"STUDY PROJECT ON COMBINATORIAL CATALYSIS"

By

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Dehradun

May, 2008

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"STUDY PROJECT ON COMBINATORIAL CATALYSIS"

A thesis submitted in partial fulfillment of the requirements for the Degree of

Master of Technology

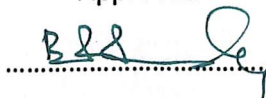(Refining & Petrochemical Engineering)

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CERTIFICATE

This is to certify that the work contained in this thesis titled **"Study Project on Combinatorial Catalysis"** has been carried out by **Vikas Malik** under my supervision and has not been submitted elsewhere for a degree.

Dr.R.P.Badoni
Distinguished Professor

Date: June 18, 2008

ABSTRACT

For a field that began just a decade ago, the combinatorial approach has risen quickly to become the best friend of chemistry. At one time, chemists had no choice but to laboriously synthesize new compounds one at a time. But with the advent of robotic technology that allows mass synthesis and screening, researchers have suddenly found themselves with perhaps more information than they can handle.

Combinatorial catalysis is not a new field in science, but an interdisciplinary topic involving many different research communities. Project shows that its success relies on combining scientist creativity and advanced technology, which should lead both to new breakthroughs and to a broadened understanding of catalysis.

This project is covering the study of Development of techniques for high throughput synthesis of catalysts and new assays for rapid throughput catalyst testing, potential combinatorial techniques, and reduction of analytical cycle time by parallel operation and automation.

Present study focused on how the combinatorial approach is helping in developing the new materials in Research and Development areas of catalytic science and technology.

Acknowledgement

It is my pleasure to present this thesis namely **"Study project on combinatorial catalysis"** as a major project of my M.Tech. programme. I am very much thankful to **Dr. R.P Badoni** who helped me with his knowledge to complete the project.

I express my heartful gratitude and my indebtness to **Dr. R.P. Badoni,** his brilliant guidance, co-operation, constructive criticism and keen interest extended most heartily to execute the ticklish task of the project.

I am also thankful to **Dr D.N. Saraf** who taught us genetic algorithm as a part of the subject of optimization principles. Without the knowledge of that subject it was not easy to complete the project.

I am also thankful to the library people of **"Indian Institute Of Petroleum Dehradun"** who gave me the help for literature reviewing.

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R080206011

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Some Technical Definitions

Computational combinatorial chemistry, like any subfield, is impregnated with its terminology. Understanding a few key words can make things a lot clearer.

BCUT-

Descriptors (see definition below) based on a fusion of atomic properties such as polarizability and charge distribution, and on molecular connectivity, which together relate to a molecule's ability to interact with a receptor.

Chemistry space-

The concept that any one compound can be assigned a position in a multidimensional space, where each axis corresponds to a structure-related property. For example, an axis could represent the presence or absence of a chlorine substituent, or of an aromatic ring. The "distance" between compounds in chemistry space can be a representation of their similarity or diversity.

Descriptors-

Molecular properties related to structure or electronic characteristics such as polarizability, aromatic ring centers, and others. Descriptors provide a way of comparing and contrasting molecules in a combinatorial library.

Diversity-

The concept of culling the most molecularly diverse set of compounds from a combinatorial library to pare the library down to a manageable size and increase the chances of discovering a potential drug candidate.

Fingerprint-

A string of yes or no answers about a molecule's properties. These can correspond to the axes used in chemistry space, for example: aromatic ring? Yes. Bromine? No. These answers can be represented as zeros and ones in a bit string, or fingerprint, unique to that compound. The fingerprints can then be analyzed for their diversity or similarity.

Metric-

Another term for descriptor.

Pharmacophore-

A descriptor based on chemical "centers" with which a ligand molecule is likely to interact at a protein receptor site. These centers include hydrogen bond donors and acceptors, positive charge centers, aromatic ring centers, lipophiles, and acids and bases. A pharmacophore contains a set of centers and a specific geometry that is necessary for the ligand to bind to the receptor.

SAR and QSAR-

Acronyms for structure-activity relationship and quantitative structure-activity relationship. The terms refer to data that, as the names imply, relate a molecular structure to its biological activity. Used to augment the number of potential drug compounds once a promising lead has been identified.

Virtual library-

A computer database of chemical compounds from which combinatorial chemists try to identify potential drugs or agrochemicals to be synthesized.

CHAPTER 1

INTRODUCTION

1.1 General

Although microporous materials synthesis has been intensively studied during the last decades and several attempts for the optimization of catalyst and growing mechanisms has been reported, the discovery and optimization of zeolites is still a mostly empirical process. In fact, the different synthesis parameters involved in the crystallization (concentration of the starting gel, reactants course, temperature, time, etc.) are strongly inter-correlated, leading to highly difficult processes for development of catalyst. Moreover, these hidden relationships among synthesis variables give rise to some information about the designation and optimization of catalyst for a specific reaction.

1.2 Introduction to Project

The construction of models for prediction of the formed zeolite and/or their structural/thermodynamic properties as a function of the synthesis variables will be of help for zeolite discovery programs aiming at mapping large spaces. Indeed, the combination of predictive modeling (such as quantitative structure/properties relationships - QSPR-) and mapping strategies can strongly reduce the required number of experiments for achieving a complete picture of the explored space (phase diagram). In addition, the application of high throughput experimentation (HTE) in this field supports the thoroughly study of multi-component

systems (and process conditions) driving to the formation of microporous materials. Recently, it has been reported the application of HTE for the synthesis under hydrothermal conditions and the parallelized XRD characterization of libraries of microporous silicoaluminates and the mixed metal oxides (MMO's).

Different machine learning (ML) methods have applied successfully to QSPR modeling in materials science as for instance in ferromagnetism, bulk mechanical properties and catalytic behaviour. Modeling of large libraries of solid materials produced by HTE techniques presents an innovative algorithm which iteratively selects the members of the library based on a biased statistical criterion. Such design differs greatly from all others since its aim is not to optimize of a given catalytic property but rather to iteratively reach a well-organized sampling distribution onto the search space in order to enhance future recognition rates when using a modeling approach in a following step. In the area of zeolite synthesis modeling, neural networks (NNs) allowed the successful modeling of complete phase diagrams studied by HTE methods. However, NNs may suffer from over fitting the training data, and lack of information regarding the classification obtained and, therefore, there is still the need to develop more robust and accurate modeling techniques for materials science.

Support Vector Machines (SVMs) are a good candidate for such purpose, since this method has shown outstanding performances in several fields as for instance, optimization of catalyst in monoliths, object recognition, material identification, and structure detection in images categorization. Moreover, SVMs techniques have been extensively applied in QSPR modeling in drug discovery and

medicinal chemistry, process engineering, physical chemistry, and very recently to heterogeneous catalysis domain. When using ML methods for QSPR modeling, input and output variables should be carefully selected in order to properly represent the different properties of the materials or the parameters/conditions involved in the synthesis process. In the case of zeolite synthesis, typically, the model output is just a categorical variable representing the type of structure obtained. It has also been reported the prediction of the achieved crystallinity of the competing phases.

However, in principle, it could also be possible to model the synthesis parameters in order to predict other zeolite properties such as structural descriptors, thermodynamic properties or even its catalytic or adsorption/diffusion behaviour. Structural descriptors are computed either using parameters derived from the idealized zeolite structure or by analyzing experimental data drawn typically from spectroscopic characterisation.

CHAPTER 2

THEORTICAL LITERATURE REVIEW

2.1 Computational methods for library design

Reaction planning and computational library design has substantially changed the process of material discovery, since it enables selection of an adapted and improved subset of experiments among an almost infinite number of candidate molecules by applying virtual screening techniques
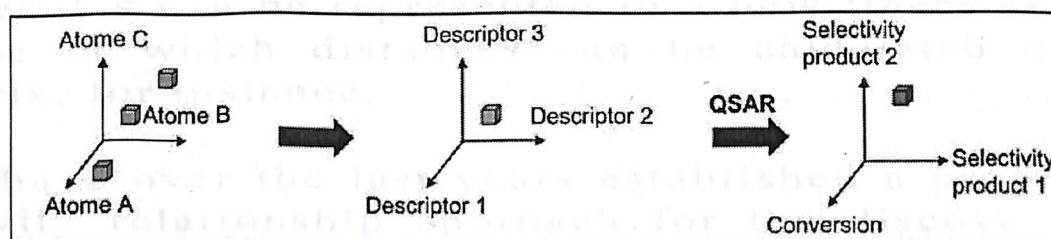
Fig. (1). Scheme representing the different parameter spaces. Composition space (left), physico-chemical descriptor space (middle) and performance space (right).

The diversity profiling of materials/molecules is the basic concept in the design of libraries of molecules. It relies on the "similar property principle", assuming that structurally similar molecules should have similar chemical activities. The similarity/diversity of two molecules can be assessed by measuring a "distance" between them, while for a molecule library it is a distance matrix. The relationship which links the molecules to their activities is captured by means of a statistical QSAR model. The quantification of distances between molecules is the key issue in the QSAR approach. For this purpose, molecules should be described in a way that all molecules can be localized in a common

linear search space, starting from their composition and structure. From the 3D structure of a molecule, a number of physicochemical features can be computed. These quantitative values, together with values obtained from the sum formula (molecular weight etc.) or the two-dimensional structure (atom connectivity, presence of functional groups) constitute the so-called "QSAR descriptors".

The set of all descriptors for a given molecule represents its fingerprint. Even if the level of information contained in the fingerprint is somewhat reduced with respect to the full 3D description of molecules, it may capture relevant information with respect to the activity profile one wants to assess. Using the fingerprints as new variables, all molecules can be represented in a new linear search space in which distances can be calculated using matrix, for instance.

We have over the last years established a property-activity relationship approach for the discovery of solid state materials.
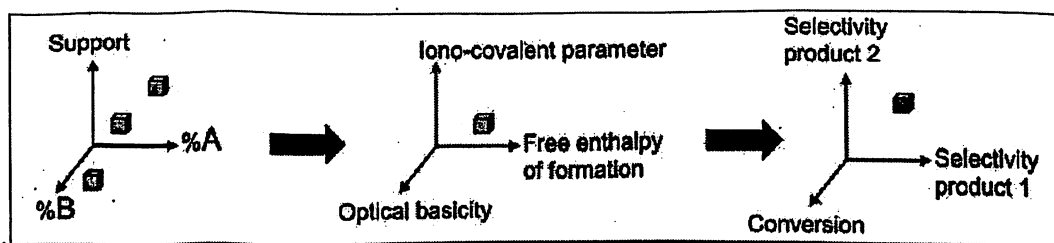
Fig. (2). QSAR approach in heterogeneous catalysis. Composition space (left), physico-chemical descriptor space (middle) and performance space (right).

