Development of new catalytic preparative gas-phase processes.

by

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Lecture Courses

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Organic Research Seminars and Colloquia - Edinburgh University Chemistry Department (3 years attendance).

Current Awareness in Organic Chemistry - Edinburgh University Chemistry Department (5 lectures, 3 years attendance).

Postgraduate Lectures in Nuclear Magnetic Resonance Spectroscopy - Edinburgh University Chemistry Department (10 lectures).

Case Studies in Industrial Chemistry - Zeneca (8 lectures).

Synthons in Organic Synthesis - Prof. E. Vilsmaier, (5 lectures)

Safety Awareness Course – Merck (3 lectures).

Medicinal Chemistry - Merck, Sharp and Dohme (5 lectures, 3 years attendance)

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Abstract

This thesis has endeavoured to apply the use of solid catalysts to Flash Vacuum Pyrolysis (FVP) and Flow Pyrolysis in order to develop preparative scale processes for specific transformations.

The development of a dehydration protocol for the transformation of amides to the corresponding nitriles has been successfully achieved. This involves the use of commercially available molecular sieves under FVP conditions. The conditions have been optimised and extended to the analogous dehydration of oximes and utilised in the preparation of a number of aromatic, aliphatic and heteroaromatic nitriles in generally excellent yields of 59-99%. The role of the molecular sieves in the process has been extensively investigated in working towards truly catalytic conditions.

Molybdenum oxide based catalysts have been applied to the dehydrogenation-aromatisation of polycyclic hydroaromatic compounds under FVP conditions. Again, after optimisation, the conditions have been applied to the preparation of a number of aromatic and heteroaromatic compounds. The mechanistic nature of the reaction has been investigated, particularly with regard to the possible presence of free radical intermediates. This would not appear to be the major reaction pathway since elimination of side-groups from appropriately substituted substrates occurs only to very small extent.

The so-called "anthranilate rearrangement" of 2-nitrotoluene to anthranilic acid has been investigated. Several stages of the mechanism of this process in the gas-phase have been elucidated using both Flash Vacuum Pyrolysis and Flow

Pyrolysis. Various flow pyrolytic conditions have been developed in an attempt to identify the problem steps of this reaction and to work towards a preparatively useful process. Solid catalysts such as porcelain and molecular sieves have been used to mediate this, with limited success.

Contents

Introduction

1. Catalytic gas phase reactions.

Chemical reactions mediated by heat alone are of the earliest and most simple processes. Over the years, gas phase chemistry has developed both in terms of refining syntheses and of the equipment and apparatus used. Flash vacuum pyrolysis and flow pyrolysis, described later, are now well defined laboratory techniques, easily reproducible.

Catalysis has likewise been extremely important in the development of chemistry, particularly industrially. The efficiency and environmental benefits that catalytic processes bring offer attractive advantages to both lab and plant scale chemistry.

However, the use of catalysts in gas-phase organic chemistry for the synthesis of fine chemicals has been largely overlooked, especially since around the 1960's, when Elvidge and Sammes[1] commented "*Where applicable, the vapour phase catalytic method is undoubtedly superior to the more conventional laboratory procedures.*" This observation, however, was not followed by a mass investigation of these methods: rather, catalytic gas-phase synthesis seemed to fall out of favour. Very early reviews on general gas-phase organic chemistry such as Hurd's[2] give some examples of this kind of work although there tends to be no real systematic approach to these observations. This chapter will collect together the important uses of solid catalysts in the gas-phase synthesis of organic fine-chemicals, while highlighting the important advantages and showing the place of such methods in the armoury of the synthetic organic chemist.

Firstly, a brief background will be provided on pyrolysis systems. These can be broadly divided into two main types: flow pyrolysis and flash vacuum pyrolysis (FVP) and the important differences between the two will be highlighted. Secondly, the scope of this literature review will be defined before finally presenting the work itself.

1.1 Flow pyrolysis

Flow pyrolysis is the earliest used and on appearance the simplest form of controlled gas-phase chemistry. In the most basic terms the system consists of a heated tube through which a substrate is delivered. A more detailed inspection of the method however reveals a vast array of variables which must be considered before undertaking a flow pyrolysis experiment. Although the apparatus used varies considerably throughout the work detailed, the skeleton of the system will be presented here and specifics highlighted when appropriate.

A black box schematic of the flow pyrolysis apparatus is shown in figure 1.

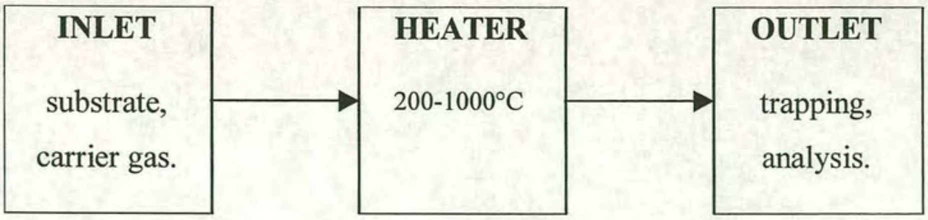


Figure 1

Inlet.

The inlet system consists of some apparatus capable of addition of the substrate at a controlled rate. This could be simply a dropping funnel or perhaps a syringe/syringe pump setup. The rate used must be optimised for any specific process but feed rates of up to tens of grams per hour can be used in some cases. In most experiments there is also a controlled flow of a carrier gas, generally inert (and usually nitrogen) but occasionally reactive.

Heater.

The heated area of the apparatus is generally a tube, most often held vertically and externally heated. In the older literature, the heating was commonly achieved by winding the tube with resistance wire and insulating with asbestos but modern tube furnaces are used more frequently in recent times. The tube itself can be made of any inert material resistant to the temperature of the study but quartz, pyrex, iron, copper and stainless steel are all relatively common. Inert packing materials as discussed later are often used as a means of increasing the efficiency of heat transfer from the apparatus to the substrate.

The other variable to be considered here is the tube dimensions. Reaction tubes are usually at least 20 cm in length and 1 cm in diameter and can range up to sizes of over a metre in length to 3 cm in diameter. Longer tubes are often used to provide space at the top for a "pre-heater" which has the sole purpose of vaporising the substrate.

In a catalytic experiment the tube will be packed with the catalyst, usually in coarsely granular or pelleted form, for some distance of its total length. The placement of the catalyst within the reaction tube is another important variable in these experiments.

Reaction temperatures vary around an average of 500-600 °C although catalysed reactions are often carried out at much lower temperature.

Outlet.

The trapping of condensable products is usually achieved using cooled traps, depending on the nature of the products and the carrier gas. Gaseous products are sometimes passed directly into a gas chromatograph for analysis. The trapping of products from flow pyrolytic experiments is a non-trivial exercise and many different cooling strategies have been employed, from simple water condensers to liquid air cooled traps.

1.2 Flash Vacuum Pyrolysis (FVP)

For flash vacuum pyrolysis, again the simple flow diagram shown in figure 1 applies. There are fewer variables to consider in these experiments when compared with flow pyrolysis and the apparatus used can be more specifically described by figure 2.

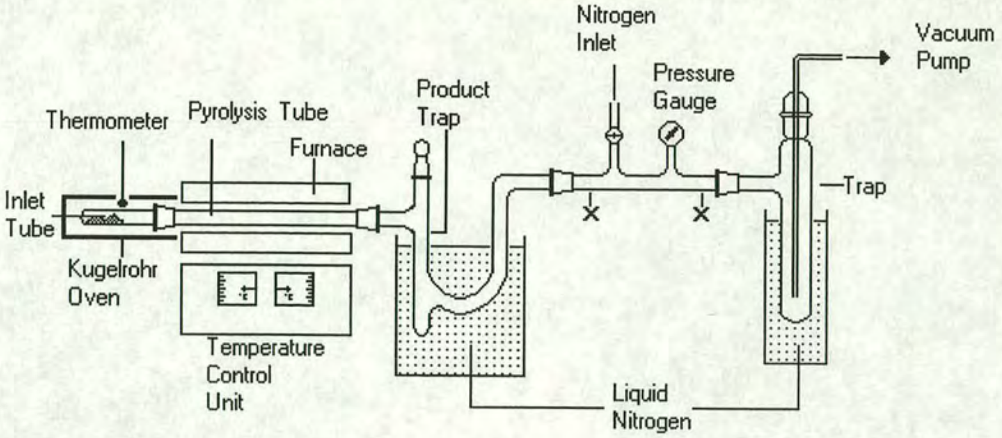


Figure 2

The compound to be subjected to FVP is placed in the inlet tube and heated to vaporisation under a vacuum of typically 10^{-2}-10^{-3} Torr. The substrate then enters the furnace tube (generally made from quartz) where the chemistry takes place. The tube is held in a furnace and heated to temperatures as high as 1100 °C but most usefully in the region of 300-750 °C. In a catalytic experiment, this tube would be packed in some region, around the centre, with a solid catalyst. The contact time of an FVP experiment *through an empty tube* is generally of the order of milliseconds: obviously the use of a solid catalyst, especially in finely granular form, will increase this somewhat. As a result of this short contact time, substrates are forced to undergo unimolecular processes, unlike flow pyrolysis where the use of atmospheric pressure means that bimolecular reactions can sometimes predominate.

Products formed are trapped using a cooling system of generally liquid nitrogen but sometimes dry-ice/acetone.

The scale of these experiments using the apparatus shown is limited only by the dimensions of the inlet and trapping systems. The throughput rate however is dependent upon the volatility of the substrate and the dimensions of the furnace tube but a rate of about 1-2 g h^{-1} is typical.

1.3 Scope of review

This introduction to pyrolytic methods using solid catalysts will deal only with methods of synthetic use in the preparation of fine organic chemicals. It will not include the heavy industrial applications such as the cracking of natural gas or polymerisation of olefins to petroleum[1] and others, many of which are reviewed by Hurd.[2] Furthermore, it will not deal with high-pressure systems such as those carried out in sealed tubes: only methods involving pressures of atmospheric level or below will be considered.

The review will try to deal with situations where any chemical transformation has been carried out solely under the influence of heat and the catalyst. Thus, flow pyrolysis reactions involving the use of a reactive carrier gas will not be reviewed here.

A varied chemistry can take place under catalytic gas-phase conditions. Eliminations are common, especially dehydrogenations and dehydrations. Rearrangements are also represented, as are bimolecular combinations such as alkylations. The nature of the catalysts used is equally diverse. Metal oxides, especially alumina are often used, as are zeolites and even noble metals such as platinum.

A differentiation must also be made between the three areas in which solid packings are used in gas-phase experiments in order to avoid confusion. Firstly, many pyrolytic processes involve the use of an inert substance such as porcelain, pumice and quartz wool, chips or tubes to provide a surface area within the furnace tube which aids heat transfer. The net result of this is an increase in the contact time, an increase, therefore, in the effective reaction temperature of the experiment. To the experimental chemist, this simply means that a lower furnace temperature can be used than normal. Such processes are disregarded for the purposes of this introduction unless some evidence for partial catalysis exists, for example, a change in selectivity.

Secondly, processes utilising a solid *reagent* – "Vacuum Gas-Solid Reactions" (VGSR) will be overlooked here. These methods, where a solid reagent packed into a furnace tube is effectively used up and transformed into something else during reaction, have been reviewed elsewhere.[3]

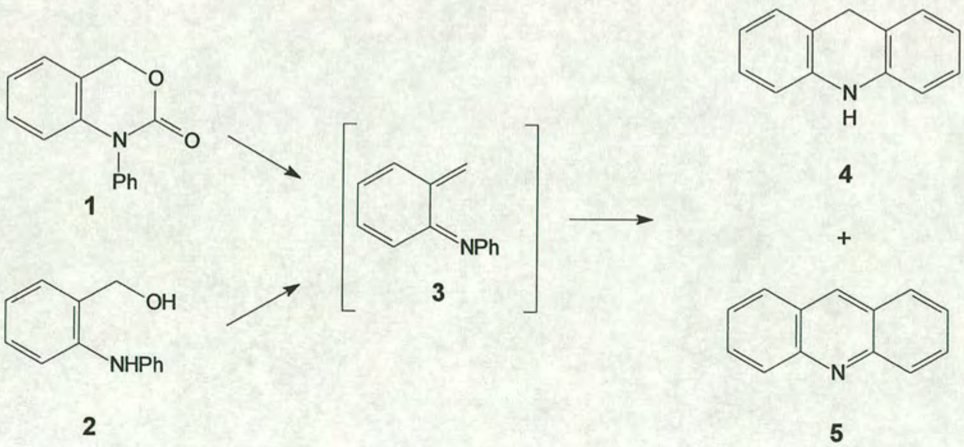
The final category, and the one with which this review shall deal, is that of a solid catalyst. This will be defined as a material which, when used in a pyrolytic system, effects a transformation not normally observed under uncatalysed gas-phase conditions. Obviously the distinctions between these three categories are blurred and in many cases, especially in the older literature, it is unclear whether a process is truly catalytic or not. Some of these grey areas will be dealt with here in an attempt to clarify the picture somewhat. Also, in many cases where a synthetic process has been found to be successful, very little interest has been attached to the nature of the solid catalyst/reagent/contact-mass used and it remains unclear to which category the experiment should belong. Again, these situations will be included.

