

Catalysis of liquid phase organic reactions using chemically modified mesoporous inorganic solids

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The modification of silicas and related materials by attachment of organic functionalities to their surface is an important area of research in heterogeneous catalysis and green chemistry. The methods available for the preparation of these hybrid organic–inorganic materials are reviewed, as are their applications as catalysts in a range of reactions.

Catalysts played a major role in establishing the economic strength of the chemical industry in the first half of the 20th century. As we approach the first half of the 21st century increasingly demanding environmental legislation, public and corporate pressure and the resulting drive towards clean technology in the industry will provide new opportunities for catalysis and catalytic processes. Some of the major goals of 'Green Chemistry' are to increase process selectivity, to maximise the use of starting materials (aiming for 100% atom efficiency), to replace stoichiometric reagents with catalysts and to facilitate easy separation of the final reaction mixture including the efficient recovery of the catalyst.¹ The use of efficient solid catalysts can go a long way towards achieving these goals.² Polymer-supported catalysts have been widely used.³ Their popularity comes mainly from the fact that product isolation is simplified and that milder conditions and higher selectivity can be attained although they can suffer from limited thermo-oxidative stability. Catalysts based on high surface area inorganic support materials should have better thermal stability and have also attracted a lot of interest as solid catalysts and reagents in liquid phase organic reactions. They form the basis of some new industrial catalysts which are used as replacements for toxic and corrosive traditional reagents.⁴ The mesoporous nature of silicas and acid-treated clays for example, allows reasonably good molecular diffusion rates and can lead to activity enhancement through the concentration of active centres.⁵ These first generation supported reagent catalysts are, however, based on physisorbed reagents, are frequently unstable in polar media and, consequently, often cannot be reused. An emerging area of research which seeks to retain the 'green benefits' of heterogenisation and enhanced activity and/or product selectivity while avoiding the drawbacks of catalyst instability and limited reusability is the development and use as catalysts of mesoporous inorganic support materials with chemically bound active centres.

Preparative methodology

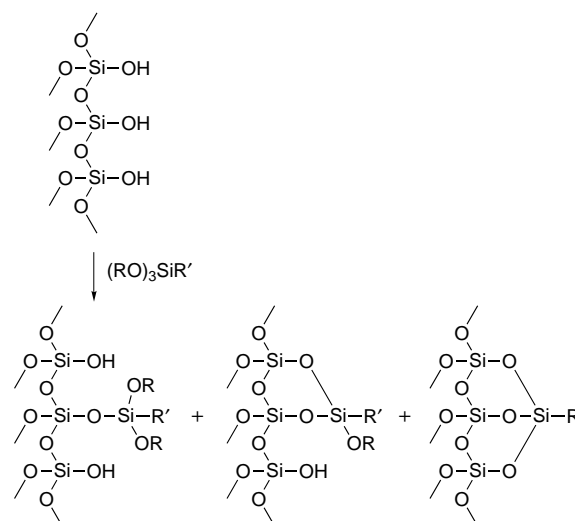
A range of possible methodologies exists for attaching organic functionality to the surface of a support. We will concern ourselves primarily with those methods which result in covalent attachment to a silica surface. Thus, purely electrostatic methods, such as those used to attach porphyrins to supports (*via e.g.* sulfonate-supported pyridinium ion pairs) will not be described. Nor will concepts such as the supported aqueous phase catalysts pioneered by Davis amongst others.

Several routes exist for the covalent attachment of organic functionality to the surface of a silica. These include grafting of functional organosilanes, surface chlorination and subsequent displacement, direct sol–gel preparation of organomodified

silicas (especially micelle templated versions) and post-functionalisation of existing organic groups at the surface.

Grafting

This remains the most popular method, mostly due to its simplicity, at least in terms of experimental procedures. The silica is reacted with an appropriate organosilane in a suitable solvent, typically toluene at reflux, although ethanol at room temperature is also effective in some cases. The resulting solid is collected and washed (Scheme 1).



Scheme 1 Simplified grafting reaction at a silica surface

This method is versatile and relatively rapid, with many silanes being commercially available. Loadings of organic groups on the surface vary from *ca.* 0.3 mmol g⁻¹ for cyanoethyl groups to *ca.* 1 mmol g⁻¹ for amine-containing silanes. Loadings for the more recent controlled porosity MCM-based materials† can be significantly higher (1–1.7 mmol g⁻¹). Pore size distributions vary little from the original silica used, although surface areas can drop by a significant amount.⁶ While this is a good method for initial studies, drawbacks can include the formation of several surface species resulting from binding *via* one, two or three Si–O–Si groups, attachment of oligomeric silanes, and the presence of physisorbed material, which must be thoroughly washed off before the catalyst can be used in reactions. Loading can often be low, resulting in the need for relatively large amounts of catalyst. Nonetheless, many catalysts have been successfully prepared by this method, and it remains the most commonly used route to new catalysts. The catalytically active group can be present in the silane which is attached to the surface, or can be introduced by subsequent post-modification reactions.