The concept of descriptors (attributes) applied here encodes some native physicochemical properties or calculated feature of a solid catalyst as a numerical value (input variable). The set of all descriptors for a given catalyst represents its descriptors vector. The coupling of the literature data with the

elemental composition of the catalysts plus information about synthesis parameters allowed the computation of highly informative attributes, which allowed prediction of catalytic performance, after establishment of a statistical model, linking the descriptors to the catalytic response. A conceptual workflow illustrating the methodology is presented in Fig. 2.

In this study, a rational methodology for the selection of highly informative descriptors is developed. In contrast to "chemical intuition" used previously, the choice of attributes by a method based on information theory and data mining techniques is described here. Investigations of discriminant descriptors which are decisive in the predictions of catalytic properties were carried out.

2.2 Genetic algorithms used in combinatorial catalysis

With the establishment of a multitude of different high throughput techniques in industrial and university laboratories the potential for a fast and efficient evaluation of a large number of materials in a short time has been enabled. However, in search for new or advanced heterogeneous catalysts various factors, beginning with the choice of the active component, the influence of dopants and support materials up to the selection of an appropriate preparation method, have to be considered. Regarding that for each parameter a large pool of compounds or methods is at the disposal, a high dimensional search space results which provides a virtually infinite number of solutions to a catalytic problem. For an efficient exploration and exploitation of such vast search spaces appropriate optimization strategies and data-mining tools are

needed to complement the experimental high-throughput technology (HTT). Typically, only little is known about a response surface at the beginning of an optimization process. Thus, to find an advanced catalyst composition an optimization method is needed that requires no fundamental mathematical model of the coherences. The most common methods providing such an approach are either deterministic algorithms, like holographic research studies (HRS) or stochastically based procedures like simulated annealing (SA) or genetic algorithms (GAs).

Most suitable to the problems of heterogeneous catalysis and thus frequently applied are genetic algorithms. The modern application of this strategy results on the work of Holland and DeJong, who first adopted this technique for combinatorial optimization problems. The two basic strategy modules are the application of random elements for a broad scan of the search space and the exchange and conservation of the thereby received information.

The advantages of genetic algorithms are their flexibility and the fact that they require no complex mathematical operations. If a general solution pattern to a given problem, i.e. a catalyst structure, is appropriately encoded and an objective function for the evaluation of the problem solving quality is defined, every further step can be affected by computation. Software routines generate a random population out of the search space whose individuals are evaluated by the objective function. Solutions that fit best to the requirements of the fitness function have the best chances of selection to participate in the build-up of a succeeding population (differential reproduction).

The basic principle in generating this follow-up population is mimicry of biological paradigms, using mutation and cross-over operators. In heterogeneous catalysis genetic algorithms have been introduced for about six years. Successful applications in several fields of catalysis have been reported since then, providing the proof of concept and the generation of new catalyst materials.

Recently the dependence of the algorithm performance on the experimental design of the algorithm has been pointed out in detail and analyses have been carried out comparing GAs to other optimization methods. Further approaches deal with the combination of GA with artificial neural networks (ANN). These strategies of interaction, referred to as soft computing techniques, are either the training of the ANN with the results of the GA or, in contrary, the simulation of experimental results with a trained ANN as a pre-screening to speed up the genetic optimization process.

Despite the well examined applicability of GA for problems of heterogeneous catalysis and its proved reliability for multidimensional optimizations, only few applications beyond scientific examinations focusing on the GA methodology itself have been published. The application of a GA on the optimization of technically relevant catalysts, which are to be optimized for more than one performance criterion, shall be introduced.

Thus, in the presented study a genetic algorithm is used as a stand-alone optimization method for a multi criteria optimization. A restricted search space of more than 150,000 mono-, bi- and trimetallic and mixed metal oxides catalyst compositions is searched for advanced catalytic assemblies in the field of selective oxidation. For a start three

consecutive generations of catalysts each with a population size of about 480 individuals have been examined. In focus is (a) an appropriate technique in catalyst evaluation composed of data derived from a primary screening as well as (b) the creation of a rather simple but flexible optimization procedure with an implementation of economical aspects.

Applying the versatile multi-channel monolith reactor, introduced before, the figure of merit for each catalyst composition can be based directly on a quantitative conversion rate of the examined components a broad temperature range. Moreover, monolithic honeycombs are vital tools in the search for supporting systems close to technically applied structures and are themselves widely used as part of technical catalysts. The use of a monolith based screening tool for selective oxidations in combination with a restricted catalyst preparation and an appropriate catalyst pre-treatment promises an easy scale up from the results of the optimization process to applications in relevant fields of catalysis.

CHAPTER 3

EXPERIMENTAL LITERATURE ANALYSIS

3.1 EXPERIMENTAL DESIGN

A simple but flexible optimization procedure based on genetic algorithms was created in Microsoft Excel using Microsoft VBA. The procedure evaluates and ranks catalyst compositions according to their performance in selective oxidation, resting upon the four criteria of the conversion rates of Carbon mono oxide and a hydrocarbon at two different temperatures.

The classical tools of a genetic algorithm (the estimation of the catalyst fitness, the selection dependent on the catalyst quality and the use of genetic operators to transform the selection into a new catalyst population) are provided and several analysis tools are available. An outline of the procedure is summarized in Fig. 3.

3.2 Preparation and Screening Technology (HTT)

A non virtual optimization procedure in heterogeneous catalysis has to rest upon a reliable benchmark test. Using the conversion rate of the two gaseous components in total oxidation as base to the figure of merit, the multi-channel monolithic reactor is a versatile tool. Due to the use of common analytical equipment in a research laboratory, a realistic evaluation of the potential of the tested catalysts is made possible by determining the activities.

The specific monolithic honeycomb structure used (Cordierit 410 from Inocermic), consists of 10x20 channels with a diameter of 2.6 mm (72 cpsi) and a channel length of 75 mm. A special pre-treatment of this material prevents a radial, channel-to-channel diffusion through the monolith walls. Each monolith channel can so be used as a single plug-flow reactor. The catalytic tests can be carried out in an array of eight rows and 16 columns, thus using 128 of the 200 columns available. To deposit the active components inside the channels, first the inner monolith walls are uniformly coated with 105 g/L of Al2O3 as catalyst support using a wash coat procedure described by Moulijn. After additional drying by 350°C for 3.5 h the coated monoliths are ready to be employed in a successional preparation and screening sequence to generate and examine the catalytic compositions submitted from the surrounding optimisation procedure.

To generate the individual catalytic species in each monolith channel, the washcoat is saturated channel by channel with a mix of precursor solutions of the desired metals, previously mixed in a deep well plate. The monolith is temporarily sealed on one side and the channels are filled individually with 300 µl of the precursor solutions. With the pore volume respectively the oxide layer's water capacity known to be 500 mL/kg for the Al2O3 coating, the desired metal content can be adjusted with high accuracy, analogously to dry impregnation or incipient wetness methods. After the necessary time for the complete saturation of the oxide layer (2 s), the dilutions are removed.
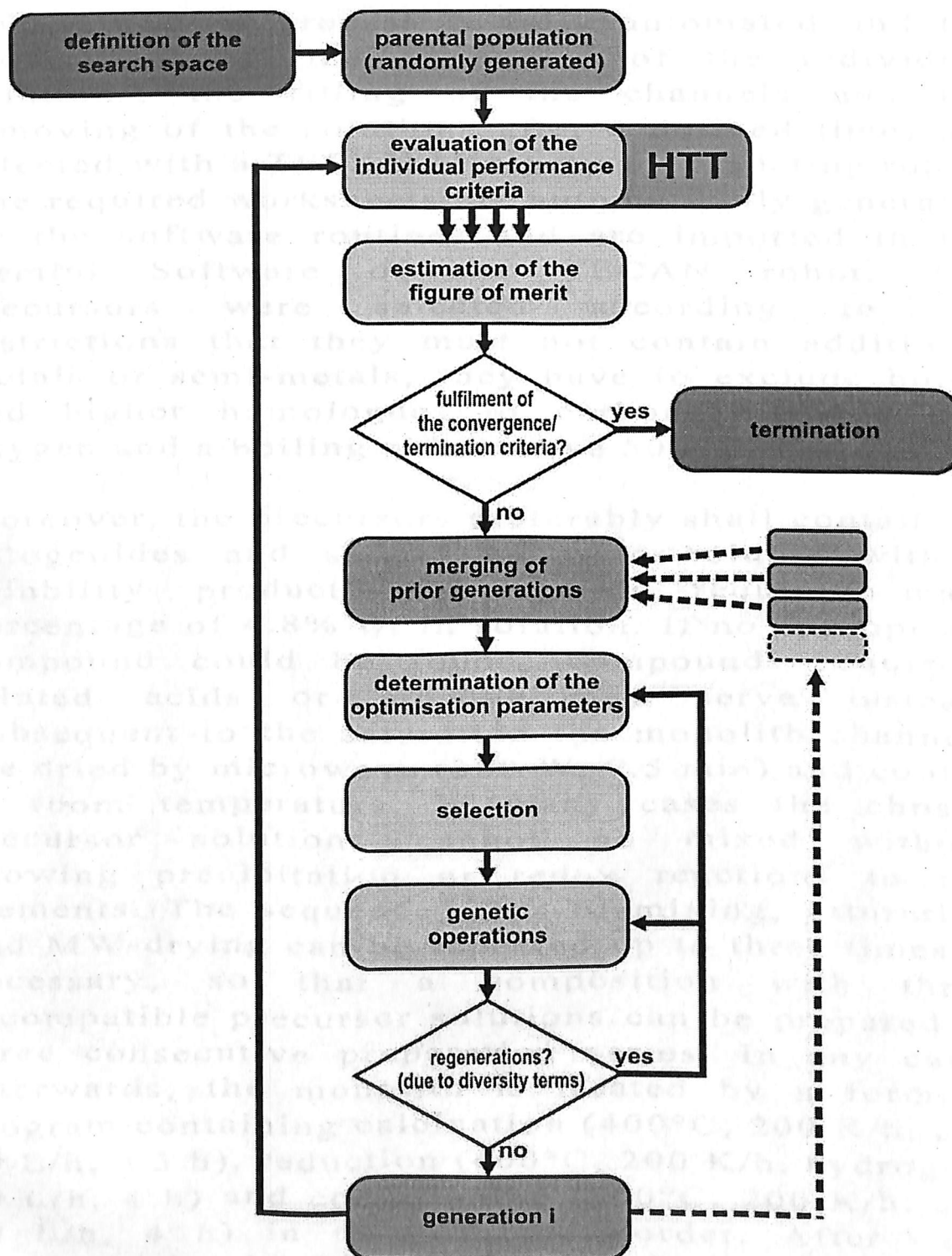
Fig 3: flowchart of the adapted genetic algorithm

The saturation process is fully automated and the required steps (the premixing of the individual solutions, the filling of the channels and the removing of the solutions after a defined time) are affected with a TECAN Miniprep 60 pippeting robot. The required worksheets are automatically generated by the software routines and are imported in the Gemini Software of the TECAN robot. The precursors were selected according to the restrictions that they must not contain additional metals or semi-metals; they have to exclude boron and higher homologues to carbon, nitrogen and oxygen and a boiling point above 500°C.

