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Combinatorial approaches to heterogeneous catalysis: strategies and perspectives for academic research

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Abstract

The application of combinatorial chemistry to heterogeneous catalysis is analysed in terms of current strategies and perspectives on the industrial and academic levels. Potential methodologies for academic research laboratories are proposed with emphasis on both theoretical and practical considerations. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Heterogeneous catalysis; Combinatorial chemistry; Optimisation algorithms

1. Introduction

Over the past 5 years, the number of articles and reviews dealing with combinatorial chemistry applied to heterogeneous catalysis has been steadily increasing. This demonstrates the growing interest of the scientific community for this new methodology, which aims at the discovery of materials whose properties may surpass those of the best industrially used formulations. Combinatorial chemistry applied to heterogeneous catalysis is a very controversial subject, however. Today, within universities as well as within public and private research centres, attitudes towards combinatorial methods run the gamut from fascination to scepticism or even outright rejection. The discussion sometimes seems to lack a rational basis and some of the concepts used may need further clarification.

In evaluating if combinatorial chemistry is a subject worth pursuing or not, one has to distinguish between the different research fields for which this technique is applied. On one hand, there is the combinatorial synthesis of new organic structures. On the other hand, there is the synthesis of new inorganic materials by combination of the most useful elements of the periodic table (about 75). In the domain of inorganic synthesis, we must differentiate between the preparation of materials with specific physical properties, such as superconductivity [1], and that of materials more precisely adapted to heterogeneous catalysis, for which the final target is a certain chemical reactivity and product selectivity with respect to certain gaseous or liquid mixtures. When complex distributions of reaction products have to be resolved, chemical reactivity is obviously more difficult to evaluate than one specific physical property.

A major source of disagreement about the future prospects of combinatorial methods in heterogeneous catalysis emanates from the highly confidential aspect of the progress accomplished by industrial research. It is very difficult to draw conclusions about the state of the art without being able to include the important activities of industrial research laboratories. In this context, it has to be stressed that combinatorial chemistry, with its relatively practical approach, is of immediate

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industrial interest, in contrast to some other new research areas.

Within academic research, general papers [2,3], as well as conferences and specialised seminars or workshops [4,29–32], are proof of a certain level of activity, while revelations regarding national and international networks or consortiums tend to be minimal. This activity is highly polymorphous, however, which makes it difficult to evaluate the efforts under way and the objectives retained. The near absence of detailed academic publications about the reality of research carried out in the laboratory (development and application of tools for the rapid synthesis of catalysts and the evaluation of their activity, software for data handling or for the piloting of catalyst preparation, concrete applications to key reactions in heterogeneous catalysis) contribute to the difficulties mentioned above. This last observation drives home the point that research in combinatorial catalysis is still at an early stage, and on the threshold of many possible applications.

2. Analysis of the combinatorial approach to heterogeneous catalysis

We have at our disposal several elements of analysis which can help provide a reasonable understanding of combinatorial catalysis. Accordingly, based on our own experience in the domain,[2] this paper shall analyse, in a non-exhaustive manner, some of the questions that academic researchers hoping to specialise in combinatorial methods for heterogeneous catalysis can legitimately ask themselves.

As a first approximation, this combinatorial approach may be viewed as two complementary methodologies.

2.1. Primary screening

Primary screening deals with the ab initio discovery of new materials via the systematic exploration of combinations of elements for the preparation of multicomponent materials. Such an approach may require considerable technical means, such as robotic systems for the chemical preparation of catalysts, coupled with set-ups for the evaluation of the catalytic activity of large numbers of formulations [5,6]. A throughput of 10 000 catalyst formulations per month has been reported for such primary screening techniques. In other cases, catalyst preparation is more inspired by surface science techniques [7], such as physical or chemical vapour deposition, than by conventional chemical techniques (impregnation, co-precipitation or sol–gel synthesis). These surface science techniques are obviously very well suited to the controlled preparation of large libraries of candidate compositions, but when larger quantities of each material are required for further testing, it may become difficult to reproduce the preparation using more technically applicable chemical preparation techniques. Typical screening techniques for primary screening are scanning mass spectroscopy [5] and infrared thermography [8].

