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Single step, solvent-free processes: examples and prospects

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An outline is given of some of the options now available — and likely to be of growing importance — for various of ways in which inorganic catalysts may be developed to effect industrially important chemical reactions in environmentally more acceptable means. One major goal is to devise ways of producing *in situ* (within the sphere of reaction) aggressive oxidants especially those that are environmentally hazardous. Two specific examples are cited: 1) one involves hydroxylamine, generated in a benign fashion, so as to effect the ammoximation of cyclohexanone to its oxime and ε-caprolactam; 2) the other involves the Baeyer—Villiger reaction (for converting cyclic ketones to lactones) *via* perbenzoic acid. The role of supported bimetallic catalysts in solvent-free hydrogenations (especially of polyenes) is also highlighted.

Keys words: bimetallic nanoparticles, cyclic polyenes, enantioselective hydrogenation, Baeyer—Villiger reaction, ammoximation.

Introduction

For this celebratory article that marks the seventieth birthday of a very fine chemist, I wish, with my co-authors, to return to the theme of environmentally responsible chemical processes.** It is a subject that flows naturally from my own specialities, heterogeneous catalysis and solid-state chemistry; and it is one that gains in importance daily because of its direct commercial relevance. In essence, we focus here on aspects of the design of simple inorganic solid catalysts that serve to effect processes that have hitherto proved either, impossible, expensive, cumbersome, inefficient or dangerous.

No great intellectual insight is required to understand that traditional approaches to the construction of industrial processes for the production of commodity chemicals as well as of fine, and pharmaceutical chemicals were usually accomplished with primacy being given to considerations of cost and convenience. Hitherto, it mattered less if the processes of industrial production involved multi-step events, or that the by-products generated were voluminous (or of little value), or that, during the course of production, some long-term damage might be inflicted upon the environment. What was of greater importance in those days was whether the desired product could be generated relatively quickly, irrespective of the considerations which nowadays loom large in the thoughts and actions of the chemical engineer and industrial chemist. Legislation, as well as strong societal pressure, has had a profound effect on the approach and design of current chemical manufacturing practice; and it is now universally recognised that, first, single-step processes are superior to multi-step ones; and that, wherever possible, solvent-free processes are to be preferred from ones that entail the use of volatile or non-biodegradable, or hazardous solvents.*

Elsewhere we have outlined[1—4] the considerable progress that has been achieved in recent years in attaining the goals of clean technology** when sustainable development was centre-stage.[5] Here we focus on two aspects of the general drive towards clean technology:

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** Twice in my life I (JMT) have participated in international conferences with Oleg M. Nefedov. The first occasion was at the Moscow meeting convened by the I.U.P.A.C committee, CHEMRAWN (Chemical Research Applied to World Needs), of which I was then chairman, in Moscow in 1992. This conference was organised by two my friends: Academicians V. A. Koptyug and O. M. Nefedov both of the Russian Academy of Sciences. The second occasion was in Switzerland, where Richard Ernst of the ETH, Zurich, organised the Engelburg Conference in 1994. At that meeting I delivered a paper entitled: "New catalysts for a cleaner environment," which was published in a somewhat obscure Austrian journal (*Chem. Raundasch.*, 1994, No. 22, pp. 20—21) and, consequently, rather widely neglected.

* Solvents such as benzene, because of their well-known carcinogenicity and volatility, are frowned upon, toluene less so; but esters such as (typically) ethyl acetate are still tolerable, principally because of their low volatility and biodegradability.

** The very subject that was at the heart of the Moscow CHEMRAWN Conference in 1992 and also the subsequent CHEMRAWN Conference in Seoul in 1996.