Moreover, the precursors preferably shall contain no halogenides and should be water-soluble with a solubility product to yield a required mass percentage of 4.8% wt in solution. If no appropriate compound could be found, compounds requiring diluted acids or ethanol may serve instead. Subsequent to the saturation the monolith channels are dried by microwave (300 W, 7.5 min) and cooled to room temperature. In many cases the chosen precursor solutions cannot be mixed without showing precipitation or redox reactions to the elements. The sequence steps of mixing, saturating and MW-drying can be repeated up to three times if necessary, so that a composition with three incompatible precursor solutions can be prepared in three consecutive preparation series. In any case, afterwards, the monolith is treated by a forming program containing calcination (400°C, 200 K/h, air, 10 L/h, 3.5 h), reduction (400°C, 200 K/h, hydrogen, 10 L/h, 4 h) and conditioning (500°C, 200 K/h, air, 10 L/h, 4 h) in the presented order. After each forming step the coated monolith is cooled back to room temperature (6 h) at the particular conditions.

The evaluation of the catalyst performance results of the quasi-simultaneous screening of each channel in a positioning system from AMTEC Inc. The conversion rates of the two target-compounds (CO, HC) supplied in parallel in a complex gaseous feed mixture (oxygen: 6% vol.) are monitored at two reaction temperatures. An Omnistar quadruple mass spectrometer (QMS) from Pfeiffer and a gas chromatograph (GS, HP 5890) with FID are applied in parallel for the quantitative detection of the desired gas phase species.

The analysis time by using the GC is about 4.5 minutes/catalyst (i.e. 10 hours for 128 channels). Fig. 4 shows the evaluation equipment. A detailed description of the monolith screening setup and its reliability is presented elsewhere.

To estimate the quality of the results, i.e. to evaluate and consider geometric and time dependent effects, an intelligent arrangement of the catalysts over the monolith has been previously introduced. At the expense of a higher throughput a distribution pattern consisting of a fourfold replication of 30 catalysts was used. The arrangement as an antidromic 'double snail' guaranteed that each of the replicated catalysts is broadly distributed over the monolith. For the use in the optimization procedure this design has been slightly modified and an antidromic snail-pattern was created, using only double replication. Examinations show that a broad distribution and the possibility of a geometric analysis are both maintained by only little qualitative losses, but a doubled capacity is won.

Preparation:
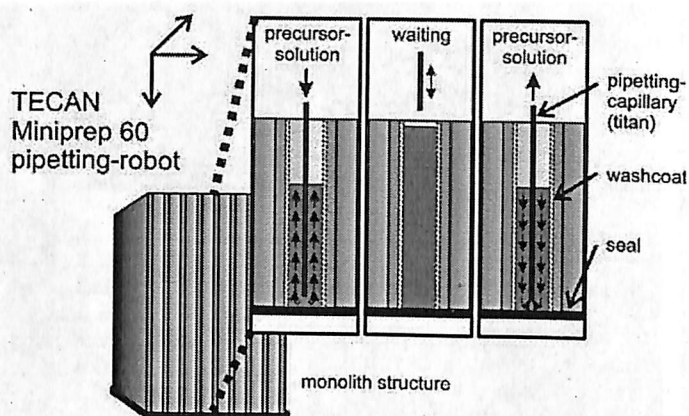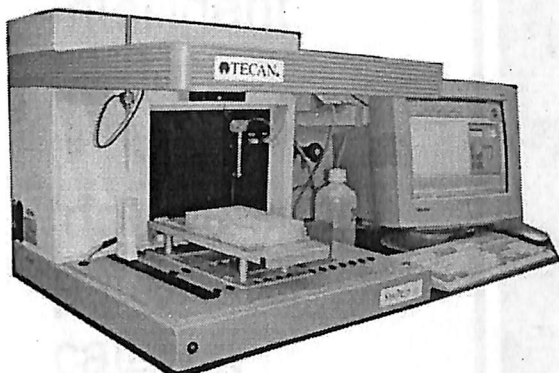
Screening:
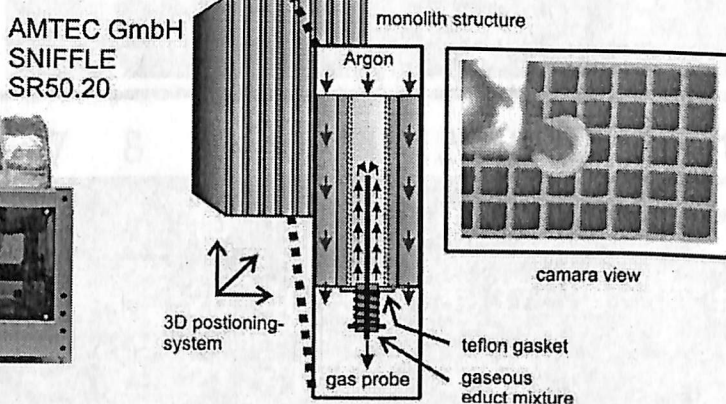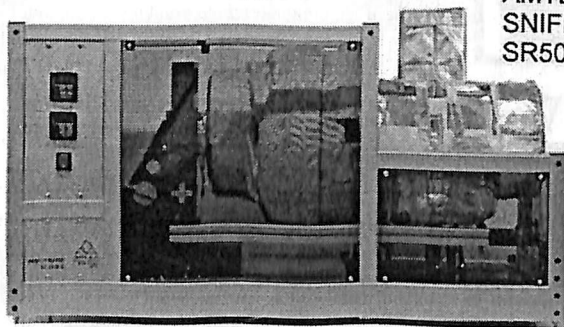
Fig 4: Experimental HT equipment for the catalyst evaluation using a pippeting robot and a 3D sampling and dosing system.

With this design each monolith contains 60 different individuals distributed over the 128 channels. Additionally each design contains four blank channels and four channels prepared with an internal standard (IS). These 62 compositions will be referred to as a monolith library.

Intelligent design:

'double snail' pattern for catalyst distribution:
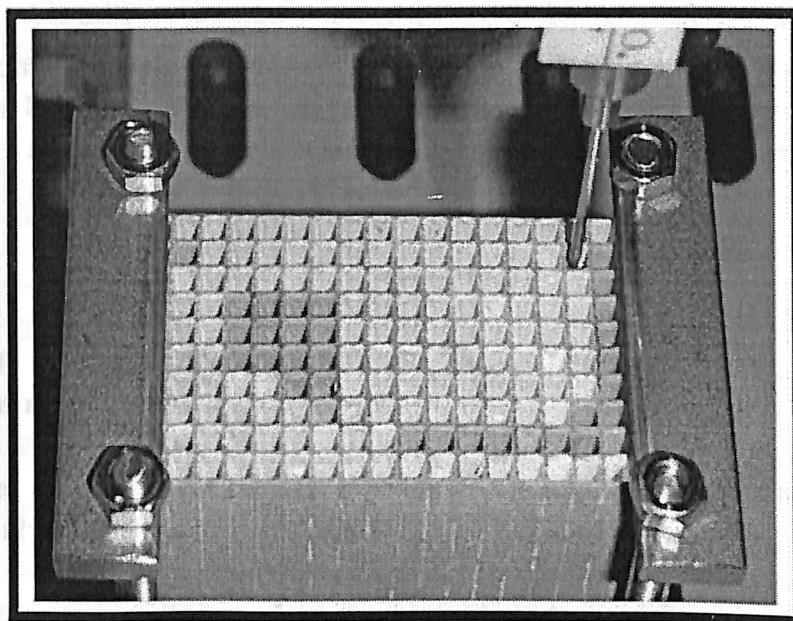
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	*a	41	42	43	44	45	46	47	19	18	17	16	15	14	13	*b
2	40	20	21	22	23	24	25	48	20	40	39	38	37	36	35	#d
3	39	19	6	7	8	9	26	49	21	41	54	53	52	51	34	12
4	38	18	5	#a	1	10	27	50	22	42	55	60	59	50	33	11
5	37	17	4	3	2	11	28	51	23	43	56	57	58	49	32	10
6	36	16	15	14	13	12	29	52	24	44	45	46	47	48	31	9
7	35	34	33	32	31	#b	30	53	25	26	27	28	29	30	#c	8
8	*c	60	59	58	57	56	55	54	1	2	3	4	5	6	7	*d

Fig 5: Advantageous catalyst distribution over the monolith in form of an antidromic double snail pattern (including four blank channels *a-*d and four channels depleted with an internal standard #a-#d)

The sequence as presented allows the preparation and screening of about three monolith libraries a week, resulting in a maximal throughput of about 750 catalyst compositions a month.

3.3 Definition of the Search Space and the Parental Generation

The search space is defined via the catalyst description and the restrictions it is thereby subjected to. To avoid an overload of information for this study a rather convenient catalyst structure was chosen, containing up to three different metals on a metal oxide in maximally nine discrete amounts. With the substrate and the preparation method predefined (compare section given before), the genetic information of each catalyst (respectively the chromosome in biological terms) can be described via the following pattern. The replacement characters $n1$ to $n3$ represent the three possible elements in its associated quantity level $y1$ to $y3$. (To both, ni and yi can be referred to as genes)

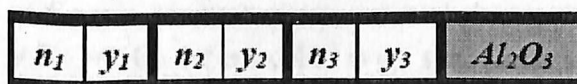| n_1	y_1	n_2	y_2	n_3	y_3	Al_2O_3

Fig 6: Search Space combinations

49 metals were selected reflecting our research interests as well as the precursor restrictions mentioned above. Each metal amount yi associated to ni can vary between the three levels of 0% wt., 0.2% wt. and 0.8% wt. In summary, a maximal depletion on the wash coat of 2.4% wt. can be achieved.

3.4 Catalyst Encoding and Generation of the Parental Population

For embedding the previously introduced catalyst information into the mathematical procedures of the genetic algorithm a suitable encoding has to be applied. In this case an encoding based on the decimal system was chosen. A code C for a composition results as described below with N representing the maximal possible elements and Y the maximum possible quantitative metal amounts.

$$C = n_1 + y_1 \cdot N + n_2 \cdot (N \cdot Y) + y_2 \cdot N(N \cdot Y) + n_3 \cdot (N \cdot Y)^2 + y_3 \cdot N(N \cdot Y)^2$$

With 49 possible metals chosen (n_i = 0 to 48; N = 49) and the determination of 3 possible amounts for each occurring metal (y_i = 0 to 2; Y = 3) in summary 166,651 different possible catalyst compositions are represented by a continuous set of 3,176,522 codes. Redundant compositions out of the encoding result (a) from the inclusion of similar catalyst compositions with different sequences and (b) from the option to set a quantitative metal amount to 0% wt. Thus, due to the latter mono- and bimetallic depletions on the wash coat are easily integrated, accepting that for instance a bimetallic catalyst encoding with y_3 = 0 (resulting to 0% wt.) yields to the same composition sequence with 49 possible options for n_3.