2.2. Secondary screening

Secondary screening targets the optimisation of already-existing formulations, without necessarily excluding the discovery of new materials. The main characteristic of this second methodology is the association of *high-throughput preparation and evaluation of materials under conditions that are as realistic as possible* with *a rational approach* which orients the investigation along predetermined paths. These techniques are usually considerably slower than primary screening techniques due to the more accurate or more detailed information obtained.

Secondary screening can be achieved by employing continuous flow parallel microreactors with identification of reaction products [9–11]. An alternative approach can be realised through kinetic investigation. Microkinetic analysis, coupled with in situ spectroscopic methods that identify important reaction intermediates, allows the development of a realistic kinetic scheme for a given catalytic reaction. Relevant kinetic data can rapidly be extracted when transient

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experiments are modelled [12,13,33]. These techniques allow the analysis of the elementary reaction steps that *determine* the global catalytic outcome. If throughput is increased by performing experiments in parallel, these techniques can be used as screening tools leading simultaneously to catalyst optimisation and to comprehension of the mechanistic changes induced by variations of catalyst composition or reaction conditions.

The distinction between primary and secondary screening is obviously somewhat arbitrary, and not necessarily appropriate for each type of catalysis. A combination of primary and secondary screening has been proposed to be most effective, because new materials discovered by primary screening can next be optimised by secondary screening techniques [5]. An alternative approach could be to limit the necessary capital investments by concentrating on "secondary screening". We believe that secondary screening, in combination with a fundamental approach and the exploration of domains insufficiently (or never) explored, is well adapted to the technical possibilities of most fundamental research laboratories.

A bottleneck in combinatorial catalysis research is the limited number of parallel screening techniques currently available for primary or secondary screening. The development of new screening techniques is another domain to which academic research could make important contributions.

3. Strategies and technologies for secondary screening

On a *conceptual level*, the goal of secondary investigation is not to prepare and test "just any catalyst," but to specifically aim for materials that present an optimal concentration of active and selective catalytic sites. We shall now illustrate the complexity of this goal by means of an example.

In the important field of oxidative dehydrogenation of light alkanes into alkenes, for which global demand is constantly increasing, one basic idea widely developed in the literature is the association of catalytic selectivity with a well-defined type of structure. As such, the orthovanadate phase of a V/MgO catalyst appears to be more selective than the pyro or ortho phases, even though proposals to the contrary have also been made [14,34]. The reality of such a chemical law would undeniably pose strict limits on a combinatorial approach, given the limited number of crystalline structures that exist for a particular V–Mg–O ternary ensemble. That said, numerous observations tend to suggest that it is, in fact, the superficial structure of supported phases (which can be completely different from that of core structures) that determines catalyst performance for this reaction. Accordingly, by optimising the vanadium content, our laboratory has demonstrated that the best yields of C_3 or C_4 alkenes occur for very low vanadium contents for which there exists no well-defined structure, just a high surface concentration of distorted VO_4^{3-} tetrahedrons (with the rapid evolution of an amorphous structure dispersed towards a spinel type crystalline structure, depending on the reaction conditions) [15,16]. As well, Ruth et al. [17] showed, through a fundamental study of Mo–V–Nb type oxides for the oxidative dehydrogenation of ethane, that the best formulations (deduced from a pre-combinatorial approach on about 10 solids) were multiphase solids, with an important role accorded to easily reducible amorphous phases . However, in contrast to this, Zanthoff et al. [18] have shown that the related catalytic system V–Sb–O behaves in the opposite manner for the ammoxidation of propane. In that case, non-crystalline surface structures of VO_x are detrimental to dehydrogenation and nitrogen insertion selectivity [19].

These observations considerably broaden the combinatorial horizons for this class of reactions, because the goal is not to discover new bulk crystalline structures, but to identify the most active and selective morphology. In the future, combinatorial methods should much more quickly help identify the optimum catalyst composition and structure for a given reaction.

On a *more technical level*, several factors must be reunited in order to form a continuous loop if a combinatorial approach to heterogeneous catalysis is to be successful.

- Chemical goals to be attained (e.g., a certain product yield, selectivity, or resistance to coking) have to be determined in order to define an objective function. The objective function is a measure of catalytic performance in relation to these chemical goals.
- The components that are to make up the catalysts, including different preparation and activation

methods, have to be defined. Their definition should be based on previous experiments or on literature data, though rarely used elements should not be excluded.

