An Approach to the Construction of Indexed Libraries for the Combinatorial Selection of Heterogeneous Catalysts

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Two series of sublibraries consisting of data for an overall 10 mixtures (five supported metal catalysts each) were constructed and tested for the selection of catalysts in terms of activity and/or selectivity in the cracking/isomerization of *n*-heptane. © 2002 Elsevier Science (USA)

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INTRODUCTION

In the last few years, combinatorial methods have been extensively used to identify and optimize heterogeneous catalysts (1–5). However, most reported approaches rely on the use of parallel synthesis and high-throughput screening techniques. Notwithstanding the impressive advances in this field, the efficiency of available methods for preparing and testing heterogeneous catalysts is rather low relative to homogeneous catalysts (6–8) and, especially, to active organic compounds, for which the libraries often contain thousands of compounds (9). Both the synthesis of heterogeneous catalysts and their testing are subject to a number of shortcomings; also, most available methods for the synthesis and deconvolution of organic compounds are inapplicable to them. An alternative methodology based on a genetic algorithm and an evolutionary approach has been successfully used to optimize the performance of heterogeneous catalysts, however (10).

Indexed (orthogonal) libraries are effective tools for deriving information from mixtures of organic compounds (11, 12). Such libraries are constructed from two series of sublibraries. Thus, for the synthesis of dimeric compounds, each building block A_n in the first sublibrary is reacted with a stoichiometric amount of an equimolar mixture of all other building blocks (B_1–B_m). In the second set, each reactant B_m is treated with a stoichiometric amount of an equimolar mixture of all other components (A_1–A_n).

Using this methodology, researchers at Glaxo constructed a library from 40 acid chlorides and 40 amines or alcohols. The process provided 80 mixtures of 40 components each, the screening of which exposed two novel leads against the neurokinin-3 receptor and the matrix metalloproteinase collagenase (11). Other example consists of the preparation of a library composed from nine alcohols and six isocyanates to formally generate 54 carbamates, which were screened against acetylcholinesterase (12). These authors consider that the goal of this method is not so much synthetic as analytic and that its purpose is to gain information on as wide a universe of structures as possible in the shortest time and with the smallest cost.

In this paper, we examine the potential of an indexed combinatorial library for selecting supported metal catalysts for the cracking/isomerization of *n*-heptane. The isomerization of low-molecular-weight paraffins is of a high current interest on account of the fact that branched isomers exhibit high octane numbers and can be used as gasoline additives to replace aromatic compounds, the usage of which should be reduced to avoid the environmental problems they pose (13). In our case, the dimeric compound was replaced with a catalytic solid consisting of two materials, viz. a metal (M) and a support (S). Five different metals (viz. Fe, Co, Ni, Pd, and Pt) were supported on as many zeolites (designated FER, ZSM-5, MOR, BEA, and USY) to obtain 10 mixtures with five components each where the identity of the metal or the support was fixed. This approach simplifies both the synthesis and the testing of catalysts; as a result, it enables catalytic activity measurements in conventional reactors and hence the identification of every reaction product.

EXPERIMENTAL

All zeolites (FER, ZSM-5, MOR, BEA, and USY) were purchased from Zeolyst Int. (refs. CP914, CBV8014, CBV90A, CP811E, and CBV760) in the following SiO_2/Al_2O_3 molar ratios: 55, 80, 90, 75, and 60, respectively. The metal precursors used were $Fe(NO_3)_3 \cdot 9H_2O$, Co $(CH_3COO)_2 \cdot 4H_2O$, $Ni(NO_3)_2 \cdot 6H_2O$, $Pd(NH_3)_4(NO_3)_2$,

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and $Pt(NH_3)_4(NO_3)_2$. The concentration of the metal solutions was 0.005 M. No reaction has been observed among them in solution.

