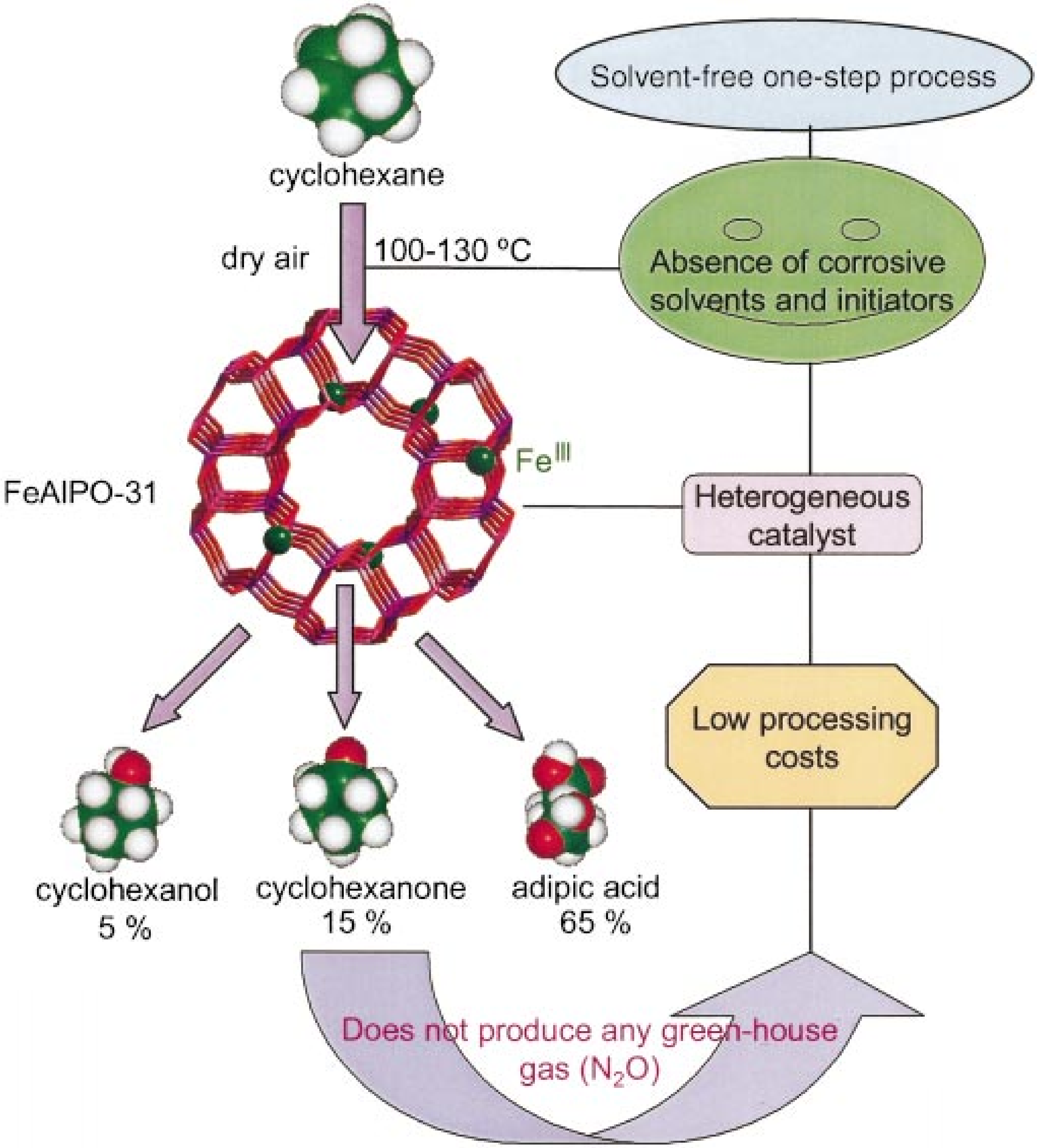


Adipic acid is currently manufactured in a costly multi-step process involving homogeneous catalysts, aggressive oxidants (conc. nitric acid) and the production of large quantities of the 'greenhouse' gas nitrous oxide. An alternative, one-step, solvent free process using air and an inexpensive microporous catalyst is shown above.