- A system allowing the preparation of "libraries" that consist of catalysts of variable composition, as well as a commercial or home-made set-up for the rapid evaluation of catalytic performance and physico-chemical properties (in the view of a selection according to certain criteria defined by the objective function), have to be available.
- A data handling and processing system is needed to cope with the increased flow of data created by the experiments. It could also include optimisation routines that direct the search towards the global maximum of catalytic performance (the maximum of the objective function). This can be achieved by creating generations of catalysts. Once the catalysts of a given generation have been tested, the algorithm calculates the next generation of catalysts to be tested, based on the test results of previous generations.

Fig. 1 illustrates the principle of these optimisation loops within the context of heterogeneous catalysis. We shall now outline this scheme, one key step at a time.

3.1. Preparation of catalyst libraries

Complete automatisation is eventually needed for the preparation of great numbers of catalyst samples of varying composition. Today, synthesis robots for the preparation of catalyst libraries are commercially available. Such a robot should ideally possess a mechanism for the automatic handling of liquids and solids. It should also be able to perform programmable agitation, filtration, heating and cooling steps. These functions correspond to the various manual steps of a conventional preparation (impregnation, co-precipitation and sol–gel). For the moment, one roadblock is that most currently available commercial synthesis robots do not simultaneously present all of these functions, which means that modifications are often necessary on the laboratory level. In any case, it is necessary to adapt the synthesis procedure to the technical possibilities of the robotic preparation system, which is by no means a trivial task as limited information on the robotic synthesis of inorganic materials is available. A second problem is the high cost of such robots, which is related to their prototypical character. The expansion of the market and the probable competition among new, specialised companies, and perhaps even commercialisation by public laboratories themselves, should render these tools more accessible in the years to come. We note, however, that most of the trailblazing laboratories in the domain of combinatorial catalysis began their work with manual micropipettes and sets of inexpensive test tubes.

3.1.1. How should one combine elements in order to build a catalyst library?

First of all, one must select the possible components that are to make up the different catalyst materials to be tested. The choice will be guided by the intuition of the chemist based on literature data, and by the results of previous experiments or of primary screening.

After the components have been selected, search algorithms can be used to reduce the number of experiments needed to find the catalyst composition with the best catalytic performance. This involves finding the maximum (or minimum) of the objective function as a function of catalyst composition. In general, the objective function is expressed in terms of the concentrations of the different catalyst components and in terms of the reaction conditions. It quantifies catalytic performance and has to be defined before a search algorithm can be applied. There are a number of search algorithms available, not all of them equally suited for catalyst optimisation. When selecting the appropriate search algorithm for a combinatorial catalyst optimisation problem, a number of requirements have to be taken into consideration.

- The algorithm should be able to find the *global maximum* of the objective function and should not be trapped by local maxima.
- Ideally, the algorithm should perform the search *in a parallel fashion*, since the central idea of combinatorial chemistry is to increase efficiency by performing experiments in parallel. The search algorithm should therefore suggest a number of new catalyst compositions at a time (as many as there are solids in a library). These compositions are tested, then values for the objective function are returned in order for the algorithm to calculate a