2. Solid catalysed pyrolysis reactions

2.1 Dehydration

This section will discuss reports of catalytic dehydrations in the gas phase. Alumina is the most commonly used catalyst in these reactions, although the use of silica and zeolites is discussed also.

The use of solid catalysis under FVP conditions has been used to lower the reaction temperature and alter the reaction selectivity in the preparation of products arising from azaxylylenes such as **3**, scheme 1.[4]

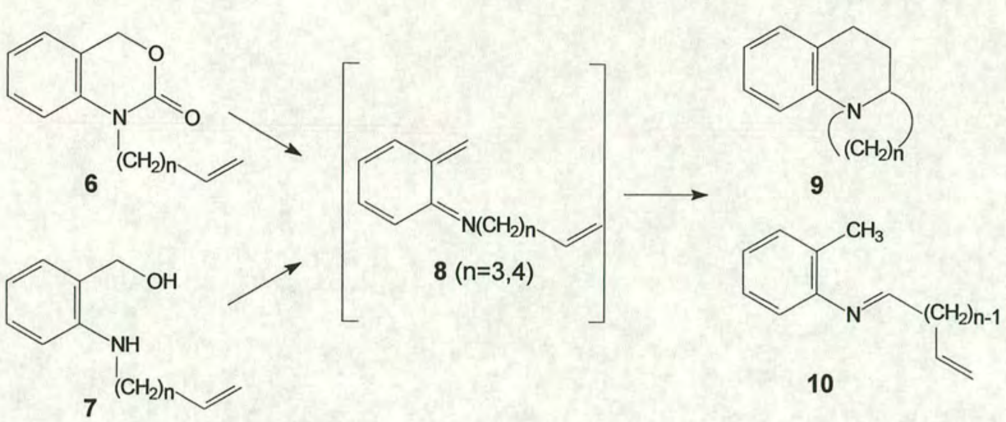


Scheme 1

Compound **3** can be generated by standard FVP from either of the precursors **1** or **2** by decarboxylation or dehydration respectively, using temperatures of at least 650 °C, resulting in mixtures of dihydroacridine **4** and acridine **5**. The proportion of dehydrogenation depends upon the exact temperature used: higher temperature promotes the formation of acridine further.

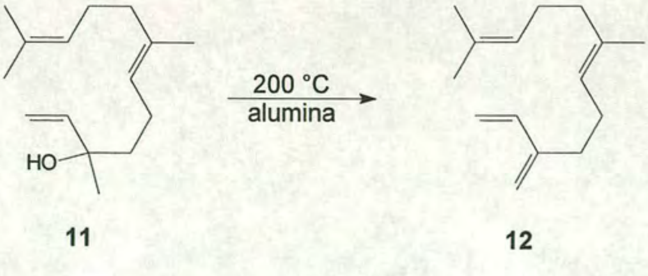
If quartz tubes, coated internally with t.l.c. grade alumina or silica are introduced into the furnace, the temperature required for generation of the intermediate is reduced to as low as 350 °C. Further, the use of alumina promotes the dehydrogenation to acridine as the major product, while silica does not. Similar introduction of molecular sieves to the apparatus results in 100% conversion to acridine from **2** at 450 °C.

A similar effect was noted by the authors in the reactions of *N*-alkylazaxylylenes **8**, scheme 2. Generated in the same way as above, these undergo both intramolecular Diels-Alder reaction to give **9** and H-shift to give **10**. The use of silica coated quartz tubes in this series again allows the use of temperatures up to 250 °C lower but also changes the ratio of **9**:**10**, interestingly favouring increased formation of **9** only when precursor **7** is pyrolysed: pyrolysis of **6** results in unaltered reaction mixtures, albeit using a lower reaction temperature.



Scheme 2

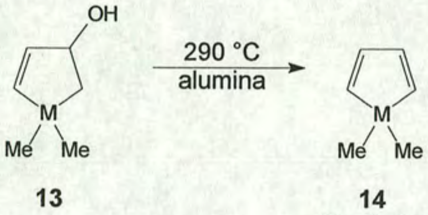
(*E*)-*β*-Farnesene **12** has been prepared by dehydration of (*E*)-nerolidol **11** using a hybrid system of flow and flash vacuum pyrolysis.[5] This compound is of interest as it forms the major component of the alarm pheromone of many aphids. The reactor consists of a vertically held tube, packed with alumina, under oil pump vacuum (0.1-0.2 Torr). The alumina, heated to 200 °C is first treated by evaporation of pyridine through the tube. Following this, the starting material **11** is dripped through the column at a rate of around 20 g h^{-1} resulting in a 65% yield of *β*-farnesenes after purification, of which 47% is the *E* –isomer.



Scheme 3

The use of neutral, untreated alumina gives only a 2% yield of **12** while treatment of the alumina with other bases such as pyrrolidine and triethylamine gives a 55% yield of *β*-farnesenes (of which 40% is *E*-isomer) and 65% of *β*-farnesenes (of which 45% is *E*-isomer) respectively.

Catalytic gas-phase dehydration provided the first convenient synthesis of siloles and germoles unsubstituted at the ring carbon atoms such as **14**.[6,7] This requires a temperature of 290 °C in essentially an FVP system (1.3×10^{-2} Torr) though featuring a vertically held reaction tube.



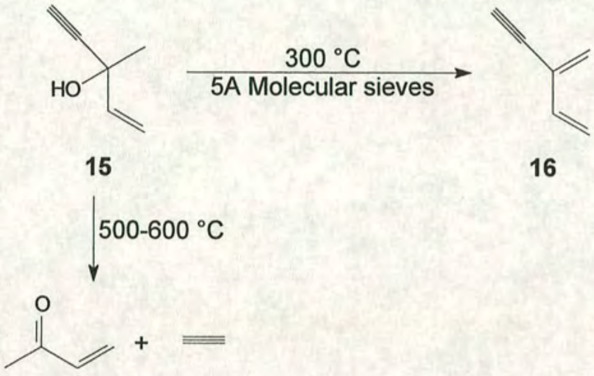
13

14
M=Si, Ge

Scheme 4

These products tend to dimerise and until this point had been prepared by elimination of benzoic acid at 540 °C from the 3-benzoylated analogue of **13** and trapped as a Diels-Alder adduct with maleic anhydride.[8] The catalytic reaction allows **14** to be simply collected from a cooled trap as normal and characterised by NMR at room temperature, a procedure which was previously not possible.

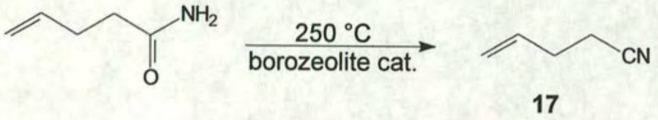
In the studies of Hopf *et al*, 2-ethynyl-1,3-butadiene **16** has been investigated as a novel diene for Diels-Alder reactions.[9] FVP provided the only preparatively useful route to this compound as shown in scheme 5.



Scheme 5

Dehydration of 3-methyl-1-penten-4-yn-3-ol **15** at 300 °C, 10^{-3} Torr over 5A molecular sieves led to an isolated yield of 63% **16**. It is important to prepare the sieves to rid them of water before reaction. This was achieved using a precisely described heating sequence. Scheme 5 also shows the pure thermal chemistry of **15**. At 500-600 °C the alcohol is cleaved to yield methylvinylketone and acetylene. This is then a good example of how catalysis can be used to modify the standard pyrolysis chemistry which can take place.

There exists in the patent literature details of a process for nitrile manufacture by dehydration of the corresponding amides.[10] This consists of a flow pyrolysis system at 250 °C using a very specific borozeolite catalyst. The starting amide, in solution, is passed over the catalyst at a rate of 5 cm^3 h^{-1} under a mixed carrier gas of nitrogen and ammonia. As an example, the preparation of pent-1-enenitrile **17** in 99% yield is given in scheme 6.

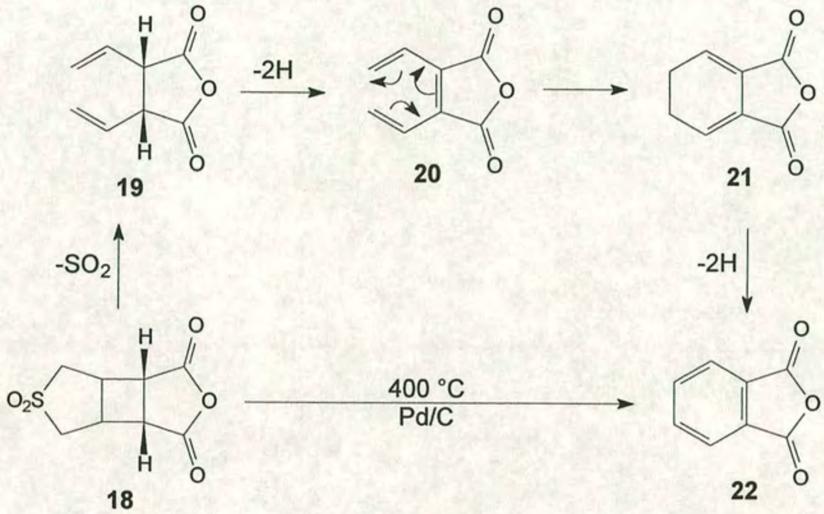


Scheme 6

2.2 Dehydrogenation

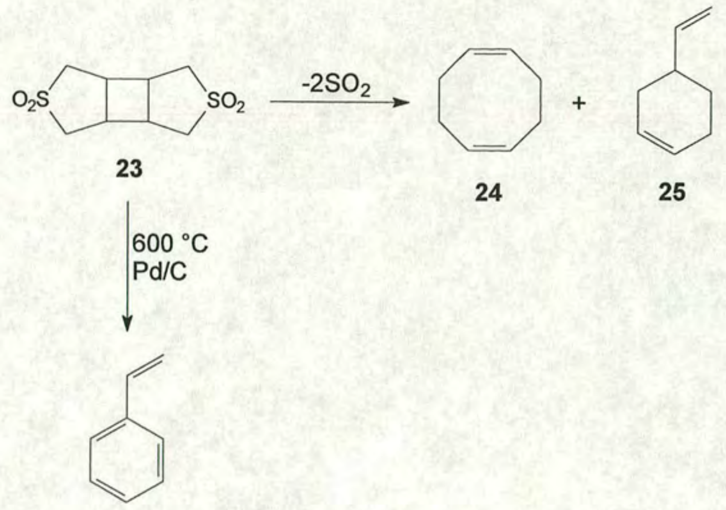
Unsurprisingly, gas phase dehydrogenation processes have been widely reported using traditional condensed phase dehydrogenation catalysts such as palladium and platinum. However, some systematic investigations of the use of metal oxides and mixed metal oxides for dehydrogenation have been carried out and these are reported here also.

Systems such as **18** have been shown to eliminate sulfur dioxide under flash vacuum pyrolysis conditions, resulting in the formation of *cis*-2,3-divinylsuccinic anhydride **19**.[11] By packing the FVP reaction tube with palladium on activated carbon, **18** can be converted to phthalic anhydride **22** in a single step, presumably *via* loss of the ring-junction hydrogen atoms from **19** followed by electrocyclisation and further dehydrogenation as shown in scheme 7.[12]



Scheme 7

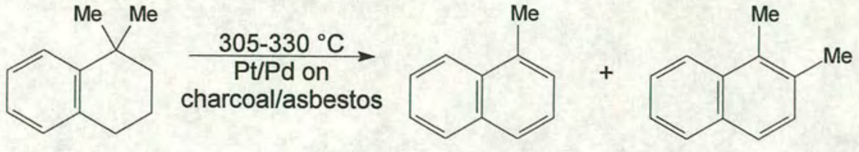
The same conditions were also used in preparation of styrene from the disulfone **23**. This compound, under standard FVP conditions, gives a mixture of cycloocta-1,5-diene **24** and 4-vinylcyclohexene **25**, where it is known that the latter is formed *via* the former.[13] If the palladium catalyst is introduced to the system, **23** is converted to styrene as main product, though in low yield (12%).



23 24 25

Scheme 8

The catalytic dehydrogenation of various hydronaphthalenes in the vapour phase has been investigated.[14] This was achieved using both platinum and palladium catalysts, supported on both charcoal and asbestos, where the reaction pathway is more dependent upon the support than the metal used. As an example, scheme 9 shows the products obtained from pyrolysis of 1,1-dimethyltetralin **26** over such catalysts.



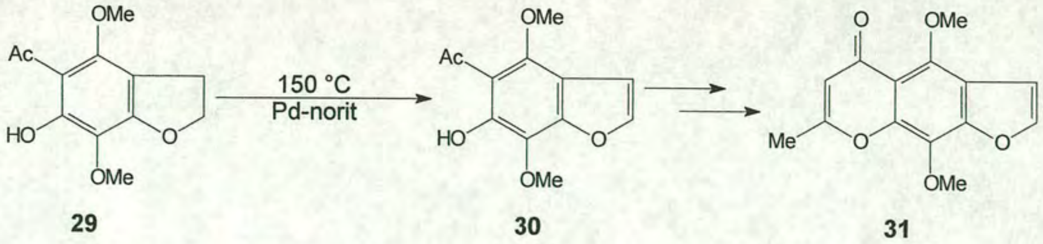
26 27 28

Scheme 9

A description of the apparatus used details a pyrex tube, held at 15° to the horizontal, under "slight suction". The substrate is introduced to this apparatus at a rate of 0.3 g h^{-1}.