The first sublibrary was constructed as follows. The precursor salt of each metal (M_x) was impregnated at incipient wetness in a mixture of the five zeolites (S_{1-5}) to obtain a final metal content of 0.5 wt%. The second sublibrary was constructed by using a solution containing the five metal precursors (M_{1-5}) to impregnate each support (S_y) to a final content of 0.5 wt% in each metal. Prior to use, the catalysts were calcined at 400°C and reduced at the same temperature in an H_2 atmosphere. The metal loading of supported catalysts is usually expressed as a weight percentage, even though the atomic composition varies from metal to metal. One other shortcoming arises from differences in pore network and specific surface area, which may lead to a differential distribution of the metal on different supports. However, zeolite supports have some advantages, such as a high specific surface area (300–600 m^2 g^{-1}) and a pore channel network that ensures efficient dispersion of the final metal loading (2.5 wt%).

By using the above-described procedure, each catalyst was formed twice. The presence of two active mixtures from both sublibraries assured the existence of one catalyst which is common to them. The 10 mixtures of five catalysts each were screened in the transformation of n-heptane, which involves two competing processes: cracking and isomerization. Catalytic activity measurements were conducted in a flow-through fixed-bed reactor (internal diameter, 7 mm) under standard conditions in the absence of diffusion (see Table 1 for reaction conditions). The reactor was fed at the top with n-heptane by means of a SAGE 351 propulsion pump. n-Heptane was transferred to an evaporator, where it was mixed with the carrier gas (N_2), which allowed the reactor's feed rate to be adjusted. The reaction products were directly inserted into a gas chromatograph and analyzed using a methyl silicone 100 m × 0.25 mm ID fused silica capillary column. Products were identified by comparison with standards and their structures confirmed by mass spectrometry.
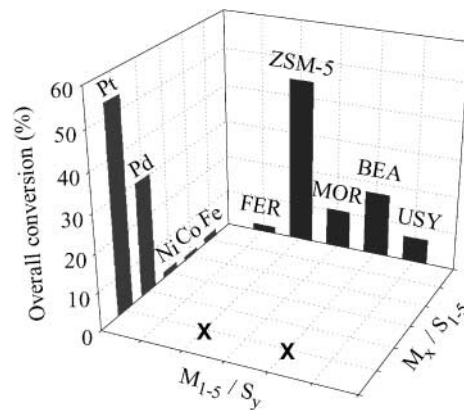

FIG. 1. Total conversion in the cracking/isomerization of n-heptane at 300°C as determined using the two sublibrary series. For reaction conditions, see Table 1.

RESULTS AND DISCUSSION

The results provided by the M_x/S_{1-5} sublibrary (Fig. 1) revealed the most active metals to be Pt and Pd—the other three were scarcely active. Also, based on the results obtained with the second sublibrary, the following activity sequence can be established: ZSM-5 > BEA > MOR > USY > FER. A comparison of these results with those provided by the first sublibrary reveals that the most active catalyst is Pt/ZSM-5, followed by Pt/BEA and so on; this is consistent with previous findings of other authors as regards both the metal and the support (14–16). Taking into account the fact that the two processes compete with each other and the significance of the liquid yield of these reactions, Fig. 2 shows the selectivity toward C_{5+} and C_{4-} hydrocarbons, defined as the weight ratio between the conversion to C_{5+} (or C_{4-}) hydrocarbons and the total conversion to n-heptane. In any case, the major compounds in the C_{4-} fraction are propane and isobutane whereas the most
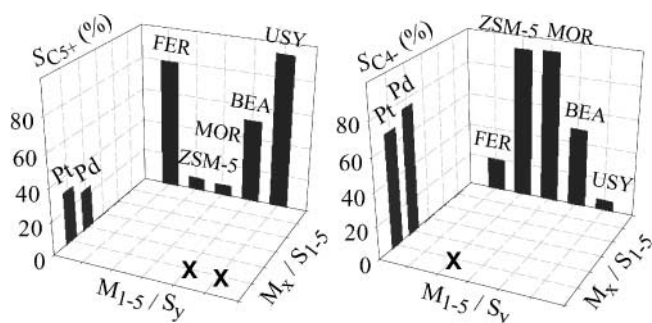
TABLE 1

Total Conversion (X_T) and Selectivity Toward Hydrocarbons (S) Obtained with the Catalysts 0.5% Pt/USY and 0.5% Pt/BEA[a]