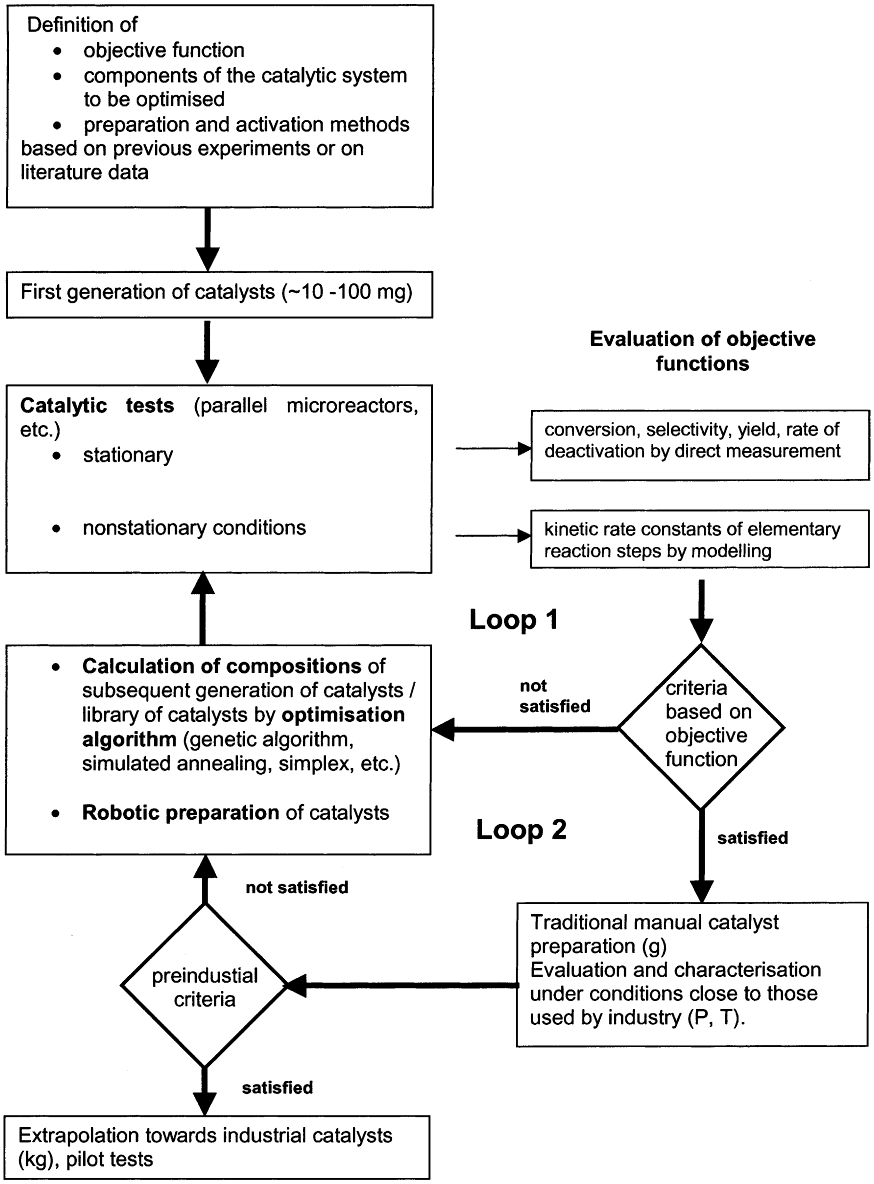

Fig. 1. Proposed optimisation process for heterogeneous catalysts.

new set of compositions to be tested. Many search algorithms operate sequentially, however, by suggesting one new experiment at a time. These algorithms can be used only if implemented in a parallel fashion, starting from several catalyst compositions at a time.

- The *objective function* (as a function of catalyst composition) is usually not available in an analytical form if it has not been determined by fitting of experimental data or by theoretical considerations. The algorithm should therefore treat it as a *black box*. Values for the objective function are determined by experiments and are then returned to the algorithm to calculate the next set of catalyst compositions. Many deterministic search algorithms, which require an objective function in an analytical form (e.g., to calculate derivatives), are not suitable.

- One has to take into consideration *the throughput of experiments that can be accomplished*. Some search algorithms require a large number of experiments because of slow convergence to the maximum of the objective function. Such algorithms would not be appropriate if the experimental set-up allowed only for very limited throughput.

Among the deterministic search algorithms, the *simplex algorithm* [20] could be adapted to combinatorial optimisation, since it does not require an objective function in an analytical form. If an objective function with n variables has to be optimised, the search is begun by defining $(n + 1)$ points to form a regular simplex. This simplex is a triangle in the case of two variables. The search then progresses by selecting the corner for which the objective function has the lowest value. New corners are then generated by reflecting the triangle about the side opposite to the worst corner, and so on.

Stochastic search algorithms employ random search techniques to some extent, in contrast to deterministic search algorithms. They have the advantage of not being as easily trapped by local maxima (or minima) and are, therefore, better suited for use as global search techniques. Convergence might be slower than with deterministic algorithms, though. Important examples of stochastic search techniques are simulated annealing and genetic algorithms. These algorithms do not require the objective function to be in an analytical form. Both are inspired by natural processes.