Further the same element can appear coexistent in position n_1, n_2 and n_3. In a monometallic composition the single element can thus appear in the discrete depletions of 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.6, 1.8, and 2.4% wt., in bimetallic compositions one element can yield the discrete quantitative

values of 0.2, 0.4, 0.8, 1.0 and 1.6% wt., whereas the second element can only exist in 0.2 and 0.8% wt. For trimetallic compositions each element amount may only vary discretely between 0.2 and 0.8% wt.

An initial population (also referred to as parental generation or parental population) is created plain randomly without any further heuristics. A random set of P numbers out of the 3,176,522 codes is selected. The population size P is determined to 480 individuals and accordingly the preparation of 8 monolith libraries per generation. In order to avoid further repetitions within a generation due to the encoding, a diversification is applied. The algorithm substitutes the redundancies automatically with new random numbers until no further identical compositions are detected in the parental set. The 480 individual catalyst compositions represent a small amount of 0.288% of the overall search space. Due to the design, however, all genes are represented in a statistic equipartition within the parental generation (Fig. 7).
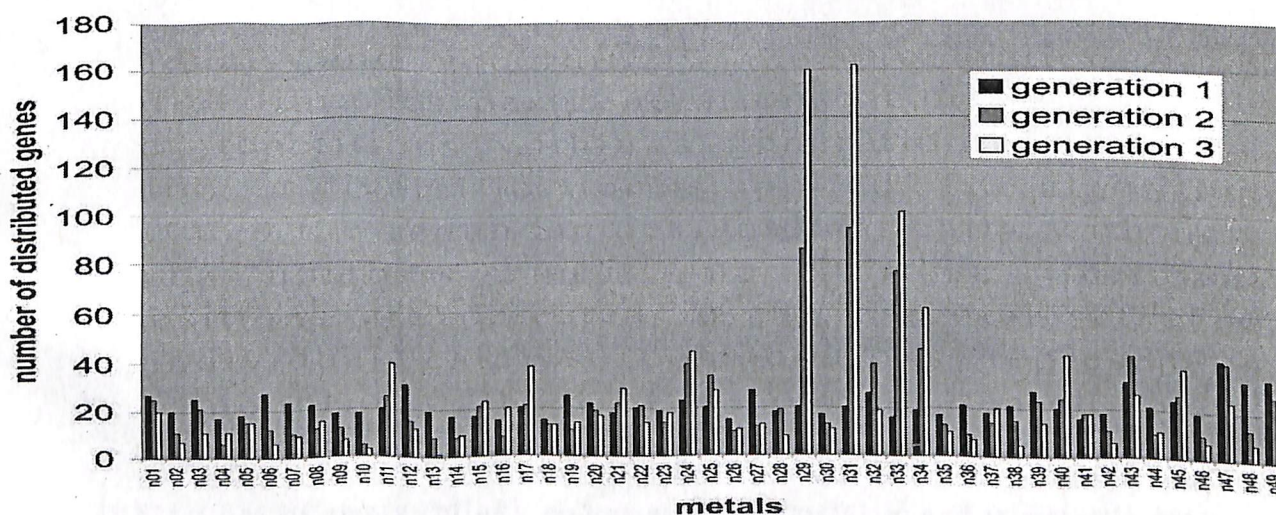
Fig. 7. Total number of the 49 metals (genes) distributed over a generation. Comparison of the distributions of the parental generation (generation 1) with the examined generations after one (generation 2) and two runs (generation 3) of the optimization procedure.

Legend:
- □ empty
- ▨ monometallic
- ▨ bimetallic
- ■ trimetallic
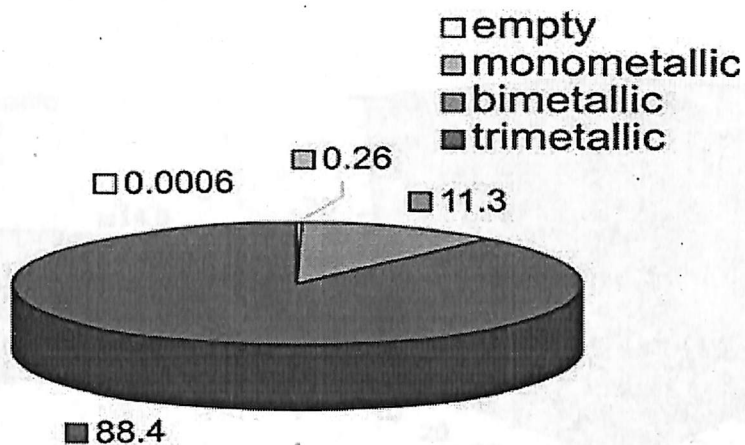
(a) real catalyst partition
- □ 0.0006
- ▨ 0.26
- ■ 11.3
- ■ 88.4
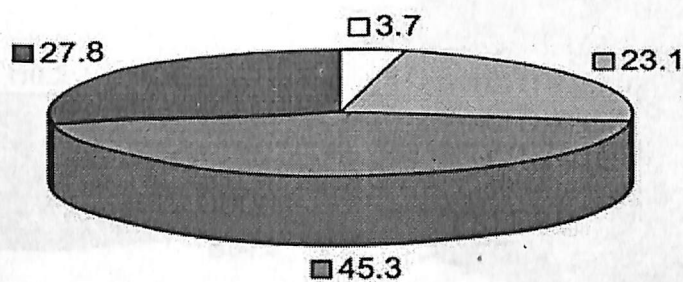
(b) selection probability
- □ 3.7
- ▨ 23.1
- ■ 45.3
- ■ 27.8
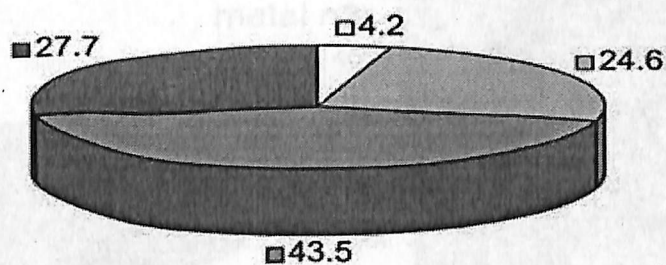
(c) parental generation (undiversified)
- □ 4.2
- ▨ 24.6
- ■ 43.5
- ■ 27.7

Fig. 8: Fractions of empty (blind), monometallic, bimetallic and trimetallic catalyst compositions resulting (a) of the actual search space in comparison to (b) of the encoded search space. The fractions of the randomly generated (undiversified) parental generations (c) reflect the latter. (All figures are presented in [%]).
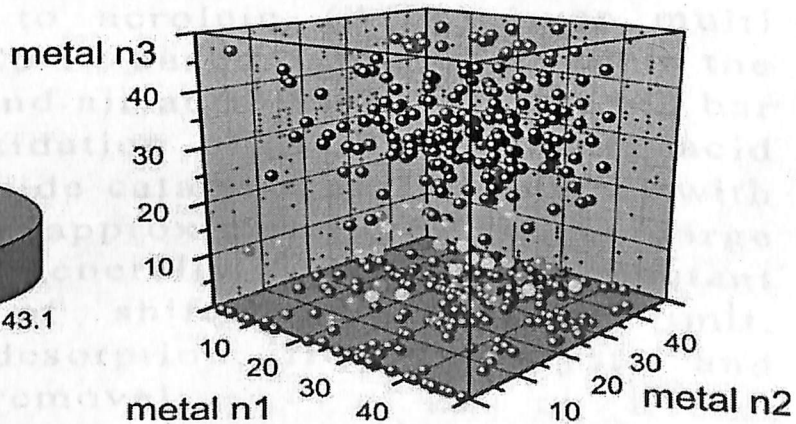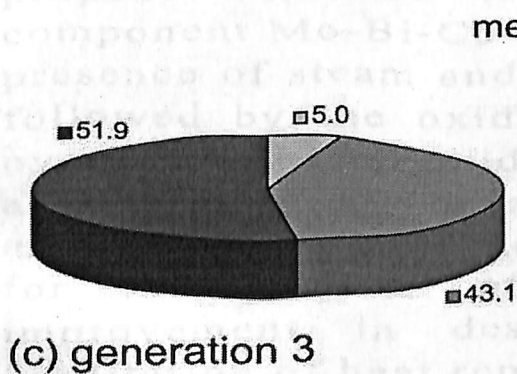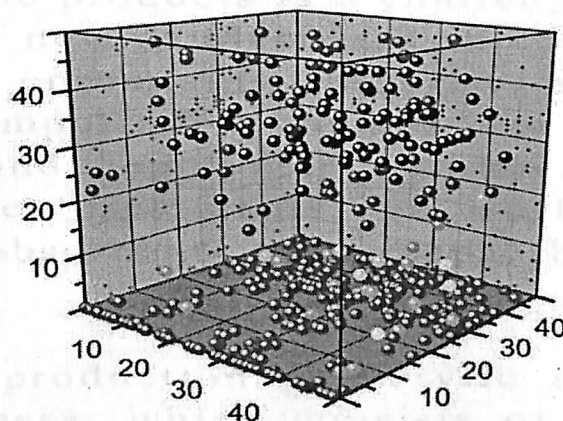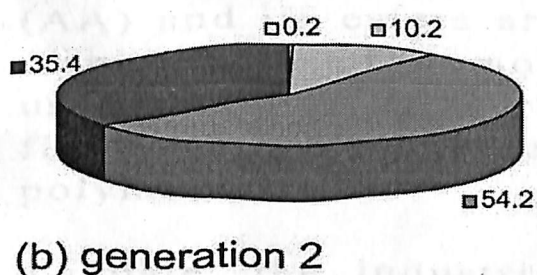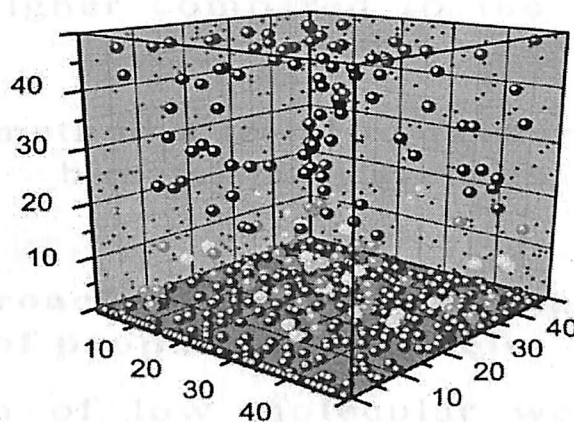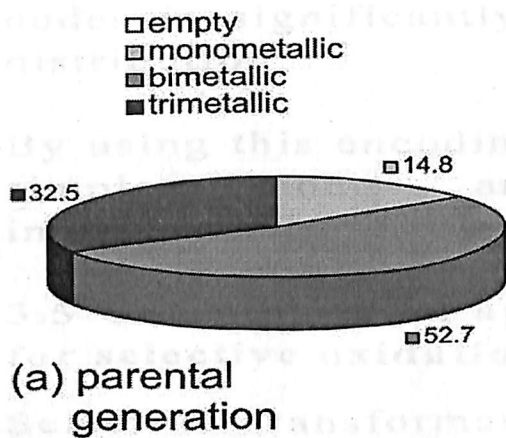
Fig. 9: Change of the fractions of empty (blind), mono-, bi- and trimetallic catalyst compositions from (a) the diversified parental generation to the following generations (b,c). Displayed are the fractions (figures are presented in [%]) itself as well as simplified visualizations (abandoning the different metal amounts) of the examined catalyst compositions in the search space.