0947-6539/01/0714-2972 $ 17.50+.50/0

Solvent-Free Routes to Clean Technology

John Meurig Thomas,*[a, b] Robert Raja,[a, c] Gopinathan Sankar,[a]
Brian F. G. Johnson,[c] and Dewi W. Lewis[d]

Abstract: A major aim for the chemical technology of the future is the avoidance of noxious and environmentally unacceptable organic solvents. In this concept article we discuss more environmentally friendly and highly selective alternatives which we have evolved for carrying out a number of important chemical conversions. These entail the use of porous heterogeneous catalysts in which the active sites have been atomically engineered and fully characterized. Such solid catalysts operate under solvent-free conditions and usually entail one-step processes.

Keywords: green chemistry · heterogeneous catalysis · oxidation

Introduction

Much publicity has been given[1] of late to the merits of both supercritical CO_2 and ionic melts as potentially important means of avoiding noxious and environmentally unacceptable organic solvents in the chemical technology of the future. But there is an equally desirable need to design reactions that proceed under altogether solvent-free conditions. A wish list that would effect a quiet revolution in chemical practice, both on an industrial and laboratory scale, includes among its desiderata developing the “art of conducting chemical reactions without solvents”.[2]

It has long been recognized[3–5] that one way of achieving this goal is to harness the combined principles of photochemistry and solid-state chemistry (more specifically crystal engineering). For example, if monomers of organic molecules are induced to crystallize in such as manner as to bring into close proximity their potentially reactive functional groups (such as olefinic bonds), they can subsequently be stimulated (by UV irradiation, for instance) to undergo preferred reactions which entail no diffusion, merely minor local atomic reorganization. Such topochemical[3] reactions yield clean products, the chemical nature of which is governed more by the molecular environment within the particular parent crystal than by the intrinsic reactivity of the molecule (see Figure 1).[5]

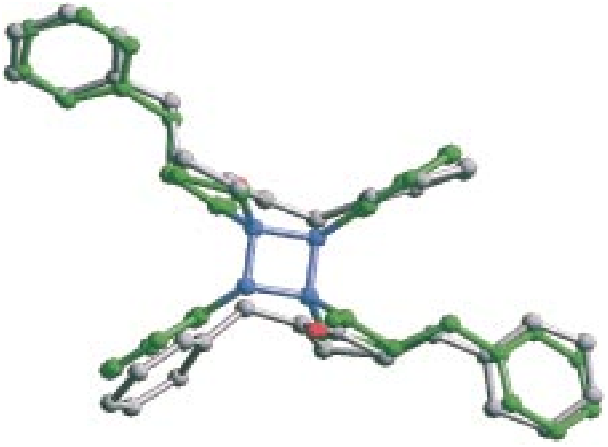


Figure 1. Two neighbouring molecules of monomer (2-benzyl-5-benzylidene-cyclopentanone) are so disposed with respect to one another in the “engineered” crystal that they readily link up when irradiated with UV light to form a dimer. The four-membered cyclobutane ring is formed from the pairs of carbon atoms linked originally by ethylenic bonds. Note how little the peripheral atoms (benzene rings) move during this diffusionless reaction.[22]

Numerous different kinds of unsaturated reactants have been converted into desirable (including optically active) dimeric, oligomeric and polymeric products in this fashion. Thanks largely to strategies pioneered in Israel, the UK, Japan and Germany[4–8] for engineering crystals that bring pairs or stacks of monomer species into close juxtaposition, considerable headway has been made in effecting a range of other