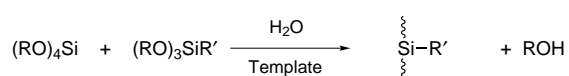
Surface chlorination and subsequent displacement

This is a much less frequently used method, although it has advantages of forming a direct Si–C bond at the surface and precludes the formation of surface bound oligomers and

variable modes of attachment. Groups are robustly bound, and are typically less prone to leaching than those attached *via* grafting. The technique is less easy to use, requiring the reaction of silica with the chlorinating agent, converting surface hydroxyls to Si-Cl bonds, and is typically achieved using thionyl chloride at reflux,⁷ or with CCl₄ in a fluidised bed reactor⁸ at 400–450 °C. The Si-Cl material thus produced is reacted with a solution of a Grignard reagent or an organolithium species, leading to displacement of the Cl and the formation of a Si-C surface bond. The main drawback in this method is that the requirement for strongly nucleophilic reagents limits the functionality which can be successfully attached. This approach has been used for silicas^{8,9} and clays.^{7,10} One article describes the exchange of Si-Cl for Si-Li,¹⁰ rather than the normal Si-R, although no reason for this inverted reactivity was given.

Templated sol-gel techniques

This methodology is essentially the co-polymerisation of a silica precursor (typically a tetraalkylorthosilicate) with an organosilicate precursor [typically a trialkoxy(organosilane) (Scheme 2).



Scheme 2 Templated sol-gel synthesis of organofunctionalised silicas

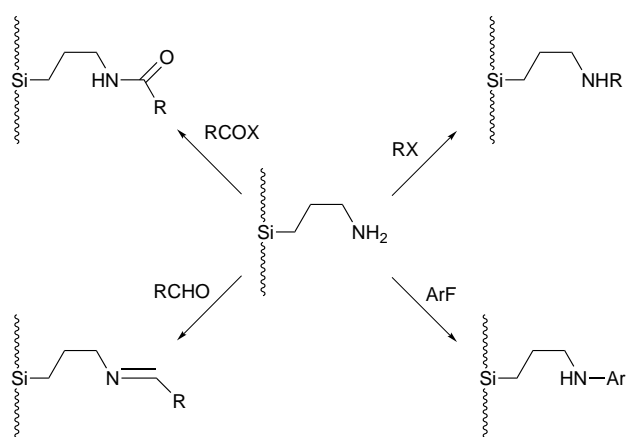
The most important impetus for this approach has come from the discovery of the MCMs, which has allowed the predictable formation of very regular mesoporous materials, which show a great deal of promise as highly selective catalysts. This technique, which was initially used for the preparation of purely inorganic materials, has been successfully extended to include organomodified materials.^{11–13}

Reaction conditions are very mild and the procedure is remarkably simple. The materials produced are very thermally stable; organic groups do not detach from the surface at temperatures lower than *ca.* 450 °C, and, as the groups are intimately bound into the surface, they are also solvolytically stable. Loadings can be very high, and are essentially independent of the silane used. We have recently prepared a material with a loading of 3.0 mmol g⁻¹, much higher than those obtainable by grafting. Loading is controlled by the ratio of silanes in the preparation. The surface areas reported are very high, ranging from 700 to *ca.* 1600 m² g⁻¹. Typical silica supported reagents have surface areas of *ca.* 75–300 m² g⁻¹.

Post modification

This is often a necessary step in the synthesis of chemically modified surfaces, since the range of silanes available is limited (they are also moisture sensitive and can be difficult to work with) and the use of Grignard or organolithium reagents means that the chlorination methodology can only be used with a few functional groups. One of the commonest grafted functions is the primary amine, usually *via* the cheap 3-aminopropyl-(trimethoxy)silane. This group behaves like a typical amine function, and can thus be derivatised by formation of amides or imines, and by alkylation. Nucleophilic aromatic substitution of suitable activated rings is also possible (Scheme 3).

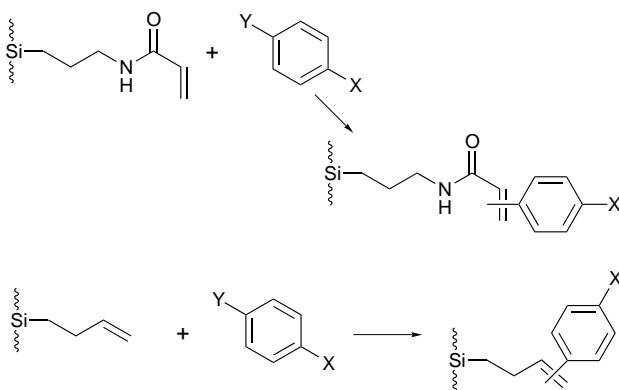
The formation of amides can be carried out with anhydrides, acids or acid chlorides. Esters will also form amides, although slowly.¹⁴ A particularly attractive option is to use acids without solvent in a vapour phase reaction at 150–170 °C. For example, 4-aminobenzoic acid can be reacted to form the silica-bound amide by mixing with the amine-functionalised silica in the absence of solvent and heating to 170 °C under vacuum.¹⁵ This allows the vapour to enter the pores of the catalyst and react. Water and excess acid are removed under the reaction conditions, leaving the surface bound amide. The supported aniline thus formed can be further functionalised *via* diazonium



