

MESOPORE IMMOBILISED BIS(OXAZOLINE) CATALYSTS FOR
ENANTIOSELECTIVE CATALYSIS

by

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Cui dono lepidium novum libellum

Arido modo pumice expositum?

Here's my small book out, nice and new,

Fresh-bound – whom shall I give it to?

Catallus

87-54? B.C.

Abstract

Mesoporous silica materials have the potential to replace many conventional silicas for uses such as supports for heterogeneous catalysis and absorbents. The large pore size and high surface area make them ideal for supporting bulky organometallic catalysts for enantioselective reactions. We have immobilised chiral bis(oxazoline) metal complexes onto the surfaces of some of these versatile supports (MCM-41 and MCM-48) *via* different tethering strategies. The resulting heterogeneous catalysts were shown to be highly active in the enantioselective cyclopropanation of styrene with ethyl diazoacetate.

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Chapter 1. Introduction

1.1 Preamble

1.1.1 Environmental issues

At present there is great interest in environmental issues, with an ever-growing number of international summits held to address the problems in this area. One of the main topics is always the amount natural resources used and the large amount of waste products and pollutants created by a few major industrial nations. These rich nations frequently oppose ideas that would benefit the environment on the grounds that they are too costly in terms of money, would place their industry at a disadvantage, or the implementation would prove to be unpopular with the voters. In addition to this, it is recognised that as the second and third world countries industrialise the amounts of pollutants produced and the strain on the resources of the planet will increase. One problem with the industrialisation of the poorer countries of the world is that the more environmentally friendly processes are more expensive than older more polluting methods.

Indeed it has been noted that environmental issues only become a concern of the general public once they have achieved a level of prosperity currently only found in the western world. In many countries legislation is being introduced to increase recycling and to bring the amounts of pollutants and waste created within agreed limits. Much of this relies heavily on financial incentives (such as landfill tax, the fossil fuel levy ⁽¹⁾ or proposed energy taxes ⁽²⁾) to reduce the amount of waste products and energy used. A large number of renewable energy projects are in the pipeline in accordance with the UK's commitment to Europe and the Kyoto treaty ⁽¹⁾. Many large chemical plants now operate combined heat and power systems to save energy but this cannot reduce the amount of waste side products

produced. As a result of this, there has been an increase in spending on projects that try to reduce the amount of waste produced.

1.1.2 Use of catalysts

For the chemical industry the waste produced usually requires specialist disposal techniques and sites, which are very costly. One method of lessening this cost is through reducing the amount of waste produced by selectively creating the desired product using catalysis. This method is now very commonly used in industry, and many of the chemicals in use today are made using catalysis. The direction that catalysis is currently taking is towards more selective catalysts, especially in drug synthesis where a single enantiomer is often the preferred option. The most widely quoted example of the problem with racemic drugs is thalidomide [even though this drug racemises in the body] (and is now being used to treat Aids, cancer and leprosy⁽³⁾). The use of only one enantiomer can be an expensive process as previously many drugs were synthesised in racemic mixtures, and this would result in at least half of the drug being thrown away. Many drugs companies are putting increasing resources into researching chiral catalysts to synthesise drugs with high enantiomeric excess.

Catalysts fall into two main classes:

- ❖ Homogeneous catalysts are in the same phase as the reactants or products.
- ❖ Heterogeneous catalysts are in a different phase to the reactants and products.

Homogeneous catalysts are usually liquid (or soluble in the solvent used in the reaction). They are frequently organometallic compounds, and the wide choice of metals and

organic ligands available means that they can catalyse a large range of reactions. They usually have greater reactivity and selectivity than heterogeneous catalysts, but require additional steps to remove the catalysts from the products (if this is even possible), which can be an expensive and time-consuming process. In some syntheses (such as drug syntheses) it may be necessary to ensure the complete removal of the catalyst, as the organometallic complexes used may themselves be harmful or have toxic side effects.

Heterogeneous catalysts are in a different phase from the reactants. They are usually solids and are insoluble in the reaction medium. They are generally easier to manufacture and cheaper to produce than homogeneous catalysts, however the chemical processes involved may be much more complex and less understood. Common examples are platinum metal catalysts in catalytic converters in cars, and ZSM-5 in the cracking of petroleum. The supported catalysts that we will be looking at will, however, be more difficult and more expensive to produce than their homogeneous counterparts. Problems associated with heterogeneous catalysts are poor selectivity and low yields. Their main advantage lies in that it is a very simple process to remove all of the catalyst after the reaction (usually by filtration) and can be easily used in continuous flow processes.

1.2 Mesoporous Materials

1.2.1 Introduction to mesoporous materials

For many years scientists have been using amorphous silica, or microporous silica based compounds such as zeolites, as catalysts and as supports for catalysts. One common use recently has been as a support for chiral organometallic catalysts. Zeolites have often been used as supports but their principal problem is that the entrance to the reactive site is much smaller than the actual site. While this can be advantageous as in “ship in a bottle” catalysts ⁽⁴⁾ where it prevents the catalysts from being leached out, it can also decrease the active lifetime of the catalyst, as some products will not be able to escape, and this can lead to diffusion problems. The other main problem is that the active sites are small which limits the range of reactants, substrates and products which these supports can be used for. Amorphous silica has also been frequently used as a support, and although it does not suffer the size exclusion problems of zeolites, the low surface area to mass ratio means that only small amounts of active catalytic sites are available. The catalyst also must be chemically attached to the surface to prevent leaching and, when compared to zeolites, the support has no structure directing capacity.

In comparison, mesoporous materials have large pores which are usually the same diameter all the way through. This means that a much wider range of reactions and reactants can be used and any products formed can easily diffuse out of the solid matrix. IUPAC defines a mesoporous material as an inorganic solid, which contains pores with diameters in the size range of 20-500 Å ⁽⁵⁾. The surface area of most mesoporous materials is also very high and usually is in excess of 700 m²/g. This gives them the ability to have a large density of chemically isolated catalytic sites in a small amount of solid.

1.2.2 History of mesoporous materials

It is usually reported that mesoporous materials were discovered by Beck *et al* in 1992^(6, 7) with a new family of materials called MCM's (Mobil Composition of Matter). These papers have indeed inspired the current interest in this area and at present there are in excess of 3800 papers that have been published in this field. However they are not the first published report of a mesoporous silicate material although they did recognise a greater significance and potential in their discovery than some of the earlier researchers. The nature of this 'first' mesoporous publication being in Nature also added to the ease in which this discovery was recognised by the rest of the scientific community.

Some of the earliest papers stem from work into modified silicas for use in chromatography or as low-density materials for use in industrial manufacturing processes. Due to the amount of research carried out in these areas in the 1960's and 70's, it was widely expected that a new preparative method that would increase the size of stable pores that could be easily synthesised would be found soon.

The earliest report that has been shown to be a synthesis of a mesoporous material is from a US patent from 1971⁽⁸⁾ for forming 'low bulk density silica' for use in the synthesis of Zn_2SiO_4 phosphors. The procedure given in this patent was tested in a recent paper⁽⁹⁾ to give a solid which exhibited all of the properties associated with the first MCM synthesised, MCM-41.

A second pre-MCM mesoporous report is from a group at Waseda University in Tokyo⁽¹⁰⁾ and describes the synthesis of silica complexes with pore sizes between 2 - 4 nm (20 - 40 Å). The synthesis method that is described is based on an even earlier paper⁽¹¹⁾ looking at the cationic exchange of layered clay materials (particularly Kanemite) by organic

surfactants. The final step of surfactant removal to make a porous material was not undertaken in the earlier paper. The method by which these are formed was slightly modified and is now used to make the FSM-type materials ⁽¹²⁾. Some confusion about the paper from Waseda University may have been caused by the title, as it refers to microporous materials not mesoporous.

The takeoff in mesoporous materials began in 1992 when a new family of porous materials was reported ^(6, 7) which had a regular array of large pores in the mesoporous size range in which the pore size could be tailored from 15 – 100 Å. Since then many more papers have been written and much of the work has been discussed in several reviews ^(5, 13, 14). The materials were called MCM-type materials (Mobil Composition of Matter after their discovery by the Mobil Oil Company) and are probably the most widely studied. Within a few years papers on several other types of silica based mesoporous materials had been published: these include FSM (Folded Sheet Mesoporous materials) materials ^(12, 15), SBA (Santa Barbara) type materials ^(16, 17), MSU-X (Michigan State University) materials ⁽¹⁸⁾ and MCF's (mesocellular foams) ⁽¹⁹⁾. All of these materials use an organic surfactant around which the structure forms, the subsequent removal of the organic material leaving a porous material. Polymers can also be used to make ordered structures; 'polymer-polymer nanocomposites' have been synthesised ⁽²⁰⁾ with a hexagonal structure similar to that of MCM-41. The final material was not porous but contained a fluorescent polymer in the spaces where pores would have been. These materials do however highlight new possible areas of catalyst support as polymeric beads and dendrimers are already used for this purpose.

1.2.3 Pore structures of mesoporous materials

Mesoporous materials can be synthesised with a wide range of pore morphologies to tailor the solid material for the intended use. There are many different types of mesoporous material and differing names for many similar structures depending on the synthesis conditions. It is not practical or possible to give descriptions of all of them here, but some of the more commonly used pore structures are described below.

MCM materials

MCM-41

MCM-41, (Figure 1.2.3.1) which is the most commonly used, has a 2 dimensional hexagonal array of pores surrounded by a matrix of amorphous material with a space group of $p6m$ ⁽²¹⁾. The pores do not interconnect within the structure and can be deemed to be straight over short distances. FSM-type materials and SBA-3 are also reported to have a similar hexagonal structure although the mechanism of formation for the materials is thought to be different (see Section 1.2.7 on mechanisms of formation).

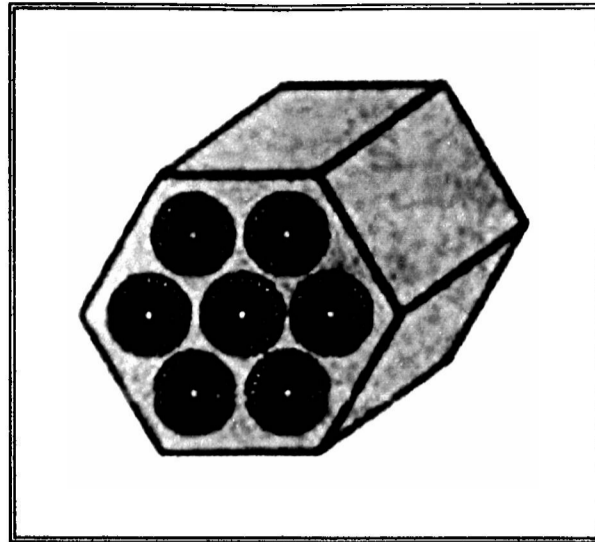


Figure 1.2.3.1: Pore structure of MCM-41 ⁽⁵⁾

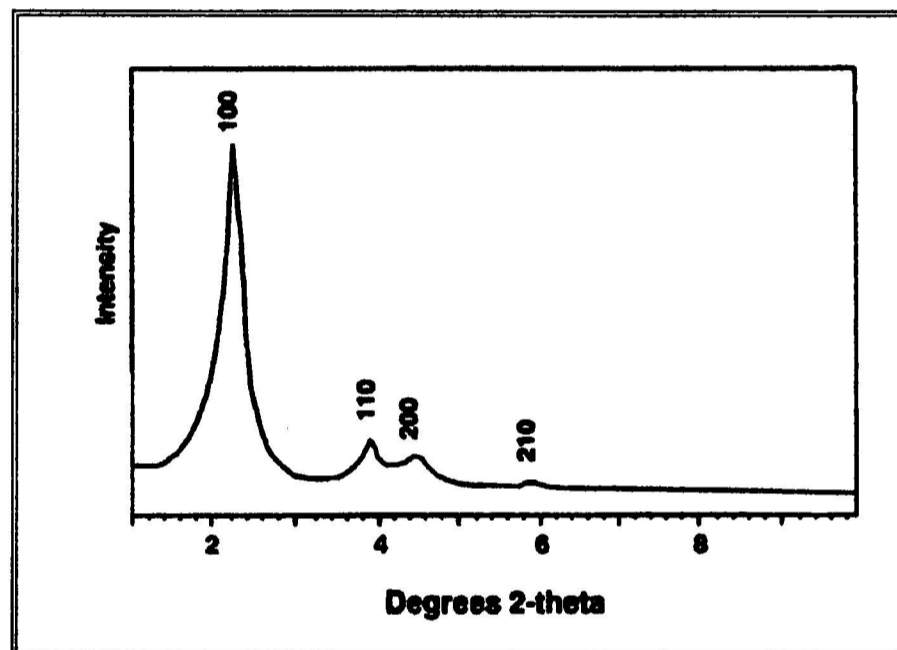


Figure 1.2.3.2: Published X-ray pattern of MCM-41 (40) ⁽⁶⁾

MCM-48

MCM-48 (Figure 1.2.3.3) is sometimes referred to as the cubic phase of MCM-41; its structure has been compared to a gyroidal minimal surface ⁽²²⁾ and has the space group $Ia\bar{3}d$. The structure has higher connectivity than MCM-41 with interconnections occurring inside the structure, which should give this material a higher diffusion coefficient and reduce the likelihood of the pores becoming blocked. The channels form two separate systems that

intertwine around each other and only connect with other channels of the same system. In spite of this greater connectivity though, there are comparatively few papers on this material when compared to MCM-41. This is probably due to problems with the reliability of the synthesis of this material, which we have also experienced at first hand.



Figure 1.2.3.3: Structure of MCM-48⁽²³⁾

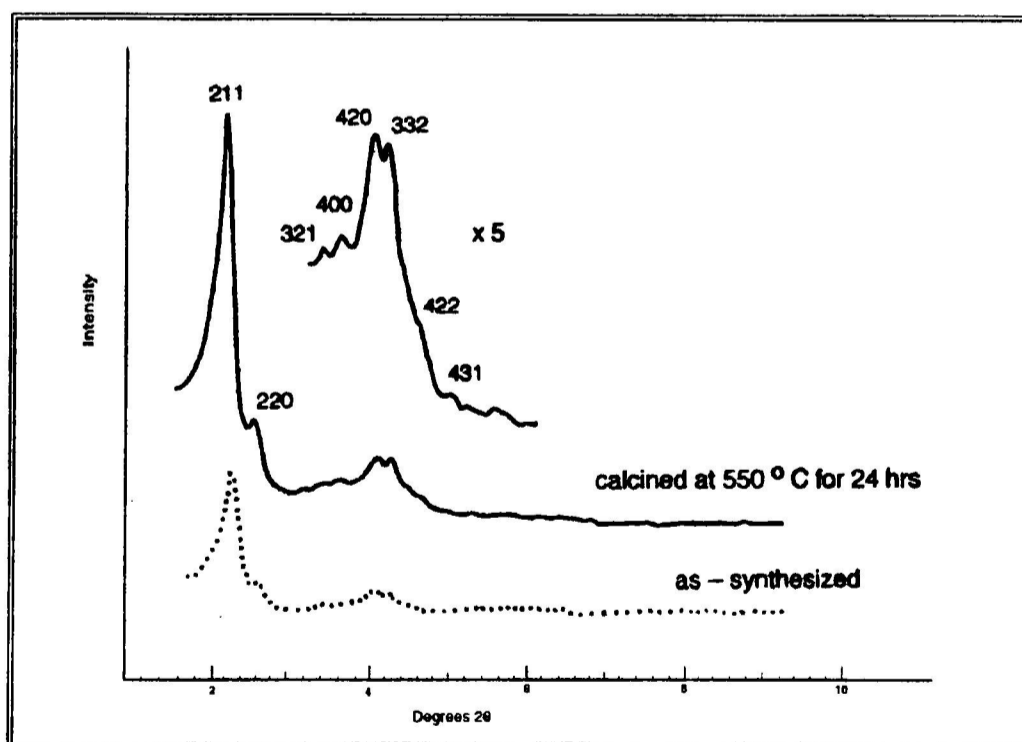


Figure 1.2.3.4: Published XRD pattern of MCM-48⁽²⁴⁾

MCM-22 / ITQ-2 / MCM-36

Another MCM structure is that of MCM-22, although this is not a mesoporous material itself, it is worth mentioning as the uncalcined precursor can be used to make either layered material or a pillared mesoporous material in addition to the microporous zeolite (Figure 1.2.3.5). The advantage of modifying these materials by pillaring or delamination is to increase access to the active sites and to reduce the problems associated with small pores.

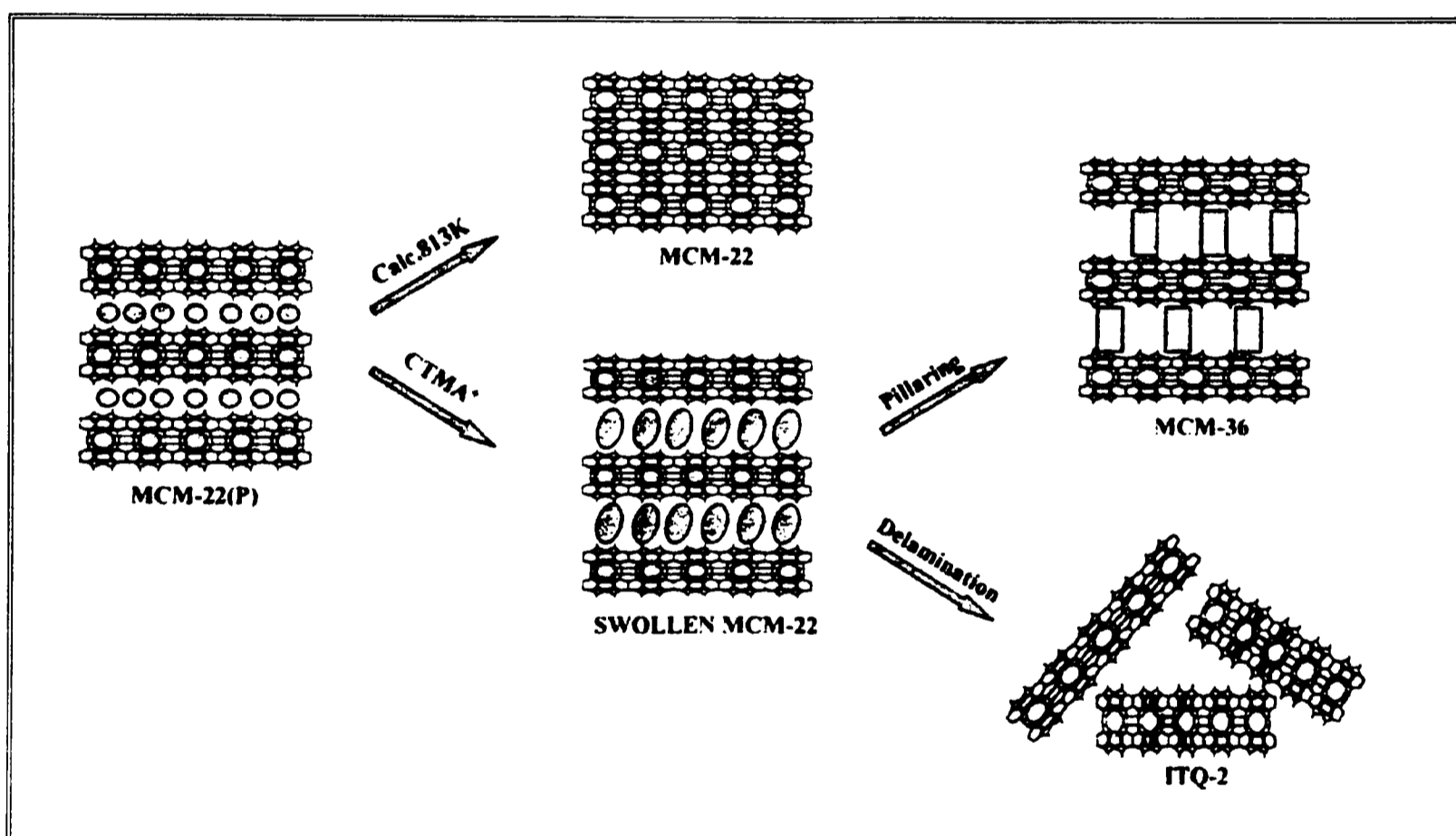


Figure 1.2.3.5: Structures of MCM-22, MCM-36 and ITQ-2 ⁽²⁵⁾

MCM-22 is an aluminosilicate material and is best described as a microporous zeolite. With MCM-22, size of reagents (as with all porous materials) is limited by the size of the pores - for MCM-22 smaller channels (10 membered rings) lead to cages which are 1.8*0.7 nm in size.

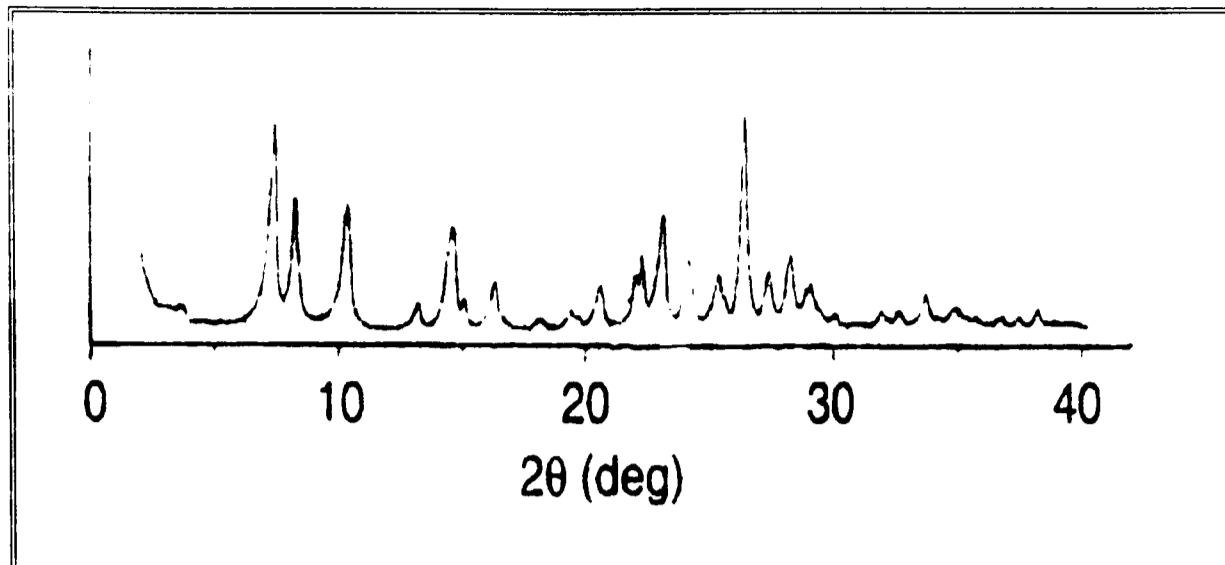


Figure 1.2.3.6: Published XRD pattern of MCM-22 ⁽²⁶⁾

The delaminated version is known as ITQ-2 (Instituto de Tecnología Química), which is made by swelling the precursor with an organic surfactant and then forcing the layers apart. The structure still possesses the chemical characteristics and activities of its zeolite counterpart but is able to cope with much larger molecules. The precursor material splits along the line of the large cages leaving a layers of material *ca.* 2.5 nm thick ⁽²⁶⁾ with a surface dominated by 0.7*0.7 nm cups ⁽²⁵⁾. The material was tested in the cracking of decane and gave similar results to the MCM-22 zeolite but with less secondary reactions ⁽²⁶⁾. The arrangement of the delaminated layers has been compared to a ‘house of cards’ presumably meaning that the overall structure is a disorganised matrix of highly crystalline layers ⁽²⁵⁾. The reduction in the size of the crystals of material caused by delamination reduces the amount of long range order within this material and can make it appear almost amorphous to X-ray (Figure 1.2.3.7).

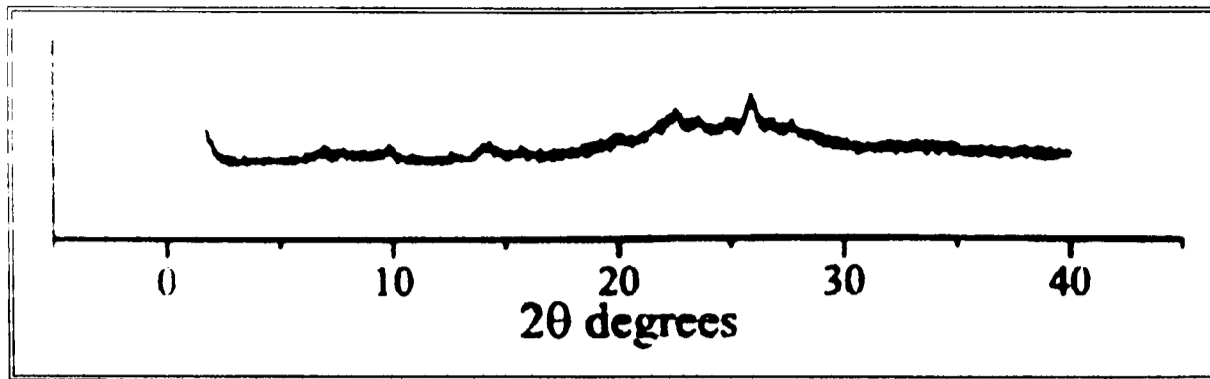


Figure 1.2.3.7: Published XRD pattern of ITQ-2 ⁽²⁵⁾

The precursor can also be swollen and then by creating pillars of solid material by hydrolysing a suitable source, a layered material MCM-36 can be synthesised. The material used to pillar the layers can be varied but most commonly silica or alumina is used ⁽²⁷⁾. Again as with ITQ-2 the surface of material will be dominated by the 0.7*0.7nm cups formed by the pushing apart of the layers. The mesoporous material formed by this method does not have the same narrow pore distributions that are associated with structures like MCM-41 and MCM-48.

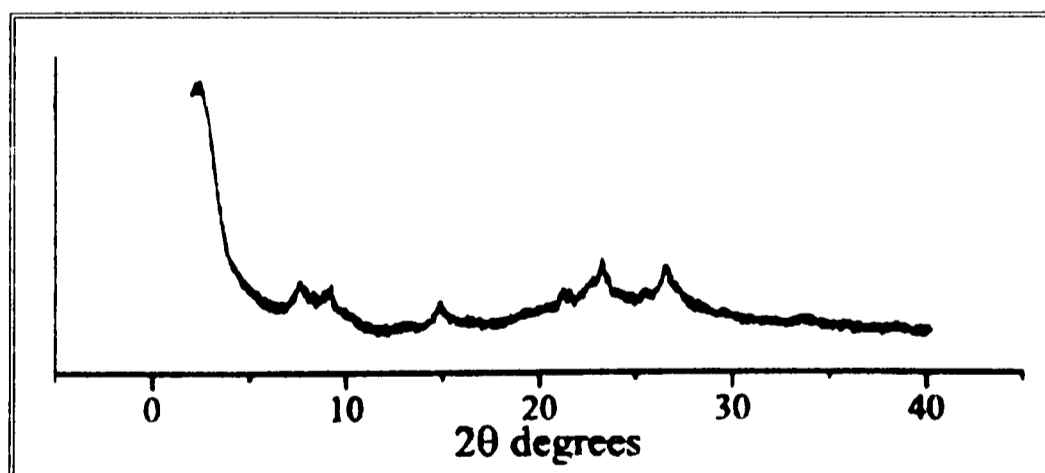


Figure 1.2.3.8: Published XRD of MCM-36 ⁽²⁵⁾

Another MCM material with a different structure not discussed in depth here is MCM-50 which has a lamellar structure.

FSM materials

FSM materials show a similar hexagonal pore structure to MCM-41 (Figure 1.2.3.1). The material is synthesised from a layered sodium silicate (kanemite) *via* a method which is very similar to that reported by Yangisawa in 1990 ⁽¹⁰⁾. Unlike the MCM materials the number after FSM does not signify the pore structure but rather the length of the surfactant chain used in the synthesis (i.e. FSM-16 would be made with a C₁₆ surfactant). As with MCM-41 the pores can be considered straight over short distances, and the similarity of the pore structures gives and almost identical XRD to MCM-41 (Figure 1.2.3.9).

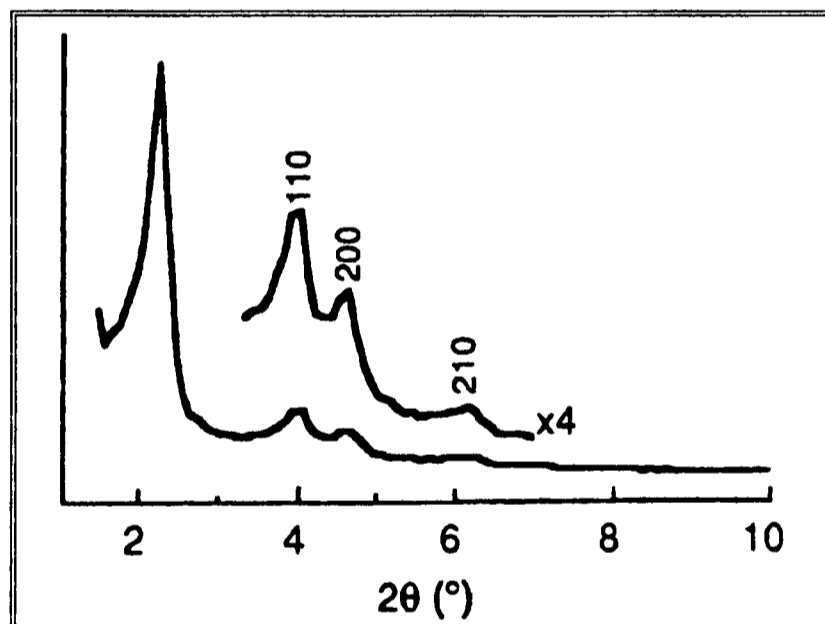


Figure 1.2.3.9: Published XRD of FSM-16 ⁽¹²⁾

SBA materials

SBA-2

This is probably best described as a mesoporous cage structure with hexagonal symmetry⁽¹⁶⁾ ($P6_3/mmc$, although it has been suggested that structure has lower symmetry⁽²⁸⁾). It consists of a 3 dimensional array of cages connected by pores (Figure 1.2.3.10), and because of this can sometimes be described as a mesoporous zeolite. This mesoporous silicate can be synthesised with cages of 77 – 102 Å in size, with the interconnecting pores having a diameter of *ca.* 35 Å. The structure also has a large internal surface area of about 600 m²/g.

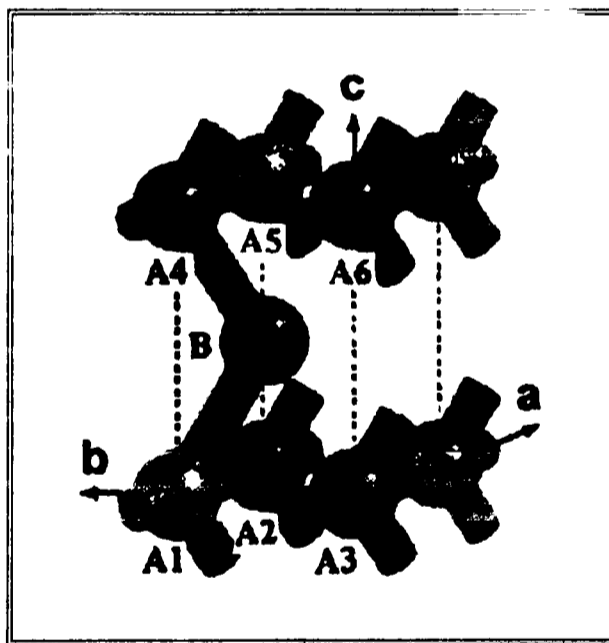


Figure 1.2.3.10: Channel system of SBA-2⁽²⁸⁾

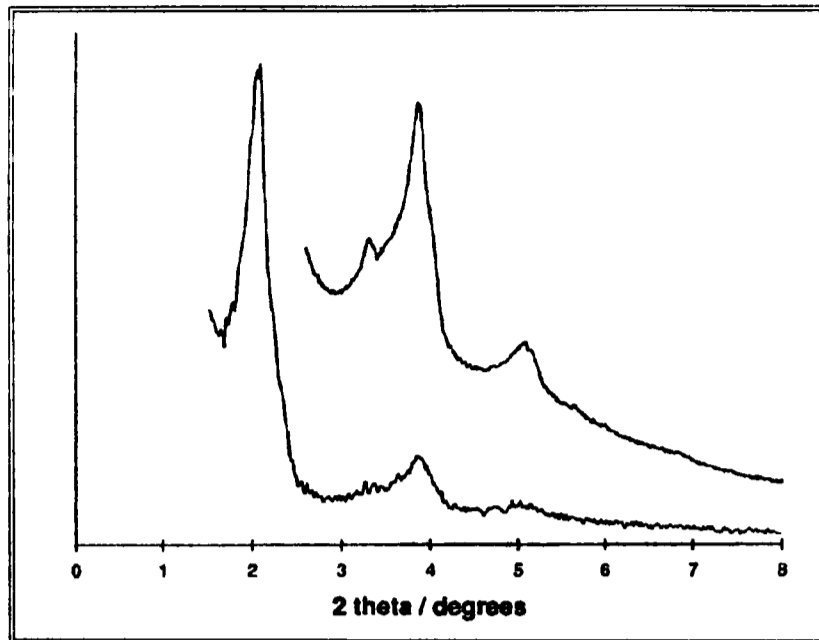


Figure 1.2.3.11: Published XRD pattern of SBA-2 ⁽²⁸⁾

SBA-3

SBA-3 is the name sometimes given to MCM-41 that has been synthesised under acidic conditions (this is also sometimes called APM, Acid Prepared Mesostructure). As such it has the same pore structure, space group and X-ray pattern as MCM-41 (Figures 1.2.3.1 and 1.2.3.2).

Other SBA structures not discussed here are SBA-1 which has a cubic structure (Pm3n), and SBA-15 which has a hexagonal structure ⁽²⁹⁾.

MSU materials

MSU-V

MSU-V materials (sometimes followed by a number *i.e.* C_n which denotes the alkyl chain length used in the synthesis) are proposed to have a lamellar structure. The pores are thought to be arranged within a gallery-confined framework with a high degree of cross-

linking⁽³⁰⁾. The structures have been synthesised with surfactants ranging from C₁₂-C₂₂ giving pores up to 2.7 nm in size.

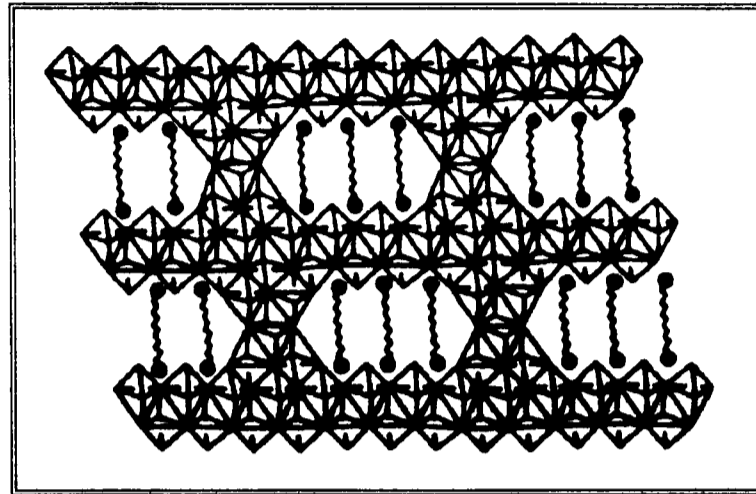


Figure 1.2.3.12: Proposed assembly structure for MSU-V⁽³⁰⁾

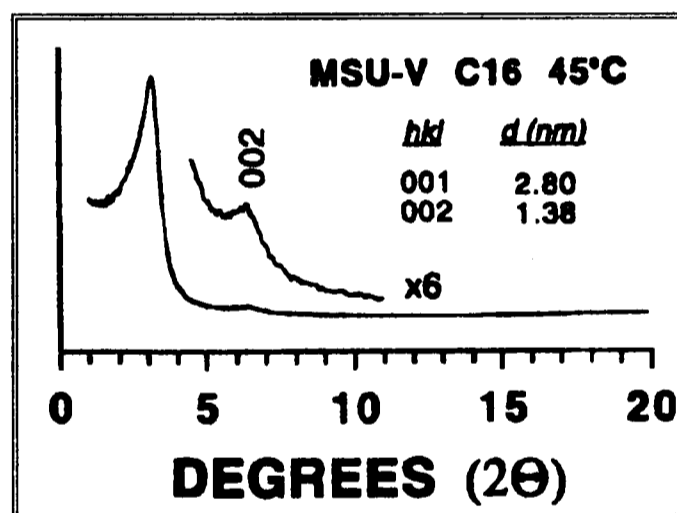


Figure 1.2.3.13: Published XRD pattern of MSU-V⁽³⁰⁾

MSU-X

MSU-X materials where x is a number relating to the material or surfactant lack a regular system of packing for the channels. They are usually described as having an interconnecting network of 'worm like' three-dimensional channels, although hexagonal and lamellar structures have also been observed, sometimes even in the same structure⁽¹⁸⁾.

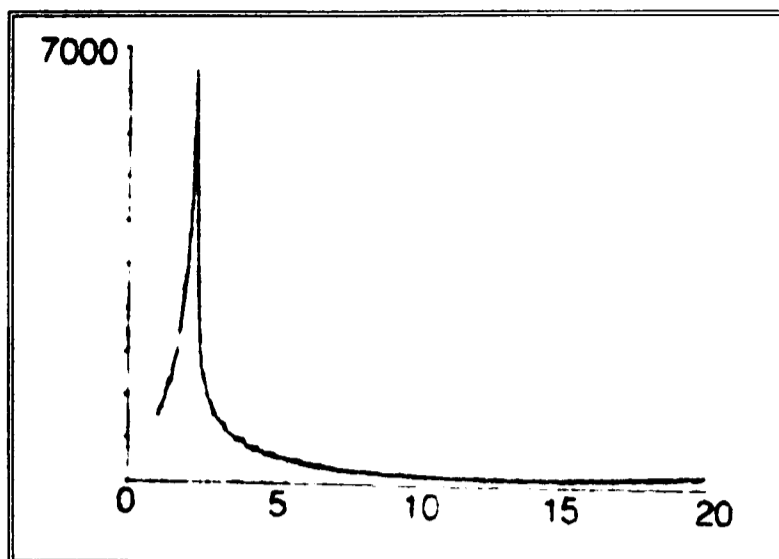


Figure 1.2.3.14: Published XRD pattern of [Ti]-MSU-1 ⁽¹⁸⁾

MCF materials

Mesocellular siliceous foams (MCF's) have large spherical cells, which are connected by windows to form a continuous matrix of pores ⁽¹⁹⁾. Their synthesis utilises an organic cosolvent that forms a microemulsion of spheres, around which the silica condenses. Altering the amount of the cosolvent present can control the size of the spherical cells and a narrow distribution of sizes is obtained; spherical cells have been synthesized in the range of 220 to 350 Å. The interconnecting windows in the structures are usually within the range 70 to 180 Å. The order that the spherical cells pack in relation to each other cannot be controlled very well and as a result the higher order peaks in the X-ray diffraction patterns cannot be indexed.

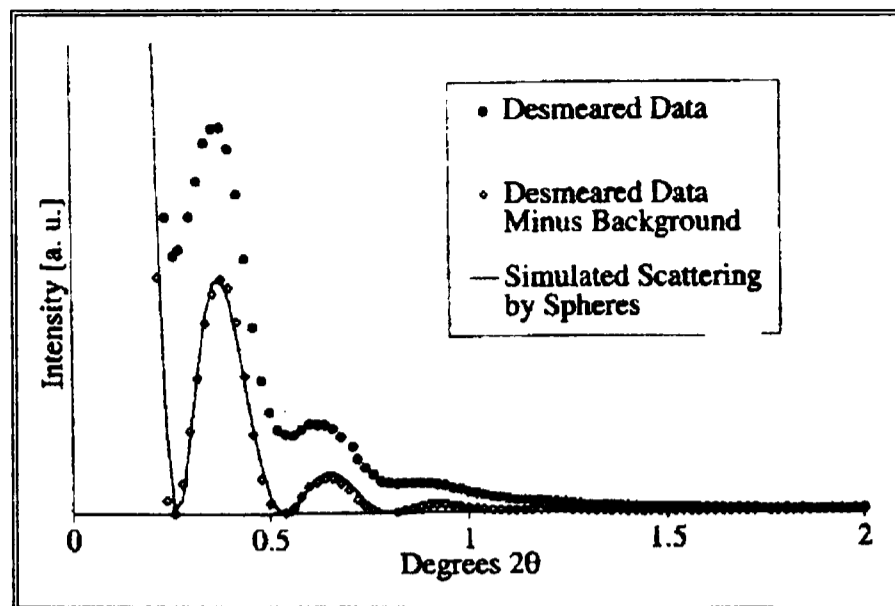


Figure 1.2.3.15: Published XRD pattern for an MCF structure with cell diameter of 33 nm ⁽¹⁹⁾

HMS materials

HMS (hexagonal mesoporous silica) materials are prepared using neutral or non-ionic surfactants. They have a similar structure (and XRD pattern) to MCM-41 and other hexagonal mesoporous materials although typically they have thicker pore walls and less long-range hexagonal order than MCM-41.

1.2.4 General synthesis methods of mesoporous materials

As mentioned earlier most mesoporous materials derive their structure from an organic template. The size of the pores is dependent on the length of the hydrophobic tail of the organic surfactant, with the most common type of surfactants used being mono alkylammonium based. This is probably for several reasons, the first being that these are the original surfactants used by Beck *et al* in his paper. The other reasons can be put down to cost and commercial availability. For example Gemini surfactants (with two alkyl

ammonium groups) have to be synthesised in the lab, and Pluronic surfactants, which are commercially available, are very expensive. To synthesise larger sized pores a swelling agent such as trimethylbenzene is frequently required, although they also may require a different method of surfactant removal due to their inherent instability.

For most of these materials there is no one definitive method for their synthesis. As will be demonstrated later in this section, each research group seems to adopt and adapt a method which is suitable for them. Sometimes groups will also rename materials produced by a different synthesis procedure, based on structure or chemical reactivity. An example of this is MCM-41 prepared in acidic medium which has also been called SBA-3 or APM (acid prepared mesostructure).

The methods of removing the organic surfactant (discussed later in Section 1.2.5) are general to almost all of the mesoporous materials, except for some large pore structures and organically modified materials, where calcination in air and ozonolysis cannot be used, as these processes would also remove the organic functionality.

FSM materials

FSM materials are prepared from a layered silicate material called kanemite (idealised as $\text{NaHSi}_2\text{O}_5 \cdot 3\text{H}_2\text{O}$), which is usually synthesised in the laboratory as part of the procedure^(15, 31). This type of material was first synthesised as a porous material in 1990⁽¹⁰⁾ yet nearly all papers on mesoporous materials do not make mention of it. This early report was analysed in 1994 by workers from Mobil⁽³²⁾ and they found that the materials synthesised did not show the high surface areas and pore sizes associated with mesoporous materials. This

may be due to the differing methods by which they synthesised the kanemite starting materials.

Both of the early papers (Yanagisawa and Beneke)^(10, 11) made their kanemite by the following method; a cold solution of 1 mole NaOH in 35 ml water is slowly added to 1 mole SiO₂ in 100 ml methanol ensuring that the temperature stays below room temperature. The slurry is then dried at 100°C (for up to 2 weeks) then calcined at 700°C for 5.5 hours, before the product is dispersed in water (to remove excess sodium) and then recovered by filtration and dried in air. The Mobil paper prepares its kanemite from sodium silicate solution (27.8% SiO₂) and mentions that it dries the initial slurry at ambient temperature rather than the 100°C reported in the other papers.

The kanemite products obtained in all 3 papers have different elemental compositions, which in itself is unsurprising, although the range is quite large. The Beneke paper produces a material with the ratio Na/Si/H₂O of 0.92 / 2 / 3.8 (for some strange reason the Mobil paper has this down as 0.8 / 2 / 4). The Yanagisawa paper does not give an accurate composition but claim that the material has the idealised ratio Na/Si/H₂O of 1 / 2 / 3. The paper from Mobil produces a material with the ratios of 0.4 / 2 / 2, and they also go on to state that the d spacings and intensities for the low angle peaks are similar to that reported by Beneke in table 1, and that they differ from the pattern published by Yanagisawa. Table 1 however only gives the structure of several dehydrated sodium silicates and not that of kanemite itself. Comparison of the XRD pattern published by Yanagisawa to recognised data finds a perfect match.

All three papers use the same method for the ion exchange, which is to stir 1 g of the kanemite with 100ml of a 0.1 M solution of an alkyltrimethylammonium chloride at 65°C for 1 week. The ion exchange is repeated to ensure most of the sodium is replaced. At this point

Beneke simply washes away excess organic components with ethanol and water. He does not calcine the material to give a porous material as he was investigating the reactivity of the sodium ions in exchange reactions. Yanagisawa washes the material with acetone to remove excess organics and dries the solid in air, calcination is by heating to 700°C with a thermal analyser. The paper by Mobil makes no mention of washing away excess organic material although this might have been combined with the filtration of the solid. Surfactant removal was by calcination in air at 540°C.

From the data presented in the papers it would seem that the starting silicate materials were not only of different composition but also of different structure and this caused the materials made by the Mobil workers to collapse when the surfactant was removed. Their own MCM materials, which are made by dissolving the silicate prior to the formation of the mesoporous material, still produced good quality mesoporous materials. The collapse of the mesoporous structure in the 1990 paper did not occur and left them with a material which shows all of the properties now associated with mesoporous materials.

The same group, that carried out the original work with extra collaborators, subsequently altered the method to give materials which we now know as FSM type materials. An example of the modern synthesis method of the mesoporous material FSM-16 is given below⁽¹²⁾:

A dried water glass powder with a SiO₂/Na₂O ratio of 2.00 is calcined at 700°C for 6 hours, 50 g of this material is then dispersed in 500ml of distilled water and stirred for 3 hours. The resulting mixture is filtered to give a wet kanemite paste, which is added to 1000ml of a 0.1 molar solution of a hexadecyltrimethylammonium chloride. The pH of the solution is adjusted to 8.5 with a 2 molar solution of HCl and the mixture left at 70°C for 3

hours. The resulting products are filtered and dried before the organic template is removed. Removal of the template can be by various methods, one of which is calcination in air at 700°C for 6 hours. A second method is dispersion in 150 ml of ethanol with 3.8 g of concentrated hydrochloric acid and stirring at 50°C for 6 hours, followed by filtration, this is then repeated to ensure complete removal of the surfactant.

It is important to note at this stage that the name of these materials are denoted by the length of the alkyl chain, i.e. FSM-16 is made with a hexadecyltrimethylammonium salt (C_{16}), and FSM-10 is made with a decyltrimethylammonium salt (C_{10}).

The material formed by the new FSM method compared to that formed in the original report is of much higher quality and several extra peaks can be seen in the analysis which are due to the regular arrangement of the pores relative to each other.

This method forms a hexagonal arrangement of pores similar to that of MCM-41 (Figure 1.2.3.1), although the layered structure is thought to be retained (see Section 1.2.7 on mechanisms of formation.)

MCM materials

MCM-type materials use the same types of surfactants (alkylammonium salts) as FSM-type materials but are usually synthesised from silica solutions, although other types of silica such as layered silicates⁽³²⁾, organosilicates, aluminosilicates⁽⁶⁾ or powdered silica may also be used. Unlike the FSM family of mesoporous materials the number after the name does not signify the surfactant used and hence give an idea of the pore size, rather it informs which of the MCM family of materials the structure is based on. This means that a material written as MCM-41 could have any pore size which can be synthesised (typically 25 – 40 Å

although they can be made with much wider range of pores). Sometimes the materials will be denoted as e.g. MCM-41 (40) where the pore size in Angstroms is denoted in the brackets.

MCM-41

Acidic Preparation

Some of the early preparations of MCM-41 use the following method ⁽⁶⁾:

40 g of water, 18.7 g of sodium silicate solution, and 1.2 g of sulphuric acid are combined and stirred together for 10 minutes. A solution of the surfactant is then added (surfactant / silica ratio = 0.5, the volume of water used is to make a 25% weight surfactant solution in water, i.e. 14.18 g of $C_{12}H_{25}(CH_3)_3N^+$ in 42.54 g of water) and the gel stirred for 30 minutes. 20 g of water is then added and the gel heated at 100°C for 144 hours (6 days) in a sealed vessel. The solid product is filtered off and washed with water, before being dried. The organic surfactant is then removed, and again this can be done using a variety of methods. The most common is to calcine at 540°C under nitrogen for 1 hour, followed by 6 hours in flowing air (or oxygen).

Mesoporous materials synthesised under these conditions may also be designated SBA-3 or APM structures.

Basic preparation

MCM's can also be synthesised in basic media, for which an example of the method used is given below ^(33, 34):

Gel composition, 1 SiO₂ : 0.5 DTMABr : 0.17 NaOH : 30 H₂O

Fumed silica was dissolved in sodium hydroxide solution and stirred for 30 minutes, DTMABr (dodecyltrimethylammonium bromide) was added and stirred for 1 hour. The mixture is placed into a sealed vessel and heated at 373 K for 6 days. The resulting solid is then treated exactly the same as the acid synthesised method.

MCM-48

MCM-48 has not been studied as much as the much more common MCM-41, and this has sometimes been put down to the ease of synthesis of MCM-41 compared to MCM-48. The solid is prepared in basic media using TEOS (tetraethylorthosilicate) as the silica source. As with all mesoporous preparations there are variations in the synthesis methods, but the most common surfactant used is the same as for most mesoporous materials CTAB (cetyltrimethylammonium bromide or chloride). Other surfactants can be used and an example of such a synthesis method for MCM-48 is given below ⁽³⁵⁾:

An aqueous solution of surfactant (cetylbenzyltrimethylammonium chloride) and TEOS was brought to a pH of 11 by addition of NaOH (normalized ratio 1 Si : 0.047 surfactant : 0.54 NaOH : 150 H₂O). The resulting mixture was kept at 100°C for 10 days in a Teflon flask. The resulting white powder obtained after filtration was heated to 500°C under argon then for 6 hours under flowing oxygen.

SBA materials

SBA-2

SBA-2 utilises Gemini surfactants in the synthesis route, these surfactants have also been used in the synthesis of other mesoporous materials such as MCM-48. They are called Gemini surfactants because they have 2 quaternary amine groups which are separated by an alkyl chain. Each head group is also attached to a hydrophobic tail group, and the general form they take is $C_nH_{2n+1}N^+(CH_3)_2(CH_2)_sN^+(CH_3)_2C_mH_{2m+1}$ which is usually written in the form C_{n-s-m} . An example of a synthesis procedure ⁽¹⁶⁾ is 0.05 M C_{16-3-1} surfactant, 0.5M NaOH, 1M TEOS and 150 ml H_2O stirred at room temperature for 5 hours. The solid product is washed and filtered and the template removed by calcination at 500°C.

MSU-X materials

MSU-X materials are synthesised with non-ionic polyethylene oxide and tri-block copolymer surfactants. The most interesting thing about the synthesis of these materials is that the pore size is dependant on the synthesis temperature. Depending on the surfactant used the pore diameter can more than double in size when the synthesis temperature is raised from 25°C to 65°C ⁽³⁶⁾ A synthesis procedure for the material MSU-1 is described below ⁽³⁷⁾

To a 0.02M solution of Tergitol 15-S-12 ($C_{15}H_{31}O(CH_2CH_2O)_{12}H$) in a sonicated bath at room temperature was added enough tetraethylorthosilicate to obtain a molar ratio of silicate to surfactant of 8.0. The mixture was sonicated for a short period of time to give a

milky suspension, then left to age without agitation for 12 hours to give a colourless solution. A 0.24M solution of sodium fluoride was added to give a ratio with the silicate of 0.025. The solution was then placed into a shaking bath with a speed of 40rpm at 25-65°C for 48 hours. The solid product was separated with a centrifuge and dried at 70°C followed by heating at 200°C for 6 hours. The surfactant was removed by traditional calcination methods.

MCF materials

Mesocellular foam materials are synthesised from an acidic solution of a Pluronic surfactant ⁽¹⁹⁾ (these are similar to the surfactants used for MSU materials but a different brand) with trimethylbenzene as an organic cosolvent. This is thought to cause a microemulsion of droplets around which the silica hydrolyses and condenses to form a continuous matrix, where two droplets touch each other a window is formed. Very few papers on these materials have been published and so little data is available on their properties.

A published synthesis procedure is as follows ⁽¹⁹⁾, 2 g of Pluronic surfactant P123 [poly(ethylene oxide)-*block*-poly(propylene oxide)-*block*-poly(ethylene oxide) triblock copolymer] (EO₂₀PO₇₀EO₂₀) is dissolved in 75 ml of 1.6 M HCl. 2 g of 1,3,5-Trimethylbenzene is added (23 mg of NH₄F can be added to obtain larger window sizes) and the mixture stirred for at least 45 minutes at 35-40°C. 4.4 g of tetraethoxysilane is added and stirred for a further 20 hours at 35-40°C and then for 24 hours at 95-100°C before the product is recovered by filtration. The organic surfactants are removed by calcination.

1.2.5 Methods of surfactant removal

It has been shown that the method of removal of the surfactant can have a profound effect on the resultant material. Here we will discuss three methods of removing the organic template and the benefits and drawbacks of each method. The three methods we will cover here are the main ones used. They are:

- Calcination
- Solvent extraction
- Ozonolysis

Calcination

Calcination involves heating the solid at high temperature in a flowing oxygen rich atmosphere to burn out the surfactant. The typical temperature used is in excess of 500°C and frequently the solid is heated to the desired temperature under an inert atmosphere to stop the surfactant charring and to reduce the amount of surfactant that is present before burning the remainder out. This method is the most commonly used by most research groups to make mesoporous materials.

The effect that this has on the solid material produced is that there is usually a slight shrinkage of the pore size compared to the starting material and there is more condensation of the silanol groups⁽³⁸⁾. Calcination gives materials a slightly better hydrothermal stability when compared to other methods of surfactant removal.

The problems with this method are that, as it is a harsh method, it is unsuitable for organically modified materials. It is also unsuitable for some of the larger pore structures (i.e. above 100Å) as it can cause the structure to collapse.

Solvent extraction

The solvent extraction method, is simply extraction of the organic template by dissolving it in a suitable solvent leaving the porous solid material behind. An example of a solvent system that has been used for this is 150 ml of ethanol with 3.8 g of concentrated hydrochloric acid added ⁽¹⁵⁾. The solid has to be washed 3 times to ensure that most of the surfactant has been removed. Solvent extraction is the only method that can be used for surfactant removal from one pot synthesis of organically modified mesoporous materials.

The method does not appear to result in the shrinkage of the 'as synthesised' pores meaning that this method could be suitable for larger pore and other less stable structures.

This method has been compared to calcination for the material FSM-16 ⁽¹⁵⁾ and whilst there was no observable difference in the thickness of the walls of the pores, the hydrothermal stability of the extracted material compared to the calcined material was greatly reduced. Examples of other solvent systems that have been used are; suspension in a 1 Mol solution of HCl in diethylether at room temperature overnight ⁽³⁹⁾, extraction with refluxing solvent (soxhlet extraction), or repeated stirring with hot ethanol ⁽⁴⁰⁾.

Ozonolysis

Ozonolysis basically is creating ozone around the material and allowing this to remove the organic template⁽³⁸⁾. The advantage of this method is that compared to calcination it is a 'mild' method and is therefore suitable for large pore structures which might become unstable by the more usual calcination methods. This method also does not result in the pore shrinkage that is seen by the calcination method, and it is also reported that the distribution of pore sizes is much narrower and more uniform. The only reported disadvantage of the ozonolysis method is that if treated for too long the structure will eventually collapse⁽⁴¹⁾. This method cannot be used for the calcination of organically modified mesoporous structures. The effect that this method of surfactant removal has on the overall stability of the structure is unknown.

1.2.6 External morphology

It is not only desirable to control the internal structure of a material to try and control the stereochemistry of a reaction; various external factors must also be taken into consideration. Factors such as particle size control are commonly used in zeolite chemistry for changing surface areas and increasing diffusion. Larger particles of mesoporous materials have been synthesised by using uncalcined material as a seed and the new material condenses around the original sample. However it is also advantageous in certain fields such as industrial catalysis to be able to control the shape of the particle formed. Mostly this is because of factors such as packing of catalysts into reactors and differing rates of diffusion. Shape selectivity in porous materials also has advantages for microscale engineering as they

can be used as templates for ultra fine materials once the surrounding material has been removed.

Various research groups have investigated the size and shape of the particles of MCM-41 and have demonstrated that it is possible to control the morphology of the particles to suit ones needs. In many studies MCM-41 has been synthesised with little concern for the size or morphology of the particles, as most of the work using MCM's has only been interested in the activity within the pores. With modifications to the initial synthesis conditions a variety of structures have been produced including hollow tubes ⁽⁴²⁾, ropes ^(43, 44), and spheres ⁽⁴⁵⁾, as well as a host of unusual shapes ^(see Figure 1.2.6.1 and also ref. 43).

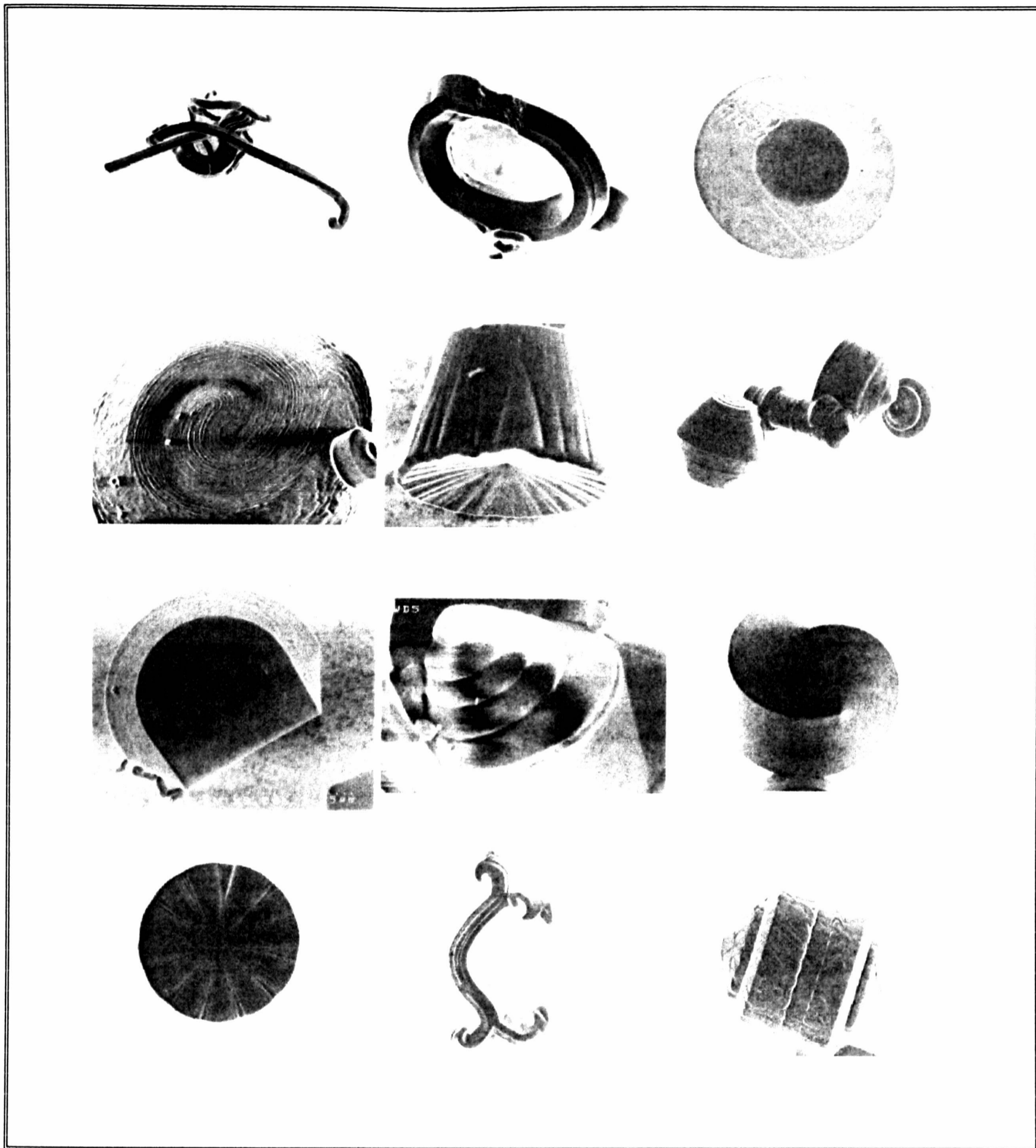


Figure 1.2.6.1: Some of the more unusual shapes of MCM-41 ⁽⁴³⁾

Of the shapes that have been synthesised the most interesting commercially are probably the rope like structures, long fibres and spherical structures.

Long fibres and 'Rope' like morphology

The 'rope like' structures have attracted interest from the electronic community as they could potentially be used for embedded conducting materials in microscale electronic devices ⁽⁴²⁾. The uniformity of the pores within mesoporous structures also pose the possibility that ultra fine wires of materials could be synthesised with uniform diameter through out their entire length. The 'ropes' can be synthesised up to almost millimetre scale from micrometer sized fibres which have the MCM-41 structure. After they have been loaded with the desired conducting material the silica exoskeleton can be removed by etching to obtain the wires.



Figure 1.2.6.2: Long hexagonal fibres of MCM-41 ⁽⁴⁶⁾

There are at least two synthesis methods for creating long fibres of MCM-41; the first involves addition to the initial surfactant mix of a polymer ⁽⁴⁷⁾, which induces the elongation of the particles. The second method of creating long fibres of mesoporous material is to use a reduced concentration of tetraethylorthosilicate in the reaction mixture and rapid stirring

⁽⁴⁶⁾, the final synthesis mixture in this case being 0.12 CTAB; 0.12 TEOS: 14.6 HCl: 100 H₂O.

The 'rope like' structures were made using nitric acid and a shear flow system ⁽⁴⁴⁾, the gel composition has an average ratio of 1 CTAB : 6-12 TEOS : 9-36 HNO₃ : 1000-2000 H₂O.



Figure 1.2.6.3: 'Rope' like organisation of MCM-41 ⁽⁴⁴⁾

Spherical morphology

The spherical particles of MCM-41 have potential applications in two main areas: industrial catalysis and as supports for chromatography.

Industrial plants use rounded particles as the diffusion throughout a fixed bed of catalysts is much more uniform and the particles do not become locked together. The uniformity of flow coupled with a very high surface area and good diffusion is also why spherical materials are ideally suited for chromatography ⁽⁴⁸⁾. With or without undergoing additional organic modification, which is quite simple to carry out (see Section 1.2.10), spherical mesoporous silicas could have the potential to be used in HPLC systems ⁽⁴⁵⁾.

These particles are synthesised by a modification of the method used to synthesise amorphous spherical particles of silica for the same purposes. This method uses the hydrolysis of a tetraalkoxysilane with ethanol and aqueous ammonia in the presence of a solution of an alkylammonium salt ⁽⁴⁵⁾. The spherical particles produced by this method varied in size from 400 to 1100nm, although the average size is around 600nm.

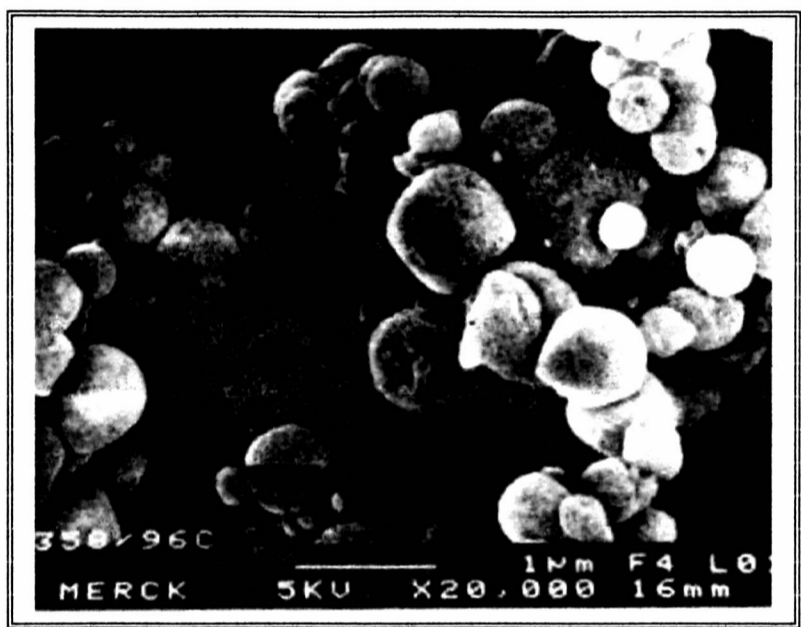


Figure 1.2.6.4: Spheres of MCM-41 ⁽⁴⁵⁾

1.2.7 Proposed mechanisms of formation of mesoporous materials

The exact mechanism by which certain mesoporous materials are formed by has still not been entirely proved. There are different mechanisms (as you would expect) for different materials but for some of the less well known structures there has been little work carried out on the subject.

FSM materials

FSM materials as mentioned earlier are formed from a layered silicate material called kanemite and an ionic surfactant. It is believed that after the sodium ions have been ionically exchanged for organic surfactant molecules the layers of silicate swell and fold around the surfactant molecules^(5, 10). Whether the layered structure is retained or whether the structure is more similar to MCM-41 is still disputed. The differences in the physical properties of the two materials suggest that it is highly likely that there is some difference in the structure of the walls of the pores, although this may be just due to the thickness of the walls.