---

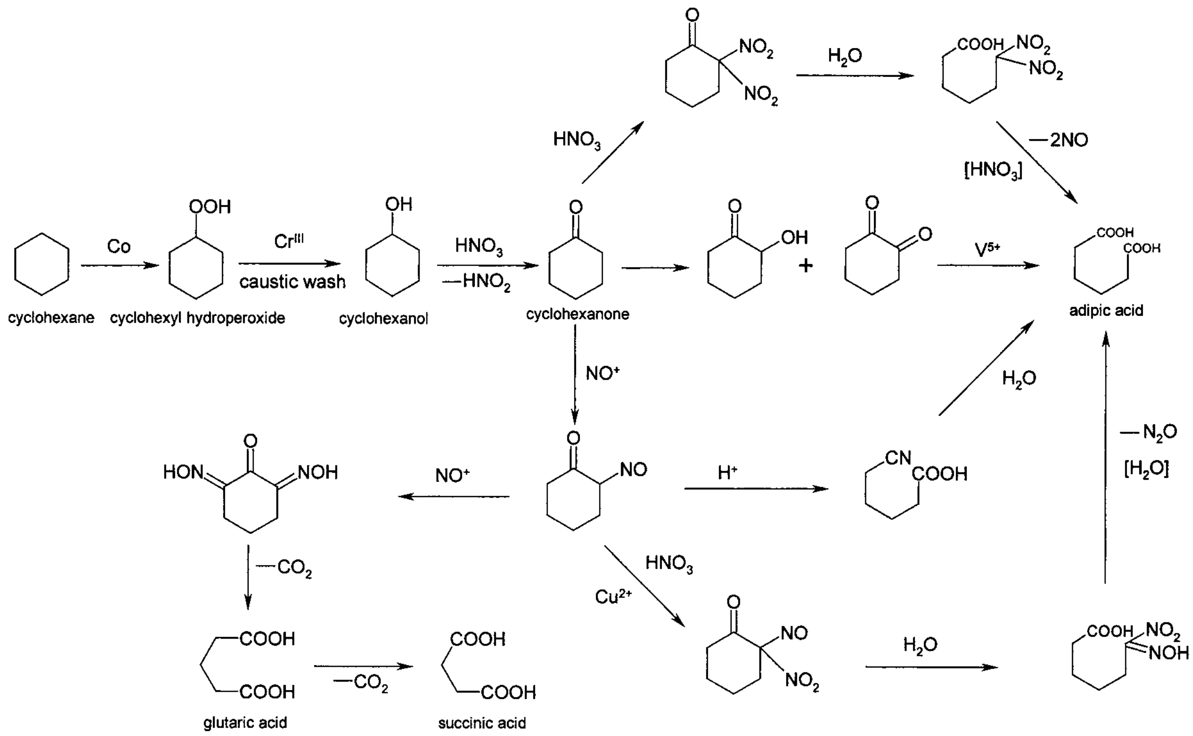
[a] Prof. Sir J. M. Thomas, Dr. R. Raja, Dr. G. Sankar
The Royal Institution of Great Britain
Davy Faraday Research Laboratory, 21 Albemarle Street
London W1X 4BS (UK)
Fax: (+44) 207-670-2988
E-mail: dawn@ri.ac.uk

[b] Prof. Sir J. M. Thomas
Department of Materials Science and Metallurgy
Cambridge University, Pembroke Street
Cambridge CB2 3QZ (UK)

[c] Dr. R. Raja, Prof. B. F. G. Johnson
Department of Chemistry, University of Cambridge
Lensfield Road, Cambridge, CB2 1EW (UK)

[d] Dr. D. W. Lewis
Department of Chemistry, University College London
20 Gordon Street, London WC1H 0AJ (UK)

0947-6539/01/0714-2973 $ 17.50+.50/0



Scheme 1.

Table 1. Production of K-A oil (cyclohexanol + cyclohexanone).

	Industrial and commercial technologies			Our solvent-free clean technology route
	Liqiud-phase oxidation of cyclohexane[a]	Boric-acid-modified oxidation of cyclohexane[b]	Hydration of cyclohexene	Liquid-phase oxidation of cyclohexane[d]
conditions	180 °C, 0.8–2.0 MPa	140–160 °C	not known	100–130 °C, 1.5 MPa
catalyst	soluble cobalt salts	soluble cobalt salts	soluble Ti, Cu, Cr	solid FeAlPO-5, CoAlPO-36
initiator/solvent	Cr^{III}	anhydrous metaboric acid	sulphuric, nitric and tungstic acids	none
conversion	< 6 %	not known	10–12 %	8–12 %
main product(s)	cyclohexyl hydroperoxide (cHHP)	cyclohexyl perborate ester	cyclohexanol	cyclohexanol and cyclohexanone
by-products	mono- and dicarboxylic acids, esters, aldehydes and other oxygenated materials	none	none	adipic and valeric acid
downstream processing	use of aqueous caustic phase containing a few ppm of cobalt to decompose the cHHP to cyclohexanol and cyclohexanone	hydrolysis of the ester to cyclohexanol and boric acid	separation of cyclohexane from mixtures of benzene and cyclohexene (costly distillation step requiring solvents); selectivity is very sensitive to impurities such as sulphur	none
advantages	low -ol/-one ratio	cyclohexyl rings are protected from further attack	high yield of cyclohexanol	absence of corrosive solvents/initiators; one-step process; heterogeneous catalyst; ease of catalyst recycle and recovery; low processing costs
disadvantages	catalyst recovery; recycle; two-step process; disposal of Cr^{III}; expensive processing costs	higher investment and operating costs (to recover and recycle the boric acid) and high -ol/-one ratio	three-step process, significantly higher investment costs than that of a conventional cyclohexane oxidation plant; the fact that main product is cyclohexanol and not cyclohexanone makes the process unattractive for caprolactam	high residence time; high -ol/-one ratio

[a] DuPont, US 3957876, US 3987100, US 4675450; BASF, GB 1382849; DSM, EP 659776. [b] Halcon, US 3665028. [c] Asahi, JP 90016736B. [d] *J. Am. Chem. Soc.* **1999**, *121*, 11926.