Scheme 3 Reactions of aminopropyl-functionalised silica

chemistry, and forms the basis for an effective base catalyst.¹⁶ The attachment of a silane to a surface often allows the selective monofunctionalisation of a doubly functional molecule. This approach has been used in the synthesis of the supported metal salt depicted in Scheme 6, a very versatile and active oxidation catalyst (see following section).¹⁷

Newer methods for the functionalisation of surface bound alkenes (from chlorination/displacement routes) include the Heck reaction.¹⁸ This methodology allows the attachment of a variety of aryl groups to the surface under solvent free conditions at temperatures between 130 and 150 °C (Scheme 4).



Scheme 4 The functionalisation of surface alkenes *via* the Heck reaction: X = H, CHO, CO₂H, CN; Y = Br, I

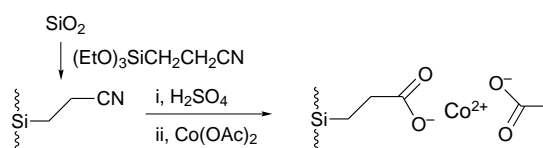
The use of the resulting materials in catalysis is currently under study.

Catalysis of oxidation reactions

Oxidation is the area where chemically modified surfaces have found most use. A wide variety of materials have been prepared, using several methods for attaching the organics to the surface, with many areas of oxidation chemistry benefiting from the materials thus derived.

We recently reported a simple immobilised form of Co(OAc)₂ which is capable of the epoxidation of alkenes.¹⁹ This material was prepared according to Scheme 5.

This is a remarkable result, since the organo-functionalised silica is shown to survive the harsh conditions required to



Scheme 5 Preparation of supported Co(OAc)₂

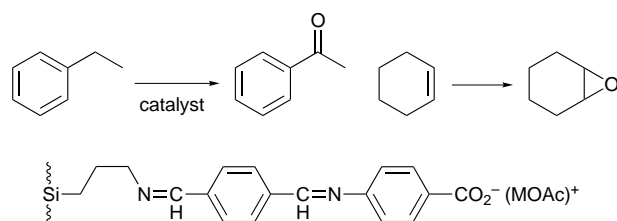
hydrolyse the nitrile group (50% H₂SO₄ at reflux, 24 h). The materials was found to efficiently catalyse the epoxidation of alkenes using sacrificial aldehydes and oxygen (Table 1).

Table 1 Epoxidation of alkenes using supported cobalt acetate

Alkene	t/h	Yield of epoxide ^a
Cyclohexene	5	85
Oct-1-ene	5	45
Octa-1,7-diene	24	48 ^b
2,4,4-Trimethylpentene	5	95
Hex-1-ene	24	30
Styrene	3	32 ^c

All reactions were carried out at 19 °C in dichloromethane with isobutyraldehyde as sacrificial aldehyde. ^a GC yield with internal standard. ^b Monoepoxide; 7% of diepoxide was also formed. ^c 5% PhCHO and 21% polymer also formed.

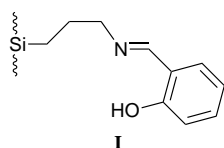
A related catalyst type has been recently reported,¹⁷ where the metal centre is supported by a longer spacer chain (Scheme 6). This material was prepared from aminopropyl-silica by reaction with terephthalaldehyde to form the monoimine (attachment of the amine to the surface precludes reaction at both ends of the dialdehyde), followed by formation of a second imine with *p*-aminobenzoic acid. The supported acid was then treated with metal acetates to generate the active catalyst.



Scheme 6 Reactions catalysed by supported metal acetates

The catalyst is active in the same epoxidation reaction as the supported Co acetate above. Interestingly, the Ni version is most active, followed closely by Cr and Cu, with Mn and Co being distinctly poorer. Of particular interest is the ability of this catalyst to carry out the oxidation of alkyl aromatics. In this case the Cr version is the best, and allows a conversion rate of 370 turnovers h⁻¹ to be achieved.