Simulated annealing [21] is inspired by the way in which the crystalline structure of a solid can be converted to its minimum energy structure by appropriate temperature treatment (annealing). A random search designed to find the global minimum of the objective function is employed. The algorithm accepts not only favourable changes (decreases) of the objective function but, with a certain probability, unfavourable changes (increases) as well, in order to escape local minima. The probability with which these unfavourable changes in the objective function are accepted depends on the "temperature" of the system. As the search progresses, the temperature is subsequently lowered, and the search converts to the global minimum of the objective function. Simulated annealing can equally be employed to search for the global maximum of the objective function. In its simplest form, it is essentially a sequential algorithm that suggests one new solution at a time. As mentioned above, it would have to be implemented in a parallel form to be useful for combinatorial chemistry.

Genetic algorithms [22] are inspired by natural evolution and are based on selection and survival of the fittest. In contrast to simulated annealing, this intrinsically parallel type of search algorithm works with populations of trial solutions. Optimisation occurs through generations of populations of trial solutions with increasing average fitness.

Neuronal networks [23] are a simplified form of artificial intelligence inspired by the working principle of natural nervous systems of humans and animals. Although they are not specifically designed as optimisation algorithms, they could also be applied to catalyst optimisation (an example is given below). Neuronal networks can be trained with sets of input data (such as catalyst compositions) and output data (such as the yield of a given product for a catalytic reaction) which are related by an unknown functional dependency (the objective function). After training, the networks are then able to approximate this unknown function and make predictions for output data on the basis of new sets of input data for which they have not specifically been trained. Neuronal networks can also be used to classify input data. They could therefore be useful to extract relationships from catalytic data for a large number of catalyst compositions.

As far as heterogeneous catalysts are concerned, we shall now discuss how the methods employing genetic algorithms and neuronal networks can be implemented.

With genetic algorithms, a first generation of catalysts is prepared by the random combination of components chosen for a function judged necessary for the catalyst to be effective. For example, for the oxidative dehydrogenation of propane as described by Wolf et al. [24], the base components are primary oxides (V_2O_5, MoO_3, Fe_2O_3, GaO, MgO and La_2O_3) which present various functions, such as acidity, basicity, strong redox potential, or the ability to easily dissociate oxygen.

For the water gas shift reaction (WGS), which is currently being studied in our laboratory, basic elements such as Co, Cu, Fe, Cr, Zn and Mo combined with oxygen as oxides have to be considered for preparing the first generation or initial library. Other elements, such as gold, that are also known to be effective in that type of chemistry, can be considered for further evolution of the catalyst generations. Each combination is coded in a manner that includes the concentration of each component and additional information about the preparation and activation protocols [24].

Then, after the performance of these various initial combinations is determined in catalytic tests, the three main mathematical operators allowing evolutionary creation of a new generation of solids are applied (Fig. 2).

- *Selection* refers to the identification of "good" formulations and the quantification of their catalytic performance with respect to the objective function.
- *Crossover* deals with the exchange of components between the selected formulations.
- The third operator, *mutation*, comes in two varieties. Quantitative mutation refers to a change of concentration of the components, while qualitative mutation occurs when a certain component (selected at random) is added or removed.

The efficiency of these genetic algorithms is fully documented in [24].

Hou et al. [25] employed a *neuronal network* to optimise catalysts for the ammoxidation of propane into acrylonitrile. The authors used a network that was trained with experimentally determined data on conversion and selectivity for a number of catalyst compositions. After appropriate training, neuronal networks were then able to predict (within certain limits of error) the catalytic performance for a new set of input data (with unknown catalyst compositions in this example). The compositions predicted to be the best were used in a second round of catalytic tests. By comparing predicted and experimental data, it is possible to estimate the ability of the network to predict catalytic performance of unknown compositions, and to determine whether more data for training are needed. By repeated rounds of experiments and training, it should be possible to approach the optimal catalyst composition.