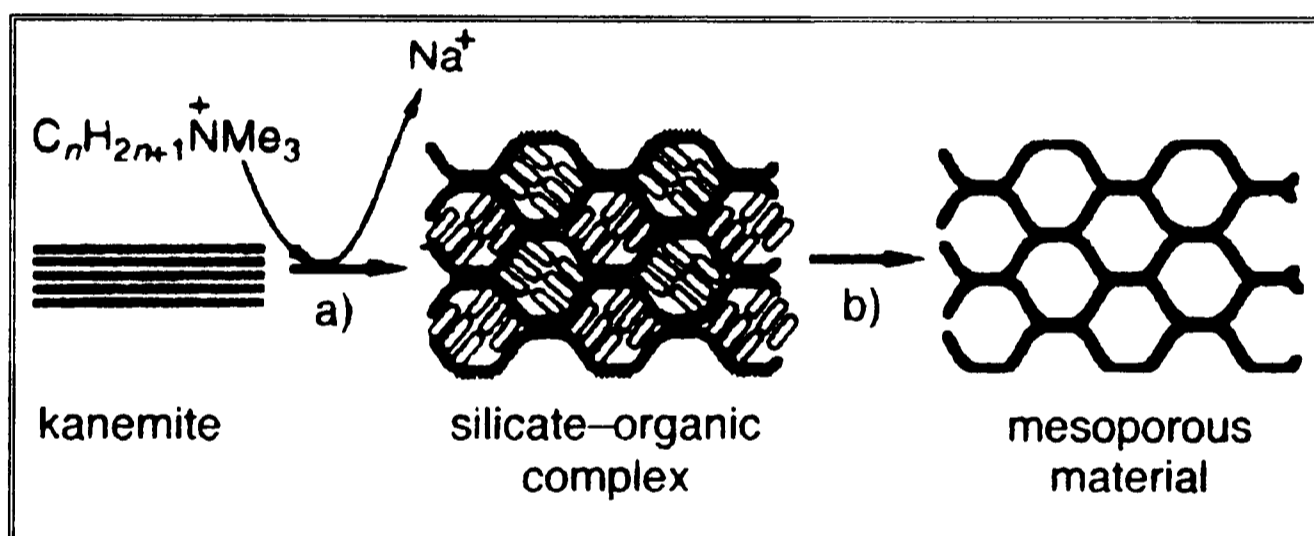


Figure 1.2.7.1: Folding of layered silicate around organic surfactant to form FSM materials,
a) Ion exchange, b) Calcination⁽⁵⁾

MCM-41

There are now two main proposed mechanisms by which MCM-41 forms (a third method has been discounted). The first of these is that MCM-41 forms from a layered starting material and that the pores are formed by charge density matching^(49, 50). This

method has a gradual increase of curvature in the layers, which slowly condense to form a hexagonal phase.

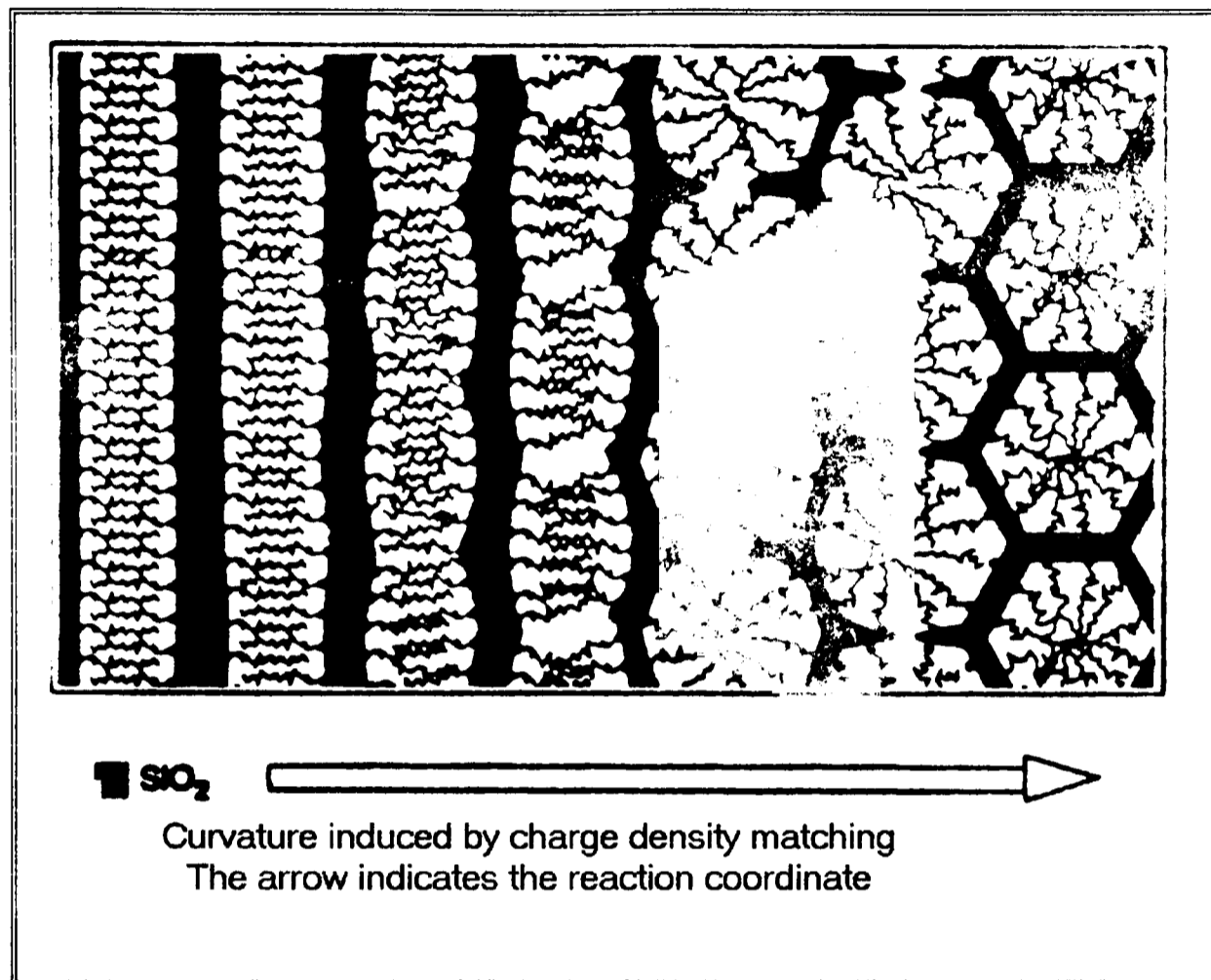


Figure 1.2.7.2: Charge density forming mechanism of MCM type materials ⁽⁵⁾

The second method involves a liquid crystal templating process, for which several possible mechanisms have been proposed.

The first is that the organic surfactant forms itself into a hexagonal liquid crystal structure and that the silicate material condenses itself around this structure. This cannot be true, as the concentration of the surfactant is far below what would be required to form such a phase.

The second suggestion is that the silica somehow mediates the formation of the hexagonal liquid crystal phase; this is the mechanism that is most widely quoted. The

mechanics behind this proposal are not very well understood although several groups are working on solving this problem. There is also a proposed variation on this theme where the silicate condenses around rod shaped micelles of surfactant and they gradually condense into a silicate encapsulated hexagonal array. All of the liquid crystal templating methods rely on the formation of rod shaped micelles of organic surfactants.

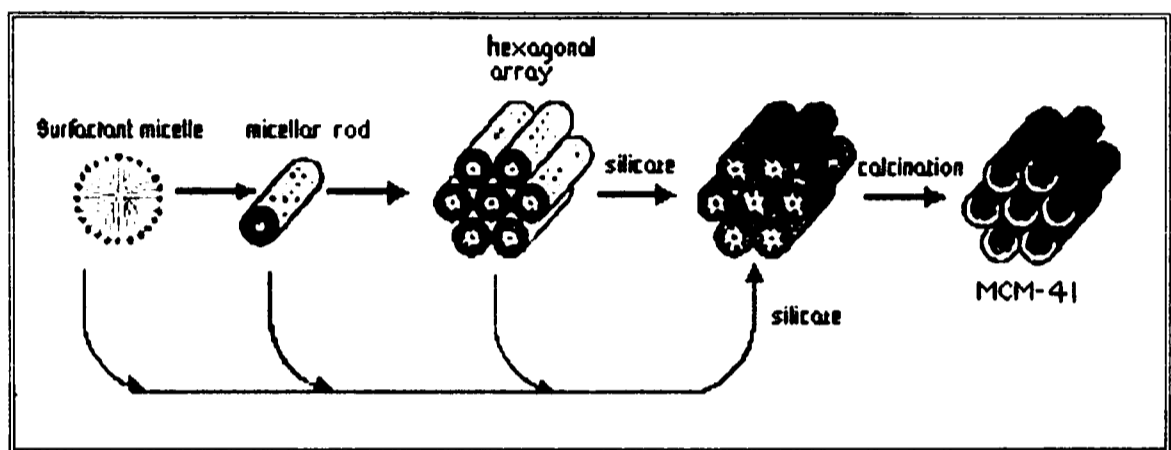


Figure 1.2.7.3: Two possible pathways for the synthesis of MCM-41 ^(5, 6)

In the above diagram (Figure 1.2.7.3) the top pathway is now known to be incorrect, as the hexagonal liquid crystal structure cannot be formed at the surfactant concentrations used. Consequently the lower pathway is thought to be more probable.

1.2.8 Physical properties and stability

Studies into the physical properties of mesoporous materials have only really been carried out on MCM-41 type materials, although a few papers exist on HMS mesoporous sieves and FSM type materials. Many of the properties such as hydrothermal and mechanical stability have been conjectured to be related to the thickness of the pore walls. Various methods have been employed to try and improve the stability of the structures and these will

be covered in Section 1.2.10 on modified materials. The results given below are for MCM-41 type materials and can therefore only be considered as guidelines and deemed accurate for the particular method and sample.

A mesoporous material by definition has to have a pore size of between 20 and 500 Å, although the larger pore sizes are less stable. The materials are usually synthesised with pores of about 30 Å, this tends to give a large surface area usually in excess of 700 m²/g and a large pore volume of 0.7-1.2 cm³/g for a typical sample ⁽⁷⁾. The thickness of the pore walls, upon which most of structural stability rests, have been reported as varying between 1.0-1.4 nm ^(13, 40).

Purely siliceous MCM-41 has been shown to retain its structure at temperatures of up to 1123 K in dry air before the structure began to collapse ⁽⁵¹⁾. The stability in moist air is slightly lower with the structure beginning to disintegrate at 1073 K with 8 torr of water vapour. It has also been reported that the mesoporous structure does not collapse even under a 100% steam flow at 770 K at atmospheric pressure ^(52, 53).

Whilst the structure may seem to be very stable, further work has shown that it does have one major instability ^(52, 53, 54). This is the complete collapse of the structure in boiling water, or even if it is placed in aqueous solution for extended periods of time. This is believed to occur by hydrolysis of the silicon - oxygen - silicon bonds by water molecules that are absorbed within the pores ^(34, 52). This is also thought to occur when the mesoporous structure is heavily compressed.

This method of collapse would also support the theory that having a thicker pore wall improves the stability. Research has been carried out to try and improve the stability in aqueous solutions, much of this work centering on pH adjustment, organic modification or

metal incorporation. These techniques will be covered in more depth later on in Section 1.2.10.

The stability of MCM-41 under mechanical compression has also been investigated⁽⁵⁵⁾. This research shows that the structure can be seriously affected by pressures as low as 86 MPa, at which pressure it is estimated that about half of the ordered structure is destroyed (this is estimated from the nitrogen adsorption data although the X-ray pattern still closely resembles MCM-41). Complete destruction of the large pores occurs before 224 MPa by which point there is very little adsorption and the XRD just shows a pattern characteristic of an amorphous material. It should be mentioned that the paper itself acknowledges that even before the results were known that the mechanical stability was expected to vary with the thickness of the pore walls. The compressibility could pose an additional problem if large pellets of mesoporous materials were required for catalytic processes. It is however possible that large particles of mesoporous materials can be grown using sequential synthesis reactions.

1.2.9 Silicon chemistry of mesoporous materials

Due to the observed differences between mesoporous materials and their silica gel counterparts in the affinity for various molecules, including water, studies on the surface chemistry of these materials has been carried out^(31, 39). Again nearly all of this work is centred on MCM-41.

The purely siliceous material has been shown to be comprised of 3 main types of silica groups, Q^4 , Q^3 and Q^2 ($Si(SiO)_x(OH)_{4-x}$). It is also reported that these materials show a similar ^{29}Si NMR pattern to amorphous silica⁽⁶⁾.

The uncalcined precursors prepared with electrostatic surfactants show a relatively low degree of cross linking between the silica groups, presumably as unlinked SiO⁻ groups are needed to balance the charge on the structure in some synthesis methods⁽⁴⁰⁾. The degree of cross-linking increases with calcination, probably due to condensation of silanol groups, giving a ratio of Q⁴/Q³ of *ca.* 1.18. This additional condensation does not occur if solvent extraction is used to remove the surfactant. Materials prepared *via* neutral surfactants (*i.e.* HMS type materials) show little extra cross-linking upon surfactant removal although the overall degree of cross-linking in the final material is substantially higher (Q⁴/Q³ *ca.* 2.68)⁽⁴⁰⁾.

It has been reported that on the surface of silica materials there are considerably less SiOH groups on MCM-41 (2.5-3.0 groups/nm²) than found on conventional silica (5-8 groups/nm²)⁽³⁹⁾ and that there are 3 different types of silanol groups. These are single silanol groups, silanol groups hydrogen bonded to their nearest neighbours, and geminal silanol groups where there are two OH groups per silicon. The lower number of silanol groups is because mesoporous materials have a more highly condensed surface due to their better ordering. It would also be expected that the number of silanol groups would be reduced by calcination in air and subsequent loss of water due to condensation of surface silanol groups.

1.2.10 Modifications of mesoporous materials

Many studies have sought to modify the properties of mesoporous materials with a view to their potential use in a range of different applications. A large number of the earlier papers on modifications were to try and optimise the synthesis mixture particularly to improve the hydrothermal stability of the resultant porous material. Most of these have only

been tried out on MCM-41 due to the ease of synthesis although many of them could be extended to other types of mesoporous or siliceous structures. The modifications can be broadly split into several areas:

- 1) pH adjustment for extra stability.
- 2) Addition of organic components to stabilise the structure and increase the hydrophobicity of the materials.
- 3) Addition of inorganic components to stabilise the structure or promote catalytic activity.
- 4) Addition of organic components for the attachment of catalysts or to promote catalytic behaviour.

1) pH adjustment for extra stability

As mentioned earlier the stability of the structure (particularly the hydrothermal and mechanical stability) is heavily dependent on the thickness of the pore walls. One way of improving the hydrothermal stability (by thickening the pore walls) is to adjust the pH of the solution several times during synthesis. However this method requires frequent interruption of the crystallisation process and can be a time consuming process ⁽⁵²⁾. The increase in the hydrothermal stability is significant but does not produce an entirely stable structure as the intensity of the X-ray diffraction peaks still decreases by over 30% after only 1 hour in boiling water.

2) Stabilisation by addition of organic components

A second way of improving the stability of the structure is to add an organosilane or other organic compound which covers the surface of the material with a monolayer of organic material. This can be done either during or after the synthesis of the mesoporous solid and the aim is to prevent the hydrolysis of the silicon oxygen bonds by increasing the hydrophobic nature of the surface ⁽⁵⁶⁾.

The procedure for modification during synthesis is simple; a small amount (about 20%) of the normal silicon source is replaced by an equivalent amount of an organosilane (usually XTriEthOxySilane – where X is an alkyl group). During the synthesis procedure the organosilanes arrange themselves around the organic surfactant micelles in a monolayer with the remaining silicon atoms forming the remaining bulk of the walls. The removal of the surfactant cannot be carried out by calcination or by ozonolysis, as this would destroy the organic monolayer. The materials formed by this method were observed to have smaller pore size and pore volume than equivalent pure silica counterparts however the surface area remained high ⁽⁵⁶⁾. The hydrothermal stability of the materials was improved considerably compared to normal MCM-41 although some reduction in peak intensity was observed. The best results were obtained using both organic modification and pH adjustment, which stabilised the structure considerably more than organic modification alone.

The addition of an organic monolayer after synthesis is also simple, although the mesoporous material must be dried first and care must be taken to avoid the presence of moisture during the reaction. As with previous modifications there are many different reagents which may be used although organosilanes still predominate. An example is the

coating of an MCM material with a monolayer of SiMe_3 groups using chlorotrimethylsilane under reflux⁽³⁴⁾. As expected this treatment reduces both pore size and surface area of the sample. The materials showed greatly increased stability to both moisture and compression and showed very little decrease in XRD peak intensity on moisture treatment for 30 days. (Moisture treatment is exposure to water vapour over a saturated NH_4Cl solution at room temperature, unmodified MCM's will lose 80% of their X-ray diffraction peak intensity within 2-3 days⁽³⁴⁾). More surprisingly even when this material was calcined again to remove the organic components the increase in hydrothermal stability was retained. With the moisture treatment both of the modified materials (calcined and uncalcined) showed about a 10% decrease in peak intensity over 30 days⁽³⁴⁾. Both of the modified materials showed greater resistance to compression than the non-modified materials although the calcined material exhibited lower stability than the non-calcined modified materials.

These modifications have also been used with mesoporous materials with an organometallic catalyst tethered to the surface⁽⁵⁷⁾. With supported catalysts problems are sometimes found with sensitivity to moisture or the build-up of side products which may eventually cause the deactivation of the catalyst. Coating any unreacted surface may reduce the amount of moisture present or lessen the rate at which side products accumulate.

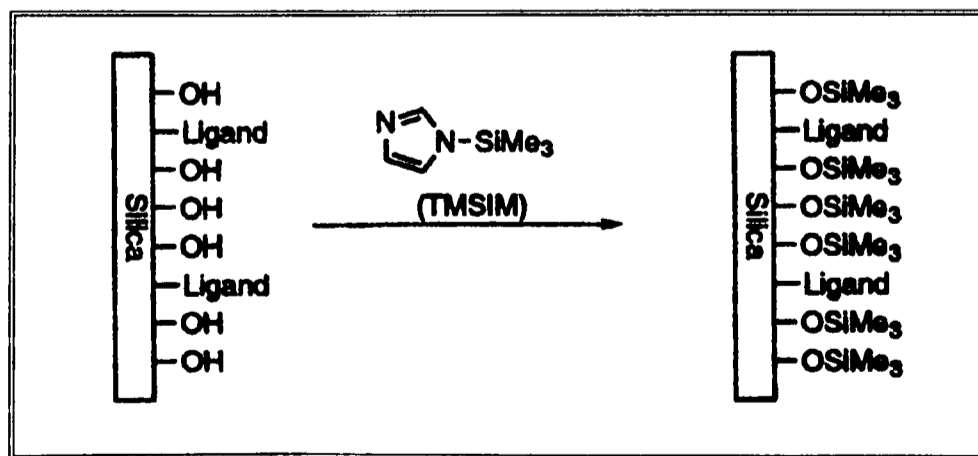


Figure 1.2.10.1. Post-synthesis surface modification of mesoporous material⁽⁵⁷⁾

3) Addition of inorganic components

The addition of inorganic components into mesoporous materials is undertaken for two main reasons which are not necessarily compatible; these are to stabilise the structure or to promote catalytic behaviour.

The structure can be stabilised during the synthesis procedure by adding certain metal salts which alter the chemical environment of the water molecules trapped in the pores, and correspondingly alter the local structure of the final material ⁽⁵²⁾ The method by which these metal salts alter the structure during the synthesis of the materials is as yet not fully understood. Analysis shows that these materials have a larger degree of condensation of the silanol groups within the solid - it is this that is believed to be responsible for the improvements in stability rather than a thickening of the pore walls. The salts used are typically sodium or potassium salts such as chlorides, bromides or organic salts like acetate or EDTA complexes. In reference 52, both pH adjustment and addition of metal salts were used in conjunction to improve the hydrothermal stability of the structure. The concentration of the metal salts used proves to be very important as does the point during the synthesis procedure when the salts were added. If the salts were added too early (before the surfactant – silica structure had completely formed) then disordered mesoporous structures may be formed. Some of the best results were obtained using a ratio of 3:1 of NaCl to surfactant with the NaCl being added after the first pH adjustment. The paper reports that this structure showed no sign of loss of intensity even after being boiled in water for 12 hours. Also reported was that one sample prepared with a sodium EDTA salt was stable enough to survive heating at 1230 K for 2 hours with no apparent loss of structural intensity. These

modifications although tedious could hold the answer to stabilising MCM type materials made in the lab, although the repeated opening and closing of the pressurised reaction vessel could cause problems for industry.

Metal atoms may also be incorporated within mesoporous materials to promote catalytic activity. The metal can be added by two different methods: incorporation into the synthesis mixture, or by binding to the surface after synthesis. One of the most common elements incorporated is aluminium to impart strong acidity to the structural framework to obtain mesoporous materials which can mimic zeolite catalysts. The main aim of this is to try to develop mesoporous versions of petroleum cracking catalysts, where it is hoped that the larger pores should decrease the amount of clogging and so increase the lifetime of the catalyst significantly and also enable the cracking of larger fractions. Some of the catalysis carried out using metal modified mesoporous materials is covered in a brief review⁽¹⁴⁾.

Mesoporous materials can be synthesised directly with various ratios of silica to aluminium although the characteristic X-ray pattern rapidly disappears with a silica:aluminium ratio of below 10. It has been mentioned previously that various silica sources can be used to make mesoporous materials, likewise in aluminosilicates a wide range of aluminium sources can also be utilised. These include sulphates, isopropoxides, orthophosphates, sodium aluminate as well as Catapal B alumina. The best source for getting the most aluminium into the framework cannot be agreed upon⁽¹⁴⁾ as different methods were used to synthesise the mesoporous materials in question. It has been reported in two studies that the acidity of aluminated MCM-41 is comparable to amorphous aluminosilicates^(58, 59) which in itself is unsurprising as the walls in mesoporous materials are effectively amorphous in structure. These aluminium containing mesoporous materials have been shown to have catalytic activity for various petroleum-related reactions⁽¹⁴⁾ In many of these processes the

reactivity of the mesoporous catalyst was shown to be higher than their corresponding amorphous aluminosilicate counterparts. This can be attributed to the greater surface area that can be used for catalysis in the mesoporous materials.

Other metals incorporated into mesoporous materials for catalysis include titanium for epoxidation of alkenes^(60, 61) and vanadium for oxidation of cyclodecane⁽³⁵⁾. There are many more papers out there on this area of mesoporous materials but as this falls outside the scope of this project a comprehensive search has not been carried out.

The second method of adding metal atoms to surface is to add them after the synthesis and calcination of the mesoporous material. The aim of this is to attach a metal centre to the surface silanol groups of the mesoporous material. There are two ways of doing this; the first is a solid-state impregnation where mesoporous material is ground up with a metal salt then heated in air to 500°C⁽⁶²⁾. This is not the most commonly used method for adding metal atoms onto mesoporous supports.

The second method is a wet impregnation, and in common with most processes involving mesoporous materials individual research groups have done this *via* different methods. One way is to add a soluble metal salt in methanol and to heat at 60°C for 3 hours before removing the solvent quickly and calcining in air at 500°C⁽⁶²⁾. This method has also been used to add aluminium by refluxing a mesoporous material with aluminium chloride in chloroform⁽⁶³⁾. Organometallic complexes can also be used, as subsequent calcination will remove the organic component to leave free metal oxide on the surface.

4) Addition of organic components to support catalysts or promote catalytic behaviour

Organic components can also be added not only to stabilise the mesoporous structure as we have mentioned earlier, but can also be used to support organometallic catalysts or to promote catalytic behaviour.

One organic group which has been added to mesoporous materials to promote catalytic activity is amino groups. For example amino modified MCM-41 has been used as a base catalyst. Mesoporous materials synthesised with varying amounts of aminopropyl(trimethoxy)silane in the synthesis mixture have been shown to be able to catalyse the Knoevenagel reaction (Figure 1.2.10.2) ⁽⁶⁴⁾ with varying success depending upon the reagents and solvent used. The maximum yield reported was 97% with in some cases catalyst turnovers of over 6000.

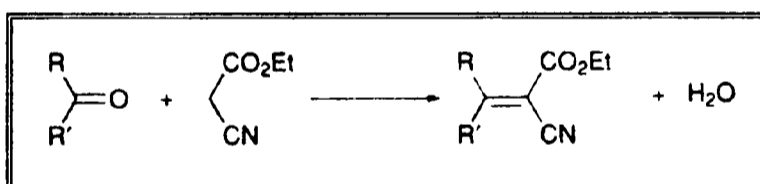


Figure 1.2.10.2: Knoevenagel reaction catalysed by aminopropyl supported MCM's ⁽⁶⁴⁾

Amino modified MCMs have also been used as catalysts in the synthesis of monoglycerides from glycidol and fatty acids (Figure 1.2.10.3) ⁽⁶⁵⁾.

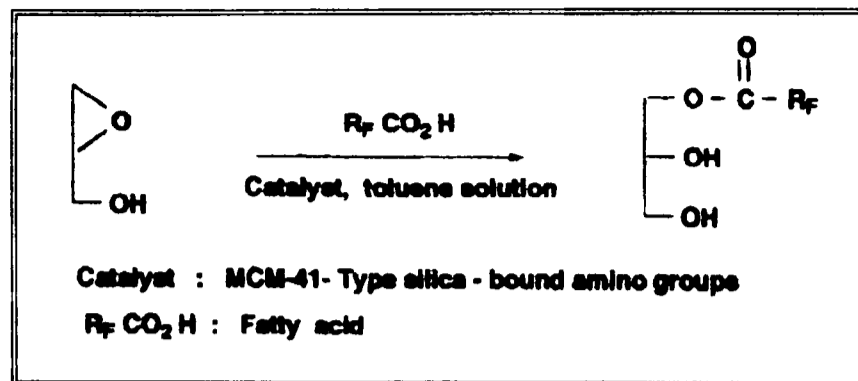


Figure 1.2.10.3 Monoglyceride synthesis catalysed by amino modified MCM's ⁽⁶⁵⁾

Organic functionalities such as amine groups can also be used to bind organometallic catalysts to the surface of mesoporous materials (Figure 1.2.10.4). This will be covered in greater depth in Sections 1.3 and 1.5.

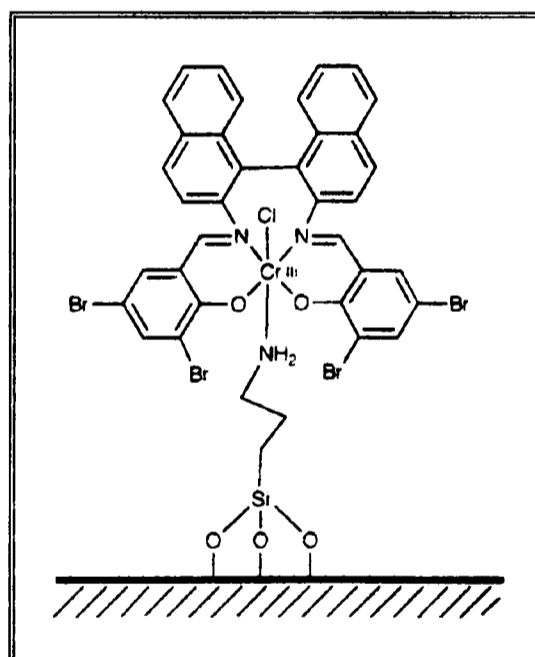


Figure 1.2.10.4: Amino modified mesoporous material used to support an organometallic catalyst ⁽⁶⁶⁾

1.2.11 Uses of mesoporous materials

As can be seen in this Chapter there are many potential uses for mesoporous materials, most of which have not been fully explored due to the recent nature of their discovery. Some of these applications include uses in chromatography and filters, large pore catalysts and supports for catalysts providing additional options to using more conventional amorphous silicas and zeolites. Some interesting examples are the use of mesoporous materials in the environmental remediation of heavy metal ions ⁽⁶⁷⁾ or as petroleum cracking catalysts ⁽¹⁴⁾. Other applications may be more exotic for example using mesoporous materials to make ultra thin wires.

As we have demonstrated in this Chapter there is currently a great deal of interest in mesoporous materials and a wide array of structures and synthesis methods have been used. The sheer number of papers on mesoporous materials is vast with over 3800 papers easily available and more being published every week. As mentioned throughout this chapter the MCM family (especially MCM-41) is the most widely studied with over 1800 papers on MCM-41 alone.

1.3 Supported Organometallic Catalysts

1.3.1 Introduction to supported catalysts

The idea of taking a successful homogeneous catalyst and making it heterogeneous without removing the reactivity and selectivity that made it attractive in the first place is not in itself a new idea. There are several ways that have already been tried with organometallic catalysts with varying amounts of success. Some of these methods are:

- i) Incorporation into an organic host material
- ii) Trapping within the pores of a microporous zeolite
- iii) Binding between layers in clays
- iv) Attaching to mesoporous solids or amorphous silica.

Several of the methods listed above have been tried recently with some of the bis(oxazoline) ligands we intend to use. Several of the catalysts discussed here are related to bis(oxazoline) ligand (such as their predecessors, the salen and semicorrin ligands) or are early uses of mesoporous materials as supports for organometallic catalysts.

1.3.2 Organic materials as catalyst supports

There are several ways of using organic materials as supports for organometallic catalysts: the first is to incorporate the catalyst into a polymer, the second is to bind the catalyst to a polymer bead, and the third is to turn the catalyst into a dendrimer.

One example of incorporating the active catalyst molecule into a polymer is the incorporation of a salen complex in a matrix of styrene and divinylbenzene ⁽⁶⁸⁾ (Figure 1.3.2.1). These catalysts were tried with and without the spacer groups shown in Figure 1.3.2.1, the effect that the spacer groups were shown to have, was to increase the selectivity of the catalyst.

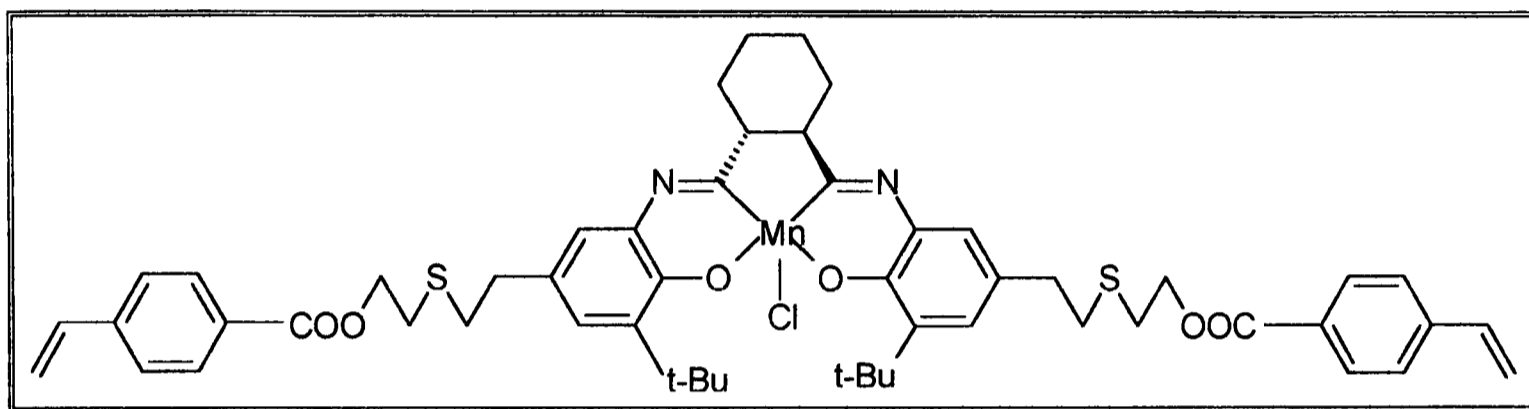


Figure 1.3.2.1: Salen type ligand with spacer groups as used in polymer bound catalyst ⁽⁶⁸⁾

The catalysts formed gave good results for some epoxidation reactions (Figure 1.3.2.2) (up to 92% conversion with a 97% yield and 62% enantiomeric excess was obtained using *cis*- β -methylstyrene as the olefin [N.B. these are the maximum results recorded in the paper]).

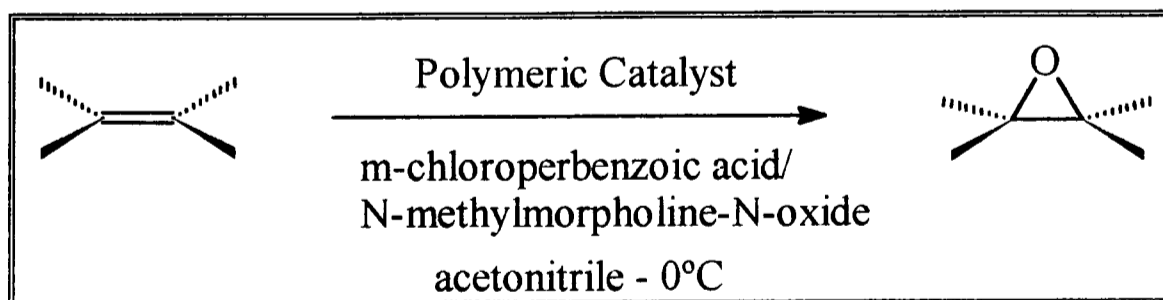


Figure 1.3.2.2: Epoxidation of olefins using polymeric bis(oxazoline) catalysts ⁽⁶⁸⁾



Depending upon the oxygen source used, the catalysts were able to be recycled at least five times with little change in selectivity. For some other oxidants tried (iodosylbenzene) the rate of reaction was low and some of the side products formed could not be completely removed from the supported catalyst matrix, which could affect the ability to recycle the catalyst. Although the yields reported are generally very good, this system does not seem to give good yields when using bulky olefins such as 1-phenylcyclohexene where the reported yield is low and over 50% starting material is recovered as side products ⁽⁶⁸⁾.

Placing the catalyst within polymeric matrices can sometimes cause problems with the diffusion of reactants and products. This can be avoided by placing the catalyst on the outside of the supporting material, and is commonly achieved by grafting the catalyst *via* a suitable tether to a commercially available polymer bead such as polystyrene (Figure 1.3.2.3) ⁽⁶⁹⁾.

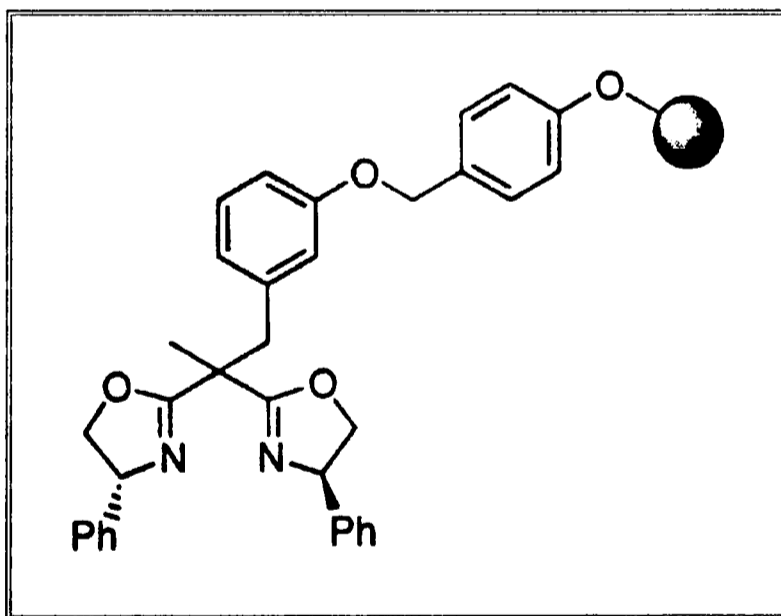


Figure 1.3.2.3: Bis(oxazoline) ligand grafted onto a polystyrene / polyoxyethylene copolymer bead ⁽⁶⁹⁾

These catalysts were used for the zinc catalysed Diels-Alder reaction (Figure 1.3.2.4) and also the palladium catalysed allylic alkylation reaction (Figure 1.3.2.5).

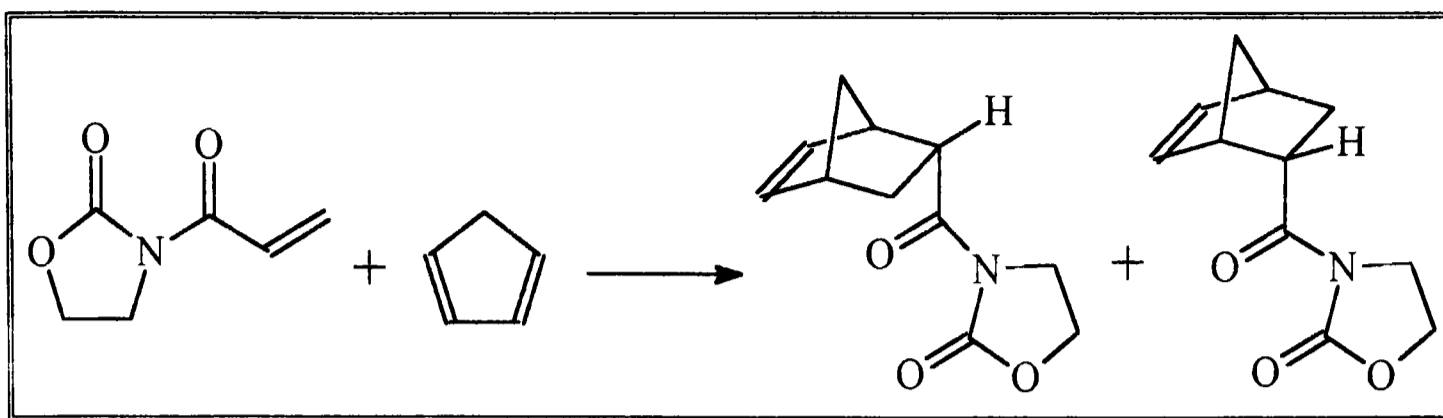


Figure 1.3.2.4: Diels-Alder reaction using cyclopentadiene and 3-acryloyl-1,1-oxazolidin-2-one⁽⁷⁰⁾

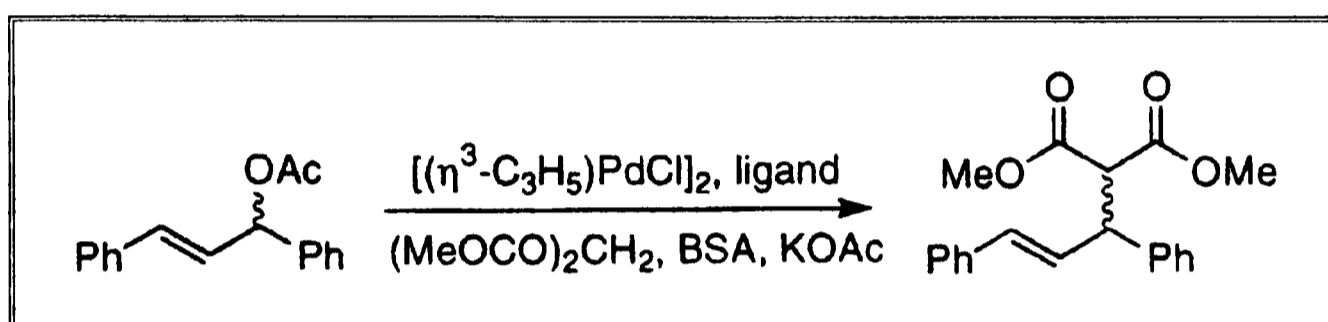


Figure 1.3.2.5: Allylic alkylation using a palladium bis(oxazoline) complex⁽⁶⁹⁾

The zinc catalyst used in the Diels-Alder reaction gave little or no products at -78°C , compared to full conversion with the homogeneous counterpart. At room temperature both the supported and homogeneous catalysts gave full conversion although the heterogeneous catalyst gave a racemic product.

The palladium catalyst showed good results giving similar selectivity to the equivalent homogeneous catalyst (94-95% ee heterogeneous, 95-96% ee homogeneous), although the yields found were generally slightly lower for the heterogeneous system. Precipitation of palladium during the reaction prevented the catalyst from being recycled and so had to be removed using potassium cyanide before reuse of the catalyst⁽⁶⁹⁾.

As an alternative to supporting a catalyst on a polymer bead a catalyst can be made into a dendrimer. This involves adding a branching organic compound to the catalyst one

layer at a time (in some respects these supported catalysts can be described as resembling a fractal diagram).

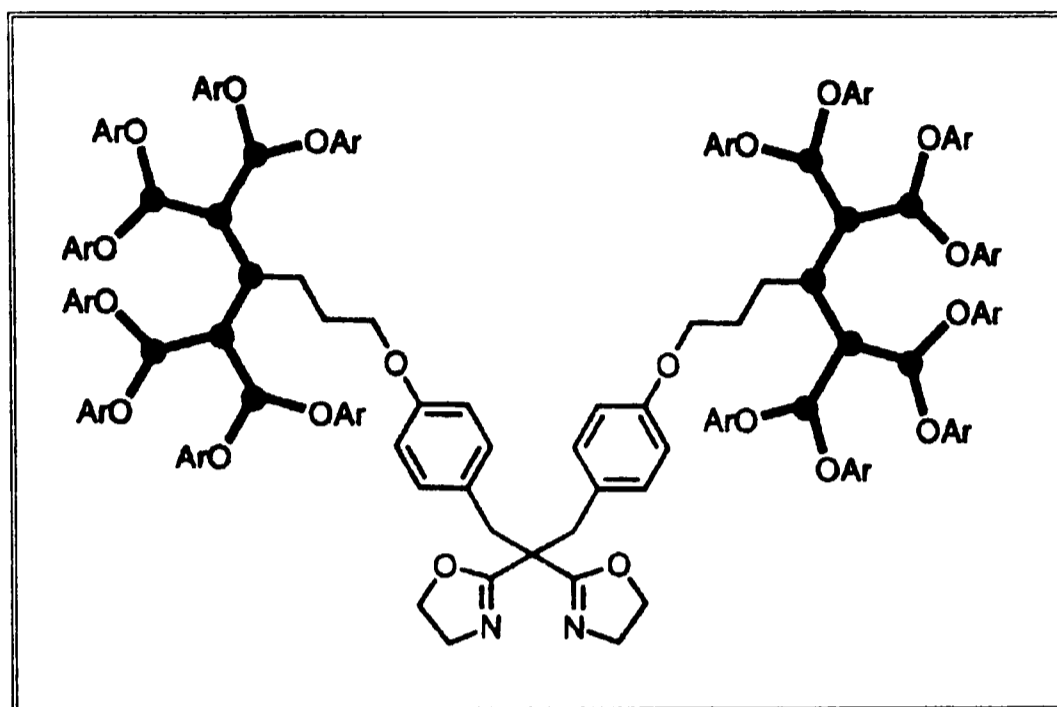


Figure 1.3.2.6: 3rd generation dendritic supported bis(oxazoline) catalyst ⁽⁷¹⁾

Differing generations of dendrimer can have a profound effect on the reactivity and stereoselectivity of the catalyst; this is caused by the steric constraints that the dendrimer places upon the active catalytic site. As the generation number increases so does the size of the supporting material until the catalytic site is completely encased within the dendrimer matrix. In the case of the dendrimer shown in Figure 1.3.2.6, which was used in the Diels-Alder reaction (Figure 1.3.2.4), the third generation showed a marked decrease in the rate of reaction compared with previous generations. This catalyst also showed an increase in selectivity compared with the homogeneous equivalent; this effect is believed to be caused by the dendrimer sterically hindering access to the active catalytic site. The authors felt that the increase in selectivity was not good enough for practical purposes, but that by modification of the dendrimer higher selectivities could be obtained ⁽⁷¹⁾.

1.3.3 Zeolites as catalyst supports

A second method of heterogenising homogeneous catalysts is to encapsulate the catalyst within a porous solid. This has been commonly used in the past, especially using zeolites as the supporting material. One common method is to synthesise an organometallic catalyst complex within the zeolite cage, the complex needs to be too large once assembled to fit through the passages interconnecting individual cages. Catalysts made by this method are often described as 'ship in a bottle catalysts'. An example of this is a manganese salen complex which has been trapped inside the pores of zeolite Y and used in the epoxidation of alkenes⁽⁴⁾. The catalyst complex (*ca.* 10-11Å) is smaller than the cages in zeolite Y (13Å), but is too large to escape through the interconnecting channels (7Å).

The supported catalyst reacts much slower than the homogeneous counterpart, with reaction time increasing from *ca.* 30 minutes to over 16 hours. The increase in reaction time is thought to be primarily due to the diffusion rate of reactants throughout the zeolite support. The supported catalyst showed increased selectivity towards *trans* products over *cis* products, based upon the size of the products, but also suffered from leaching of the manganese metal from the complex (approximately 20% of the metal leached out after 16 hours), and a decrease in catalytic activity associated with blocking of the zeolite pores.

1.3.4 Clays and layered materials as catalyst supports

A third method of supporting organometallic catalysts is by the use of clays or layered materials ^(72, 73). An example of a clay supported catalyst is a chiral bis(oxazoline) copper compound for use in cyclopropanation reactions ⁽⁷²⁾. In this case the catalyst complex was exchanged with the supporting clay to obtain a heterogeneous catalyst. The results showed that the supporting clay could have a large effect on the yield and selectivity. The rate of reaction was slower and lower yields were obtained when compared to the homogeneous catalyst in most cases. The main advantage of these catalysts is the ease of recoverability for reuse (although as the ligand is only held in by electrostatic interactions it does gradually leach out, causing deactivation).

Most layered clay materials used are either naturally occurring or are synthetic analogues of naturally occurring clays. Other layered structures may also be used as supports for catalysts - examples include an $Mg_5Al_{2.5}$ -layered double hydroxide which has been used to support (and stabilise) a cobalt (II) phthalocyaninetetrasulfonate catalyst. This catalyst is used for oxidation of organic molecules and the authors note the potential for use in water treatment ⁽⁷³⁾.

1.3.5 Mesoporous and amorphous silicas as catalyst supports

As we have already mentioned in Section 1.3.3 porous materials can be used as supports by trapping the catalyst within the pore of a caged structure such as a zeolite. These catalysts sometimes suffer from diffusion problems and can only be used for a limited range of reactants and products due to the size limitations imposed by the porous structure. Other

materials such as amorphous silica have been used as supports, but this often requires modification of either the support or catalyst to effectively bind the two together. Amorphous silica also suffers from a low surface area meaning that only a small amount of active catalyst can be supported on a solid. Some mesoporous materials, as we have discussed in Section 1.2, can often be considered as being similar to amorphous silica although with much higher surface areas, while others have a composition similar to zeolites which may enable the use of different binding strategies.

There are several methods for supporting catalysts within a mesoporous material. The first is to use ionic exchange to immobilise the catalyst onto the surface of the material ⁽⁷⁴⁾. Alternatively the metal complex may be grafted directly to the supporting material (Figure 1.3.5.1) ^(75, 76). This method will result in any organic ligand being leached out faster than the metal, so is useful for catalysts where the metal salt is particularly toxic or the organic ligand is commonly available.

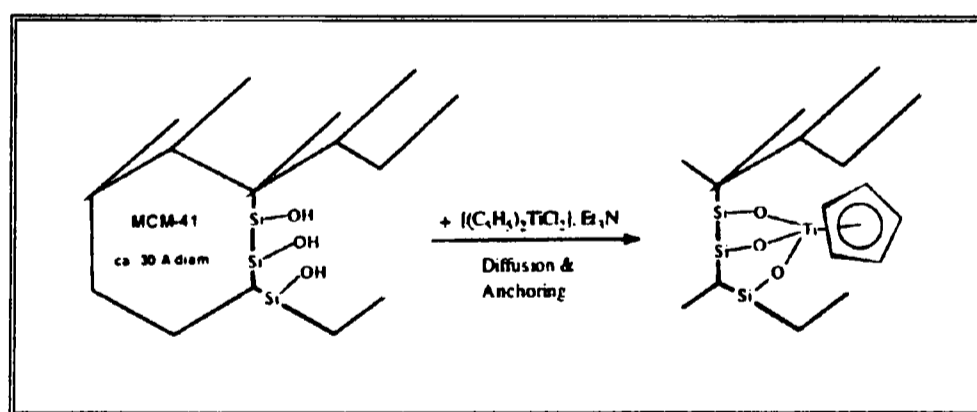


Figure 1.3.5.1: Titanium catalyst grafted onto MCM-41 ⁽⁷⁶⁾

A second method is to use interactions between counter ions and the surface to immobilise the catalyst complex on the surface. This method has been used to immobilise a rhodium catalyst on the surface of a mesoporous silica using hydrogen bonding between

triflate counter ions and surface silanols to bind the catalyst to the supporting matrix (Figure 1.3.5.2)⁽⁷⁷⁾. This is a simple and easy method for supporting catalysts, but care must be taken when choosing reaction conditions for catalysis, as the catalyst complex is only weakly bound to the surface and may be easily removed.

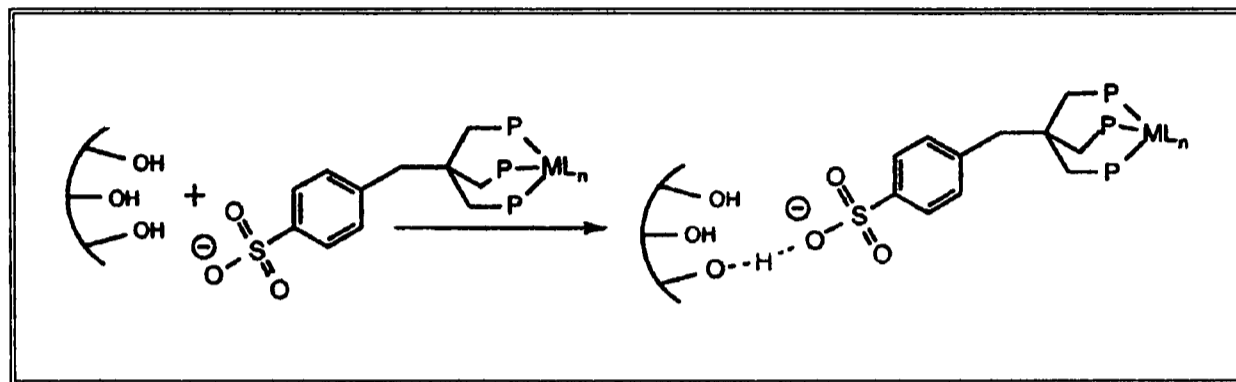


Figure 1.3.5.2: Catalyst bound *via* hydrogen bonding from counter ion⁽⁷⁷⁾

Catalyst complexes can also be bound to the surface of a supporting material using tethers, these tethers can either be attached to the ligand or the metal itself.

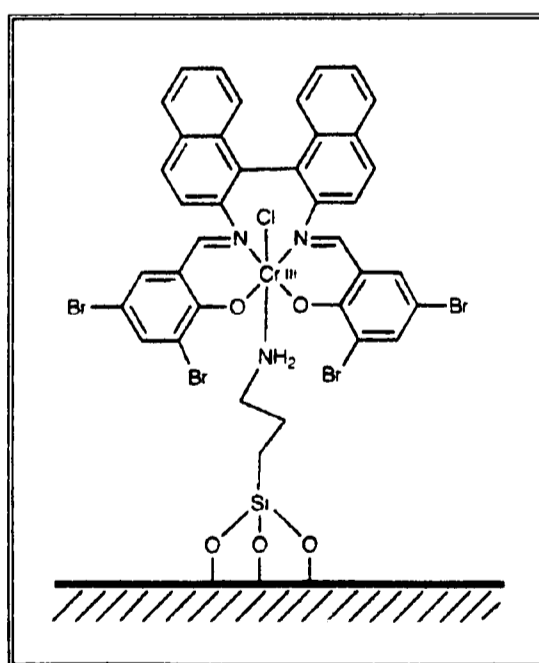


Figure 1.3.5.3: Catalyst complex immobilised *via* tether attached to metal centre⁽⁶⁶⁾

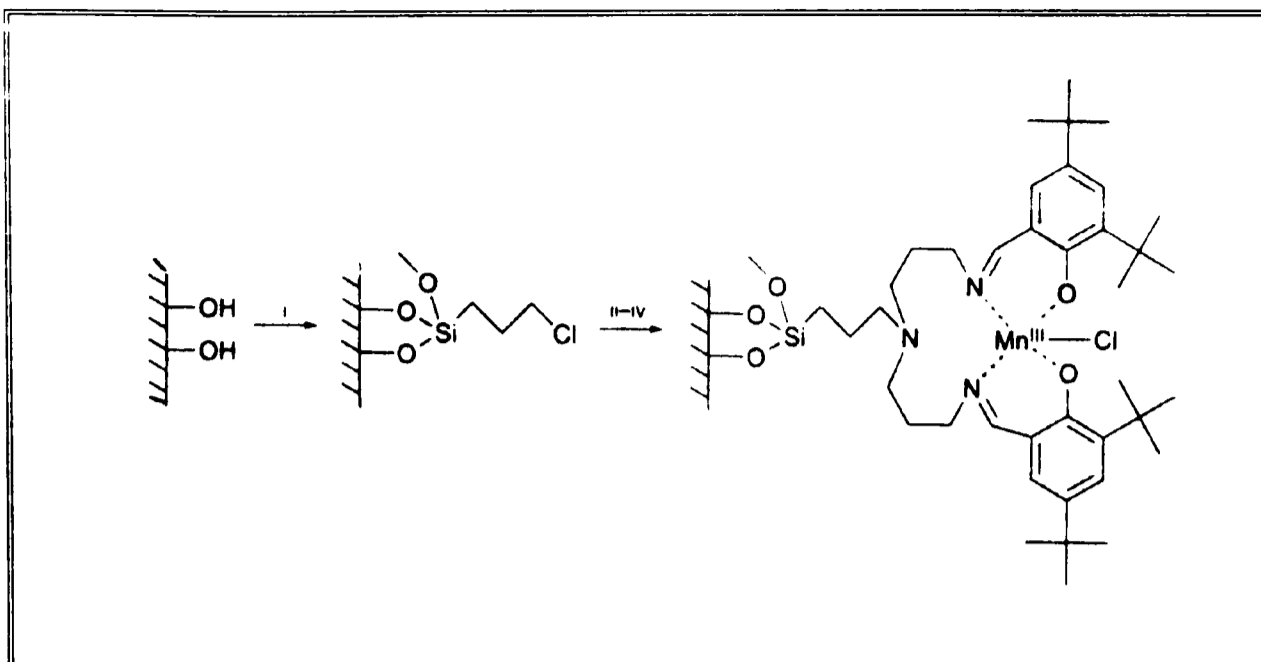


Figure 1.3.5.4: Catalyst complex immobilised *via* tether attached to ligand ⁽⁷⁸⁾

The use of tethers attached to the ligand is often harder and more expensive than other methods of immobilising catalyst complexes. This idea is particularly attractive though for chiral catalysts as the expensive part (the chiral organic ligand) is covalently attached directly to the support and is less likely to be leached out.

1.4 Bis(Oxazolines) as Ligands for Catalysis

1.4.1 History of Bis(oxazolines)

Bis(oxazoline) compounds have been known for more than 60 years ⁽⁷⁹⁾ but until recently very little work has been carried out using these compounds except as reagents for polymerisation ⁽⁸⁰⁾ or as part of the investigations into penicillin. They are related to semicorrins and salen type ligands (Figures 1.4.1.1 and 1.4.1.2) that have been used as ligands in organometallic catalysis for many years ^(68, 81, 82). An advantage that bis(oxazoline) ligands have over salen ligands is that they have a more rigid structure so it might be expected that they could have a greater effect on stereochemistry. It is therefore not surprising that people should look at bis(oxazolines) as an alternative source of new ligands for catalysts. As can be seen in the previous chapter some of these ligands have already been converted into heterogeneous catalysts by various methods.

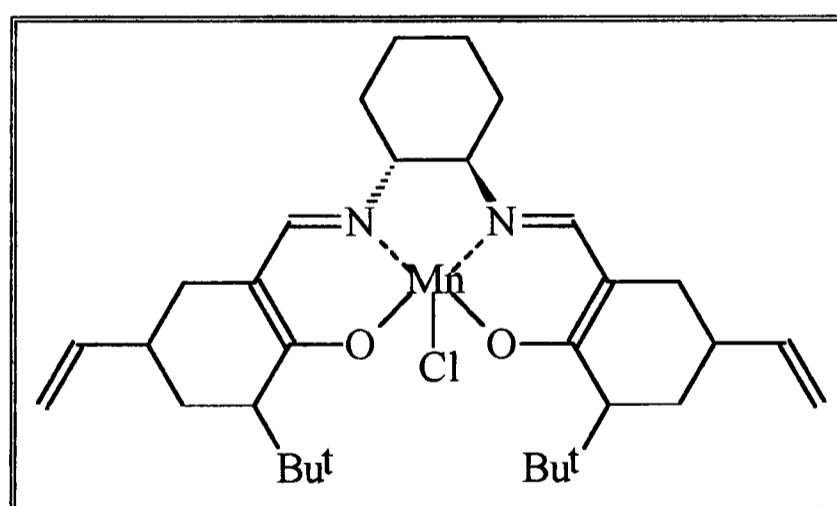


Figure 1.4.1.1: (R,R)-N,N'-Bis(3-*t*-butyl-5-vinylsalicylidene)-1,2-diphenyl-1,2-ethanediamine manganese (III) chloride complex (salen ligand complex) as used by Minutolo ⁽⁶⁸⁾

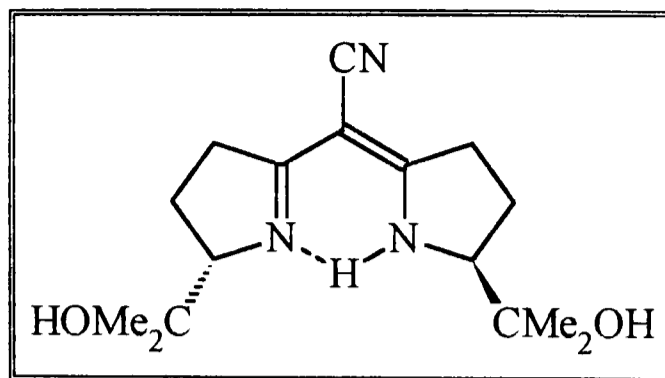


Figure 1.4.1.2: Semicorrin ligand as used by Pfaltz ⁽⁸²⁾

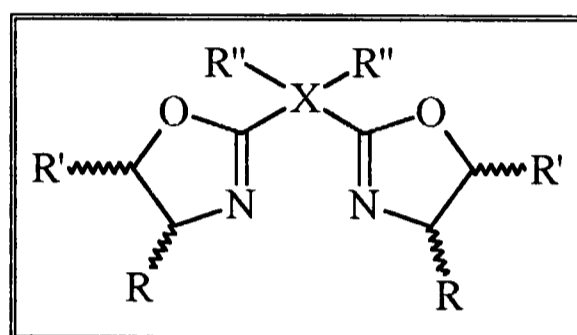


Figure 1.4.1.3: Bis(oxazoline) ligand (4 position =R, 5 position =R')

1.4.2 Structure of Bis(oxazolines)

From Figure 1.4.1.3 we can see that bis(oxazoline) ligands consist of three main parts which can be easily changed:

- ❖ The groups on the oxazoline rings (R and R')
- ❖ The groups attached to the bridge (R'')
- ❖ The organic bridge joining the oxazoline rings together (X)

In addition to these 3 aspects the number of oxazoline rings in the ligand can also be altered, of course it is then no longer a bis(oxazoline), but oxazoline ligands have been synthesised as unsymmetrical mono(oxazolines) ⁽⁸³⁾, and also as tris(oxazolines) ^(84, 85). However, we are primarily interested in bis(oxazolines) as ligands because of the large number of reactions that they have been shown to catalyse with good yield and selectivity.

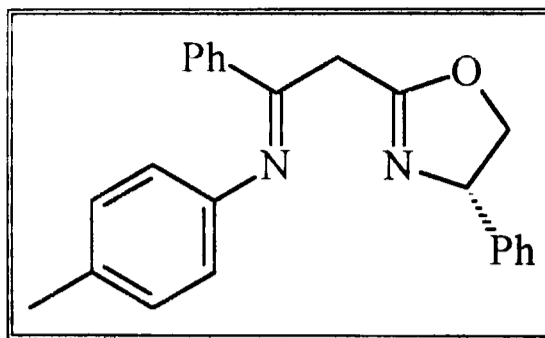


Figure 1.4.2.1: [1-phenyl-2-((4*S*)-phenyl-4,5-dihydrooxazol-2-yl)vinyl]-*p*-tolylamine ligand (mono(oxazoline) ligand) as used by Andersson ⁽⁸³⁾

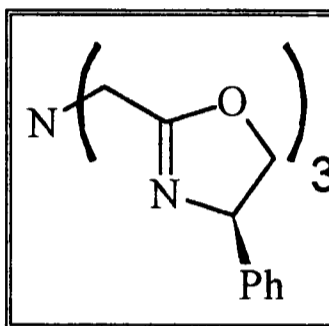


Figure 1.4.2.2: Tris(oxazoline) as used by Kohmura ⁽⁸⁴⁾

The first part of the ligand which can be altered, (in most cases research groups stick to using one family or group) is the organic bridge between the oxazoline rings. Various groups have investigated the effect that the length of the alkyl chain in the organic bridge (see Figure 1.4.1.3) has on the ligand ⁽⁸⁶⁾. One of the more commonly used bridging groups contains a 1 carbon spacer in between the two rings. It has been suggested that the reason that this is so successful is because when a metal is added to form a complex the resulting system forms a stable 6 membered ring. The alkyl organic bridging groups that have been tried vary from 0 - 3 carbons. In some cases an aromatic system such as a benzene ring, a pyridine (Figure 1.4.2.3) or even a polycyclic system (Figure 1.4.2.4) have been used to replace the alkyl chain.

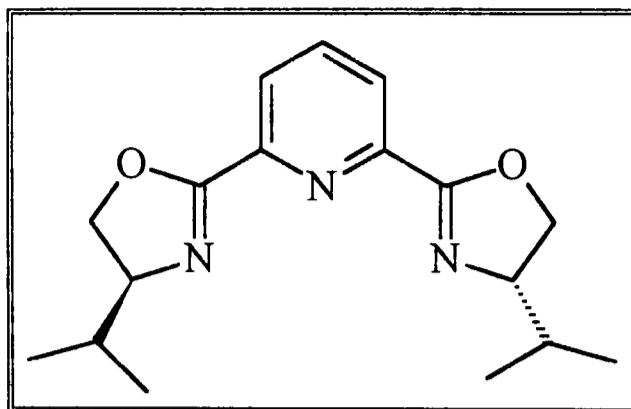


Figure 1.4.2.3: Pyridyl bis(oxazoline) as used by Pfaltz ⁽⁸⁷⁾

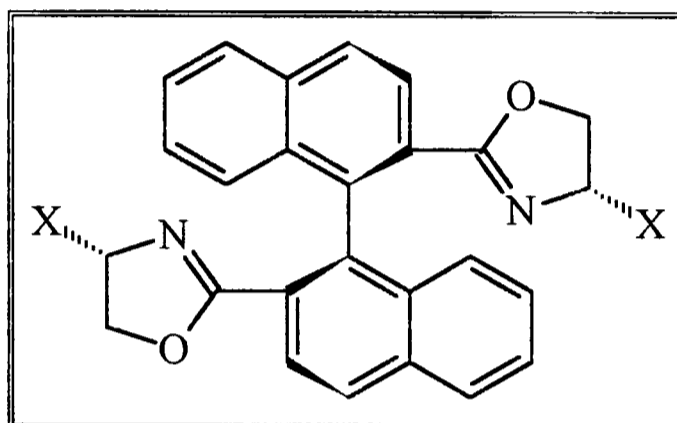


Figure 1.4.2.4: 2,2'-Bis(oxazolyl)-1,1'-binaphthyl ligand as used by Uozumi ⁽⁸⁸⁾

The second part of the ligand that may be altered are the organic groups on the oxazoline rings, which are very important, as this is where chirality is usually incorporated into the molecule. As with many chiral ligands much of the selectivity is caused by bulky organic groups forcing molecules co-ordinating to the active centre to adopt a specific configuration due to steric hindrance. The choice of organic functionalities that can be used is varied, but the most widely used groups for catalysis are all bulky such as phenyl, *iso*-propyl and *tertiary*-butyl groups, which have the necessary size to effectively direct the stereochemistry. Other than phenyl, *i*-propyl and *t*-butyl bis(oxazolines) one of the other ligands which has shown good results in catalysis reactions (these will be discussed later) and has been used repeatedly by various research groups contains both the 4 and 5 positions of the oxazoline ring linked together with an aromatic ring (Figure 1.4.2.5).