The importance of the catalyst support is emphasised by the results obtained using platinum. Over platinised charcoal, 85% dehydrogenation takes place. (This is not an isolated yield of product but is measured from gas evolution.) If platinised asbestos is used, only 16% dehydrogenation takes place. The migration of a methyl group to **28** is a minor product: the elimination of a methyl group to give 1-methylnaphthalene **27** is a general reaction for alkylhydronaphthalenes over these catalysts.

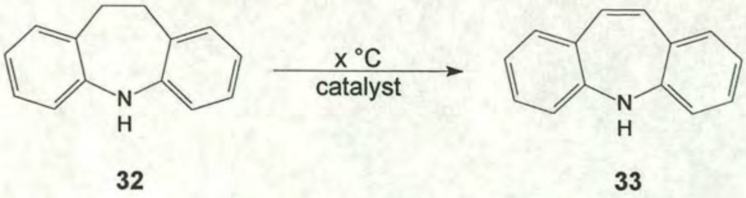
Catalytic dehydrogenation has also been used in the synthesis of khellin **31**.[15] This compound was reported in 1930 as being an active component of a traditional Eastern Mediterranean medicine,[16] and was further identified as a treatment for asthma in 1947.[17] The authors described the sublimation of the starting material **29** through a column of palladium-norit on glass wool under reduced pressure followed by trapping on a cold finger. This yields khellinone **30**, which is then further elaborated to khellin.



Scheme 10

This gives a yield of 81% with no other side-products reported, such as those which would result from cleavage of ring substituents.

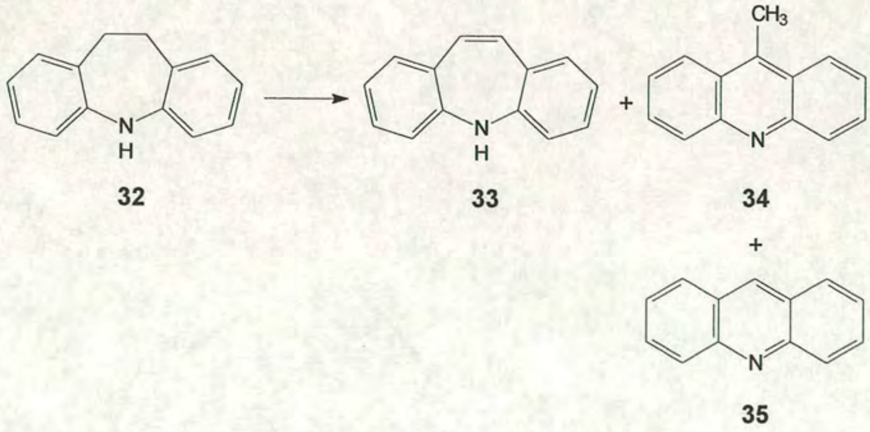
Iminostilbene **33** (dibenz[*b*,*f*]azepine) is the nucleus of a family of compounds which have been widely used in the pharmaceutical industry. Iminostilbene derivatives show antidepressant activity in particular, as well as exhibiting properties of antiallergic, antiepileptic and fungicidal action amongst others.[18] The synthesis of this nucleus has been investigated extensively in the gas phase and dehydrogenation catalysts have been important mediators of this process. A Swiss patent[19] describes the preparation of **33** from iminodibenzyl **32** using an iron (III) oxide catalyst at 400-450 °C. A British patent[20] gives a more detailed description of a vertically held tube (50 cm × 3 cm diameter) filled with Raschig rings over which a nickel/silica catalyst is distributed. The starting material is sublimed under vacuum and carried by a "weak stream" of nitrogen from the bottom of the column, while the products formed are collected in a cooled trap at the top. The reaction is carried out at 600 °C.



Scheme 11

The method described for the synthesis of khellinone above has also been used in the preparation of iminostilbene **33**.[21] Details of the system describe a vertically held tube, packed with palladium-charcoal sprinkled on glass wool. The starting material, iminodibenzyl **32**, is placed in a flask beneath the column and a slow stream of nitrogen is passed through the system, which is evacuated to 0.5 Torr. On sublimation of **32** at a rate of 1.25 g h^{-1} through the tube at 160-170 °C, a mixture of starting material and iminostilbene **33** is obtained which can then be separated by column chromatography. On repeated pyrolysis of the recovered starting material, a maximum yield of 50% could be obtained. This was reported as giving superior results to those obtained using the traditional condensed-phase dehydrogenative methods of sulfur, selenium and palladium.

This pyrolytic preparation of iminostilbene has been further studied by Inoue.[22] Several metal oxide catalysts were evaluated for their conversion and selectivity properties for the reaction shown in scheme 12.



Scheme 12

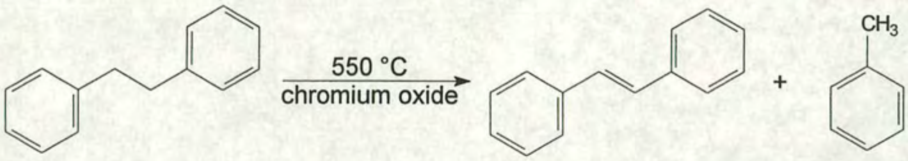
These reactions were carried out using the generic flow pyrolysis apparatus described in section 1.1. Heat-melted iminodibenzyl was introduced at 2.5 g h^{-1} from a dropping funnel to a 25 cm quartz tube at 550 °C under a carrier gas mixture of nitrogen and steam. The results obtained using various catalysts are summarised in terms of conversion and selectivity.

Palladium and nickel oxide catalysts gave rise to a reaction so violent that only gaseous products were formed. Cobalt, iron and manganese oxides gave reasonable conversion to products, with a maximum yield of 41% iminostilbene. This was accompanied in each case by 5-10% yields of 9-methylacridine **34** and acridine **35**. Zinc and tin oxides gave poorer conversion to products but greater selectivity – only iminostilbene was formed in these reactions. Oxides of chromium, cerium and magnesium were found to be all but inactive under these conditions.

In particular, the reaction over manganese oxide was studied. Conversion to products increased with temperature in the range 500-600 °C but at temperatures over 575 °C, the formation of side-products **34** and **35** increased substantially. This led to an investigation of the use of binary catalysts. Admixture of tin oxide (itself shown to give 100% selectivity) in various ratios was evaluated: a reasonably high conversion to products (~ 50%) accompanied by good selectivity for iminostilbene formation (> 90%) was achieved using a ratio of around 8:2 (manganese oxide : tin oxide) at 550 °C.

The gas-phase reaction of aromatics over dehydrogenation catalysts has been studied in a number of reports.[23-26] Reactions of benzene and toluene over metals and metal oxides generally do not yield clean products, rather affording mixtures of biphenyls, triphenylenes, diphenylbenzenes and other polycyclic aromatics. The reactions of bibenzyl under similar conditions yield mainly anthracene, some stilbene (the expected dehydrogenation product) and toluene.

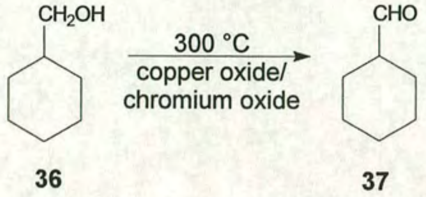
It has been reported that using a chromium oxide catalyst on alumina support, cleaner dehydrogenation than that previously obtained is possible.[27] For example, bibenzyl is converted to stilbene in 43% yield accompanied by 27% yield of toluene, presumably formed simply by homolytic cleavage of the CH_2—CH_2 bond and hydrogen abstraction.



Scheme 13

The reaction is carried out by passing the bibenzyl in benzene solution through the reactor at 550 °C giving a 95% recovery of material by weight.

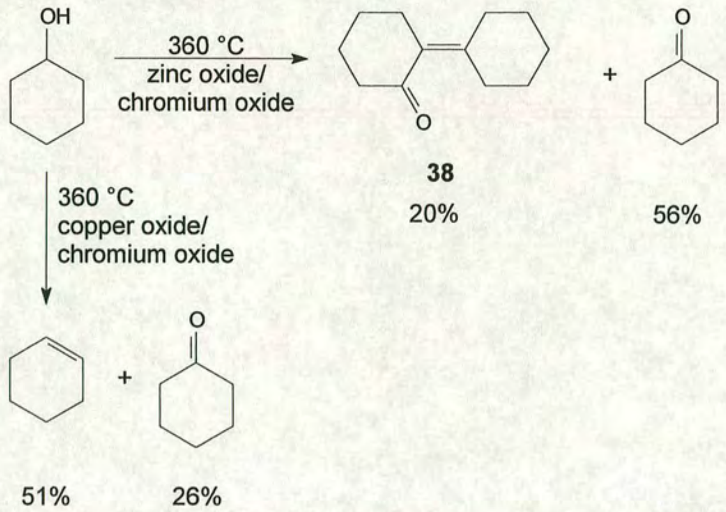
A report from the 1930's details what was claimed at the time to be the most satisfactory method for the oxidation of alcohols to aldehydes and ketones by gas-phase dehydrogenation.[28] This involves the use of a binary copper oxide-chromium oxide catalyst in a flow pyrolytic system at atmospheric pressure. An example process is shown in scheme 14.



Scheme 14

Interestingly, the authors report the vital influence of the rate of addition of the starting material. If cyclohexylcarbinol **36** is added at a rate of 2 cm^3 min^{-1}, 61% yield of **37** is obtained, based upon recovered alcohol. If the rate of addition is adjusted to 1 cm^3 min^{-1}, 75% yield is obtained. The method was used in the preparation of a number of aliphatic aldehydes from primary alcohols in yields in excess of 90% allowing for recovered alcohol, on scales of up to 150 g.

The formation of side-products arising from dehydration or aldol condensation does not seem to be a problem in the reactions of primary alcohols. However, the dehydrogenation of cyclohexanol is more problematic.



Scheme 15

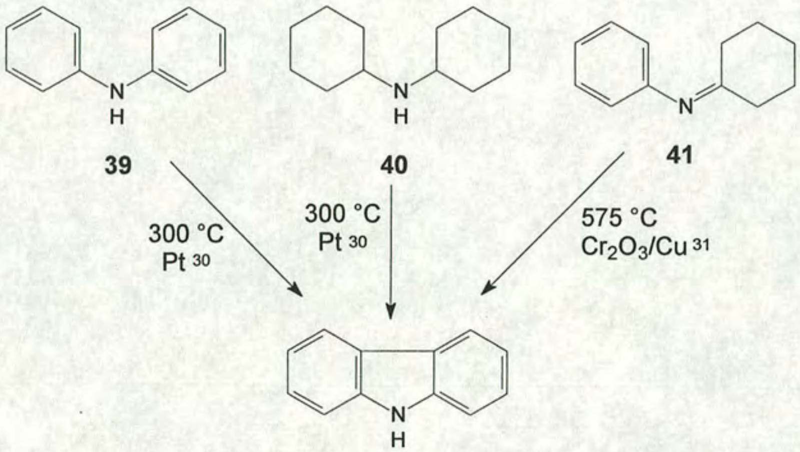
Over a zinc oxide/chromium oxide catalyst, the formation of 2-cyclohexylidene-cyclohexan-1-one **38** is an important side reaction, formed by aldol condensation of cyclohexanone followed by dehydration. If the copper oxide-chromium oxide catalyst is used, dehydration is the main pathway followed, giving 51% yield of cyclohexene.

2.3 Dehydrocyclisation

The dehydrocyclisation reaction, where a ring, usually aromatic, is formed by removal of hydrogen from two or more points in the molecule, has been extensively studied in the vapour phase. This topic has been the subject of a review by Hansch in 1953,[29] containing many references to the catalysis of such processes. A vast array of catalysts has been employed: metals (Pt, Pd, Ni, Cu) and metal oxides (Cr_2O_3,

Mo_2O_3, V_2O_5, ThO_2, Al_2O_3, TiO_2) were particularly common. Metals, usually supported on carbon or asbestos, have the advantage of activity at lower temperatures (300-400 °C) where metal oxides are generally used at temperatures of 450-600 °C.

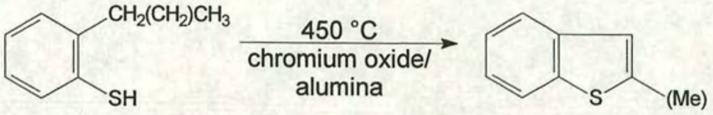
Particular attention is drawn to the suitability of this method in the preparation of heterocycles. Carbazole can be prepared by catalytic dehydrocyclisation from several precursors, as shown in scheme 16.



Scheme 16

Both diphenylamine and dicyclohexylamine are converted to carbazole by the action of platinum at 300 °C while a higher temperature is needed to convert *N*-cyclohexylideneaniline to carbazole using a copper/chromite catalyst.

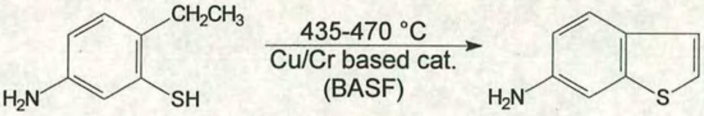
Benzothiophenes can also be prepared by this method (scheme 17).[32]



Scheme 17

Benzothiophene and 2-methylbenzothiophene have been prepared by this method in yields of 10-30%. These processes are run at an incredibly high throughput rate of 30-40 g h^{-1}, this having been optimised by a series of test experiments.