Catalyst	T (°C)	X_T (wt%)	S_{C5+}	S_{C4-}
Pt/USY[b]	350	26.8	90.3	7.3
Pt/USY[c]	400	16.9	76.4	15.7
Pt/BEA	300	39.1	84.4	15.6
Pt/BEA	350	80.3	50.6	47.7

[a] Reaction conditions: WHSV, 37 h^{-1}; catalyst weight, 0.100 g; H$_2$ flow rate, 40 ml min^{-1}; H$_2$/HC = 2.6.
[b] S_{C5+} = 83.6 at X_T = 38.1%.
[c] S_{C5+} = 63.0 at X_T = 38.4%. This catalyst was strongly deactivated under the reaction conditions used.

FIG. 2. Selectivity toward C_{5+} and C_{4-} hydrocarbons in the cracking/isomerization of n-heptane at 300°C as determined using the two sublibrary series. A total conversion of ca. 14% was selected in all cases except with the M_{1-5}/FER sublibrary (X_T = 3%). For reaction conditions, see Table 1. The selectivity values provided by the M_x/S_{1-5} sublibraries are not shown owing to the very low conversions obtained with them.
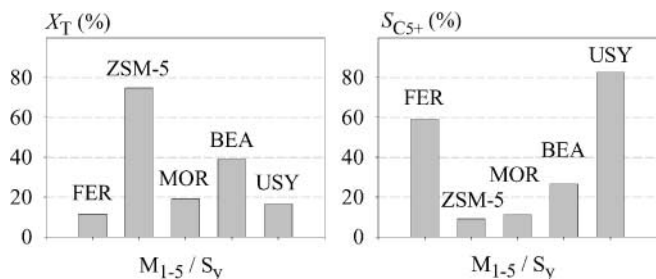
FIG. 3. Total conversion and selectivity toward C_{5+} hydrocarbons in the cracking/isomerization of n-heptane at $350°C$ as determined using one of the sublibrary series. For reaction conditions, see Table 1.

abundant products in the C_{5+} fraction are C_7 isomers. As can be seen, the catalyst mixtures containing Pt were more selective toward C_{5+} hydrocarbons (i.e., they result in less cracking) than those containing Pd. Based on the data for the second sublibrary, the following C_{5+} hydrocarbon selectivity sequence can be established: USY > FER > BEA > ZSM-5 ≈ MOR. The catalytic activity measurements provided by the M_{1-5}/S_y sublibrary were also tested at a higher temperature ($350°C$) and found to lead to the same conclusions as regards both total conversion and selectivity toward C_{5+} hydrocarbons (Fig. 3).

In view of the previous results, the ideal catalyst for the cracking process would be Pt/ZSM-5, and those for the isomerization reaction Pt/USY and Pt/BEA—the former being more selective toward liquid products and the second more active overall. Catalyst Pt/FER is a poor choice of isomerization catalyst on account of its low activity.

These conclusions were checked by preparing catalysts Pt/USY and Pt/BEA separately (both containing 0.5 wt% metal), which yielded the results shown in Table 1. As can be seen, the BEA zeolite exhibited higher activity than the USY zeolite, consistent with previous results. Also, the selectivity toward C_{5+} hydrocarbons was as good with BEA as it was with USY (on similar conversions); this seems to contradict the results provided by the sublibraries, which suggested that support USY was more selective. The discrepancy, however, can be ascribed to the increased activity of the Pt/BEA catalyst relative to Pt/USY, which allows the former to operate at a lower temperature and hence minimizes cracking (13).

A comparison of the results provided by the Pt/BEA and Pt/USY catalysts with those derived from the M_{1-5}/BEA and M_{1-5}/USY libraries reveals that the former yields better conversions and selectivities toward C_{5+} hydrocarbons. This suggests that the presence of other metals has an adverse effect on the activity of Pt metal sites. In addition, the presence of Pd results in increased cracking, which accounts for the selectivity differences observed. The differences in conversion and selectivity obtained by comparing the two approaches was to be expected, as the process is influenced by many variables that can introduce slight changes in the