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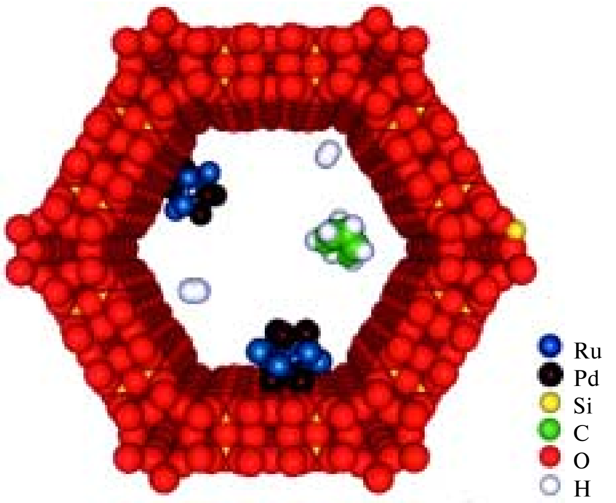

Fig. 1.* Computer graphics model of Pd_6Ru_6 nanocatalyst clusters anchored (originally in their carbonylated form *via* pendant silanol groups) to the inner walls of mesoporous silica. The nanocatalyst is akin to $Cu_4Ru_{12}C_2$, Ru_6Sn, and Ru_5Pt clusters. A typical reactant polyene (norborna-2,5-diene) and H_2 are also shown in the mesopore channel, which has a diameter of *ca.* 30 Å.

the need to reduce greatly the number of steps employed in traditional methods of manufacture; and the desire to rely less — even abandon altogether — the use of solvents as a medium for effecting chemical conversions.

Novel examples of solvent-free hydrogenations

Here we focus on the value of using nanoparticles of bimetallic catalysts, prepared from mixed-metal carbonylates (as hitherto described[6—9]) so as to disperse and anchor them in a spatially uniform fashion along the inner walls of mesoporous silica. The carbonyl "coatings" of the metal core in the parent carbonylates are driven off by gentle thermolysis, so as to yield the naked cluster of the kind shown in Fig. 1.

The parent mixed-metal carbonylate ions from which the nanoparticles of the active bimetallic catalysts are derived are illustrated in Fig. 2. The atomic structures of the parent carbonylate ions are determined by conventional X-ray crystallographic methods. But the structures of the bound bimetallic nanocatalysts are deduced[2,6—9, 12—15] by a combination of X-ray absorption fine structure spectroscopy and electron microscopy: it