This preparative method has recently been used and improved for the preparation of 6-aminobenzothiophene **42.**[33]



42

Scheme 18

This report includes a detailed description of a relatively sophisticated reactor. The starting material is fed by infusion pump at between 2 and 11 cm^3 h^{-1} into a long (57 cm) vertically held pyrex tube, the top third of which is packed with Raschig rings to provide a pre-heater. The middle third is packed with a commercial binary catalyst of copper and chromium oxides and the lower third is empty. The desired product crystallises in an uncooled flask at the bottom of the reactor in yields of 39-65%, depending upon feed rate, temperature and catalyst used.

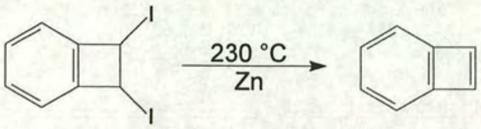
Other recent work on the dehydrocyclisation of *n*-paraffins to aromatics, a key reaction in the preparation of high octane fuels, has been carried out using titania-zirconia catalysts.[34] This paper gives references to the huge body of work which exists in this area, mainly in the pre-war era, and further references can also be found in Hansch's review.[29]

2.4 Other eliminations

This section incorporates a small number of eliminative procedures other than those discussed already. These include dehalogenation, decarboxylation, deoxygenation, extrusion of carbon monoxide and dealkylation.

Dehalogenation reactions have been carried out in the gas phase over metallic "catalysts". These reports do not investigate the role of the metal or its final oxidation level and could be thought of as VGSR reactions with the metal being converted to MX_n. This work will be reported here but it should be borne in mind that the metals may not be catalytic in the process.

One such example is the generation of benzocyclobutadiene **44** in the gas phase.[35] This has been prepared by flash vacuum pyrolysis of 1,2-diiodobenzocyclobutene **43** over zinc powder at 230 °C.

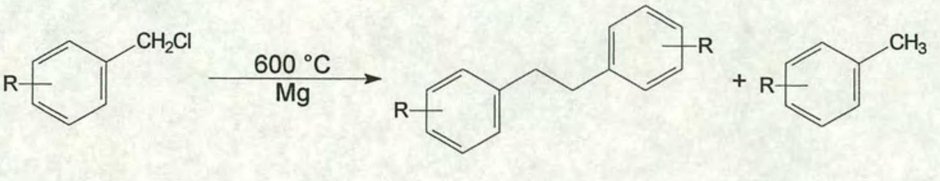


43 **44**

Scheme 19

This highly reactive species, which dimerises at >75 K, was characterised by IR using matrix isolation in argon and was first prepared by this method.

Another such dehalogenation using FVP incorporating a metal catalyst/reagent has been forwarded as a useful method for C—C bond formation.[36] Such combination is rare under FVP conditions: most processes involve rearrangement or fragmentation. This report details a preparation of bibenzyls **46** from the corresponding benzyl chlorides **45** as depicted in scheme 20.



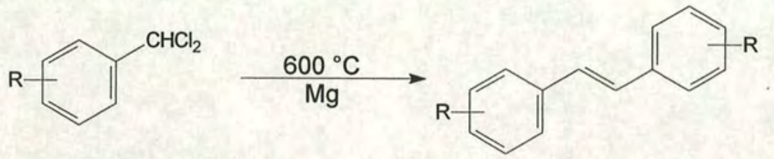
45 **46** **47**

Scheme 20

Bibenzyls incorporating 2,3 and 4 substituents have been prepared in this way in yields ranging from 37-80%. Toluenes **47** are an ever present side-product.

The authors provide some evidence for the consumption of magnesium by reaction with an excess of benzyl chloride. Conversion to magnesium chloride is assumed.

The process is also effective in the preparation of stilbenes **49** from the corresponding benzylidene chlorides **48** in yields of 36-63%. This reaction is complicated by the presence of reduction products **46** and **47**.

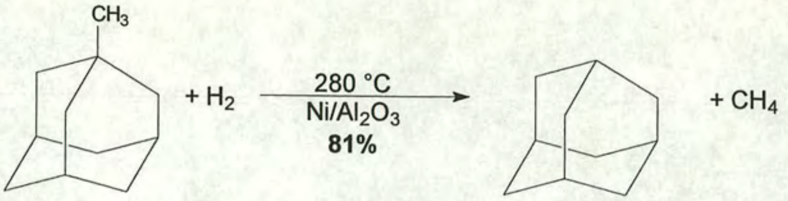


48 **49**

Scheme 21

In 1980, Schleyer *et* al reported a catalytic hydrogenolysis of alkyl-substituted adamantanes over a nickel/alumina catalyst.[37] This catalyst has been used for a variety of eliminative reactions by the authors since then and these applications will be discussed together here.

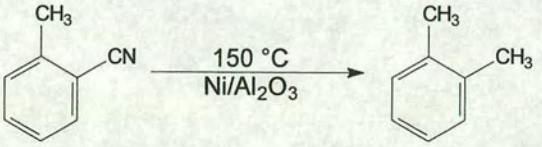
The dealkylation of adamantanes in the gas phase is carried out using a horizontally held flow pyrolysis system. The substrate is heated in an oil bath and carried over a nickel/alumina catalyst, held in a pyrex furnace tube at 200-300 °C by a slow stream of hydrogen (20-30 cm^3 min^{-1}). Products are trapped by cooling on exiting the furnace tube. An example is shown in scheme 22.



Scheme 22

Several alkyl substituted adamantanes, diamantanes and triamantanes were dealkylated by this method in variable yields, though sometimes quantitative. At higher temperatures, the adamantane skeleton is broken – this provides further side-products in the reactions of di- and triamantanes.

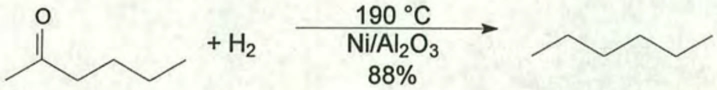
The same catalyst has been used for the catalytic hydrogenolysis of nitriles, furnishing the corresponding methyl substituted compounds as shown in scheme 23.[38]



Scheme 23

This process is carried out using the same apparatus and procedure as that described for the adamantane work. At temperatures of 120-150 °C, several aromatic and aliphatic nitriles have been transformed in this way, in yields of 52-92%. Side-reactions include the reduction of aromatic rings at higher temperatures. The authors note the absence of amines in any product mixture, but the odour of ammonia was detected on opening of the apparatus.

Further use has been made of this defunctionalisation method in the deoxygenation of ketones.[39] Exactly the same apparatus and procedure are used to effect the transformation as exemplified by 2-hexanone in scheme 24.



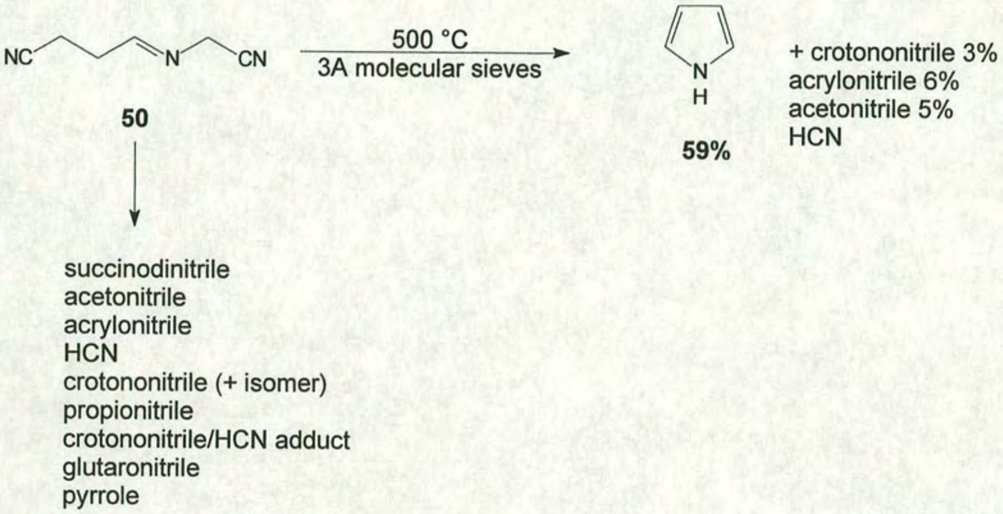
Scheme 24

Unsurprisingly, selectivity is noted as the main drawback of this process – other functionalities are affected by these conditions as we have seen previously. Other limitations include the low conversion to products observed when sterically encumbered ketones are subjected to the procedure.

Finally, the nickel/alumina catalyst has been employed to effect the decarboxylation of carboxylic acids.[40] The success of this process was found to be restricted to the decarboxylation of aromatic and tertiary aliphatic carboxylic acids. However, use of a palladium catalyst at higher temperatures (330 °C) provides a much more general procedure for this elimination.

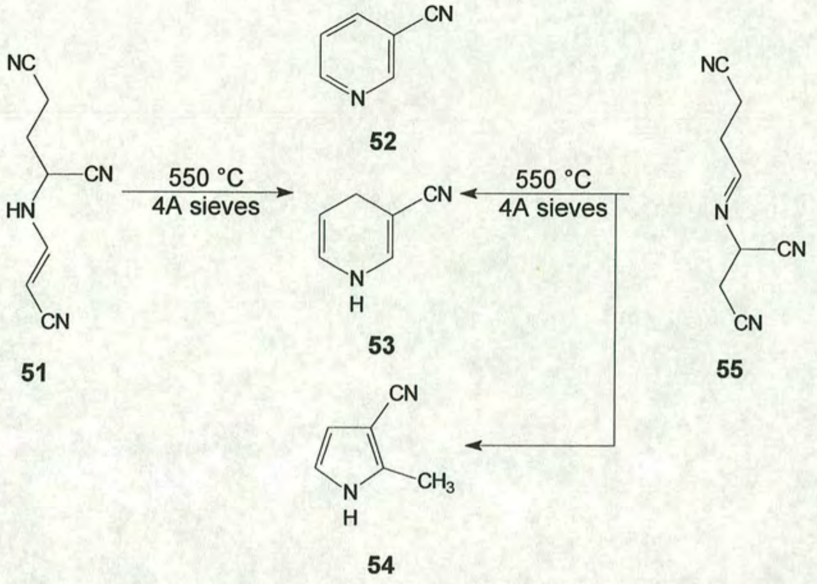
In a series of reports on the chemistry of α-aminonitriles,[41,42] Eschenmoser has discussed the elimination of hydrogen cyanide by a pyrolytic pathway. Scheme

25 indicates how this can be observed under traditional FVP conditions but how the selectivity of the reaction is greatly increased by use of molecular sieves as catalyst.



Scheme 25

In the second report of this series, this seemingly catalytically aided elimination of HCN is used further as shown on scheme 26.

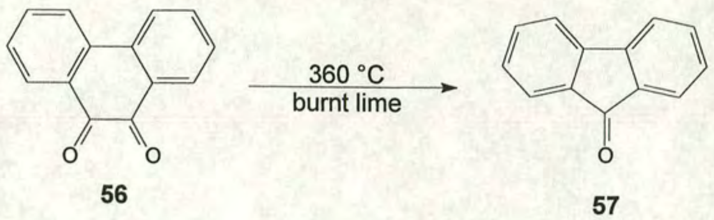


51 52 53 54 55

Scheme 26

From both **51** and **55**, nicotinonitrile **52** is the main product, accompanied by 2-methylpyrrole-3-carbonitrile in the pyrolysis of **55**. The dihydro compound **53** is observed in both cases in small amounts, but most is converted to **52** under the reaction conditions. Yields are observed to be low, and interestingly, strongly dependent upon the volatilisation rate of the substrate. Several other examples of this elimination of HCN followed by cyclisation are discussed in the reports.

There exists a report on the distillation of phenanthraquinone **56** over "burnt lime".[43] This results in carbon monoxide extrusion to give fluorenone **57** as shown in scheme 27.



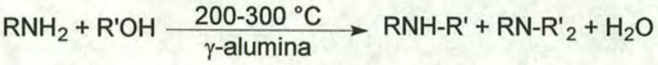
Scheme 27

Normally, **56** distils at 360 °C without decomposition: the extrusion is only seen under catalytic conditions. Other similar extrusions of carbon monoxide under FVP conditions can be found in the work of Schaden.[44]

2.5 Combinative processes

As was stated earlier, most pyrolytic processes involve fragmentation of some sort: breakage of a weak bond or elimination of a small molecule are common processes. There are however some instances of gas phase processes taking place which involve a combination which is not simply dimerisation or polymerisation. By necessity, these processes are generally carried out under flow pyrolysis conditions since the high vacuum and short contact time of the flash vacuum experiment negates such bimolecular reactions. Already discussed, in section 2.4, is a dimerisation process, which relies upon the elimination of halogens for the preparation of symmetrical bibenzyls.[36]

Another such catalytic gas phase system has been applied to the *N*-alkylation of amines using alcohols as the alkylating agent.[45] This is carried out using an archetypal flow reactor with a catalyst bed of γ-alumina, according to the general equation shown in scheme 28.