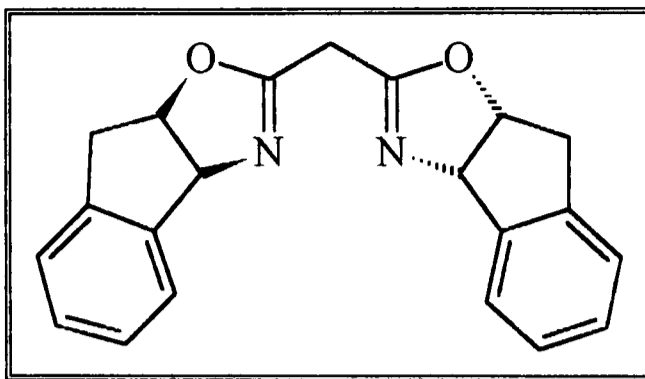


Figure 1.4.2.5: Inda-bis(oxazoline) ligand as used by Davies ⁽⁸⁶⁾

Computer modelling has been used to investigate the effect that different R groups in the 4 and 5 positions on the oxazoline ring have on the angle between the two nitrogens and a metal centre which is termed the bite angle ⁽⁸⁹⁾. A general trend could be seen where the catalysts with higher bite angles are those which exhibit greater selectivity.

The only limiting factor to the choice of R groups on the rings is that the groups in identical positions are usually the same as each other. This is because it is very difficult to make in a reasonable yield a material where the R groups in identical positions on the oxazoline ring are different from each other. Much of the work to make unsymmetrical bis(oxazolines) is directed towards synthesis of fragments of natural products with interesting properties ⁽⁹⁰⁾. The yields reported for these unsymmetrical ligands are below 50% per step, compared with over 88% over all yield for the standard symmetrical bis(oxazolines) ⁽⁹¹⁾.

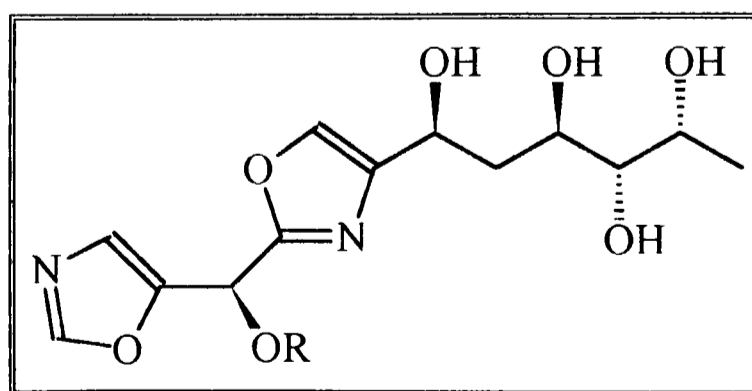


Figure 1.4.2.6: Bengazole A-G a natural bis(oxazoline) fragment ⁽⁹⁰⁾
R= Fatty acid

It has been acknowledged that it is not only the organic groups in the 4 position of the oxazoline ring that can have a profound effect on the selectivity of the final catalyst. The group in the 5 position of the oxazoline ring can also have a great influence on the selectivity of the ligand, especially if it is a large bulky group that can restrict the orientation that the reagents can adopt when interacting with the catalytic centre. An example of this is a 5,5-diaryl oxazoline with two bulky aromatic groups in the 5 position of each oxazoline ring where the usual preference for *trans* isomers in the cyclopropanation of styrene can be reversed *i.e.* preference for the *cis* isomer is found⁽⁹²⁾.

The final part of the ligand which can be altered easily are the groups attached to the bridge between the oxazoline rings. There are two main reasons for adding different groups in this position. The first is to try and promote better activity, whilst the other is to add functional groups so that the molecule can be reacted further. In homogeneous catalysts the most common change to these groups is to replace the original hydrogen groups with two methyl groups. This prevents the ligand rearranging by losing hydrogen from the bridge and donating electrons to the metal with which it is complexed. In effect this changes the ligand from an electron donating to a neutral ligand, meaning that the metal must find some other way of neutralising its charge.

1.4.3 Synthesis of Bis(oxazolines)

Various methods exist for the synthesis of bis(oxazoline) ligands. The most commonly used methods at present all use amino alcohols from the chiral pool to give an enantiomerically pure product. The R groups on the finished oxazoline ring can be almost

any group that can be synthesised with 1,2-aminoalcohol functionality. A few of the more popular methods are given below (Figures 1.4.3.1, 1.4.3.2 and 1.4.3.3).

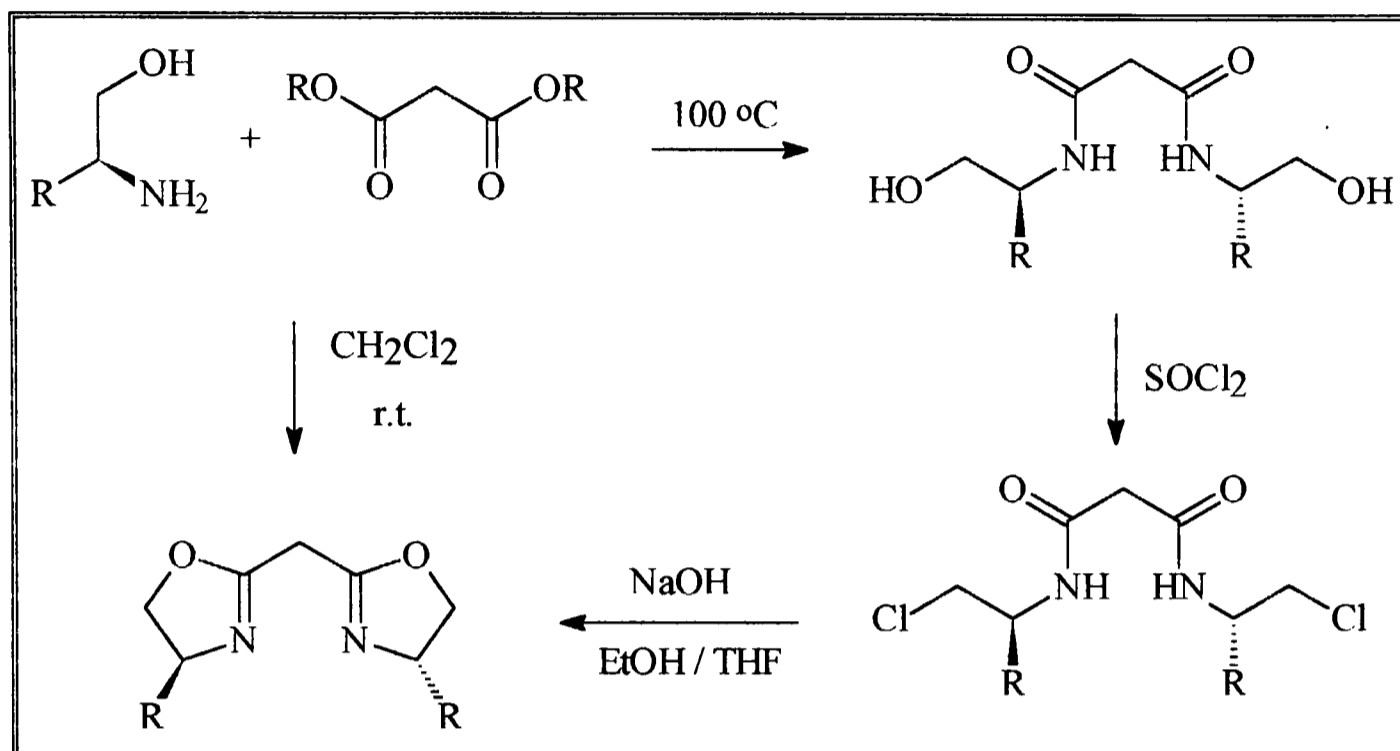


Figure 1.4.3.1: Bis(oxazoline) synthesis from malonic ester and amino alcohol (based on diagram from ref. 93)

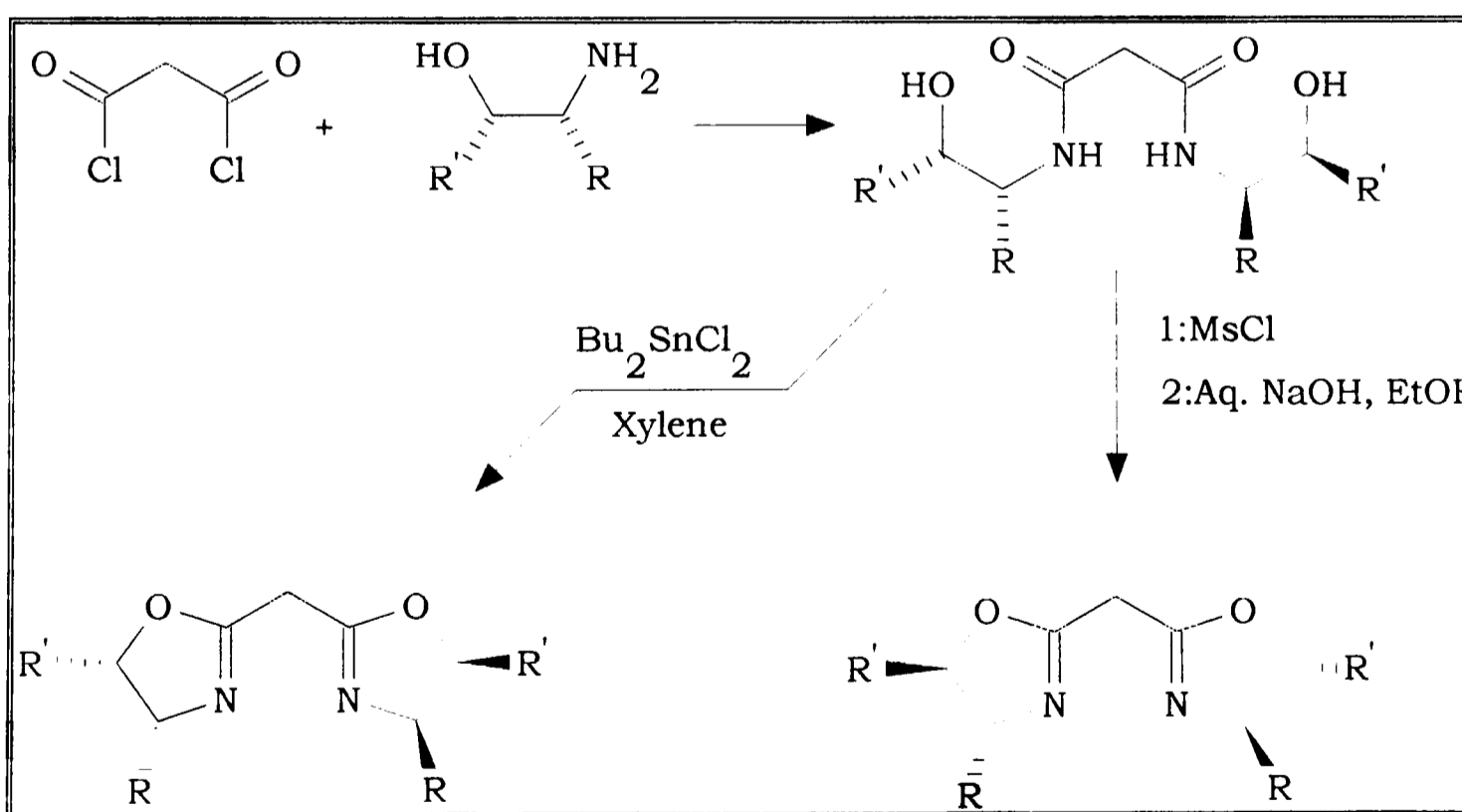


Figure 1.4.3.2: Bis(oxazoline) synthesis from malonyl dichloride and amino alcohol (reproduced from ref. 94)

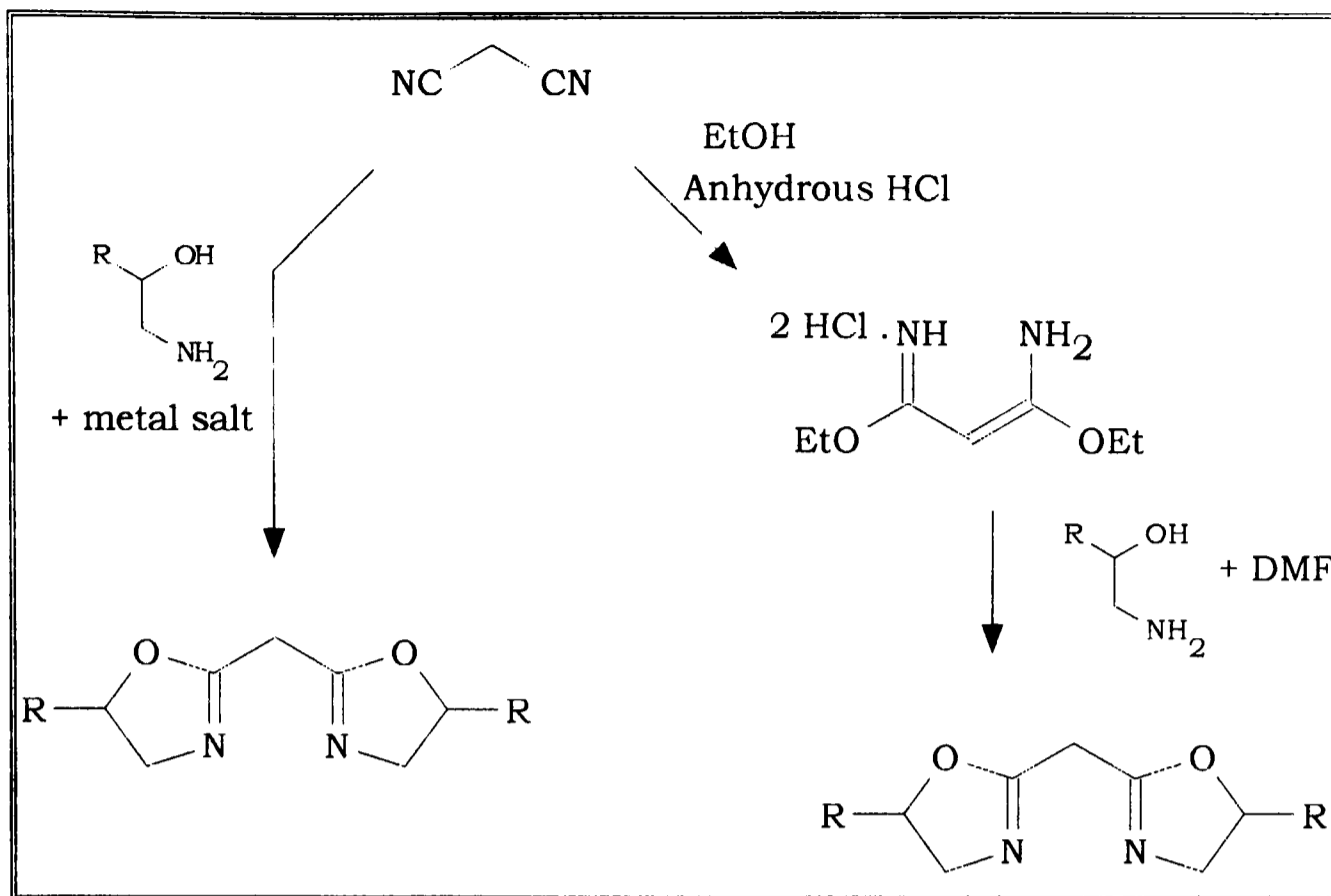


Figure 1.4.3.3: Bis(oxazoline) synthesis from malonylnitrile and amino alcohol^(based on diagram from ref. 94)

(N.B. For metal catalysed reactions with malonylnitrile see refs. 95 and 96)

In all of the above synthesis methods it is traditional to use a slight excess of the chiral amino alcohol (about 0.05 M *i.e.* 2.1 M amino alcohol: 1 M malonate). From the literature the most commonly used method for synthesising these ligands is to react an amino alcohol with malonyl dichloride to give the diamide complex (Figure 1.4.3.2). At this stage ring closure can be achieved *via* many different routes, with the two most common ones using thionyl chloride (Figure 1.4.3.1) or methane sulphonyl chloride (Figure 1.4.3.2 right hand route). It has been reported that methane sulphonyl chloride is better at closing oxazoline rings of more sterically hindered ligands than thionyl chloride⁽⁹⁷⁾.

Although malonyl dichloride is commercially available its extreme sensitivity to moisture makes it desirable to synthesise it as it is required from malonic acid. There are many papers which involve the synthesis of this intermediate^(98, 99, 100) some of which report up to 85% yield. The basic method is to heat malonic acid in thionyl chloride then distil the

malonyl dichloride under reduced pressure. To maximise yield in this reaction it is recommended that the malonic acid be finely powdered and that a conical flask is used to maximise surface area. It is also recommended that the reaction be heated gently to reduce charring⁽⁹⁸⁾.

The second most widely quoted method is the Masamune protocol (Figure 1.4.3.2 left hand route) which refluxes a malonate ester with an amino alcohol to form the diamide and then uses dichlorodimethyl stannane to close the oxazoline rings. The ring closure *via* this method gives retention of the stereochemistry at the 5 position of the ring whilst most other methods give inversion. All of the methods mentioned above give good yield of bis(oxazoline) in the literature (*ca.* 60 – 80 %).

The synthesis from malonylnitrile using a catalytic amount of a metal salt is not commonly used. Typically the reagents are refluxed in toluene under nitrogen with a catalytic amount of metal salt (usually zinc (II) chloride) to give the final bis(oxazoline) ligand. In some cases the product recovered was found to be a mix of isomers meaning that extra care must be taken with this method⁽⁹⁶⁾.

1.4.4 Metal complexes of bis(oxazolines)

Bis(oxazolines) are ideal materials to be reacted with metals to form complexes, part of this is due to the structure of many of the commonly used ligands meaning that stable six membered rings can be formed. The metal complexes are very easy to synthesise, merely requiring the ligand to be mixed in solution with an appropriate metal salt. Depending on the ratio of ligand to metal, mono or di-complexes can be formed (Figures 1.4.4.1 and 1.4.4.2). The vast majority of complexes are formed are mono-complexes as these can be made with

all types of bis(oxazoline) ligand, whereas the di-complexes usually require a charged bis(oxazoline) ligand. In some cases both the mono- and di- complexes have been shown to catalyse the same reaction with good reactivity and selectivity.

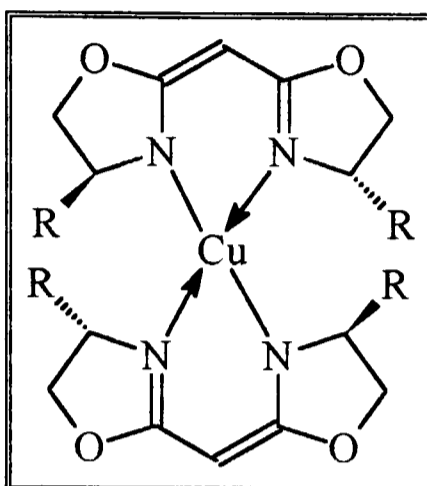


Figure 1.4.4.1: Structure of the di-bis(oxazoline) copper (II) complex as proposed by Masamune (R=Phenyl, *t*-butyl, *i*-propyl) ⁽⁹¹⁾

As mentioned in Section 1.4.2 bis(oxazoline) ligands can be either electron donating or neutral depending upon the groups on the bridge between the oxazoline rings. Where the ligand is neutral the ligand usually forms a mono-complex with the metal, as a counter ion is still required to balance the charge (Figure 1.4.4.2).

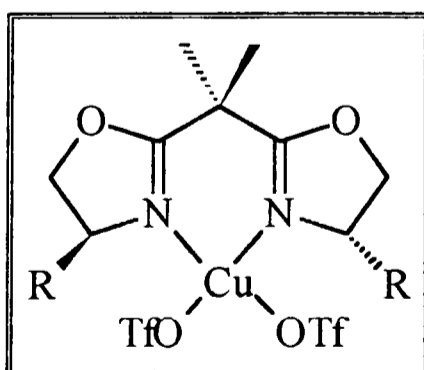


Figure 1.4.4.2: Structure of the mono-bis(oxazoline) copper (II) triflate complex as used by Jorgensen (R=phenyl, *t*-butyl) ⁽¹⁰¹⁾

Complexes can be formed with a wide variety of metals including Cobalt⁽¹⁰²⁾, Copper^(103, 104), Europium⁽¹⁰²⁾, Iron^(70, 105), Lanthanum⁽¹⁰²⁾, Magnesium⁽⁷⁰⁾, Palladium^(96, 106), Nickel⁽⁹⁶⁾, Ruthenium⁽¹⁰⁷⁾, Scandium⁽¹⁰²⁾, Ytterbium⁽¹⁰²⁾ and Zinc^(108, 109).

1.4.5 Catalysis by bis(oxazoline) complexes

Since the 1990's it has been reported that bis(oxazoline) metal complexes can act as stereoselective catalysts for a variety of important organic reactions (for reviews see refs. 94 and 110). Some examples include the use of Cu complexes for cyclopropanations^(91, 93, 103, 104), Diels-Alder reactions^(70, 86) Hetero Diels-Alder reactions⁽¹⁰¹⁾, Michael additions⁽¹¹⁰⁾, Allylic oxidations⁽¹¹¹⁾ and the synthesis of aziridines⁽¹¹²⁾. Pd complexes have been used for allylic substitutions⁽¹⁰⁶⁾, Ru complexes for epoxidations⁽¹⁰⁷⁾ and hydrosilation reactions⁽¹¹³⁾. Zn complexes for Allylation reactions⁽¹⁰⁸⁾, Fe^(70, 105) and Mg⁽⁷⁰⁾ complexes have also been reported as catalysing Diels-Alder reactions. Complexes with Mg, Ni, Co, Zn, Sc and Ce have also been tested for the Mukaiyama-Michael reaction (Figure 1.4.5.1) with varying degrees of success⁽¹⁰²⁾.

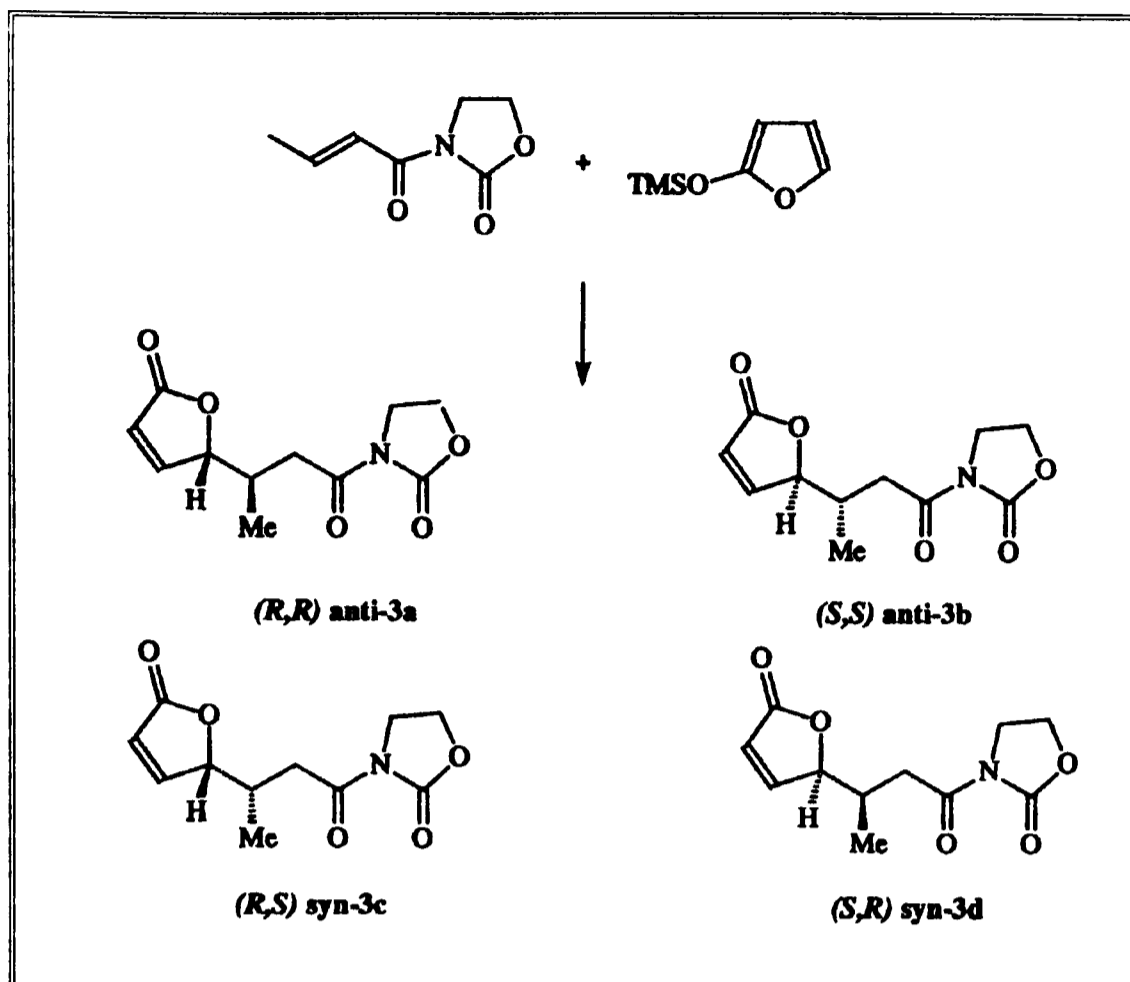


Figure 1.4.5.1: Mukaiyama-Michael reaction between (E)-3-crotonyl-1,3-oxazolidin-2-one and 2-trimethylsilyloxyfuran ⁽¹⁰²⁾

The two reactions that appear most often in papers on catalysis using bis(oxazoline) ligands are the cyclopropanation of styrene with ethyldiazoacetate (Figure 1.4.5.2), and the Diels-Alder reaction between 3-acryloyl-1,3-oxazolidin-2-one and cyclopentadiene (Figure 1.4.5.3).

Cyclopropanation reaction

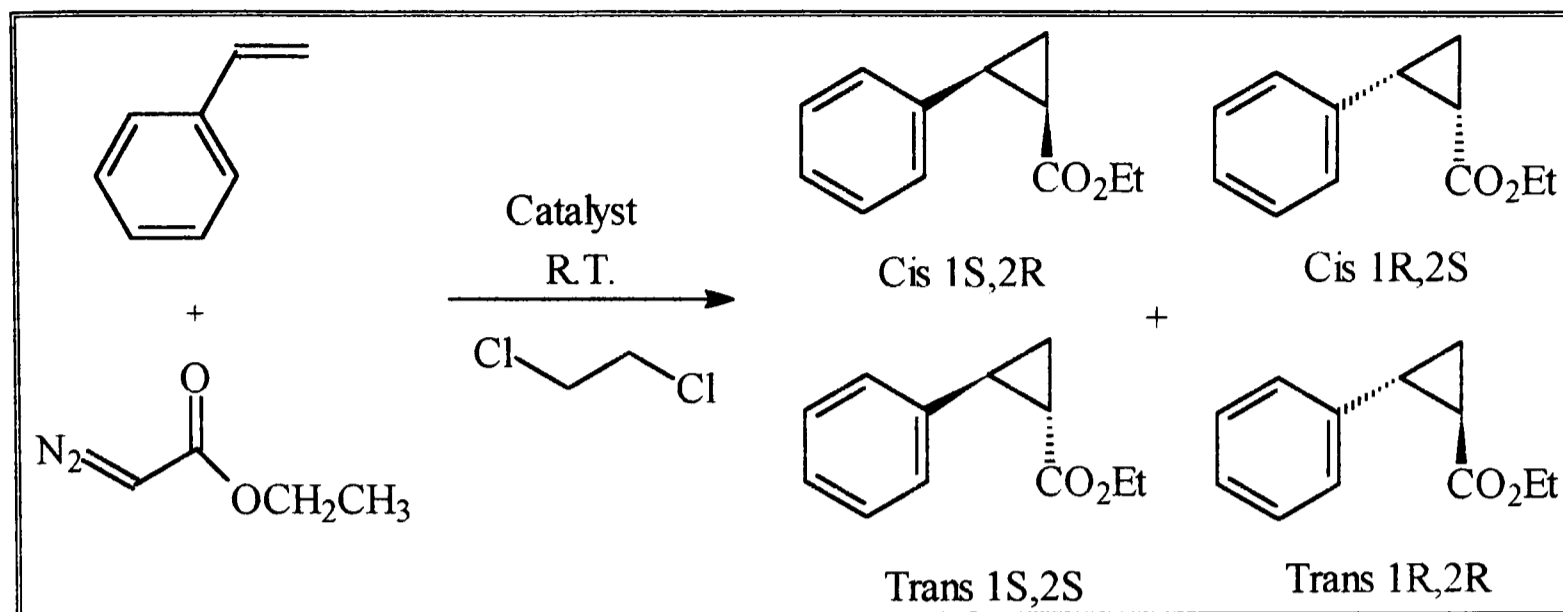


Figure 1.4.5.2: Cyclopropanation of styrene with ethyldiazoacetate⁽⁹¹⁾

The standard benchmark cyclopropanation used to test catalytic reactivity for this reaction is the reaction between styrene and ethyldiazoacetate (Figure 1.4.5.2). This reaction usually produces 4 main products as well as 2 side products formed by the dimerisation of the diazoacetate. The main products are the 4 isomers of ethyl 2-phenylcyclopropane carboxylate, of which two are *trans* (1*R*, 2*R* and 1*S*, 2*S*) and two *cis* (1*R*, 2*S* and 1*S*, 2*R*). With bis(oxazoline) ligands the metal usually used for this reaction is copper, as it has been known for as least 20 years that it is a suitable catalyst for this reaction⁽¹¹⁴⁾. Early experiments to synthesise chiral cyclopropanes used chiral diazoacetates to incorporate chirality into the molecule⁽¹¹⁵⁾. Whilst both copper (I) and copper (II) complexes have been used to catalyse this reaction, it is generally accepted that the active catalytic species is a copper (I) complex⁽¹¹⁴⁾. Therefore, although copper (II) is much more stable and the complexes can be easily stored, an activating agent such as phenylhydrazine is required to convert it into a copper (I) species prior to commencing the reaction.

Typically an excess of styrene and slow addition of the diazoacetate is used to maximise the yield of cyclopropanes by reducing the amount of side products produced.

Some of the best results obtained to date use a di-complex (Figure 1.4.4.1, R=*t*-butyl)⁽⁹¹⁾. This catalyst gave an 80% yield with a *trans*: *cis* selectivity of 3:1, and enantiomeric excesses for the individual stereoisomers of 90% for the *trans* isomers and 77% for the *cis*. The best results using a mono complex⁽¹⁰³⁾ use 2,2'-isopropylidenebis(4-*t*-butyl-2-oxazoline) as a ligand with a copper triflate (trifluoromethane sulphonate) salt (Figure 1.4.4.2, R=*t*-butyl). This catalyst gave comparable yield (77%) to the di-complex above, slightly worse stereoselectivity (73:27 *trans*: *cis*) but better enantioselectivity (99 and 97% respectively).

As it is easy to obtain both isomers of an amino alcohol it is easy to synthesise a bis(oxazoline) ligand to give the opposite enantioselectivity, although adding bulky groups to the 5 position on the oxazoline ring sometimes has the effect of driving selectivity in the opposite direction and can result in lower enantiomeric excess. They can also in some cases alter the stereoselectivity to show a preference for the *cis* isomer to be formed⁽⁹²⁾. Ligands with a 1-carbon spacer as a bridge normally show a preference for the *trans* isomers to be formed. However, where the oxazoline rings are directly linked without a bridging group (Figure 1.4.5.3, R=cyclohexyl) a large preference (over 2:1) was shown for the *cis* isomer⁽¹¹⁶⁾. Unfortunately the enantiomeric excesses for this ligand were very poor in comparison to the more usual bis(oxazoline) ligands where a bridging group is used.

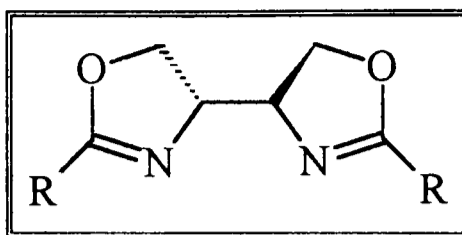


Figure 1.4.5.3: Bis(oxazoline) ligand as used by Mosset and Saalfrank

(R=*t*-butyl, cyclohexyl, phenyl, adamantyl)⁽¹¹⁶⁾

Diels-Alder reaction

A second reaction which has been shown to be catalysed by bis(oxazoline) ligands and has attracted a great deal of attention is the Diels-Alder reaction. The most common form of test for selectivity is the reaction between 3-acryloyl-1,3-oxazolidine-2-one and cyclopentadiene (Figure 1.4.5.4). The products from this reaction have been used as the basis for attempts at synthesising natural product fragments which have shown interesting antiinsectal properties⁽¹¹⁷⁾. The Diels-Alder reaction is especially important as it is one of the main carbon-carbon bond forming reactions used in organic chemistry.

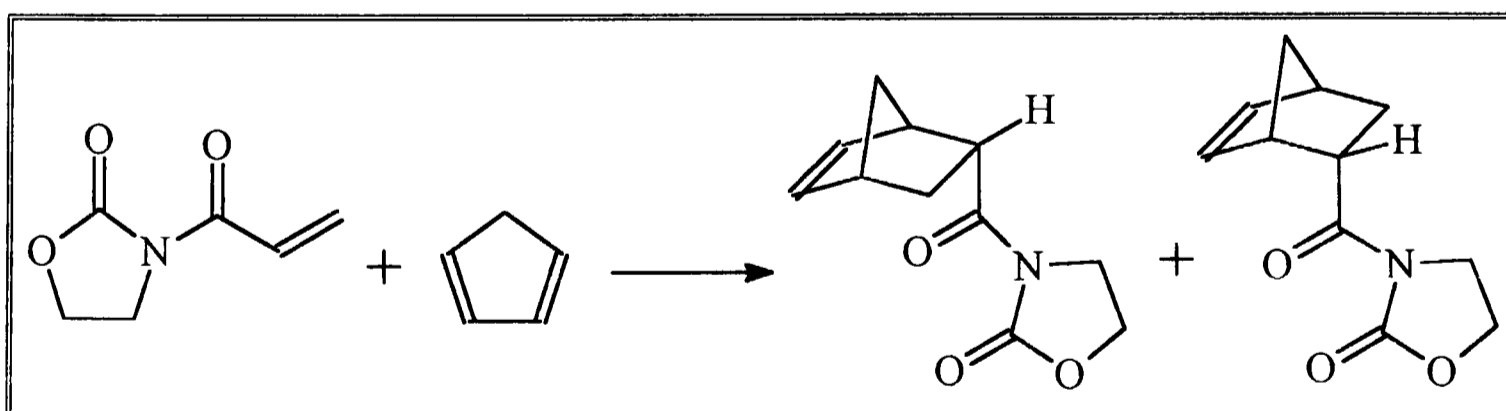


Figure 1.4.5.4: Diels-Alder reaction between 3-acryloyl-1,3-oxazolidine-2-one and cyclopentadiene⁽⁷⁰⁾

Bis(oxazoline) metal complexes have been shown to catalyse the Diels-Alder reaction with a number of different metals. Some of the metals that have been used include copper

⁽⁸⁶⁾, cobalt ⁽¹¹⁸⁾, iron ⁽¹⁰⁵⁾, magnesium ⁽⁷⁰⁾, and zinc ⁽¹¹⁸⁾. Unlike the cyclopropanation reaction, however, only single ligand complexes are used to catalyse this reaction, and the ligands used are in their neutral form. As with the cyclopropanation reaction described previously the majority of the ligands which show the best selectivity all have bulky groups in the 4 position on the oxazoline ring.

The best results to date have been derived from using the neutral (S)-2,2'-isopropylidenebis(4-*t*-butyl-2-oxazoline) ligand and copper (II) triflate (Figure 1.4.4.2, R=*t*-butyl). This gave 86% yield with 98% of the product being the endo form, and also giving over 98% enantioselectivity ^(70, 118). As with all catalysts, changing the metal will alter the activity and may require a different ligand to achieve the best results. This is certainly the case with these ligands; the neutral ligand (R=phenyl) only gives 30% enantioselectivity when used with copper, but gives up to 80% ee with iron. In some cases, when using magnesium based systems, a co-catalyst such as AgSbF₆ was found to improve the selectivity ⁽¹¹⁹⁾.

It has been shown that the co-ordination of the metal centre plays a vital part in determining the selectivity in this reaction. With a catalyst formed from magnesium perchlorate and the neutral (*R*)-2,2'-isopropylidene-bis(4-phenyl-2-oxazoline) both the *S* and *R* enantiomers can be obtained as the major enantiomer. With a dry catalyst, which forms a tetrahedral complex, the *S* enantiomer is obtained with 70% ee. If the catalyst is formed with 2 equivalents of water present an octahedral complex is formed and the *R* enantiomer is synthesised with up to 65% ee ⁽⁷⁰⁾.

Allylic oxidation (Karash Sosnovsky reaction)

The Karash Sosnovsky reaction, also described as the allylic oxidation of olefins, is essentially the decomposition of a perester and its reaction with an alkene at high temperature (<80°C), which was first described in 1958⁽¹²⁰⁾. The original papers show that at this time it was known that the reaction was catalysed by copper or cobalt salts such as halides or ethylhexoate.

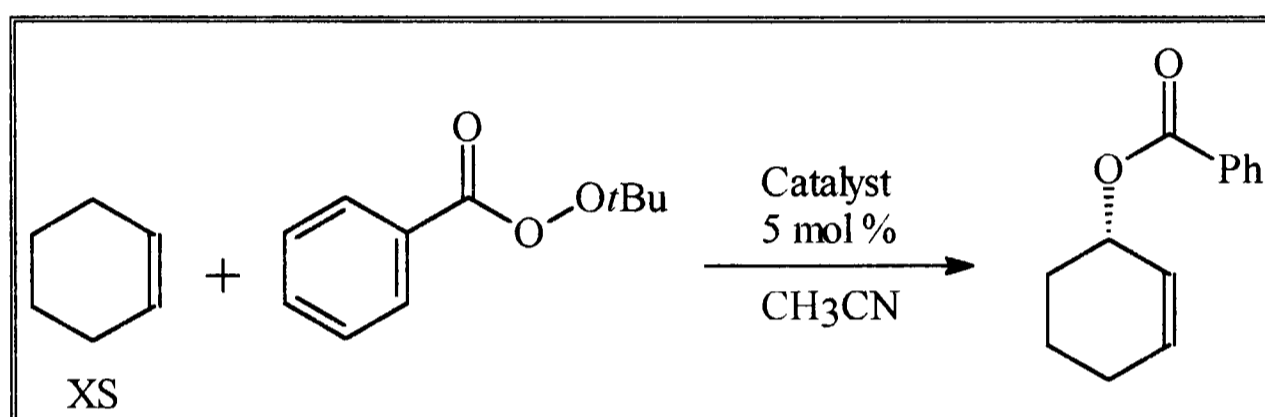


Figure 1.4.5.5: Kharasch Sosnovsky reaction between cyclohexene and *t*-butyl perbenzoate

In these early papers it is unsurprising that there is no reference to chirality as no ligands with structure directing capabilities were employed in these reactions. In refluxing benzene with a 2.5 fold excess of the alkene (cyclohexene) and *t*-butyl perbenzoate, a yield of 77% was reported⁽¹²¹⁾. The idea of using this reaction to give chiral products again is not a new idea, in the 1960's it was discovered that if an optically active copper salt such as copper α -ethyl camphorate was used as the catalyst, then in some cases the product also showed some optical rotation⁽¹²²⁾. The degree of rotation was determined by converting the product ester into an alcohol and measuring its rotation. The amount of induced rotation in the product material was very small in comparison to the pure single isomers.

This reaction was re-examined in 1995 using chiral bis(oxazoline) ligands such as the 2,2'-isopropylidene-bis(4-*t*-butyl-2-oxazoline) and copper (II) triflate (Figure 1.4.4.2)^(123, 124) and some pyridal bis(oxazoline) ligands (Figure 1.4.2.3)⁽¹²⁵⁾. With these ligands yields of up to 58% with enantioselectivities of 81% have been reported using cyclohexene as the alkene⁽¹²⁵⁾. The reaction conditions used today use much lower temperatures than in the original synthesis (rt. compared with 80°C). The modern synthesis methods at the lower temperature result in lower yield of product compared to the original synthesis (35-63% vs. 70%).

Allylation of aldehydes and ketones

The allylation of aldehydes and ketones is yet another important reaction frequently used by organic chemists to make their desired products. This reaction is very slow unless an activating agent such as either a Lewis acid or a catalyst is used⁽¹²⁶⁾.

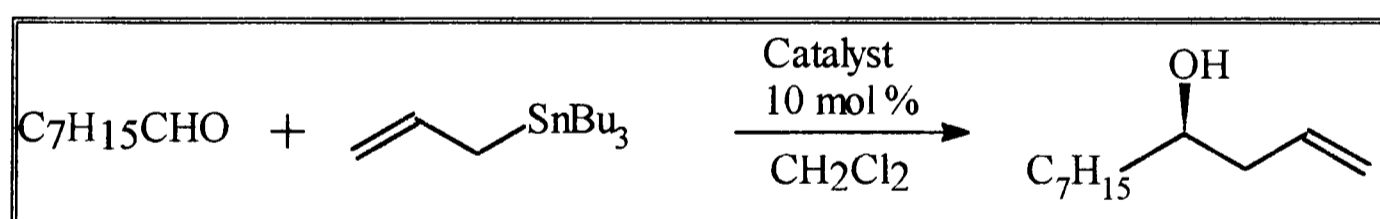


Figure 1.4.5.6: Allylation of octanal with allylstannane⁽¹²⁷⁾

The reaction between octanal and allyltri-*n*-butyl tin (Figure 1.4.5.6) has been tested with a variety of bis(oxazoline) ligands and metals⁽¹²⁷⁾. With a common bis(oxazoline) ligand [methylenebis(4-*S*-phenyl-2-oxazoline)] a large number of metals were shown to catalyse the reaction, but in most cases enantioselectivity was very low or non-existent. The exception to this was zinc, which gave consistent enantioselectivity of 40% irrespective of the

counter ion used. Conversely it is clear that the counter ion plays a very important part in the yield, which improves from 10% to 78% upon changing from chloride to iodide ⁽¹²⁷⁾.

However all of these catalysts are homogeneous, and so additional steps are required to remove the catalyst from the product.

1.5 Supported Bis(oxazoline) catalysts

1.5.1 Introduction to supported bis(oxazolines)

Bis(oxazoline) complexes have been known to catalyse many organic reactions for a long period of time (see Section 1.4). As has already been mentioned these ligands are related to the salen and semicorrin type ligands, which have already been supported upon various solid supports^(66, 68, 78). As many of the reactions that bis(oxazolines) have been shown to catalyse require high ratios of catalyst to substrate, using these ligands can be expensive. The next obvious stage in the development of bis(oxazoline) catalysts is to support them on a wide range of solids to try to make them easier to handle and to make recovery and reuse possible. There are many variations on the methods by which a bis(oxazoline) ligand may be supported, but essentially these may be grouped into four methods;

1. Covalent bonding at the bridging position (where it has been shown there is little effect on the selectivity).
2. Ion exchange to bind the metal to a suitable support.
3. Use weak binding forces to hold the catalyst on the supporting matrix.
4. Size exclusion or 'ship in a bottle' catalysts.

When this project was started this field was still in its infancy, with very few papers on supported bis(oxazoline) catalyst systems. The first papers on supported Bis(oxazoline) catalysts came out in 1997, one of which involved use of a dendrimer as a support⁽⁷¹⁾, and the second involved immobilisation by cationic exchange with clays⁽¹²⁸⁾. In recent years many more groups have started to work in this field covering a much wider array of supports and

supporting methodologies. Much of the recent work is not covered in this Chapter due to the recent nature of the publications and the increasing proliferation of publications in the field, although a review on heterogeneous bis(oxazoline) catalysts has recently been published⁽¹²⁹⁾.

1.5.2 Dendritic bis(oxazolines)

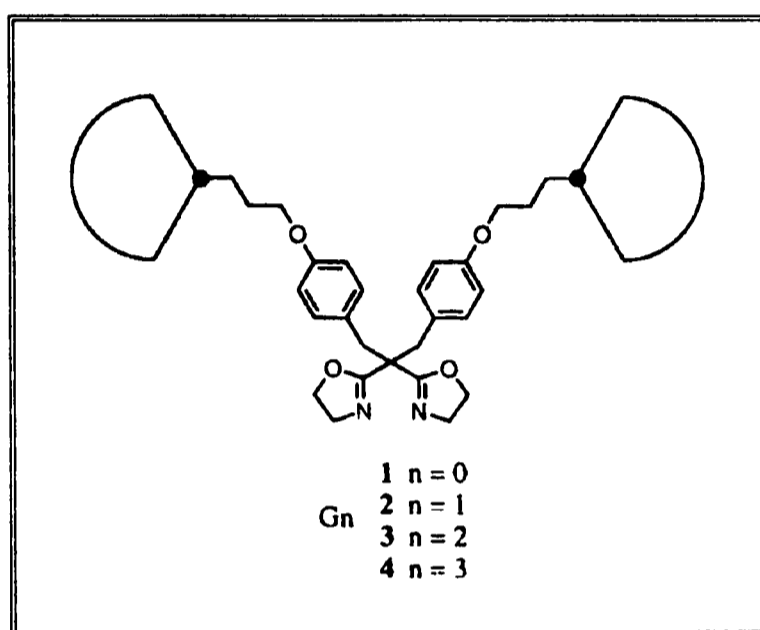


Figure 1.5.2.1. Dendritic bis(oxazoline) ligand as used by Chow⁽⁷¹⁾

In one of the earliest papers relating to bis(oxazoline) catalysts supported using dendrimers⁽⁷¹⁾, in which the catalysts prepared were tested for Diels-Alder reactions, the primary concern was with the effect that each succeeding generation of dendrimer had on the rate of reaction. Unlike most of the later papers on heterogeneous bis(oxazoline) catalysts it does not use a chiral ligand. The choice of ligand is even more unusual as there are no organic functionalities at all upon the 4 or 5 positions on the oxazoline ring (Figure 1.5.2.1). The catalysts developed showed that the rate of reaction dropped sharply for the 3rd generation dendrimers, but also that some selectivity based upon size was marginally improved. This is believed to be caused by the size of the dendritic host itself, as the authors concluded that in the early generations of dendrimer the catalytic centres were on the outside

surface. As the dendrimer increases in size the catalyst becomes embedded within the matrix which has the effect of impeding the diffusion of the reagents to the catalytic centre, and imposing steric limits upon the products of the reaction.

1.5.3 Polymeric Bis(oxazoline) systems

Organic supports have been used by creating polymer bound bis(oxazoline) ligands, either by direct synthesis of polymeric bis(oxazolines) ^(130, 131) or by grafting to commercially available polymeric beads ^(69, 131, 132). Soluble polymers have also been used so that the reactions can be carried out almost homogeneously, but the catalyst can still be recovered and reused ⁽¹³³⁾.

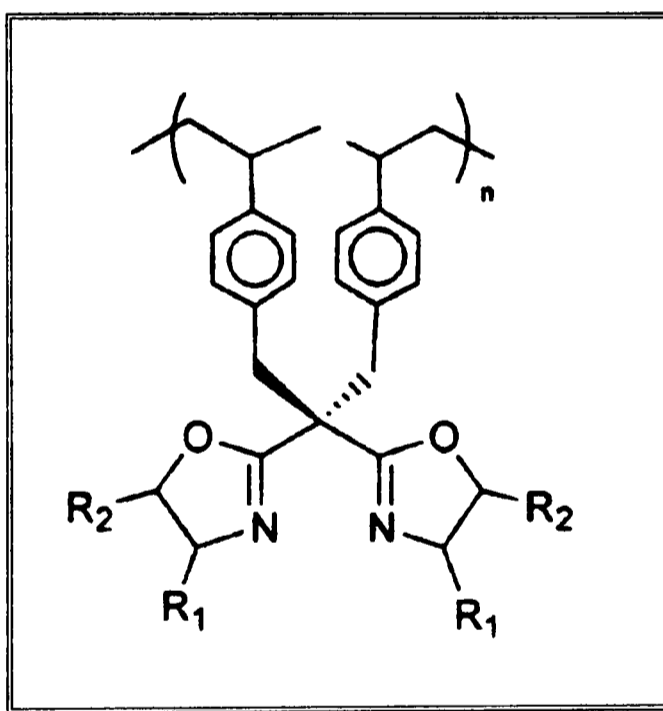


Figure 1.5.3.1: Polymeric bis(oxazoline) ligand as used by Luis and Mayoral ⁽¹³⁰⁾

R₁ = *t*-butyl or phenyl, R₂ = H or R₁, R₂ = inda group (see Figure 1.4.2.5)

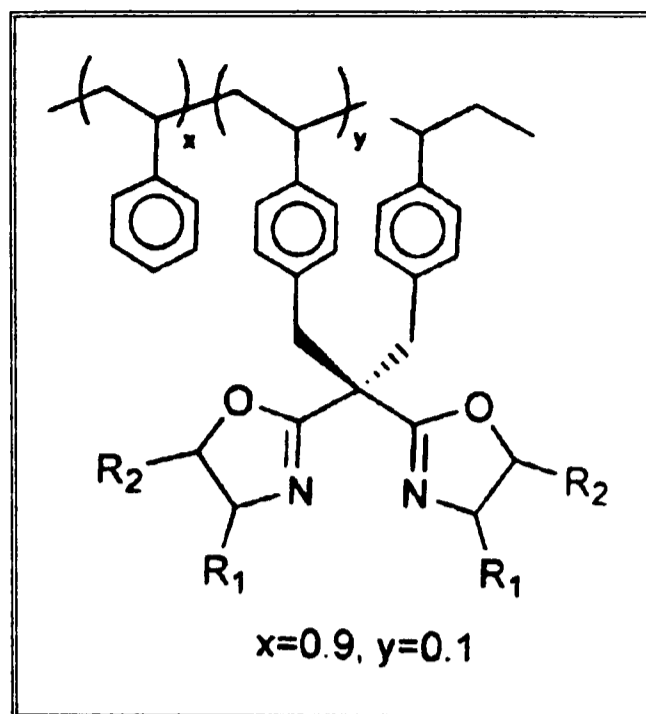


Figure 1.5.3.2: Polymeric bis(oxazoline) ligand as used by Luis and Mayoral ⁽¹³⁰⁾

$R_1 = t$ -butyl or phenyl, $R_2 = H$ or R_1 , $R_2 =$ inda group (see Figure 1.4.2.5)

The method of direct synthesis is fairly straightforward. The bis(oxazoline) ligand is modified so that terminal styrene groups occupy the positions on the bridging group which makes the ligand easily polymerisable. The polymers used are frequently styrene based, with some utilising self polymerisation and others with added reagents to make them porous using radical initiation. Some of these catalysts gave good results when compared to the homogeneous equivalents (with toluyl groups upon the bridge) for cyclopropanation reactions. The basic self-polymers gave enantioselectivities which were only slightly higher than those observed for the homogenous catalyst (51% ee compared with 50% for the *trans* isomer [Figure 1.5.3.1, $R_1 =$ phenyl]). Those using toluene or dodecanol as porogenic agents showed higher selectivities than were observed for the homogeneous catalyst complex (61% ee using toluene as a porogenic agent). The unsymmetrical polymers (Figure 1.5.3.2, $R_1 =$ phenyl) showed only a slight reduction in the enantioselectivity of the products (46% compared to 50%). In all cases, these polymeric catalysts showed lower selectivity in the *cis* and *trans* isomeric ratio than the homogeneous catalyst, although in one case the usual

preference was actually slightly reversed (*trans: cis* 70:30 for the homogeneous and 47:53 for the homopolymer).

When a cross-linking agent was also added to the mixture the enantioselectivity of the products was vastly reduced (down from 50% to either 18% or 8% depending on the cross-linking agent)⁽¹³¹⁾. The cross-linked polymers also have a disadvantage, as the cyclopropanation must be carried out at elevated temperatures in order to obtain sufficient yield. From these results it is clear that for these polymeric ligands that the polymer has a large effect upon the catalyst system, with a porous polymer seeming to be much better than a cross-linked one, or even a homo polymerised one. A theory has been proposed that part of the change in selectivity is related to the loading of catalyst upon the support. It proposes that lower catalyst loading can lead to higher selectivity by reducing unfavourable steric interactions between catalyst complexes. A decrease in selectivity would be expected for catalytic systems where the active sites are not sufficiently isolated and interaction between separate catalyst sites can occur⁽¹²⁹⁾. This could pose a dilemma for industrial usage of supported bis(oxazoline) systems due to competing demands of yield and turnover rate per gram of catalyst verses selectivity.

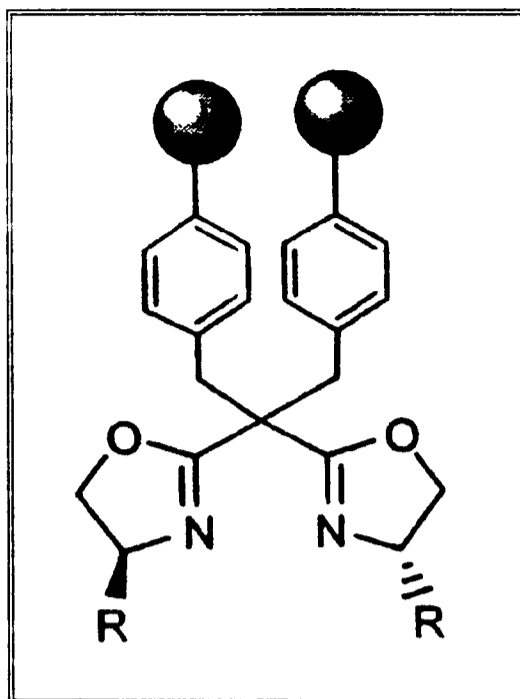


Figure 1.5.3.3: Bis(oxazoline) ligand supported on polymer beads as used by Mayoral ⁽¹³⁴⁾

The catalysts supported on commercially available polymer beads ^(131, 134) created by the same group as the directly polymerised oxazolines showed approximately half of the selectivity of the homogeneous catalyst. The ligands were proposed to be bound to the polymers through both of the bridging positions, although it is thought unlikely that all of the ligands are bound in this manner ⁽¹²⁹⁾. The polymeric support used in this case was a chloromethylated divinylbenzene modified polystyrene. To obtain reasonable yields in the catalytic cyclopropanation reaction elevated temperatures (60°C) were required.

Most of the other researchers investigating polymer bound bis(oxazoline) catalysts have opted to use single tether systems. This gives greater certainty on the conformation of the ligand, which cannot be guaranteed on di-modified bis(oxazolines) without chromatographic separation. It also however reduces the symmetry of the ligand (loss of the C₂ axis), although this does not seem to have a significant effect on the selectivity of the products.

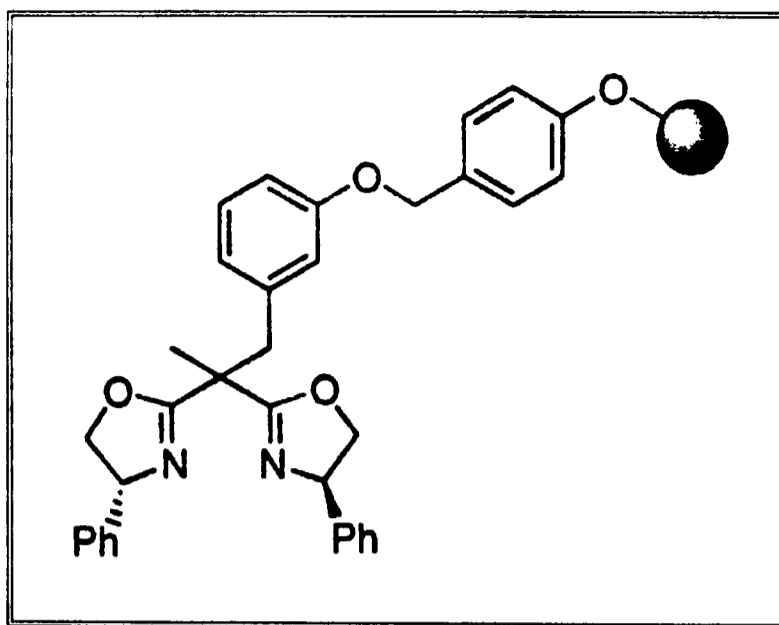


Figure 1.5.3.4: Single tether polymer supported 1,1'-ethylenebis(4-phenyl-2-oxazoline) as used by Moberg ⁽⁶⁹⁾

The choice of polymers on which to graft these catalytic systems is as varied as the reactions on which they have been tested. Supports have included modified poly(ethylene glycols) ⁽¹³³⁾, argogels ⁽⁶⁹⁾, tentagels ⁽⁶⁹⁾ as well as the more common polystyrene matrices ⁽¹³²⁾.

With palladium, the argogel supported complexes were tested for the allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. The supported ligand (Figure 1.5.3.4) was compared to commercially available 2,2'-isopropylidenebis(4-phenyl-2-oxazoline) both being complexed with Pd. The results indicate that the supported palladium complex gives lower overall yield of products compared to the homogeneous version (67-95% homogeneous, 28-70% supported) ⁽⁶⁹⁾. The enantioselectivity remained virtually unchanged with only a 1% decrease between the homogeneous version and the supported complex.

The zinc complex was tested for the Diels-Alder reaction between 3-(2-propenoyl)-2-oxazolidone and cyclopentadiene (Figure 1.4.5.4) ⁽⁶⁹⁾. The results were disappointing, as at the usual temperature employed for this reaction (-78°C) only trace amounts of product were detectable after 2 days. In contrast the homogeneous equivalent gave full conversion after only 15 hours. In order to achieve full conversion of the starting materials with the polymeric

discovered that by deactivating the remaining surface hydroxyl groups the enantioselectivity could be improved from 65% to 81% at room temperature. The authors also found that a longer reaction time was needed to ensure complete deactivation of all remaining surface hydroxyl groups on the silica than was suggested in the previous literature.

Covalently bound catalysts on commercially available silica have also been used in the cyclopropanation of styrene with ethyldiazoacetate (Figure 1.4.5.2) ⁽¹³⁴⁾. Some of these systems have been synthesised by Mayoral *et al* who have already been mentioned in connection with the polymeric and ionic supported systems, and so the method of synthesis therefore understandably borrows heavily from the earlier polymer work. They showed that, although the catalysts could be easily supported on modified silica, the selectivity is reduced compared to both the homogeneous and most of the polymeric versions of the catalyst. The best selectivity was again obtained with the inda-bis(oxazoline) ligand (Figure 1.4.2.5) which gave 35% yield, stereoselectivity of 47:53 and an ee of 52% for the *trans* isomer. This is compared to 69% ee for the polymer system and 83% for the homogeneous ligand ⁽¹³⁴⁾. Their attempt to use modified methylenebis(4-*t*-butyl-2-oxazoline) as the ligand, which is widely regarded as giving some of the best selectivities for this reaction, gave little enantioselectivity (6%). The reason why *t*-butyl ligands do not work well when covalently bound to silica supports is not known, as this ligand has been used fairly successfully when bound to polymers ⁽¹³⁶⁾ and also when ionically bound to certain clays ⁽¹³¹⁾.

Mesoporous silica supported catalysts were published shortly after normal silica versions ⁽¹⁴⁰⁾ and were published concurrently with our results described in this Thesis. The methodology used is a two step strategy similar to that used for the ordinary silica supported catalyst, as the same bis(oxazoline) ligand is used and as the catalysts are tested in the same

catalytic reaction a comparison between the amorphous and the mesoporous silica supported catalysts is possible.

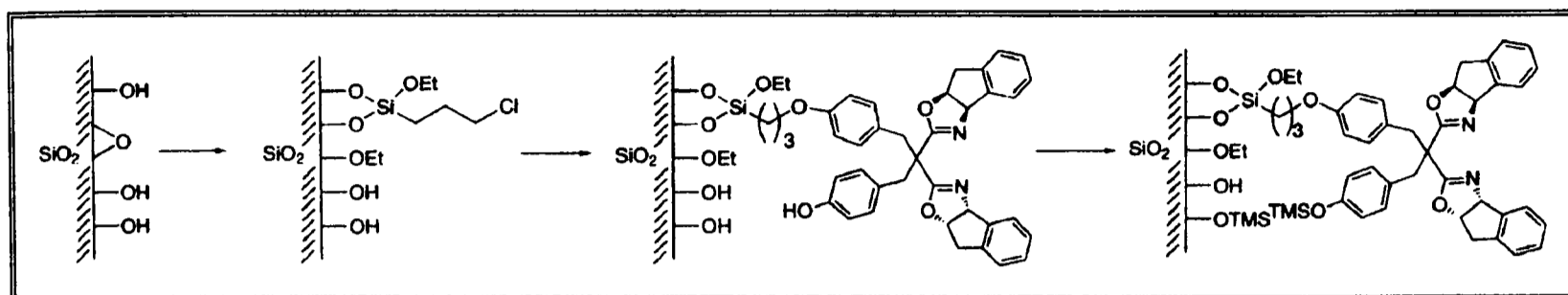


Figure 1.5.6.3: Inda-bis(oxazoline) ligand supported on a mesoporous material as by Park ⁽¹⁴⁰⁾.

Both the amorphous silica supported catalysts and the mesoporous silica supported catalysts for the Diels-Alder reaction used a copper triflate catalyst with a similar loading of catalyst ($0.17 - 0.25 \text{ mmol g}^{-1}$) ^(57, 140). At low temperature (-78°C) the mesoporous catalyst gave 98% yield (no reaction time is given for this), 9:1 endo/exo selectivity and 78% ee. The silica catalyst gave a lower yield (82%) after 48 hours, slightly better endo/exo selectivity (96%) and better enantioselectivity (87%). It would seem that there is almost no difference between the catalysts supported on commercially available silica and those on a mesoporous host. This is not surprising, as the only major difference that we would expect is a higher maximum loading of the catalyst upon the support. When the remaining hydroxyl groups on the mesoporous support were removed by reaction with hexamethyldisiloxane there was no increase in the selectivity of the reaction, unlike that seen in the amorphous silica with the copper (II) perchlorate catalyst.

1.6 Project aims

At the start of this project very few papers pertaining to supported bis(oxazoline) catalysts existed and bis(oxazolines) supported upon mesoporous silicas were completely unknown. The aim of this project is to synthesise mesoporous silicate materials, to bind chiral bis(oxazoline) catalyst complexes to the supports and to test the resulting heterogeneous catalysts. These catalysts will be tested in catalytic reactions where homogeneous bis(oxazoline) catalysts have been shown to produce isomerically enhanced products. The heterogeneous catalysts will be compared against the homogeneous catalysts and where possible recycled several times.

Chapter 2. Instrumentation

Although all of the techniques used in this project are well established some are much less commonly used than others. Techniques such as IR, NMR, UV-Vis and CHN analysis require no explanation, other techniques such as low angle XRD (which is only used for mesoporous materials) and solid state NMR are less commonly used and so a brief discussion of these techniques is given here.

2.1 Low angle X-ray Diffraction

2.1.1 History of X-rays

X-rays have been known for over 100 years (discovered in 1895 by Roentgen), initially, and as with all new discoveries, they were not well understood at first (they were even named X-rays because their nature and ability to penetrate solid matter was not understood).

The term X-ray is used to define electromagnetic radiation of wavelength *ca.* 1Å. The definition is not exact and various literature sources give the X-ray region as *ca.* 1Å⁽¹⁴¹⁾, <3nm⁽¹⁴²⁾, 0.5 - 2.5Å⁽¹⁴³⁾ or 10nm - 100pm⁽¹⁴⁴⁾. Although the SI unit of measurement for X-rays is nanometers (nm), in practice angstroms (Å) are much more frequently used (1nm = 10⁻⁹ m = 10Å).

2.1.2 X-ray diffraction

X-rays are produced when high-energy charged particles collide with matter, the collision causes a loss of energy which is emitted as a wide frequency of X-ray radiation known as 'white radiation'. In an X-ray machine a beam of high-energy charged particles is aimed at a metal target so that in addition to the 'white radiation' emission lines characteristic to the target metal are also generated. These emission lines are caused by ionisation of K shell electrons leaving the atom in an excited high-energy state. One of the outer shell electrons immediately falls into the vacancy in the K shell emitting energy. The energy is emitted as radiation of definite wavelength. As an electron from any of the outer shells may fill the K shell vacancy a series of emission lines of definite wavelength are formed. The radiation is then filtered to give a single emission line; with the most commonly used metal target, copper, the lower intensity radiation is filtered off leaving $K\alpha$ radiation of wavelength 1.5418\AA . Other commonly used sources are chromium ($K\alpha$, 2.2909\AA), iron ($K\alpha$, 1.9373\AA) and molybdenum ($K\alpha$, 0.71069\AA).

When a beam of X-rays hits the electron density surrounding atoms it is scattered in all directions. The scattered beams all travel a different distance between the X-ray source and the detector and so are not in phase with each other, which results in most cancelling each other out (this is termed 'destructive interference'). A regularly arranged structure, such as a crystal, can act as a diffraction grating, resulting in some of the beams scattered in the same direction being in the same phase as each other; these reinforce each other (this is termed 'constructive interference') to give maxima at specific positions in space.

If we consider a crystalline solid to be built up of layers which act as semitransparent mirrors (this is not entirely accurate but serves as a useful comparison), scattered rays will

then be in phase if the extra distance that the beam travels between different layers is equal to a whole number n of wavelengths, as shown by Figure 2.1.2.1 below.