So, from generation to generation of catalysts, an evolution towards optimised formulations is theoretically possible. We must, however, emphasise *the great*

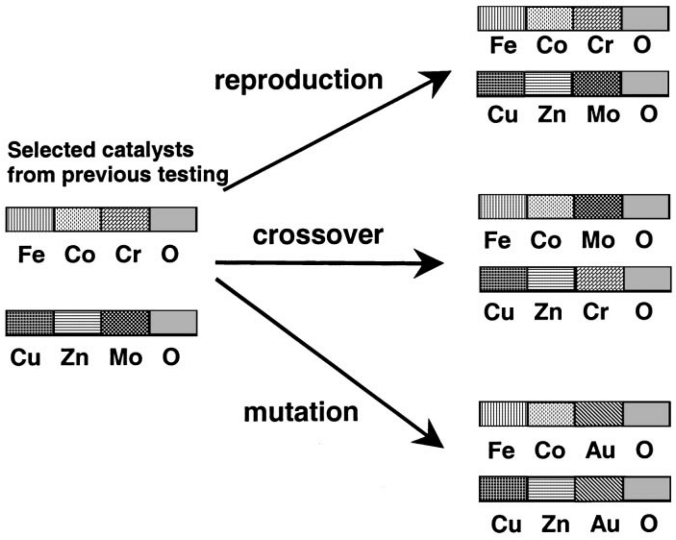

Fig. 2. Illustration of how the main genetic algorithm operators may produce new catalysts from two samples selected within a previous generation. These formulas represent typical WGS catalysts. For computing, the use of binary codes is required (i.e., using 1 when a given element is present and 0 when it is absent) and the actual concentration of each element has to be considered, as detailed in [22].

importance of the initial choices made by the chemist regarding the catalytic components that will be useful. These choices are also dictated by the possibility or impossibility of physically and chemically combining these components. Oxides can easily be combined for oxidative dehydrogenation, while different metals, prepared by various vapour deposition techniques or by reduction of precursor salts, cannot necessarily be as easily combined. This illustrates that the combinatorial approach is complex and, above all, can quickly lead to success in certain cases but just as quickly to failure in others.

3.2. Catalyst evaluation

Numerous systems for the rapid evaluation of catalysts, providing different types of information and of various degrees of technical advancement, have already been proposed in the literature. For example, infrared thermography on sample plates [8,26] allows the measurement of catalytic activity via the related temperature changes. The development of continuous flow parallel reactors coupled to methods of rapid analysis, such as gas chromatography and/or mass spectrometry, is useful for the determination of the global values of reactivity (conversion, selectivity and ageing) [9–11]. Finally, through the modelling of transient signals, non-stationary kinetics [12,13,27,33] gives quick access to the intrinsic kinetic parameters for the elementary reaction steps (Figs. 3 and 4). Other methods of evaluation, using in situ physicochemical measurements, e.g., are also technically feasible on the laboratory scale. We believe that special emphasis should be placed on *the most informative methods of evaluation* because they allow the establishment of selection criteria that are directly related to the properties essential to the catalytic act. There again, the fundamental knowledge of the reaction concerned, and particularly of its intrinsic kinetics, remains necessary for the efficiency of the method [28].

The evaluation technique obviously must be compatible with the rotational speed desired in the first optimisation loop of Fig. 1. Selection is carried out based on preestablished criteria quantified by the objective function (objective functions = yield, deactivation rate, heat of adsorption of a reactant or of desorption of a key product, sticking coefficient, rate of diffusion of lattice oxygen, redox constant, and so on).