0947-6539/01/0714-2974 $ 17.50+.50/0

kinds of organic photochemical reactions in the absence of solvents.

Valuable as this approach to solvent-free reactions has been, it is not sufficiently versatile—even allowing for the many sophisticated variants of organic photochemistry that entail the incarceration of reactant or sensitiser species inside zeolite cages[9]—to cover the wide sweep of processes that are a feature of present-day chemical technology. Moreover, photochemical processes are not, in general, favoured on an industrial scale partly because of their cost, but also because of their practical inconvenience; thermally activated processes are generally more favoured.

There are, however, other more practicable routes which we have evolved for carrying out a number of important chemical conversions (see Tables 1–4 below). These entail the use of porous heterogeneous catalysts in which the active sites have been atomically engineered and fully characterized. Such solid catalysts operate under solvent-free conditions and usually entail one-step processes. Moreover, all the oxidation catalysts designed by us require only benign oxidants (dioxygen or air), and consist of inexpensive, readily preparable, transition-metal-ion-substituted aluminophosphate molecular sieves. Their mode of operation, explained fully elsewhere,[10–13] relies on shape-selective and/or regioselective free-radical processes of a spatially constrained kind. These heterogeneous catalysts facilitate separation of product from reactant and may be readily regenerated when their activity declines.

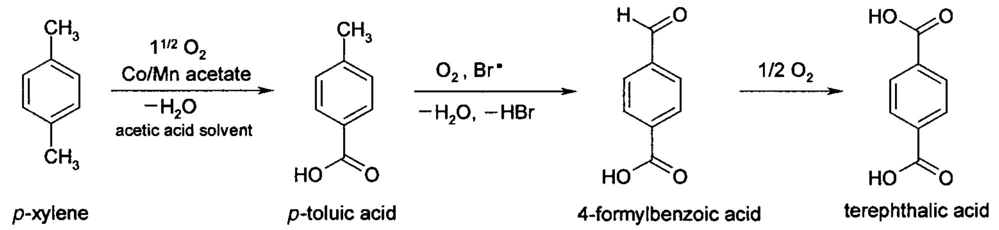
Selective Oxidation of Hydrocarbons and Aromatics

Illustrative examples of industrial significance: Many key precursors and products in the polymer industry are generated in costly and polluting processes that involve the selective oxidation of cyclohexane (Scheme 1). Intermediates such as cyclohexanol and cyclohexanone, known as K-A oil (Table 1), are the stepping stones for the production of caprolactam (the monomer for nylon 6) and adipic acid (Table 2), which, in turn, is a building block for a series of

Table 2. Production of adipic acid.

	Industrial and commercial technologies			Our solvent-free clean technology route
	Nitric acid oxidation of K-A oil[a]	Butadiene-based routes A[b]	B[c]	Aerial oxidation of cyclohexane[d]
conditions	60–120 °C, 0.1–0.4 MPa, 60 % HNO_3	two-step carbomethoxylation of butadiene with CO and MeOH	two-step dihydrocarboxylation of butadiene	one-step process, 100–130 °C, 1.5 MPa, air
catalyst	V^{5+}, copper metal	homogeneous cobalt catalyst	Pd, Rh, Ir	solid FeAlPO-31
initiator/solvent	none	excess pyridine	halide promoter such as hydroiodic acid and a saturated carboxylic acid (e.g., pentanoic acid) is used as solvent	none
yield	90 %	70 %	not known	65 %
main product(s)	adipic acid, glutaric and succinic acid	3-pentenoate and dimethyl adipate	3-pentenoic acid, adipic acid	adipic acid and cyclohexanone
by-products	nitrous oxide and other oxides of nitrogen, CO_2, plus lower members of dicarboxylic acids	none	2-methyl glutaric acid and 2-ethyl succinic acid	glutaric and succinic acid
downstream processing	product stream passed through a bleacher to remove nitrogen dioxides and then to an absorber to recover nitric acid	hydrolyis of diester to adipic acid and methanol	recycle the 3-pentenoic acid produced by the first hydrocarboxylation step	hydrolysis of diester to adipic acid
advantages	high yield of adipic acid	suppression of lower carboxylic acids	2-methyl glutaric acid and 2-ethyl succinic acid could be isomerized to adipic acid by the same catalyst system	molecular oxygen (air) used as oxidant; corrosive solvents/promoters not needed; does not produce any greenhouse gas (N_2O); heterogeneous catalyst; ease of catalyst recycle and recovery; low processing costs
disadvantages	2.0 mol of nitrous oxide produced for each mole of adipic acid (a serious problem as nitrous oxide is a greenhouse gas that is vented to the atmosphere); due to the corrosive nature of nitric acid, plants are constructed of titanium or stainless steel; the reac tion is very exothermic (6280 kJ kg^{-1}); catalyst recovery and recycle are very expensive.	catalyst recovery and recycle; recovery of excess pyridine, very high pressures	recovery and recycle of solvent; transport and disposal of promoter; costly extraction procedures	long reaction time (24 h)