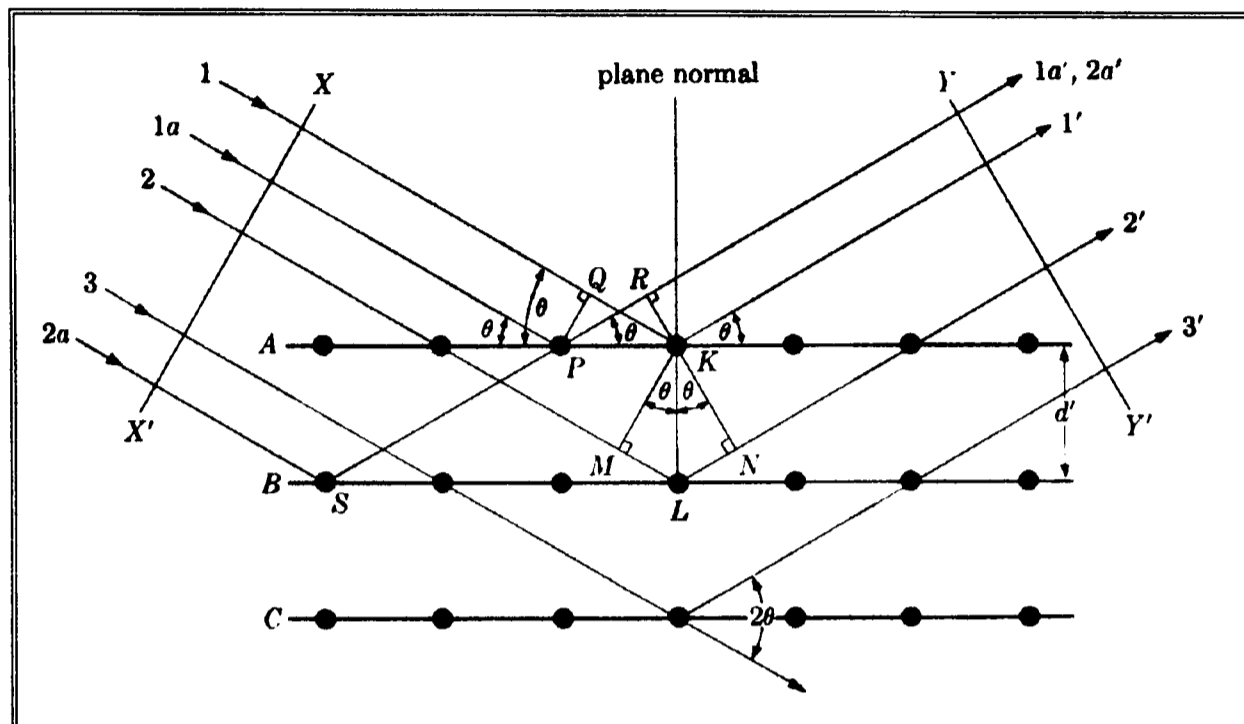


Figure 2.1.2.1: Diffraction of X-rays by a crystal ⁽¹⁴⁵⁾

This is the basis of the most fundamental equation in X-ray diffraction, Bragg's law ($\lambda=2d \sin\theta$) [where λ is the wavelength of the radiation, d is the distance between planes of atoms and θ is the angle of diffraction]. If Bragg's law is satisfied constructive interference occurs, otherwise there is destructive interference ⁽¹⁴⁶⁾.

The intensity of the diffraction maxima are stronger than the randomly scattered beams (due to the reinforcement and the destructive interference occurring) but are much lower than the intensity of the incident beam as only a fraction of the light is diffracted in any one direction.

X-rays have been used to study the internal structure of solids by diffraction for over 90 years (Friedrich, Knipping and Laue 1912) ⁽¹⁴⁷⁾.

2.1.3 Low angle X-ray diffraction

From Bragg's law it can be seen clearly that the lower the angle (θ) the greater the distance is between the repeat units in the structure. For most crystalline materials, the repeat distances found within the structures are of such dimensions that recording of the diffraction pattern between *ca.* $2\theta = 10 - 90^\circ$ will provide all the information necessary for details of the structural order present, and where the data is of sufficient quality structure solution or refinement is possible enabling more detailed information on molecular packing and interatomic distances to be determined.

The study of mesoporous materials does not lend itself to such analysis from powder diffraction as, due to the much larger crystallographic repeat distances, the X-ray diffraction pattern obtained is "compressed" so that only peaks at low angle (typically between *ca.* $2\theta = 1.5 - 8^\circ$) are observed. Further, many mesoporous materials (and certainly the ones we have been investigating) possess a regular arrangement of pores but have no short-range interatomic order, as the structure of the pore walls is essentially amorphous. Hence, the only structural information that can often be obtained from X-ray diffraction studies of mesoporous solids is the repeat distance between the pores themselves and the symmetry or packing arrangement of the pores relative to each other. Nevertheless, this information is still useful in determining which mesoporous phase has been prepared.

The instrumentation used to record low angle XRD data was the same as used for conventional XRD data, although extra precautions were taken to ensure that at the very low angles used the intense incident beam could not damage the detector. All samples were mounted on a specially designed, X-ray transparent flat plate sample holder on which the sample compartment was *ca.* 2 cm diameter (hence requiring more sample than other

traditional methods) as the spread of the beam over the sample surface at low angle is large. Data was recorded in reflection mode and low angle calibration of the diffractometer was carried out using a Mica standard

2.2 Solid State Nuclear Magnetic Resonance

2.2.1 Introduction to NMR

The effect that is now known as NMR was first observed in 1946, although it was not until *ca.* 1960 that this technique became commonly used in chemistry. With the advent of Fourier transform NMR in the 1970's ⁽¹⁴⁸⁾ it is now one of the fundamental spectroscopic techniques used to investigate organic structures. NMR can also be used to investigate localised atomic environment of any atom having an isotope possessing nuclear spin e.g. ²⁹Si, ³¹P etc. To determine if an atom possesses nuclear spin the following rules can be applied ⁽¹⁴⁹⁾.

1. Nuclei with numbers of protons and neutrons both even (*i.e.* both charge and mass even) have no spin
2. Nuclei with odd numbers of protons and neutrons (*i.e.* charge is odd but total mass is even) have integral spin (whole numbers *i.e.* 1,2 etc.)
3. Nuclei with an odd total mass have half-integral spins (*i.e.* $\frac{1}{2}$, $\frac{3}{2}$ etc.)

Technological advances in magnets have gradually increased the power of these instruments from about 60MHz in 1960 to over 1GHz today.

2.2.2 Theory of Resonance

An atom which has nuclear spin can be viewed as a tiny bar magnet which is floating in space. When an external magnetic field is applied to these tiny magnets they can either be aligned with the magnetic field (the most energetically favoured state) or against the magnetic field (the high energy state), these are termed the α and β states respectively. In the normal state there will be more nuclei in the α state than the β state in accordance with energy distribution laws. Over the entire sample this will give a small magnetic moment in the direction of the magnetic field.

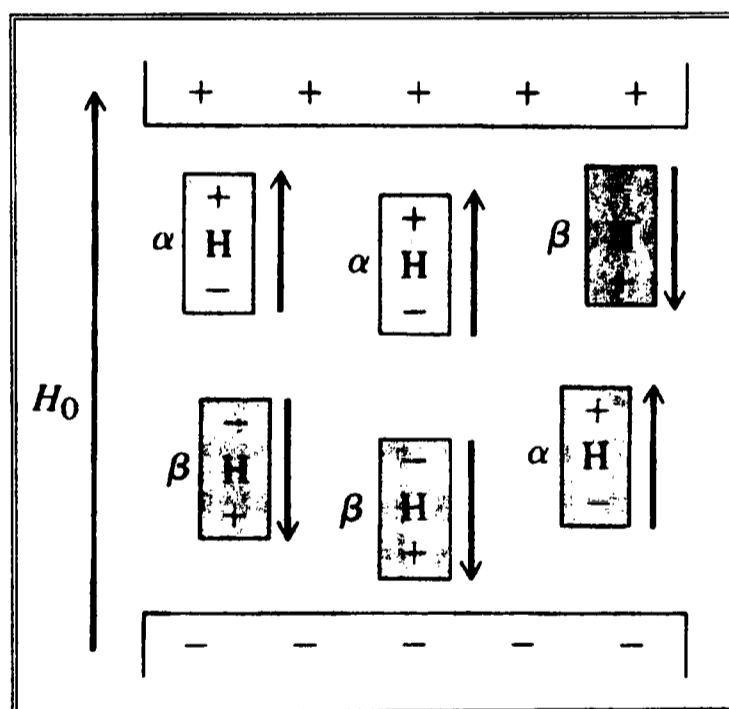


Figure 2.2.2.1: Nuclear spins aligned with and against the magnetic field ⁽¹⁵⁰⁾

These nuclei are not stationary in the magnetic field, as according to quantal laws the dipole moment of a spinning nucleus cannot be exactly in the direction of the magnetic field. This causes an effect known as the 'Larmor Precession'.

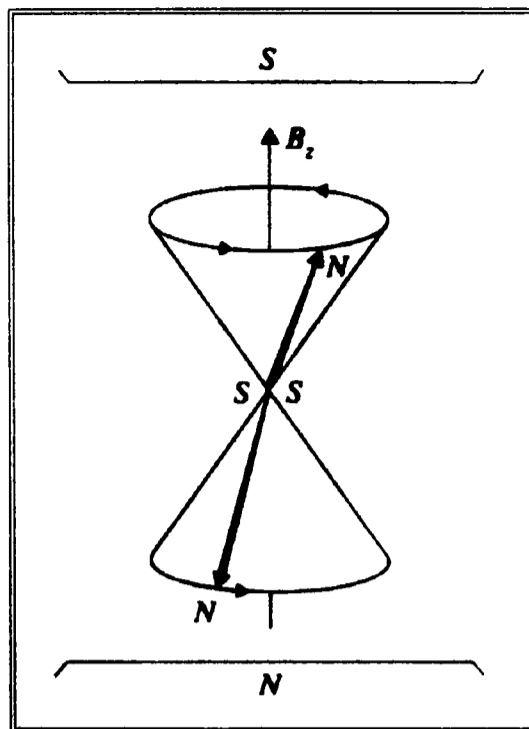


Figure 2.2.2.2: Larmor precession of a nucleus with spin $\frac{1}{2}$ ⁽¹⁴⁹⁾

The α state can be excited to the β state by irradiation of the sample with enough energy to bridge the gap between the two states. The amount of energy required to excite the atom is dependent on the strength of the external magnetic field, the type of atom and its local environment. The nuclei can only interact with a beam of energy if the frequency of the radiation is the same frequency as the precession; this is known as resonance. The energy required to excite the atom is supplied by electromagnetic radiation (for NMR the energy required usually falls into the radio wave frequency).

NMR spectra can be recorded by two different methods: continuous wave and pulse.

In continuous wave NMR either the magnetic field or the radio frequency is slowly scanned and the absorbance recorded directly as the spectra. This method is no longer commonly used, as it requires several minutes to complete a single scan, and many individual scans may be required to reduce random noise to an acceptable level.

In pulse NMR (or Fourier Transform NMR as it is more commonly called) pulses of radio waves which cover the whole frequency range are used. The source of the radio pulse and the detector are at right angles to each other to ensure that there is no direct interaction

between the two. The spectra are recorded as a function of the decay of the excited species. This method is most commonly used today as large numbers of scans can be quickly recorded and combined to give a higher quality of spectra.

The pulse of radio waves is applied at right angles to the applied magnetic field, this creates an oscillating magnetic field at right angles to the applied field. This new magnetic field has the effect of tipping the overall magnetic moment of the sample. The degree of tipping (Θ) is given by:

$$\Theta = \gamma B_1 t_p$$

Where γ is the magnetogyric ratio (the strength of the individual nuclear magnetic field which is unique to each type of nuclei), B_1 is the strength of the oscillating magnetic field and t_p is the duration of the magnetic pulse. The duration of the pulse is often chosen so that $\Theta=90^\circ$.

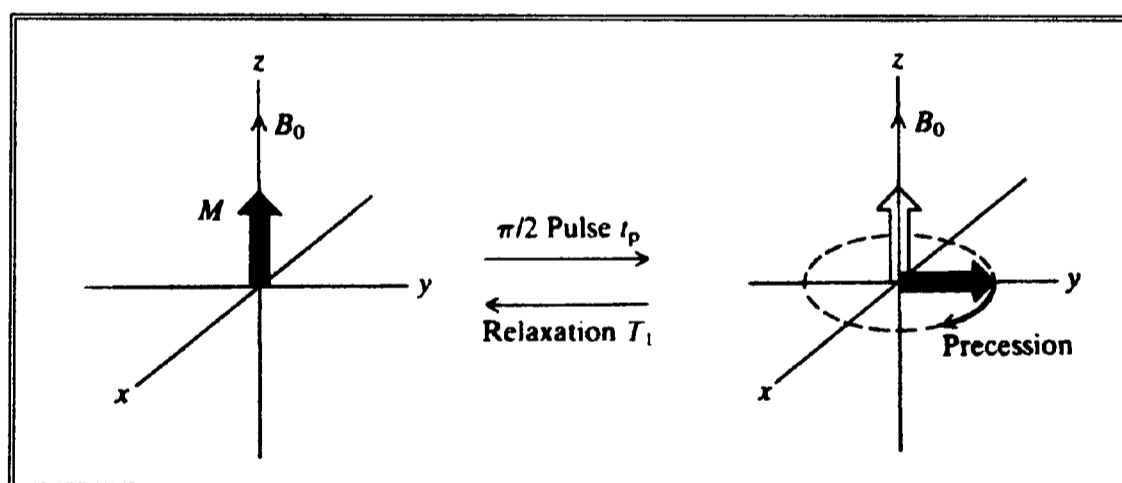


Figure 2.2.2.3: Effect of 90° pulse on the net magnetic moment of a sample ⁽¹⁵¹⁾

The net magnetic moment decays to the ground state (aligned with the applied magnetic field), and the energy released as this occurs is picked up by the receiver and is called the free induction decay (FID). This is a complex waveform which requires the application of a mathematical Fourier transformation before the spectrum can be displayed.

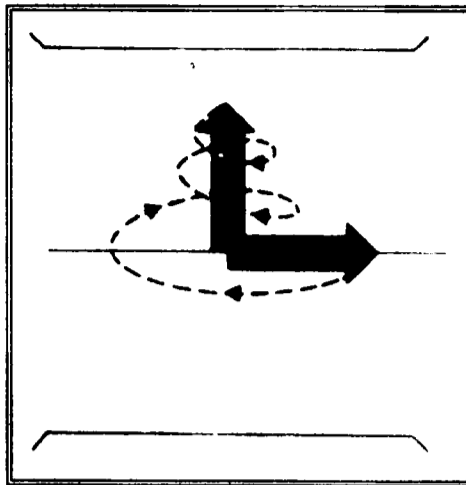


Figure 2.2.2.4: Decay of a 90° pulse back to the ground state ⁽¹⁴⁹⁾

2.2.3 Solid State NMR

Most NMR spectroscopy is involved with the investigation of liquid samples, however NMR can also be used to investigate solid samples. Although the basic theory for solid state NMR is the same as for standard NMR techniques several important problems which do not affect liquid samples must be solved first.

The frequency at which each nuclei resonates is dependent on several factors, the most important of which include direct and indirect dipole-dipole interactions between magnetic nuclei and electron shielding. All of these have an effect on the total magnetic field affecting individual nuclei. Essentially this means that nuclei have a large effect on the magnetic field of surrounding nuclei, this effect is known as dipolar coupling. The effect that each nucleus has is proportional to the distance between the nuclei ($1/r^3$), the angle between the two nuclei and the applied field ($3 \cos^2\theta - 1$). In gaseous and liquid samples rapid molecular tumbling reduces direct dipole - dipole interactions to zero and indirect dipole - dipole interactions to the coupling constant (J). In a solid sample molecular tumbling cannot occur as the molecules

or nuclei are fixed (or are in spatially restricted orientations). This means that direct dipole-dipole interactions give variations in the magnetic moment of each nucleus through dipolar coupling, resulting in much broader peaks. Also in a powdered sample all orientations of a molecule or nucleus relative to external magnetic field are present. Each orientation will have a different chemical shift which also leads to the broadening of peaks. Broader peaks cause problems, as they are much harder to resolve (due to peak overlap) and are much harder to observe as the intensity is spread over a wider area causing a decrease in the signal to noise ratio.

We can however use mechanical means to reduce the $(3 \cos^2\theta - 1)$ term to zero and eliminate line broadening due to chemical shift anisotropy. If the sample is spun rapidly at an angle of 54.7° to the applied magnetic field so that $3\cos^2\theta=1$ we can provide an approximation of molecular tumbling. This angle is known as the 'magic angle' and the process is often called magic angle spinning. In practice though it is not possible to rotate the sample fast enough to completely remove chemical shift effects and each peak is split into a set of equally spaced lines one of which is the isotropic peak and the others spinning side bands. The spacing between lines is equal to the frequency at which the sample is rotated.

Dipole-dipole interactions can also be reduced by magic and spinning although again in practice it is not possible (with current technology) to spin the sample fast enough to completely remove this effect.

The way in which magic angle spinning affects the chemical shift anisotropy and dipole-dipole interactions is different. At slow spinning speeds magic angle spinning will break up a spectrum line-broadened by chemical shift anisotropy into the series of equally spaced lines. With a spectrum broadened by direct dipole-dipole interaction the line width

will only be significantly reduced when the spinning speed is in the region of (or greater than) the magnitude of the dipole-dipole interaction.

Magic angle spinning solid state NMR was used in the investigation of the organic ligand tethered to the silica support.

Chapter 3. Results and Discussion (Synthesis)

3.1 Mesoporous Material Synthesis

As the intention was to tether an organometallic catalyst complex to the synthesised mesoporous material only pure silica materials were synthesised. This also meant that we would be able to directly compare our mesoporous supported catalyst complexes to those supported on commercially available silica. During the synthesis of the mesoporous silicate materials plasticware was used to avoid contamination by material dissolved from normal glass laboratory equipment.

3.1.1 MCM-41

Synthesis

The first material synthesised was MCM-41, and two different synthesis methods were used. The first method used was an acidic method which was essentially the same as that used in the initial synthesis by Beck and co-workers in 1992 ⁽⁶⁾. An alternative basic preparative method was tried later for comparison and is also based upon Becks early work. Both methods gave MCM-41 in good yields (*ca.* 60%) although the secondary peaks in the majority of the preparations in acidic media were better defined than in the sample prepared in basic synthesis media. The increased definition in the secondary peaks is characteristic of a more ordered sample where the arrangement of the pores is much more regular. Multiple syntheses were carried out throughout the course of the project and it was found that the quality of the mesoporous materials synthesised differed slightly between batches due to small variations in the conditions. It is also expected that the surface chemistry of the final

mesoporous product differs slightly between the acidic and basic synthesis methods. The differences would be in the thickness of the pore walls and in the framework charge ⁽⁵⁾. To date however there is little work comparing the surface chemistry of these materials, and none which directly compare the surface chemistry of the materials prepared by acidic and basic routes. It is also known that the pH of the reaction has an effect on the morphology of the particles, and that pH modification can improve the stability of the final mesoporous material ⁽⁵¹⁾. In order not to introduce additional unnecessary variables to the catalyst preparative process later on in our study, which may influence activity, we concentrated on preparing MCM-41 by the acidic method. Only a small amount of the basically prepared material was synthesised and was not used in the preparation of the main series of catalysts studied. The principal analysis technique for these materials was low angle XRD and subsequent comparison to published material. A cross section of samples were submitted for nitrogen absorption measurements to determine pore size and surface areas, and a few samples were also studied using TEM.

X-ray diffraction pattern analysis

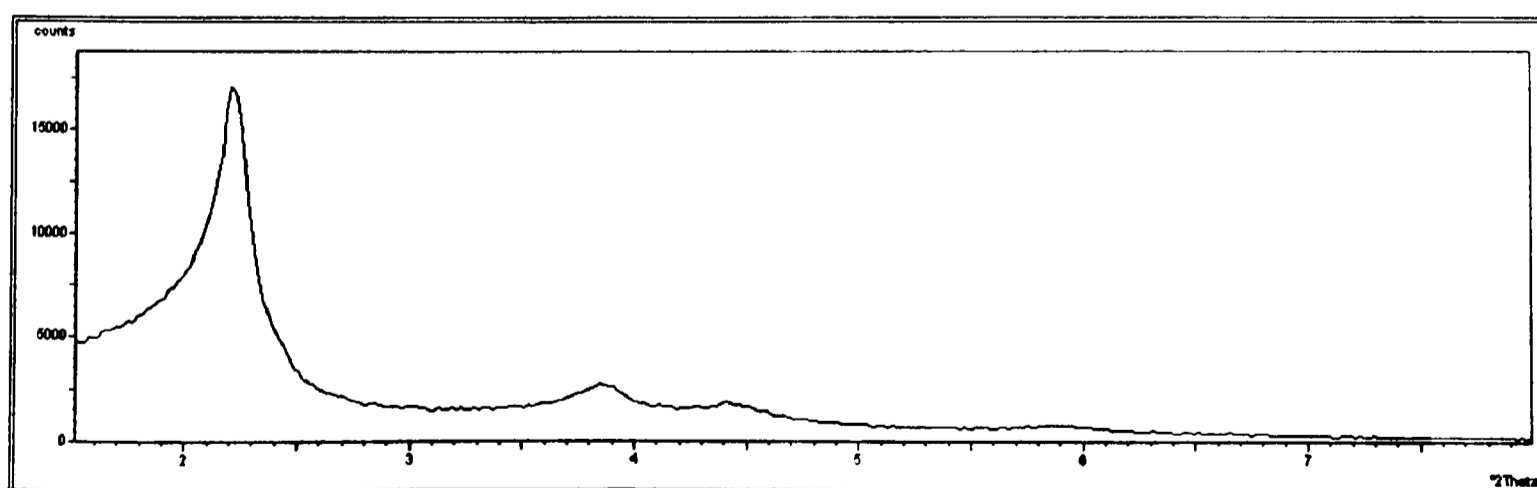


Figure 3.1.1.1: XRD pattern of calcined MCM-41

The X-ray pattern above (Figure 3.1.1.1) is comparable to the published data for this material - in MCM-41 it is common to see up to four peaks between 2θ values of about 2-6°. These correspond to the 100, 110, 200, and 210 reflections, and a fifth peak (300 reflection) can occasionally be seen for very good samples at $2\theta \approx 5.8^\circ$ ⁽¹³⁾, although this peak is very weak and requires extended XRD data collection time to be seen clearly. The first peak is indicative of the ordering of the individual channels, and as such the position is dependent upon the size of the pore. In conjunction with N₂ adsorption measurements it can be used to give an estimation of the pore diameter or the thickness of the walls between pores^(6, 15, 40). The subsequent peaks are caused by the packing arrangement of the channels with respect to each other as a consequence of the symmetry of the material – for MCM-41 the indexing of the peaks is consistent with the hexagonal arrangement of the pores. All the peaks shift to slightly higher 2θ values upon calcination due to contraction of the pores when the template is removed; this is most noticeable for the 100 reflection. The amount of pore shrinkage is dependent upon the sample and the calcination method used but is clearly observed and occurs with all mesoporous materials⁽³⁸⁾. In some preparations it was difficult to see the 210 reflection due to lack of intensity, and occasionally the 110 and 200 peaks were not easily distinguishable. While not all of the materials synthesised had these well-defined secondary peaks all showed an intense peak around $2\theta \approx 2.2^\circ$, indicating that a mesoporous material had formed. The lack of definition of the secondary peaks in some of the samples is indicative of the samples having a lack of long range order of the pores within the sample, although the lack of definition may be compounded by either sample packing effects or from the nature of the XRD scans used (as due to time constraints scan times were sometimes limited to *ca.* 15 minutes). We have noticed that occasionally a poor XRD pattern which has little definition

can be vastly improved by repacking the same sample. In the later work on supporting the bis(oxazoline) catalysts only the better crystalline batches of MCM were used.

Infra-Red spectra analysis

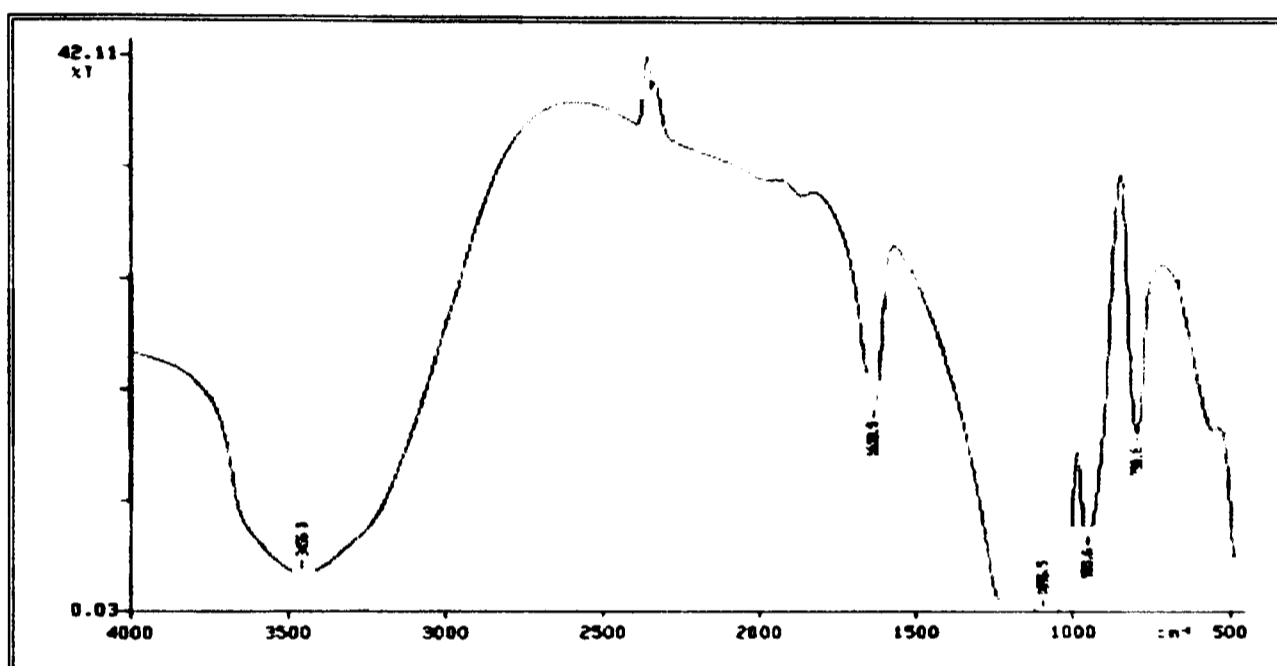


Figure 3.1.1.2: IR Spectra of calcined MCM-41

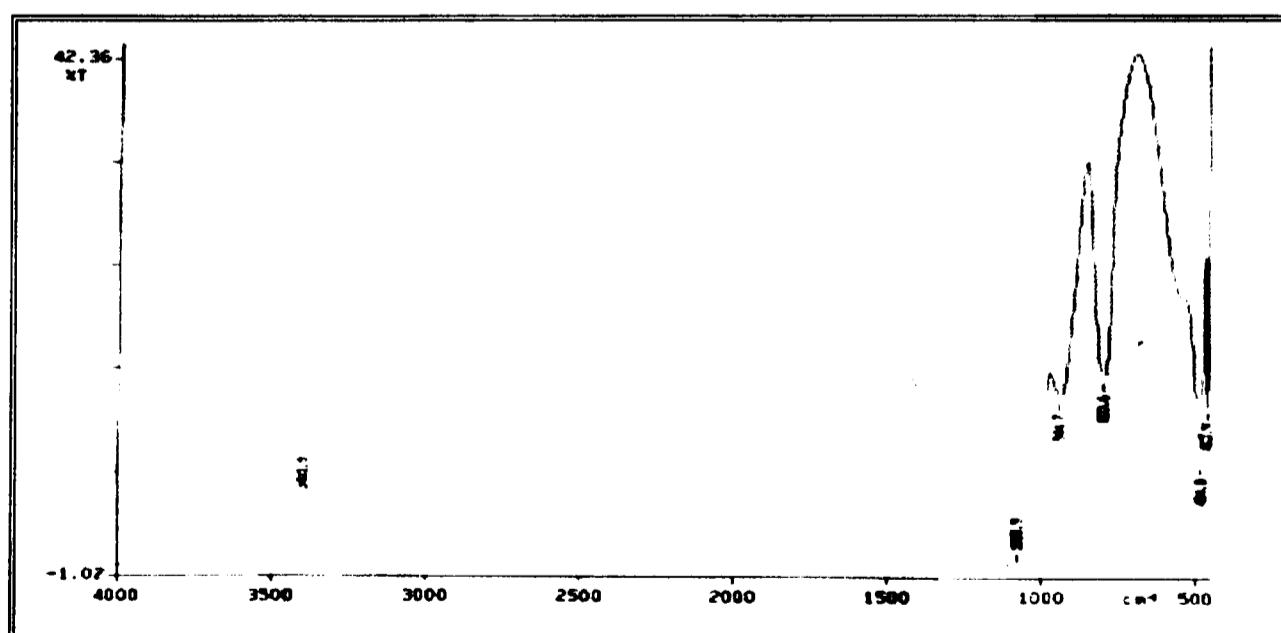


Figure 3.1.1.3: IR spectra of dried calcined MCM-41

IR spectra were also recorded for these materials and show no difference to that of commercially available silica. The two spectra above (Figures 3.1.1.2 and 3.1.1.3) are from the same batch of MCM-41, but for the second spectra the sample has been dried at 140°C under vacuum for several hours. Both spectra show a broad peak at *ca.* 3450 cm⁻¹ which corresponds to the OH stretch of silanol groups and residual water trapped in the pores. The peak at *ca.* 1640 cm⁻¹ is associated with the bending mode of water and the broad peak *ca.* 1080 cm⁻¹ and the peak at *ca.* 800 cm⁻¹ correspond to Si-O asymmetric and symmetric stretching. Peaks at *ca.* 950 cm⁻¹ can be attributed to Si-O⁻ surface groups and are commonly found in silicas and zeolites which contain a high concentration of surface defects. The major differences between these spectra are fairly obviously that the peak at *ca.* 3450 cm⁻¹ (OH) has decreased in size and the peak at *ca.* 1640 cm⁻¹ (H₂O) has almost disappeared. This is due to water, that was either trapped in the pores or hydrogen bonded to the surface hydroxyl groups of the silica, being removed. It is important to note that the peaks caused by the support are fairly broad and intense and that even with drying the peak at *ca.* 1640 cm⁻¹ has not completely disappeared. The reasons for noting this will be made clear when discussing the supported bis(oxazoline) catalyst systems.

Nitrogen absorption analysis

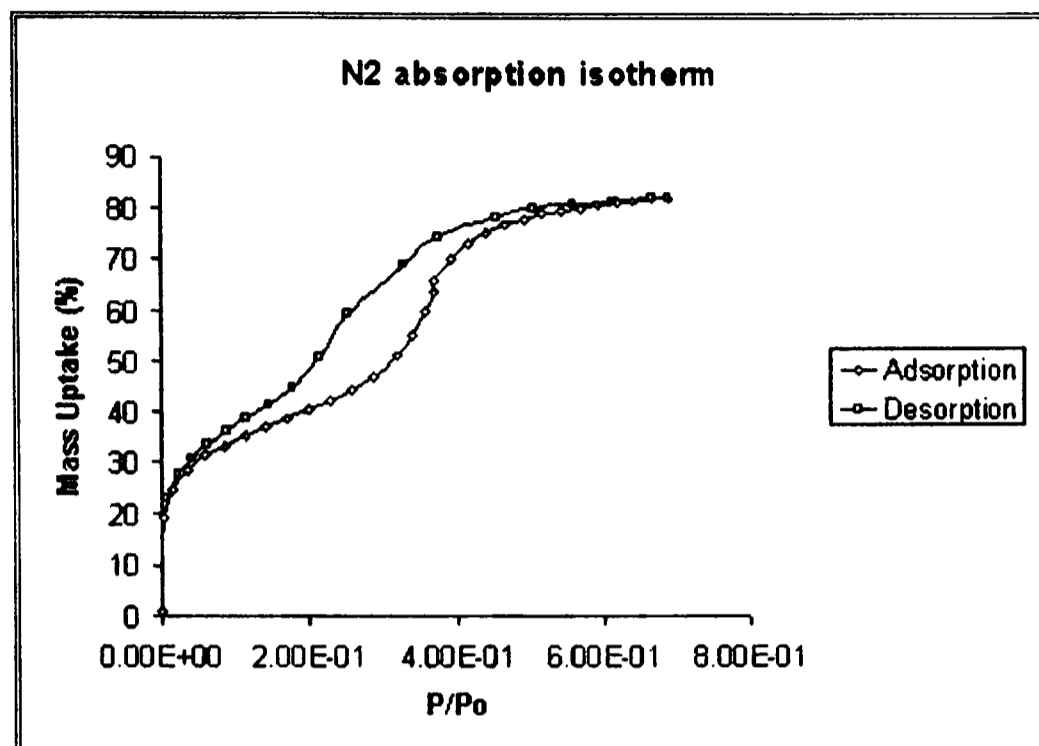


Figure 3.1.1.4: Nitrogen absorption plot for MCM-41

Nitrogen absorption experiments were performed on an automated system at St Andrews University. Previously a manual set up was used which took a long time especially for samples with high surface areas such as most mesoporous materials.

Figure 3.1.1.4 shows a type IV isotherm which is typical of that obtained for mesoporous materials. With the automated system the surface area is calculated automatically using a BET isotherm, and pore radii are then also calculated using a cylindrical BJH model. The results obtained for the MCM-41 samples are shown in Table 3.1.1.1.

Sample	Surface area m ² /g	Pore radius Å
MCM-41 (A)	1391.8	11.4
MCM-41 (B)	917.8	13.0
Catalyst complex with MCM-41 (A)	661.7	14.0
Catalyst complex with MCM-41 (B)	253.1	14.1

Table 3.1.1.1: Automated nitrogen absorption measurements for samples of MCM-41

The apparent surface areas for these materials are within the expected ranges with the surface areas being in excess of 900 m²g⁻¹ for both of the pure MCM-41 samples. Variance between the different samples tested is entirely expected, as minor differences in the synthesis conditions for each batch of MCM prepared means that each experiment will give slightly different results for pore sizes and surface area. Some difference in the pore radius would also be expected, as the pores in each sample will shrink upon calcination. The difference seen, however, is much larger than expected, one of the samples (MCM-41 (A)) showing a pore radius of 11.4 Å and the second (MCM-41 (B)) 13.0 Å. With the surfactant used (cetyltrimethyl ammonium bromide) a slightly larger pore radius *ca.* 15 Å would be expected from the literature ⁽⁷⁾. The difference between the published radii and MCM-41 (B) is most likely a small difference in the pore size itself compounded by the small number of data points collected by the automated equipment. On several samples less than 10 data points were collected for the desorption branch (which is used to calculate the pore radius) which translates to measurement intervals of 2 - 3 Å. This limits the accuracy, although broad trends can still be observed. With the manual equipment used for the MCM-48 sample (Figure 3.1.2.2) over 40 data points were collected giving an accuracy of *ca.* 0.2 Å. MCM-41 (A)

though is much further from the published value and when a catalyst complex was tethered inside this batch of support (MCM-41 (A)) a pore radius of 14.0 Å was recorded. This increase cannot be explained by either the small number of data points taken or by inconsistencies within the sample.

These results can be double checked using the XRD pattern ^(6, 15 and 40) or TEM measurements, unfortunately our TEM measurements do not have an internal scale making this very unreliable. Using the 2θ values from the XRD measurements and Bragg's law ($\lambda=2d \sin\theta$) the value for d is calculated for the main 100 peak. Taking into account the hexagonal structure (repeat unit $a_0=2d\sqrt{3}$), we can obtain an estimate of the distance between the centres of adjacent pores. The thickness of the pore walls must then be subtracted, although again this is not an accurate measurement, as this will differ between each synthesis method and sample. The thickness of the pore walls has been reported in the literature to vary between *ca.* 1.0-1.4 nm ^(13, 40) (using the calculations above and the pore size measurements from the absorption measurements the pore wall thickness for MCM-41 (B) is 1.32 nm). Using these published values for pore wall thickness this gives pore radii of 13.5 - 15.5 Å for sample MCM-41 (A) and 12.5 - 14.5 Å for the catalyst complex with MCM-41 (A). This suggests that it is most likely that the nitrogen absorption measurement for sample MCM-41 (A) is incorrect. If it were then assumed that the pore measurements for the catalyst complex with MCM-41 (A) are correct this would give a pore wall thickness of 1.11 nm.

TEM analysis of MCM-41

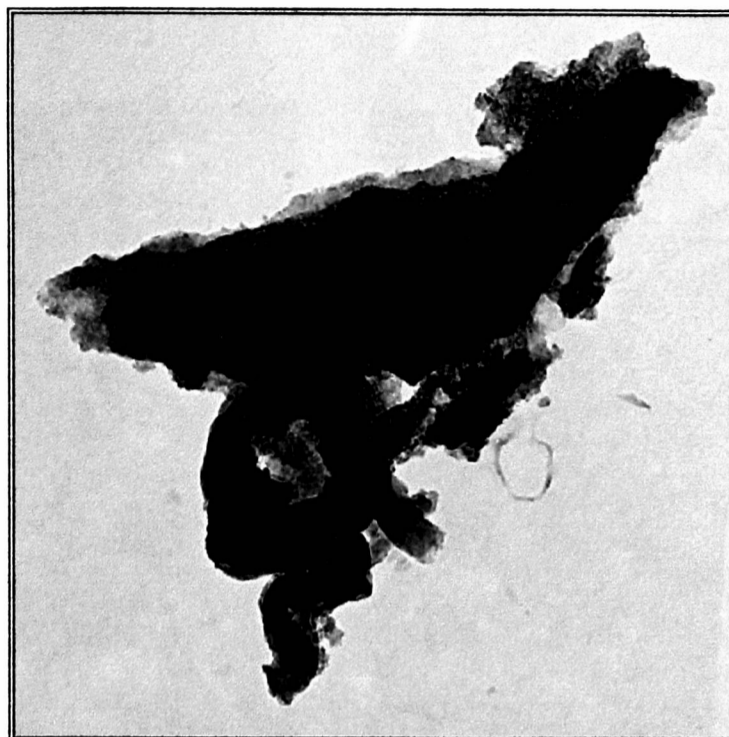


Figure 3.1.1.5: TEM of calcined MCM-41 (27,500 * magnification)

The TEM scans showed that the particles of mesoporous material did not have a specific morphology or size (Figure 3.1.1.5) but rather a random structure. This is not surprising as a great number of studies have been carried out which show that to obtain a specific morphology precise control has to be taken with stirring rates, reagent concentration, pH and a host of other factors, and even then it can not be guaranteed that all of the sample will contain the same morphology. In our study here we are primarily interested in supporting catalysts within the pores of the solid, and so the external morphology should not greatly affect the catalysis results, the only possible exception being added complications with the diffusion of reagents to the active sites. Some of the TEM scans show clear evidence of the network of channels, with both the long straight lines associated with ‘side on’ views of the channels (Figure 3.1.1.6) and the classical ‘head on’ hexagonal structure of MCM-41 (Figure

3.1.1.7). These can only be easily seen at the edges of the material where it is thinner, but show that we have synthesised a well-ordered mesoporous structure.

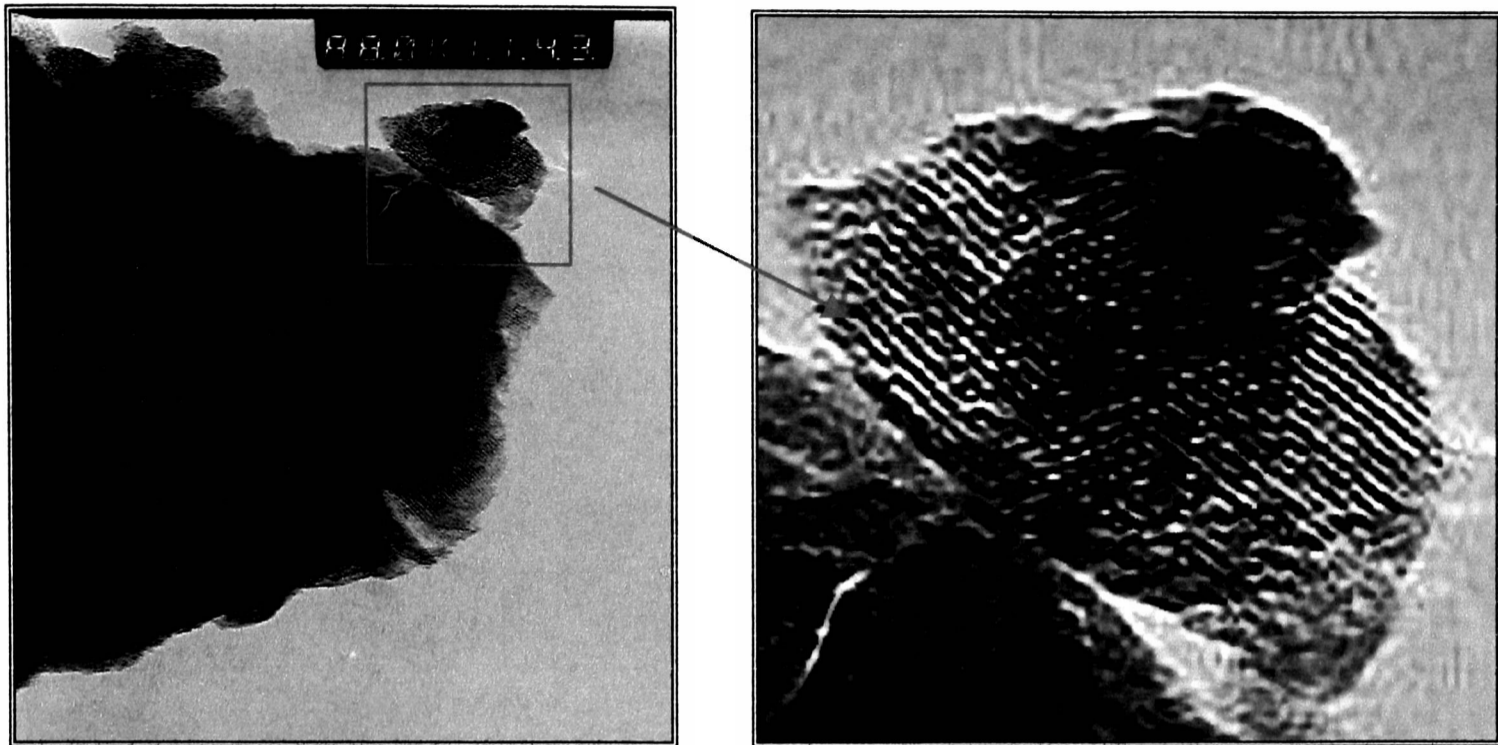


Figure 3.1.1.6: TEM scans showing side on views of mesoporous channels (88,000 * magnification)

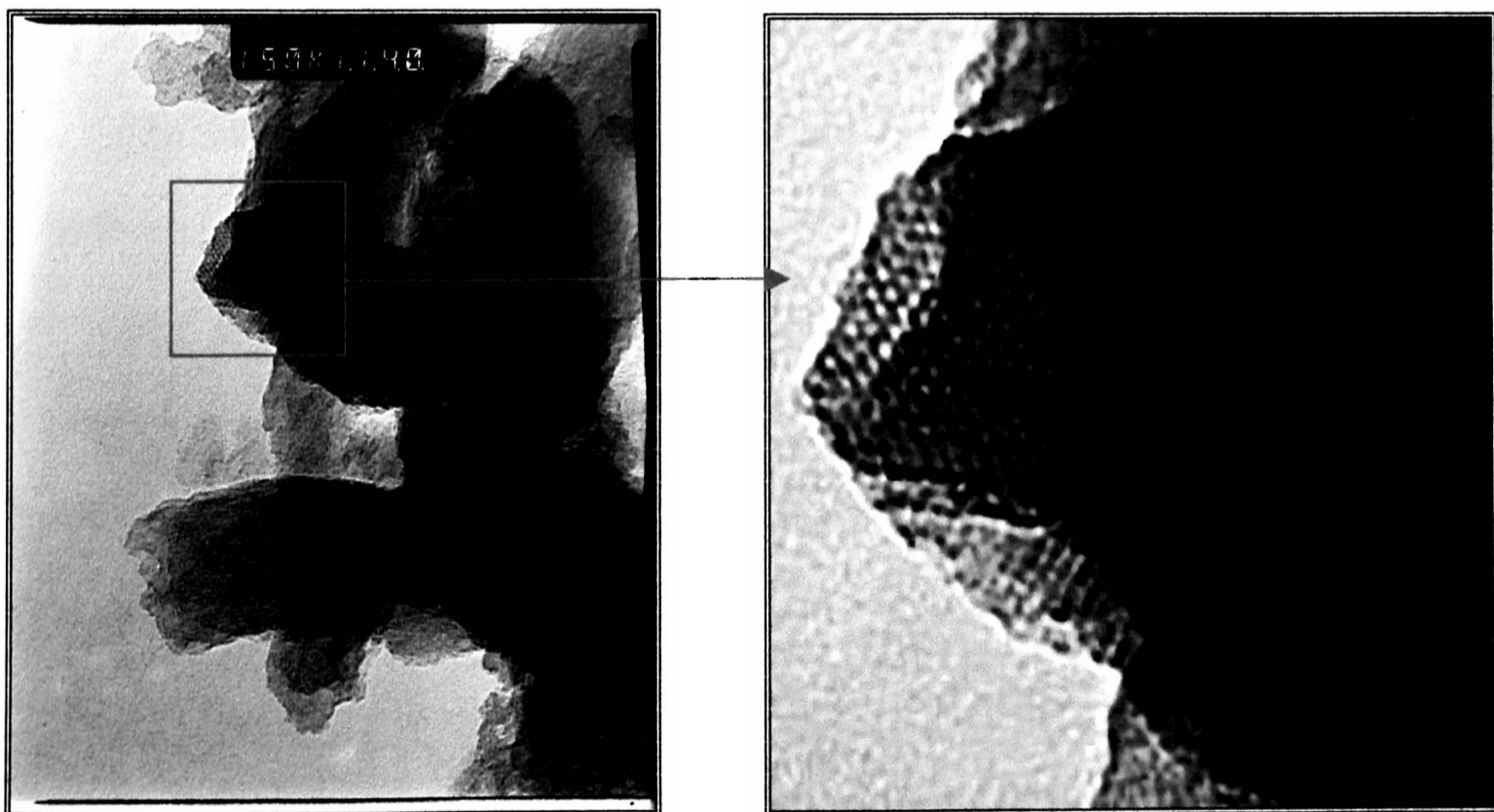


Figure 3.1.1.7: Top view of the channels in MCM-41 (150,000 * magnification)

3.1.2 MCM-48

Synthesis

The second mesoporous material synthesised was MCM-48, for which two different methods were tried. The first method used the ratios quoted in the literature,⁽²²⁾ while the second used more water in the mixture and a slightly modified mixing procedure. This second method was found to give a better yield of material than the experiment using the literature method and ratios (51% compared to 36%). There is still the question of which method gives a better quality of material as this can be arguably more important than the yield which is obtained. Both methods give samples which are pure MCM-48, on this occasion the literature method (method 1 in the experimental section) seems to have given a better quality material. It must be stressed though that this is only one observation as each synthesis will produce a slightly different product and direct comparison of the different methods requires many reactions for a comparison to be made with confidence.

The relative scarcity of papers using MCM-48 in comparison to MCM-41 (mainly due to synthesis problems) can also be understood. Whilst in the first year of study at St Andrews University the synthesis of MCM-48 was carried out 4 times. In each case MCM-48 was obtained very easily, however whilst in the second and third years of study at Birmingham University we were unable to synthesise any MCM-48 by either method which had previously worked in St Andrews, in most cases the product obtained being MCM-41. Undergraduate project students working on similar projects also attempted to synthesise MCM-48 using literature methods without success. In both cases the TEOS used was from Aldrich and the sodium hydroxide pellets from Fisher. The cetyltrimethyl ammonium bromide for the St Andrews materials was either an old bottle of BDH brand or from Aldrich which was also

used in the failed Birmingham syntheses. The possibility that the water used may have some effect was also investigated as St Andrews uses a glass-distilled system whilst Birmingham uses ion exchange. We therefore obtained some of the water from St Andrews and used this to try and make more material, however this was also unsuccessful. Why we were able to synthesise MCM-48 every time in St Andrews and were completely unable to make any in Birmingham is still unclear. It does however go some way towards explaining why in spite of having greater connectivity, and therefore being a better supporting material as diffusion through the support should be faster and the pores are less likely to become blocked, it is much less commonly used. As with MCM-41 the principle method of analysis for these structures is by low angle XRD.

X-ray diffraction analysis

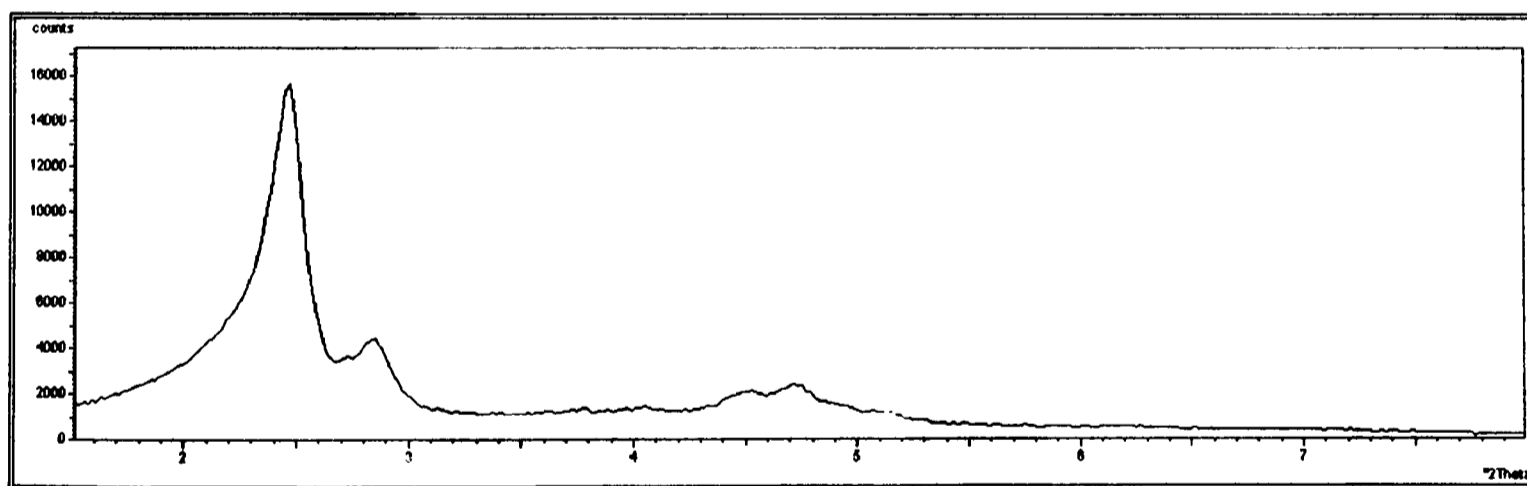


Figure 3.1.2.1: XRD pattern of calcined MCM-48

The X-ray patterns for MCM-48 is much more complex than that of MCM-41, on some samples in the literature over 18 peaks have been clearly identified between 2θ values of $2.5\text{-}8.0^\circ$ ⁽²¹⁾. The largest peak at 2θ *ca.* 2.5° corresponds to the 211 reflection, with the 220

reflection appearing slightly higher at $2\theta \approx 2.8^\circ$. The remaining peaks are all much less intense than these and often appear as an unresolvable cluster with the 321 and 400 reflections at approximately 4.0° and the 420, 332, 422 and 431 reflections between 2θ 4.5 and 5.2° ⁽²¹⁾. The other peaks are unlikely to be distinguishable from the base line without a very good sample and a large amount of XRD run time. The X-ray patterns recorded in the literature show good correspondence to the predicted $Ia\bar{3}l$ cubic structure.

Nitrogen absorption analysis

Whilst most of the nitrogen absorption experiments were performed on an automated system at St Andrews University the sample of MCM-48 was recorded on a manual set up which took a long time due to the high surface area of the sample.

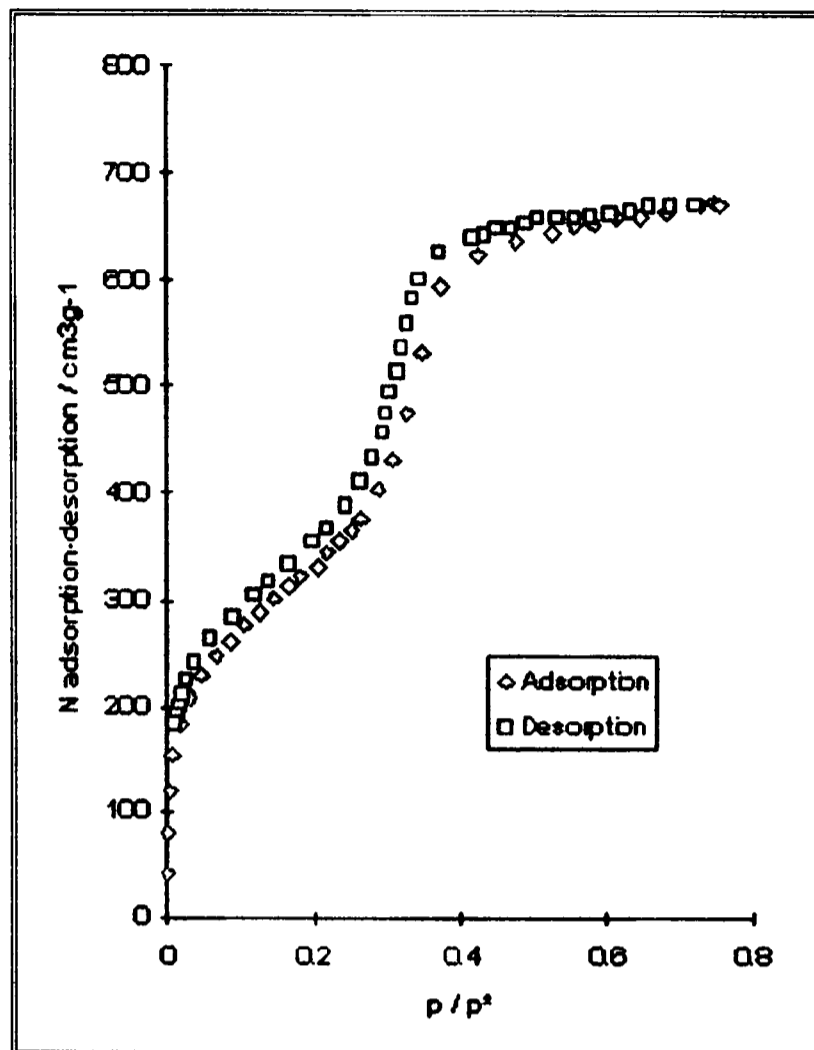


Figure 3.1.2.2: Plot of nitrogen absorbed vs. pressure for MCM-48

Figure 3.1.2.2 above shows a type IV isotherm which is typical of that obtained for mesoporous materials. The surface area can either be calculated using the BET isotherm or by estimation of the “B” point (the point at which the graph goes linear for the first time). At this point there is monolayer coverage of nitrogen on the surface of the mesoporous material. In the graph above this occurs at $240 \text{ cm}^3 / \text{g}$, which gives an approximate surface area of $1074 \text{ m}^2/\text{g}$.

The pore size can be calculated (usually from the desorption curve) and a plot of $\Delta v_p / \Delta r_p$ vs. r for the pores shows the pore radius as a maximum on the graph (Figure 3.1.2.3) (this only works well for pore sizes within the mesoporous range as can be seen by the fluctuations in the graph at lower pore radii).

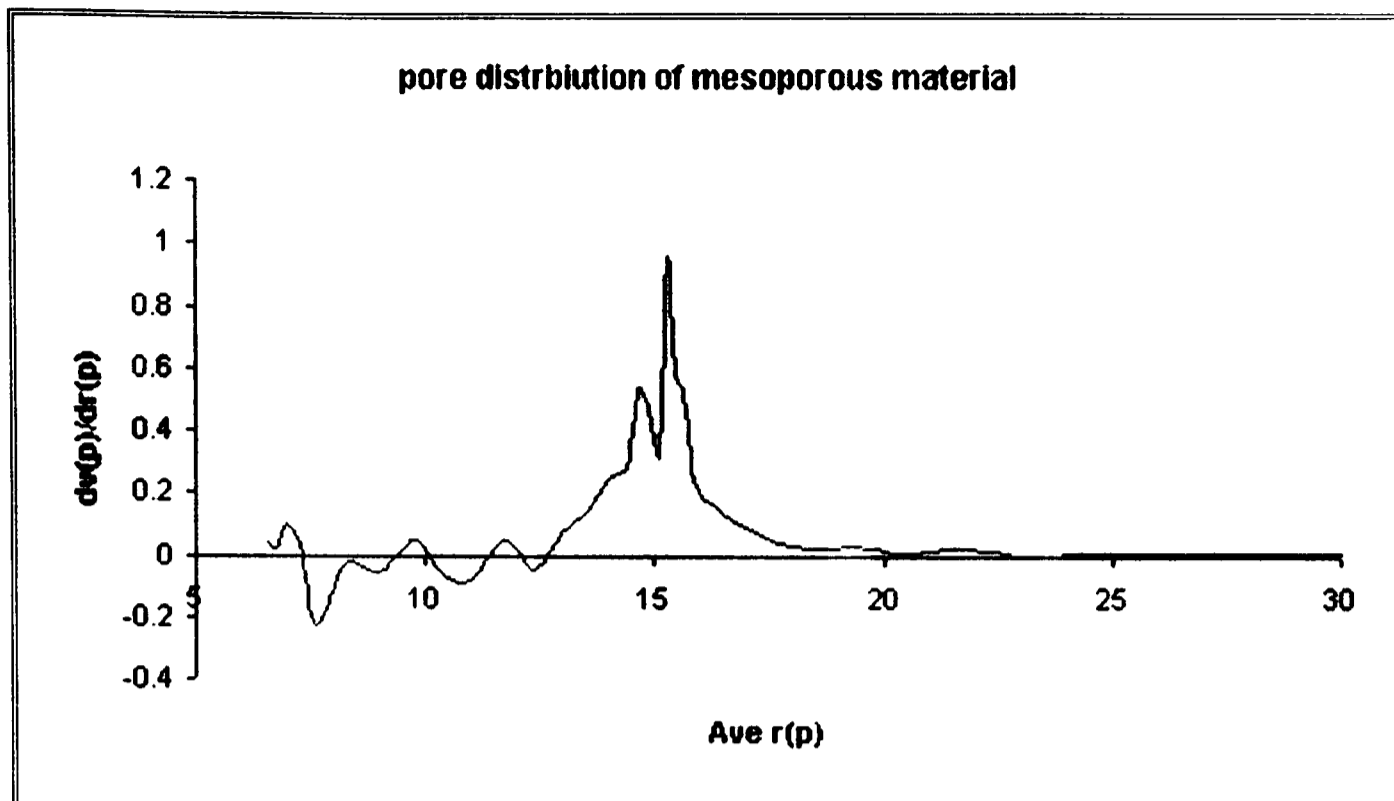


Figure 3.1.2.3: Pore size distribution plot for MCM-48

N.B. the sudden decrease in the centre of the peak is due to an erroneous point in the experimental data.

3.1.3 Surfactant rich samples

Although most of these mesoporous materials are usually easily synthesised care must be taken during the calcination process. If the washing is insufficient there can be too much surfactant present in the synthesised material, and a potentially explosive reaction can sometimes take place. It is thought this is caused by a high concentration of vaporised surfactant, which, upon changing the gas from nitrogen to oxygen can spontaneously combust. The presence of excess surfactant in the sample can be seen in the precalcination X-ray pattern with large peaks due to crystalline surfactant occurring at 2θ values of 3.4° and 6.8° (Figure 3.1.3.1). The remainder of the XRD patterns in these cases often appears of poor quality, although the final calcination product is usually of good quality. If a sample was

found to be surfactant rich it was calcined in smaller amounts and / or left under nitrogen for an additional hour.

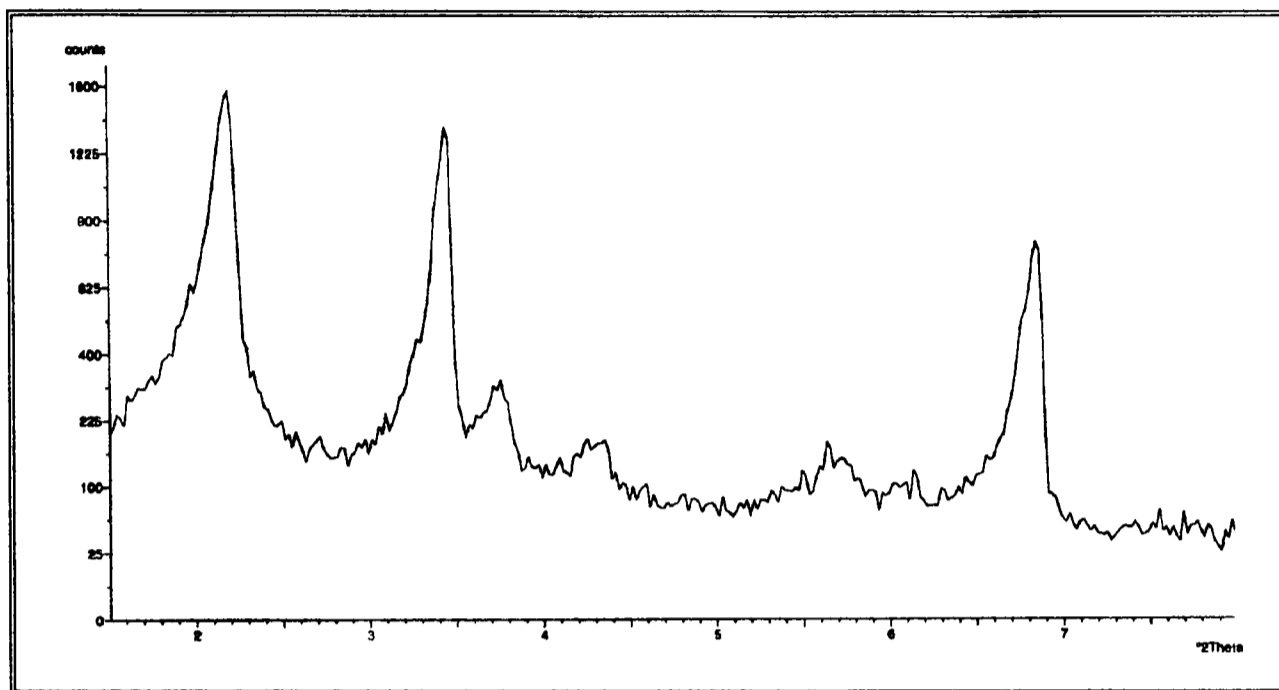


Figure 3.1.3.1. XRD of MCM-41 with excess surfactant still present

3.2.1 Modification of mesoporous materials with chloro and amino functionalised organic tethers

Synthesis

The tethers initially selected for testing were alkylsilane based, terminating with either chloro or amino groups, as the procedures for the reactions of these with the hydroxyl groups on silica supports was well known^(5, 152). The chloro functionality according to the available literature, should easily react selectively with the bridging group on a bis(oxazoline) ligand. The amino functionality could be used either to bind to a metal, which is co-ordinated to a bis(oxazoline) ligand, or be used to react with a modified ligand where an appropriate functionality had been added to the oxazoline bridge.

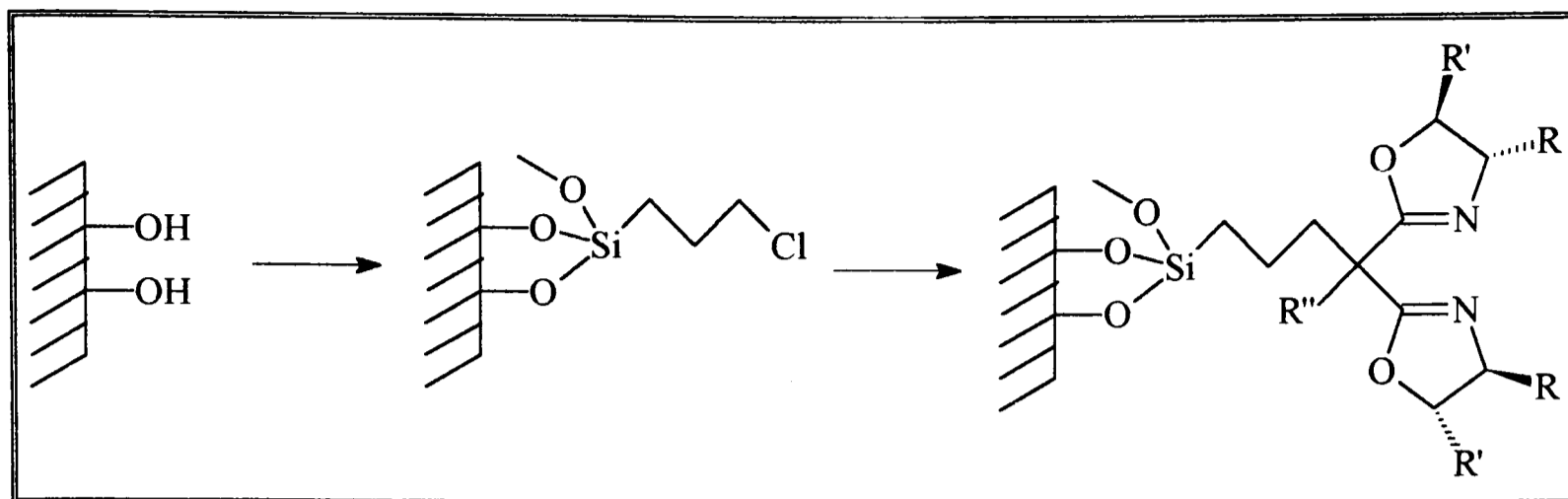


Figure 3.2.1.1: Proposed method of tethering bis(oxazoline) ligand with a chloro tether

The exterior surface of the mesoporous materials represents only a small fraction of the total surface area, but as many of the organosilane tethers are highly reactive it can be assumed that the limiting step in the reaction is the rate of diffusion. This would make the exterior surface much more likely to react than the interior surfaces. In order to try and ensure that all of the active catalytic species end up inside the pores of the support (rather than on the external surface) the surface hydroxyl groups would have to be capped first. This was achieved by the addition of a small amount of dichlorodimethylsilane. The organic species tested as tethers initially were 3-aminopropyltrimethoxysilane and 3-chloropropyltrichlorosilane. The amount of tether successfully bound to the surface could only be determined by CHN analysis. For the amine tethers this was relatively simple as a comparison could be made between the carbon and nitrogen results. For the chloro derivatives, in which no nitrogen is present, it was much harder to determine the exact loading of the tether, as residual solvent could still remain within the pores even after several hours under vacuum. A prime example of this is an early MCM-48 experiment to add chloropropyltrichlorosilane to the surface where even after several days of being gently heated on a high vacuum system CHN results were still showing a 150% theoretical yield!