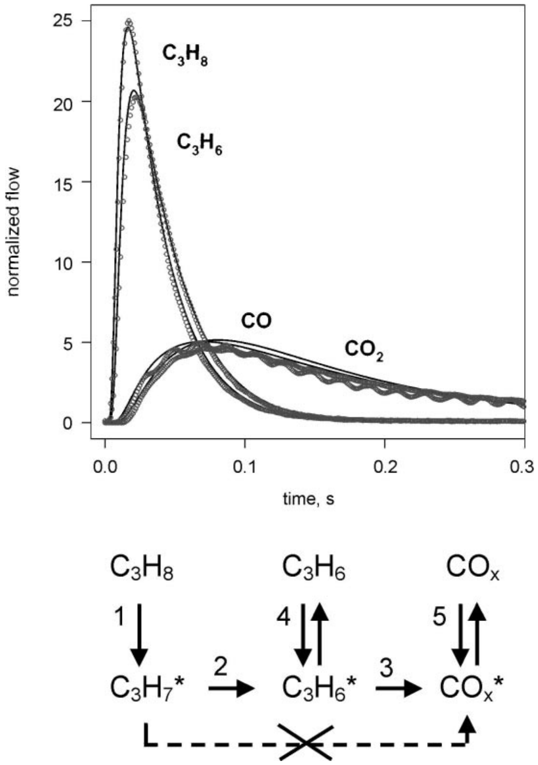

Fig. 3. Experimental (circles) and model (lines) transient responses at 600°C from a pulse of propane/oxygen = 2 admitted over a V/MgO catalyst in the TAP reactor. From this fast response analysis, all the kinetic parameters corresponding to the above scheme of the oxidative dehydrogenation of propane are determined [13].

We note that the commercialisation of these evaluation techniques (such as parallel microreactors, scanning XRD and infrared thermography) is not yet as widespread as the commercialisation of systems for combinatorial preparation.

3.3. Extrapolation towards materials that meet industrial requirements

One major criticism of the combinatorial approach is that it can lead to poorly reproducible formulations that are difficult to extrapolate for use under real industrial conditions (though this argument could also be advanced against the preparation of model catalysts in academic laboratories). We believe that a solution to this problem is provided by the use of a second

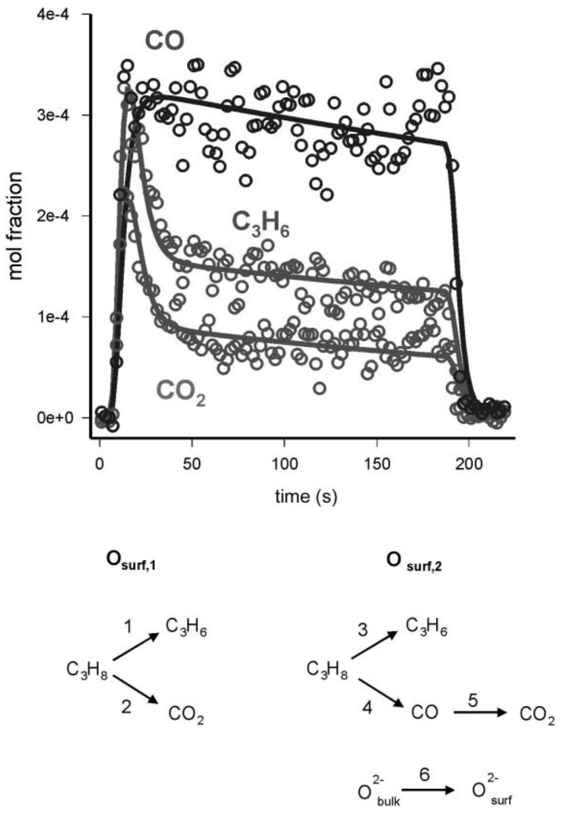

Fig. 4. Experimental (circles) and model (lines) transient responses at 550°C after a step transient of propane admitted over a V/MgO catalyst under anaerobic conditions [27]. From the data it can be concluded that two different oxygen species ($O_{surf,1}$: more selective site and $O_{surf,2}$: less selective site) are present on the catalyst. These different species cause the biexponential decays for propane and CO_2. The fast decay stems from the more selective sites while the slow decay stems from the less selective sites. CO is only formed on the less selective oxygen sites. The applied kinetics were obtained in a short time (very few experiments) using spectroscopic results and optimised catalyst compositions and preparation methods.

optimisation loop (rotating more slowly and with no automated process), based on the conventional preparation of gram or kilogram quantities of catalyst, the characterisation and the evaluation of the best catalysts of the first loop (Fig. 1).

4. Conclusions

Once concepts and strategies have been clarified, the combinatorial approach seems like a real opportunity to grasp in this initial phase of extension to the vast field of heterogeneous catalysis, especially for academic research. The basic technical and theoretical tools of combinatorial catalysis already exist and, in the short term, advancements of varying degrees depending on the chemistry attempted can reasonably be envisioned. Though considerable human and material investments are necessary for the expansion of combinatorial catalysis, we must remember that this approach that combines *discovery and comprehension* is at the heart of the goals of research. In this way, it can only reinforce the creativity of our laboratories.

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