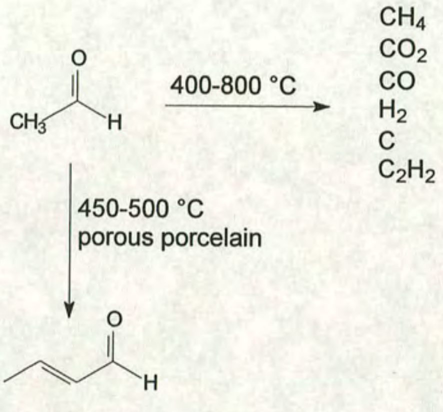
$$RNH_2 + R'OH \xrightarrow[\gamma\text{-alumina}]{200\text{-}300\ ^\circ C} RNH\text{-}R' + RN\text{-}R'_2 + H_2O$$

Scheme 28

The amine is introduced to the reactor in solution with the alcohol with which it is to be alkylated at a rate of 2 $cm^3\ h^{-1}$. Nitrogen is used as the carrier gas. Products are trapped in an ice-cooled flask beneath the reactor.

In these reactions there is a trade off between selectivity for mono- or disubstitution and % conversion. Increased temperature increases the conversion but decreases the selectivity. For example, in alkylating aniline with methanol, 90% selectivity for *N*-methylaniline can be achieved at only 45% conversion. Several other amines and alcohols have been evaluated for their suitability in this reaction also. Propan-1-ol, hexan-1-ol and benzyl alcohol are all excellent alkylating agents while propan-2-ol gives poor conversion. Importantly, on methylation of chirally pure α-methylbenzylamine, no racemization occurred, even at 300 °C.

In a study of the thermal decomposition of acetaldehyde, very different results were obtained in the absence or presence of porous porcelain, a material not normally considered to be a catalyst.[46] Under standard flow pyrolytic conditions through an empty tube, acetaldehyde is broken down to carbon and gases only: pyrolysis at above 400 °C results in varying amounts of methane, acetylene, carbon dioxide, carbon monoxide and hydrogen, the abundance of each being dependent on the temperature used. However, as shown in scheme 29, pyrolysis of acetaldehyde over porous porcelain follows a different path.



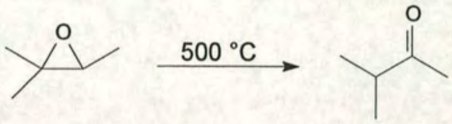
58

Scheme 29

No indication of yield is given for crotonaldehyde **58** but an aldol condensation has evidently been promoted which cannot take place in an unpacked tube. A similar aldol process is observed in the gas phase preparation of cyclohexanone, as discussed earlier (scheme 15, p24.) This may be due to a simple increase in the contact time of the experiment, allowing the bimolecular reaction to take place, but no further study on the system has been carried out. This then is a good example of a "grey area" between catalytic and non-catalytic reactivity.

2.6 Rearrangement

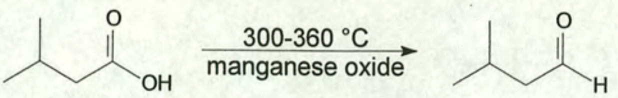
In 1903 it was recognised that in the pyrolysis of epoxides at 500 °C, cleavage of the ring occurred to yield aldehydes or ketones, as depicted in scheme 30.[47]



Scheme 30

However, at this temperature, side-products are formed by decomposition of the product ketone. The authors found that these side-products could be eliminated by the use of an alumina catalyst and much lower temperatures of 250-260 °C. In fact, if the side-products are formed by product decomposition then it is probable that the alumina acts only as a contact mass, and the lower temperature used allows the ketone product to remain intact.

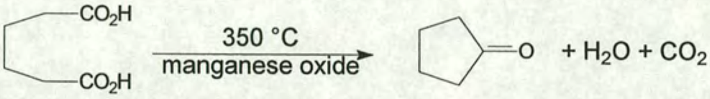
The use of manganese oxide as a catalyst in the gas phase conversion of carboxylic acids to yield the corresponding aldehydes has been reported.[48] This surprising reduction takes place at temperatures of 300-360 °C as depicted by the example shown in scheme 31.



Scheme 31

The authors report the preparation of a number of aliphatic aldehydes in 50-70% yields.

A departure was noted, however, in the pyrolysis of adipic acid **59**, which was found to cyclise and furnishes cyclopentanone

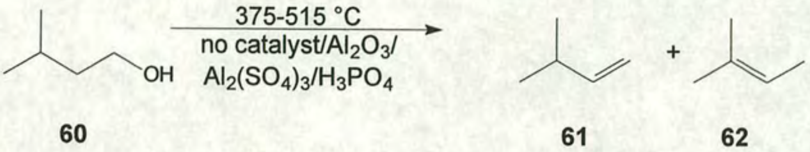


59

Scheme 32

Indeed, this transformation is observed under uncatalysed pyrolysis at 500 °C – giving a 20% yield. However, under catalysis, 80% yield is possible.

In a study of the dehydration of isoamyl alcohol **60** to isopropylethylene **61** in the gas phase, several catalysts were used and their properties evaluated.[49] Isopropylethylene also rearranges to trimethylethylene **62** under these conditions and the extent to which this occurred was monitored. The apparatus used for this work consisted of a four foot long silica tube of one inch in diameter heated with resistance wire and insulated with asbestos. Products are trapped in an ice-cooled flask on emergence from the reaction tube. Scheme 33 shows the results obtained using alumina, aluminium sulfate and phosphoric acid on pumice as catalysts.



Scheme 33

When isoamyl alcohol is introduced to an empty tube at 515 °C at a rate of around 1.7 mol h^{-1}, dehydration occurs to 33%, of which the hydrocarbon mixture is of the ratio 2:1 (**61**:**62**). Carbonisation of the empty furnace tube causes the conversion to hydrocarbons to drop to 9%. If the alcohol is reacted at a lower rate of 1 mol h^{-1}, the conversion to dehydrated products is increased to 41%.

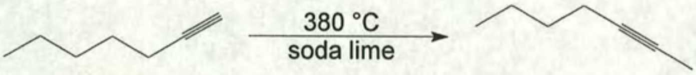
Use of alumina as catalyst at 375-450 °C gives an increased dehydration of 48-58%. Further, no rearrangement of isopropylethylene **61** to trimethylethylene **62** is observed. At 500 °C however, dehydration occurs to 67% while rearrangement occurs to around 10%.

Aluminium sulfate proved extremely efficient in terms of both dehydration and rearrangement. At 345 °C, dehydration occurs to a degree of 57%. Of the hydrocarbon mixture produced, only 21% are present as isopropylethylene.

The use of phosphoric acid at 405 °C gives a conversion to hydrocarbons of 50% - of the order produced using alumina as catalyst. However, phosphoric acid is more active in mediating the rearrangement to trimethylethylene, the product mixture produced consisting of approximately equal amounts of **61** and **62**.

It can be seen that these acidic catalysts not only promote the dehydration of alcohol to alkene but also mediate the rearrangement of **61** to **62** at lower temperatures than is possible under uncatalysed conditions. This can be rationalised in terms of the likelihood of a protonation-deprotonation mechanism taking place under acidic conditions. This would result in the more stable alkene to be formed as expected from Zaitsev's rule, *i.e.*, trimethylethylene **62**.

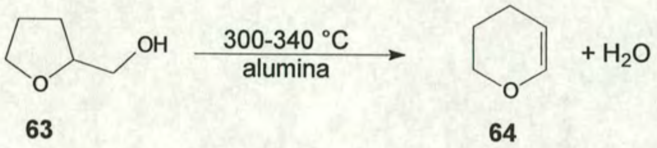
Soda lime has been found to be an active catalyst for the rearrangement of hept-1-yne to hept-2-yne in the gas phase as shown in scheme 34.[50] The apparatus consists of a tube tilted from the horizontal , fitted with a dropping funnel at the top end and a condenser at the bottom.



Scheme 34

The rearrangement occurs to an extent of 70%. In an uncatalysed experiment using pumice as a contact mass at 350 °C, far less rearrangement was observed. The product mixture consisted of 68% starting material and the reaction was accompanied by the "copious evolution of white fumes".

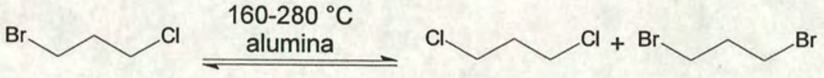
Dihydropyran **64** can be prepared via the catalytic dehydration of tetrahydrofurfuryl alcohol **63** in the gas phase.[51] The rearrangement takes place following a dehydration step mediated by alumina, as shown in scheme 35.



Scheme 35

The alcohol is introduced to a 90 cm furnace tube inclined slightly from horizontal at a rate of 50 cm^3 h^{-1} giving a 70% yield of dihydropyran.

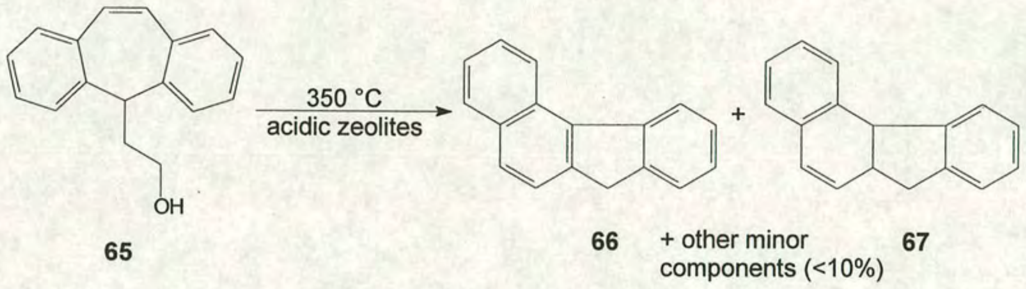
The disproportionation of 1-bromo-3-chloropropane to 1,3-dibromopropane and 1,3-dichloropropane has been carried out according to scheme 36.[52]



Scheme 36

The reaction is carried out in a flow pyrolysis system consisting of a vertically held, electrically heated pyrex tube of 30 cm × 2.6 cm. At a temperature of 280 °C, the conversion of 1-bromo-3-chloropropane to products is 50%, of which 95% consists of the dichloro and dibromo species. Minor products include allyl bromide and allyl chloride. It is quoted in the report that these latter compounds are the main products formed in the normal pyrolysis of 1-bromo-3-chloropropane by dehydrohalogenation. Evidence is also presented to rule out a mechanism of dehydrohalogenation followed by hydrohalogenation as being responsible for the formation of the dichloro and dibromo species. It would appear that a possibly alumina-bound carbocation formed by loss of halide does not complete elimination and is subsequently attacked by a halogen anion.

Scheme 37 shows a summary of the products obtained from the pyrolysis of 5-*β*(hydroxyethyl)-5H-dibenzo[*a,d*]cycloheptene **65** over acidic zeolites.[53]

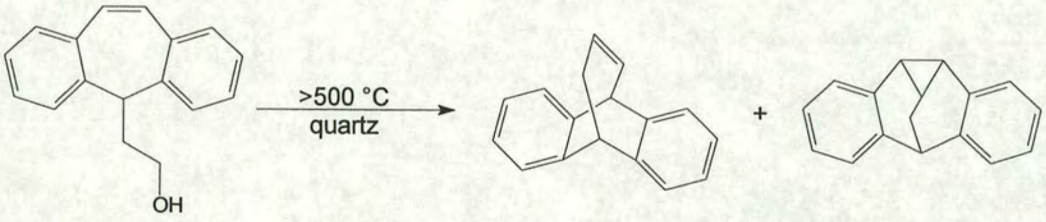


Scheme 37

The reaction is carried out using a hybrid system of flow and flash vacuum pyrolysis. The sample was introduced under argon (6 cm^3 min^{-1}) at a pressure of 0.65 mbar to a vertically held 70 cm long quartz tube. The tube is packed for 20 cm of its length with the zeolite catalyst. The zeolites used are specially prepared and not commercially available.

In reactions over 7 different zeolites the benzofluorene **66** is the main product in each case, in yields of 16-52%. The dihydro derivative **67** is the next most abundant in yields of 7-23%. A mechanism for the reaction is proposed by the authors, citing protonation followed by elimination of water as the probable initial steps. The mechanism is supported by the presence of the proposed intermediates as minor products in the pyrolysate of **65**.

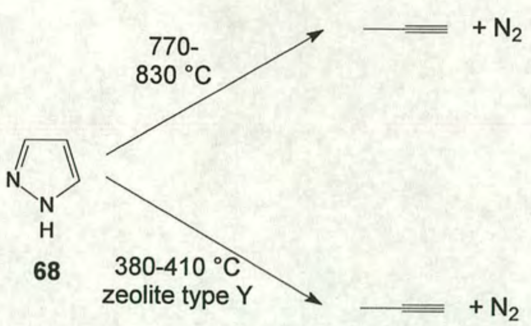
In contrast, the uncatalysed pyrolysis of **65** over quartz as a contact mass yields the main products shown in scheme 38.