As a further result of the encoding technique the selection probability of monometallic and bimetallic codes is significantly higher compared to the true distribution.

By using this encoding method a trend to favour the simpler mono- and bimetallic systems is implemented.

3.5 Combinatorial approach to develop a catalyst for selective oxidation of propane to acrolein

Selective transformation of low molecular weight alkanes into more valuable products is a challenging task. The development of new catalysts for selective oxidation is considered promising. Acrylic acid (AA) and its esters are important monomers for the manufacture of homo- and copolymers, which are used mainly as surface protectants, in surface finishing, and as super absorbents (super absorbent polymers, SAP).

To date, the industrial production of acrylic acid involves a two-step process, which consists of the propene oxidation to acrolein (ACR) over multi component Mo-Bi-Co-Fe based oxide catalysts in the presence of steam and air at 330-370 °C and 1-2 bar followed by the oxidation of ACR to acrylic acid over Mo-V based oxide catalysts at 260-300°C, with an overall yield of approximately 87 %. A large amount of water is generally added to the reactant for the purpose of shift of explosion limit, improvement in desorption from catalyst, and facilitation of heat removal.

Propene is produced directly in the catalytic cracker from higher molecular weight fractions during petrochemical refinement of crude oil and by catalytic dehydrogenation from propane.

To substitute the production of propene and the current two-steps propene-to-acrolein and acrolein-to-acrylic acid process, the single-step direct oxidation of propane to AA has attracted growing attention in the past decade in both academia and industry. By now, three well-known categories of catalyst systems, vanadium pyrophosphate (VPO) type catalysts, heteropoly compounds catalysts and multi-component or mixed metal oxides catalysts (MMO), have been extensively studied for the selective oxidation of propane to AA.

Among these, MMO catalysts are commonly considered to have a possibility to replace the traditional catalysts in the existing industrial two-step process via propylene. Among those MMO catalysts systems, the most promising catalyst appears to be the Mo-V-Cr-Nb mixed oxide, proposed by the Mitsubishi Chemicals, which is reported to achieve more than 40% of acrylic acid yield. An appropriate Mo-V-Te-Nb metal ratio is critical for the formation of high catalytic activity. Although Mo-V-Cr-Nb and Mo-V-Sb-Nb mixed oxides are known to be effective for the selective oxidation of propane to AA, the catalytic performance is not yet sufficient for industrial applications.

Therefore, substantial investigations of new catalytic system are necessary to find a more active or stable catalyst. Demand for the discovery of such a new viable catalyst leads to the combinatorial approach applying high-throughput technologies. The major advantage of the combinatorial approach lies in the possibility to test a large number of samples in a short time under comparable reaction conditions, which increases the chances of discovery of totally new and unexpected catalysts and their optimization.

The development and application of high-throughput methods for the rapid discovery and optimization of solid state catalysts has led to promising results during the last few years. Since the technology available for the selective oxidation studies were not suitable to study the conversion to AA, the conversion of propane to ACR was selected as an indicator for the chances to find new catalysts for the reactions of interest. In the present work, diverse libraries of MMO catalysts for the selective oxidation of propane to ACR were synthesized via a modified sol-gel method using a synthesis robot and library design software, and tested in a high-throughput mass spectrometer (MS) screening setup described previously.
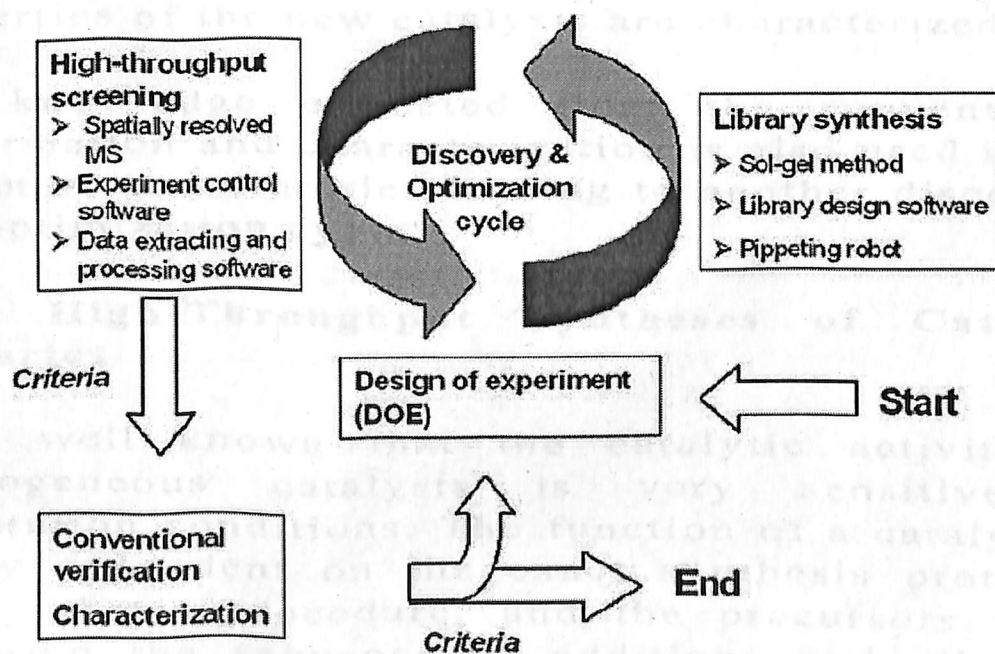
Fig 10: Flow chart of the high-throughput experimentation in the present study

3.5.1 A High-Throughput Experiment

Efficient implementation of high-throughput experimentation (HTE) requires the complete combinatorial workflow with no bottleneck. The general strategy for high-throughput experimentation in the present study involves not only the discovery and optimization cycles with the creation and evaluation of catalyst libraries but also conventional verification and characterization. The typical HTE procedure in this study is demonstrated in Fig. 10. The discovery and optimization cycle containing library design, synthesis and performance testing is carried out until the most promising catalysts to satisfy the desired properties are found. The catalysts with promising results are reproduced and validated in a conventional manner, and the properties of the new catalysts are characterized.

The knowledge extracted from the conventional confirmation and characterization is also used in the design of new libraries leading to another discovery and optimization cycle.

3.5.2 High-Throughput Syntheses of Catalyst Libraries

It is well known that the catalytic activity of heterogeneous catalysts is very sensitive to preparation conditions. The function of a catalyst is highly dependent on the exact synthesis protocol, the synthesis procedure, and the precursors used. Changing the sequence of additions and allowing different drying times and calcination temperatures will result in a variety of different materials of identical composition, but different catalytic activity and selectivity. Thus, variations in chemical composition with a wide range of elements must be carried out with a common synthesis procedure that

is tolerant to such compositional changes. Many conventional catalyst preparations are not suitable for such a search.

Highly tolerant synthesis recipes have been developed, which allow the broad screening of elemental compositions based on sol–gel procedures. These recipes have been used to prepare a large variety of mixed oxides, which can then be tested for catalytic performance. Because all catalyst materials were mixed oxides and the oxidation state of the oxides was not determined and may change during the experiment, the materials are identified only by the metal ions and atomic ratio given as a subscript; for example, $Mo_{0.3}Cr_{0.7}$ means a mixed oxide comprising 30 molar % of Mo and 70% of Cr oxides.

Typically, 0.5 M metal precursor solutions except for molybdenum (0.1 M) and tungsten (0.226 M) were prepared by metal alkoxides (vanadium (V) triisopropoxide, iron (III) ethoxide, niobium (V) ethoxide, tanthalum (V) ethoxide, manganese (II) propionate, tungsten (VI) isopropoxide in ipropanol, and bismuth (III) 2-ethylhexanoate, molybdenum (V) hexanoate in n-propanol), nitrates (chromium(III) nitrate in i-propanol) or anhydrous metal chlorides (antimony (V) chloride, tellurium (IV) chloride, niobium (V) chloride in ipropanol). The automated synthesis of catalysts was done using a commercial pippeting robot (LISSY, Zinsser Analytic). In the procedure, the prepared metal solutions were positioned in 10 mL vials and used to formulate the final reaction mixture by transferring the aliquots of each stock solution into 2-mL vials, positioned in racks of 50 vials.

The synthesis of the combinatorial catalyst libraries was accelerated using the Plattenbau library design

software. This software calculates, based on a parameterized recipe, the volumes of the different solutions of starting materials, as required for the preparation of the individual samples. It also generates an optimized pippeting list, which can be transferred directly to the pippeting robot. For the synthesis of MMO catalysts, a modified acid catalyzed sol–gel method was applied, based on the procedures described in detail previously. The molar ratio of metal:water:acid (propionic acid):complexing agent (4-hydroxy-4-methyl-pentanone):alcohol (i-propanol) was 100:100:6:300:6500.

The prepared samples are identified by the central elements with the expected mol% from the composition of the starting sol given in subscripts. The total molar amount of central elements was set as 200 μmol per sample. After the pippeting process of an entire rack (50 vials) was completed, this rack was covered and placed on an orbital shaker (Titramax 100; Heidolph) for 3 h. After removing the lid, the resulting sols were dried for 5 days at 40°C to allow gel formation and catalyst drying.

All samples were calcined in an oven at 65°C for 5 h and at 250 °C for 5 h. The catalyst powders obtained were ground with a glass rod in the vials and manually transferred into 207 hexagonally positioned wells (3.5 mm) in a stainless steel library plate (99 mm). Some wells were left empty for background, and one well was filled with a reference catalyst ($Mo_{0.6}V_{0.2}Cr_{0.13}Nb_{0.07}$, prepared by the conventional slurry method) for comparison. The activity of each well was represented relative to the activity of the reference catalyst. The prepared library was calcined again at 600 °C for 2 h in an oven with inert condition.

3.5.3 High-Throughput Testing of Catalyst Libraries

The open-well, high-throughput reactor system connected to a quadrupole mass spectrometer was used for a rapid sequential primary screening, which has been described in detail previously. The catalyst library is placed in a special reactor with a heating system and insulation. In the reactor system, a capillary bundle containing both the educts gas supply and the product gas sampling system is inserted sequentially into each well of the library plate. The position of the capillary bundle is fixed while the complete reactor is moved by an xyz-stage. The high throughput screening was controlled by the Test Rig software by controlling xyz-stage movements and sampling.