Kurusu and Neckers have also prepared simple complexed metal species on silica, based on the salicylimine species **I**:



The metals complexes show some activity in the oxidation of cyclohexane^{20,21} and in alkylaromatics.²¹

Jacobs and coworkers have prepared an active epoxidation catalyst based on supported metal complexes with the triaza-cyclononane ligand system.²² Both silicas and MCMs were used as supports. The catalysts were prepared by the reaction of the cyclic ligand with a supported glycidyl material, in the case of the MCM, and with both glycidyl and chloropropyl in the case of the silica. The ligand system was then modified by reacting the two free amines with propylene oxide, and subsequent metal complexation. The epoxidation of styrene was used as a test reaction. Selectivities and turnover numbers (mol h⁻¹) were higher in the case of the MCM-derived materials than the silicas, regardless of the nature of the supported ligand.

Metalloporphyrins have also been the subject of much work, and several routes have been developed to attach them to

heterogeneous supports. Porphyrins are expensive, and thus recovery becomes economically important. It is also possible that attachment to a surface may hinder destructive oxidation of the electron rich ring system, a factor which traditionally limits their useful lifetime. The use of charged groups, typically ammonium or sulfonate attached to the periphery has been used to enhance adsorption to polar supports such as silica and magnesium oxide.^{23,24} Direct covalent binding to silica surfaces has been achieved by coordinative binding of the metal centre to supported imidazoles, pyridines, *etc.*^{25,26} The second mode of attachment is *via* aryl groups attached to the periphery of the ring system. Thus, Mansuy and coworkers have used aminopropyl silica to tether a perfluorophenyl-substituted porphyrin.²⁷ These approaches are summarised in Fig. 1.

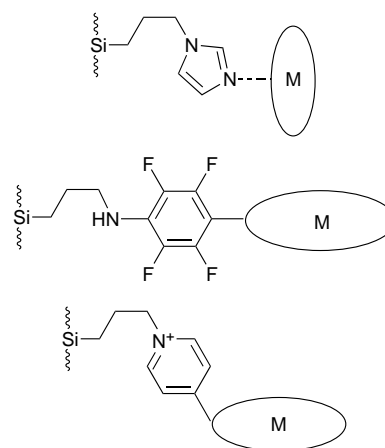


Fig. 1 Examples of covalently bound porphyrins

A second approach is the nucleophilic displacement of chloride from chloropropylsilica with a pyridine-substituted porphyrin.²⁸ These materials are active in the epoxidation of alkenes, where iodosylbenzene is the preferred oxidant, and in the oxidation of alkanes to alcohols and ketones.

A further example of this approach is the copolymerisation of a porphyrin containing four attached trimethoxysilane groups with tetraethoxysilane, leading to an active hybrid silica-porphyrin.²⁹

Finally, one problem relating to the oxidation of hydrocarbons with hydrogen peroxide is the difficulty of having appreciable concentrations of the non-polar substrate and the polar oxidant together at the catalytic centre. One elegant solution has recently been published by Neumann and Wange.³⁰ They have shown that attachment of a mixture of poly(ethylene oxide) and poly(propylene oxide) to a silica, followed by the physisorption of methylrhenium trioxide allows the efficient mixing of both reaction partners (Fig. 2). The catalyst allows the efficient epoxidation of alkenes with hydrogen peroxide.

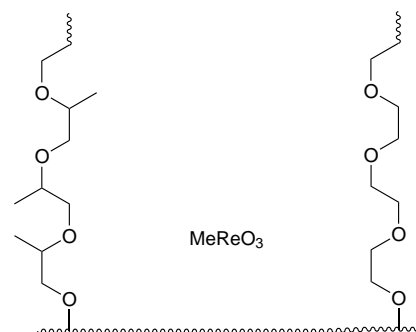


Fig. 2 Polyether modified supported methylrhenium oxide

A mix of the two polymeric chains was shown to be better than a single type of chain. This is attributed to a combination

of the relatively hydrophilic poly(ethylene oxide) and the more hydrophobic poly(propylene oxide) giving the right balance of properties, and allowing optimum mixing of the two reagents.

Solid acid catalysts

Solid acids are the most widely studied and commonly used heterogeneous catalysts. Their use however, is heavily biased towards large-scale continuous vapour phase processes such as catalytic cracking and alkane isomerisations. There is also a great need for solid acid catalysts which are effective in liquid phase organic reactions such as those employed in many batch-type reactors by fine, speciality and pharmaceutical intermediate chemical manufacturers. These include Friedel–Crafts alkylations, acylations and sulfonylations, isomerisations, dehydrations, oligomerisations and aromatic halogenations and nitrations. At present these reactions are commonly catalysed by mineral acids such as H_2SO_4 and HF and by Lewis acids such as AlCl_3 and BF_3 . These traditional reagents suffer from many drawbacks including hazards in handling, corrosiveness, and difficulty in separation along with the inevitable production of often large volumes of toxic and/or corrosive waste. Solid acids based on organic polymers such as ion-exchange resins and Nafion are available but suffer from poor stability or high cost whereas supported reagents such as ‘clayzic’ (acid-treated clay supported zinc chloride)³¹ have a limited range of applications and their weak support–reagent interaction may result in leaching of metal ions into polar media. The development of active and truly catalytic, heterogeneous alternatives to traditional soluble or liquid acids is a very important goal in green chemistry and while solid acids based on organically modified supports are relatively uncommon, significant progress using supports which have been chemically modified by reaction with Lewis acids has recently been made in our laboratory and elsewhere.