65

Scheme 38

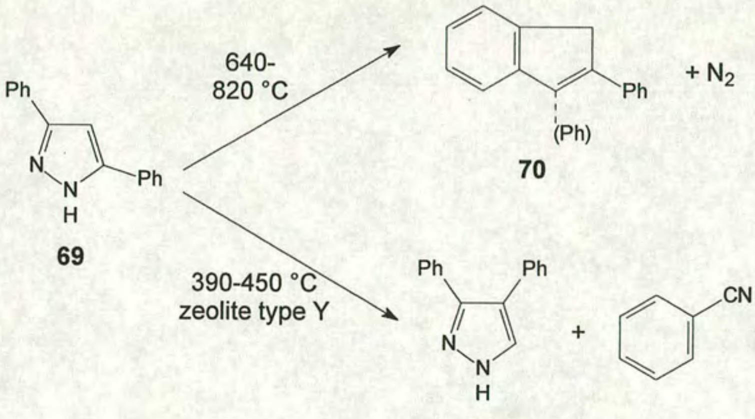
In an attempt to prepare vinylcarbene intermediates from pyrazoles by nitrogen extrusion, FVP has been employed.[54] The reaction has been studied on two precursors: the parent pyrazole **68** and also 3,5-diphenylpyrazole **69**. Schemes 39 and 40 illustrate the contrasting reaction pathways of these precursors and the effect of zeolites on the process.



68

Scheme 39

It can be seen that no difference occurs when using a zeolite catalyst in the FVP system other than allowing the reaction to be run at much lower temperature. In each case, nitrogen extrusion occurs, affording propyne.



69

70

71

Scheme 40

In the pyrolysis of 3,5-diphenylpyrazole **69**, zeolite catalysis does indeed change the product profile. Nitrogen extrusion from **69** occurs under standard FVP conditions to yield 2- and 3-phenylindenes **70** while zeolites mediate only isomerisation to **71** and presumably N-N bond cleavage to give benzonitrile. Polyaromatics are also formed as by-products in this reaction.

Discussion

1. Catalytic dehydrations under FVP conditions

1.1 Preparation of nitriles by dehydration

1.1.1 Introduction

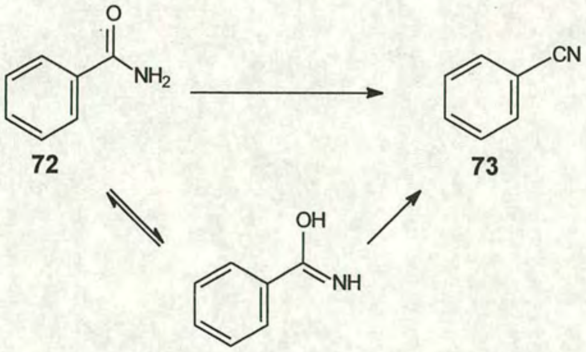
The dehydration of a carboxylic amide to the corresponding nitrile is a widely used process and there have been many solution phase methods developed for carrying out this transformation. However, there remains a need for a general and mild method and gas phase methodology, especially catalytic, is well suited to this kind of simple elimination.

Traditional solution phase methods for amide dehydration include the use of phosphorus reagents such as phosphorus pentoxide[55] and phosphorus oxychloride.[56] Thionyl chloride has also been used[57] to effect this transformation. These methods collectively suffer from several drawbacks, for example the liberation of toxic gases, conditions exclusive to certain examples, work-up difficulties, long reaction times or tedious purification. As a result, several other methods, involving more exotic reagents have been developed. These include the use of Burgess reagent,[58] ethyl iodide/silver oxide,[59] trifluoroacetic anhydride/pyridine,[60] and silazanes,[61] Again however, the limitations ascribed to the more common methods apply in many cases here and in some examples the methods are complicated further by the necessary preparation of the dehydrating reagent.

In the introduction to this thesis, a section devoted to dehydration reactions discussed the literature precedent for the use of gas phase chemistry in this kind of process. The primary aim of the work described in this section is to develop such a method for the preparation of nitriles from amides using the technique of Flash Vacuum Pyrolysis and the influence of solid catalysts.

1.1.2 Optimisation of amide dehydration conditions

The development and optimisation of a catalytic gas phase amide dehydration method was carried out using the test reaction shown – the dehydration of benzamide **72** to benzonitrile **73**.



Scheme 41

The reaction can formally be described as a β elimination from the enol form of the amide as shown.[62] Firstly, to determine whether benzamide was a suitable substrate for FVP, the reaction was carried out under purely thermal conditions, without the use of any catalyst packed into the furnace tube. (The Flash Vacuum Pyrolysis method is described in the introduction, section 1.2, p.5). Although this experiment yielded no nitrile at 700 °C, the amide was sublimed smoothly from the inlet tube without decomposition and was collected quantitatively unchanged in the product trap. This then was encouraging for the development of a useful process.

The thermal dehydration of benzamide was then attempted using porcelain chips as a packing material in the furnace tube. This was regarded to be an inert packing and was used to effectively increase the contact time of the experiment without raising the furnace temperature. Benzamide, when reacted at 700 °C over such packing, yielded a mixture of benzonitrile and unreacted starting material, in a ratio of approximately 1:1. The work up of this reaction mixture was very simple. Collection of the pyrolysate into methanol followed by evaporation under reduced pressure rids the mixture of any water formed during reaction. It was clear at this stage from the clean nature of this process that the development of a gas phase amide dehydration protocol was indeed possible, but to carry this out required a suitable analytical procedure. NMR spectroscopy provided the most suitable method for this. ^{13}C NMR spectroscopy was found to be ideal since this allows us to view individual peaks easily, with no multiplicity problems and would quickly highlight the presence of any undesired by-products. It was also a straightforward procedure to quantify these reactions by this method due to the fact that the product mixture contains only 2 components. The ^{13}C NMR spectrum of an authentic 50:50 mixture of benzamide and benzonitrile was first recorded. Conversion to nitrile was thus calculated as the ratio of intensity (product peak x) versus intensity (reactant peak x) normalised against the same intensity ratio in the 50:50 mixture. This process was repeated for each product peak referenced against each reactant peak, resulting, in the case of these 5 peak compounds, in a matrix of 25 ratios. The mean average value of these ratios was taken as the conversion to benzonitrile. The validity and the accuracy of this method is confirmed by the example spreadsheet shown on p.183, experimental section where there is no more than 15% difference in the ratios to be averaged.

This method was then used to determine the conversion to benzonitrile obtained from reaction of benzamide at a range of furnace temperatures with the results shown in figure 3.

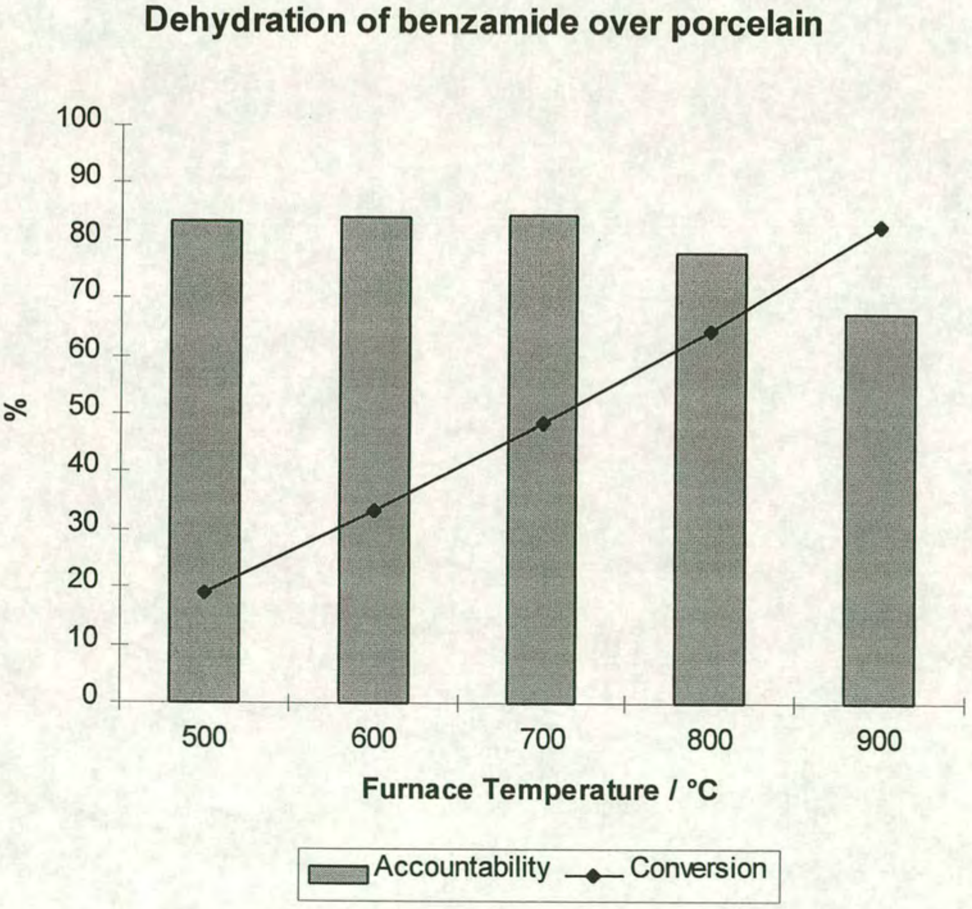


Figure 3

Accountability is the amount of material recovered, expressed as a percentage of the amount expected, allowing for water loss. It is estimated from repeated reactions that the error inherent in this figure is approximately ± 5%. Figure 3 shows that although the increase in conversion is fairly linear, the accountability drops at temperatures over 700 °C. This is to be expected in FVP reactions - higher temperature allows other decompositions to take place, e.g., to polymeric material and indeed, at 900 °C the porcelain chips were heavily blackened by the reaction. As a result the actual percentage yield of benzonitrile obtained was never above 60 % (figure 4).

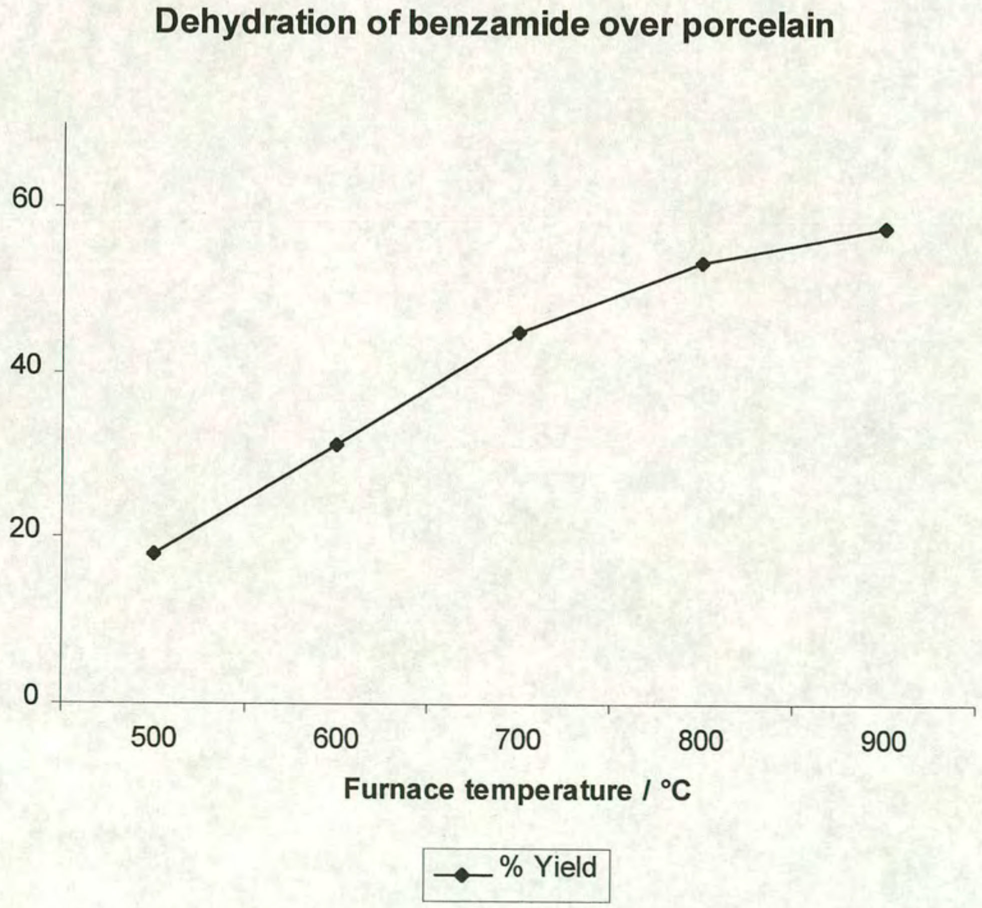


Figure 4

The percentage yield shown is not based on isolated product but on the data displayed in figure 3, *i.e.*, calculated from the ^{13}C NMR spectrum.

The dehydration was then attempted using the gas phase dehydration conditions reported by Storr and detailed in the introduction.[4] This consisted of packing the furnace tube with lengths of silica tubing (5 cm × 6 mm) coated in t.l.c. grade silica before conducting the pyrolysis, again using a temperature of 700 °C. This resulted in 27% conversion to benzonitrile, obviously poorer than the result obtained using porcelain at this temperature and so this method was not pursued further.