The maximum loading achieved with an amine tether was 2.02 mmol g^{-1} (based on the % nitrogen), whilst for the chloro it was much lower at around 0.7 mmol g^{-1} . The maximum loadings reported are usually in the range of $1 - 1.7 \text{ mmol / g}$,⁽¹⁵³⁾ but this varies with the sample used and the synthesis method. Each of these tethers has its own particular problems. For the amine tethers, the reaction with dichlorodimethylsilane produces HCl gas which must be removed prior to addition of the tether otherwise it may deactivate the functional group. An early experiment with a chloro tether showed that a base is frequently required to ensure a complete reaction, but if too much base is added this may deactivate the functional group. These experiments were analysed by XRD, CHN and IR, some samples were submitted for ^{13}C solid state NMR.

Infra-Red spectra analysis

The IR rarely shows any additional peaks compared to pure mesoporous materials (Figures 3.1.1.2 and 3.1.1.3) and cannot be used as proof of the addition of the tether as residual solvent may cause additional peaks and low loadings of tether may not be discernible from the mesoporous support. This can be seen with a comparison of Figures 3.2.1.2 and 3.2.1.3 below, Figure 3.2.1.2 has a much higher loading of tether and this can be seen by the additional peaks at *ca.* 2935 cm^{-1} (CH_2 stretch) and 1500 cm^{-1} (CH_2 deformation). On the second Figure 3.2.1.3 the loading is too low to be able to be seen clearly over that of the mesoporous support.

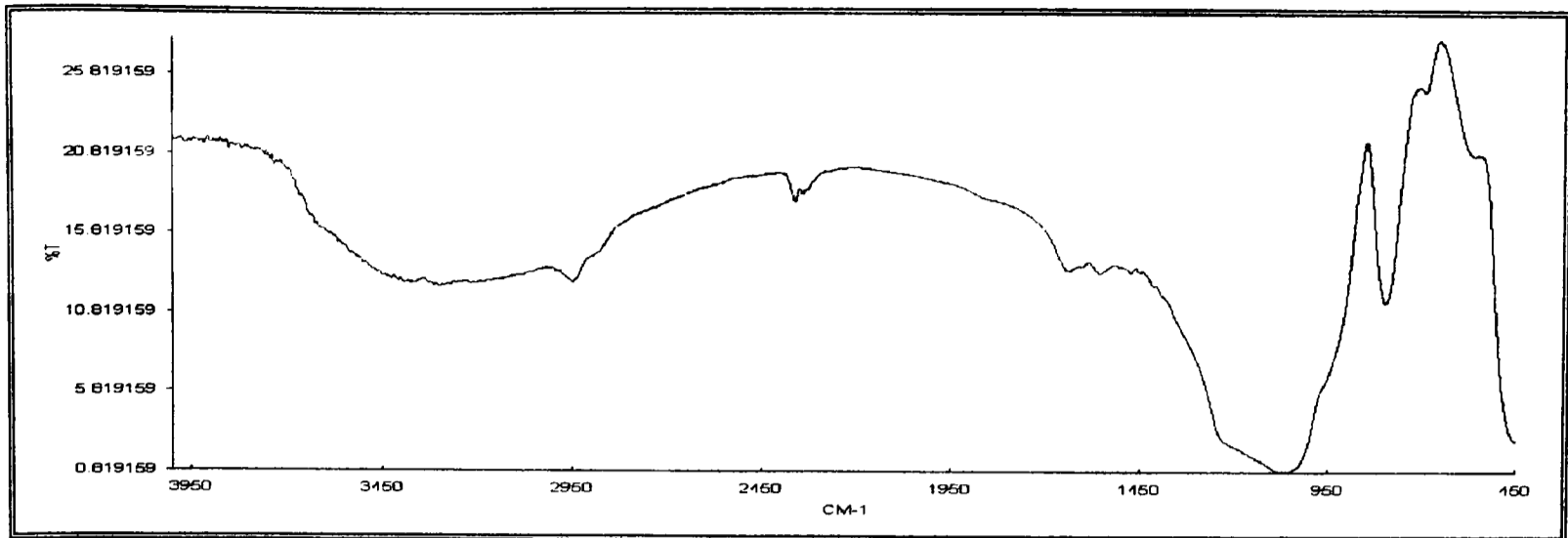


Figure 3.2.1.2: IR spectra of MCM-41 modified with 3-aminopropyltrimethoxysilane

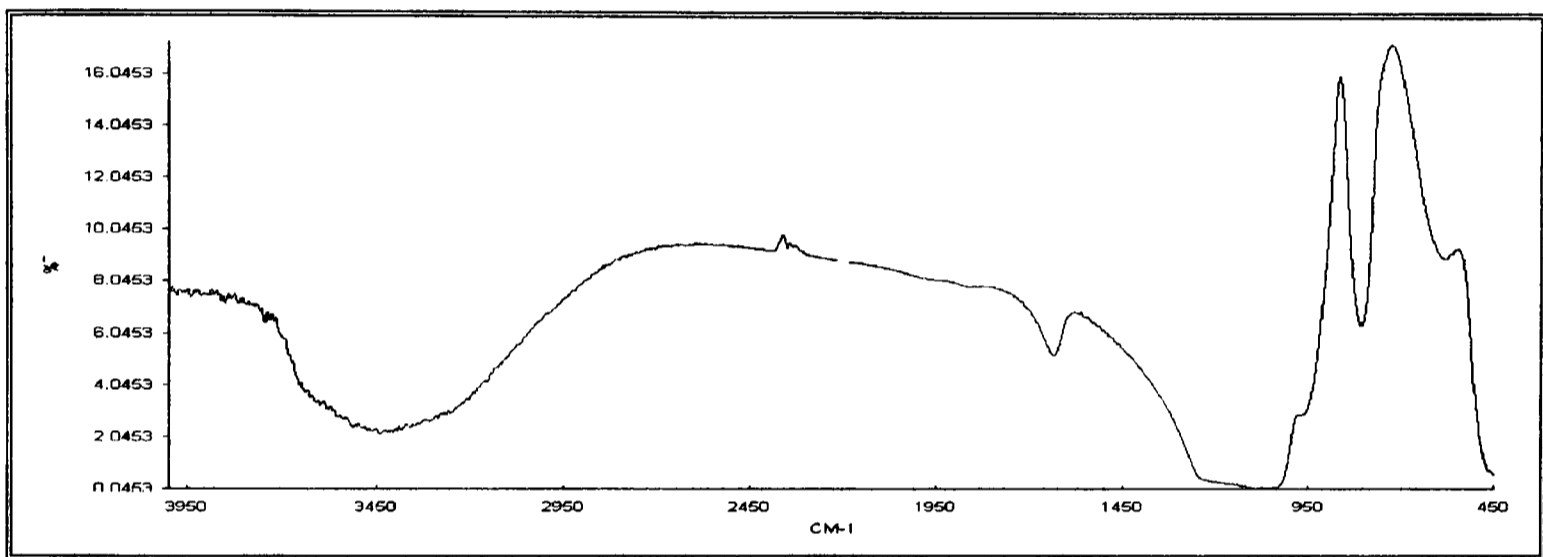


Figure 3.2.1.3: IR spectra of MCM-41 modified with 3-chloropropyltrichlorosilane

X-ray diffraction pattern analysis

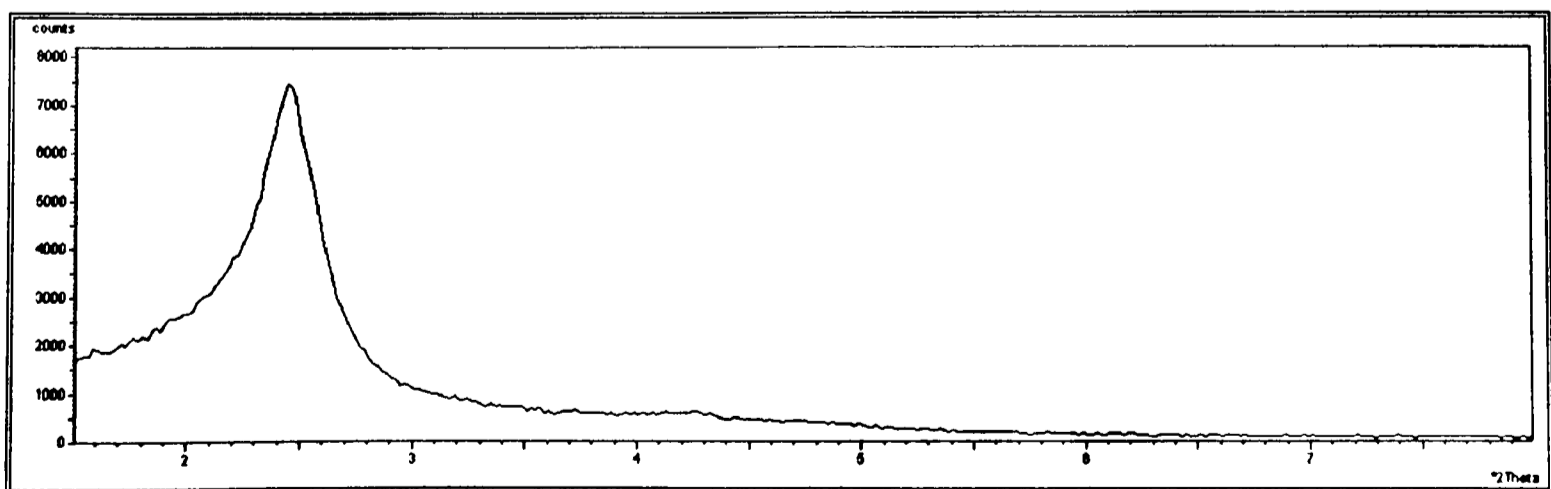


Figure 3.2.1.4: XRD pattern of MCM-41 modified with 3-aminopropyltrimethoxysilane

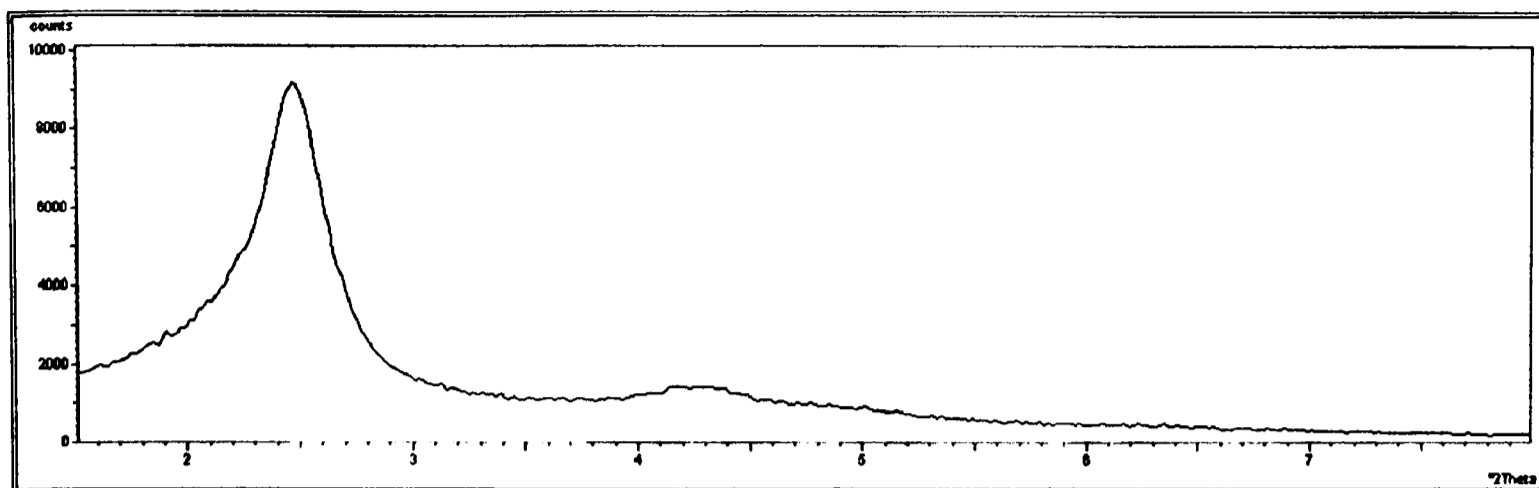


Figure 3.2.1.5: XRD pattern of MCM-41 modified with 3-chloropropyltrichlorosilane

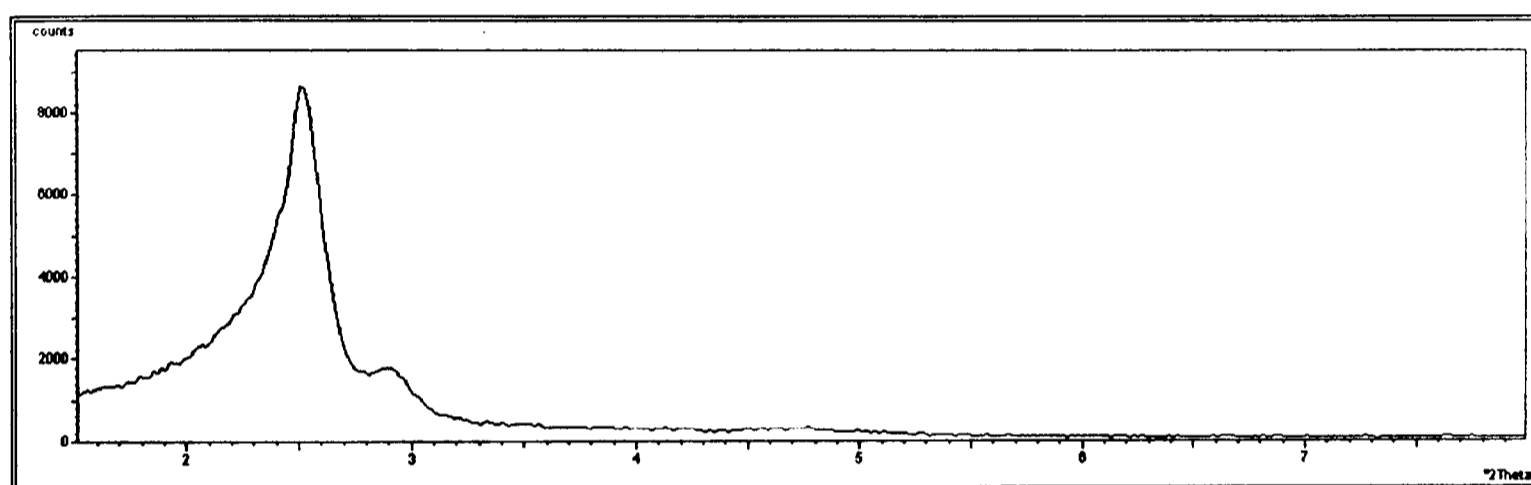


Figure 3.2.1.6: XRD pattern of MCM-48 modified with 3-chloropropyltrichlorosilane

As can be seen from the above X-ray diffraction patterns (Figures 3.2.1.4, 3.2.1.5 and 3.2.1.6) the addition of the organic moiety reduces the clarity of the secondary peaks in the diffraction patterns. This is probably caused by the tether and trace amounts of solvent left in the pores increasing the amount of variance in the repeat units of the mesoporous support although the possibility of degradation of the mesoporous host cannot be ruled out.

The loadings found in these early experiments were much too high to ensure that once the ligand was added each catalytic centre would be isolated from each other. If due to the loading the catalytic centres are too close to each other then interactions between individual catalytic sites may occur. These interactions could cause a decrease in selectivity by forcing

the catalyst (by means of steric interference) to adopt unusual conformations which may have an adverse affect on selectivity compared with the 'free' homogeneous counterparts. High loading could also reduce the activity of the catalyst by reducing the effective pore size and restricting the flow of reactants and products to and from the active catalytic site. Calculations from the CHN measurements for the amine tether also indicate that at the current high loadings not all of the methoxy groups react. It can be determined that only an average of 2.5 out of every 3 methoxy groups react at these concentrations. It was decided to reduce the concentration of the tethering species, and to react the remaining surface hydroxyl groups to stabilise the structure. This was decided as several papers show that the main weakness of mesoporous materials is their ease of destruction by water, and that deactivating the surface silanol groups with an organo-silane can significantly reduce this problem. Additionally the capping of the remaining silanol groups should reduce the residual acidity of the mesoporous support which may prove to be important in controlling selectivity in catalytic applications *e.g.* prevention of the ring opening of epoxides. The deactivation was also desirable from the viewpoint of the bis(oxazoline) ligands we propose to tether as one paper reported problems with these ligands decomposing on a silica column ⁽¹⁵⁴⁾. The capping group chosen (chlorotrimethylsilane) was similar to that used to deactivate the external surfaces of the mesoporous supports. It would be unsuitable to use this capping agent where amine tethers were present (for reasons discussed previously) but by the time we were using this capping procedure we were no longer using 3-aminopropyltrimethoxy silane as a tether.

The external surfaces were deactivated using a highly reactive alkyl silane (dichlorodimethylsilane). The rate of the reaction between the alkyl silane and Si-OH groups is sufficiently rapid that very little reagent will be able to diffuse into the pores and so will react with the external surface.

^{13}C Solid State NMR

Some of the tethered samples experiments were submitted for ^{13}C solid state NMR, but in the majority of cases the loading of organic material was insufficient to obtain good resolution unless the support was saturated with the organic tether.

Where sufficient resolution was achieved the carbon atoms in the tethers could be seen clearly, although in addition to these peaks further peaks were sometimes observed for residual solvent which was not removed from the pores. This can be seen in Figure 3.2.1.7 which shows the peak due to the tether at *ca.* 9 ppm (Si-CH₂), 26 ppm (CH₂) and 46 ppm (CH₂Cl) and also peaks due residual solvent at *ca.* 11 and 66 ppm.

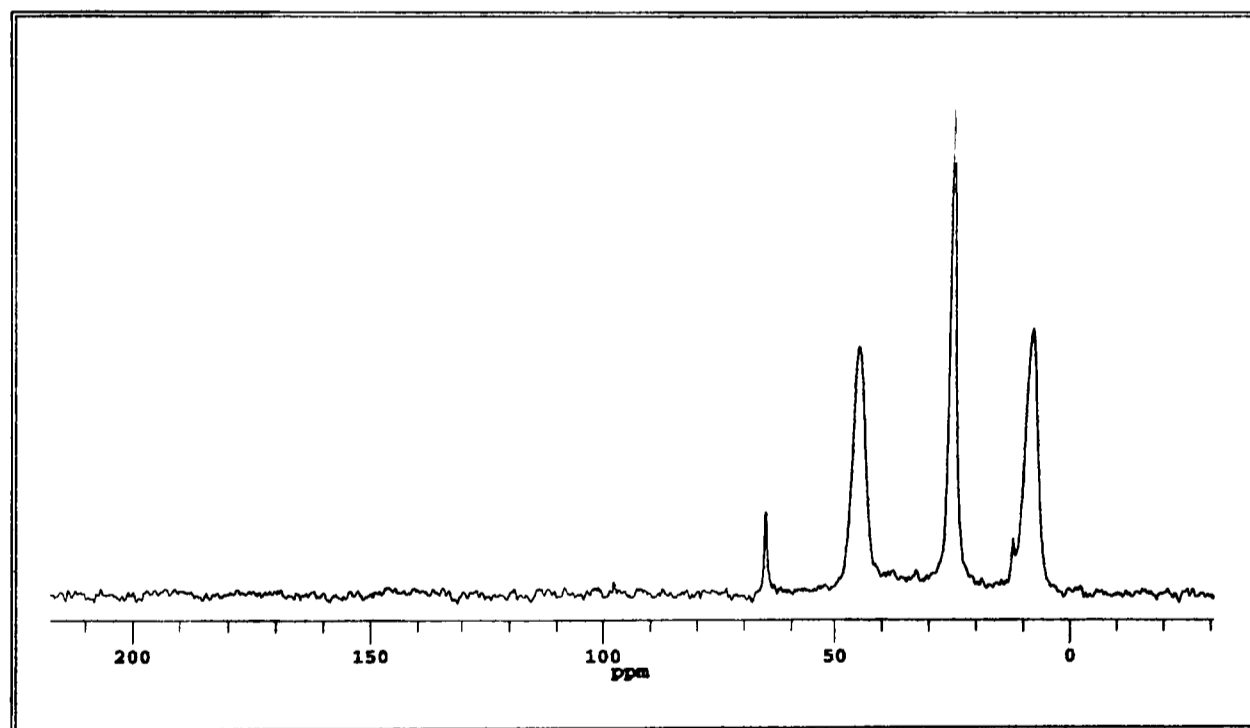


Figure 3.2.1.7: ^{13}C solid state NMR of 3-chloropropyltrichlorosilane modified MCM-41

3.3 Synthesis of bis(oxazoline) ligands

3.3.1 Introduction

The synthesis of bis(oxazoline) ligands was undertaken for 2 main reasons: the first was to gain experience at making these types of ligands in order to determine whether synthesis inside the pores of mesoporous materials was practical (this is the method most commonly used for making the related supported salen type catalysts). The second was to synthesise bis(oxazoline) ligands that were similar to those reported as being suitable ligands for catalysis but which were not commercially available.

Various difficulties were encountered with literature methods, mostly being problems with purification of the final product *via* chromatography. In the vast majority of syntheses of bis(oxazoline) ligands, a silica column is suggested for the purification with various solvent mixes being used (e.g. ethyl acetate/ ethanol 40/1 ⁽¹⁰⁶⁾, dichloromethane/ acetone 10/1 ⁽⁹⁷⁾, cyclohexane/ ethyl acetate 65/35 ⁽¹⁵⁵⁾). Whilst in the earlier experiments we also used silica columns it has also been reported in one paper that silica columns can cause decomposition of bis(oxazoline) ligands ⁽¹⁵⁴⁾. The later and more successful syntheses that we carried out therefore followed the Masamune protocol which uses a neutral alumina column to purify the product. Initial attempts to synthesise bis(oxazoline) ligands were carried out using cheap achiral aminoalcohols, which were already present in the lab, in an attempt to obtain large quantities of test ligand which could be screened for a range of different tethering strategies. This caused some problems as the aminoalcohols used lacked the necessary organic bulk to ensure that during some of the purification stages the product did not migrate to the aqueous phase.

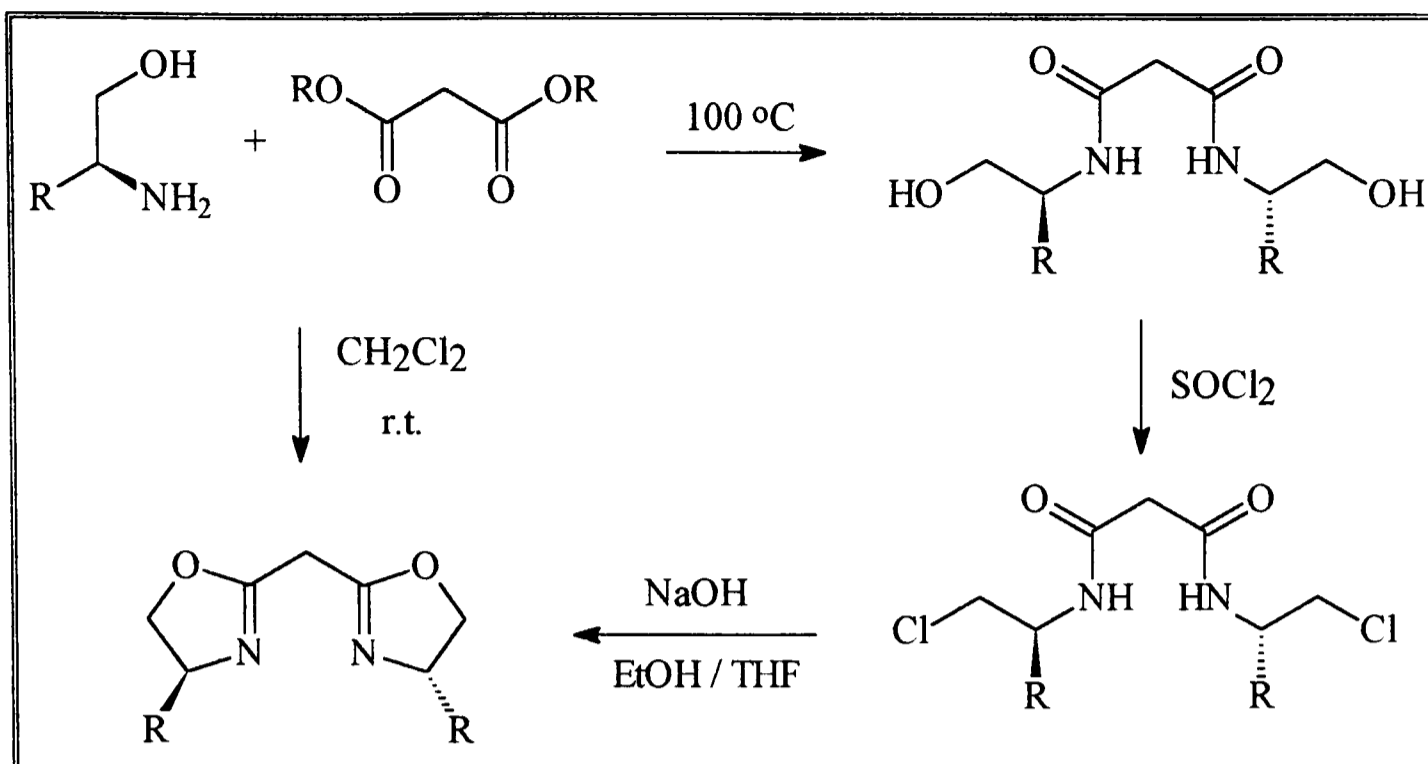


Figure 3.3.1.1: Synthesis of bis(oxazoline) ligands ^(based on a diagram in ref. 93)

In nearly all synthesis methods for bis(oxazolines) the diamide is formed first and then the oxazoline rings are closed. The different methods of ring closure can be applied to the diamides once they are formed, and so the first compound that must be synthesised therefore is the diamide intermediate.

3.3.2 Diamide synthesis *via* reflux of diethylmalonates

The synthesis that was attempted first (and seemed to be the easiest) was based on a method used by Pfaltz, ⁽⁹³⁾ which involved refluxing a malonic ester and an amino alcohol in toluene to form the diamide intermediate (top right in Figure 3.3.1.1). Originally ethanolamine was used with two different malonic esters which were diethyl-2-bromo-2-methyl malonate and diethyl phenylmalonate as it was thought that these would be suitable for reacting with the modified MCM materials described previously. The bromo containing bis(oxazoline) would be expected to react with an amino functionalised mesoporous material,

whereas the phenyl containing bis(oxazoline) would have a single hydrogen on the bridging position between the oxazoline rings which should react with a halide tether.

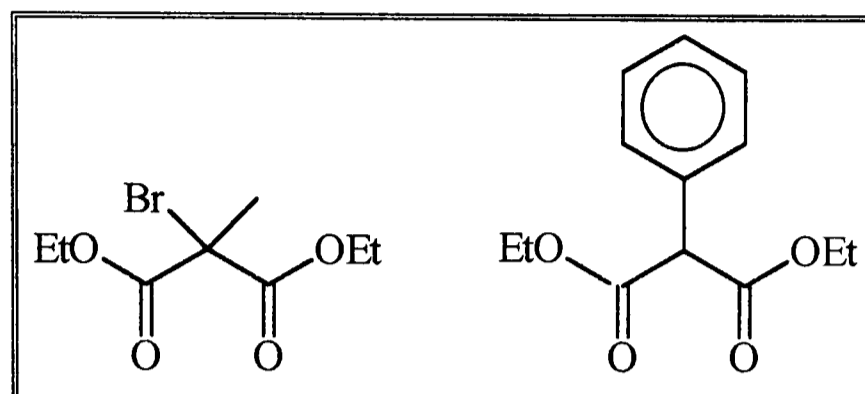


Figure 3.3.2.1: Structures of diethyl-2-bromo-2-methyl malonate and diethyl phenyl malonate

The purification of the diamide product was initially attempted by column chromatography on silica where the unreacted malonic ester starting materials were recovered easily. The diamide stuck to the column and required methanol to remove any product, and was subsequently impure. The amount of recovered malonic ester was over 50% of the initial amount and even in the literature the maximum yield stated for this method is only 85%⁽⁹³⁾ (compared with up to 98% for other methods)⁽¹⁵⁵⁾. In much of the literature the diamide intermediate has either not been purified or has been purified by recrystallisation, but for the ethanolamine derivative the product remains liquid and so recrystallisation was not possible. Our preparation may have been affected by the use of simple aminoalcohols, such as ethanolamine, in place of the much larger aminoalcohols used in the literature which can be purified *via* recrystallisation.

3.3.3 Bis(oxazoline) synthesis using malonitrile

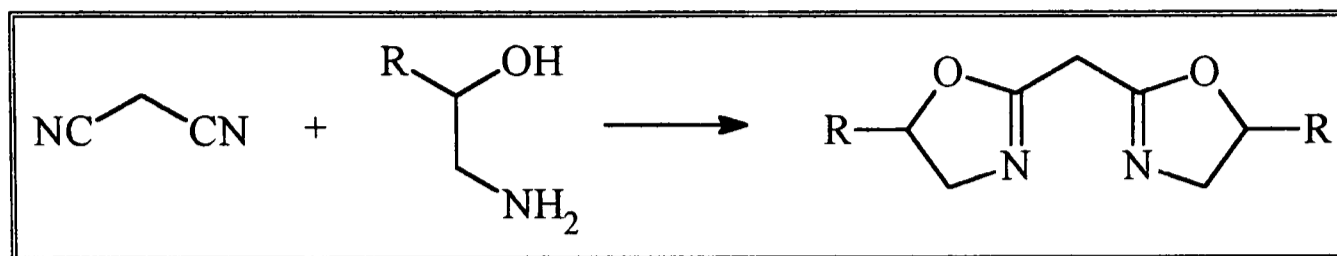


Figure 3.3.3.1: Synthesis of Bis(oxazoline) using malonitrile⁽⁹⁵⁾

In view of the low yield it was decided to try some of the other methods of synthesising bis(oxazoline) ligands. The next method tried used malonitrile with zinc acetate as a catalyst⁽⁹⁵⁾ (Figure 3.3.3.1) again with ethanolamine in refluxing toluene. No product was observed for this reaction.

3.3.4 Diamide synthesis using malonyl dichloride

The next method tried is much more commonly used than either of the first two, involving the use of a much more reactive reagent to react with the amino alcohol (Figure 3.3.4.2). The first stage is the synthesis of malonyl dichloride from malonic acid (Figure 3.3.4.1)^(99, 100); this synthesis is straightforward although care must be taken to obtain good yield and purity of the final product. In early experiments with this method very little product was recovered, and sometimes the product was impure, one of the main problems being that a large amount of charring occurs which drastically reduces the yield. The reasons for this low yield have been traced to too intense heating and low solubility of malonic acid in thionyl chloride and several ways of improving the yield and purity of the product have been suggested⁽⁹⁸⁾. These include powdering the malonic acid and the use of flat-bottomed conical

flasks to increase the surface area. Following this advice improved both the yield and purity of the final product. In our work maximising the yield was felt to be of secondary importance compared with purity, especially when using the expensive chiral aminoalcohols which would become the limiting factor. The malonyl dichloride produced compared well to the published data although the sensitivity to moisture meant that the product was used immediately in the diamide synthesis.

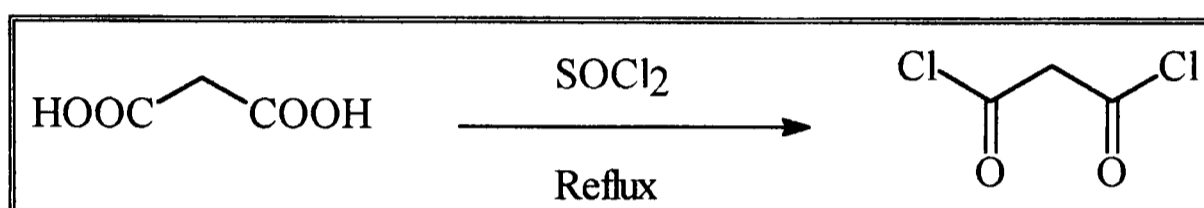


Figure 3.3.4.1: Synthesis of malonyl dichloride

In addition to malonyl dichloride we also synthesised phenylmalonyl dichloride, the synthesis of which was straightforward as any problems had already been encountered and solved during the previous syntheses of malonyl dichloride. The reason for synthesising this compound was to add additional organic bulk to the diamide intermediates to try to ensure that the product was soluble in the organic phase.

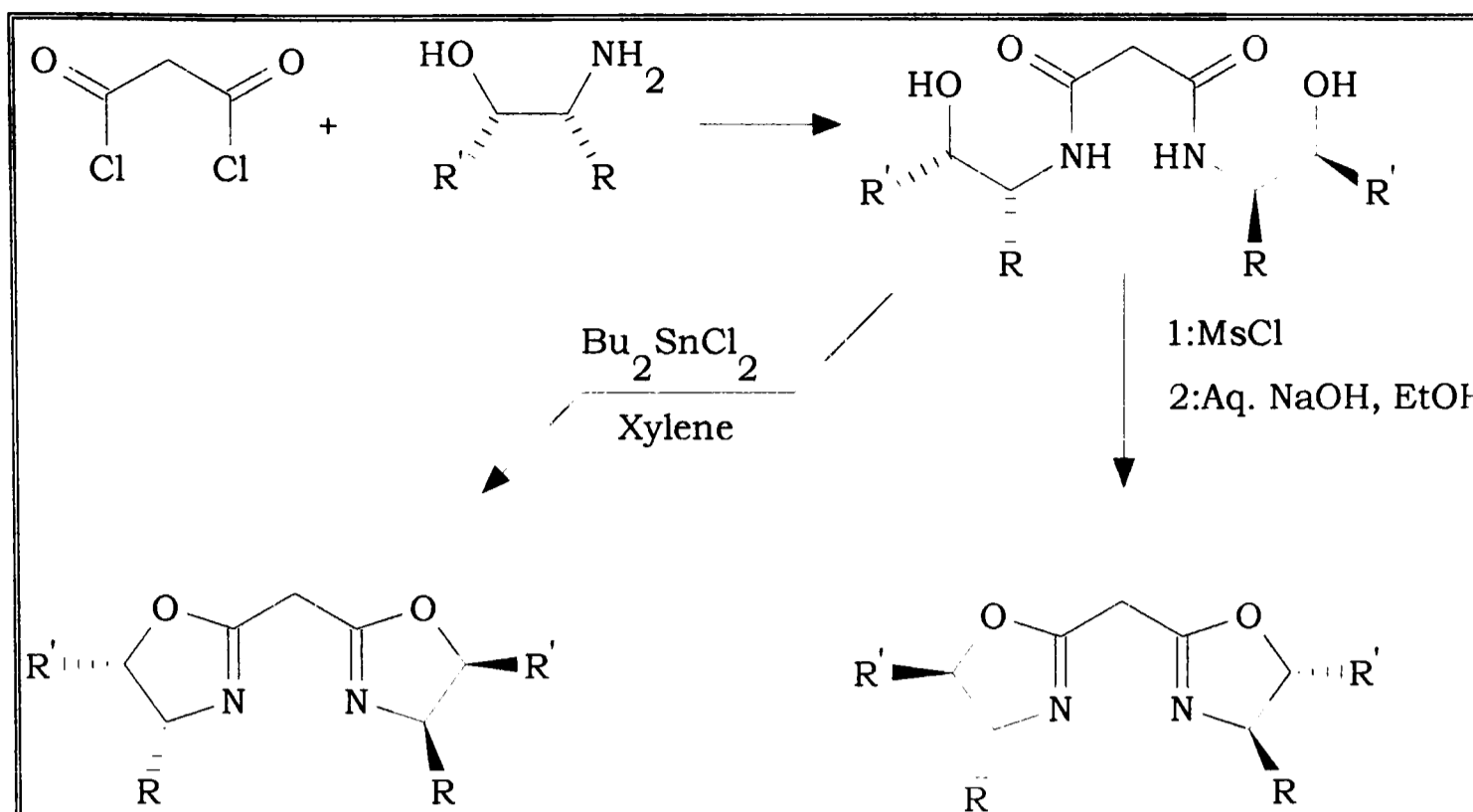


Figure 3.3.4.2: Bis(oxazoline) synthesis from malonyl dichloride and amino alcohol (reproduced from ref. 94)

The reaction of the dichloride with the aminoalcohol also proceeds fairly smoothly. It is characteristically carried out in cold dichloromethane with triethylamine as a base. In some literature studies, where the diamide intermediate is sufficiently bulky (such as with the pyridyl bis(oxazolines) (Figure 1.4.2.3) the product can just be filtered off and recrystallised⁽¹⁰²⁾. Other papers suggest diluting the solution with more dichloromethane before quenching the reaction with ice water^(106, 155) and washing with dilute HCl and sodium hydrogen carbonate solutions. In several of our experiments a fine powder was found at the bottom of the reaction vessel, however in all cases this turned out to be a chloride salt of triethylamine. Also in the early experiments with ethanolamine, butanolamine and 2-amino-2-methylpropan-1-ol little or no product was found in the organic phase. This might be expected for some of the smaller diamide intermediates as they contain 2 alcohol groups and 2 secondary amines. As the range of large racemic aminoalcohols is limited this led us to try a much larger amino alcohol 1,2-aminophenol. Using 1,2-aminophenol the products were found as expected in the organic phase and in reasonable yield. We were though unable to close the two oxazoline

rings by the usual synthesis methods suggested in the literature (using thionyl chloride or methane sulphonyl chloride followed by reflux with an aqueous alcohol/ base solution). The failure to close the rings is probably due to the amino alcohol (1,2-aminophenol) being incompatible with the method tried due to lack of flexibility in the phenyl ring. The completed bis(oxazoline) with 1,2-amino phenol has been reported in the literature as a by-product in an unsuccessful synthesis of a diaminobenzo macrocycle ⁽¹⁵⁶⁾.

3.3.5 Bis(oxazoline) synthesis via the Masamune protocol

We then tried the Masamune protocol ^(91, 104) which had been reported as the most successful method in some of the other papers. This method is essentially a 1-pot synthesis where the diamide intermediate is formed by reflux and the oxazoline rings are closed by using dichlorodimethyl stannane (also called dimethyl tin dichloride). This method uses a higher boiling solvent (xylene instead of toluene) than the previously tried reflux method, and also has the advantage that as a 1-pot method the diamide is constantly being removed forcing the reaction to completion. The reason that it is not always used is because closing the oxazoline ring by using this method does not reverse the stereochemistry on the 5 position on the oxazoline ring. Closing the oxazoline rings by use of either thionyl chloride or methanesulphonyl chloride causes inversion at this position on the oxazoline ring. This means that the different methods work by different routes and the steric effects that bulky groups in the 5 position will affect each method differently. Some studies using bis(oxazolines) with substituents on both the 4 and 5 positions on the oxazoline ring have shown that the steric effect from the group in the 5 position of the oxazoline ring can have a large effect on the selectivity of any resultant catalyst ⁽⁹²⁾. For this method the early

experiments used phenylglycinol as the aminoalcohol as this had been previously used in the literature and so was not expected to give any of the problems previously encountered with other aminoalcohols, and the analytical data for this compound had been previously published (93).

The first time we attempted this method a lower boiling solvent than was suggested in the literature was used (toluene instead of xylene). The expected bis(oxazoline) ligand had not formed in any great quantity, but the NMR showed that a small amount of the ring open diamide intermediate had been formed. This did not survive Kugelrohr distillation to try to obtain any ligand formed. With the correct solvent (xylene) the bis(oxazoline) ligand was produced although a large number of impurities were present. Purification was undertaken on a silica column pretreated with triethylamine followed by Kugelrohr distillation although a pure product was not obtained. Problems were encountered during the purification process as the bis(oxazoline) ligands are difficult to see on TLC at low concentrations either using a normal UV lamp or with iodine. The yields were still very low compared to the literature and a reason for this was found in a subsequent experiment with leucinol and using a neutral alumina column to purify the product. This only gave us 2 products, the diamide intermediate and a product where only one of the two bis(oxazoline) rings had closed. This suggested that the Dean-Stark apparatus was not efficiently removing all of the water and the dimethyl tin dichloride was being deactivated. Greater care to ensure dryness resulted in the bis(oxazoline) ligand being produced in reasonable yield (44%) with a similar amount of diamide precursor and mono(oxazoline) recovered. Some subsequent reactions used molecular sieves in a soxhlet extractor to effect removal of moisture.

3.3.6 Conclusions of bis(oxazoline) Syntheses

Given the above problems it was decided that the synthesis of bis(oxazolines) *in situ* in the pores of mesoporous materials would be unlikely to succeed by the methods that we had tested. The yield obtained in homogeneous reactions showed that it would be impossible to obtain a pure supported ligand by this method. The hydroxyl groups on the surface of the mesoporous materials, coupled with difficulties in removing all of the moisture, would cause too many problems for either the malonyl dichlorides or the Masamune ring closure procedure using dimethyl tin dichloride which appears to be sensitive to moisture. The alternative ring closure method, which involves refluxing with an aqueous alcoholic base is unsuitable for use with MCM type materials as it has been reported that boiling in water rapidly destroys the structure^(52, 54).

On prolonged storage over the course of the project it was found that the ligands also partially decomposed! Samples stored for two years from their initial synthesis we found to be a much darker orange colour, and when we attempted to use these to form the purple copper (II) di-bis(oxazoline) complex no purple colour was observed. Subsequent NMR analysis showed that a large part of the ligand had decomposed. This also explains why the commercially available bis(oxazolines) often differ in colour to those reported in the literature, and why the NMR of the purchased products often show that they contain more impurities than the label suggests (Figure 3.3.6.1). Attempts to purify the purchased ligands by Kugelrohr distillation before use tended to result in low yield and further decomposition of the ligand.

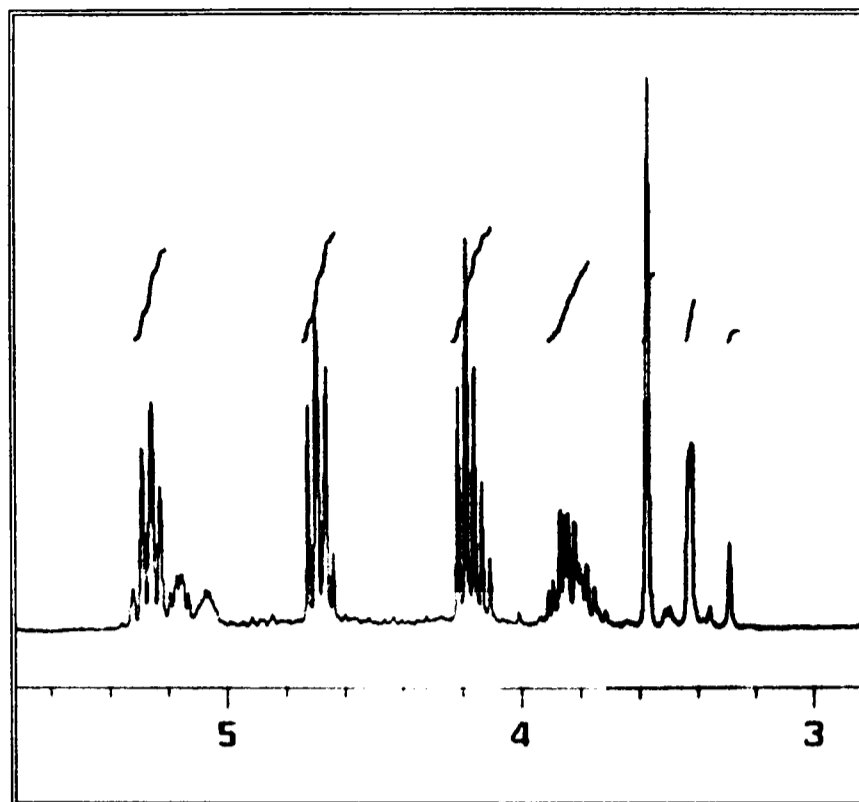


Figure 3.3.6.1: Expansion of the ^1H NMR of purchased methylenebis(4-*S*-phenyl-2-oxazoline) showing the bridging and oxazoline ring protons.

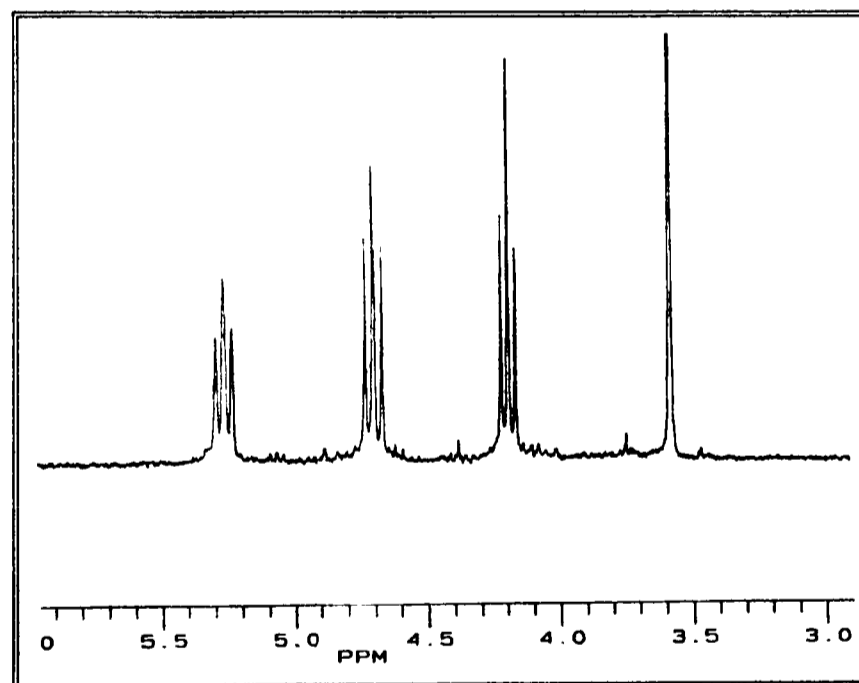


Figure 3.3.6.2: Expansion of the ^1H NMR of pure methylenebis(4-*S*-phenyl-2-oxazoline)

In comparison to figure 3.3.6.1, the peaks due to the bis(oxazoline) ligands can be easily determined in figure 3.3.6.2. These have been interpreted as 5.25 ppm H-C(4,4'); 4.69 ppm H_a-C(5,5'); 4.19 ppm H_b-C(5,5') and 3.57 ppm C(2)-CH₂-C(2).

3.4. Tethering of Bis(oxazoline) ligands to supports via haloalkane tethers

3.4.1 Chloro tethers

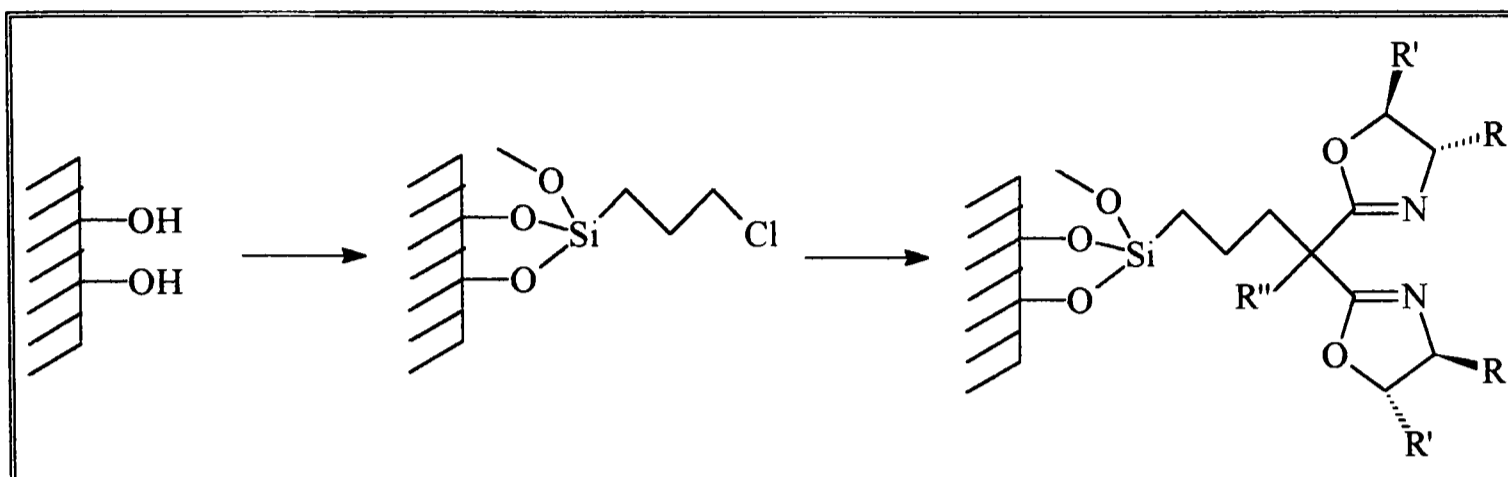


Figure 3.4.1.1: Proposed method of tethering bis(oxazoline) ligand with a chloro tether

With the MCM's modified with 3-chloropropyltrichlorosilane various methods were tried to react bis(oxazoline) ligands with the tether which would have been expected to yield the supported ligands based on the available organic literature ⁽¹⁵⁷⁾. The standard method involves reaction of the ligand with a slight excess of n-butyl lithium which should deprotonate the bridging group of the bis(oxazoline), rendering it open to react with a suitable electrophile. However, we were unable to get this reaction to proceed even when using promoting agents such as TMEDA (tetramethylethylenediamine). The initial method used was to add the bis(oxazoline) ligand to a mesoporous material modified with a chloro tether, to enable any unreacted ligand to be recovered; no supported ligand was observed by this method. With materials which were not completely modified, the failure of the reaction may have been caused by the presence of the remaining silanol groups present on the surface. In some of the later experiments where the surface silanols had been deactivated with alkylsilanes the solid state NMR showed that the reaction seemed to be removing many of the capping alkylsilane groups. Attempts to react the bis(oxazoline) ligand with 3-chloropropyl

trimethoxysilane and then add the supporting material also failed. A test reaction between purchased methylenebis(4-*S*-phenyl-2-oxazoline) and 2-chlorooctane showed no reaction, instead only a purer bis(oxazoline) being recovered after purification (Figure 3.4.1.2). The extent of the reaction can be easily seen in the NMR even without completely separating the products, as the peak for the hydrogens on the bridge group can be used as an indicator: they shift downfield and split for a single tether, and disappear completely when two tethers have been added to the same bridging methylene group (Figure 3.4.2.1). The oxazoline ring protons can be used to determine how much of the di-tethered species is formed as on the chiral ligand they separate into easily distinguishable groups for which the intensity can be easily determined.

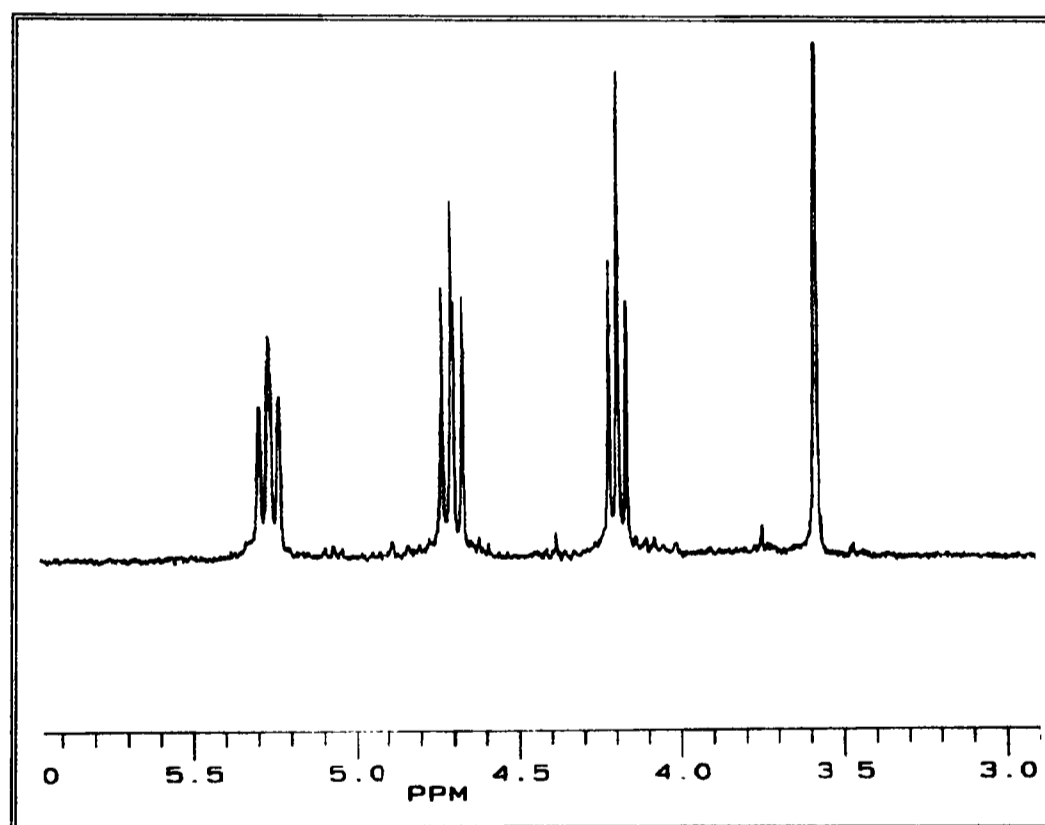


Figure 3.4.1.2: Enlargement of the ^1H NMR spectra of methylenebis(4-*S*-phenyl-2-oxazoline) (recovered from a chloro experiment) showing only the peaks caused by the unreacted oxazoline ring protons and bridging protons

The findings confirmed that the bis(oxazoline) ligand did not react by either method using 3-chloropropyltrichlorosilane or 3-chloropropyltrimethoxysilane to form a supported species. This is in contrast to the literature which suggests the reaction between an oxazoline

and an organic halide using butyl lithium should proceed selectively at the bridging position⁽¹⁵⁷⁾. In order to get this reaction to work either a harsher reagent such as *t*-butyl lithium, or methyl lithium or a better leaving group would be required. The simplest method was to increase the ability of the leaving group by moving down group 17 in the periodic table. Tests using 2-bromooctane with TMEDA as a promoter showed the reaction occurring, proving that this strategy was sound. The reaction was then tested with 1-iodobutane (as 3-iodopropyltrimethoxysilane was readily available, and a better leaving group might make it possible to avoid using TMEDA or other unnecessary reagents).

3.4.2 Iodo tethers

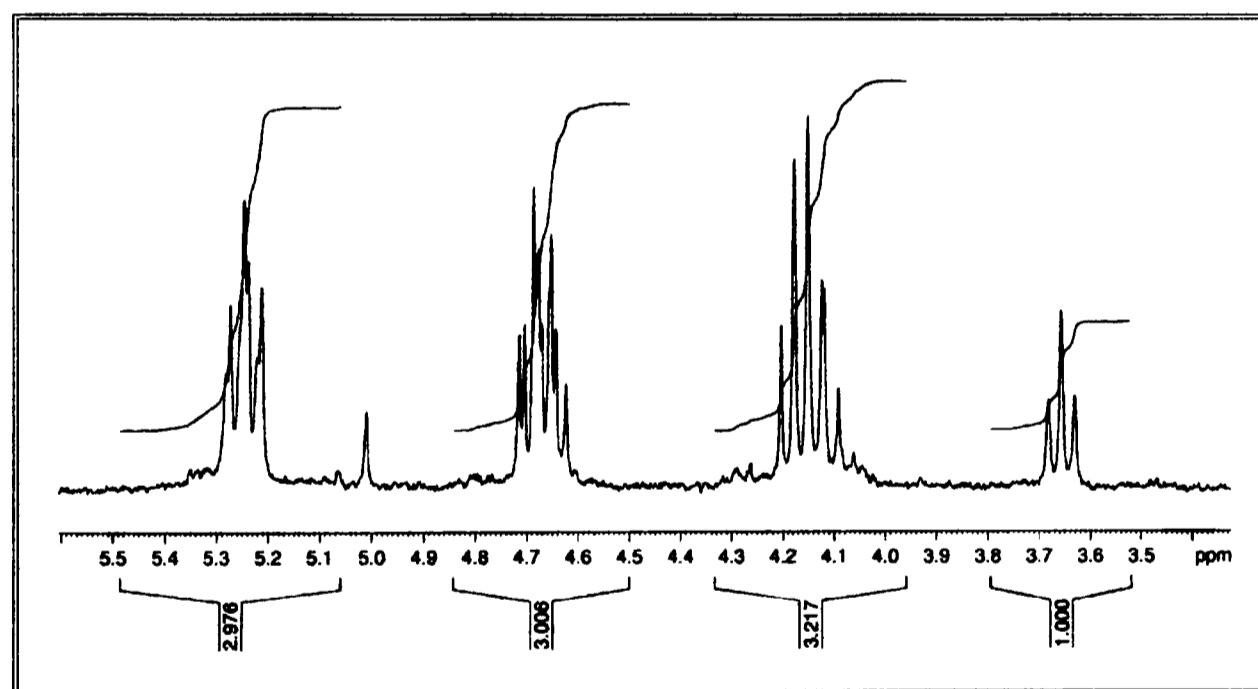


Figure 3.4.2.1: Enlargement of ¹H NMR spectra of methylenebis(4-*S*-phenyl-2-oxazoline) reacted with 1-iodobutane and TMEDA.

Figure 3.4.2.1 shows that the reaction proceeds well and that all of the ligand has reacted with a 2:1 ratio in the final product between the mono and the di modified species with 1 and 2 tethers respectively. The reaction also showed signs of self-indication, as the

further the reaction proceeds more liberated iodine is present in the solvent, eventually turning the solution a deep red colour.

Based on this work it was decided that the best course of action was to react the tether (3-iodopropyltrimethoxysilane) and the bis(oxazoline) ligand together first and then to add the product to the mesoporous support. Due to the reactive nature of the tethering species and especially as the final aim is to bind this to silica, separation of the mono-tethered and di-tethered products is very difficult. Given that the modified tethers are moisture sensitive (due to the presence of the trimethoxysilyl group) and react with silica this meant that the only purification strategy that might work was reverse phase chromatography (fractional distillation would also cause the methoxysilyl groups to condense).

Reverse Phase HPLC

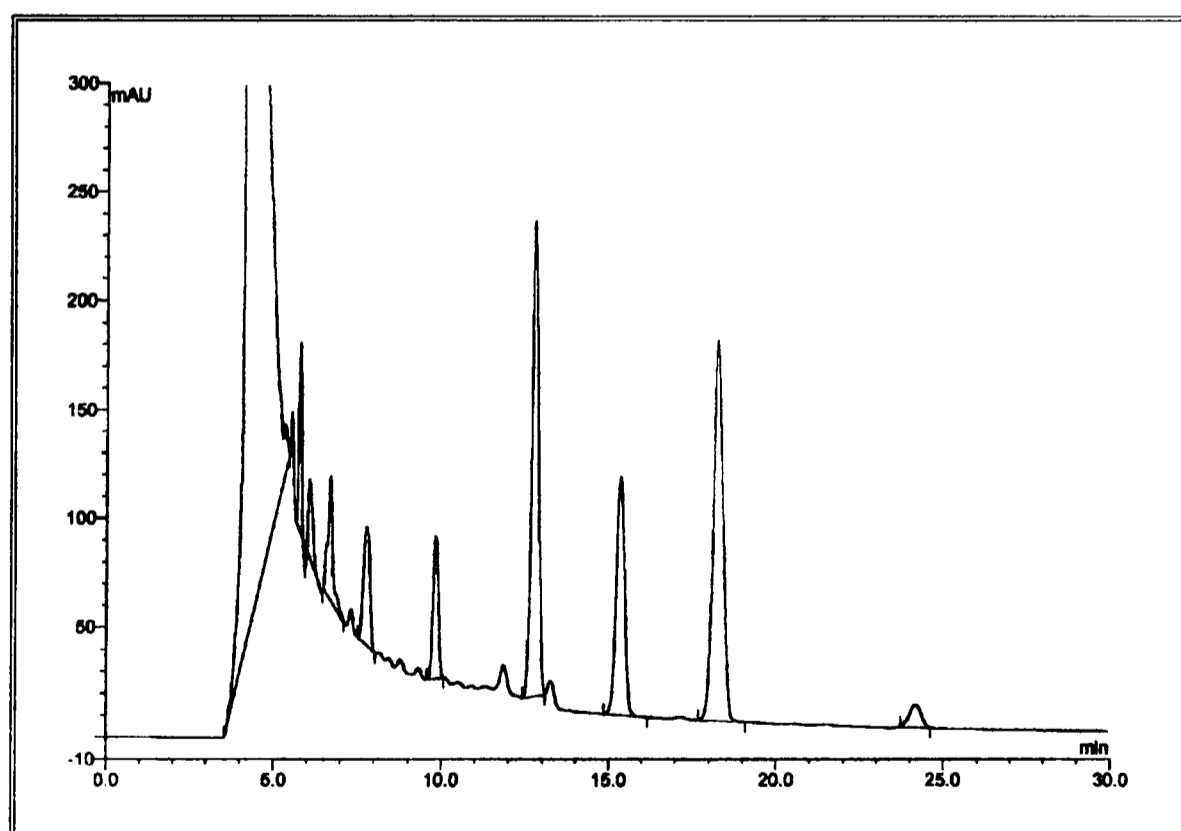


Figure 3.4.2.2: Reverse phase HPLC trace of modified bis(oxazoline) ligand

Reverse phase HPLC was used to try and separate the bis(oxazoline) ligand with one and two tethers attached. Due to concerns with the methoxysilyl groups condensing and solidifying in the column, the range of solvents was restricted to acetonitrile. This did partially separate at least 10 fractions (Figure 3.4.2.2) although only 3 had sufficient separation to obtain pure samples in sufficient quantity for further analysis. None of these samples when investigated by mass spectra and IR showed any form of the bis(oxazoline) ligand present.

The best course of action at this stage was seen as to accept that both mono and di-tethered species would be present, as in some polymeric systems the loss of C_2 symmetry caused by addition of only one tether to the bridging group does not adversely effect the selectivity of the catalyst⁽⁶⁹⁾. In subsequent experiments the products were not separated and a one-pot strategy was used. The first stage of the reaction proceeded well, the colour indication provided by the liberated iodine showing that the reaction had taken place, and the addition to the MCM was carried out in the same manner as the previous additions of tethers. Soxhlet extraction was used to ensure that any ligand that was detected in the analysis was bound to the surface. The IR spectrum showed the additional peaks in the C-H stretching region similar to those in Figure 3.2.1.2, but the most characteristic peak for oxazolines (the C=N bond at *ca.* 1667 cm^{-1}) was obscured by the OH bending absorption band from the mesoporous support (and absorbed water) meaning that IR could not be used for definitive identification. CHN analysis failed to show any nitrogen present, but from calculations based on the carbon the amount of nitrogen present for the ligand this would have been very small (less than 0.25 %) and below the detection limit of the analyser. In addition TMEDA and ethylenediamine were also used in the reaction and so the presence of nitrogen does not necessarily indicate the presence of the ligand. The sample was submitted for solid state

NMR but the noise on the spectrum was very large and only one peak could be determined with 100% certainty. This peak was at 128 ppm and belongs to the phenyl aromatic ring system on the methylenebis(4-*S*-phenyl-2-oxazoline) and as no other aromatic compounds were used in the synthesis we were able to conclude that the ligand had been successfully bound to the surface. The reaction was repeated with enough methylenebis(4-*S*-phenyl-2-oxazoline) to saturate support to get conclusive data to support the theory. The IR again showed the extra peaks associated with C-H stretching but again conclusive results could not be drawn from these measurements. The CHN showed nitrogen present but as indicated earlier this does not confirm presence of the ligand. Solid state NMR was used on this sample and the resulting spectra (Figure 3.4.2.3) showed peaks which compare very well to the published literature values for the ligand and the tether. The peaks reported for the homogeneous ligand occur at 163.0 ppm (C 2,2'), 142.0 ppm (aromatic C), 128.7, 127.6, 126.7 ppm (aromatic CH), 75.4 ppm (C 5,5'), 69.8 ppm (C 4,4') and 28.4 ppm (bridging C). Peaks at low ppm values are difficult to interpret due to the presence of both mono and di-tethered bis(oxazoline) ligands and unreacted tether which gives peaks at 19, 26 and 46 ppm. The broadness of the peaks may be due to disorder and the largest peak for the phenyl group at *ca.* 128 ppm has side bands. These are additional peaks which are shifted from the main peak by a frequency corresponding to the spinning speed of the sample (in this case 5 kHz). They tend to be observed for strong peaks corresponding to carbons which have slow relaxation times such as aromatic groups.