Aluminium chloride is one of the most widely used inorganic reagents in organic chemistry, being highly soluble and very active. However, its many drawbacks, such as its corrosive nature, difficulties in separation and recovery, and the large volumes of environmentally hazardous waste associated with its use, make it a prime target for heterogenisation.^{4,32} We have reported an active heterogeneous form of aluminium chloride which is highly effective at least in Friedel–Crafts alkylation reactions.³³ The material **II**, which is believed to contain a mixture of OAlCl_2 and O_2AlCl sites, is prepared by reaction of a surface-hydroxylated high surface area mesoporous inorganic solid such as silica gel or acid-treated montmorillonite with aluminium chloride in a low-polarity aprotic organic solvent (Scheme 7).



Scheme 7 Preparation of supported aluminium chloride

The optimum loading is support dependent with the higher surface area mesoporous silica gel having an optimum loading (1.5 mmol g^{-1}) twice as high as that of K10 montmorillonite. The former catalyst is also a little more active and selective towards monoalkylation although K10 is a less expensive support material.

Previous attempts at preparing immobilised aluminium chloride have met with limited success. Catalysts prepared in the vapour phase or from a CCl_4 solution have proved to be active in the gas phase (*e.g.* in cracking reactions) but their activity in liquid phase reactions has generally been poor.³⁴ Catalysts of this type should be differentiated from those which undergo a final high temperature calcination stage after treatment with a soluble aluminium salt. Thus various mesopor-

ous materials such as MCM-41, MCM-48, SBA-1 and KIT-1 have been treated with reagents including ethanolic solutions of AlCl_3 and $\text{Al}(\text{NO}_3)_3$ and slurries of $\text{Al}(\text{OPr}^i)_3$ in non-polar solvent (*e.g.* hexane) followed by calcination of the resulting solid at temperatures of $>800 \text{ K}$ to give solid acids.^{35,36} This typically results in the formation of tetrahedral (framework) and octahedral (non-framework) Al. Such materials are more commonly associated with vapour phase reactions such as cracking.³⁶

The catalyst represented by **II** shows excellent activity in the room temperature alkylation of benzene with alkenes.³³ Its activity is comparable to that of aluminium chloride but it shows improved selectivity towards monoalkylation compared to AlCl_3 itself and is readily recoverable and reusable (unlike AlCl_3 which need to be removed from the reaction after one use, typically by a water quench). The reaction can be extended to alkylbenzenes but halobenzenes are considerably less reactive presumably because of complexation of the polarisable halogen centre to active catalyst centres (Table 2).

Table 2 Activity of (optimised) supported aluminium chloride solid acids in the alkylation of aromatic substrates [2:1 mol ratio of ArH to alkene; 10 g catalyst (mol ArH^{-1})]

Substrates	Catalyst	Reaction conditions t/h ($T/^\circ\text{C}$)	Monoalkyl-aromatic yield (GC%)
PhH + oct-1-ene	AlCl_3	2(20)	61.6
PhH + oct-1-ene	$\text{SiO}_2(70 \text{ \AA})\text{-AlCl}_3$	1.25(20)	78.3
PhH + oct-1-ene	K10- AlCl_3	2(20)	76.3
PhH + hex-1-ene	K10- AlCl_3	2(20)	69.2
PhH + dodec-1-ene	K10- AlCl_3	2(20)	77.3
PhH + hexadec-1-ene	K10- AlCl_3	2(20)	71.0
PhMe + oct-1-ene	K10- AlCl_3	1.5(20)	80.9
PhEt + oct-1-ene	K10- AlCl_3	3.5(20)	74.3
PhF + oct-1-ene	K10- AlCl_3	4(20)	29.6
PhCl + oct-1-ene	K10- AlCl_3	4.5(20)	14.2

It is interesting that reaction of mesoporous silica gel with MeAlCl_2 under similar conditions gives a catalyst with comparable activity to that prepared using AlCl_3 . In contrast, reaction of MeAlCl_2 with K10 gives an appreciably less active catalyst, an observation that is consistent with the theory that the HCl released during the reaction of AlCl_3 with the clay helps to convert the more microporous clay structure into a more mesoporous silica structure³⁷ (MeAlCl_2 reacts with the surface hydroxyls by elimination of CH_4). Remarkably, MeAlCl_2 itself is less active again³³ suggesting that the methyl group is more deactivating than the support surface although the presence of isolated Lewis acid sites on the surface, rather than dimers in solution, may be a more important factor.