Commercially available molecular sieves are extensively used as drying agents in organic chemistry but have also been utilised as a catalyst in dehydration processes.[9] These are zeolite materials which have a basic crystalline structure consisting of a three dimensional framework of SiO_4^{4-} and AlO_4^{5-} polyhedra. These polyhedra are linked by all their corners to give a generally open framework containing regular channels and cavities. Although naturally occurring, most commercial types are synthetically prepared. The most commonly used molecular sieves for drying purposes are designated as "Zeolite A" type and subdivided into types 3A, 4A and so on.[63] The number indicates the approximate size of the entrance to the zeolite channels in Angstroms and is controlled by the size of the metallic counter ion associated with the aluminosilicate. The cheapest material, 4A, incorporates sodium and has a pore size of 4.2 Å. Potassium exchanged zeolite A is designated 3A while calcium exchanged material has a pore size of 4.9 Å and is designated 5A.

It was clear that these materials, available as powders or as beads of varying size, could be advantageously used as solid catalysts in the context of FVP. Molecular sieve 3A, which is generally accepted as the best for drying organic solvents since the pore dimensions preclude the absorption of organic materials,[63] was chosen as the material most likely to mediate the dehydration of benzamide and beads of 1-2 mm were used for ease of handling. It is known that 1 g of 3A molecular sieves has the capacity to absorb approximately 0.25 cm^3 of water, based upon the approximate density and the crystal structure of zeolites.[64] However, there are approximately 8% of the active sites which display a higher activity due to cation occupancy within the zeolite.[64] This means that 1.5 g of 3A molecular sieves could, using these highly active sites, dehydrate approximately 1 mmole of substrate. It was thus decided to use 10 g of molecular sieves initially and to operate experiments on such a scale that this would be in excess in terms of water absorbency (up to a 1 g reaction scale). Also, a 10 g portion gives a conveniently sized (2-3 cm) plug, held in the central hot zone of the furnace tube by plugs of quartz wool.

On purchase, molecular sieves are generally wet and it was necessary to devise a preparation protocol to render the sieves fully active. This was achieved by heating for 2 h at 400 °C in air and for a further 0.5 h under vacuum. Heating the molecular sieves for only 1 h did not fully rid the zeolite of water while heating for longer than 2 h gave no increased activity.

Having found a suitable preparation protocol, the molecular sieves were then used to catalyse the test dehydration of benzamide to benzonitrile under FVP conditions. This was carried out at a range of temperatures using the NMR-based analysis procedure detailed earlier, giving the results depicted in figure 5.

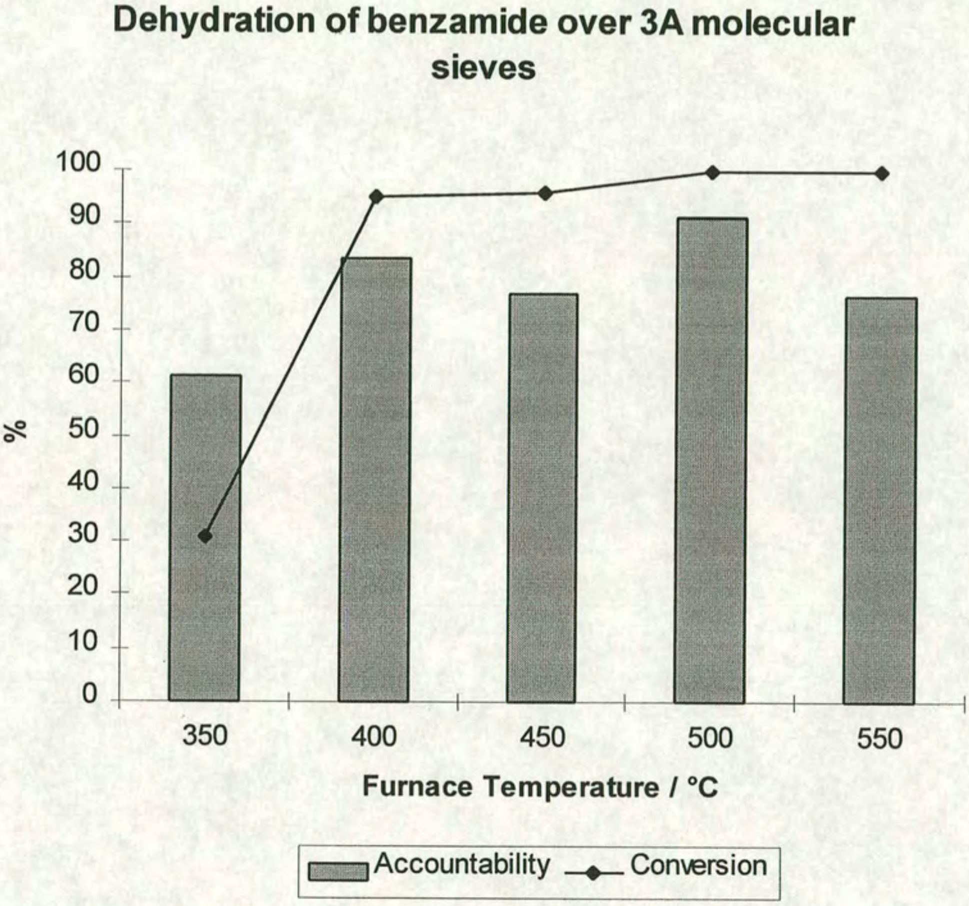
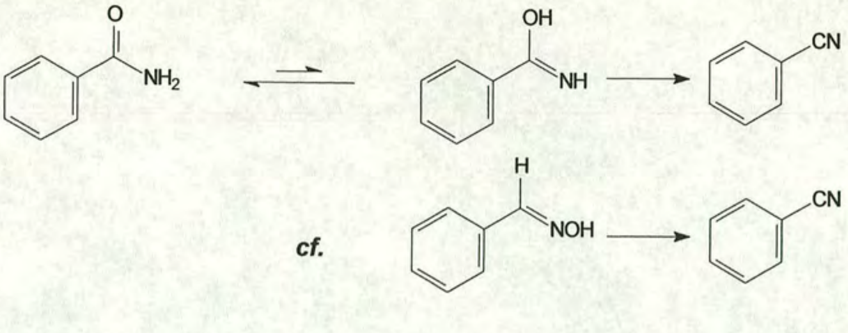


Figure 5

Noticeably, the reaction temperatures being used here are around 300-400 °C less than those used for the dehydration of benzamide over porcelain. Also, it can be seen that the graph of conversion rises much more steeply to total conversion than that plotted for reaction over porcelain. Again the recovery drops at higher temperature as decomposition takes place. The low accountability obtained at 350 °C however is more difficult to explain. This is unlikely to be due to trapping of organic material in the zeolite pores since the zeolite pore size of 3 Å should preclude entrance to organics. More likely is that at this furnace temperature, unreacted benzamide is condensed near the exit of the furnace tube, where the temperature may be sufficiently cooler. This would imply that the conversion to benzonitrile shown for this reaction, 31%, is artificially high since not all of the unreacted starting material was collected. The optimum conditions for dehydration were chosen as 500 °C since this gives full conversion to benzonitrile at high accountability.

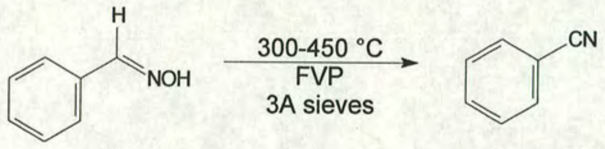
1.1.3 Optimisation of oxime dehydration conditions

The dehydration of oximes to the corresponding nitrile is in many ways an analogous process to amide dehydration. Indeed, many of the traditional reagents and conditions described earlier are also used for this purpose. This can be easily understood in terms of the similarities between the oxime structure and that of the enol form of the amide. Since the amide dehydration process can be formally described as a β elimination from the enol form (see scheme 41), usually where the reagent helps augment the leaving of the OH group, it could be imagined that the oxime dehydration should progress more easily (scheme 42).



Scheme 42

The dehydration of oximes was therefore optimised on the test dehydration of benzaldehyde oxime **74** over 3A molecular sieves at temperatures of 300-450 °C. Benzaldehyde oxime **74** was first prepared in 92% yield by simple condensation of benzaldehyde and hydroxylamine hydrochloride.



74 **73**

Scheme 43

Reaction at all temperatures gave almost complete conversion to benzonitrile (based on ^{13}C NMR analysis as before). However, only reaction at 350 °C was shown to give a good recovery of material – the accountability was less than 65% for all other temperatures. 350 °C was therefore chosen as the optimum temperature for the dehydration of oximes.

1.1.4 Role and activity of molecular sieves

Although the optimisation experiments described up to this point seem to have provided a useful nitrile dehydration method, the role of the molecular sieves in the reaction remains unclear. Several questions must be answered before a claim can be made for a robust process and several others arise from a mechanistic viewpoint. A number of experiments was therefore carried out to determine catalyst deactivation pathways, the fate of water produced and whether these profiles could be altered by the use of different commercial molecular sieves. All of these experiments described are carried out using an amount of 10 g of catalyst in the furnace tube.

Pyrolysis of up to 1 g of benzamide under the optimised conditions (500 °C) yields only benzonitrile – no unreacted benzamide is found in the product trap. An experiment was carried out to determine the reaction scale limit at which this would cease to be the case. This was carried out by placing a large quantity of benzamide in the inlet of the FVP apparatus and conducting the pyrolysis under optimised conditions until benzamide appeared unchanged in the product trap. This could be easily determined due to the relative volatilities of starting material and product. Benzamide condenses almost immediately on exiting the furnace whilst benzonitrile remains in the gas phase until reaching the liquid nitrogen level in the product trap. The reaction was then monitored by eye and was stopped when benzamide was seen to condense in the outlet. On collection, drying and weighing of the pyrolysate it was found that approximately 10^{-2} moles of reaction had taken place, just over 1 g. It was also found that some 80% of the water released by the reaction had been collected in the product trap. Although the 20% discrepancy may be responsible for the deactivation of the sieves it seems more likely that this is within the bounds of realistic experimental error for the procedure as described. In a later experiment, described below, water passed through sieves at 500 °C was recovered quantitatively, though the sieves were deactivated as a result. On subjecting the sieves to the usual preparation protocol (in an attempt to regenerate them to full activity) and then repeating this experiment, benzamide was seen to condense in the product trap immediately. The activity of the molecular sieves is therefore damaged irreparably by reaction.

The stability of the molecular sieves to prolonged heating was investigated by a similar experiment. The procedure as described above was carried out after heating the catalyst at 500 °C for 16 h beforehand. This was certainly found to have a deactivating effect. Only ~ 250 mg of benzamide was reacted before it was seen to condense unchanged in the FVP outlet. This corresponds to a 75% drop by comparison with the untreated catalyst. However, it is not clear whether the catalyst has simply “switched off” or whether it is still active, while not giving 100% conversion to nitrile. To investigate this, a batch of 5 g of benzamide was pyrolysed under the standard conditions. This gave a 4.17 g (85%) yield of benzonitrile while 0.67 g of unreacted benzamide was also collected. This shows that the zeolite is still active, if less so, for dehydration on scales greater than 1 g. The continued deactivation of the catalyst was followed by a further series of experiments. Benzamide was pyrolysed over molecular sieves at 500 °C, prepared as normal, in successive batches of 5 g, *i.e.*, a batch of amide (5 g) was reacted, the products collected, and another batch of amide (5 g) was immediately reacted. This was repeated for 5 batches giving the results shown in figure 6.

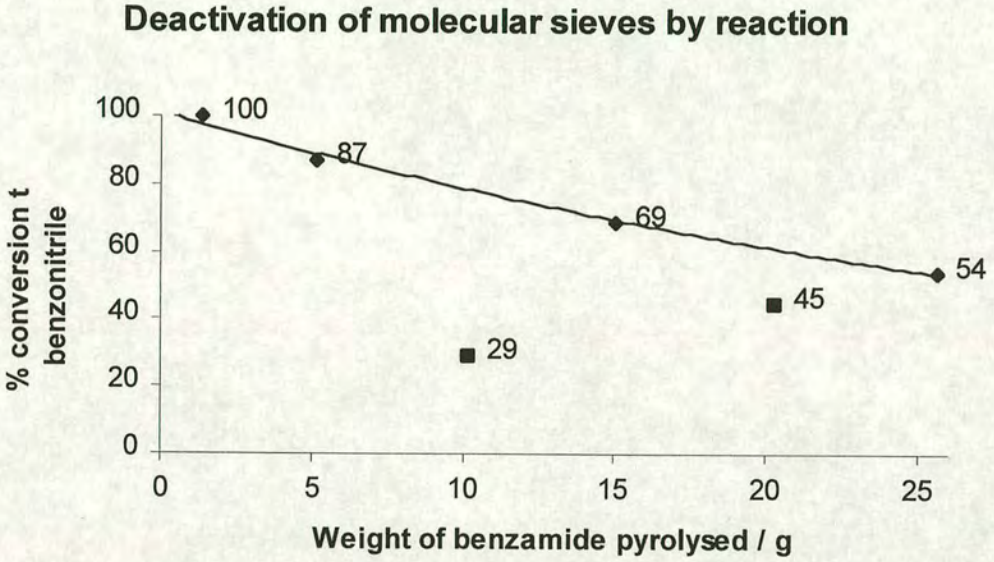


Figure 6

The first thing to note from the graph is that 54% conversion is still achieved, even after reaction up to a 25 g scale. It should be reiterated at this point that only nitrile and unreacted amide are present in the product mixture. The points at 10 and 20 g which have been omitted from the trend line reveal another interesting point to note. These figures result from an experimental anomaly arising from a change in inlet tube geometry. This resulted in the introduction of benzamide to the furnace at an increased rate which in turn resulted in a decrease in conversion. For example, the third point on the graph arose from a reaction occurring over 40 mins while the second was complete over two hours, with the same inlet temperature and amount of starting material. This apparent sensitivity to throughput rate is not usually observed in a normal, uncatalysed FVP experiment except in extreme cases.[65] It can easily be imagined that an increased concentration of reactant at the catalytic sites would result in this decrease in activity.