operation conditions and give rise to phenomena with a direct impact on the final results. However, in order to avoid drawing spurious conclusions in applying this combinatorial approach to heterogeneous catalysis, one should take into account the following recommendations: (a) all catalysts should exhibit a similar kinetics during the process (i.e., all should possess a low catalytic activity in order to enable proper activity and selectivity comparisons); (b) side reactions should be minimized or suppressed in order to avoid interferences; (c) deactivation and poisoning reactions should be inhibited, as they are bound to affect each catalyst to a different extent; and (d) synergetic and catalytic inhibition effects resulting from the mutual presence of some catalysts (or metals) should be avoided unless they are to be used for some specific purpose. In this way, the catalytic activity results obtained will be accurate and consistent. Probably most of these assumptions hold for our system. However, it is important to recognize that the testing of mixtures makes possible interactions between compounds that could lead to either an increase (synergism) or decrease (antagonism) in the measured activity/selectivity compared to that of the pure compounds. The latter is a "false negative," possible in any screening effort. This is also the case for libraries of drugs (12) and homogeneous catalysts (7). Provided that the library is diverse enough to find a sufficient number of interesting leads or catalysts, such antagonism can be tolerated. These effects could be useful to detect interactions between components by employing experimental-design techniques (8).

In summary, the straightforward approach proposed in this paper, based on the use of indexed libraries, allows the efficient selection of heterogeneous catalysts for the cracking/isomerization of n-heptane. Further experiments will be needed in order to investigate the scope of this methodology for its application to other reactions and catalytic systems. Their use could be extended not only to other two-component systems, but also to catalysts with a variable component subjected to different physical or chemical treatments. Also, catalytic systems of three or more components could be considered provided all had a mutually independent, additive effect. Likewise, the combinatorial approaches traditionally applied to drug synthesis and testing could be used for the selection of heterogeneous catalysts by choosing appropriate variables. Finally, their joint use with automated, high-throughput screening techniques could increase their usefulness even further.

REFERENCES

1. Jandeleit, B., Schaefer, D. J., Powers, T. S., Turner, H. W., and Weinberg, W. H., *Angew. Chem. Int. Ed. Engl.* **38**, 2495 (1999).
2. Schlögl, R., *Angew. Chem. Int. Ed. Engl.* **37**, 2333 (1998).
3. Senkan, S. M., *Nature* **394**, 350 (1998).
4. Orschel, M., Klein, J., Schmidt, H.-W., and Maier, W. F., *Angew. Chem. Int. Ed. Engl.* **38**, 2791 (1999).
5. Holzwarth, A., Denton, P., Zanthoff, H., and Mirodatos, C., *Catal. Today* **67**, 309 (2000).
6. Crabtree, R. H., *Chem. Commun.* 1611 (1999).
7. Shimizu, K. D., Snapper, M. L., and Hoveyda, A. M., *Chem. Eur. J.* **4**, 1885 (1998).
8. Pescarmona, P. P., van der Waal, J. C., Maxwell, I. E., and Maschmeyer, T., *Catal. Lett.* **63**, 1 (1999).
9. Balkenhohl, F., von dem Bussche-Hünnefeld, C., Lansky, A., and Zechel, C., *Angew. Chem. Int. Ed. Engl.* **35**, 2289 (1996).
10. Wolf, D., Buyevskaya, O. V., and Baerns, M., *Appl. Catal. A* **200**, 63 (2000).
11. Smith, P. W., Lai, J. Y. Q., Whittington, A. R., Cox, B., Houston, J. G., Stylli, C. H., Banks, M. N., and Tiller, P. R., *Biomed. Chem. Lett.* **4**, 2821 (1994).
12. Pirrung, M. C., and Chen, J., *J Am. Chem. Soc.* **117**, 1240 (1995).
13. Belloum, M., Travers, Ch., and Bournonville, J. P., *Rev. Inst. Fr. Pétrol.* **46**, 89 (1991).
14. Zhang, W., and Smirniotis, P. G., *J. Catal.* **182**, 400 (1999).
15. Lugstein, A., Jentys, A., and Vinek, H., *Appl. Catal. A* **166**, 29 (1998).
16. Blomsma, E., Martens, J. A., and Jacobs, P. A., *J. Catal.* **165**, 241 (1997).