[a] *Ullmann's Encyclopedia of Industrial Chemistry*, 5th ed., A1, **1993**, p. 271. [b] BASF, US 4310686. [c] DuPont, US 5145995. [d] Ref. [11].



Scheme 2.

synthetic polyamide fibres, such as nylon 66 and polyurethane resins. Other applications include plasticizers, reinforced plastics, lubricants, speciality foams, lacquers, adhesives, surface coatings, acidulant in gelatins and jams and as a buffering or neutralizing agent in foods. Textile and synthetic fibres such as polyester (Terylene) are made from terephthalic acid, which is currently produced commercially by using aggressive reagents such as bromine and acetic acid (Scheme 2). Our molecular sieve catalysts achieve these conversions under benign conditions (see Table 3).

Another important industrial oxidation reaction is that known as the Baeyer–Villiger process for the conversion of cyclic ketones into lactones. This is a reaction of great commercial value with applications spanning antibiotics, steroids and many aspects of agrochemistry.[14] The peracids (e.g., peroxomonosulphuric acid H_2SO_5, otherwise known as Caro's acid) used for the first half-century or so of Baeyer–Villiger oxidations (discovered in 1899) are now increasingly frowned upon (when not already banned) because of environmental and other reasons, notably safety. The withdrawal

Table 3. Production of terephthalic acid.

	Industrial and commercial technologies			Our solvent-free clean technology route
	Oxidation of *p*-xylene using bromine and acetic acid: Amoco oxidation[a]	Oxidation of *p*-xylene with an activator and/or bromine in acetic acid: Eastman Chemical[b]; Mobil Chemical[c]	Toluene route without solvent (acetic acid): Mitsubishi Gas Chemical[d]	Liquid-phase oxidation of *p*-xylene in air
conditions	175–225 °C, 1500–3000 kPa	120–140 °C	complex between toluene and $HF-BF_3$ is first formed, which is subsequently carbonylated with carbon monoxide to *p*-tolualdehyde	130–150 °C, 2.5 Mpa
catalyst	soluble cobalt/manganese/ bromine system	soluble cobalt, manganese	manganese/bromine system	solid CoAlPO-36
initiator/solvent	acetic acid	acetaldehyde, 2-butanone, bromine, acetic acid	none	none
main product(s)	toluic acid, 4-formylbenzoic acid, terephthalic acid	4-formylbenzoic acid, terephthalic acid	*p*-tolualdehyde, terephthalic acid	toluic acid, 4-formylbenzoic acid, terephthalic acid
by-products	vapours of acetic acid, nitrogen and carbon oxides	vapours of acetic acid	none	none
downstream processing	condensing the vapour and refluxing the condensate; recovery of terephthalic crystals by solid-liquid separation; solvent recovery	crude terephthalic acid was leached using excess acetic acid followed by sublimation and centrifugation	the complex has to be decomposed before *p*-tolualdehyde can be oxidised in water with a manganese/bromine catalyst	esterfication of terephthalic acid
advantages	excellent yield	titanium-lined vessels are not needed where bromine is not required	toluene as a potential feedstock is cheaper than *p*-xylene; acetic acid is not required	no need for corrosive solvents; activators and bromine; heterogeneous catalyst—hence ease of separation and recycle
disadvantages	highly corrosive bromine/ acetic acid environment requires the use of titanium-lined equipment; highly exothermic reaction ($2 \times 108\ J\,Kg^{-1}$) rerequiring solvent evaporation; disposal of bromine salts; solvent/catalyst recovery and recycle; high solvent loss; purification step to remove 4-formylbenzoic acid impurities	costly activators; catalyst recovery and recycle; purification step, solvent recovery (distillation); recycle and disposal	complexities of handling hydrogen fluoride/boron trifluoride and the need for carbon monoxide make the process very expensive; catalyst recovery and recycle	low yield; high residence times, purification step to remove 4-formylbenzoic acid