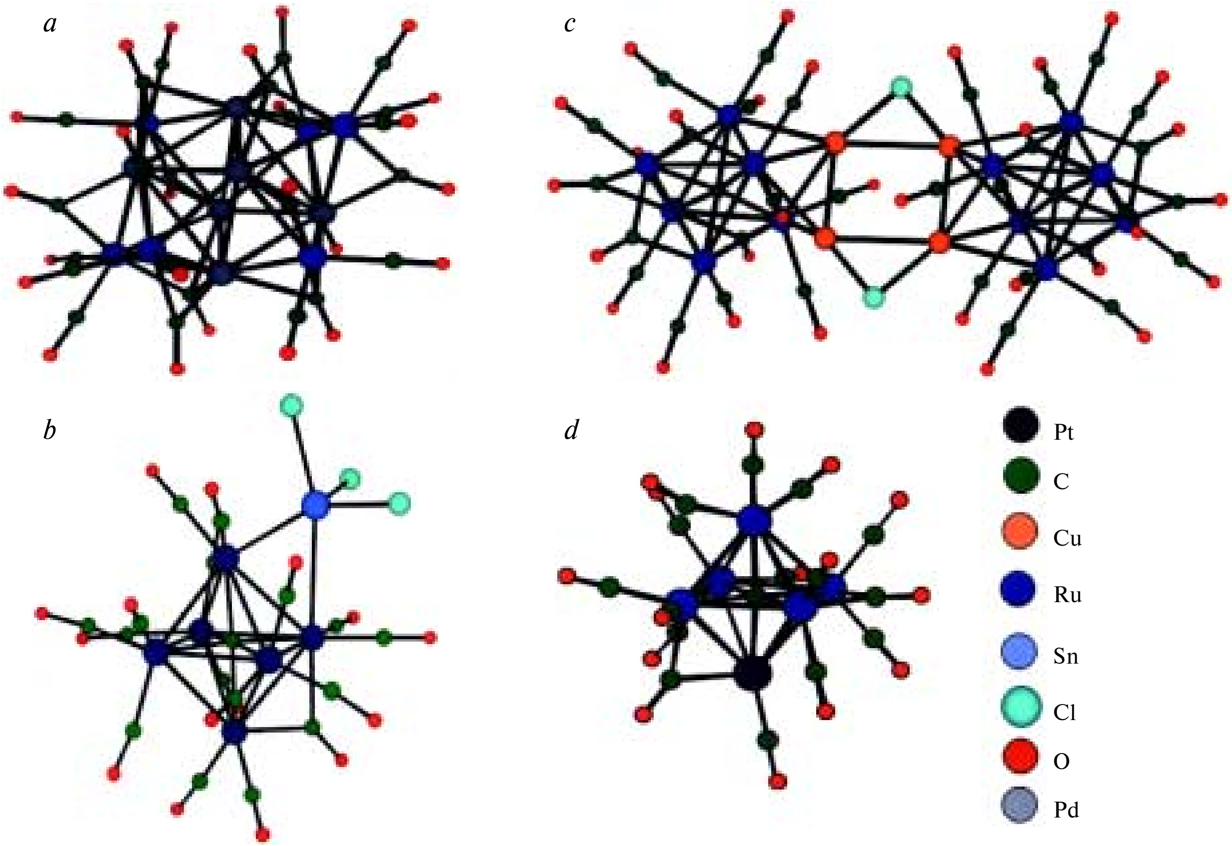

Fig. 2.* Typical parent carbonylates from which naked nanoparticle (10 to 15 Å diameter, depending upon the constituents of the bimetallic core) catalysts are generated: *a*, $[Pd_6Ru_6(CO)_{24}]^{2-}$; *b*, $[Ru_6C(CO)_{16}SnCl_3]^{-}$; *c*, $[Ru_{12}C_2(CO)_{32}Cu_4Cl_2]^{2-}$; and *d*, $[Ru_5PtC(CO)_{15}]^{2-}$.

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* Figures 1 and 2 are available in full color in the on-line version of the journal (http://www.wkap.nl/journalhome.htm/1066-5285) and on the web site of the journal (http://rcb.ioc.ac.ru).

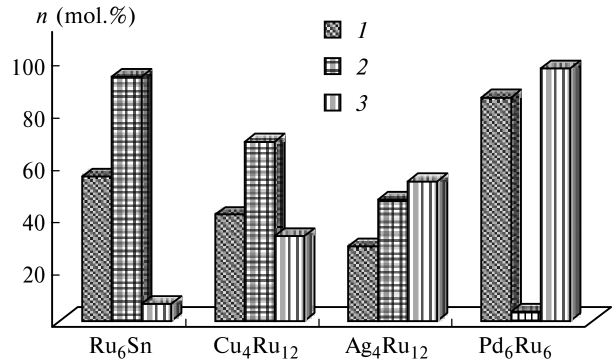


Fig. 3. Solvent-free selective hydrogenation of norborna-2,5-diene using a variety of bimetallic nanocatalysts (333 K; 10 h; P_{H_2} = 30 bar; catalyst 25 mg and norborna-2,5-diene ~50 g): *1*, conversion; *2*, norbornene; and *3*, norbornane.

is simply not possible to use X-ray crystallography because of lack of long-range order.

The catalysts prepared by us were intended (see below) to be employed under solvent-free conditions for the hydrogenation of norborna-2,5-diene and of cyclododeca-1,5,9-triene. The monoenes of these two polyenes are used extensively as intermediates in the synthesis of bicarboxylic aliphatic acids, ketones, cyclic alcohols, lactones and as intermediates for other purposes. In particular, the selective hydrogenation of cyclododeca-1,5,9-triene to cyclododecane and cyclododecene is industrially important in the synthesis of valuable organic and polymer intermediates, such as 12-laurolactam and dodecanedioic acid,[16] which are important monomers for nylon 12, nylon 612, copolyamides, polyesters and for coating applications.

