proline isomerase¹⁰, so this hypothesis cannot be taken for granted. Indeed, the one known example of a host protein being required for virion assembly, facilitation of filamentous phage assembly in prokaryotes by the host protein thioredoxin, has proven not to require the enzymatic activity of this folding catalyst¹¹. So it remains to be seen just what role cyclophilin A plays in the HIV-1 life cycle.

An issue raised by this research is whether cyclosporin A (or, more likely, a non-immunosuppressive analogue) could be useful in the treatment of AIDS. We are inclined to be pessimistic in this regard, for two reasons. First, the levels of the drug required to prevent HIV-1 replication are also sufficient to block the enzymatic activity of the cyclophilins. Any long-term inhibition of cyclophilin-mediated proline isomerase activity would probably result in significant toxicity. Second, because the closely related SIV is not dependent on cyclophilin A for infectious virion production, it seems that HIV-1 may well be able to mutate to a cyclosporin-A resistant form. Such

mutants, if they could be obtained, might however provide insights into the role of cyclophilin A in the HIV-1 life cycle; they might also help to answer the intriguing question of why HIV-1 is apparently unique among retroviruses in requiring this particular form of host-cell assistance. □

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CATALYSIS

Fine-tuning metal clusters

Michel Boudart

MANY industrial catalysts used today are metals that are spread over the internal surface of porous materials acting as carriers or supports. Such catalysts have enormous surface areas of many square metres of metal exposed per gram of catalyst. The metal is usually in the form of clusters containing 10–100 atoms. Many, sometimes close to 100 per cent, of the metal atoms in each cluster are exposed to the reacting mixtures, and this is especially desirable in the case of expensive platinum-group metals. But as the clusters are so tiny (1–10 nm), the question arose as to the effect of cluster size on catalytic activity. Answering that question becomes hard when the clusters contain fewer than about 50 atoms, in part because of the difficulty of synthesizing clusters of uniform size with a known number of atoms per cluster. Collections of free clusters have been made in the past decade, but now, in work reported on page 346 of this issue¹, Gates and colleagues have succeeded in producing supported clusters for catalytic testing.

First, some definitions. A catalyst is a substance that brings about a chemical reaction by providing a cyclic path along which reactants become products, while the catalyst is recovered at the end of the cycle. The activity of the catalyst is expressed by the number of revolutions of the cycle per second, expressed as a turnover frequency (TOF). The latter is a

true measure of the activity of the catalyst while the number of observed turnovers before a catalyst dies is the expression of catalyst life.

The work of Gates and colleagues is the culmination of a long effort to synthesize supported metallic clusters of known identical size and structure from known organometallic clusters. The latter precursors consist of tetrahedra or octahedra of iridium atoms, denoted Ir₄ and Ir₆, respectively, stabilized as carbonyls by carbon monoxide ligands. These precursors are adsorbed in the pores of various powders (magnesium oxide, γ -alumina, sodium Y-zeolite). Then the carbon monoxide ligands are removed by heating in helium at 300 °C. The authors show by X-ray absorption that the original tetrahedra and octahedra are preserved at the end of the preparation, as well as after the catalytic reaction. The reactions chosen were the hydrogenation of cyclohexene and of toluene, because previous work had shown that their TOF did not depend on the size of the clusters. But no one knew what would happen to the TOF on clusters containing six or fewer metal atoms.

Now, when TOF values for Ir₄ and Ir₆ clusters are compared to those measured on conventional supported iridium clusters, the following conclusions are reached. First, TOF values are markedly smaller for Ir₄ and Ir₆ than for conven-

tional Ir clusters. Second, these inferior TOF values are different for Ir₄ and Ir₆, being somewhat higher for Ir₆. Third, they depend on the nature of the support, so it appears that the support interacts strongly with these tiny clusters. On the one hand, the support acts as a ligand that stabilizes their structure and prevents the clusters from coalescing; on the other hand, it is also responsible for a partial loss in catalytic activity.

In a sense, the smallest identified clusters are too small, as their TOF is less than found on larger clusters. But it should not be concluded too hastily that this milestone in a long search is disappointing. Indeed, the proof of concept is that stable, identical and identified clusters can be supported and are catalytically active. The synthetic strategy behind this result can now be exploited in two ways. First, instead of focusing on activity, a future goal might be selectivity. There is an empirical rule in catalysis according to which an increase in selectivity can sometimes be bought at the expense of activity. An example of selectivity might be the selective hydrogenation of a C=C bond in a molecule with both a C=C bond and a C=O bond, as may be desirable in the preparation of fine chemicals. Second, the next synthetic strategy might be to prepare clusters containing two different metals.

Both ideas have indeed been pursued by two collaborating groups at the University of Notre Dame, one led by Thomas Fehlner and the other by Eduardo Wolf^{2,3}. Their synthetic strategy is to prepare non-supported bimetallic porous particles of clusters by controlled thermal decomposition of single-source precursors containing both metals. These new catalysts, containing cobalt and another metal such as molybdenum, copper or zinc, have been tested for selective hydrogenation of butadiene to butene: the selectivity is higher than that observed with conventional catalysts. Another more challenging reaction, the selective hydrogenation of crotonaldehyde to crotyl alcohol, is being investigated.

In conclusion, if it is accepted that selectivity is a more important catalytic attribute than activity — as is the case for enzymes — then the synthetic strategies discussed above show promise for producing new catalysts for the rapidly growing industry in fine chemicals. □

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