[a] W. Partenheimer in *Catalysis of Organic Reactions*, (Ed.: D. W. Blackburn) Marcel Dekker, NY **1990**, p. 321. [b] G. I. Johnson, J. E. Kiefer (Eastman Kodak Company) US 4447646, **1983**. [c] *Chem. Eng. Prog.* **1971**, *67*, 69. [d] *Chem. Eng. (New York)* **1976**, *83*, 27.

from the market of the potentially explosive 90 percent H_2O_2 (the replacement for Caro's acid) has prompted the use of lower grade peracids, and also the use of H_2O_2 in the presence of inorganic materials, such as methyltrioxorhenium. Our approach[15] relies entirely on Mn^{III}-framework-substituted (or Co^{III}) microporous aluminophosphates, in which air (or O_2) and a sacrificial aldehyde are used. A per-carboxylic acid (e.g., perbenzoic acid) is formed in situ, and functions as an environmentally successful oxygen donor to convert the cyclic ketone into the corresponding lactone (see Figure 2). A similar approach, again using a sacrificial aldehyde, serves to epoxidize a range of alkenes[16] in O_2 (air), with the same kind of molecular sieve catalyst.

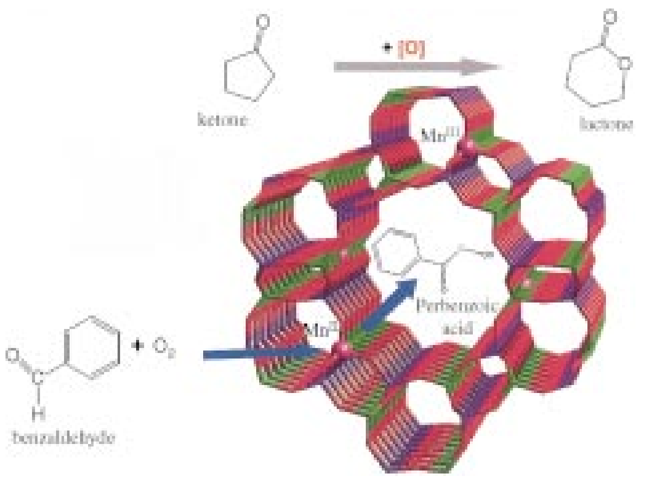


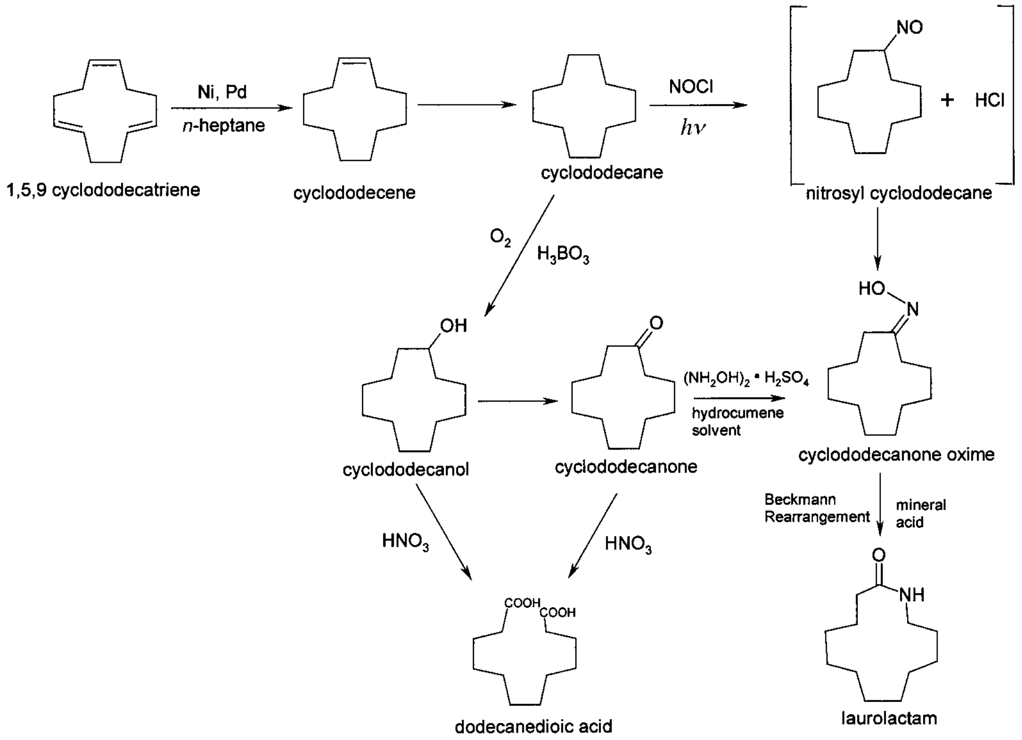
Figure 2. Graphical representation of the MnAlPO-36 catalyst, showing the Baeyer–Villiger oxidation of a cyclic ketone to the corresponding lactone, via the in situ formation of perbenzoic acid from benzaldehyde, effected by Mn^{III} ions and molecular O_2.