We have shown that it is possible to extend the methodology for supported aluminium chloride for liquid phase applications to the relatively new hexagonal mesoporous silicas as supports (HMSs).^{38,39†} Activity in the alkene alkylation of alkylaromatics is again comparable to that of AlCl_3 itself, and the solid acids are also easily recovered and can be reused. Most significantly, the increase in selectivity towards monoalkylation through the use of the heterogenised Lewis acid is further enhanced (Fig. 3). By using external site poisons such as Ph_3N (to block external acid sites through complexation) or Ph_3SiCl (to destroy external hydroxyl groups), there is a still greater increase in selectivity with close to 100% monoalkylation being achievable with hexadec-1-ene. This may be the first significant illustration of zeolitic like effects (in-pore selectivity) in catalysts based on these structured mesoporous materials operating in the liquid phase. The extension of this phenomenon from the small molecules transformed by zeolites to large molecules is clearly very important. It promises significant improvements in product selectivity, while maintaining the

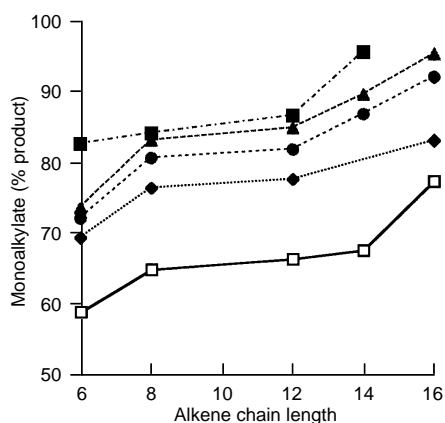
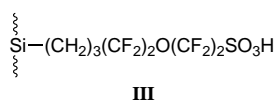


Fig. 3 Selectivity vs. chain length for a series of alkenes with HMS catalysts. (□) AlCl₃, (◆) AlCl₃/K10, (●) AlCl₃/HMS24, (▲) AlCl₃/HMS24-TPS, (■) AlCl₃/HMS24-Ph₃N; TPS = triphenylsilyl. HMS24 refers to a parent HMS with av. pore diameter 24 Å.

relatively fast reaction rates that mesoporous catalysts can give in liquid phase organic reactions.

It seems likely that heterogeneous versions of other very active Lewis acids can be prepared by similar methods although there are few other references to this in the existing literature. Iron(III) chloride should be reactive enough to form surface OFeCl₂ bonds for example and a stable form of supported FeCl₃ has been recently reported.⁴⁰ The material has been used to catalyse liquid phase Friedel–Crafts benzoylations⁴⁰ reminiscent of a commercial catalyst⁴¹ although the surface structure and activity on reuse of the catalyst have not been described.

Brønsted acids can also be fixed to the hydroxylated surfaces of support materials. Most spectacularly surface attached perfluorosulfonic acids have been reported⁴² which supercede the perfluorinated sulfonic acid resin (Nafion)-silica composites reported a year earlier.⁴³ The route to these requires the preparation of the new reagent (OH)₃Si(CH₂)₃(CF₂)₂O-(CF₂)₂SO₃⁻M⁺ which is then bonded to an existing support or incorporated in an *in situ* sol-gel technique to give the novel silica based solid acid **III**.



The materials are catalytically active for a number of typically acid-catalysed liquid phase organic reactions such as alkene alkylations of aromatics (although they are considerably less active than the supported aluminium chloride described above) and the benzoylation of activated aromatics such as *m*-xylene. They are orders of magnitude more active than conventional acidic ion exchange resins.

On a somewhat more mundane level, there are various reports of solid Brønsted acids derived from reaction of support materials with conventional liquid acids although the nature of the support-acid interaction and catalyst stability are generally not well understood. Thus simple treatment of silica gel with sulfuric acid followed by mild drying gives a solid acid that is active in various aromatic nitrations (nitric acid or isopropyl nitrate as nitrating agent).⁴⁴ Activity of the solid acid is comparable to the more expensive Nafion-H.