The library plate temperature was set to 420 °C for each measurement. The composition of the reactant gas mixture was 8.7 vol% C_3H_8, 4.9 vol% O_2, 10 vol% H_2O, and Ar balance with a total flow rate of 5 ml min^{-1}. A liquid mass flow controller (MFC) connected to an autoclave was used to inject desirable amounts of water. The injected water was well mixed with reactant gas in a micro mixer (SSIMM, IMM). In addition, the whole educts and product line was heated with thin heating elements controlled by a thin thermocouple to prevent liquid condensation. The products were monitored on-line by a quadrupole mass spectrometer (GSD 300 T2, Balzers). The monitored products m/z were 18 (water), 29 (C_3H_8), 40 (Ar), 41 (C_3H_6), 44 (CO_2), 55 (acrolein), and 72 (acrylic acid). The argon intensity was chosen for internal standardization as representative within the chronological progress recording the detection sensitivity over the whole experiment. In a standard experiment, it took about 120 s (100 s inside the hole for reaction, 10 s

outside the hole for waiting, and another 10 s for xyz-stage moving) to evaluate the catalytic activity for each material. Therefore, the activity test of 207 catalysts took approximately 7 h. The data obtained were analyzed computationally with the software MS Express

CHAPTER 4

Results came out by screening and testing of the catalyst

4.1 Screening of a Library Containing Mixed Oxides Based on 11 Elements

In a first library, 11 elements were selected (Mo, V, Te, Ta, Nb, Sb, W, Cr, Bi, Mn, Fe). The selection was based on the interesting dehydrogenation and/or oxidation properties of the associated oxides. This library contained only ternary mixed oxides with a molar composition of (0.33, 0.33, 0.33), resulting different 165 catalysts as shown in Fig. 11

This library was calcined and activated as mentioned above, and library plate was loaded into a reactor and heated up to 420°C. Since the primary screening was conducted at low propane conversion (less than 2%) due to short contact time, the concentration of reactant remain almost constant for all the catalysts screened.

Therefore the activity and selectivity of catalysts screened only reflects their initial values, eliminating the complication caused by reactant depletion. The high activities for the ACR formation are found at the Mo-Cr-Te (# 18, # is indicating channel number), V-Cr- Sb (#58), and Mo-V-Cr (#2) as shown in Fig. 12

In the figure presentation, the performance of reference catalyst ($Mo0.6$ $V0.2Te0.13Nb0.07$) was set to 100 % and a color tone was adjusted between the lowest and highest intensity of MS signal for

ACR and CO2. Maximum intensity of MS signal for ACR and CO2 was set to white and minimum intensity of MS signal for ACR and CO2 was set to black irrespective of percentage. The Mo0.33Cr0.33Te0.33 and V0.33Cr0.33Sb0.33 catalysts show high ACR formation and relatively low CO2 formation. About 25 % of the prepared samples from the library produced more CO2 than the reference catalysts. Because the CO2 is product originated from undesirable total oxidation reaction, these samples have been excluded from further studies. The formation of AA was negligible for all the samples except for catalyst of identical composition as the reference catalysts, but prepared by the sol-gel procedure. The best catalysts towards ACR with low CO2 formation are listed in Table 1.

4.2 Screening of the Newly Prepared Library Composed of MoCrTe, VCrSb, and MoVCr

Based on the results of the library of ternary mixed oxides composed of 11 elements, we have chosen the MoCrTe, VCrSb, and MoVCr as potential catalysts for the propane oxidation to ACR or AA. A spread of the composition library was prepared, where all the three elements were allowed to vary between 0 and 100 mol% in steps of 10 mol%. Each library contains 66 discrete compositions and thus a total of 198 samples with the various compositions of ternary samples were obtained as shown in the Fig. 13. The sample powders were dried and calcined in the same way as mentioned above and then catalytic performance was screened.
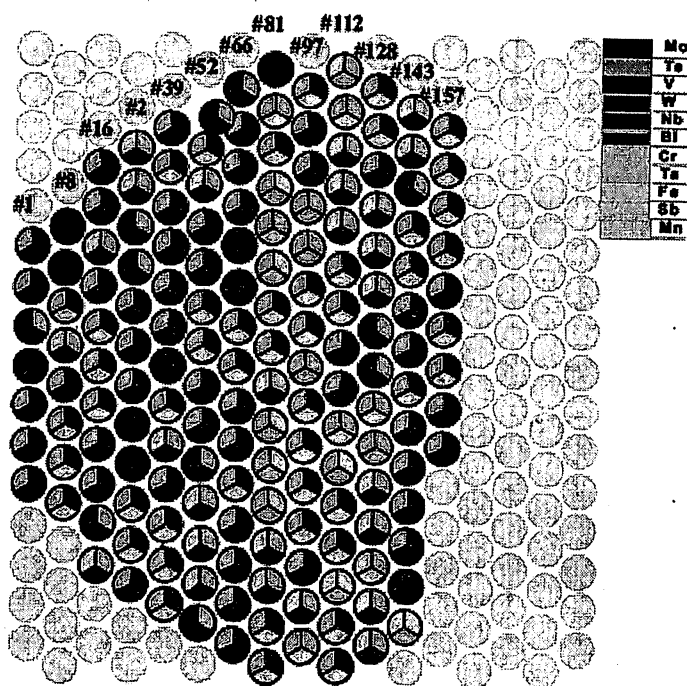
Fig 11: Sample position of ternary mixed libraries and and composition of each sample

4.2.1 Catalytic Activity Test of VCrSb Oxides

Fig.14 illustrates the performance of the ternary mixed oxides of V-Cr-Sb. The three corners in this figure correspond to 100% V, 100% Cr, and 100% Sb, respectively. The composition increment is therefore 10% per matrix element. The data clearly show a high activity for the ACR formation is near the composition of $V0.1-0.4Cr0.3-0.4Sb0.2-0.6$ (Fig. 14a). The most active catalyst is $V0.2Cr0.2Sb0.6$ which shows about 250 % higher ACR formation compared to the reference catalyst. The CO_2 formation as shown in the Fig. 14b is increased in the region $V0-0.1Cr0.6-0.9Sb0.1-0.3$, which indicates that the total oxidation is major reaction in this region and selectivity does not correlate with elemental composition.
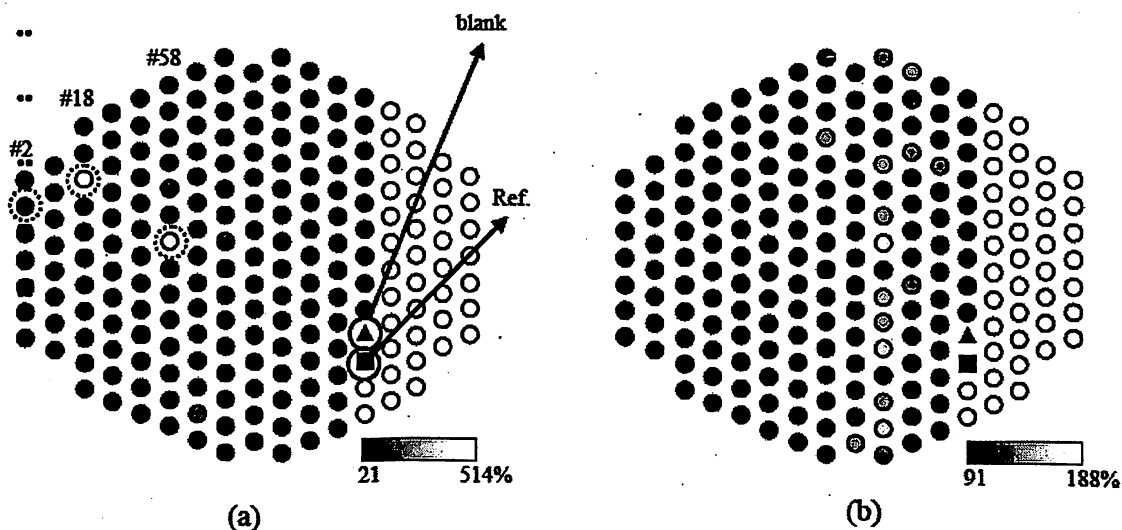
Fig.12: Relative performance of ternary mixed oxides catalyst library at 420 °C (a) ACR, (b.) CO2 formation. The composition of #2, #18, and #58 is Mo0.33V0.33Cr0.33, Mo0.33Cr0.33Te0.33, and V0.33Cr0.33Sb0.33, respectively.

4.2.2. Catalytic Activity Test of MoCrTe Oxides

Fig. 15 shows the performance of the ternary mixed oxides of Mo-Cr-Te. The highest activity for ACR formation is observed at Mo0.3-0.4Cr0.4-0.5Te0.1-0.2. The most active catalyst in this region is found at Mo0.3Cr0.5Te0.2. This catalyst is much more active, which shows 480 % higher activity for ACR formation compared to the reference catalyst. Fig. 15b shows that the total oxidation mainly occurs at the chromium rich regions, indicating some element-specific selectivity.

4.2.3. Catalytic Activity Test of MoVCr Oxides

The relative performance of the ternary mixed oxides of Mo-V-Cr is depicted in the Fig. 16. In this case, the catalytic activity is sensitive to the catalyst composition, with those along the Mo and Cr binary axis and V and Cr axis with small amount of Mo producing high amount of ACR. The highest activity for the ACR formation is found in the region with

Mo0.1-0.4V0-0.3Cr0.5-0.7 (Fig. 16a). The most active catalyst for ACR formation is Mo0.3Cr0.7 which shows 250 % higher activity than the reference catalyst. The CO_2 formation is observed only in the chromium rich region similar to the VCrSb and MoCrTe oxides. It was found that the VCrSb, MoCrTe, MoVCr oxides systems show promising catalytic performance for the direct formation of ACR associated with a reduced activity for CO_2 formation (chemo selectivity).