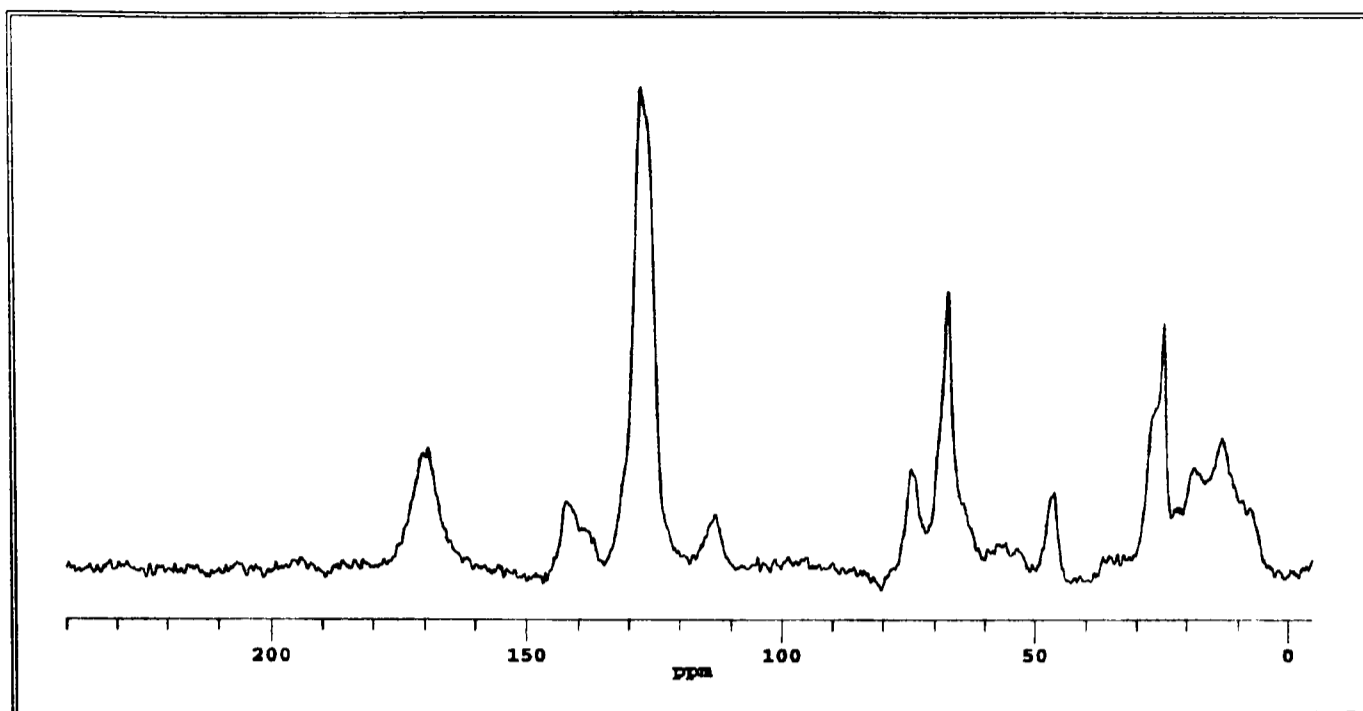


Figure 3.4.2.3: Solid state ^{13}C NMR of methylenebis(4-*S*-phenyl-2-oxazoline) tethered to MCM-41 using 3-iodopropyltrimethoxysilane

Further experiments showed that the reaction between the tether and the bis(oxazoline) ligand still occurred in the absence of TMEDA but required a longer period of time before the indicative colour change was observed. The vast majority of reactions to support the ligands were therefore carried in the absence of TMEDA.

3.5 Bis(oxazoline)-Copper (II) catalyst complexes

3.5.1 Complexes supported *via* alkyl halide tethers

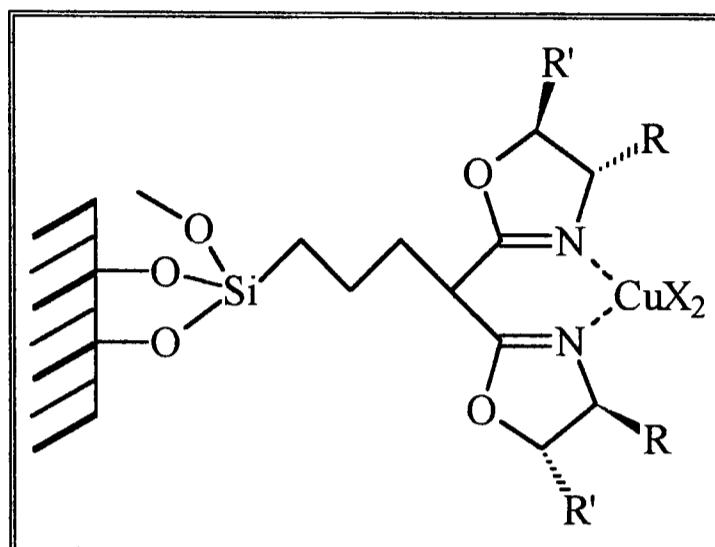


Figure 3.5.1.1: Bis(oxazoline) copper (II) complex supported *via* alkyl tether

Our first attempts to create the supported catalyst complex were derived from the products of the experiments to support methylenebis(4-*S*-phenyl-2-oxazoline) on mesoporous silicas. With copper (II) and bis(oxazoline) ligands two products could be expected to be observed: a mono complex with a 1:1 ratio between the bis(oxazoline) ligand and copper similar to the polymer supported catalysts, which would be expected to be green. The second product would be a di-complex containing two bis(oxazoline) ligands per copper atom which has been used in homogeneous catalytic reactions⁽⁹¹⁾ and which would be purple or violet in colour.

Initially, the preparation of supported di-complexes were attempted by sequential addition of copper (II) chloride and a second equivalent of methylenebis(4-*S*-phenyl-2-oxazoline) to a methylenebis(4-*S*-phenyl-2-oxazoline) modified mesoporous material. In all cases the products were pale green powders, indicating that the product contained only the mono-complex and that the di-complex was not formed. The filtrate in each case was purple

in colour indicating that the copper (II) di-methylenebis(4-*S*-phenyl-2-oxazoline) complex was present in solution. Attempts to try and increase the diffusion through the solid and increase the chance of obtaining the supported di-complex by gently heating caused the solution to turn brown in colour indicating that the complex was being degraded. The reasons for the failure to support the di-complex are unclear although possible reasons may involve diffusion problems and steric constraints due to pore size or pore blocking, or the possibility of other binding sites involving unreacted tether which may react with the second equivalent of ligand.

A second attempt to support the di-bis(oxazoline) copper complex was tried using a one-pot synthesis method, reacting two equivalents of bis(oxazoline) ligand with 3-iodopropyltrimethoxy silane before adding 1 equivalent of copper then reacting the formed complex with the supporting matrix. The products obtained from this reaction were also green in colour, although the filtrate turned slightly purple when a small quantity of methylenebis(4-*S*-phenyl-2-oxazoline) was added, indicating that there is more copper than bis(oxazoline) present in the filtrate. A similar test with a small amount of Copper (II) chloride showed no change in colour. UV-Vis spectra on the solid product gave only weak spectra (due to the dilute nature of the sample) meaning it was hard to determine the exact position of the maximum although this appeared to be at *ca.* 690 nm. This peak is not consistent with that observed for the purple di-complex which occurs at *ca.* 536 nm, so the conclusion that can be drawn from this is that each time synthesis of the di-complex was attempted the principal product was the single ligand mono-complex. While there may be trace amounts of the di-complex present it is not expected to be sufficient to greatly affect any catalytic reactions. Following these tests, all syntheses of supported systems synthesised were

carried out using a 1:1 ratio of ligand to metal, and nearly all used the one-pot strategy described above (Figure 3.5.1.2).

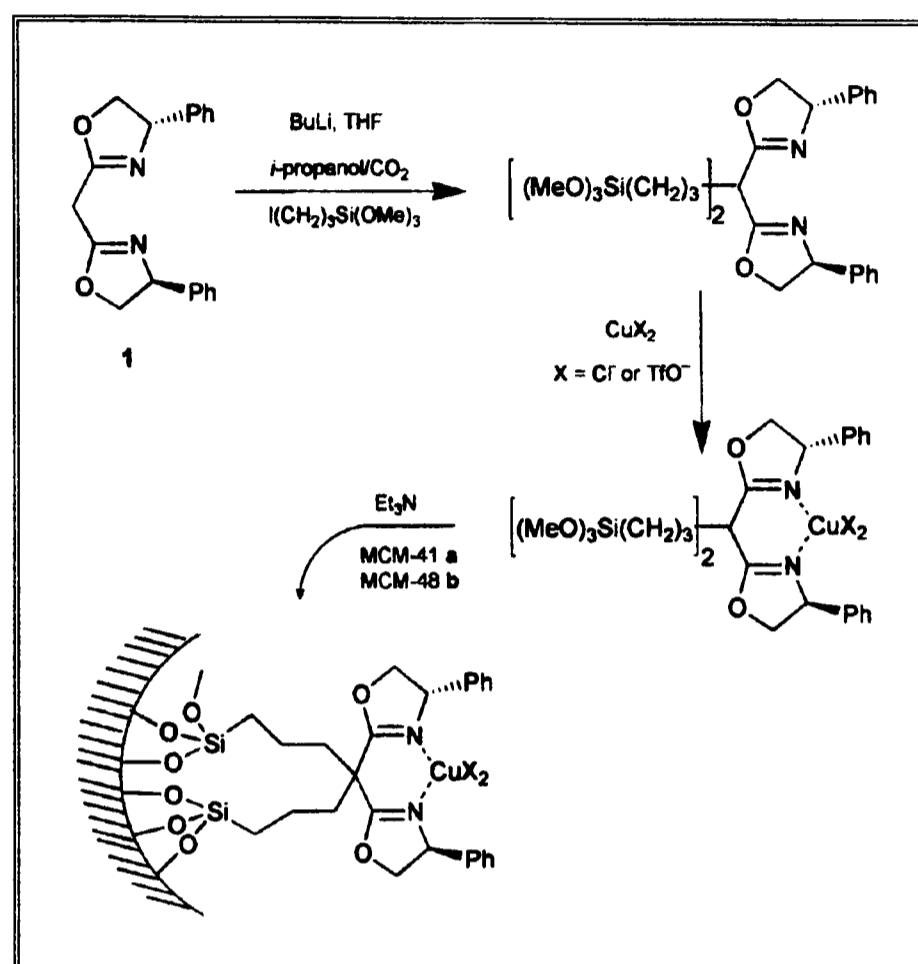


Figure 3.5.1.2: One pot synthesis method of forming supported bis(oxazoline) catalysts ⁽¹⁵⁸⁾

Using the one-pot method, mono-bis(oxazoline) copper (II) complexes were readily synthesised, using the colour of the liberated iodine (discussed in Section 3.4.2) to determine when the reaction was sufficiently complete to add the metal salt. All of the recovered solids were pale green in colour indicating that the mono-bis(oxazoline) copper complex was formed. The copper salts used were copper (II) chloride (which was also used for synthesis of the homogeneous di-bis(oxazoline) systems) and copper (II) triflate (for comparison with the homogeneous mono-bis(oxazoline) systems). The ligands used were methylenebis(4-*S*-phenyl-2-oxazoline), methylenebis(4*R*,5*S*-diphenyl-2-oxazoline), methylenebis[(4-*S*-(2-methylpropyl)-2-oxazoline] and methylenebis(4-*S*-*t*-butyl-2-oxazoline). The supporting

materials used were MCM-41, MCM-48 and amorphous silica (Cab-o-sil) [although not all were used for all the ligands, due to problems with MCM-48 synthesis (see Section 3.1.2 for details) and time constraints for the methylpropyloxazoline].

The loading of the catalyst was determined by the amount of copper present using AAS, and where possible this was compared to CHN results and theoretical yields. CHN results are not always particularly useful in this regard, as there is the possibility that there may be uncomplexed ligand and unreacted tether bound to the surface, residual solvent, or even by-products from reactions with triethylamine trapped in the pores.

The copper loadings found indicate that the reaction is not very efficient as only 20% of the ligand ends up as an active catalytic complex bound to the support. If we look back at Figure 3.4.2.1 we can see that there is no unreacted ligand present after the reaction between the bis(oxazoline) ligand and the iodoalkane. This suggests that the problem of low yield is not in this stage of the reaction. This means the problem of low yield is with either the addition of the tether to the surface, deactivation of the trimethoxysilyl tethering group prior to the addition of the solid or metal being leached out during soxhlet extraction.

It is likely that all three reasons above have some effect contributing towards the low yield. Looking back at early experiments to tether the ligand rather than the complex to the surface we also observe low yield (*ca.* 23-35%). In some cases this may be due to saturation of the surface in experiments designed to give maximum loading for solid state NMR analysis. In other experiments where the loading was suitable for catalytic reactions, comparisons between carbon and nitrogen analysis cannot be used to determine the loading of ligand due to the low amount present. In many cases the catalytic working levels contain amounts of nitrogen below the detectable levels for the instrument and we have had to base calculations on carbon measurements alone.

The main cause of the low loading is most likely a combination of deactivation of the tether prior to addition of the supporting matrix and low yield in the reaction between the tether and the support. This will be discussed again later in Chapter 5 (Future work).

The external surfaces of the supporting materials in the majority of cases were not deactivated before addition of the complex, and in most cases the remaining surface hydroxyl groups were not deactivated after the addition of the catalyst either. Partly this was as some early experiments with the failed chloro tethers seemed to show the capping groups were removed when the reaction between a modified material and a bis(oxazoline) ligand was attempted. There were additional concerns as to the effect that highly reactive chlorosilanes (used for capping) might have on the amine functionalities of the bis(oxazoline) rings. Some catalysts were created with these additional modifications, which have already been discussed in Section 3.2.1.

Samples of supported catalysts generated using copper (II) chloride and copper (II) triflate in MCM-41 were submitted for EXAFS analysis. This analysis was carried out to answer questions arising from unexpected results obtained using the mesopore supported copper (II) chloride systems (Section 4.1.7).

The catalyst generated using copper (II) triflate showed the expected results with the copper atom being surrounded by two nitrogen and two oxygen atoms. Due to the weakness of the sample the noise could not be completely removed from the spectrum resulting in a relatively high R factor of 45.10 (R = goodness of fit of experimental compared to theoretical, generally a good R factor \approx 30) (Figure 3.5.1.3). The Cu-N bond lengths (1.904Å) are similar to those found by Evans for the isopropylidenebis(4-*t*-butyl-2-oxazoline) copper (II) triflate dihydrate complex (1.921, 1.955Å)⁽¹¹⁸⁾. The Cu-O bond lengths for the triflate groups (1.957Å) are however not similar to the Evans complex, which has one triflate group only

weakly bound to the metal and the second completely dissociated, although they are similar to those found by Evans for Cu-O (water) in the complex (1.979, 1.958Å).

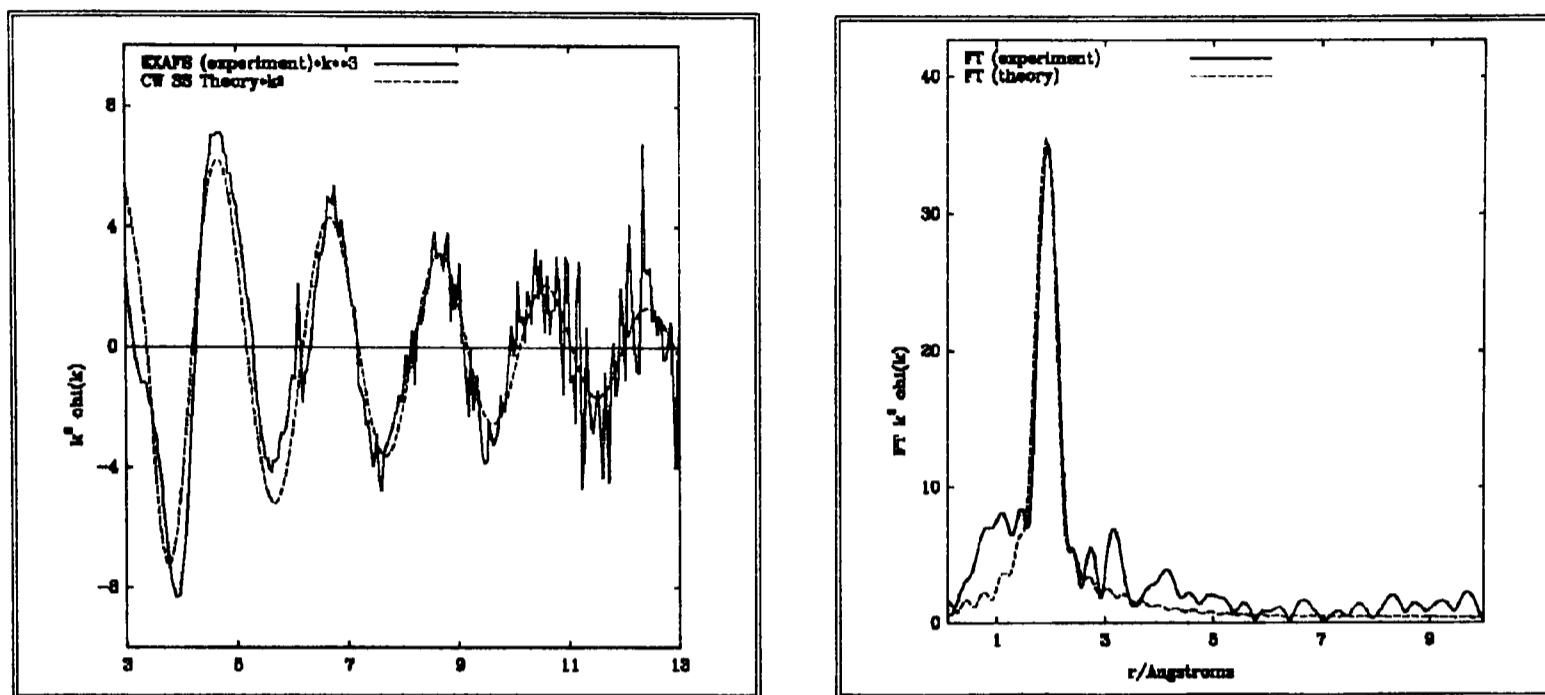


Figure 3.5.1.3: EXAFS plots for methylenebis(4-S-phenyl-2-oxazoline) copper (II) triflate complex supported on MCM-41 *via* an iodopropyl tether

Atom type	Number of atoms	Distance (Å)	R value	Debye-Waller factor (σ^2)
Cu	1	0.000	45.10	0.005
N	2	1.904	45.10	0.004
O	2	1.957	45.10	0.004

Table 3.5.1.1: EXAFS data for methylenebis(4-S-phenyl-2-oxazoline) copper (II) triflate complex supported on MCM-41 *via* an iodopropyl tether

The catalysts generated using copper (II) chloride however did not show as expected chlorine atoms bound to copper. The results indicate that the chlorine has been exchanged with either nitrogen or oxygen. Due to the experimental conditions, which uses triethylamine, silver nitrate tests (which show the presence of chloride ions) and the requirements of the

metal for charge balancing we believe a possible explanation is that the chloride ions have been replaced by a triethylamine plus chloride counter ion. The results show Cu-N bond lengths of 1.951 and 1.964 Å with an R factor of 35.09 (Figure 3.5.1.4). In later sections catalysts described as chloride catalysts refer to catalysts generated using copper (II) chloride, which may also have undergone exchange of chloride ions.

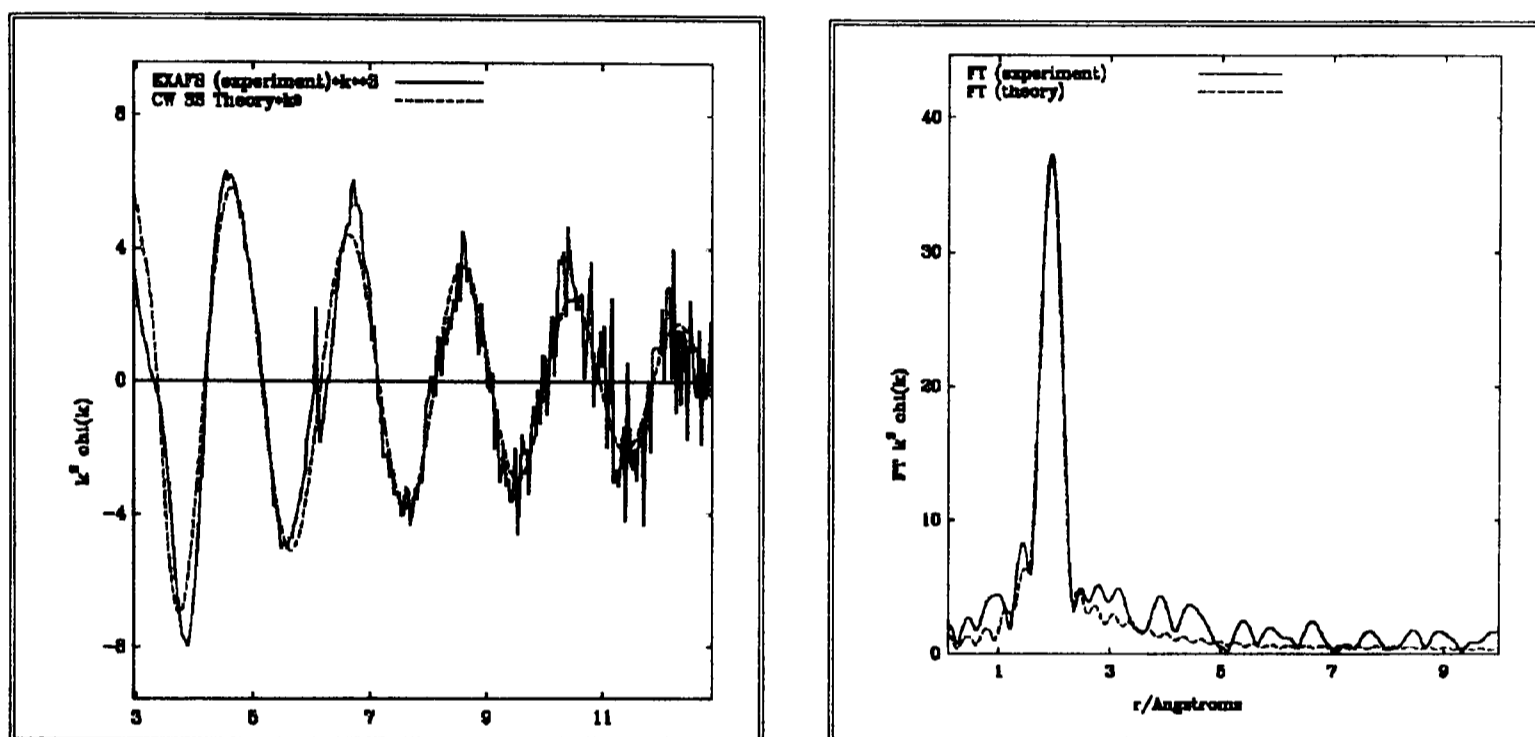


Figure 3.5.1.4: EXAFS plots for methylenebis(4-S-phenyl-2-oxazoline) copper (II) chloride generated catalyst supported *via* an iodopropyl tether on MCM-41

Atom type	Number of atoms	Distance (Å)	R factor	Debye-Waller factor (σ^2)
Cu	1	0.000	35.09	0.005
N	2	1.951	35.09	0.004
N	2	1.964	35.09	0.004

Table 3.5.1.2: EXAFS data for methylenebis(4-S-phenyl-2-oxazoline) copper (II) chloride generated catalyst supported *via* an iodopropyl tether on MCM-41

3.5.2 Complexes supported *via* hydrogen bonding with the surface

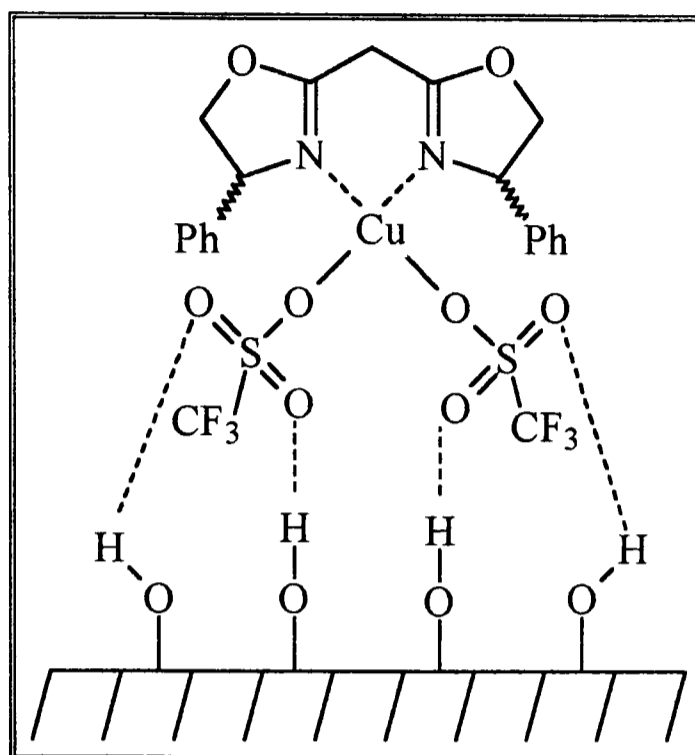


Figure 3.5.2.1: Methylenebis(4-phenyl-2-oxazoline) copper (II) triflate complex supported by hydrogen bonding

Covalently bonding catalyst complexes as described in section 3.5.1 is not the only way of supporting catalysts. The hydrogen bonding between sulfonate groups and surface hydroxyls on silicas have been used to as a method of supporting catalyst complexes on silica surfaces ⁽¹⁵⁹⁾. We have used this technique to support methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) triflate complex on the surface of MCM-41. The supported complex was synthesised by the addition of a 1:1 solution of methylenebis(4-*S*-phenyl-2-oxazoline) and copper (II) triflate in DCM to a suspension of MCM-41 in the same solvent. The solution of the ligand initially turns purple upon addition of the copper salt (indicating the formation of the di-complex) but gradually turns green as the remaining copper triflate dissolves and complexes. When this solution was added to MCM-41, the solution became colourless and the solid took up the green colour. The filtrate was tested separately by addition of a copper (II) solution and a solution containing free bis(oxazoline) ligand, but neither of these tests gave a

positive result (forming the purple di-bis(oxazoline) copper complex), indicating that all of the metal and ligand had been successfully bound to the surface.

The catalyst complex however was only weakly bound to the surface of the supporting mesoporous material and could be completely removed by addition of any polar solvent. It was, however, stable in nonpolar solvents (e.g. DCM) even when soxhlet extracted for several hours. The amount of copper present was determined by AAS and the result proved to be a close match for the amount of bis(oxazoline) ligand present as determined by CHN analysis. Unfortunately, this catalyst proved to be disappointing in catalytic trials (these will be discussed in Chapter 4) and so the experiment was not repeated for other bis(oxazoline) ligands.

3.5.3 Complexes supported *via* metal centres to diamine tethers

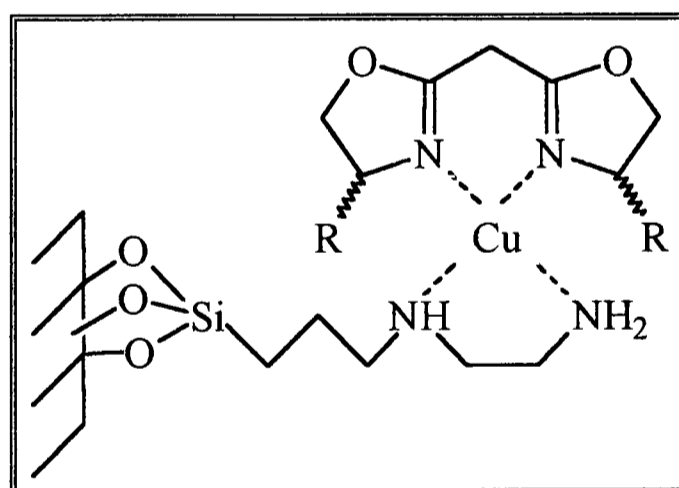


Figure 3.5.3.1 Bis(oxazoline) complex supported *via* diamine tether

The idea of using mono-amino tethers to react with specially designed bis(oxazoline) ligands (Section 3.3.2) had been discontinued at an early stage (due to synthesis problems with the bis(oxazoline) ligands), but the use in the literature of both the mono and di-complexes of bis(oxazoline) ligands for catalysing the same reaction with similar results

posed some interesting ideas. If one of the chiral bis(oxazoline) ligands in the complex was replaced by a organic tether (attached to a supporting material) which was able to complex with the metal in a similar fashion to a bis(oxazoline) ligand then a pseudo supported di-complex could be synthesised without any modification of the ligand. The catalytic activity of the pseudo di-complex would be expected to compare more favourably to the mono-complex than to the di-complex. As bis(oxazoline) ligands complex with the metal *via* bonding through the nitrogen atoms in the oxazoline ring the obvious reaction was to replace the second bis(oxazoline) ligand with a commercially available diamine tether. Using a diamine should keep the potential of the metal centre similar to that in the di-complex, and selecting a diamine with an appropriate alkyl chain between the amine groups should give similar spatial co-ordination and ligand bite angle around the metal. The tether that was tested in this case was N-[3-(trimethyloxysilyl)propyl]-ethylenediamine.

Initial experiments to obtain the (trimethoxysilyl)propylethylenediamine bound to the surface of MCM-41 used the same methods as applied earlier for the mono-amine tethers. CHN analysis showed that only two out of three of the silylmethoxy groups had reacted with the surface, as had been noticed previously for mono-amine tethers (Section 3.2.1). ¹³C Solid state NMR which showed the presence of the tether bound to the surface (Figure 3.5.3.2).

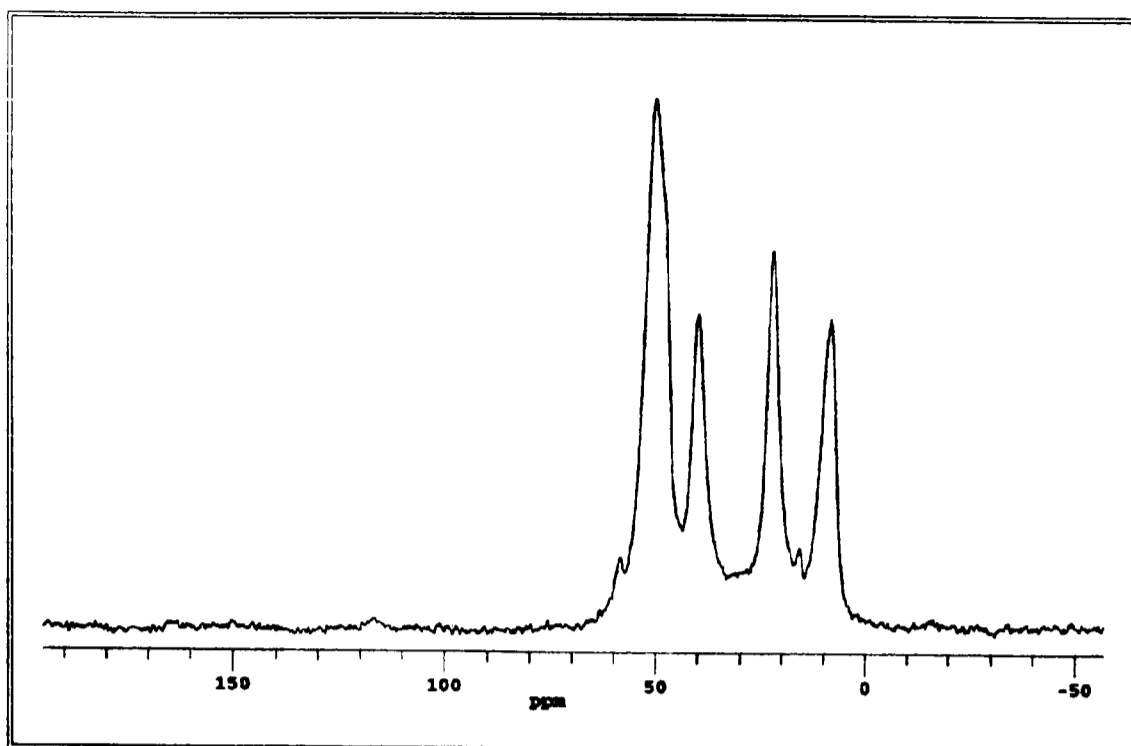


Figure 3.5.3.2: Solid state ^{13}C NMR of [3-(trimethoxysilyl)propyl] ethylenediamine on MCM-41

When a 1:1 mix of methylenebis(4-*S*-phenyl-2-oxazoline) and copper (II) chloride was added to the (trimethoxysilyl)propylethylenediamine modified MCM-41 a blue solid was recovered. This showed an absorption maxima at *ca.* 592 nm compared with *ca.* 536 nm for the homogeneous di-methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) complex. A subsequent control experiment without bis(oxazoline) ligand gave identical results. CHN analysis showed a similar ratio between carbon and nitrogen for both the initial supported tether and the copper complex. AAS compared with nitrogen analyses showed that the ratio between copper and the diamine tether was approximately 1:3 for both the experiments with and without bis(oxazoline) ligand. This suggests that instead of the desired product with one tether and one bis(oxazoline) ligand (Figure 3.5.3.1) we instead have a supported copper (II) (silylpropyl)ethylenediamine complex.

Although the copper to tether ratio would suggest 3 diamino tethers bound to each copper this is very unlikely. Even homogeneously the reaction between copper (II) and ethylenediamine the maximum is two ethylenediamines per copper, with the remaining co-

ordination sites occupied by solvent or water. This has also been observed as the case for the reaction between mesopore supported amine tethers and copper⁽¹⁶⁰⁾.

When synthesised, the homogeneous equivalent (copper (II) bis(ethylenediamine) was a similar blue colour to the heterogeneous version when kept under organic solvents. However upon exposure to air this gradually absorbed moisture and changed colour to a deep purple. This colour change was not observed for the supported complex.

The loading of diamine tether (*ca.* 1.5 mmol/g) in these early experiments was obviously too high as the copper preferentially formed a di-complex with the tether rather than the 1:1 tether:bis(oxazoline) ligand intended.

The loading of diamine tether on MCM-41 was reduced (*ca.* 0.091 mmol/g) to try and obtain isolated diamine binding sites. With this lower loading and a 1:1 mix of copper (II) chloride and methylenebis(4-*S*-phenyl-2-oxazoline) a small amount of a pale green powder was obtained. The loading of copper was determined to be 0.065 mmol/g which although closer to the idealised 1:1 ratio still shows that there is probably still some bis(diamine) copper complex present in addition to uncomplexed tether.

3.5.4 Homogeneous Bis(oxazoline) copper (II) complexes

In order to determine the quality of our supported catalyst systems it is necessary to test them against the equivalent homogeneous systems and compare the results to those obtained by other groups using the same catalysts. Two types of bis(oxazoline) copper complexes have been used in catalytic reactions, containing either one or two bis(oxazoline) ligands. Those containing two ligands use almost exclusively bis(oxazoline) ligands which can become charged (by loss of a proton from the bridging group and subsequent

rearrangement of double bonds). These di-complexes are usually crystalline and can be easily synthesised and purified. The mono complexes are usually prepared *in situ* in the catalysis reaction vessel.

Synthesis of di-bis(oxazoline) complexes

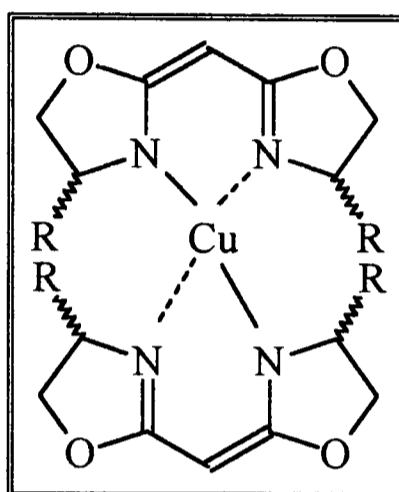


Figure 3.5.4.1. Di-methylenebis(oxazoline) copper complex as proposed by Masamune ⁽⁹¹⁾

The di-bis(oxazoline) copper complexes have been used in cyclopropanation reactions ⁽⁹¹⁾, and are usually synthesised from halide salts. Following the published synthesis route using copper (II) chloride a di-complex (Figure 3.5.4.1 R=S-phenyl) was easily synthesised. The yield obtained was slightly lower than that quoted for the same complex in the literature. This is due to the use of smaller quantities of reagents, absorption of the complex onto the filter paper during filtration and incomplete recrystallisation.

Whilst the phenyl derivative was easily synthesised following the literature method, the complex using methylenebis(4-*S-t*-butyl-2-oxazoline) initially gave some problems. This was eventually traced to the quality of the purchased ligand, as it transpired that the ligand obtained from the first supplier was not the desired compound, whilst the IR spectrum was sufficiently close to the desired ligand to escape detection at first. The reaction between

methylenebis(4-*S-t*-butyl-2-oxazoline) and 0.5 eq. of copper (II) chloride with 2.5 eq. of *n*-butyl lithium should give purple crystals as the product (similar to those obtained for the phenyl derivative). The only product from this reaction was always dark green in colour and would not crystallise. In the available literature the *t*-butyl ligand is perceived to be harder to react than the phenyl derivative ⁽⁹³⁾ as it requires additional purification steps and harsher conditions. This caused additional time to be wasted on repeat and modified experiments.

Suspicion aroused, submission of the ligand for ¹H NMR analysis showed that the desired ligand was not even the major component present and did not appear to be present at all. A second supply of this ligand was obtained which easily gave the desired di-complex following literature methods. The yield of this reaction was again lower than the published value, due to not all of the complex being recrystallised and the decomposition of the bulk of the remaining solution.

In addition to the phenyl and *t*-butyl derivatives a version where R=2-methylpropyl was also synthesised. This final di-bis(oxazoline) complex was synthesised towards the end of available laboratory time and we were unable to get this particular product to crystallise. The colour of the product was the same as those observed for both the phenyl and *t*-butyl complexes, leading us to believe that the product contained the desired complex but was prevented from crystallising, possibly by impurities from the ligand synthesis.

Synthesis of mono-bis(oxazoline) copper (II) complexes

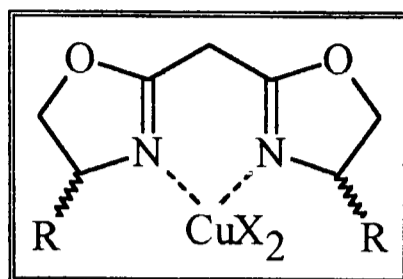


Figure 3.5.4.2 Methylenebis(oxazoline) copper (II) complex

Mono-bis(oxazoline) copper complexes are frequently synthesised using neutral ligands (which have no hydrogens on the bridging group which can be removed) although any bis(oxazoline) ligand may be used. They are usually synthesised just prior to the commencement of the catalytic reaction, often in the actual catalysis vessel itself to reduce the chances of decomposition occurring. Most often the copper salt used is a triflate (trifluoromethanesulfonate) as complexes of this salt have been shown to be highly reactive in some catalytic reactions (although other salts such as $\text{CuClO}_4(\text{CH}_3\text{CN})_4$ and CuOtBu have also been used⁽¹⁰⁴⁾). In some literature preparations copper (I) salts are preferred, as they are the active catalytic species for some catalytic reactions whereas copper (II) salts (which are more stable and easier to store) must be activated first. In our syntheses we only used copper (II) salts as the intention was to compare the homogeneous complexes to supported complexes which were prepared using copper (II) salts for ease of synthesis and storage.

The synthesis of mono-bis(oxazoline) copper (II) triflate complexes was carried out by dissolving a 1:1 ratio of copper (II) triflate and the appropriate ligand in THF. The solutions would briefly turn a purple colour before fading to a deep green as equilibrium was achieved. The products obtained were difficult to handle, as we were unable to obtain a crystalline form, and the products were recovered as a thick sticky oil. This was found to be the case for both

methylenebis(4-*S*-phenyl-2-oxazoline) and methylenebis(4-*S*-*t*-butyl-2-oxazoline). Some of these products were used in subsequent catalytic reactions although in most cases the mono-bis(oxazoline) catalytic systems were synthesised *in situ* in the reaction vessel.

3.6 Bis(oxazoline) zinc catalyst complexes

Although the majority of catalysts synthesised were copper-based, some heterogeneous systems (especially alkyl tether and diamine tether based see Figures 3.5.1.1 and 3.5.3.1 for examples) were also synthesised using zinc salts (chloride and iodide) which were intended for use in different catalytic systems such as allylation reactions. It was more difficult to obtain proof that the zinc metal was present, as the zinc complexes are colourless and so no colour change could be observed. As with the copper bis(oxazoline) complexes the low loading of catalyst meant that some common analytical techniques (e.g. IR, CHN) could not provide conclusive evidence. Also we did not have access to analysis by AAS for zinc (due to no zinc lamp being available). Samples were submitted for EXAFS (Extended X-ray Absorption Fine Structure) analysis which confirmed the presence of zinc in the sample. The analysis showed similar results those obtained for the copper (II) chloride generated catalysts where the halide counter ion had been replaced by a much lighter element (probably nitrogen).

For the first sample (methylenebis(4-*S*-phenyl-2-oxazoline) zinc (II) iodide complex supported *via* iodopropyl tether), Zn-N distances were 1.944 (2N) and 1.987Å (2N) with a good of R factor 28.16 (Figure 3.6.1.1).

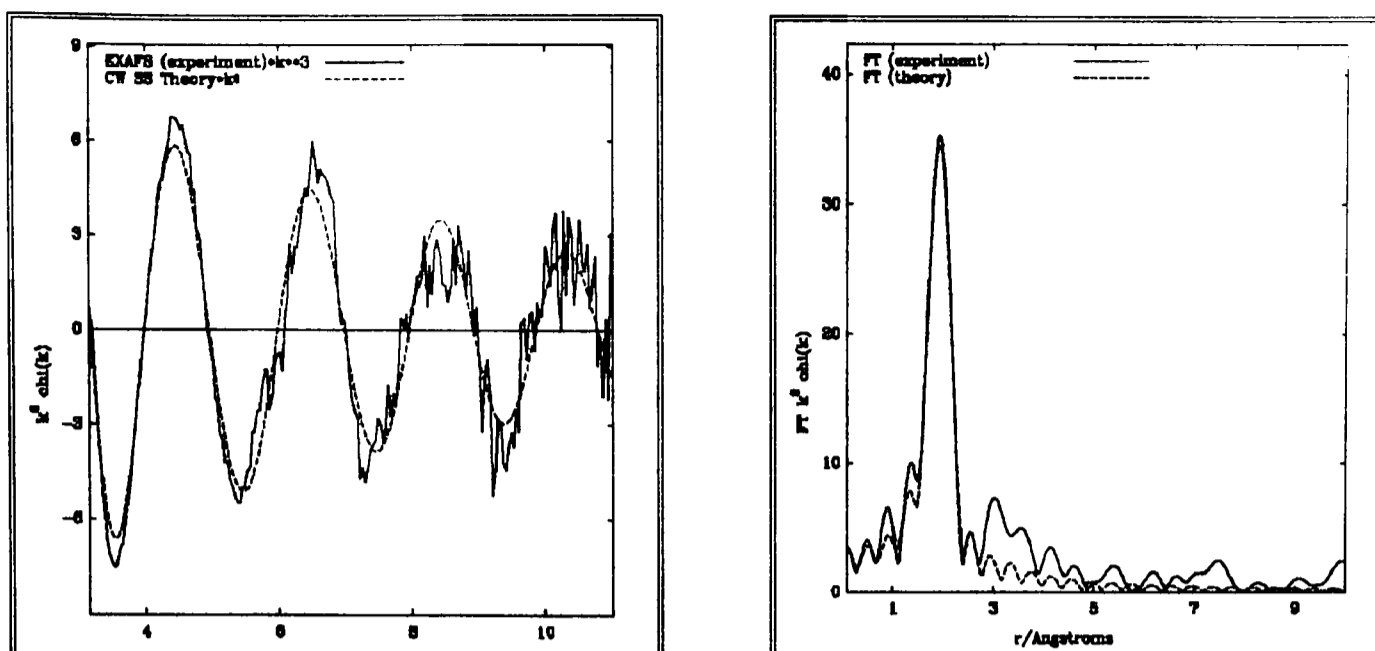


Figure 3.6.1.1. EXAFS plots for methylenebis(4-*S*-phenyl-2-oxazoline) zinc (II) iodide generated catalyst supported *via* iodopropyl tether supported on MCM-41

Atom type	Number of atoms	Distance (Å)	R factor	Debye-Waller factor (σ^2)
Zn	1	0.000	28.16	0.005
N	2	1.944	28.16	0.0035
N	2	1.987	28.16	0.0035

Table 3.6.1.1: EXAFS data for methylenebis(4-*S*-phenyl-2-oxazoline) zinc (II) iodide generated catalyst supported *via* iodopropyl tether supported on MCM-41

A second sample containing methylenebis(4*R*, 5*S*-diphenyl-2-oxazoline) supported complex produced identical results showing that the iodine atoms were no longer directly bound to the metal centre. Interatomic distances were similar to the previous sample (Zn-N 1.927 (2N) and 1.998Å (2N)) with a good fit of experimental to theoretical data (R=29.34).

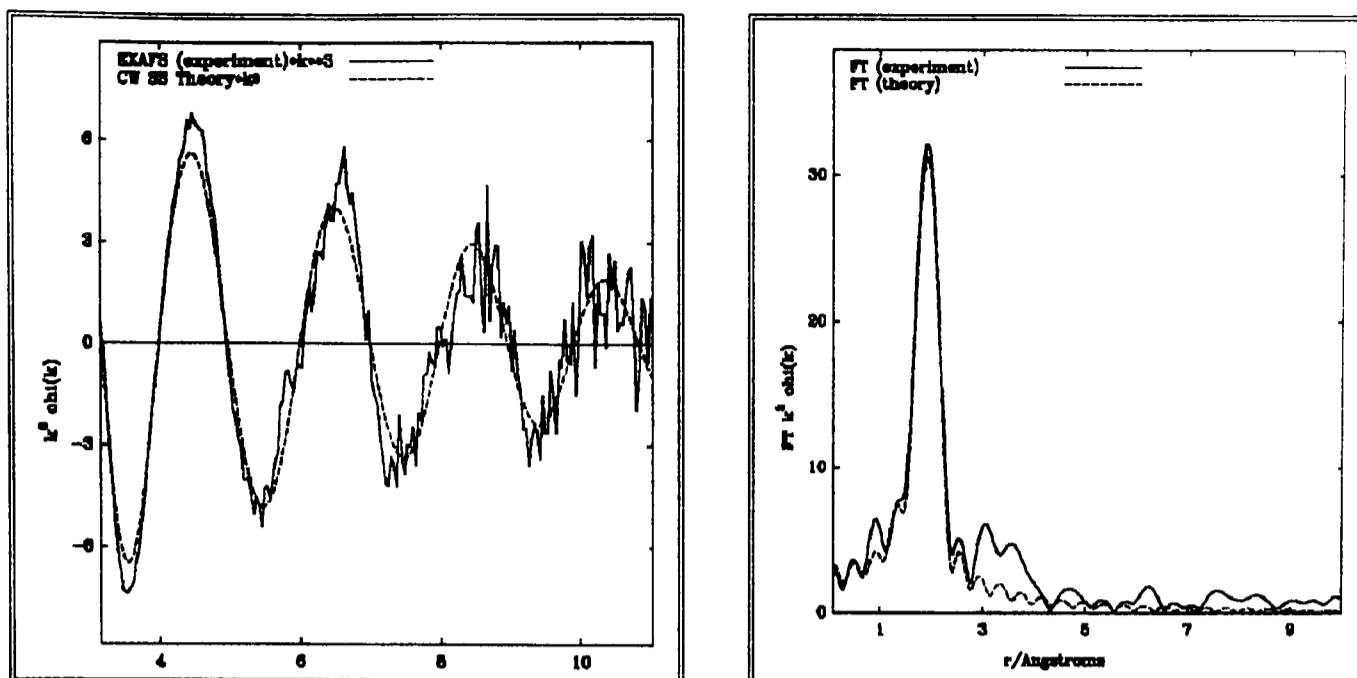


Figure 3.6.1.2: EXAFS plots for methylenebis(4*R*,5*S*-diphenyl-2-oxazoline) zinc (II) iodide generated catalysts supported *via* iodopropyl tether on MCM-41

Atom type	Number of atoms	Distance (Å)	R factor	Debye-Waller factor (σ^2)
Zn	1	0.000	29.34	0.005
N	2	1.927	29.34	0.004
N	2	1.998	29.34	0.004

Table 3.6.1.2: EXAFS data for methylenebis(4*R*,5*S*-diphenyl-2-oxazoline) zinc (II) iodide generated catalysts supported *via* iodopropyl tether on MCM-41

Heterogeneous zinc catalysts were not used for catalysis as insufficient progress had been made in finding and calibrating suitable internal standards for analysis by chiral GC for the products of the catalytic reactions.

Chapter 4. Results and Discussion (Catalysis)

4.1 Catalysis of cyclopropanation reactions using bis(oxazoline) copper complexes

4.1.1 Cyclopropanation reaction

The cyclopropanation reaction is one of the basic tools in organic synthesis, it is also one method by which chirality can easily be incorporated into a molecule. The standard benchmark test reaction for cyclopropanation uses styrene and ethyldiazoacetate. The reasons for choosing to concentrate primary testing of the catalysts on this reaction were:

1. Well proven results for a variety of bis(oxazoline) ligands
2. Comparisons possible with other supported systems (e.g. polymers, clays etc)
3. Ease of analysis of products
4. Commercially available starting materials

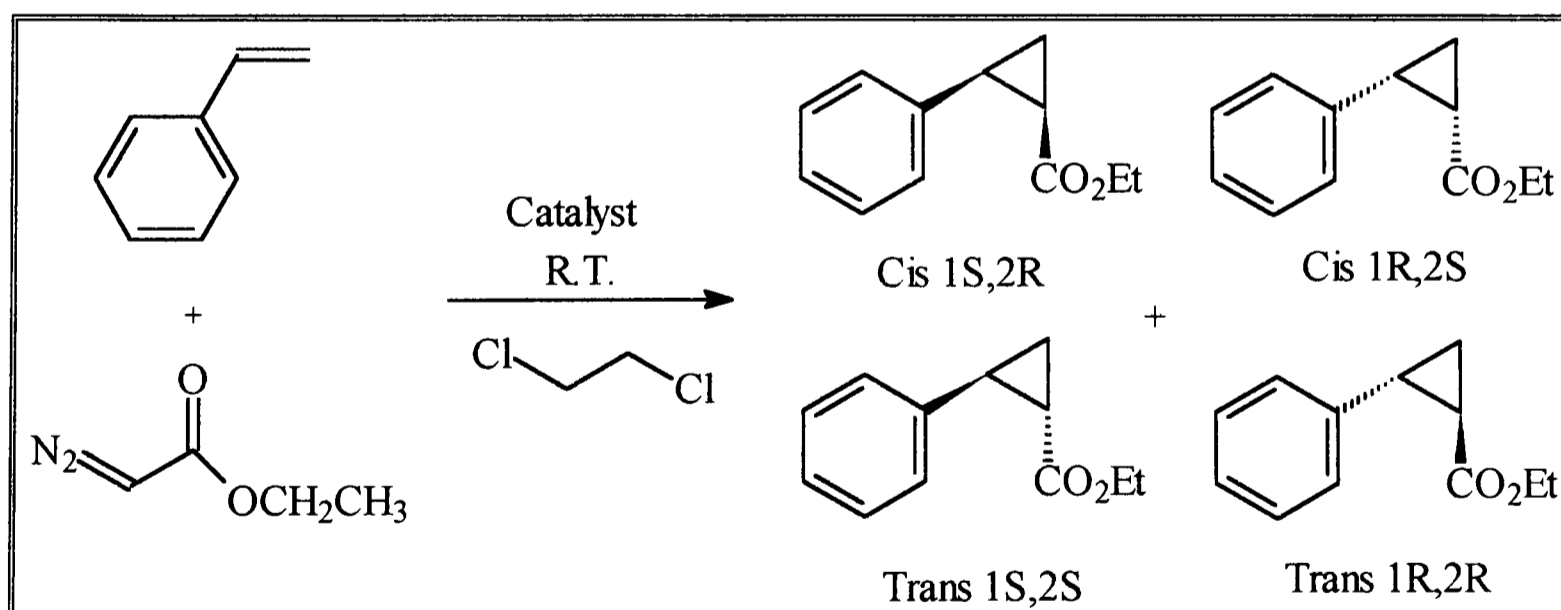


Figure 4.1.1.1: Cyclopropanation reaction between styrene and ethyldiazoacetate to form ethyl 2-phenylcyclopropane-1-carboxylate

It has been known a long time that copper complexes can catalyse cyclopropanation reactions, and it has also been shown that the active catalytic species is copper (I) ⁽¹¹⁴⁾. The catalysts we have synthesised are copper (II) complexes primarily for their stability and ease of handling (nearly all research into supported copper bis(oxazoline) catalysts use copper (II) complexes as only heterogeneous systems where the catalyst complex is synthesised *in situ* use copper (I)). This means that we must reduce the metal in our catalysts prior to commencing the cyclopropanation reaction. The most common method used for this is addition of a small amount of phenylhydrazine (although heating to 65°C in the presence of ethyldiazoacetate has also been shown to have the same effect ⁽¹⁰³⁾).

4.1.2 Early cyclopropanation experiments

Identification of products

Although many groups have studied the cyclopropanation of styrene previously, we still need to perform several experiments before commencing studies using our supported catalysts.

In many reports the standard analysis method for the cyclopropanation products is chiral GC, and this is also the preferred method for our analysis of cyclopropanation products due to ease of analysis. The GC conditions (flow rate, column temperature etc.) were based upon those quoted in the literature ^(161, 162). Samples of all starting materials were tested to give retention times, which could be compared to the results to determine which peaks corresponded to the products. Purification of individual optical isomers was not attempted (many use either chiral HPLC, or recrystallisation of menthyl esters to separate different isomers) and assignment was based on the elution order of peaks as given in the literature;

these are in elution order, (1S,2R), (1R,2S), (1R,2R) and (1S,2S) ^(72, 137, 161). Throughout the project the selectivity found with differing ligands was compared with literature values. Attempts were made to purchase an isomerically pure product to confirm the identification of the products (one isomer of ethyl 2-phenylcyclopropane-1-carboxylate was listed in a suppliers catalogue, however they were unable to supply this and it did not appear in subsequent catalogue issues).

Initial test reactions were performed using a 2:1 ratio of methylenebis(4-*S*-phenyl-2-oxazoline) and copper (II) chloride; the catalyst complex was assembled *in situ* in the reaction vessel and was not purified prior to commencement of the catalytic reaction. GC of the crude product showed several additional peaks to those expected for the products. Most of these were trace impurities which were removed by published purification procedures.

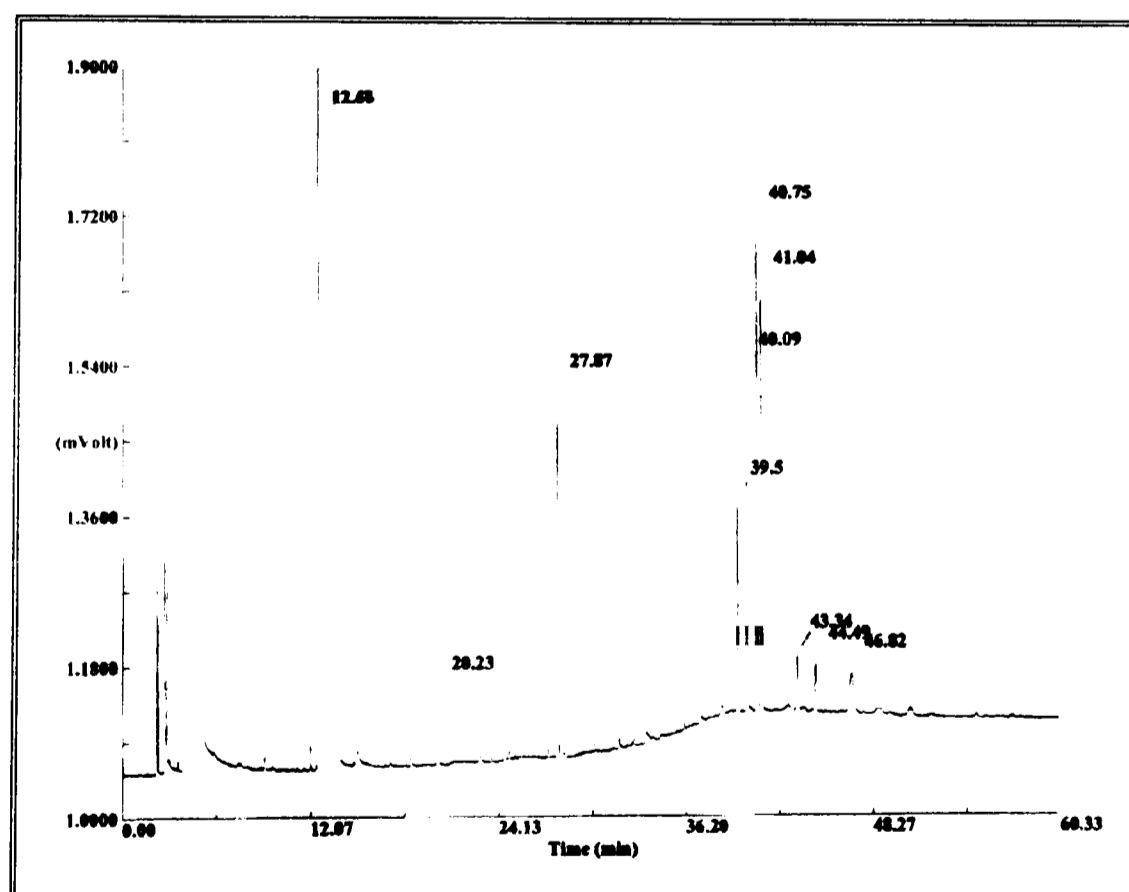


Figure 4.1.2.1: Chiral GC trace of the crude product of the cyclopropanation of styrene with ethyldiazoacetate

Figure 4.1.2.1 shows the GC of the reaction prior to purification. The major peaks at this stage are solvent (DCM) at *ca.* 4 minutes, unreacted styrene at *ca.* 12.0 minutes, *cis* and *trans* 2-butenedioic acid ethyl ester at 27.41 and 27.81 minutes and the desired products in a cluster between *ca.* 39.5 and 41.0 minutes. These desired products elute in the following order *cis* (1S,2R) ethyl 2-phenylcyclopropane-1-carboxylate (*ca.* 39.5 minutes), *cis* (1R,2S) ethyl 2-phenylcyclopropane-1-carboxylate (*ca.* 40 minutes), *trans* (1R,2R) ethyl 2-phenylcyclopropane-1-carboxylate (*ca.* 40.5 minutes) and *trans* (1S,2S) ethyl 2-phenylcyclopropane-1-carboxylate (*ca.* 41.0 minutes). The remaining peaks are either trace impurities or break down products. This first test experiment had diethyladipate as an internal standard added after purification (Figure 4.1.2.2) which has a retention time of *ca.* 36.0 minutes.

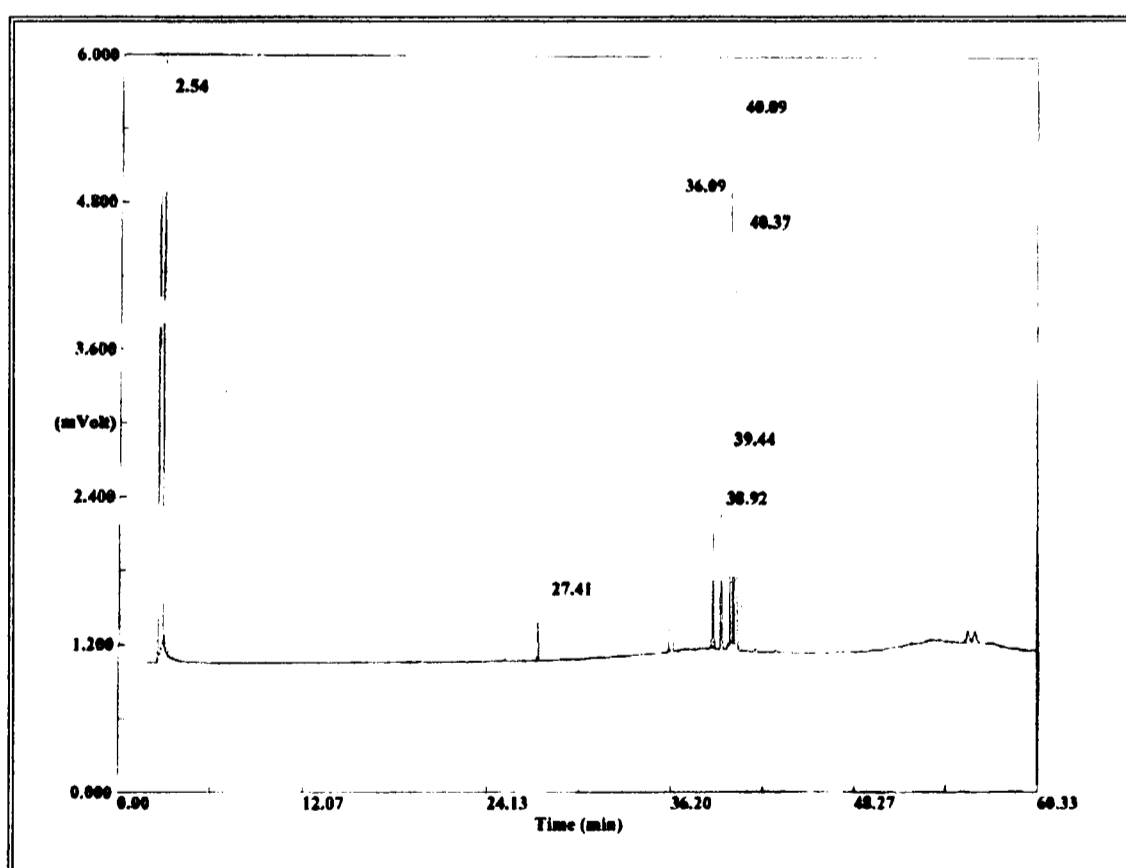


Figure 4.1.2.2: Chiral GC trace of the products shown in Figure 4.1.2.1 after purification, diethyladipate has been added as a standard

The purification process suggested in the literature passes the product through a short silica column, but in nearly all cases we found that this did not result in a pure product (even with multiple fractionation). The resulting 'purified' product usually contained two impurities at *ca.* 27.4 minutes (although only one of these is observed in Figure 4.1.2.2), and occasionally small quantities of styrene were also observed. It was found to be possible to pass the internal standard through the purification process without changing the ratio between the standard and the products. The purification method suggested in the literature is more concerned with removing the homogeneous catalyst complex (in order to stop the reaction) and some minor impurities rather than to completely purify the product.

To identify the two impurities at *ca.* 27 minutes (and to confirm that the four peaks between *ca.* 38 and 41 minutes were the desired products) some samples were analysed using chiral GC-MS. The retention times observed differed slightly (due to differences between the GC instruments).

The results showed that the four peaks between *ca.* 38 and 41 minutes were consistent with those expected for the products. The maximum molecular mass was found to be 190-191 and the fragmentation pattern compared favourably to 2-phenylcyclopropanecarboxylic acid which was the closest match in the GC-MS computers library. The impurities at *ca.* 27 minutes were identified as a side product formed by dimerisation of ethyldiazoacetate to form *cis* and *trans* 2-butenedioic acid diethyl ester (Figure 4.1.2.3).

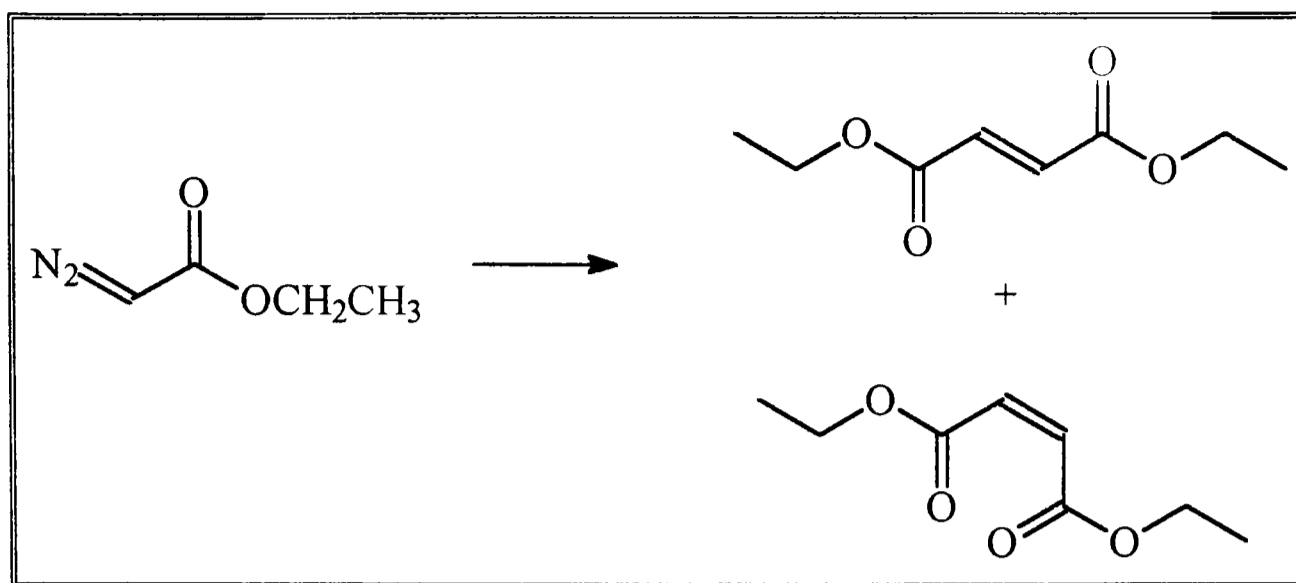


Figure 4.1.2.3: Dimerisation of ethyldiazoacetate showing *cis* and *trans* products

Test reactions were then carried out in order to determine what effect various parts of the catalyst would have on the outcome of the reaction. In our supported systems there may be unforeseen side effects caused by the support, e.g. phenylhydrazine may be deactivated before it can reduce the copper, reagents may be unable to reach active sites or products may react with the support.