The bar charts shown in Figs 3 and 4 illustrate how efficient the various bimetallic nanoparticle catalysts prepared by us, are, in effecting selective, solvent-free hydrogenations. Previously used catalysts for these selective hydrogenations, such as Raney nickel, and supported palladium or platinum or cobalt, all require the use of organic solvents such as *n*-heptane and benzonitrile (see, for example Refs. **17** and **18**).

A single-step enantioselective hydrogenation

As described elsewhere,[7,19] chiral chelate ligands based on 1,1′-bis(diphenylphosphino)ferrocene (dppf) are particularly attractive for tethering on to mesoporous silica; and the superior performance of the chiral, heterogenised catalyst, compound with the unconfined homogeneous analogue in the allylic animation reaction between cinnamyl acetate and benzylamine has been highlighted previously by us.[20]

This kind of confirmed dppf catalyst displays remarkable increases in both enantioselectivity and activity in the one-step hydrogenation of ethyl nicotinate to ethyl nipecotinate (Scheme 1). The previously available procedure for producing the biologically relevant nipecotinate entailed a two-step process and the use of a chiral modifier such as dihydrocinchonidine in one of steps.

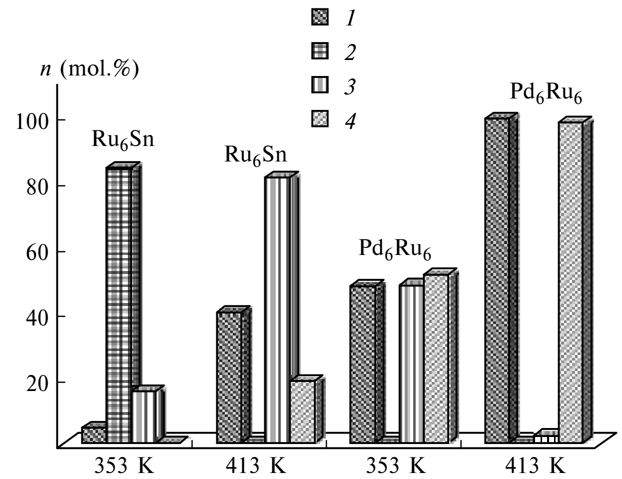
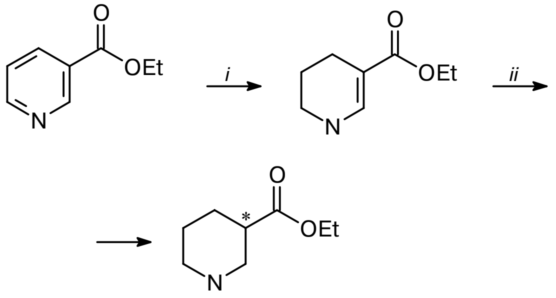


Fig. 4. The effect of temperature in the solvent-free selective hydrogenation of cyclododeca-1,5,9-triene: a comparison between Ru_6Sn and Pd_6Ru_6 after 8 h (reaction time) at 353 K and 413 K, respectively (p_{H_2} = 30 bar, catalyst 25 mg and cyclododeca-1,5,9-triene ~50 g): *1*, conversion; *2*, cyclododeca-1,9-diene; *3*, cyclododecene; and *4*, cyclododecane.