The highest CO_2 formation was found at chromium rich region which can be conjectured as good total oxidation catalysts. The major product ACR is an important industrial chemical used as an intermediate to produce AA or methionine an aminoacid used for the poultry feeding. In literature there are some reports on direct oxidation of propane to ACR. For instance, the Mo1.3V0.3Te0.3Ox/MCM-41 catalyst appeared to be interesting with ca. 16% yield of ACR. The active metal components of Mo, V, Te are well known where the Mo oxide was regarded to favor the formation of partial oxidation product, V oxide to promote the activation of C-H bond, and the Te oxide, particularly Te4+ is responsible for the H-abstraction from propene and O-insertion into allyl species, which is a reaction intermediate.
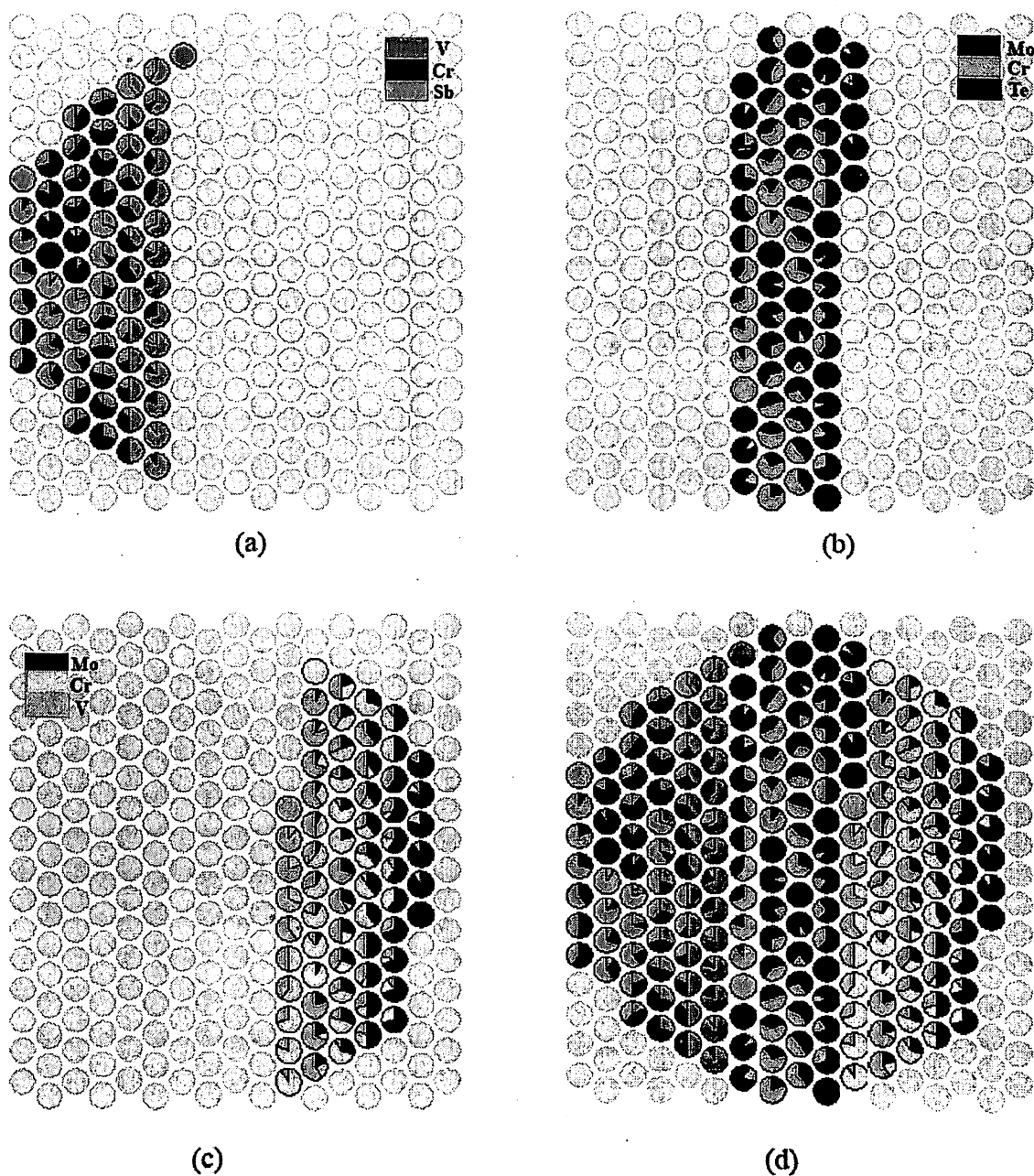
Fig 13: Ternary library composition and position of (a) VCrSb oxides, (b) MoCrTe oxides, (c) MoVCr oxides, and (d) whole spread with 0 ~ 100% Mo, 0 ~ 100% V, 0 ~ 100% Cr, 0 ~ 100% Te, 0 ~ 100% Sb in 10% increments.
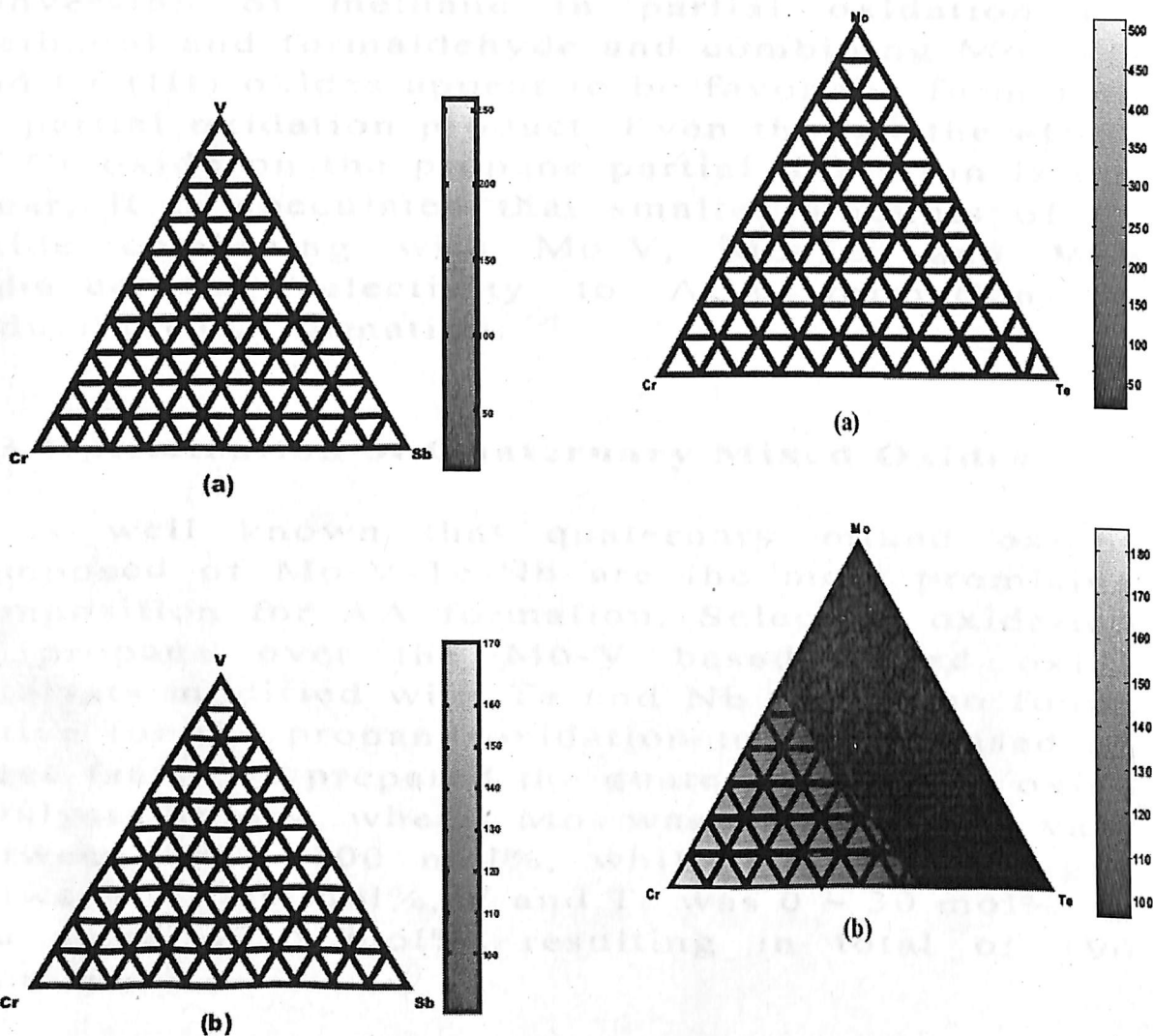
Fig.14: Relative performance of 66 member
V-Cr-Sb oxides (a)ACR, (b) CO2

Fig.15: Relative performance of 66 member
Mo-Cr-Te oxides (a) ACR, (b)CO2.

On the other hand, the effect of Cr oxide on the
selective oxidation of propane selective oxidation to
ACR has not been reported yet. Generally, Cr-
containing catalysts are one of the most effective
catalysts for the partial oxidation of methane to
methanol/formaldehyde, cycloalkanes to
cycloalkenes, and n-butane to maleic anhydride. Han
et al., reported that Cr oxide improves the

conversion of methane in partial oxidation for methanol and formaldehyde and combining Mo (VI) and Cr (III) oxides appear to be favor the formation of partial oxidation product. Even though the effect of Cr oxide on the propane partial oxidation is not clear, it is speculated that smaller amounts of Cr oxide combining with Mo-V, Mo-Te, and VSb enhance the selectivity to ACR formation by reducing CO_2 formation.

4.3 Optimization of Quaternary Mixed Oxides

It is well known that quaternary mixed oxides composed of Mo-V-Te-Nb are the most promising composition for AA formation. Selective oxidation of propane over the Mo-V based mixed oxide catalysts modified with Te and Nb were also found active for the propane oxidation to ACR. Based on these facts, we prepared the quaternary mixed oxide catalyst library where Mo was allowed to vary between 50 ~ 100 mol%, while Nb was changed between 0 ~ 20 mol%, V and Te was 0 ~ 30 mol%, in the steps of 5 mol%, resulting in total of 190 samples.

Fig. 17 summarizes the performance of the composition spread of the quaternary mixed oxides of Mo-V-Te-Nb. The highest activity for the ACR formation is found at the region of $Mo0.65-0.8V0.1-0.25Te0-0.05Nb0.05-0.1$ (Fig. 17a). The most active catalyst for ACR formation is $Mo0.7V0.25Te0Nb0.05$, which shows 145 % higher ACR formation compared to the reference catalyst. In addition, the formation of CO_2 (Fig. 17b) was low at high active regions where the formation of ACR is high. The best catalysts towards ACR with low CO_2 formation are listed in Table 2.