Tables 1–3 highlight the advantages of the solvent-free clean technology approach that we have pursued using our designed molecular sieve catalysts. In every instance, this approach, when appropriately scaled up, has the potential to replace the currently employed, environmentally repugnant processes.

Industrial hydrogenations

So far as hydrogenations are concerned, it is relevant to note that the chemical industry is turning increasingly for its feedstocks to biological molecules extracted from the plant kingdom, rather than to the constituents of oil in the production of high added value materials. Because such molecules are too large to enter the inner surfaces of microporous catalysts, it is appropriate for mesoporous catalysts (diameter in the range 30–100 Å) to be used so as to facilitate access of reactants to, and diffusion of products away from, the catalytically active sites that are (ideally) distributed in a spatially uniform manner over the high-area solid. In a number of studies[17–19] we have demonstrated how large concentrations of nanoparticle bimetallic catalysts dispersed inside mesoporous silica possess the high intrinsic activity required for the solvent-free hydrogenations. The selective hydrogenation of a polyene such as 1,5,9-cyclododecatriene is quite an important procedure in the synthesis of organic and polymeric intermediates, such as 12-laurolactam, 12-aminododecanoic acid and dodecanedioic acid, which are important monomers for nylon 12, nylon 612, copolyamides, polyesters and coating applications (Scheme 3).

Figure 3 illustrates the distribution of individual Ru_6Sn bimetallic catalyst nanoparticles inside mesoporous silica



Scheme 3.

Table 4. Selective hydrogenation of polyenes.

	Existing processes/technologies Hydrogenation of polyenes[a]	Our solvent-free clean technology route Solvent-free, low-temperature selective hydrogenation of polyenes by using bimetallic nanoparticle heterogeneous catalysts[b]
conditions	140–190 °C, 0.2–0.3 MPa	50–80 °C, 1.5–2.0 MPa
catalyst	homogeneous Ni, Pd, Pt, Co and mixed transition metal complexes	heterogeneous bimetallic nanoparticles (Ru_6Sn, Pd_6Ru_6) anchored on mesoporous silica (MCM-41)
typical reactants	1,5,9 cyclododecatriene, 1,5 cyclooctadiene, 2,5 norbornadiene	1,5,9 cyclododecatriene, 1,5 cyclooctadiene, 2,5 norbornadiene
initiator	9,10-dihydroanthracene (hydrogen donors)	none
solvent	*n*-heptane, benzonitrile, etc	none
conversion	95–98 %	90–95 %
main product(s)	cyclododecene, cyclododecane, cyclooctene, cyclooctane, norbornene, norbornane	cyclododecene, cyclododecane, cyclooctene, norbornene
by-products	isomerized products arising from starting material, complete hydrogenation	none
advantages	high yields	high yields and selectivity; catalyst stability; no need for costly initiators and solvents
disadvantages	costly initiators; solvent recovery; recycle and disposal; declining catalyst activity; as a consequence of double-bond migration; isomerization of the naturally occurring all-*cis* olefins into *trans* olefins	none

[a] DE 1230790, GB 826832. [b] Ref. [19].

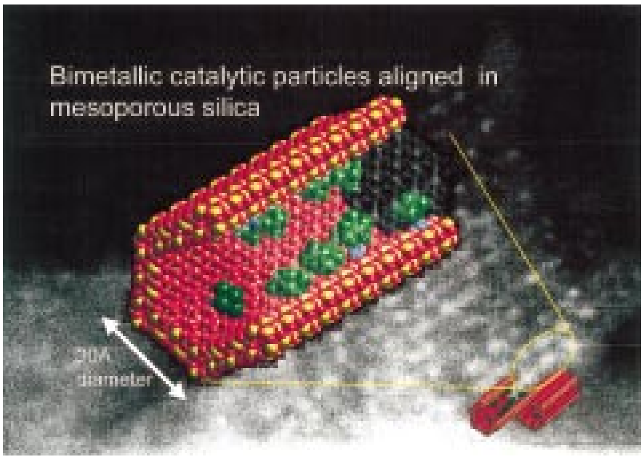


Figure 3. Clusters of Ru_6Sn, anchored at the inner surfaces of mesoporous silica function as powerful catalysts in the solvent-free selective hydrogenation of a variety of polyenes.[19] In the background electron micrograph, the linearly arranged white spots demarcate the anchored bimetallic clusters (diameter ca. 10 Å).