Scheme 1



i. 2 H_2, Pd/C; *ii.* H_2, Pd/C, chiral modifier

Selective oxidations and ammoximations with reagents produced *in situ*

First we consider the Baeyer—Villiger reaction which is of great commercial importance in the process of converting cyclic ketones to cyclic lactones. Originally,[22] peroxomonosulfuric acid (Caro′s acid), H_2SO_5 was the oxidant used for this process. For environmental and other reasons, the use of H_2SO_5, or of alternatives such as the potentially explosive 90% H_2O_2 is nowadays discouraged. One approach, favoured by some, is to use milder forms of H_2O_2 in the presence of inorganic materials such as methyltrioxorhenium. Our approach (Fig. 5) relies[23] on Mn^{III} (or Co^{III}) framework-substi-

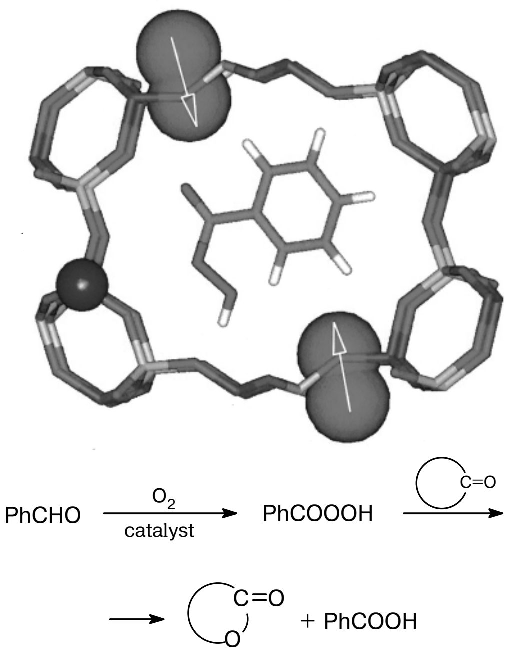


Fig. 5. Graphical representation of the reaction scheme for the *in situ* formation of the perbenzoic acid intermediate inside the micropores of the Mn^{III}AlPO-36 catalyst using benzaldehyde and molecular O_2.

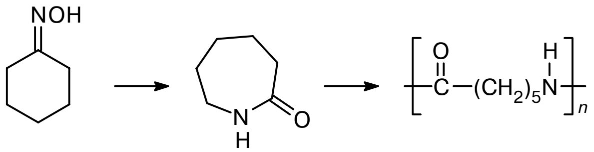
Note. This peroxy acid is subsequently involved in a nucleophilic attack at the carbonyl carbon, of a ketone or alkene, leading to production of the corresponding lactone or epoxide.

tuted MAlPOs (metal (framework)-substituted aluminophosphates[16]), in which air (or oxygen) and a sacrificial aldehyde (typically benzaldehyde, as described by Mukaiyama[24]) are used. These constituents produce, *in situ* perbenzoic acid, and this functions as an environmentally successful oxygen donor to convert the ketone to the corresponding lactone. It is to be noted that benzaldehyde molecules may freely enter the large internal areas of MAlPO-36 (M = Co and Mn). In both these microporous solid catalysts we are exploiting the ease[25] of autoxidation of aldehydes which leads, first, to the production of PhCO$^\cdot$ radicals and then PhCOOO$^\cdot$ radicals, and which, subsequently,[3] through a sequence of well-identified steps, produce perbenzoic acid. An approach similar to this *in situ* form of the Baeyer—Villiger reaction may also be used[26] to epoxidize a range of alkenes in air with the same kind of microporous catalysts employing a Mn^{III} (or Co^{III}) active site in its framework.

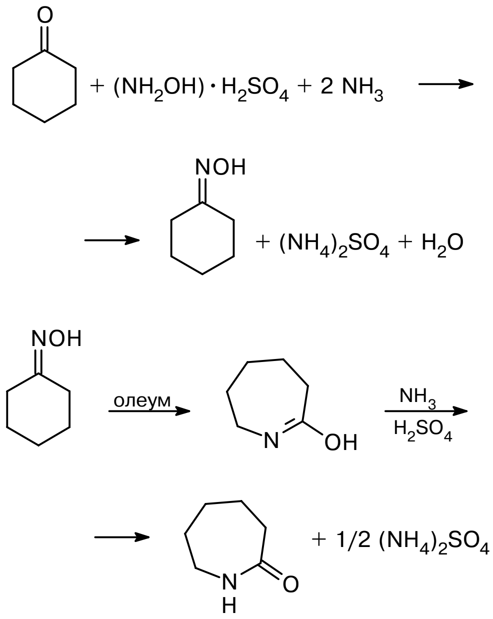
Now we turn to the much more demanding task of effecting the single-step, solvent free ammoximation of cyclohexanone. The conversion of the latter first to its oxime and then, by Beckmann rearrangement, to ε-caprolactam (Scheme 2) are important steps in the manufacture of nylon-6.