Effect of uncomplexed copper (I) and (II) on cyclopropanation reactions

Without any catalyst complex present only trace amounts of cyclopropanation products were observed. This made analysis inexact, as baseline noise could not be discounted. No enantioselectivity was observed although a small preference towards the *trans* isomer (*ca.* 58% *trans*, 42% *cis*) was found. No peaks were observed for the products of dimerisation of ethyldiazoacetate.

With copper (II) chloride present (but not reduced to copper (I) by phenylhydrazine or by heating the reaction) again only trace amounts of products were observed. The amount

present was too small to determine if there was a preference towards any isomer. Again no products were observed for the dimerisation reaction.

With copper (II) chloride reduced to copper (I) (but without any directing ligand) the cyclopropanation products were observed in large quantity. A preference was found towards the *trans* isomers, with 67.5% of the products being in this form, no enantioselectivity was observed. The dimerisation side-product was also formed in large quantities with little or no preference shown towards either isomer.

We can conclude that unless the catalyst is present and activated there will be little or no cyclopropanation reaction, and also note that a preference towards the *trans* stereoisomers does not necessarily indicate the presence of any directing ligand. If any uncomplexed copper were to remain trapped in the support (and then reduced to copper (I)) this would lower the enantioselectivity of the cyclopropanation products.

Calibration of internal standard

In order to easily determine the yield of cyclopropanation products by GC an internal standard is required (this is a measured amount of a similar compound to which other peaks can be compared). Standards used previously in the literature include decane and diethyladipate. We have chosen to use diethyladipate as an internal standard due to the similar retention time.

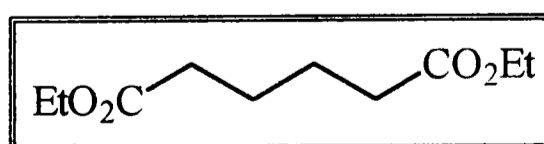


Figure 4.1.2.4: Structure of diethyladipate

It is known that different molecules will burn in slightly different ways (in terms of the signal received by the detector), which means that one mole of standard and one mole of product will produce different intensities. The ratio between the intensity of each peak and the amount of molecules present will however be constant. It had been hoped that we could calibrate the internal standard using measured amounts of the purchased single isomer product, however as this was unavailable (and none of the literature states the value they use) this would have to be calibrated by other means.

The NMR of the internal standard, when compared to that of the products, showed only one peak from the standard was totally separate from that of the products. The different isomers of products often produce different peaks rendering most unsuitable for calibration with the internal standard. However in most reactions the products were the only molecules present which possessed aromatic protons; these could be compared to the separate internal standard peak, and be used for calibration purposes. The internal standard was then calibrated by using the ratio between these separate peaks for the standard and the four product isomers found by GC and NMR over several experiments. This relative response factor between the intensity of the GC peak and the molecules of internal standard (compared to that of the cyclopropanation products) was found to be 0.758. To determine the amount of the cyclopropanation product the following equation can be applied:

$$\frac{\text{Area of product peaks}}{\text{Area of standard peak}} * \text{relative response factor} * \text{moles of internal standard} = \text{moles of products}$$

Throughout we have used 10 μ l of diethyladipate as the internal standard, which is 0.054 mmol. The equation now reads:

$$\text{Ratio of product to standard} * 0.758 * 0.054 = \text{mmol of cyclopropanation products}$$

The above equation has been used to determine the yield in subsequent reactions.

4.1.3 Effect of addition rate of ethyldiazoacetate

In many cyclopropanation studies the diazoacetate is added over a period of time (this varies between 5 minutes⁽¹⁶³⁾ and 24 hours⁽⁹¹⁾). The reasoning behind this is that adding the diazoacetate over a period of time will result in a lower concentration in solution, which should improve the yield by reducing the amount of dimerisation side product produced⁽¹⁶⁴⁾. Using an excess of styrene also has the effect of increasing the yield (viewed as diazoacetate conversion) by increasing the chances of the copper-diazoacetate intermediate reacting with a styrene molecule instead of a second diazoacetate. In many studies in the literature between 3 and 5 fold excesses have been used, in our experiments a three-fold excess of styrene was used unless stated otherwise.

Experiments on the effects of the rate of addition were carried out using a methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) chloride complex supported *via* an iodopropyl-tether on MCM-48. We found that the reactions using a syringe pump to add ethyldiazoacetate over a long period of time gave lower overall yield than those where the ethyldiazoacetate was added in one injection 5 minutes after catalyst activation (typically *ca.* 14-20% compared with 34%) (Table 4.1.3.1). However this is misleading as the low yield is probably caused by incomplete addition of the ethyldiazoacetate (some liquid would have remained in the needle used to add the reagent. In most cases the height of the reaction vessel and the large distance between the seal and the liquid surface required a long needle which would have retained more solution). Also adding the ethyldiazoacetate slowly required it to

be diluted in solvent resulting in a larger overall volume which may have caused dilution effects causing the reaction to proceed to lesser degree.

If we compare the intensities of cyclopropanation product peaks and the dimerisation side product peaks we find that less side product is formed for slower addition times. When the ethyldiazoacetate was added in one injection 5 minutes after catalyst activation the desired product peaks were *ca.* 4.5-6.3 times larger than the peaks for the side products. This is increased to 6.5-7.5 when the ethyldiazoacetate was added over 16 hours and with the addition time slowed to 39 hours virtually no dimerisation product could be detected in some reactions.

Addition time	Yield %	<i>Cis/Trans</i>	ee % <i>Trans</i>	ee % <i>Cis</i>
5 minutes (1)	34.9	1/1.69	50.6	45.8
5 minutes (2)	26.4	1/1.63	46.4	44.2
16 hours (1)	8.4	1/1.86	44.9	43.8
16 hours (2)	13.1	1/1.97	42.8	43.0
39 hours (1)	18.7	1/1.90	47.0	44.8
39 hours (2)	11.1	1/1.83	47.8	46.6

Table 4.1.3.1: Results of the cyclopropanation of styrene with ethyldiazoacetate for the 1st and 2nd use of MCM-48 iodo tether supported methylenebis(*l*-*S*-phenyl-2-oxazoline) copper (II) chloride catalysts

N.B. catalyst *ca.* 0.16 mol%, catalyst loading 0.0212 mmol g⁻¹

The enantioselectivities of all three series of experiments (addition after 5 minutes, over 16 hours and 39 hours) showed little difference for the initial run. The single addition gave slightly better *trans* enantioselectivity over the slow additions (*ca.* 3.6-5.7%) for the first use of the catalyst. *Cis* selectivities showed little change for the same experiments.

Consistent differences were found in the stereoselectivity between the timed and single additions of ethyldiazoacetate. The single instant addition gave 37.2% of the cyclopropanation products in the *cis* form, in comparison the timed addition gave 35.0% and 34.5% *cis* for the 16 and 39 hour additions respectively. The lower stereoselectivity for the single addition continued with further reuse of the catalysts.

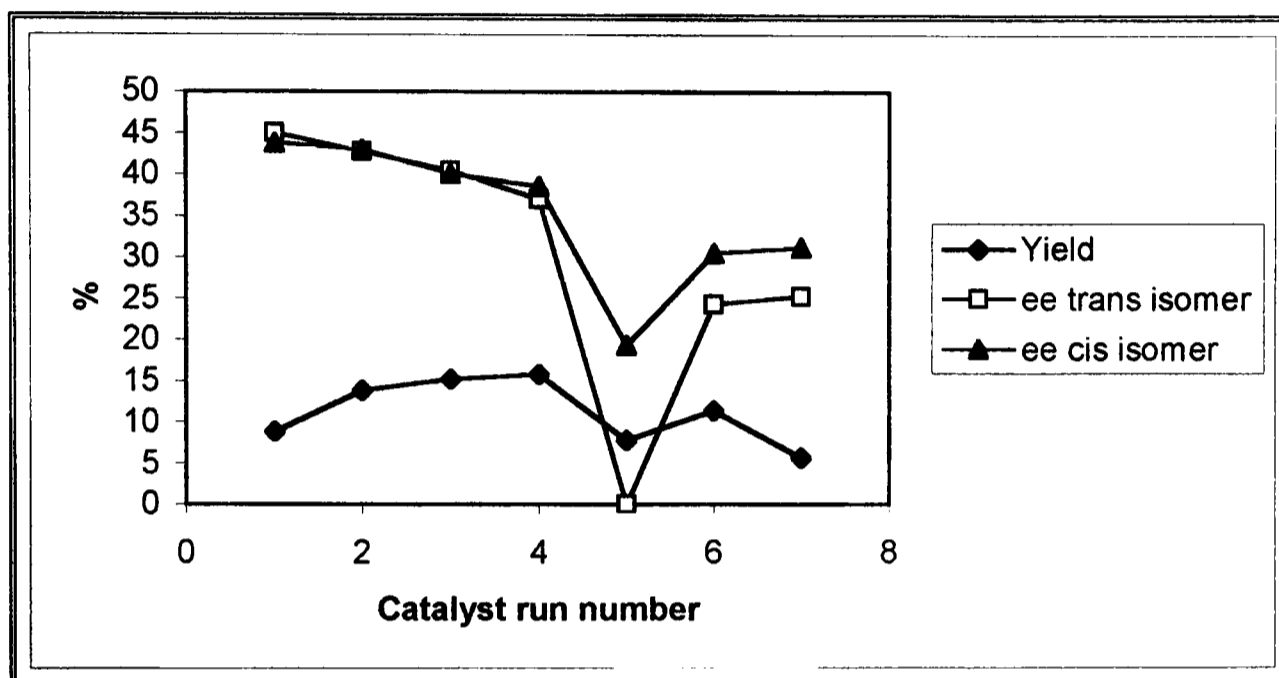


Figure 4.1.3.1: Graph showing results of cyclopropanation of styrene with addition of ethyldiazoacetate over 16 hours using an MCM-48 iodotether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride complex.

N.b. The catalyst was stored for 1 month between runs 4 and 5

It was shown that the MCM-48 supported methylenebis(4-*S*-phenyl-2-oxazoline) copper catalyst could be recycled at least 4 times with a gradual decrease in the selectivity (Figure 4.1.3.1). In some cases these used catalysts were left for *ca.* 1 month before being reused again. The catalysts showed decreased yield and selectivity upon reuse after storage, continuing to recycle these catalysts improved the yield and/or selectivity although this never reaches similar levels to those before the gap in testing.

Over the course of all the catalytic experiments (not just for the timed addition experiments) it was found that the decrease in enantioselectivity was generally faster for the

trans isomers than for the *cis*. This decrease in selectivity is probably due to gradual poisoning of the catalysts, the most probable cause of poisoning being by styrene polymerisation blocking access to catalytic sites.

4.1.4 Effect of increased temperature on catalysts

Some groups using heterogeneous bis(oxazoline) catalysts have reported that to obtain reasonable catalytic activity for certain supports the reaction had to be performed at elevated temperature (typically *ca.* 50-60°C) ⁽¹³¹⁾. Although the yields we have obtained are comparable (and in some cases better) to previously reported heterogeneous catalysts they do not compare favourably with equivalent homogeneous systems (81% homogeneous yield ⁽⁹¹⁾). Increasing the temperature of the cyclopropanation reaction may result in increased yield or enable reduced reaction times, increasing catalyst turnover.

Comparisons between cyclopropanation reactions carried out at 60°C and room temperature showed initially a slightly higher yield for the reactions carried out at elevated temperature. The catalysis performed at 60°C continued to show higher yield than those performed at room temperature upon reuse of the catalysts (Table 4.1.4.1).

Catalyst run	Yield of cyclopropanation products	
	Room temperature	60°C
1	34.5%	36.2%
2	26.4%	33.8%
3	33.6%	37.9%

Table 4.1.4.1: Yield of cyclopropanation products using MCM-48 iodo tether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride complex at different temperatures

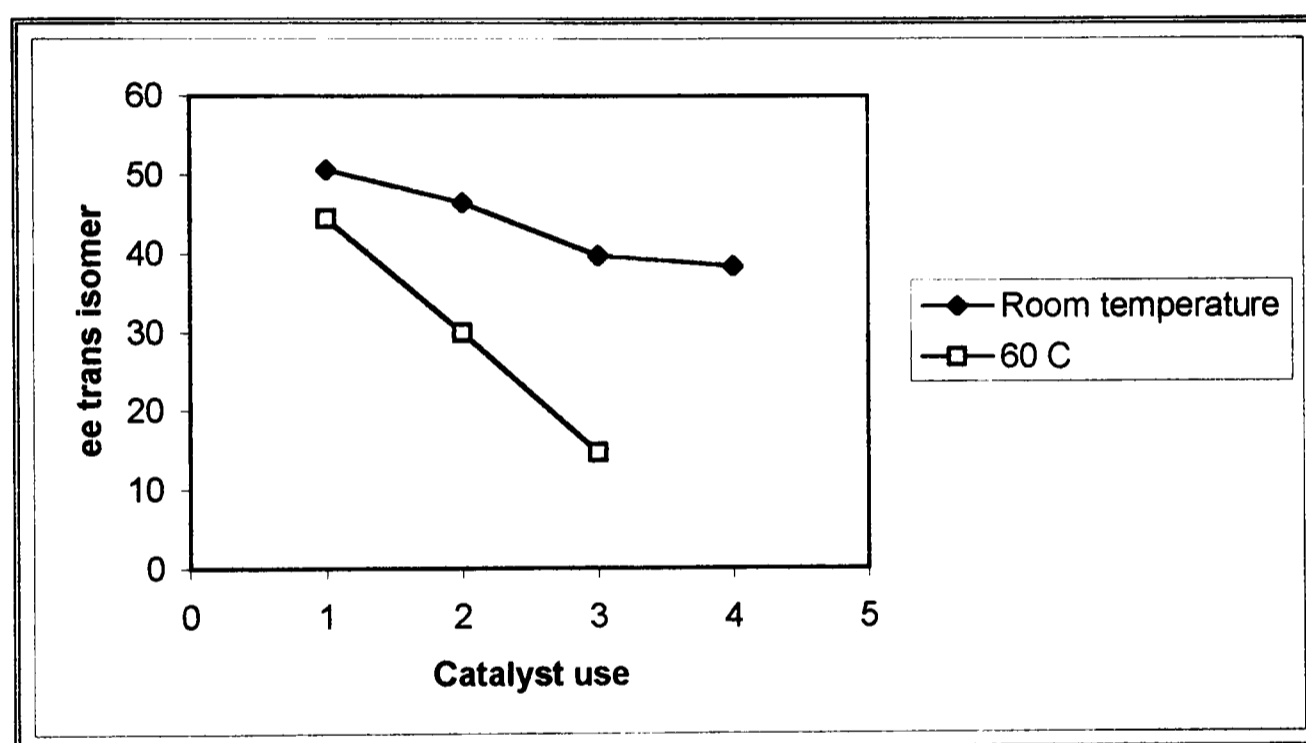


Figure 4.1.4.1: Enantioselectivity of *trans* cyclopropanation products showing faster loss of selectivity at higher temperature

The stereoselectivity for both the 60°C and room temperature were nearly identical for the initial catalyst use, however the catalysts used at elevated temperature show a faster decrease in stereoselectivity upon reuse. The enantioselectivity was also significantly reduced at the higher temperature and decreased much faster (Figure 4.1.4.1).

The results show that increasing the temperature improves the yield slightly, although the small size of the initial increase in yield may indicate that diffusion effects may be the

limiting factor in the rate of reaction. They also show that the increased temperature does not affect the initial stereoselectivity of the catalyst for the first catalyst use. However it is also apparent that the increased temperature increases the rate at which the catalyst is poisoned. The poisoning usually decreases both yield and selectivity, in this case the increased temperature keeps the yield high and the effect of the poisoning can only be seen affecting the stereo and enantioselectivity. The rapid decrease in selectivity makes repeated reuse of our supported catalysts unfeasible at these increased temperatures.

4.1.5 Effect of equimolar quantities of styrene and ethyldiazoacetate

In most studies into the cyclopropanation of styrene with ethyldiazoacetate an excess of styrene is used to reduce the amount of dimerisation side product produced and increase the yield. This effect has been mentioned earlier in connection with the rate of addition of ethyldiazoacetate (Section 4.1.3). In experiments so far we have followed this trend and used a three-fold excess of styrene. In the previous section (Section 4.1.4) we have shown that the rate at which catalyst performance is degraded can have a major effect on reusability. Whilst the exact cause of catalyst degradation is unknown (possibly a combination of metal leaching and build up of styrene and other side products), reducing the styrene to the same concentration as the ethyldiazoacetate may result in lower yield but may also prolong the life span of the supported catalysts.

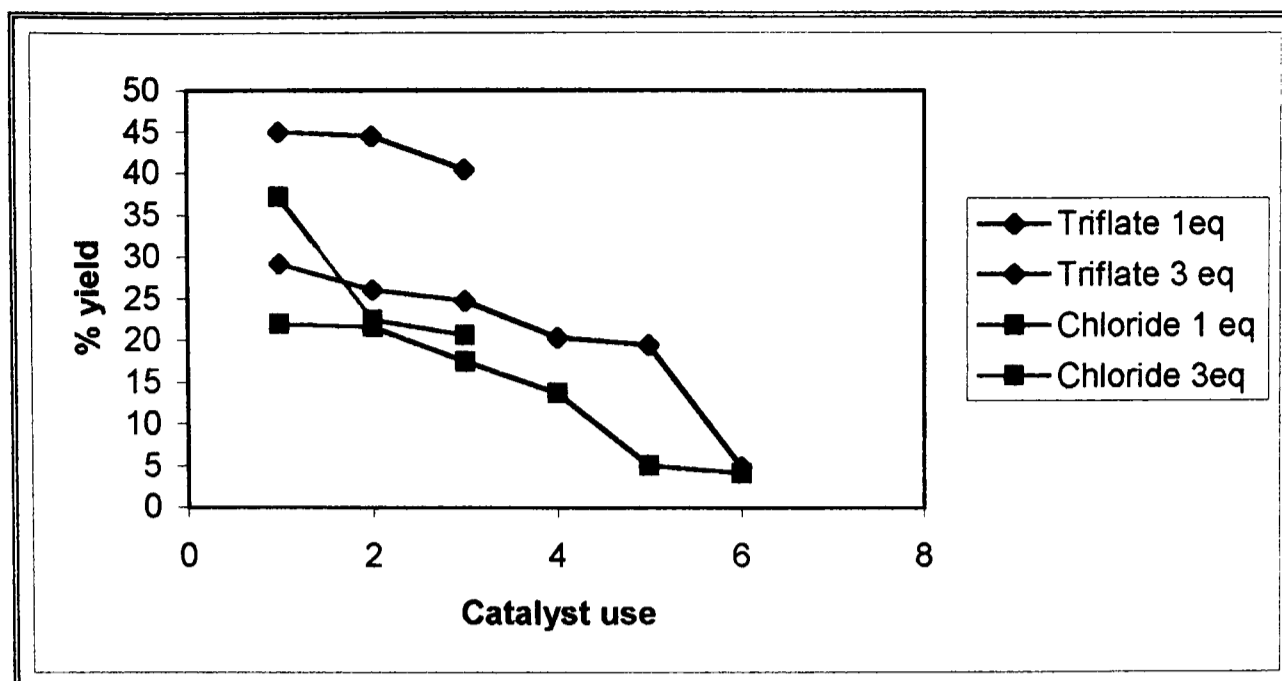


Figure 4.1.5.1: Yield of cyclopropanation products for supported copper bis(oxazoline) catalysts with equimolar and three-fold excess of styrene

Using MCM-41 iodotether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper catalysts, lower yields were found when only 1 equivalent of styrene was used for both copper (II) chloride and copper (II) triflate generated catalysts (Figure 4.1.5.1). For both chloride and triflate salts the initial yield was *ca.* 15% lower with 1 equivalent of styrene, while similar stereo and enantioselectivities were observed for the initial experiments (Figure 4.1.5.2). The chloride catalyst with a three-fold excess of styrene showed a large decrease in yield between the first and second use although the subsequent yields are still higher than those using equimolar quantities of styrene and ethyldiazoacetate. The triflate catalyst performs better than the chloride catalyst, consistently giving a higher yield of cyclopropanation products. The decrease in yield in all cases is probably a combination of effects including pore blocking (and a subsequent increase in diffusion effects) combined with some of the metal leaching from the supported catalyst.

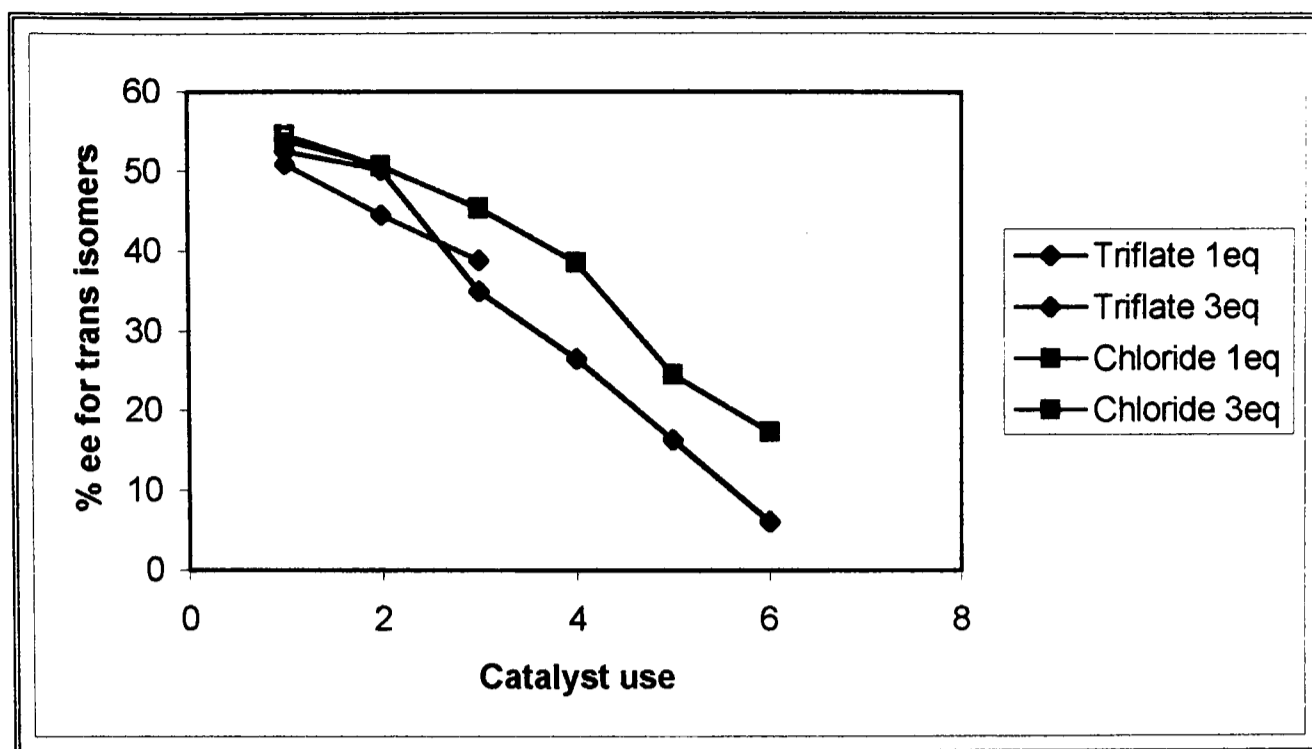


Figure 4.1.5.2: Enantioselectivity of *trans* cyclopropanation products with different styrene concentration

Figure 4.1.5.2 shows the enantioselectivity of the *trans* isomers for both the chloride and triflate generated catalysts. All show a gradual decrease in selectivity although the sharp decrease for the single styrene equivalent triflate catalyst between the second and third uses seems to defy the general trend but may be explained in part by the lower decrease between the first and second use.

The copper (II) chloride catalysts show almost no difference in the rate of catalyst degradation for selectivity for different quantities of styrene. The rate of decrease in yield however is much higher for the chloride with three-fold excess of styrene, which may be caused by build up of styrene at the entrances of the pores reducing access to the channels where many of the active catalytic sites may occur.

The results show that using one equivalent of styrene drastically reduces the yield but does not result in an equivalent increase in catalytic life span. All subsequent experiments were carried out using a three-fold excess of styrene.

4.1.6 Effect of TMEDA on catalytic selectivity

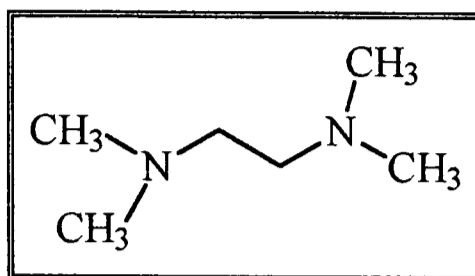


Figure 4.1.6.1: Structure of tetramethylethylenediamine (TMEDA)

The main problem encountered so far with our supported systems is the low yield for the reaction to support the catalyst upon the surface. In some earlier experiments concerning the tethering of bis(oxazoline) ligands to mesoporous silica surfaces TMEDA (Tetramethylethylenediamine) was used to promote the reaction between butyl lithium and the bis(oxazoline) ligand. Whilst the reaction to attach the tether to the bis(oxazoline) ligand was shown to still occur without the presence of TMEDA it is known that its presence does accelerate the reaction. The yield of catalyst complex upon the surface for an MCM-41 iodotether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) triflate catalyst was 27.1% (from AAS) for a supported catalyst prepared without using TMEDA, but this was increased to 45.3% for a similar supported catalyst complex synthesised using TMEDA. The use of TMEDA however is not ideal, especially in one-pot syntheses, due to possible side reactions. The structure of TMEDA (Figure 4.1.6.1) is similar in structure to the diamine compound that we have occasionally used as a tether (Figure 3.5.3.1). There remains the possibility that any TMEDA remaining may bind to the metal instead of the ligand or replace the counter anions on the metal which may change the selectivity of the catalyst complex. Also in most reactions we have used triethylamine to activate the silyl methoxy groups to bind to the surface of the support. TMEDA may result in premature activation of the methoxy

groups, which may cause clusters of catalytic sites which could adversely effect selectivity. Also the premature activation of methoxy groups could cause the catalyst to polymerise and solidify before it is added to the support.

The effect of TMEDA was tested using MCM-41 iodotether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) triflate complexes. The experiments described in preceding sections have been carried out using single batches of catalyst to eliminate factors such as catalyst loading and surface area. This is not possible in this case as we are looking at the effect that an alteration in the synthesis conditions of the catalyst has on the outcome of the cyclopropanation reaction. The loadings of catalyst in this case are 0.073mmol g⁻¹ (0.36 mol%) for the catalyst generated using TMEDA and 0.0479mmol g⁻¹ (0.24 mol%) for the catalyst without TMEDA.

Catalyst use	Yield %	
	TMEDA	No TMEDA
1	41.3	45.0
2	40.8	44.4
3	39.7	40.5

Table 4.1.6.1: Yield of cyclopropanation products for catalysts prepared with and without using TMEDA

Both the catalysts synthesised with and without using TMEDA showed good yield of cyclopropanation products with the catalyst without TMEDA showing a slightly higher yield. The catalyst prepared without TMEDA was only used three times, and Table 4.1.6.1 shows that this catalyst shows a slightly faster decrease in yield than the catalyst prepared with

TMEDA. The catalyst using TMEDA however drops sharply for the fourth use to 24.0% and to 18.0% when used for the fifth time.

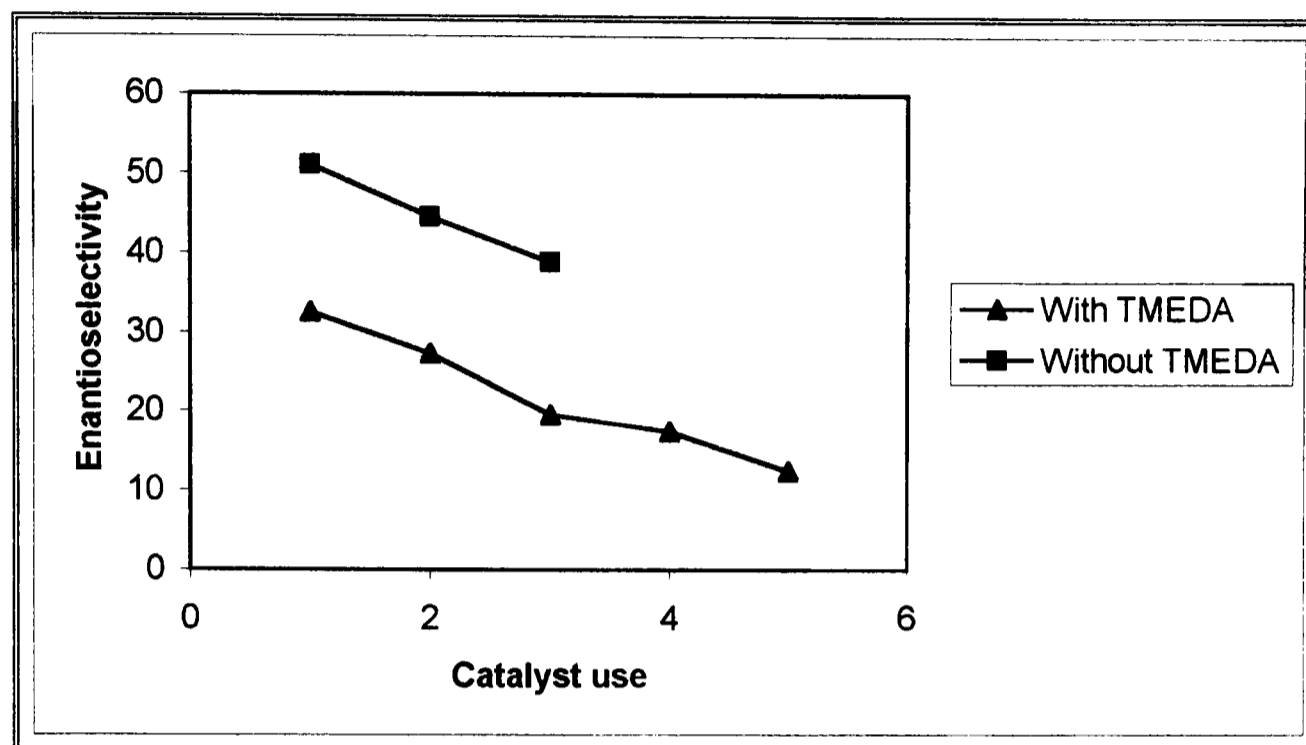


Figure 4.1.6.2: Enantiomeric excess of *trans* isomers for catalysts synthesised with and without using TMEDA

Although TMEDA does not seem to greatly affect the overall yield of the products it does have an adverse effect on both the stereo and enantioselectivity of the products. The ratio of *trans* isomers to *cis* isomers is 1.84 (64.8% *trans*) for the catalyst without TMEDA and 1.63 (62% *trans*) for the catalyst synthesised using TMEDA. Whilst these are not large differences (most of the catalysts have given *ca.* 65% *trans* : 35% *cis*) the difference (and decrease in selectivity upon reuse) is consistent over the entire range of catalysts studied.

The decrease in enantioselectivity is much more pronounced for the catalyst using TMEDA with a decrease of *ca.* 20% (Figure 4.1.6.2). The rate of degradation of selectivity with catalyst reuse is similar for both catalysts. The higher loading of the TMEDA generated catalyst may be the cause of some of the initial lower selectivity due to interaction between separate catalytic sites. Such interaction between a few catalytic sites is unavoidable due to

the random distribution of the catalyst over the surface of the support, and at higher loading more sites will be in close proximity to each other and exert an influence upon its neighbours selectivity. Note however that the higher loading by no means represents saturation of the surface, as we have previously synthesised MCM supported catalysts with over *ca.* 0.2mmol g⁻¹ of methylenebis(4-*S*-phenyl-2-oxazoline) bound to the surface *via* the same tether.

Catalysts which had been made sequentially using TMEDA (rather than *via* a one-pot synthesis, Section 3.5.1) also showed similar enantioselectivity (29.7% ee *trans* isomers) to the one-pot synthesis using TMEDA.

TMEDA greatly improves the low yield previously found in the synthesis of the catalyst complexes supported *via* alkylhalide tethers. The yield of the cyclopropanation reaction is unaffected by either the higher concentration of catalytic sites upon the surface or by any side reactions with TMEDA in the synthesis of the catalyst. The selectivity of the reaction is adversely affected by using TMEDA in catalyst synthesis, as the effect is too large to be entirely caused by the concentration of the catalyst upon the surface from random distribution. Low selectivity was also observed for a catalyst where soxhlet extraction should have ensured that no free TMEDA remained before addition of the metal salt. This means that the TMEDA must either be causing the catalytic sites to form clusters (which would greatly increase the amount of steric interaction between individual sites) or forming sites where the metal can be tethered to the surface without binding to a chiral ligand.

4.1.7 Effect of supporting material on methylenebis(4-*S*-phenyl-2-oxazoline) catalysts

For most studies into supported bis(oxazoline) catalysts one of the most commonly used ligands used is methylenebis(4-phenyl-2-oxazoline). Although this ligand does not result in the best reported selectivity (for the cyclopropanation reaction of styrene with ethyldiazoacetate the best selectivity is obtained using methylenebis(4-*t*-butyl-2-oxazoline)) it does give reasonable selectivity, and is much cheaper and is more reactive than some of the more selective bis(oxazoline) ligands.

The catalysts were supported on one of three different silica supports: MCM-41, MCM-48 and a commercially available silica Cab-o-sil. The catalysts were synthesised without using TMEDA and the cyclopropanation reaction with styrene was carried out at room temperature with a three-fold excess of styrene and the ethyldiazoacetate added in a single injection (unless stated otherwise), in accordance with observations made in previous experiments. For comparison to our supported systems three different homogeneous catalyst complexes were also studied; a di-bis(oxazoline) copper (II) chloride complex, and mono-bis(oxazoline) complexes with either copper (II) chloride and copper (II) triflate.

In comparing the different supported catalysts the effect of the interaction of catalytic sites cannot be ignored (as the surface area of the support and the loading will vary from sample to sample, as has been mentioned previously in Section 4.1.6).

Copper (II) chloride catalysts

In homogeneous catalysis two methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) chloride complexes have been tested as catalysts, involving either one or two bis(oxazoline)

ligands (see Figures 3.5.4.1 and 3.5.4.2). In the literature the di-ligand complex (as used by Masamune ⁽⁹¹⁾) has been reported to give good results with 81% yield 70:30 *trans: cis* selectivity and ee of up to 60% for *trans* isomers. Preparation of this di-complex was easily accomplished (see Section 3.5.4), but the catalytic results obtained were much lower compared with the literature (Table 4.1.7.1). Given the diazoacetate addition was over 16 hours (rather than the 24 hours used in the paper) and that the total volume of solvent was larger, coupled with effects mentioned in Section 4.1.3 the lower yield (13.6%) can be partially explained. The stereoselectivity was found to be slightly decreased (63:37 *trans: cis*) but the enantioselectivity was much lower (22.1% for *trans* isomers). The cause of this lower selectivity is unknown, but may be due to poor quality of the purchased ligand (this is however unlikely as catalysts prepared at a similar time resulted in more comparable selectivity). Throughout the supported catalysts will be compared against the published results.

Non-neutral mono-bis(oxazoline) copper (II) chloride complexes are not commonly used, even for comparisons with heterogeneous systems, as most supported catalysts are tethered to the supporting matrix *via* the bridging group, effectively rendering the ligand neutral. For our supported catalysts some ligands are only bound to the surface by a single tethering group attached to the bridge and may still be able to act as charged ligands. The published results for neutral mono-bis(oxazoline) copper chloride complexes show poor enantioselectivity (*ca.* 4-6% ⁽⁷²⁾) compared to catalysts synthesised with copper triflate.

The synthesis of the mono-ligand chloride complex was carried out *in situ* in the reaction vessel. The final colour of the catalyst complex before commencement of the catalytic reaction was pale green, indicating that there is no di-ligand complex present. The di-ligand complex is deep purple in colour which can be seen even at low concentrations.

Note also a small amount of uncomplexed copper chloride will be present in solution which will have a slight negative effect on selectivity.

The yield found was much lower than expected for a homogeneous catalyst (18.4%), the stereoselectivity was comparable to published results for the di-ligand complex (71:29 *trans: cis*). Again enantioselectivity was found to be low (20.5% ee *trans* isomers), although this is higher than reported for the neutral mono-ligand chloride complexes which result in nearly racemic products.

Catalyst	Catalyst mol %	Yield	<i>Trans: Cis</i>	ee <i>trans</i> isomer
Published di-complex ⁽⁹¹⁾	1	81 %	70:30	60 %
Synthesised di-complex	1	13.6 %	63:37	22.1 %
Mono-complex	1	18.4 %	71:29	20.5 %
MCM-41	0.18	37.2 %	66:34	53.8 %
MCM-48	0.16	34.5 %	63:37	50.6 %
Cab-o-sil	0.05	10.4 %	65:35	44.2 %

Table 4.1.7.1: Results of the cyclopropanation of styrene with ethyldiazoacetate for homogeneous and heterogeneous copper chloride catalysts supported on silicas.

N.B. the catalysis for the synthesised di-ligand complex was carried with slow addition of ethyldiazoacetate

As can be seen in Table 4.1.7.1 the amount of catalyst used in each experiment varies, the homogeneous catalysts used 1 mol% (compared to the ethyldiazoacetate). The amount of supported catalyst used varied between *ca.* 50-75mg, and so the amount of actual catalyst depends on the loading of catalyst upon the support. This loading may also have an effect on selectivity, as has been mentioned previously and will be investigated further later.

Most supported bis(oxazoline) catalysts use neutral variants of the ligands often with copper (II) triflate salts, and additionally many different solvents have also been used for the catalysis reactions, making direct comparisons between our catalysts and other published systems difficult especially for catalysis generated using copper chloride.

The yield for the supported systems in many cases was better than that found for the homogeneous equivalents, (for the di-ligand complex this may be explained by incomplete addition of reagent as explained in Section 4.1.3). The low yield found for the mono-ligand complex is consistent with results found in studies using neutral mono-ligand chloride complexes which have given low conversion in other studies⁽⁷²⁾. The mesopore-supported catalysts give higher yield than the amorphous silica supported catalyst, which in part may be due to the amount of catalyst complex present as the Cab-o-sil reaction has less than a third of the catalyst found in the other supported reactions. The Cab-o-sil silica used was not porous, the reasonable surface area arising from the small particle size, but this caused problems with the recovery process for the catalyst, as the small particle size required higher pressure for filtration making the process much slower

The stereoselectivity is slightly lower for all three of the supported catalysts compared to the published di-ligand complex and the homogeneous mono-complex. However the stereoselectivity is nearly identical for all three of the silica supporting materials tested.

The enantioselectivity for all three of the supported catalysts is much better than found in our synthesised homogeneous catalysts although is worse than the results for the published di-complex. The selectivity for the catalysts supported on mesoporous materials is similar, while the lower selectivity for the catalyst supported on amorphous silica is probably caused by the lower surface area of the support, meaning that even though the catalyst loading is lower the concentration of catalyst per unit area is much higher. The enantioselectivity for the

cis isomers is slightly lower than that for the *trans* isomers (the maximum decrease is *ca.* 5%). Our supported catalysts therefore do not suffer the same problem that affects the laponite supported catalysts made with copper chloride and phenyloxazolines ⁽⁷²⁾ i.e. whilst the enantioselectivity for the *trans* isomers is high (46%) the *cis* isomers are almost racemic (3%).

The catalysts were easily recovered and reused, but it was found that the catalyst supported upon commercial silica only had a short lifetime as by the third use the yield had decreased to *ca.* 3%, in contrast the mesopore supported catalysts still gave over 20% yield after a similar time. MCM-48 supported catalysts show a slower decrease in yield compared to MCM-41 supported catalysts (presumably, as the cross-linked channels do not become blocked as fast).

The MCM-48 supported catalyst which retained its activity the best was reused the most giving 27.3% yield for a fourth use, after which it was not used for over a month and upon reuse again only showed 2.9% yield. This negative effect of storage on the catalyst after it has been used has been noticed previously during the investigations into the rate of addition of ethyldiazoacetate (Section 4.1.3).

The stereoselectivity showed little change upon reuse (Figure 4.1.7.1). The Cab-o-sil supported catalyst surprisingly did not show faster decrease in selectivity than the mesopore supported catalysts to accompany the rapid decrease in yield, although the low yield for the final result does increase the amount of experimental error.

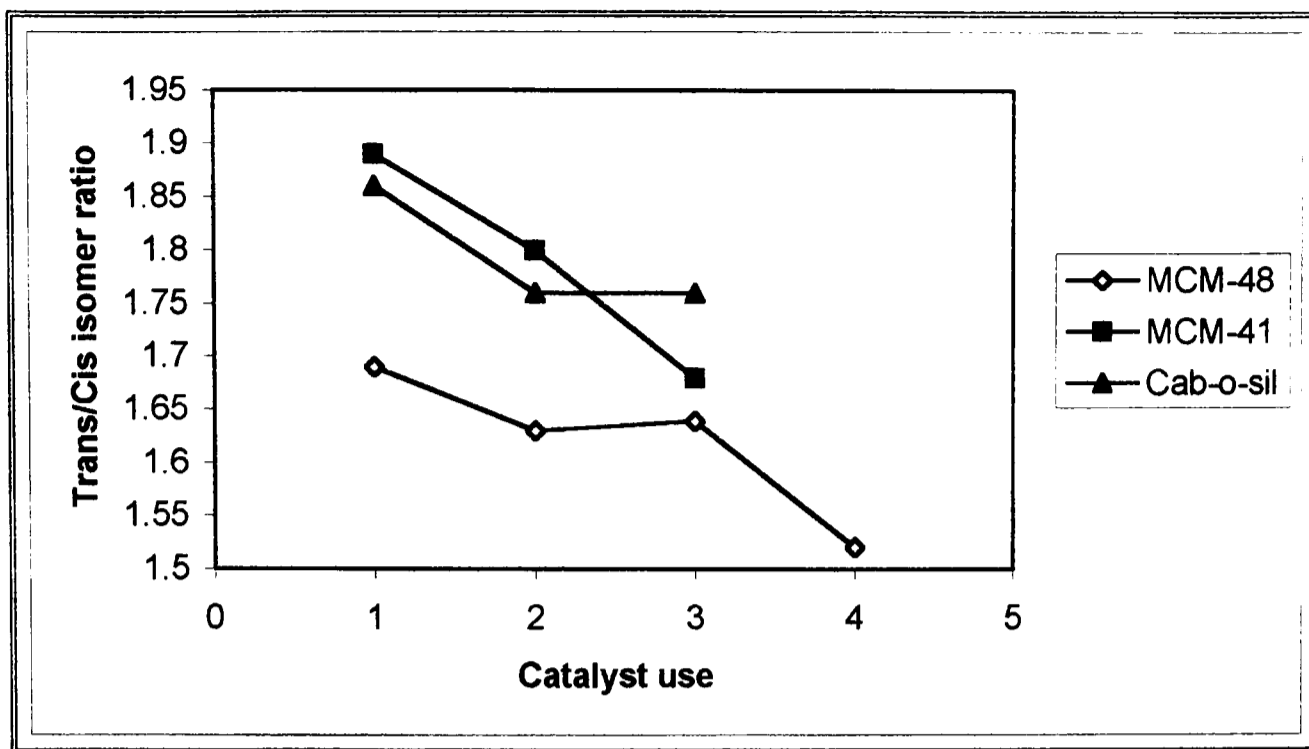


Figure 4.1.7.1: Stereoselectivity of supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride generated catalysts on reuse

The enantioselectivity decreases gradually upon reuse of the catalyst (Figure 4.1.7.2). The sharp decrease for Cab-o-sil for the third use (combined with the low yield for the same reaction) would indicate that the catalyst is becoming poisoned, although the low yield does increase the amount of experimental error. The poisoning of the catalyst seems to occur much faster for low surface area silica than for the mesoporous materials, which have large surface areas. This indicates that the poison may be binding directly to the silica surface and the high surface area of the mesoporous materials allows more poison to bind before the catalyst is overwhelmed. As with other supported catalysts there will be an effect caused by interaction between individual catalytic sites caused by the loading. This effect may be the cause of the lower selectivity shown for the MCM-48 and Cab-o-sil supported catalysts compared to those supported on MCM-41.

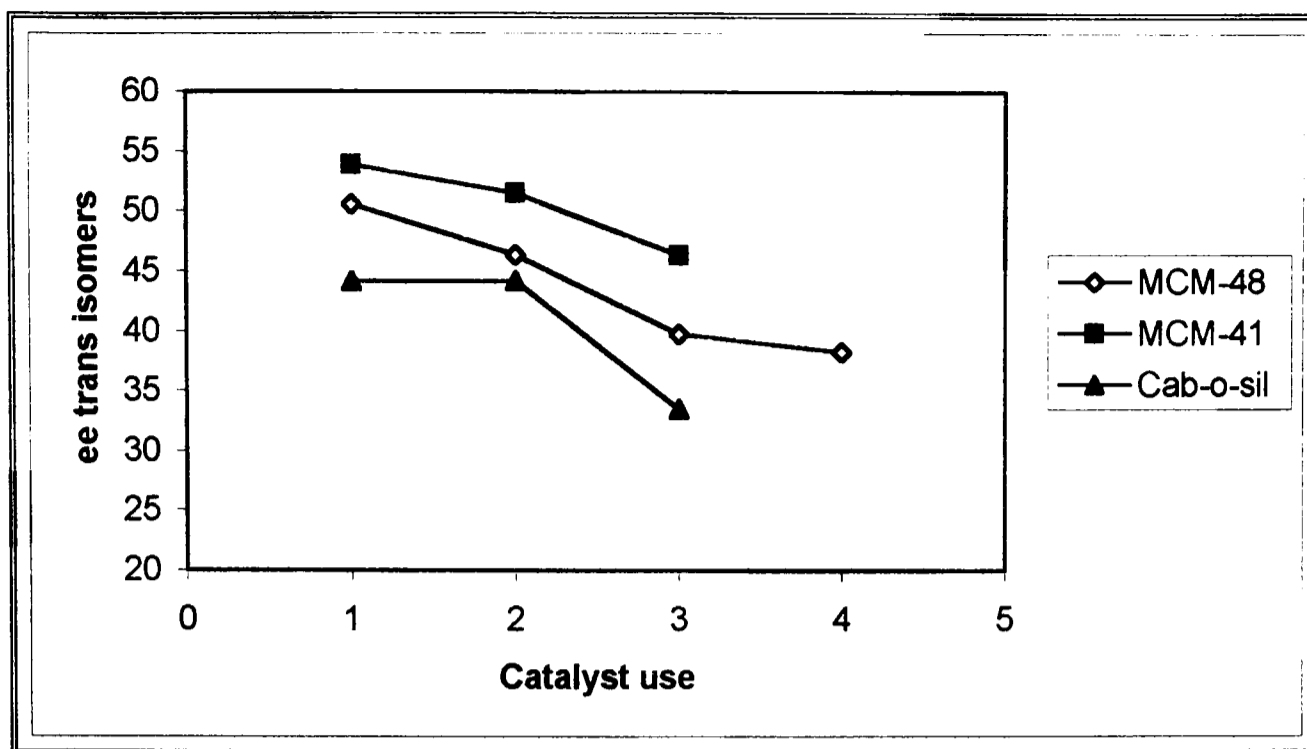


Figure 4.1.7.2: Enantiomeric excess of *trans* isomers for supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride generated catalysts upon reuse

The effect that the supporting material has on these copper (II) chloride generated catalysts is diverse and not all questions can be answered. The mesoporous materials are better supports than commercially available silica especially in terms of how many times a catalyst can be reused and the amount of catalyst which can be supported upon the surface without too adversely affecting the selectivity. Many of the other questions as to which of the mesoporous materials is best will require further surface area measurements to determine the effect that catalyst interaction has on the selectivity.

It is known that the counter ion can have a significant effect on the selectivity, and the differences between the homogeneous mono-ligand complexes (both for our synthesised versions and published ones) raised the possibility that the counter ion may have become substituted.

Silver nitrate tests on catalysts synthesised using copper chloride showed positive results for chloride ions although the amount of chloride present in each case was insufficient for anything other than the most basic tests. These results are not conclusive as they only

show that there are chloride ions present in the solid. In order to try and determine whether substitution of the counter ion had occurred samples were submitted for EXAFS analysis (see Section 3.5.1). This showed that there was no chlorine atoms bound directly to the copper atoms, and that it had been replaced by a lighter element (probably nitrogen).

Copper (II) triflate catalysts

Copper triflate has been used for supported bis(oxazoline) catalysts in the majority of cases. We can therefore make much better comparisons between our supported catalysts and those created by other groups than we could previously for the chloride catalysts.

The synthesised homogeneous mono-ligand complex gave good results (44% yield, 2.05 *trans/cis* selectivity and 57.7% ee *trans*, 49.2% ee *cis*). This is comparable to those reported for the homogeneous mono-neutral-ligand complex with methyl instead of hydrogen on the bridging group (49% yield, 2.1 *trans/cis* selectivity and 60% ee *trans*, 51% ee *cis*)⁽¹³¹⁾.

Catalyst	Catalyst mol %	Yield	<i>Trans: Cis</i>	ee <i>Trans</i>
Homogeneous	1	44.0 %	2.05	57.7 %
MCM-41	0.24	45.0 %	1.95	50.9 %
MCM-48	0.22	30.6 %	1.93	54.0 %
Cab-o-sil	0.19	37.1 %	1.84	50.5 %

Table 4.1.7.2: Cyclopropanation of styrene and ethyldiazoacetate using homogeneous and silica supported copper (II) triflate catalysts

We can see from Table 4.1.7.2 that the selectivities for all of the catalysts are similar and that the only significant difference between the different supported catalysts is for the yield. Interestingly, although the loadings of catalyst per gram are much higher for the triflate catalysts (0.0374-0.0479 mmol g⁻¹) than for the chloride catalysts (0.0063-0.0212 mmol g⁻¹) this does not seem to have adversely affected the selectivity of the catalyst. This would appear to indicate that the triflate catalysts are less susceptible to the effects of interaction between individual catalytic sites than the chloride catalysts.

The yields obtained for our supported catalysts compare very favourably with or exceed (in the case of the MCM-41 supported catalyst) those reported for the best heterogeneous bis(oxazoline) catalysts. Polymeric catalysts have given *ca.* 28-40% yield^(60, 130), catalyst-exchanged clays up to 37% (the highest yields were obtained at elevated temperatures)⁽¹³¹⁾ and those supported on silica (*via* different tethers) 24-37%⁽¹³⁴⁾.

The selectivities found for our supported catalysts show no change between the different supports (total range in Table 4.1.7.2 is 66:34 – 65:35). These compare well to other silica supported catalysts which also show about 66:34 *trans: cis* selectivity⁽¹³⁴⁾ as well as the polymeric catalysts (up to 66:34 *trans: cis* selectivity)⁽¹³⁰⁾ and those immobilised by ionic exchange (up to 67:33 *trans: cis* selectivity). Catalysts showing higher stereoselectivity usually show vastly reduced yield or enantioselectivity (e.g. Dowex supported catalyst gives *trans/cis* ratio of 2.1 but only 17% enantiomeric excess⁽¹³¹⁾).

The enantioselectivity found for our silica-supported catalysts is much better than found for the majority of supported bis(phenyl-oxazoline) catalysts previously reported. Catalysts supported on silica (*via* different tethers) have shown a maximum of 33% ee whilst those supported on laponite layered clays have frequently shown good selectivity for *trans* isomers but poor selectivity for *cis*. The best results for bis(phenyl-oxazoline) supported

catalysts by other groups are either certain polymeric systems using toluene and AIBN during polymerisation (61% ee *trans* isomer) which requires elevated temperature to achieve good yield ⁽¹³⁰⁾ (although other methods of polymerisation resulting in slightly reduced selectivity can be run at room temperature), nafion supported catalysts (also requiring elevated catalysis temperature) (59% ee *trans* isomer) ⁽¹³¹⁾ or nafion-silica exchanged catalysts (57% ee *trans* isomer) ⁽¹³¹⁾.

The catalysts also gave good yields upon reuse; both the MCM-48 and the Cab-o-sil supported catalysts gave over 25% yield after 3 uses. The catalyst supported on MCM-41 showed little decrease in the yield giving over 40% yield after the third use (a similar trend was also seen for this catalyst when used for the experiments with one equivalent of styrene).

The stereoselectivity decreased slowly for all three supported catalysts (although again the way in which the data is shown magnifies any changes). The Cab-o-sil and MCM-41 supported catalysts were only used three times showing a slow decrease in the stereoselectivity to 1.78 and 1.64 *trans/cis* respectively. The decrease for the most reused catalyst (MCM-48) levelled off after the fourth use at a *trans/cis* ratio of 1.53 (*ca.* 60:40 *trans: cis*, initially 66:34 *trans: cis*) and stayed at this level upon additional reuse of the catalyst.

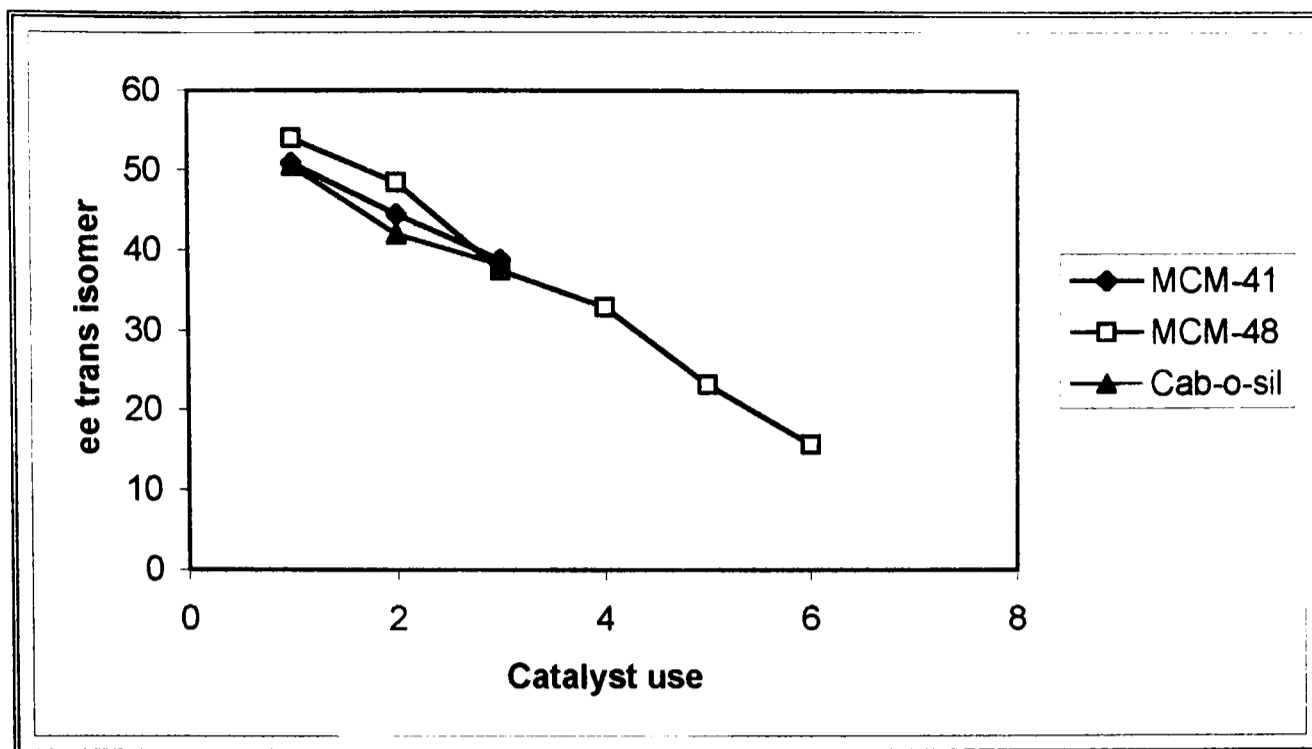


Figure 4.1.7.3: Enantiomeric excess of *trans* isomers for supported methylenebis(*4-S*-phenyl-2-oxazoline) copper triflate catalysts upon reuse

The enantioselectivity decreased gradually for both isomers on all three supported catalysts. The rate of decrease of the enantioselectivity in general is similar to that found for the chloride-generated catalysts.

Comparing the reusability of our catalysts with other supported systems shows varying degrees of comparison. Although some published catalysts have been reused up to 5 times⁽¹³⁰⁾ in most cases only data for the first 2 uses are shown. The published results as expected show that some supports are much more suitable for reuse than others. At one extreme some supported catalysts (usually catalysts that only give moderate selectivity initially) a sharp decrease to a nearly racemic product is seen upon reuse. At the other extreme almost no decrease in either yield or selectivity is shown for the second use (nafion-silica catalysts⁽¹³¹⁾). Our supported catalysts exhibit behaviour in-between these two extremes as they show a gradual reduction in yield, stereoselectivity and enantioselectivity. The selectivity found for our supported catalysts are promising for the first use. The gradual deactivation (which is believed to be caused by build-up of side products [probably both

styrene and dimerisation products of ethyldiazoacetate]) does place a limit upon the catalytic lifespan.

Changes in selectivity over the catalytic run and addition of extra reagents

In some published studies it has been noticed that the selectivity of the catalyst changes during the course of an experiment. The Dowex supported catalysts which overall result in a product with 17% ee for the *trans* isomers show better selectivity (39% ee *trans* isomers) at low levels of conversion ⁽¹³¹⁾. The single injection catalytic experiments were carried out with run times of 40 hours. Although the duration of the experiments should be sufficient to obtain maximum yield it was decided that monitoring over a prolonged period of time would show if we were utilising the full potential of the catalysts. Also it was decided to investigate whether the supported catalysts could be reused by the addition of more reagents without the need for reactivation by addition of phenyl hydrazine. This test was carried out using a copper (II) chloride catalyst supported on MCM-48.

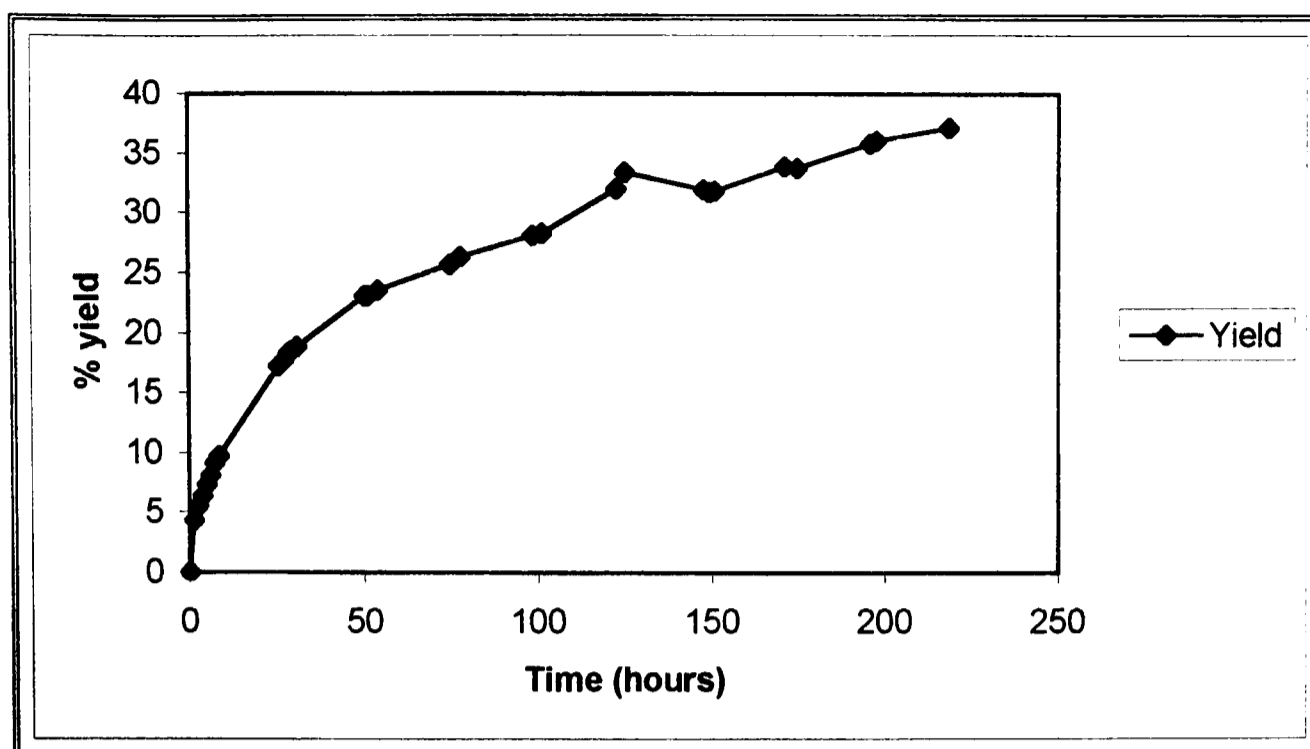


Figure 4.1.7 4: Graph showing the increase of yield over time

N.b. evaporated solvent replaced after 122 hours, a second equivalent of ethyldiazoacetate added after 149 hours

The reaction proceeds much more slowly than found for the normal catalytic experiments, this is due to some catalyst (and some reagents and products) becoming trapped on the walls of the reaction vessel (effectively reducing the amount of catalyst present) and the low temperature of the experiment. The trapping of products on the walls of the reaction vessel can also be used to explain the erroneous data points at *ca.* 122 - 125 hours at which time due to solvent evaporation additional solvent was added. The yield stops increasing after *ca.* 122 hours but upon addition of a second equivalent of ethyldiazoacetate (after 149 hours) the yield starts to increase. The rate of increase is not as dramatic as found initially when the catalyst was first activated.

Stereoselectivity does decrease slightly at higher yield, initially the *trans/cis* ratio was 1.75 after 1.5 hours, which gradually decreased to *ca.* 1.57. Upon addition of the second equivalent of ethyldiazoacetate this briefly increased again before rapidly falling back to *ca.* 1.57.

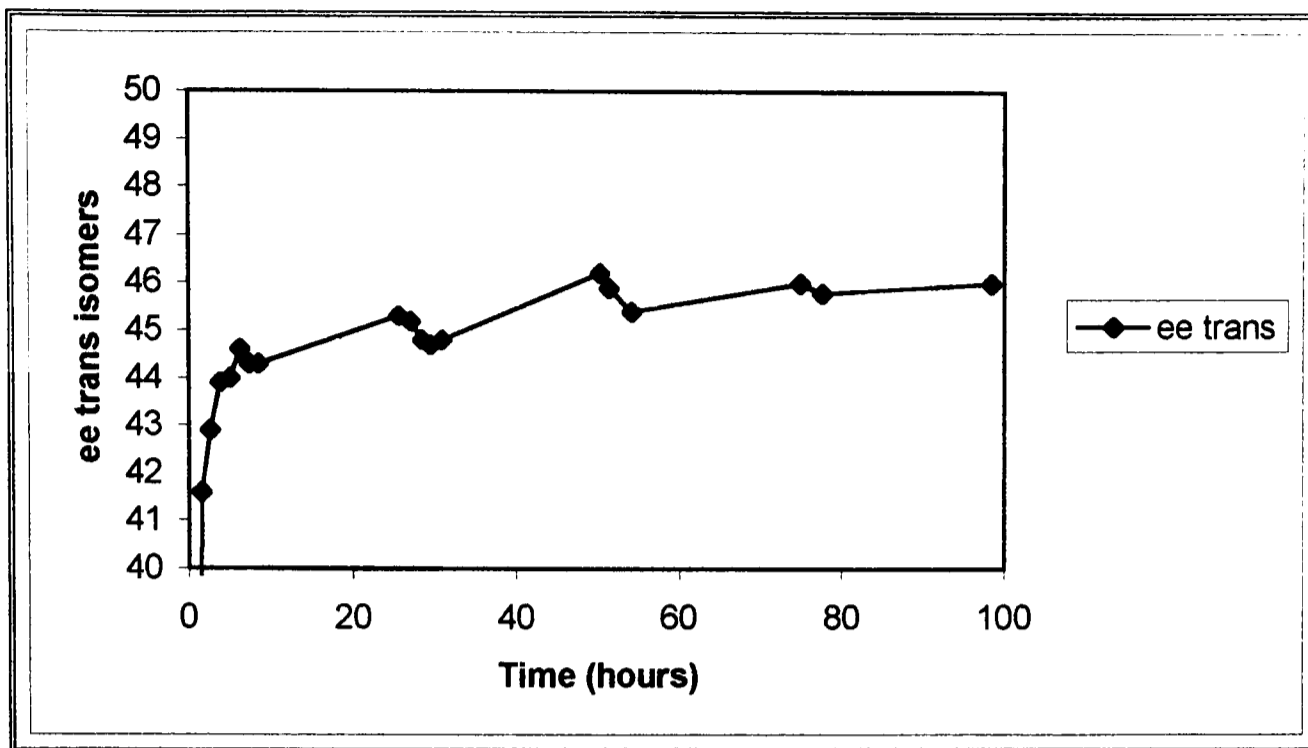


Figure 4.1.7.5: Enantioselectivity of *trans* isomers vs. catalytic run time for MCM-48 iodopropyl tether supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride catalyst

Enantioselectivity varied for both *trans* and *cis* isomers; they both show an initial increase in selectivity (*ca.* 2-3 %) over the first 5-6 hours. The enantioselectivity then decreased slightly during the day but increased at night (Figure 4.1.7.5). The reason for this is temperature related, and whilst previously we looked at the effect of increased temperature on our catalysts in order to try and increase the yield (Section 4.1.4) we did not investigate the effect of decreased temperature. Some homogeneous studies have tested catalysts both at room temperature and at 0°C, showing enhanced selectivity at the reduced temperature⁽⁹²⁾. Our experiment (Figure 4.1.7.5) also shows the same effect of increased selectivity at reduced temperature. The decrease in temperature is due to the experiment being performed during February and the heating in the laboratory being switched off at night.