(pore aperture 30 Å). This catalyst exhibits high performance in the solvent-free, selective hydrogenation of 1,5,9-cyclododecatriene (Table 4). With an ever-expanding range of mesoporous materials, with diameters up to 500 Å, now becoming available[20, 21] there is abundant scope further to pursue the solvent-free catalytic approach outlined here in future technology.

---

[1] D. Adam, *Nature* **2000**, *407*, 938–940.

[2] S. J. Lippard, *Chem. Eng. News* **2000**, *78*, 64–65.

[3] a) M. D. Cohen, G. M. J. Schmidt, F. I. Sonntag, *J. Chem. Soc.* **1964**, 2000–2013; b) J. M. Thomas, *Philos. Trans. R. Soc. London A* **1974**, *277*, 251–289.

[4] B. S. Green, M. Lahav, D. Rabinovich, *Acc. Chem. Res.* **1979**, *12*, 91–98.

[5] J. M. Thomas, *Nature* **1981**, *289*, 633–634.

[6] H. Nakanishi, W. Jones, J. M. Thomas, M. Hasegawa, W. L. Rees, *Proc. R. Soc. London A* **1980**, *369*, 307–325.

[7] K. Tanaka, F. Toda, E. Mochizuki, N. Yasui, Y. Kai, I. Miyahara, K. Hirotsu, *Angew. Chem.* **1999**, *111*, 3733–3736; *Angew. Chem. Int. Ed.* **1999**, *38*, 3523–3525.

[8] G. Kaupp, M. Haak, *Angew. Chem.* **1996**, *108*, 2948–2951; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2774–2777.

[9] A. Joy, V. Ramamurthy, *Chem. Eur. J.* **2000**, *6*, 1287–1293.

[10] J. M. Thomas, R. Raja, G. Sankar, R. G. Bell, *Nature* **1999**, *398*, 227–230.

[11] M. Dugal, G. Sankar, R. Raja, J. M. Thomas, *Angew. Chem.* **2000**, *112*, 2399–2402; *Angew. Chem. Int. Ed.* **2000**, *39*, 2310–2313.

[12] J. M. Thomas, R. Raja, G. Sankar, R. G. Bell, *Acc. Chem. Res.* **2000**, *34*, 191–200.

[13] J. M. Thomas, *Angew. Chem.* **1999**, *111*, 3800–3843; *Angew. Chem. Int. Ed.* **1999**, *38*, 3588–3628.

[14] G. Strukul, *Angew. Chem.* **1998**, *110*, 1256–1267;*Angew. Chem. Int. Ed.* **1998**, *37*, 1198–1209.

[15] R. Raja, J. M. Thomas, G. Sankar, *Chem. Commun.* **1999**, 525–526.

[16] R. Raja, G. Sankar, J. M. Thomas, *Chem. Commun.* **1999**, 829–830.

[17] D. S. Shephard, T. Maschmeyer, G. Sankar, J. M. Thomas, D. Ozkaya, B. F. G. Johnson, R. Raja, R. D. Oldroyd, R. G. Bell, *Chem. Eur. J.* **1998**, *4*, 1214–1224.

[18] R. Raja, G. Sankar, S. Hermans, D. S. Shephard, S. T. Bromley, J. M. Thomas, B. F. G. Johnson, *Chem. Commun.* **1999**, 1571–1572.

[19] S. Hermans, R. Raja, J. M. Thomas, B. F. G. Johnson, G. Sankar, D. Gleeson, *Angew. Chem.* **2001**, *113*, 1251–1255; *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 1211–1215.

[20] Y. H. Sakamoto, M. Kaneda, O. Terasaki, D. Y. Zhao, J. M. Kim, G. Stucky, H. J. Shim, R. Ryoo, *Nature* **2000**, *408*, 449–453.

[21] M. J. MacLachlan, T. Asefa, G. A. Ozin, *Chem. Eur. J.* **2000**, *6*, 2507–2511.

[22] H. Nakanishi, W. Jones, J. M. Thomas, M. B. Hursthouse, M. Motevalli, *J. Phys. Chem.* **1981**, *85*, 3636–3642.