Heterogeneous versions of heteropoly acids have also been prepared. Apart from direct deposition into support materials, they can be more firmly bonded to the surface through chemical surface modification. Acids such as 12-tungstophosphate (PW₁₂) will react with silica gels which have been treated with aminoalkylsilanes.⁴⁵ The acidic site of PW₁₂ reacts with the surface-bound amino group. The activities of such catalysts are generally higher than those of supported reagents prepared by direct deposition⁴⁵ and it is likely that further improvements are

achievable by using the structured hexagonal mesoporous materials.⁴⁶

Base catalysis

The use of supported basic groups as heterogeneous catalysts has been researched by a few groups over the last decade. The majority of work has been carried out on the simple 3-amino-propyl-derivatised silica. A variety of papers has been published describing the use of this material as an efficient catalyst for the Knoevenagel reaction.^{47–49} Most of the papers deal with the relatively facile reaction of benzaldehyde with nucleophiles such as ethyl cyanoacetate and malononitrile. We have carried out an indepth study of this reaction system with a variety of aldehydes and ketones, and have shown that this simple material is indeed a versatile and active catalyst.¹⁴ Several important features have emerged. One of the most important parameters is the solvent, a recurrent theme in heterogeneous liquid phase catalysis. In this case the solvent must play two roles. Firstly it must remove water from the system. The reaction is reversible, and the rates of all but the simplest reactions are significantly reduced by the presence of water. Secondly, the partitioning of reactants between the solvent phase and the catalyst surface is important. Since the catalyst surface is probably the most polar phase in the system, the use of non-polar solvents will allow the reagent to preferentially adsorb onto the catalyst surface (polar solvents will compete for the surface). Both these criteria are met by hydrocarbon solvents such as alkanes. Indeed it was found that the rates of reaction varied with solvent according to the following order: cyclohexane > toluene > 1,2-dichloroethane > chlorobenzene when the reaction was performed at the boiling point of each solvent. Even the higher temperature used with toluene and chlorobenzene did not bring about a rate close to that of cyclohexane (Fig. 4).

Interestingly, the much more polar⁵⁰ catalysts based on aminopropyl groups incorporated into hexagonal mesoporous silicates (HMS)^{51,†} show essentially the same trend, although

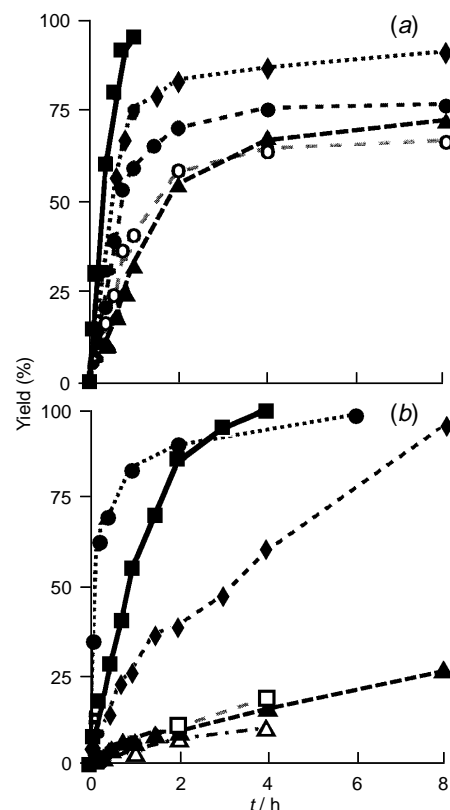


Fig. 4 Solvent effects in the Knoevenagel reaction using aminopropyl silica (a) and aminopropyl HMS catalysts (b); (■) cyclohexane, (●) toluene, (◆) hexane, (▲) 1,2-dichloroethane, (□) chloroform, (○) chlorobenzene, (△) ethyl acetate

the more polar surfaces of the HMS materials mean that toluene is the optimum solvent, with partition onto the catalyst surface still being favourable even with the more polar solvent. Increasing the solvent polarity further again reduces the rate dramatically.

Reaction studies on both sets of catalysts showed that both materials were active for a variety of reactions (Table 3).

Table 3 Knoevenagel reactions catalysed by aminopropyl substituted catalysts

R, R'	Catalyst	T/°C	t/h	Yield ^a (%)	TON ^b
Ph, H	1	82	0.1	99	—
Ph, H	2	82	36	94	—
<i>n</i> -C ₅ H ₁₁ , H	1	82	0.2	97	—
<i>n</i> -C ₅ H ₁₁ , H	2	82	0.1	99	> 6000
<i>n</i> -C ₇ H ₁₅ , H	1	82	0.2	98 ^a	—
<i>n</i> -C ₇ H ₁₅ , H	2	82	0.15	98	> 6000
<i>c</i> -C ₅ H ₁₀	1	82	1	98	650
<i>c</i> -C ₅ H ₁₀	2	110	2	92	2450
Et, Et	1	82	2	97	265
Et, Et	2	82	4	97	1127
<i>n</i> -C ₄ H ₁₀ , Me	1	82	4	98	350
<i>n</i> -C ₄ H ₁₀ , Me	2	110	4	95	1244
<i>t</i> -C ₄ H ₁₀ , Me	1	82	24	22	—
Me, Ph	1	82	24	68	250
Me, Ph	2	110	36	48	47
Ph, Ph	1	82	72	8	—

^a GC yields with *n*-dodecane as internal standard. Isolated yields are 5–10% lower. ^b Number of mol product per mol of NH₂ groups. Catalyst 1 is aminopropyl-silica; catalyst 2 is aminopropyl-HMS.