Catalysts supported *via* hydrogen bonding or *via* diamine tethers

Previously we have only looked at catalysts supported *via* iodo-propyl tethers on silica materials. We have also synthesised catalysts using methylenebis(4-*S*-phenyl-2-oxazoline) and a copper salt supported *via* hydrogen bonding (Figure 3.5.2.1) and *via* a propylethylenediamine tether (Figure 3.5.3.1). Both of these catalysts were supported on MCM-41. The hydrogen bonded catalyst was synthesised using copper (II) triflate and the diamine tethered catalyst used copper (II) chloride.

The catalyst supported by hydrogen bonding gave a good yield of cyclopropanation products (30.8%) with the stereoselectivity only slightly worse than found for the catalysts supported *via* alkyl tethers. However the products showed little or no enantioselectivity (the maximum enantiomeric excess was 1.1% for the *trans* isomers). The high loading of the catalysts (*ca.* 0.153 mmol g⁻¹) may have had some effect on the selectivity.

The catalyst supported *via* a diamine tether again gave good yield (29.8%) and showed reasonable stereoselectivity (1/1.70-1/1.65 *cis/trans*). Two different batches of catalyst were synthesised, with the first showing an enantiomeric excess of 13.6% for the *trans* isomers, while the second gave a racemic product. Analysis of these catalysts showed that the theoretical loading of active catalyst complex were 0.091 and 0.0741 mmol g⁻¹ respectively, while the loading of diamine tether (theoretically) was nearly identical in both cases.

Whilst the first batch shows that this method of supporting bis(oxazoline) catalyst is capable of producing a catalyst which can give an enantiomerically enhanced product the second batch of catalyst suggests that the method is much less robust than the route we have developed using alkyl tethers.

4.1.8 Catalysis using other alkyl tethered bis(oxazoline) copper catalysts

Methylenebis(4-*S-t*-butyl-2-oxazoline) catalysts

As has been mentioned earlier whilst methylenebis(4-*S*-phenyl-2-oxazoline) catalysts are frequently used in supported cyclopropanation reactions they have not shown the highest enantioselectivity in tests with homogeneous catalysts.

The methylenebis(oxazoline) catalyst showing highest enantioselectivity is the tertiary butyl derivative (methylenebis[4-*S-t*-butyl-2-oxazoline]).

Our early experiments using this ligand were unsuccessful as we were unable to obtain even a homogeneous catalyst which showed any selectivity. The problems found with these early catalysts were traced to the poor quality of the purchased ligand (see Section 3.5.4). A significant amount of time was wasted testing these catalysts synthesised using the faulty ligand before the problem was identified. The following results were obtained using a fresh supply of methylenebis(4-*S-t*-butyl-2-oxazoline).

The homogeneous di-methylenebis(4-*S-t*-butyl-2-oxazoline) copper (II) chloride complex gave good yield and selectivity (31.2% yield, 75:25 *trans*: *cis* selectivity, 79.3% ee *trans* isomers and 66.4% ee *cis* isomers). These results are not as good as those reported in the literature for the same catalyst⁽⁹¹⁾ (80% yield, 75:25 *trans*: *cis* selectivity, 90% ee *trans* isomers and 77% ee *cis* isomers), however this is due to differences in experimental conditions and impurities within the purchased ligand.

The homogeneous mono-ligand complex with copper (II) triflate did not perform as well as expected. In the literature this catalyst has shown over 98% ee for *trans* isomers⁽¹⁰³⁾, but we only obtained moderate enantioselectivity of 18% for this catalyst. This again may be

due to impurities within the ligand or the presence of uncomplexed metal which will drastically reduce the selectivity. The difference between the results for the di-ligand complex and the mono-ligand complex may be explained by the synthesis procedure for the di-ligand complex which included a purification stage which will remove any uncomplexed metal which is not possible in the synthesis of the mono-ligand complex.

Due to time constraints only one supported methylenebis(*4-S-t*-butyl-2-oxazoline) catalyst was synthesised with the new ligand. This was a copper (II) triflate catalyst supported *via* the iodoalkyl tether on MCM-41. The yield obtained was comparable to those previously obtained for the phenyl-based catalysts (31.5%). The stereoselectivity was much lower than found for either of our homogenous comparisons and the products showed very little enantioselectivity (*ca.* 5%) (see Table 4.1.8.1).

Catalyst	Yield	<i>Trans: Cis</i>	<i>ee trans</i>	<i>ee Cis</i>
Published homogenous di-complex ⁽⁹¹⁾	80%	75:25	90%	77%
Published homogeneous mono-complex ⁽¹⁰³⁾	N/A	77:23	98%	93%
Synthesised homogenous di-complex	31.2%	75:25	79.3%	66.4%
Synthesised homogenous mono-complex	38.1%	67:33	18%	16.4%
MCM-41 tethered catalyst	31.5%	59:41	4%	5.4%

Table 4.1.8.1: Results for the cyclopropanation of styrene with ethyldiazoacetate using methylenebis(*4-S-t*-butyl-2-oxazoline) copper catalysts.

Various other groups have synthesised supported methylenebis(*4-S-t*-butyl-2-oxazoline) copper catalysts for use in cyclopropanation reactions. Most of these have also met with limited success, the most successful supported catalysts being those supported on

polymers. These polymeric catalysts have shown enantioselectivities of up to 77%,⁽¹³⁰⁾ however a reversal in the stereoselectivity was observed with the products predominantly *cis* isomers. With catalysts immobilised within layered clays the best results were found for laponite clays, which showed 69% ee (*trans* isomers), for the first use, but decreasing rapidly upon reuse (showing only 43% ee for the second use)⁽¹³¹⁾. Catalysts supported on silica have only shown a maximum of 26% ee (*trans* isomers) and have also shown reduced stereoselectivity compared to homogeneous equivalents⁽¹³⁴⁾.

Much of the problems associated with supporting methylenebis(*t*-*S*-*t*-butyl-2-oxazoline) catalysts has focused on the size of the bulky *t*-butyl groups which make the catalyst so effective in the first place. It can be proposed that either the pores of the supporting material are too small to accommodate the complex⁽¹³¹⁾, that the steric interaction between the *t*-butyl groups and the surface is too large to allow the catalyst to operate effectively or that the tethering species is too short.

Methylenebis(4*R*,5*S*-diphenyl-2-oxazoline) catalysts

Another ligand which is commercially available is methylenebis(4*R*,5*S*-diphenyl-2-oxazoline), but complexes of this ligand have not often been used in cyclopropanation reactions in spite of good results with an array of sterically hindered olefins and diazoacetates⁽¹⁰⁴⁾.

With styrene and ethyldiazoacetate the homogeneous mono-ligand complex with copper (II) triflate gave a good yield of products (57.7%). The stereoselectivity was also good 68:32 *trans*: *cis* and reasonable enantioselectivity was also observed (43.5% *trans* isomers).

With this ligand unlike for the phenyl and *t*-butyl ligands the enantioselectivity was reversed with the (S,R) and (S,S) isomers being predominant.

The catalyst supported *via* an alkyl tether on MCM-41 also gave good yield (although as usual this was less than found for the homogeneous catalyst). Stereoselectivity was slightly reduced (63:37 *trans*: *cis*) compared to the homogeneous catalyst. The enantioselectivity showed a larger reduction being approximately half of that found in the homogeneous reaction (Table 4.1.8.2).

Catalyst run	Yield	<i>Trans</i> : <i>Cis</i>	ee <i>cis</i>	ee <i>trans</i>
Homogeneous	57.7%	2.17	34.5%	43.5%
1	35.7%	1.69	16.6%	20.5%
2	29.8%	1.64	17.0%	18.0%
3	11.8%	1.70	15.2%	15.6%

Table 4.1.8.2: Cyclopropanation reaction of styrene and ethyldiazoacetate using MCM-41 supported methylenebis (4*R*,5*S*-diphenyl-2-oxazoline) copper (II) triflate catalysts

The catalyst was reused several times with only a slight decrease in selectivity, as can be seen in Table 4.1.8.2. Whilst the yield gradually decreases, stereoselectivity is kept almost constant and the decrease in enantioselectivity is slow.

Methylenebis(4-*S*-iso-propyl-2-oxazoline) catalysts

The homogeneous di-ligand copper (II) chloride complex showed the best enantioselectivity (30.7% ee *trans* isomers) and also showed good stereoselectivity (63:37

trans: cis). However the yield obtained for this catalyst was disappointing (5.8%), the mono-ligand homogeneous complex with copper (II) triflate gave a much better yield (39%). The stereoselectivity was also good (64:36 *trans: cis*) but the enantioselectivity was lower than found for the di-ligand complex (16.8% ee *trans* isomers).

The heterogeneous catalyst supported *via* an iodoalkyl tether onto MCM-41 also showed good yield for the initial use (33.8%). The stereoselectivity was reduced compared to the homogeneous systems (*ca.* 60:40 *trans: cis*), the products obtained showed little or no enantioselectivity (*ca.* 0.4% ee *trans* isomers). Interestingly with this ligand the enantioselectivity for the *cis* isomers was found to be slightly higher (*ca.* 2%) than the *trans* isomers, this was found for both the homogeneous and heterogeneous catalysts.

Upon reuse the heterogeneous catalyst showed a marked decrease in yield (12.2%), stereoselectivity was virtually unchanged but enantioselectivity decreased even further to give a racemic product.

4.1.9 Catalysis using organically modified mesoporous materials as supports

One of the major problems which affects a supported catalyst is the gradual degradation of catalytic performance usually by poisoning due to build-up of side products. The supported catalysts that we have synthesised have shown a gradual decrease in performance which is characteristic of this phenomenon. If the build-up of side products could be eliminated, reduced or made easy to remove, then the active life span of the catalyst may be increased. Controlling the concentration of reactants present in solution can reduce the amount of some side products, such as the dimerisation product of ethyldiazoacetate. Alternatively modification of the surface of the supporting material will not reduce the

amount of side products produced, but may be able to reduce the rate at which side products build up by minimising possible sites where they may become bound to the supporting material.

The surface of the mesoporous silica support consists of large numbers of silanol groups which may be able to act as sites where either reagents or products may build up. If we modify these groups to be more similar to the non-polar solvent used in catalysis it may reduce the rate of catalyst degradation.

The first surface modified catalyst tried was MCM-48 based where the external surface (rather than the internal surfaces of the pores) had been modified with dichlorodimethyl silane before addition of the catalyst complex. The methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) chloride complex was tethered to the surface using an alkyl halide tether.

The yield obtained with this catalyst was fairly low (13%), the stereoselectivity (63:37 *trans: cis*) was slightly reduced compared with previously synthesised supported methylenebis(4-*S*-phenyl-2-oxazoline) copper chloride catalysts. The enantioselectivity (45.6% ee *trans* isomers) was comparable to the other catalysts.

The yield decreased slowly upon reuse as did the stereoselectivity (Table 4.1.9.1); the enantioselectivity however decreased faster than the equivalent catalysts synthesised without any organic modifications to the supporting materials surface. The enantioselectivity shows a sharp decrease between the second and third use, and although previously we have shown that once the catalyst is activated any prolonged period of storage will result in a loss of selectivity no such period of storage was used for this catalyst.

Catalyst use	Yield %	<i>Trans:Cis</i>	ee <i>cis</i>	ee <i>trans</i>
1	13.0	1.69	40.7	45.6
2	12.5	1.66	37.4	40.5
3	9.9	1.65	29.3	29.5

Table 4.1.9.1: Cyclopropanation of styrene using externally modified MCM-48 supported methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) chloride catalyst

Presumably with this catalyst all of the active sites are located within the internal pore structure of the supporting material (due to the external surfaces being deactivated before catalyst addition). This may partially explain the lower yield, as with previous catalysts some catalytic sites would have been on the external surface of the support and been much less susceptible to diffusion related effects. This also raises the possibility that in previous catalysts the majority of catalytic sites were on the external surfaces (and only a minority within the pores) although the possible diffusion related effects noticed at elevated temperatures (Section 4.1.4) suggest this is unlikely. The faster decrease in selectivity may then be due to the side products building up on the only accessible surfaces available which would be the internal pore surfaces near to where the catalytic sites are located.

The second modified catalyst which was tried again used methylenebis(4-*S*-phenyl-2-oxazoline) but contained the more active copper (II) triflate salt. With this catalyst the modifications were carried out after the addition of the catalyst complex with the aim of deactivating any remaining surface silanol groups using chlorotrimethylsilane.

This catalyst was not very successful, as copper AAS measurements showed that there was almost no metal present in the final product. This catalyst therefore gave very little yield

(*ca.*1.3%) and also showed reduced stereoselectivity and vastly reduced enantioselectivity (60:40 *trans: cis*, 2.2% ee *trans* isomers, 8.3% ee *cis* isomers).

Chapter 5. Conclusions and Future work

5.1 Conclusions

Supported bis(oxazoline) copper (II) catalysts have been successfully synthesised *via* a number of routes and tested in the cyclopropanation reaction between styrene and ethyldiazoacetate. From the methods of binding the catalyst to the surface tested (namely, tethering using iodopropyltrimethoxysilane, hydrogen bonding to the surface and complexation with ([trimethoxysilyl]propyl)ethylenediamine) the most effective (in terms of catalytic results for the cyclopropanation reaction) is the tethering using iodopropyltrimethoxysilane. The synthesis yield for catalysts synthesised by this method however is low compared to some other methods (this will be discussed further in Section 5.2 – Future work). The catalysts gave results which were only slightly worse than found for existing equivalent homogeneous catalysts but are comparable to the best of those reported for bis(oxazoline) catalysts immobilised in layered clays, tethered to silicas or incorporated into polymer matrices.

The other methods of supporting catalysts tested gave the following results, those supported *via* hydrogen bonding gave good yield both for catalyst synthesis as well as in the catalytic reaction, however the selectivity for the catalytic reaction was poor. Catalyst complexes using diamine tethers gave inconclusive results, with one catalyst showing some selectivity and the other producing racemic products. The selectivity found was much lower than that observed for the alkyl halide tethered catalysts.

We have also shown that by using large surface area mesoporous materials a higher loading of catalyst can be tolerated before interaction of individual catalytic sites reduces selectivity compared to catalysts supported on conventional amorphous silica materials.

5.2 Future work

Comparing the amount of research into homogeneous bis(oxazoline) catalyst systems and the relatively few papers on heterogeneous bis(oxazoline) systems it is obvious that there is still much to investigate. Concerning the immobilisation of bis(oxazoline) catalysts upon mesoporous materials, much more research needs to be carried out to improve the synthesis yield, yield and selectivity of catalysts, and to test different metals, bis(oxazoline) ligands, supporting materials, tethers and supporting methods as well as testing more of the catalytic reactions which homogeneous bis(oxazoline) catalysts have been shown to selectively catalyse. Also the exchange of counter ions observed by EXAFS for the copper chloride and zinc iodide generated catalysts needs further investigation to accurately determine the active species. Much of this is explained in greater detail below:

One of the main concerns with the synthesis of the catalysts supported using alkyl halide tethers is the low yield for the reaction to tether the catalyst to the surface, and the subsequent inability (due to the method used) to recover unreacted ligand.

There are many alterations that may be used to try and improve the yield of this reaction. One possible method is to alter the reagents used during the tethering process, we have used a methoxysilane end group for our tethering reaction to react with the silica surface. This is not the most reactive group commonly available, trichlorosilanes are much more reactive and may help to improve the yield of the tethering reaction (although extra care would have to be taken to exclude moisture from the reaction vessel).

A second method would be to alter the conditions used for the tethering process, currently this process is carried out at room temperature in the presence of base. Trimethoxysilane compounds are frequently reacted with silica surfaces under elevated

temperatures such as by refluxing in toluene, this method may prove to increase yield of the reaction. This method may also retain the halide counter ions.

Although we were unable to obtain tethered catalysts using alkyl-chloride tethers it may still be possible to use these tethers by using a more reactive lithium reagent such as *t*-butyl lithium or methyl lithium. This would enable the use of a wider array of commercially available tethers.

Other variations in reagents may also be tried similar to those used by Fraile ⁽¹³⁴⁾ where the silica surface is modified with a tethering group and the ligand is modified with a stable but compatible group. This method has several advantages in that unreacted ligand may be recovered, and that solely mono or di-functionalised ligands may be selectively used, although extra purification stages are required during the synthesis procedure.

As has been mentioned in the previous Chapter [Results and Discussion (Catalysis)] whilst the yield obtained in the catalytic reaction is favourable compared to other heterogeneous catalysts it is low when compared to equivalent homogeneous catalysts. The stereo and enantioselectivities found are also slightly lower than those for equivalent homogeneous systems.

There are several ways in which the selectivity and yield of individual catalysts can be altered, some of which we have briefly investigated. The slow addition of reagents (especially ethyldiazoacetate) would appear to reduce the amount of side products produced and may enable a higher overall yield to be obtained. Likewise increasing the overall temperature of the reaction may also improve the yield but at the expense of selectivity. We have also noticed that decreasing the reaction temperature may increase the selectivity of the catalyst, but this may decrease the rate of reaction.

The best course for maximising the yield and selectivity of the catalytic reaction is (as it has always been) the correct choice of catalyst. For heterogeneous systems this also includes the choice of supporting material and method as well as other effects such as catalyst loading. To further this aim different catalysts need to be tested; a prime example for cyclopropanation reactions is the copper methylenebis(4-*S-t*-butyl-2-oxazoline) catalyst complex which performs well in homogeneous reactions but which we were unable to make work in a heterogeneous system.

We concentrated our research upon a small number of mesoporous silica materials as supports but there still remains a wide variety of unused supporting materials, many of which are described in Chapter 1.2. Many of these supports do not share the same chemical make up as MCM-41 and MCM-48 which we used and so it is fair to assume that they would behave in different ways towards catalyst complexes immobilised within them. There is also a wide array of synthesis procedures for supporting materials that we used, and although we limited these to one synthesis procedure for each material, some of these (especially synthesis of MCM-41 in basic conditions, or even synthesis of organically modified materials) might give rise to different catalytic environments.

Another factor which must be investigated involves altering any remaining surface (after addition of the catalyst) with an inert organic layer (this may reduce the rate of side product build up and therefore prolong the lifespan of the catalyst).

As has been demonstrated in the literature a wide range of bis(oxazoline) ligands can be used with a number of different metals to tailor these catalysts to a number of different catalytic reactions (see Chapter 1.4 for details). In our research we primarily concentrated upon copper complexes (using triflate and chloride salts) using some commercially available

ligands. There are still many catalytic reactions, ligands and metals to test to achieve the maximum potential of these versatile catalysts.

Chapter 6. Experimental

IR spectra were recorded as Nujol mulls for organic solids, KBr disks or self supported wafers for mesoporous materials and thin films for liquids on a Perkin Elmer 1710, a Perkin Elmer series 1600 or a Perkin Elmer Paragon 1000 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a Bruker AC300 or AV300 MHz spectrophotometer and referenced to either internal Me₄Si or CHCl₃. Solid state ¹³C NMR were recorded using a Chemagnetics Infinity CMX300 (75MHz). X-ray spectra were recorded on a Philips powder diffractometer using Cu K α radiation (1.54056Å) or on a Siemens D5005 using Cu K α radiation (1.54056Å), CHN analysis and mass spectra were performed using the departmental service. Diffuse reflectance UV-Vis was recorded using a Unicam 500 series spectrophotometer and Chiral GC were recorded using a CE instruments Trace GC with a 25m*0.25mm β -cyclodextrin coated Al₂O₃/KCl fused silica column using an FID detector. Melting points were taken on an electrothermal melting point apparatus and are uncorrected. Flash column chromatography was performed using Acros Neutral Aluminium oxide (50 – 200 micron). TLC was carried out on 0.25mm precoated silica plates (Whatman PE SIL G/UV, polyester backing) and compounds were visualised using UV fluorescence or iodine.

Pore size and surface area measurements for MCM-41 samples were recorded by Alfonso Garcia at St Andrews University. TEM images were recorded by Liam Worboys at Birmingham University

Cu K-edge and Zn K-edge EXAFS data were collected in fluorescence mode using station 9.2 at the Daresbury Synchrotron Radiation Source using a double crystal Si(220)

monochromator set at 50% harmonic rejection. The data was collected and analysed by Ian Shannon.

Malonic acids were purchased from Lancaster, triethylamine was purchased from Avocado and some amino alcohols were purchased from Acros. Cetyltrimethylammonium bromide was either from Fisons, BDH, or purchased from Acros or Aldrich; all other chemicals were purchased either from Aldrich or Fluka. All reagents are a minimum of 97% pure, most are 99% pure and were used without further purification.

The solvents used were either distilled before use or of Analar quality; dry solvents were taken from continuous stills or distilled over CaH_2 .

6.1 Synthesis of mesoporous materials

Synthesis of MCM-41

Method 1

Sodium silicate solution (18.58 g, *ca.* 83.6 mmol SiO_2) was added to distilled water (40 g, 2.22 mol) in a plastic beaker with stirring. Concentrated H_2SO_4 (1.24 g, 12.6 mmol) was added and stirred for 15 minutes. A solution of cetyltrimethylammonium bromide (CTABr) (16.78 g, 46.0 mmol) in distilled water (50.45 g, 2.80 mol) [prepared in a plastic beaker] was added and stirred for 45 minutes. The product was placed into two sealed polypropylene bottles and heated at 98°C for 7 days. The solid residue was filtered and washed with distilled water until neutral pH was reached. The resulting white solid was then dried in air.

The white solid was calcined by heating under flowing N_2 at 10°C / minute to 550°C . After 1 hour at 550°C the furnace was placed under flowing O_2 and heated for a further 6

hours before cooling to room temperature under flowing O₂. The resulting fine white powder (typical yield *ca.* 3.03 g, 60.4%) was collected and analysed by powder XRD; XRD patterns were compared to published material. $\nu_{\text{max}}/\text{cm}^{-1}$ 3424 (vbr), 1624, 1045 (br), 944, 797, 559. Surface area by nitrogen absorption for 2 different samples was 917.8 m²g⁻¹ and 1391.75 m²g⁻¹ with pore diameters 26.0 Å and 22.8 Å respectively.

This method as been successfully repeated several times.

Method 2

Tetramethylammonium hydroxide (3.3 ml of 25% solution in water, 9.2 mmol) was added to distilled water (45 ml, 2.50 mol) at 30°C with stirring. Cetyltrimethylammonium bromide (6.5577 g, 18.0 mmol) was added and stirred until it was dissolved (*ca.* 2 hours). Fumed silica (4.0029 g, 66.6 mmol) was added slowly and the mixture stirred for 2 hours at room temperature. The mixture was left to stand at room temperature for 20 hours before being placed into 2 teflon lined stainless steel bombs for 67 hours at 150°C. The solid residue was filtered and washed with distilled water until neutral pH was reached. The resulting white solid was then dried in air.

The white solid was calcined by heating under flowing N₂ at 10°C / minute to 550°C. After 1 hour at 550°C the furnace was placed under flowing O₂ and heated for a further 6 hours before being cooled to room temperature under flowing O₂. The resulting fine white powder (2.5772 g, 64.4 %) was collected and analysed by powder XRD. XRD patterns were compared to published data. $\nu_{\text{max}}/\text{cm}^{-1}$ 3430 (vbr), 1633, 1081, (br), 961, 805, 550.

Synthesis of MCM-48

Method 1

Ratio used 1 TEOS (Tetraethylorthosilicate): 0.25 Na₂O: 0.65 CTABr: 62 H₂O

Sodium hydroxide pellets (0.9806 g, 24.5 mmol) were dissolved in distilled water (20 ml, 1.11 mol). A solution of CTABr (11.3770 g, 31.2 mmol) in distilled water (20 ml, 1.11 mol) was added and stirred for 30 minutes. TEOS (10.079 g, 48.4 mmol) was added slowly and the solution stirred for 30 minutes. The product was placed into two sealed polypropylene bottles and heated at 95°C for 4 days. The solid residue was filtered and washed with distilled water until neutral pH was reached. The solid product was then dried in air.

The white solid was calcined by heating under flowing N₂ at 5°C / minute to 550°C. After 1 hour at temperature the furnace was placed under flowing O₂ and heating continued for 6 hours before cooling to room temperature under flowing O₂. The resulting white powder (1.05 g, 36.2%) was analysed by powder XRD and the results compared to published data.

Method 2

Ratio used 1 TEOS: 0.25 Na₂O: 0.65 CTABr: 164 H₂O

Sodium hydroxide pellets (1.05 g, 26.2 mmol) were dissolved in distilled water (150 ml, 8.3 mol). CTABr (11.88 g, 32.6 mmol) was slowly added with stirring and then stirred for 30 minutes. TEOS (11.3 ml, 50.7 mmol) was added slowly and the solution stirred for 1 hour. The product was placed into two sealed polypropylene bottles and heated at 98°C for 4

days. The solid residue was filtered and washed with distilled water until neutral pH was reached. The product was then dried in air.

The white solid was calcined and analysed as in method 1.

The resulting product was a fine white powder (1.56 g, 51.2%)

This synthesis has been successfully repeated several times.

N₂ Adsorption of MCM-48

MCM-48 (0.1596 g) was dehydrated at 350°C under high vacuum for 2 hours, followed by heating at 250°C under high vacuum for a further 16 hours. The solid was then degassed at 350°C under very high vacuum (1.7×10^{-5} bar) for a further 3 hours. The sample was cooled to room temperature and then placed in a constant volume of liquid nitrogen. Measured volumes of gaseous nitrogen were slowly adsorbed and desorbed onto the solid.

Surface area was calculated by estimation of the 'B' point on a BET type 4 isotherm

Surface area (calculated) $1074 \text{ m}^2\text{g}^{-1}$

Pore diameter measured 30.6 \AA

6.2 Addition of tethers to mesoporous solids

Addition of amine tether to MCM-41

MCM-41 (1.0005 g) was dehydrated at 160°C under high vacuum for 1 hour. The solid was placed under argon and suspended in dry diethylether (*ca.* 5 ml) in a dry ice / isopropanol bath. Dichlorodimethylsilane (0.017 ml, 0.14 mmol) was added *via* syringe and stirred for 1 hour. The solvent was removed under vacuum and the residue heated gently (40

- 50°C) for 10 minutes under vacuum. The solid product was placed under argon and suspended in dry diethylether (*ca.* 5 ml) in a dry ice / isopropanol bath. 3-aminopropyltrimethoxysilane (0.6 ml, 3.43 mmol) was added *via* syringe and the mixture stirred for 2 hours in the dry ice bath, 1 hour at room temperature and 1 hour at 40°C. Triethylamine (0.5 ml, 3.5 mmol) was added *via* syringe and the mixture stirred for 2 hours. The solution was filtered under argon and the solid residue washed with several portions of diethylether. Residual diethylether was removed under high vacuum. The product was collected as a fine white powder (1.1095 g). CHN found: C, 8.96; H, 2.04; N, 2.83%. $\nu_{\max}/\text{cm}^{-1}$ 3250 (vbr), 2933, 1615, 1537, 1043 (br), 790, 689, 548. A powder XRD pattern was recorded and compared to previous experiments to ensure retention of structure. Loading of tether calculated from nitrogen analysis 2.02 mmol g⁻¹ (65.3% yield).

Addition of chloro tether to MCM-41

MCM-41 (1.0014 g) was dehydrated at 180°C under high vacuum for 1 hour. The solid was placed under argon and suspended in dry DCM (*ca.* 5 ml) in a dry ice / isopropanol bath. Dichlorodimethylsilane (0.017 ml, 0.14 mmol) was added *via* syringe and stirred for 90 minutes. Trichloro-3-chloropropylsilane (0.6 ml, 3.8 mmol) was added *via* syringe and allowed to warm to room temperature with stirring and stirred for an additional 2 hours. The solution was filtered under argon and the solid residue washed with several portions of diethylether. Residual diethylether was removed under high vacuum. The product was collected as a fine white powder (0.8889 g). CHN found: C, 1.09; H, 0.49; N, 0.0%. $\nu_{\max}/\text{cm}^{-1}$ 3312 (vbr), 1620, 1155 (br), 1007, 807, 580. A powder XRD pattern was recorded and compared to previous experiments to ensure retention of structure.

Loading of tether calculated from carbon analysis 0.23 mmol g^{-1} (5.4% yield).

Complete modification of MCM-41

MCM-41 (0.8290 g) was dehydrated at 160°C under high vacuum for 3 hours. The solid was placed under argon and suspended in dry DCM (*ca.* 5 ml). Dichlorodimethylsilane (0.014 ml, 0.115 mmol) was added *via* syringe and stirred for 1 hour. The suspension was cooled in a dry ice / isopropanol bath and trichloro-3-chloropropylsilane (0.1 ml, 0.63 mmol) was added *via* syringe and stirred for 1 hour before being left to stand overnight at room temperature. The mixture was heated gently for 30 minutes and triethylamine (0.08 ml, 0.56 mmol) added *via* syringe and stirred for 30 minutes. The solvent was removed under vacuum and the residue heated gently. The residue was suspended in dry DCM (*ca.* 5 ml) under argon and chlorotrimethylsilane (1.5 ml, 11.8 mmol) was added *via* syringe and stirred for 5 hours. The suspension was filtered under argon and the resulting solid washed with dry DCM and several portions of diethylether. Residual solvent was removed by gently heating under high vacuum. The product was collected as a fine white powder (1.0414 g). CHN found: C, 9.29; H, 1.84; N, 0.0%. Theoretical maximum loading 0.62 mmol g^{-1} . A powder XRD pattern was recorded and checked against starting material to ensure the retention of the structure.

Addition of diamino tether to MCM-41 (high loading)

MCM-41 (0.6667 g) was dehydrated at 120°C under high vacuum for 8 hours. The solid was placed under argon and suspended in dry diethyl ether (10 ml) in a dry ice / isopropanol bath. N-[3-(Trimethyloxysilyl)propyl]-ethylenediamine (360 μl , 1.89 mmol) was

added and stirred for 1 hour in the bath and 2 hours at room temperature before being left to stand overnight. The mixture was then stirred and heated to 40°C for 2 hours at which time triethylamine (0.3 ml, 2.15 mmol) was added and stirred for 3 hours then left to stand at room temperature overnight. The solid product was filtered off and washed with diethyl ether. Any residual solvent was removed by drying the solid under vacuum to yield a fine white powder (0.8376 g, 77.6 %). CHN found: C, 10.71; H, 3.035; N, 4.215%. $\nu_{\max}/\text{cm}^{-1}$ *ca.* 3300 (vbr O-H), 2938 (C-H), 1634 (br), 1463, 1021 (vbr), 799. δ_{C} (75Mhz solid state) 51.1, 49.3, 40.0, 23.1, 16.9, 9.3. Loading calculated from CHN 1.50 mmol g⁻¹.

Addition of Diamine tether to MCM-41 (low loading)

Mesoporous material MCM-41 (0.4942 g) was treated at 150°C under high vacuum for 3 hours to remove residual water. The dry solid was placed under nitrogen and suspended in dry THF (16 ml) in a dry ice / isopropanol bath. [(Trimethoxysilyl)propyl]ethylenediamine (10 μl , 0.052 mmol) was added and stirred for 1 hour at temperature and 2 hours at room temperature. Triethylamine (0.3 ml, 2.15 mmol) was added and the mixture stirred for 2 hours and left to stand overnight. The solid product was filtered off and washed with THF and dried to give a white powder (0.5458 g) which still contains some THF in the pores. $\nu_{\max}/\text{cm}^{-1}$ 3321 (vbr O-H), 1633, 1463, 1064 (br), 804. Theoretical loading 9.19×10^{-5} mol g⁻¹ or *ca.* 1/20 surface coverage.

6.3 Diamino tether copper complexes

Attempt to make MCM-41 supported oxazoline–Cu-diamine (high loading)

Methylenebis(4-*S*-phenyl-2-oxazoline) (0.0590 g, 0.192 mmol) was added to THF (10 ml). Copper (II) chloride (0.0331 g, 0.246 mmol) was added and the solution stirred until a dark green colour was observed. The solution was added to diamino tether modified MCM-41 (high loading) (0.3858 g, theoretical 0.58 mmol diamine tether) (see Section 6.2) and stirred for 1 hour then left to stand overnight. The mixture was then refluxed for 5 hours and left to stand for 48 hours before the solid was recovered by filtration and washed with THF. The recovered solid was Soxhlet extracted with THF and dried on an oven to give a blue / purple solid (0.4162 g) which still contains some residual THF in the pores. CHN found: C, 12.615; H, 3.0; N, 3.85%. $\lambda_{\text{max}}/\text{nm}$ 592. $\nu_{\text{max}}/\text{cm}^{-1}$ 3247 (vbr OH), *ca.* 2900 (C-H), 1632, 1462, 1090 (vbr), 800, Cu-AAS 0.51 mmol g⁻¹. Yield from Cu analysis 86.3%.

This solid was subsequently identified as copper-bis[(ethylenediamine) propyl-MCM-41].

Confirmation of product from previous experiment

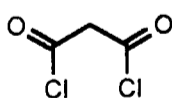
Copper (II) chloride (10.3 mg, 0.076 mmol) was added to THF (5 ml) and stirred for 30 minutes. The solution was added to diamino tether modified MCM-41 (high loading) (0.1414 g, theoretical 0.21 mmol diamine tether) and heated at reflux for 2 hours before being filtered and washed with THF. The resulting solid was Soxhlet extracted with THF and dried under vacuum to yield a blue/purple solid (0.1282 g). $\nu_{\text{max}}/\text{cm}^{-1}$ 2900-3700 (Vbr), 1641, 1464, *ca.* 1090 (vbr), *ca.* 800 (br). Cu-AAS 0.488 mmol g⁻¹. Yield from Cu analysis 82.3%.

Synthesis of MCM-41 diamino tether supported copper methylenebis(4-*S*-phenyl-2-oxazoline)

Diamino tether modified MCM-41 (low loading) (0.0573 g, diamino tether theoretical loading 0.005 mmol) was placed under high vacuum for 2 hours to remove excess moisture from the solid. The dry solid was placed under nitrogen and suspended in dry THF (*ca.* 3 ml). Copper (II) chloride (1.1 mg, 0.008 mmol) was added and the suspension stirred for 45 minutes, a pale green colour was observed. A solution of methylenebis(4-*S*-phenyl-2-oxazoline) in dry THF (146 μ l) was added (solution turns purple). The suspension was stirred and gently heated till the solution turns colourless (*ca.* 2 hours at 40 °C). The solid product was filtered off under positive pressure of N₂ and soxhlet extracted with THF. The solid product was dried under vacuum to yield a pale green / grey powder (0.0375 g). $\lambda_{\text{max}}/\text{nm}$ 670. $\nu_{\text{max}}/\text{cm}^{-1}$ 3341 (vbr O-H), 2986, 2886, 1629, 1464, 1031 (br), 969, 803. Theoretical loading 0.091 mmol g⁻¹.

6.4 Synthesis of bis(oxazolines)

Synthesis of malonyl dichloride

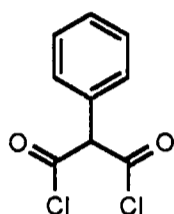


Dry malonic acid (10 g, 96 mmol) was added to thionyl chloride (32 ml, 0.44 mol) and the mixture heated under reflux with a calcium chloride drying tube until no solid malonic acid remained (*ca.* 6 – 8 hours). The excess thionyl chloride was removed by distillation under reduced pressure. The product was then distilled under reduced pressure as a clear (or

yellowy liquid) (*ca.* 3 ml, 32%). bp. 47 - 50°C (*ca.* 19mm/Hg) lit. 57°C (28mm/Hg) $\nu_{\max}/\text{cm}^{-1}$ 2935, 1777, 1387, 1303, 1197, 1028, 972, 803, 624.

This product was used immediately in the synthesis of diamide compounds.

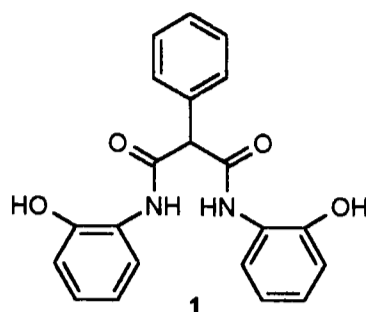
Synthesis of phenylmalonyl dichloride



Dry phenylmalonic acid (6.78 g, 37.6 mmol) was added to thionyl chloride (30 ml, 0.41 mol) and the mixture heated under reflux with a calcium chloride drying tube until no solid phenylmalonic acid remained (*ca.* 7 hours). The excess thionyl chloride was removed by distillation under reduced pressure. The product was then distilled under reduced pressure as a golden oil. (*ca.* 3 ml, 48%). bp. 112°C (*ca.* 19mm/Hg). $\nu_{\max}/\text{cm}^{-1}$ 3062, 2337, 2133, 1750, 1596, 1497, 1450, 1265, 1068, 1001, 751, 692, 645.

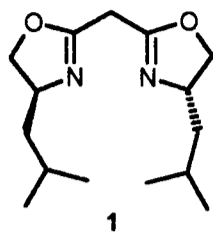
This product was used immediately in the synthesis of diamide compounds.

Synthesis of diamide from phenylmalonyl dichloride and aminophenol



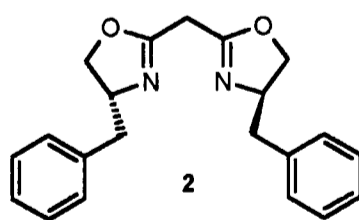
Into a solution of 2-aminophenol (3.2561 g, 29.8 mmol) in dry DCM (*ca.* 30 ml) was added triethylamine (10 ml, 71.7 mmol). The mixture was cooled in an ice bath and placed under flowing nitrogen. Crude phenylmalonyl dichloride (3 ml, 18 mmol) in dry DCM (*ca.* 10 ml) was added slowly *via* a dropping funnel with stirring. The reaction mixture was stirred for 1 hour in the ice bath. It was capped with a calcium chloride drying tube and stirred at room temperature for 12 hours. The reaction was quenched with water and the organic layer washed successively with 30 ml portions of saturated ammonium chloride solution, 5% HCl solution and saturated sodium hydrogen carbonate solution. The solvent was removed to yield a yellow crystalline compound (5.7687 g, 88%). mp. 110°C (from DCM). NMR showed this compound to be impure. This crude compound was dissolved in DCM and washed with 5% HCl solution, the organic layer was cooled (dry ice) and cold filtered. Successive cold filtrations gave cream coloured crystals (3.6101 g, 55%). mp. 174°C (from DCM). $\nu_{\max}/\text{cm}^{-1}$ 3173 (O-H, vbr), 2913 (C-H), 1667 (NC=O), 1596, 1520, 1454, 1376, 1273, 1179, 1103, 746. δ_{H} (300 MHz, CDCl_3) 9.27 (2H, s, NH), 7.54-6.88 (13H, m, ArH), 4.86 (1H, s, PhCH).

Synthesis of 2,2'-methylenebis[4-S-(2-methylpropyl)-2-oxazoline]



To dry xylene (50 ml) was added (S)-leucinol (1 ml, 7.8 mmol) and diethylmalonate (0.55 ml, 3.6 mmol). The mixture was heated under reflux with Dean-Stark apparatus for 3 hours after which a small amount of dichlorodimethyl stannane (*ca.* 0.03g, 0.14 mmol) was added. The mixture was heated under reflux with Dean-Stark apparatus for 64 hours and the mixture was reduced to *ca.* 5 ml. Column chromatography on neutral alumina with ethylacetate - hexane (3:2) as the eluent yielded the product as a colourless oil which gradually turns yellow with time (0.42g, 44%). CHN (found: C, 64.83; H, 11.77; N, 9.36. Calc. for C₁₅H₂₆N₂O₂: C, 67.9; H, 9.5; N, 10.6) $\nu_{\max}/\text{cm}^{-1}$ 2957 (C-H), 1667 (C=N), 1590, 1469, 1387, 1368, 1226, 1172, 985. δ_{H} (300 MHz, CDCl₃) 4.36 (2H, dd, $J = 8.8, 9.3$, CH₂O), 4.16 (2H, m, CHN), 3.85 (2H, t, $J = 7.9$, CH₂O), 3.32, (2H, s, N=CCH₂C=N), 1.75 (2H, m, CHCH₂CH), 1.60 (2H, m, CHCH₂CH), 1.28 (2H, m, CH₃CHCH₃), 0.93 (12H, dd, $J = 4.9, 6.6$, CH₃).

Synthesis of 2,2'-methylenebis[(4R)-4-(phenylmethyl)-2-oxazoline]



To dry xylene (25ml) was added (R)-2-amino-3-phenyl-1-propanol (0.5496 g, 3.6 mmol) and diethylmalonate (0.23 ml, 1.5 mmol). The mixture was heated under reflux with dry molecular sieve in the condenser for 3 hours, but due to solvent build up in the condenser

the experiment was cooled down. The molecular sieve was placed in a soxhlet extractor and the mixture heated under reflux for 90 minutes. Dichlorodimethylsilane (*ca.* 0.03g, 0.14 mmol) was added and the mixture refluxed for 40 hours, and left at room temperature for 96 hours. The solvent was reduced to *ca.* 3 ml, column chromatography on neutral alumina with ethylacetate - hexane (3:2) as the eluent yielded the product as a light yellow oil (0.1175 g, 23.4%). $\nu_{\max}/\text{cm}^{-1}$ 3292 (O-H), 3025, 2918 (C-H), 1659 (C=N), 1582, 1495, 1455, 1359, 1236, 1170, 1031, 981, 743, 696. δ_{H} (300 MHz, CDCl_3) 7.32 – 7.19 (10H, m, ArH), 4.39 (2H, m, CHN), 4.24 (2H, t, $J = 8.5$ CH_2O), 4.02 (2H, t, $J = 8.2$, CH_2O), 3.32 (2H, s, $\text{N}=\text{CCH}_2\text{C}=\text{N}$), 3.13 (2H, dd, $J = 4.9, 13.6$, PhCH_2), 2.69 (2H, dd, $J = 8.9, 13.7$, PhCH_2), 1.60 (10H, s, H_2O).

6.5 Addition of alkyl halide tethers to bis(oxazoline) ligands

Attempt to react methylenebis(4-*S*-phenyl-2-oxazoline) to chloro tether completely modified MCM-41

To a solution of methylenebis(4-*S*-phenyl-2-oxazoline) (31.6 mg, 0.1 mmol) in THF (*ca.* 1.5 ml) under argon in a dry ice / isopropanol bath butyl lithium (0.05 ml of 2.21 M solution, 0.11 mmol) was added and left to stand for 10 minutes. The solution was added to a suspension of completely modified MCM-41 (0.2548 g) in dry THF under argon in a dry ice / isopropanol bath. The mixture was stirred at in the bath for 30 minutes and at room temperature overnight. The residue was soxhlet extracted with dry THF and the residual solvent removed under vacuum. A white power was recovered (*ca.* 0.2g) CHN found: C, 12.09; H, 1.84; N, 0.0%. $\nu_{\max}/\text{cm}^{-1}$ 3425 (vbr), 2958, 1623, 1068 (br), 945, 846, 795, 553.

Powder XRD pattern was recorded and compared to the previous experiment to check the stability of the structure.

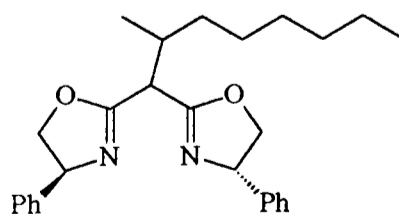
This experiment was unsuccessful.

Alkyl halide test reactions

Modification of methylenebis(4-*S*-phenyl-2-oxazoline) with chlorooctane and TMEDA

Methylenebis(4-*S*-phenyl-2-oxazoline) (70.3 mg, 0.23 mmol) was dissolved in dry THF (9 ml) under a nitrogen atmosphere. The solution was cooled in a dry ice / isopropanol bath and *N*-butyl lithium (92 μ l of a 2.5 mol solution, 0.23 mmol) and TMEDA (32.5 μ l, 0.215 mmol) was added and stirred for 1 hour in the bath and 30 minutes at room temperature. The solution was placed back into the bath and 2-chlorooctane (39 μ l, 0.23 mmol) was added and stirred for 1 hour then allowed to warm to room temperature and left to stand over night. The solvent was removed *in vacuo* and the products passed through a short column (neutral alumina, ethyl acetate: hexane 3:2). The first fraction off the column was obtained as a colourless liquid (11.6 mg) which rapidly turned red/brown in colour, this was analysed by NMR and was shown to be impure. The product was identified as unreacted methylenebis(4-*S*-phenyl-2-oxazoline). The product was not purified or analysed further.

Modification of methylenebis(4-*S*-phenyl-2-oxazoline) with bromooctane and TMEDA



Methylenebis(4-*S*-phenyl-2-oxazoline) (0.0507 g, 0.165 mmol) was dissolved in dry THF (*ca.* 9 ml) under a nitrogen atmosphere. The solution was cooled in a dry ice /

isopropanol bath and N-butyl lithium (66 μl of a 2.5 mol solution, 0.165 mmol) and TMEDA (25 μl , 0.165 mmol) was added and stirred for 1 hour in the bath and 30 minutes at room temperature. The solution was placed back into the bath and 2-bromooctane (29 μl , 0.16 mmol) was added and stirred for 1 hour and allowed to warm to room temperature and left to stand overnight. The solvent was removed *in vacuo* and purified by column chromatography (neutral alumina, ethyl acetate : hexane, 50:50). The first fraction was recovered as an orange oil (6.6 mg, 9.5%) $\nu_{\text{max}}/\text{cm}^{-1}$ 3306 (O-H), 2956, 2926, 2855, 1659, 1493, 1454, 1356, 989, 756, 699, NMR subsequently showed the product to be impure. This was identified as the monomodified product. The product was not purified or analysed further.

Modification of methylenebis(4-*S*-phenyl-2-oxazoline) with iodobutane

A solution of methylenebis(4-*S*-phenyl-2-oxazoline) (97.6 mg, 0.319 mmol) in dry THF (15 ml) in a nitrogen atmosphere was placed into a dry ice / isopropanol bath. N-butyl lithium (127 μl of 2.5 mol solution, 0.318 mmol) and N,N,N',N'-tetramethylene ethylene (48 μl , 0.32 mmol) was added and the solution stirred for 1 hour. 1-iodobutane (59 μl , 0.518 mmol) was added and the solution was allowed to warm to room temperature and left to stand for 2 days after which the solution was a pale yellow colour. The solution was purified by chromatography (neutral alumina, ethyl acetate / hexane 3:2) to give a pale orange / golden oil (34.9 mg) NMR analysis showed this to be comprised of the mono and the di-butyl derivatives in a ratio of *ca.* 2:1, further purification and analysis were not undertaken.

Immobilisation of methylenebis(4-*S*-phenyl-2-oxazoline) on MCM-41 *via* iodopropyl tether

Methylenebis(4-*S*-phenyl-2-oxazoline) (0.1269 g, 0.41 mmol) was dissolved in dry THF (6 ml) under a nitrogen atmosphere. The solution was cooled in a dry ice / isopropanol bath and *n*-butyl lithium was added (0.412 ml of a 2.5 mol solution, 1.0 mmol) and stirred for 30 minutes. Iodopropyltrimethoxysilane (0.240 ml, 0.84 mmol) was added and stirred for 6 days until a deep red colour had evolved.

MCM-41 (0.2079 g) was heated at 145°C under vacuum for 4 hours to remove residual moisture and suspended in dry THF (8 ml) under a nitrogen atmosphere. The oxazoline solution and triethylamine (0.5 ml, 3.5 mmol) were added and stirred overnight after which time more triethylamine (0.5 ml, 3.5 mmol) was added and stirred for 2 hours. The solid product was recovered by filtration under positive pressure of nitrogen. This was soxhlet extracted with THF for 16 hours and dried under high vacuum to give a white solid (0.2467 g). CHN found: C, 12.4; H, 2.47; N, 0.57%. $\nu_{\max}/\text{cm}^{-1}$ 3400(vbr), 1660, 1560, 1470, 1060 (br), 800. δ_{C} (75mhz solid state) 169.5 (C 2,2'), 142.5 (aromatic C + side band), 128.1 (br, aromatic C), 113.3 (side band), 75.0 (C 5,5'), 67.8 (C 4,4,'), 46.8, 27.3, 25.3, 19.3 (br), 13.7 (br), 8.0 (br). Loading calculated from CHN (nitrogen analysis) 0.20 mmol g⁻¹.

6.6 Immobilisation of copper bis(oxazoline) complexes on mesoporous supports

Immobilisation *via* hydrogen bonding of methylenebis(4-*S*-phenyl-2-oxazoline) copper (II) triflate complex on MCM-41

MCM-41 (0.3481 g) was dehydrated at 140°C under high vacuum for 2.5 hours then placed under nitrogen in DCM (10 ml).

A solution of methylenebis(4-*S*-phenyl-2-oxazoline) (21.5 mg, 0.07 mmol) in DCM (10 ml) was added to copper (II) triflate (26.9 mg, 0.074 mmol) and stirred for 1 hour. The solution was added to the MCM suspension and stirred for 10 minutes then left to stand overnight. The solid product was filtered off under nitrogen and soxhlet extracted with DCM for 8 hours. The recovered solid was dried under vacuum to yield a pale green powder (0.3641g, 77.4%). CHN found: C, 4.86; H, 0.905; N, 0.43%; $\nu_{\max}/\text{cm}^{-1}$ 3367.1 (vbr, OH surface and H₂O), 1633 (br), 1076 (vbr), 932, 799, 700, 643, 575; AAS (Cu) 0.156 mmol/g. Loading from CHN 0.153 mmol g⁻¹.

Immobilisation *via* iodopropyl tether of methylenebis(4-*S*-phenyl-2-oxazoline) copper complex

A solution of methylenebis(4-*S*-phenyl-2-oxazoline) (111.3 mg, 0.36 mmol) in dry THF (10 ml) under a nitrogen atmosphere was placed in a dry ice / isopropanol bath. To this solution N-butyl lithium (170 μl of a 2.5 mol solution, 0.425 mmol) was added and stirred for 1 hour in the bath and 5 minutes at room temperature. The solution was placed back into the cold bath and 3-iodopropyltrimethoxysilane (210 μl , 0.74 mmol) was added and gradually warmed to room temperature and stirred for 6 days till the solution was a deep red colour.

Copper (II) chloride (24.7 mg, 0.18 mmol) was added and stirred for 2 days. The solution was split into 2 portions and added to 2 separate mesoporous materials as detailed below:

1) To a suspension of MCM-41 (0.5863 g) in 15 ml of THF a portion of the oxazoline solution (5 ml) was added and stirred for 15 minutes. Triethylamine (0.5 ml, 3.6 mmol) was added and stirred for 30 minutes then left to stand for 16 hours after which time more triethylamine (0.6 ml, 4.3 mmol) was added and stirred for 30 minutes. The solid product was filtered under positive nitrogen and soxhlet extracted with THF for a total of 24 hours. The solid product was collected as a pale green powder (0.7503 g, solvent still present). Subsequent XRD analysis showed that the mesoporous structure of this material had collapsed. AAS (Cu) 0.0379 mmol g⁻¹. λ_{max} /nm 690. Yield from Cu analysis 12 %.

2) To a suspension of MCM-48 (0.4878 g) in 15 ml of THF a portion of the oxazoline solution (2.6 ml) was added and stirred for 15 minutes. Triethylamine (0.5 ml, 3.6 mmol) was added and the suspension stirred for 30 minutes and left to stand for 16 hours after which time more triethylamine (0.6 ml, 4.3 mmol) was added and stirred for 30 minutes. The solid product was filtered under positive nitrogen and soxhlet extracted with THF for a total of 24 hours. The solid product was collected as a pale green powder (0.5598 g, solvent still present). XRD analysis showed the retention of the mesoporous structure. AAS (Cu) 0.0212 mmol/g. Yield from Cu analysis 9.7 %.

This method has been repeated for different supporting materials, oxazoline ligands and copper salts.

Immobilisation *via* iodo tether of methylenebis(4-*S-t*-butyl-2-oxazoline) copper (II) triflate complex on MCM-41

A solution of methylenebis(4-*S-t*-butyl-2-oxazoline) (21.1 mg, 0.079 mmol) in dry THF (5 ml) in a nitrogen atmosphere was placed into a dry ice / isopropanol bath. *N*-butyl lithium (80 μ l of a 2.5 mol solution, 0.20 mmol) was added and the solution stirred for 30 minutes in the bath and 5 minutes at room temperature. The solution was replaced in the bath and 3-iodopropyltrimethoxysilane (34 μ l, 0.17 mmol) was added and the solution allowed to warm to room temperature and stirred for 8 days till a red colour had developed. Copper (II) triflate (29.7 mg, 0.082 mmol) was then added and the solution stirred for 24 hours.

A suspension of MCM-41 (0.4175 g) in dry THF (15 ml) in a nitrogen atmosphere was created and the oxazoline solution added and stirred for 1 hour. Triethylamine (0.5 ml) was added and the solution stirred overnight after which a further portion of triethylamine (0.5 ml) was added and the solution stirred for 2 hours. The solid product was removed by filtration under positive nitrogen and washed with THF. The solid was then soxhlet extracted with THF for 20 hours and dried under vacuum to yield a pale green powder (0.4382 g, 27.8 %). AAS (Cu) 0.0503 mmol g⁻¹.

Synthesis of supported complex of Methylenebis(4-*S*-phenyl-2-oxazoline) Copper (II) chloride on externally deactivated MCM-48

A solution of methylenebis(4-*S*-phenyl-2-oxazoline) (54.9 mg, 0.18 mmol) in dry THF (5 ml) under a nitrogen atmosphere was placed into an ice bath. To this solution *n*-butyl lithium (179 μ l of a 2.5 mol solution, 0.45 mmol) was added and stirred for 45 minutes. 3-

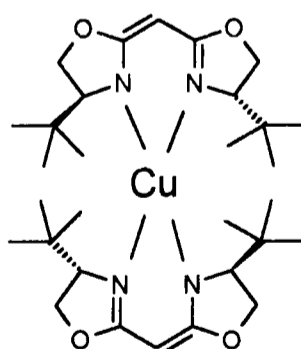
iodopropyltrimethoxysilane (104 μl , 0.53 mmol) was added and stirred at room temperature till the solution was a deep red colour (11 days). Copper (II) chloride (11.9 mg, 0.09 mmol) was added along with a small amount of dry THF (2 ml) and stirred for 24 hours.

MCM-48 (0.7330 g) was heated at 140°C under vacuum for 3 hours to remove residual water then suspended in dry DCM (15 ml) in a nitrogen atmosphere. The suspension was placed into an ice bath and dichlorodimethylsilane (12.5 μl , 0.1 mmol) added and stirred for 1 hour. The solid product was filtered off under positive pressure of nitrogen and washed with THF and dried under vacuum.

This solid product was suspended in dry THF (15 ml) in an inert atmosphere and the oxazoline solution added and stirred for 5 minutes. After this time triethylamine (0.5 ml) was added and the solution stirred for 15 minutes the left to stand overnight. The solid product was filtered off washed with THF, soxhlet extracted with THF and dried under vacuum to yield a very pale green powder (0.8421 g). $\nu_{\text{max}}/\text{cm}^{-1}$ 3431 (br), 1644 (br), 1086 (vbr), 805.

6.7 Synthesis of homogeneous bis(oxazoline) copper complexes

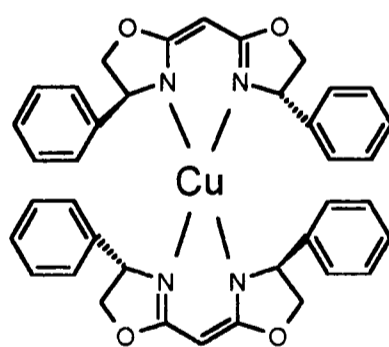
Synthesis of di-methylenebis(4-*S-t*-butyl-2-oxazoline) copper II complex



A solution of methylenebis(4-*S-t*-butyl-2-oxazoline) (19.4 mg, 0.073 mmol) under a nitrogen atmosphere in dry THF (5 ml) was placed in a dry ice / isopropanol bath. To this

solution n-butyl lithium (31 μl of a 2.5 mol solution, 0.0775 mmol) was added and stirred for 30 minutes in the bath and 5 minutes at room temperature. Copper (II) chloride (4.8 mg, 0.036 mmol) was added and the resulting purple solution stirred for 19 hours. The solution was reduced to *ca.* 1 ml and purified by chromatography (neutral alumina, ethyl acetate: Hexane; 3:2) to yield a purple solid (18.8 mg, 87.8 %). The purple solid was then recrystallised from cyclohexane to yield purple crystals (3.9 mg, 18.2 %) The residue was also initially purple in colour but decomposed to a brown solid (11.4 mg) before further crystals could be recovered. CHN calc: C, 60.63; H, 8.48; N, 9.43%, found: C, 60.54; H, 8.41; N, 9.55%. mp (cyclohexane) 216°C decomposes. Lit 225°C (dec) ⁽⁹¹⁾. $\nu_{\text{max}}/\text{cm}^{-1}$ 3435 (br), 2957, 1595, 1545, 1480, 1364, 1309, 1226, 1208, 1194, 1153, 1086, 1060, 1024, 996, 745, 654.

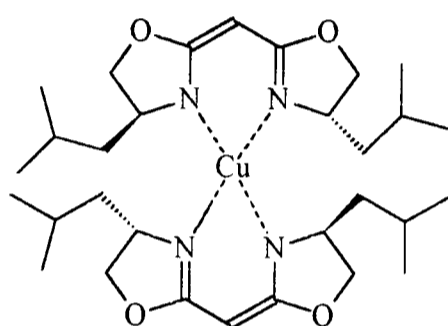
Synthesis of di-methylenebis(4-S-phenyl-2-oxazoline) copper (II) complex



A solution of methylenebis(4-S-phenyl-2-oxazoline) (89.6 mg, 0.29 mmol) in dry THF (10 ml) in a nitrogen atmosphere was placed into a dry ice / isopropanol bath. N-butyl lithium (120 μl of a 2.5 mol solution, 0.3 mmol) was added and stirred for 30 minutes in the bath and 30 minutes at room temperature. Copper (II) chloride (19.6 mg, 0.14 mmol) was added and the purple solution stirred for 24 hours. The solution was reduced to *ca.* 1 ml and purified by

chromatography (neutral alumina, ethyl acetate:hexane 3:2). The solid product was recrystallised from cyclohexane to give the product as purple crystals (46.2 mg, 48.9 %). CHN calc: C, 67.69; H, 5.08; N, 8.31%, found: C, 67.21; H, 4.86; N, 8.49%. $\lambda_{\text{max}}/\text{nm}$ 549. Mp 148°C (decomposes) $\nu_{\text{max}}/\text{cm}^{-1}$ 3027-2848 (m), 1600, 1538, 1446, 1376, 1351, 1311, 1267, 1226, 1214, 1149, 1057, 1040, 743, 698.

Synthesis of di-methylenebis(4-*S-iso*-propyl-2-oxazoline) Copper (II) complex



Methylenebis(4-*S-iso*-propyl-2-oxazoline) (8.2 mg, 0.034 mmol) was dissolved in dry THF (5 ml) under a nitrogen atmosphere. The solution was placed into an ice bath and *n*-BuLi (15 μl of a 2.5 mol solution, 0.0375 mmol) was added and the solution stirred for 30 minutes. The solution was allowed to warm to room temperature and Copper (II) Chloride (2.0 mg, 0.015 mmol) was added and the resulting purple solution stirred for 30 minutes. The solvent was removed and the product purified by chromatography (short silica column, ethyl acetate: hexane 3:2). An attempt made to recrystallise the product from cyclohexane was unsuccessful. $\nu_{\text{max}}/\text{cm}^{-1}$ 3369 (br), 2958, 1667, 1602, 1532, 1469, 1367, 1260, 1066, 1018, 801. This compound was used directly for catalysis reactions.

6.8 Cyclopropanation reactions

Heterogeneous catalysis of Styrene with ethyldiazoacetate

(general procedure)

Supported catalyst (ca 50 mg, *ca.* 0.002 mmol) was suspended in dichloroethane (2ml) under a nitrogen atmosphere. Styrene (343 μ l, 3 mmol) and phenyl hydrazine (50 μ l of a 1% solution) was added and stirred for 5 minutes. Ethyldiazoacetate (105 μ l, 1 mmol) was added and diethyladipate (10 μ l, 0.054 mmol) added as an internal standard. The reaction was stirred for 40 hours after which the catalyst was filtered off and washed with DCM.

The solvent was removed and the crude product analysed by chiral GC as a solution in DCM (1ml). Peaks observed were characterised by retention of known samples, comparison to literature data and by GC-MS; retention time (minutes). 11.99; styrene, 27.18 + 27.45; *cis/trans* 2-butenedioic acid diethyl ester, 36.07; diethyladipate (internal standard), 38.79; (S,R) ethyl 2-phenylcyclopropane-1-carboxylate, 39.31; (R,S) ethyl 2-phenylcyclopropane-1-carboxylate, 40.00; (R,R) ethyl 2-phenylcyclopropane-1-carboxylate, 40.31; (S,S) ethyl 2-phenylcyclopropane-1-carboxylate.

The product was purified on silica (hexane : ethyl acetate, 15 : 1) and a second GC recorded as a solution in DCM (1ml). $\nu_{\max}/\text{cm}^{-1}$ 3436 (br), 2928, 2360, 1726, 1606, 1460, 1411, 1337, 1323, 1186, 1042, 1018, 854, 755, 697. δ_{H} (300 mhz, CDCl_3) *trans* isomers 7.31 – 7.09 (5H, m, aromatic H), 4.18 (2H, q, $J = 7.1$, CH_2CH_3), 2.52 (1H, m, CHCO_2Et), 1.90 (1H, m, CHPh), 1.59 (1H, m, CHCH_2CH), 1.28 (4H, t, $J = 7.1$, CH_2CH_3 , CHCH_2CH). *cis* isomers 7.31-7.09 (5H, m, aromatic H), 3.88 (2H, q, $J 7.1$, CH_2CH_3), 2.58 (2H, dt, $J 7.8 + 8.8$, CHCH_2CH), 2.07 (1H, m, CHCO_2Et), 1.73 (1H, m, CHPh), 0.97 (3H, t, $J = 7.1$, CH_2CH_3). m/z 190.

Homogeneous catalysis of styrene with ethyldiazoacetate

(general procedure)

Catalyst complex (*ca.* 6.9 mg, 0.01 mmol) was dissolved in dichloroethane (2ml) under a nitrogen atmosphere. Styrene (343 μ l, 3 mmol) and phenylhydrazine (50 μ l of a 1% solution) was added and stirred for 5 minutes. Ethyldiazoacetate (105 μ l, 1 mmol) was added and diethyladipate (10 μ l, 0.054 mmol) was added as an internal standard, the reaction was then stirred for either 17 or 39 hours. After the allotted time the solvent was removed *in vacuo* and the crude product analysed by chiral GC as a solution in DCM (1 ml). The product was purified on silica (hexane : ethylacetate 15 : 1) and a second GC recorded as a solution in DCM (1 ml). GC results were compared to known samples, literature values and to GC-MS data.

Slow rate addition catalysis of styrene with ethyldiazoacetate

Catalyst (*ca.* 50 mg for heterogeneous, *ca.* 6 mg for homogeneous, 0.002 – 0.01 mmol) were suspended in DCE (3 ml) under a nitrogen atmosphere. Styrene (343 μ l, 3 mmol) and phenylhydrazine (50 μ l of a 1% solution) was added and stirred for 5 minutes. Ethyldiazoacetate (105 μ l, 1 mmol) was dissolved in DCE (2 ml) and added using a syringe pump at either 0.127 ml/h or 0.0508 ml/h (over 16 or 40 hours). The reactions were then allowed to stir for an additional 8 hours. The heterogeneous catalysts were recovered by filtration and the solvent removed *in vacuo*. Diethyladipate (10 μ l, 0.054 mmol) was added as an internal standard and the crude sample analysed by GC as a solution in DCM (1 ml). The product was purified on silica (hexane : ethylacetate 15 : 1) and a second GC recorded as a solution in DCM (1ml). GC results were compared to known samples, literature values and to GC-MS data.

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