Catalyst	Rel. C_3H_8 Conversion to ACR (%)	Rel. C_3H_8 Conversion to CO_2 (%)
(#133) $Mo_{0.7}V_{0.25}Te_0Nb_{0.05}$	245	102
(#109) $Mo_{0.65}V_{0.3}Te_0Nb_{0.05}$	208	105
(#153) $Mo_{0.75}V_{0.2}Te_0Nb_{0.05}$	215	100
(#165) $Mo_{0.8}V_{0.1}Te_0Nb_{0.1}$	220	108
(#168) $Mo_{0.8}V_{0.15}Te_0Nb_{0.05}$	235	126
Reference	100	100

However, formation of AA is still negligible except for the reference catalysts. It seems that different preparation methods make an effect on metal oxidation state and bulk phase of catalysts, resulting in different products. The lack of AA-formation may in part be attributed to the experimental set-up since AA has a low vapor pressure and does not diffuse effectively through the capillary connecting the HT reactor with the mass spectrometer.
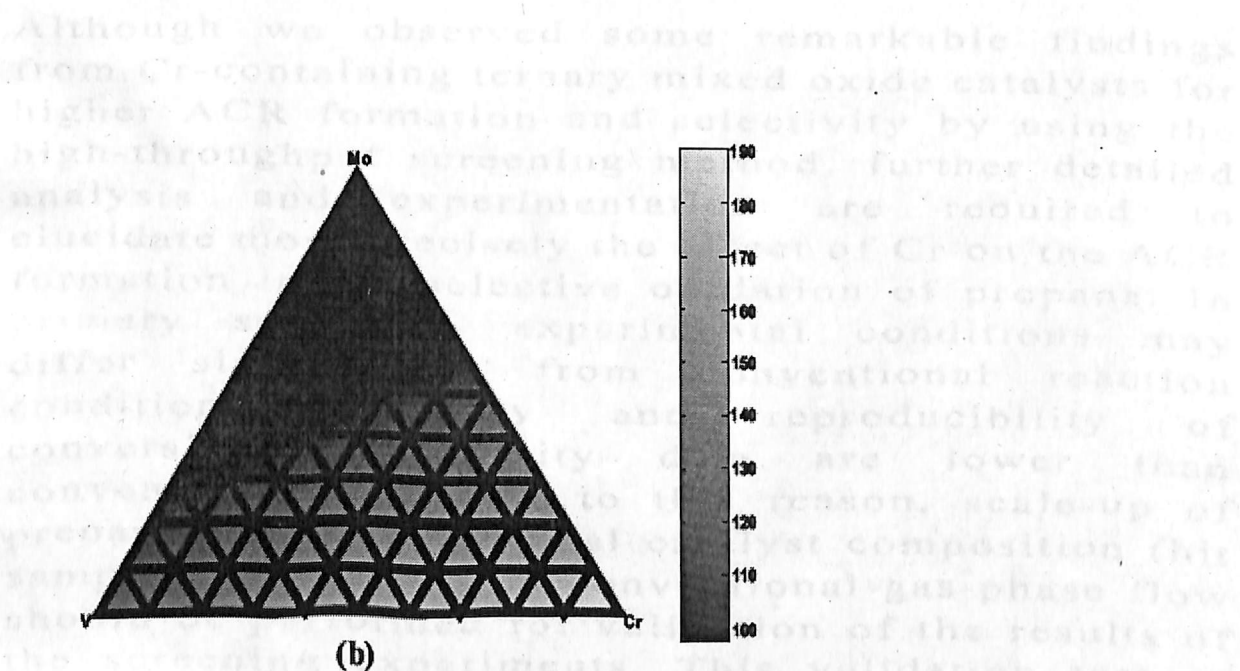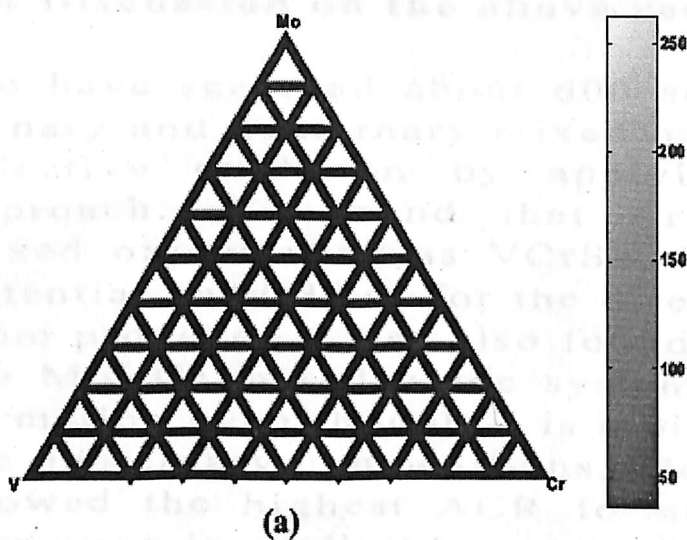
Fig 16: Relative performance of 66 member Mo-V-Cr oxides (a) ACR, (b) CO2.

4.4 Discussion on the above results

We have screened about 600 samples consisting of ternary and quaternary mixed oxides for the propane selective oxidation by applying a combinatorial approach. We found that Cr containing ternary mixed oxides such as VCrSb, MoCrTe, MoVCr are potential candidates for the direct formation of ACR from propane. It was also found that, $Mo0.3Cr0.7$ in the MoVCr mixed oxide system shows a high ACR formation even though it is a binary composition. In the quaternary compositions, $Mo0.7V0.25Te0Nb0.05$ showed the highest ACR formation. However, AA formation is negligible.

Although we observed some remarkable findings from Cr-containing ternary mixed oxide catalysts for higher ACR formation and selectivity by using the high-throughput screening method, further detailed analysis and experimentation are required to elucidate more precisely the effect of Cr on the ACR formation in the selective oxidation of propane. In primary screening, experimental conditions may differ significantly from conventional reaction conditions, accuracy and reproducibility of conversion or activity data are lower than conventional test. Due to this reason, scale-up of preparation of the optimal catalyst composition (hit samples) and testing in conventional gas-phase flow should be performed for validation of the results of the screening experiments. This validation test of primary screening and conventional testing could give a chance to find out the relationship between different metal compositions and catalytic performance.

But we can see above that the highest conversion is given by ternary mixed oxides. We should suggest the industries to use only ternary oxides for the

higher selectivities and higher activities. so the following is the list for the ternary mixed metal oxides which can be used as a catalyst for this reaction.

- For ternary MMO's
    1. V-Cr-Sb
    2. Mo-Cr-Te
    3. Mo-V-Cr

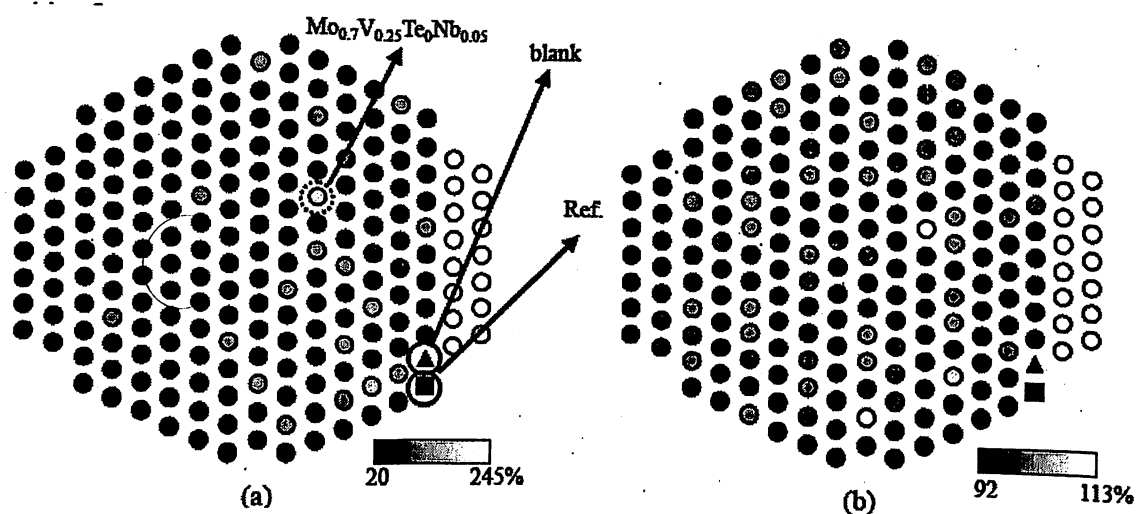- For quaternary MMO's
    1. Mo-V-Te-Nb

Fig 17: Relative performance of quaternary mixed oxides (MoVTeNb) catalyst library at 420 °C (a) ACR, (b) CO2 formation.

CHAPTER-5

Proposals for the futuristic work for universities and industries related to this project

- ❖ As it is shown in the project study that we can develop and screen the bulk amount of catalyst by the combinatorial approach we should implement this technique in the industries and universities where the catalyst work is going on.

- ❖ For the reactions like selective oxidation of propane, we have to think about the method to be implemented so that we can make or develop a better catalyst for this kind of reaction.

- ❖ Future work should be done on the selective oxidation of side chain in the benzene ring, because in these reaction only benzoic acid is the product whatever be the side chain i.e. either it is 2 membered or three membered or much more.

- ❖ The catalytic cracking catalyst should also be screened once more so that much more efficiency could be achieved.

- ❖ Zeolite synthesis should also be done by this method only so that zeolite with much more higher selectivities can be discovered and synthesized.

- ❖ In the reaction of selective oxidation of propane we can use the catalyst of ternary compositions. Because the ternary compositions are giving much better results for the activity relative to the reference catalyst. So in future we should study all of these ternary compositions to get these compositions at the industrial scale.

CHAPTER-6

CONCLUSION OF PROJECT

The following points can be concluded by the study which has been done.

> The combinatorial catalysis approach gives the better catalysts for the industries.

> This approach gives the method by which the catalyst can be scaled up to industry level from laboratory level with a superior efficiency.

> In india there is very less work done on combinatorial approach, so we should go for this approach of making new chemicals and materials.

> By this approach of making new materials we can decrease the time of testing and screening of the catalysts.

> This is economical approach for making the industrial catalysts because in screening and testing of catalysts by the traditional approach we spent a lot of money and manpower.

> Less manpower and economy is used in this approach.

➢ Genetic algorithms and artificial neural network systems are used to optimize the catalysts libraries which are proved to be successful systems to make an efficient catalyst.

➢ Catalyst libraries are used to characterize by the machines like mass spectrometer, gas chromatograph, FTIR spectroscope, etc which are readily available in any university or industrial laboratories.

➢ The selectivity of the catalyst is of the main concern in the industries so here is the procedure to get the most selective catalysts, because we can improve the selectivity of the catalysts by making the libraries and taking the genetic algorithms of first generation, second generation, third generation and so on.

➢ The efficiency of the catalyst which are made by using the combinatorial approach at the laboratory level and at the industrial level are approximately the same.

➢ Characterization of the catalysts is easy.

➢ The catalysts which can transform selectively low molecular weight compound into valuable products are easy to make by this technique.

➤ It is easy to select a catalyst from the different choices that which one is the better catalyst for a particular reaction.

➤ Relative performance of the catalysts can easily be calculated by this approach of developing a catalyst.

➤ It has a big advantage in the pharmaceutical industries also.

➤ We can study qualitative structure-property relationship and qualitative structure activity relationship for any molecular material made by high throughput technology.

➤ In the selective oxidation of propane we have better options to choose now, i.e. we have ternary and quaternary mixed metal oxides which may better work in the selective oxidation.

➤ By combinatorial approach we can get the proper compositions of the ternary and quaternary mixed metal oxides.

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