Industrially, a popular procedure is to employ hydroxylamine sulfate, and the sulfuric acid that is liberated is neutralized by ammonia (with the attendant production of large quantities of ammonium sulfate) (Scheme 3).

Scheme 2



Scheme 3



We have recently succeeded[27] in developing, on a laboratory scale, the solvent-free, one-step production of cyclohexanone oxime and ε-caprolactam with a mixture of air and ammonia using bifunctional molecular sieve catalysts. This process of benign ammoximation again uses the microporous MAlPO-36 as the key framework catalyst. To be specific the catalysts are (M^{II} M^{III}) AlPO-36 with M = Co and Mn; these solids have pore apertures of 6.5×7.5 Å. It is known from our prior work that ~4% of the framework Al^{III} ions that are isomorphously replaced by M, transition-metal ions, approximately 50% are in the M^{II} and 50% in the M^{III} state. The bifunctionality of these catalysts consists of Brönsted acid sites together with redox active ones. M^{II} ions, since they have protons loosely bound to an adjacent framework oxygen atom are the loci of the Brönsted sites, and the M^{III} ions are demonstrably the redox active sites. The pore dimensions of this molecular sieve catalyst are large enough to permit ingress of air, ammonia and hydroxylamine (which is formed *in situ* from the air and ammonia at the M^{III} sites) to the interior surface of the sieve. The hydroxylamine, NH_2OH, converts the cyclohexanone to its oxime either inside or outside the pores; and, at the Brönsted sites, this oxime (which is small enough to gain access to the sites) is isomerized to the ε-caprolactam. We have also shown that a deliberate increase in the concentration of the Brönsted sites — readily effected by the incorporation of more M^{II} ions into the framework — boosts the production of ε-caprolactam.

Conclusion

Many other processes, apart from those involving oxidations and reductions, may also be effected in a single-step and often in a solvent-free fashion. We cite just two examples: many more exist.

The first is the formation of ethyl acetate by direct addition of acetic acid, in the vapour phase, to ethylene. This reaction was discovered by one of us (JMT) and his colleagues in the University of Wales some twenty years ago.[28] The Brönsted acid catalyst devised by the inventors was a montmorillonite clay, the performance of which, in so far as percentage conversion and selectivity are concerned, is the best so far discovered. But the clay catalyst has less attrition resistance and is otherwise less robust than a polyoxymetallate (Keggin ion) type catalyst,[2,29] which is the one used in the newly commissioned Hull (UK) plant operated by BP-Amoco, who produce 220,000 tonnes per annum of ethyl acetate by direct addition of acetic acid.

The other example concerns the para-selective nitration of halogenobenzenes[32] and toluene.[31] (It is to be recalled that nitration, as well as many other operations such as sulphuration and halogenation are widely used in the manufacture of dyestuffs in ways that are not environmentally satisfactory). Smith et al.[31] has shown that nitration of halogenobenzene using the H^+ form of zeolite beta (with a Si/Al ratio of *ca.* 25) as a catalyst and a combination of liquid N_2O_4 and gaseous O_2 as the nitrating reagents leads to high yields and significant para-selectivity (*e.g.*, 85:14 of *para* to *ortho*) for chlorobenzene at 0° in a solution of 1,2-dichloroethane. But Kwok et al.[32] carried out the nitration of toluene with just *n*-propylnitrate in the presence of H-ZSM-5 as catalyst. The *ortho* : *para* ratio for a Si/Al ratio of *ca.* 1000 was 5:95, and the isolable yield of product was in excess of 50%.

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