Aldehydes and ketones (aliphatic and aromatic) both react readily, as had been shown by previous authors and turnover numbers are generally good (200–600). The poisoning mechanism was also shown to be due to amide formation by reaction of the amine with the ester group of ethyl cyanoacetate. The HMS catalysts are generally slightly less active when compared directly, but their ability to function well in toluene, and the much higher loadings achievable (2.5 *cf.* 1.0 mmol g⁻¹) means that under optimum conditions they can match the silica catalysts in terms of rate. Their turnover numbers are typically higher by a factor of 4–5, and the poisoning mechanism is different. These materials thus display a great deal of promise as novel catalysts. Rates, selectivity and conversion were found to be much higher than for typical homogeneous conditions (piperidine as base).

Brunel and coworkers⁵² have studied aminopropyl-grafted MCMs as catalysts for this reaction. They used Me₂SO as solvent, and achieved complete conversion of reactants (benzaldehyde and ethyl cyanoacetate) after 100 min. They also found that a supported piperidine catalyst (prepared by reaction of piperidine with chloropropyl-MCM) was significantly less active as a catalyst. Unfortunately, the different conditions used preclude meaningful comparison with the materials mentioned above at this time.

We have recently described the preparation and use of two novel base catalysts (Fig. 5) which have phenolates as the basic centre.¹⁶ One was prepared using the amidation/diazonium chemistry described above, the other using alkylation of surface bound amine groups with a polyether tosylate. The catalysts are active in the Michael addition, and extension of the methodology to enantioselective catalysis is currently underway.

Solid catalysts for other applications

The concept of triphase catalysis, whereby a phase transfer catalyst (PTC) is immobilised onto a support material and the

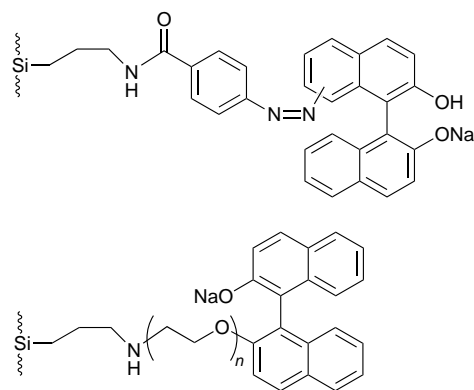
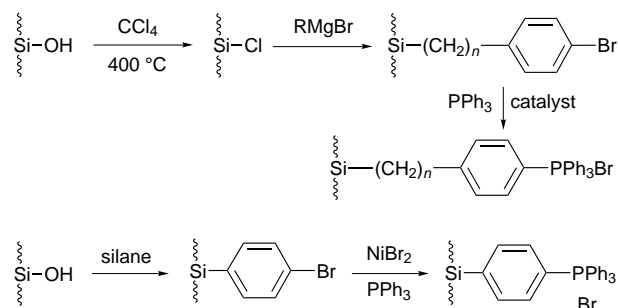


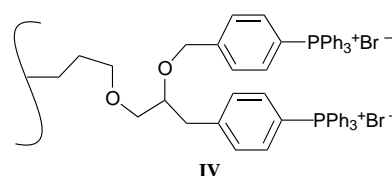
Fig. 5 Supported phenolates derived from diazotisation of surface bound aniline and from alkylation of surface bound amine

resulting supported PTC is then used in a biphasic aqueous–organic solvent reaction mixture is well established. We have recently reported a series of supported tetraarylphosphonium PTCs which show particularly high thermal stabilities and useful activities in nucleophilic substitution reactions and aromatic oxidative brominations.^{9,53,54} The catalysts are often reusable and are effective in non-polar solvents such as hydrocarbons even when the unsupported phosphonium salt is inactive (owing to poor solubility, the supported catalysts are believed to operate at the aqueous–organic interface). The catalysts can be prepared by a variety of methods as shown in Scheme 8.



Scheme 8 Preparation of heterogeneous phase transfer catalysts

The most remarkable of these catalysts is the mesoporous silica based material which contains two adjacent phosphonium centres referred to as a ‘bicipital supported phosphonium phase transfer catalyst’ IV.⁹



This catalyst is considerably more active than other supported phosphonium salts in the model nucleophilic substitution reaction of 1-bromooctane with potassium iodide. It is also very dependent on the pore size of the silica with an average pore diameter of *ca.* 100 Å giving the highest activity; this is consistent with more simple physisorbed silica-based supported reagents and seems to support the view that for liquid phase reactions catalysed by porous solids, a reasonably large pore is required to give a good molecular diffusion rate.^{2,5} Most significantly, the analogous material with only one of the aromatic rings substituted with a phosphonium group is significantly less active per phosphonium centre than the bicipital material. It is likely that the neighbouring centres can

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