Since it had already been established that the molecular sieve catalyst could be deactivated both by reaction and simply by heating, further investigation of the result depicted in figure 6 was necessary. Looking at the graph, the conversion of 54% achieved after reaction of ~25 g of benzamide may have been caused by prolonged heating alone. The molecular sieves had, prior to reaction of this final portion, remained in the furnace at 500 °C for 9 h. A further experiment in which benzamide (5 g) was pyrolysed over molecular sieves which had been heated for 9 h but not exposed to reaction gave high (84%) conversion. Benzamide was seen to condense in the product trap immediately upon starting this reaction. This correlates with the conversion achieved (87%) in the pyrolysis of the first 5 g portion. However, the appearance of unreacted benzamide in the product trap immediately on commencing the reaction indicates that prolonged heating does have a deactivating effect on the initial high activity of the catalyst though it is not responsible for the further deactivation observed in figure 6. This apparent discontinuity in the behaviour of the active sites of the catalyst seems to suggest the presence of sites of differing activity within the catalyst, with differing stability. Very active sites are responsible for 100% conversion (under our optimised conditions) on a small scale of up to 1 g: these sites are also deactivated more easily, especially by heating alone.

Other, slightly less active sites are however more stable to heating and retain activity on a larger reaction scale.

Although we know from earlier experiments that water formed during the dehydration is largely unretained in the molecular sieve, it was thought that it could nonetheless be responsible for the deactivation. To investigate this, an experiment was devised in which the molecular sieves were first treated by vaporising water through the system and then used in the reaction of a 5 g batch of benzamide. The amount of water passed across the catalyst was equal to the calculated amount which would have been formed during reactions of the first four 5 g batches depicted in figure 6, *i.e.*, the amount to which the sieves were exposed before the final batch was reacted. In mimicking the conditions (with regard to water) under which this final batch was reacted, a startling correlation was discovered. This reaction gave 47% conversion to benzonitrile (*cf.* 54%). Thus the deactivation of catalyst by reaction is almost completely caused by the water formed during the deactivation *even though the majority of this water is collected intact afterwards*. This is the case except for a small proportion of very active sites which are unstable to heating at 500 °C.

The initial high activity of the catalyst, defined by the amount of reaction which can take place at a level of 100% conversion, was also shown to be sensitive to water. The deactivation of these highly active sites with respect to water was investigated in a controlled manner. Weighed amounts of water were vaporised over molecular sieves (fresh for each experiment) and the subsequent dehydration of benzamide was carried out. In each case the water which passed through the furnace was collected and weighed before carrying out the dehydration reaction, with no discrepancy between the amount used and the amount collected. The conversions achieved before the appearance of unreacted starting material in the product trap in these experiments are shown in figure 7.

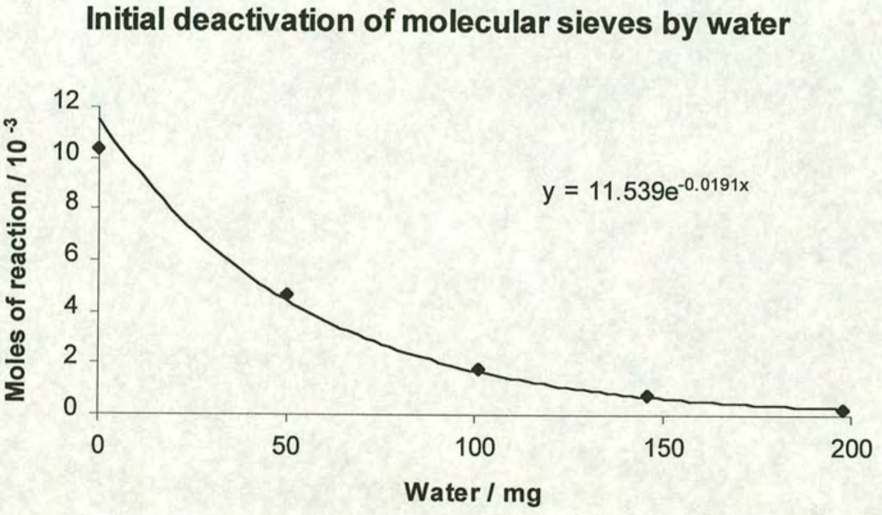


Figure 7

This graph shows a remarkable exponential relationship between the initial activity of the catalyst and its exposure to water. This correlates to a first order deactivation of these active sites with respect to the presence of water. Figure 8 demonstrates this further, plotting log (moles of reaction) versus water.

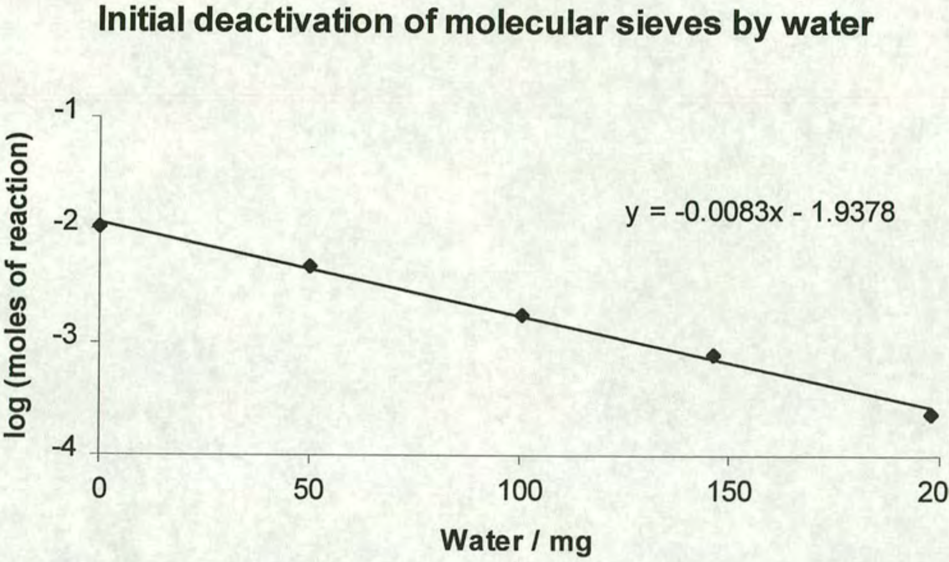


Figure 8

This first order dependence of destruction of zeolite active sites with respect to water cannot be fully explained without further experimentation. As was mentioned earlier, the pore size of 3A molecular sieves precludes entry to the framework by organic materials. This being the case, we would expect the dehydration reaction to take place on the surface of the zeolite. The damage done to the zeolite surface by contact with water could possibly be investigated by X-ray powder diffraction which would perhaps clarify this first order relationship.

Summary of 3A molecular sieves as dehydration catalyst

The deactivation of 3A molecular sieves as a catalyst in the dehydration of benzamide to benzonitrile was investigated by a number of key reactions. The main points to note are:

1. The sieves are deactivated by reaction on a reaction scale >1 g substrate per 10 g catalyst. After reaction of 25 g of benzamide the catalyst operates at only about 50% activity.
2. Different types of active site are present in the catalyst. The most active sites are the most easily deactivated, sensitive to reaction and heating. Other, more robust active sites are stable to heating but not to reaction.
3. During reaction, it would appear to be the water formed which is responsible for the deactivation, though this is not retained in the molecular sieve.
4. This deactivation by water can be described mathematically with a strong exponential correlation between amount of water to which the sieves have been exposed and amount of reaction.

Clearly, although the method developed to this point looks useful for small scale preparation, it is of little use in terms of a realistic process. Since 3A molecular sieves appear to be too sensitive to the reaction other commercial molecular sieve catalysts were investigated.

Firstly, 5A molecular sieves were used. As discussed in section 1.1.2, these incorporate calcium as counter ion rather than sodium, accounting for the increase in effective pore size to around 5 Å. Although these are generally regarded as a less useful drying agent than 3A sieves, it was hoped that catalytic activity would still be apparent. Indeed this turns out to be the case. On packing the furnace tube with 10 g of 5A sieves and preparing them for use as before, a 5 g batch of benzamide was dehydrated to benzonitrile with 87-94% conversion. This is basically the same conversion achieved using 3A sieves. Benzamide was seen to condense in the product trap immediately on commencing the reaction so the initially very active sites observed when using 3A sieves do not appear to be present. Once again, no side reactions had taken place and unreacted starting material was the only other compound present in the product mixture.

To investigate the stability of the 5A sieves to reaction, an experiment was carried out using consecutive 5 g batch reactions over the same portion of catalyst, as previously carried out for 3A sieves (see figure 6). The results obtained from these reactions are shown in figure 9.

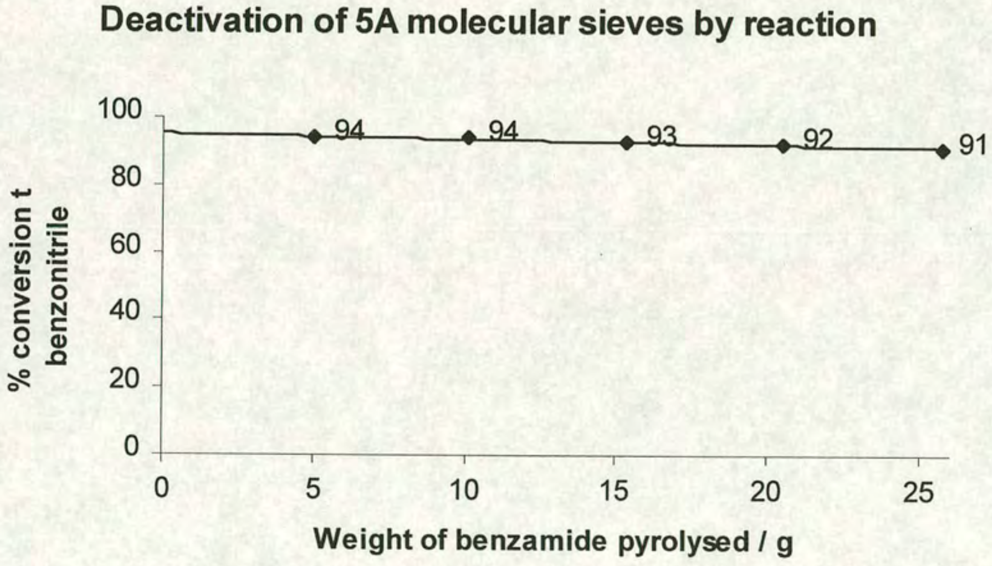


Figure 9

It can be clearly seen from the graph that 5A molecular sieves offer increased stability to 3A, giving greater than 90% conversion even after reaction of 25 g of benzamide over 10 g of molecular sieves. This stability increase can be explained in terms of the cation occupancy of the zeolite. It is known that A type sieves have 8 sites per unit cell which are "preferred" cavities for cation occupancy. In 3A molecular sieves, which contain potassium ions (and indeed any other A type sieve with univalent cations), 12 cations compete for these cavities. In 5A, which contain divalent calcium ions, only 6 compete for these cavities. Therefore it is not the 5A molecular sieve which has special stability, but the 3A which is destabilised by its cation occupancy characteristics.

Given this increased stability, it was thought that perhaps the 5A molecular sieves could be used at higher temperatures. Reaction of benzamide (5 g) at 600 °C however gave 95% conversion to benzonitrile but with reduced accountability, resulting in only 77% yield. A small amount of benzamide is recovered unconverted.

A third type of molecular sieve was also tried as a potential catalyst for this reaction. Li^+ exchanged sieves were prepared in the hope of creating a more hygroscopic zeolite than the commercially available A type sieves. The method of preparing ion-exchanged sieves used is a simple one, based upon a literature method,[63] but which nonetheless exhibited some practical problems. Basically, the 4A (Na^+) zeolite is heated at reflux in relatively concentrated lithium chloride solution for 2 days. The solution is then drained and the process repeated a further twice. This is a more rigorous method than that described in the reference given, whereby the sieves were soaked in LiCl solution for several hours and the process was not repeated a further twice. This apparently straightforward procedure, however, proved troublesome. If the mixture was not stirred then extremely violent bumping of the solution occurred, leading to ejection of material from the top of the condenser. If the mixture was stirred (this required mechanical stirring) then the molecular sieve pellets were effectively ground down to a very fine powder, unsuitable for use in the FVP system. Thus a balance had to be found between excessive stirring and excessive bumping and this was achieved to some extent by stirring slowly and also protecting against the effects of bumping by fitting a length of tubing to the top of the condenser leading to the sink. It would seem that the practicalities of the ion-exchange process are more compatible with powdered molecular sieves than with those which are already in pelleted form. Nonetheless, sufficient beads were prepared intact for use in the gas phase catalytic dehydration of benzamide. The incorporation of lithium into the molecular sieve was not measured, having followed the literature procedure and enhancing it to ensure completion.

Unfortunately, the Li^+ exchanged molecular sieves offered no improvement in activity over 3A or 5A sieves as shown in figure 10.

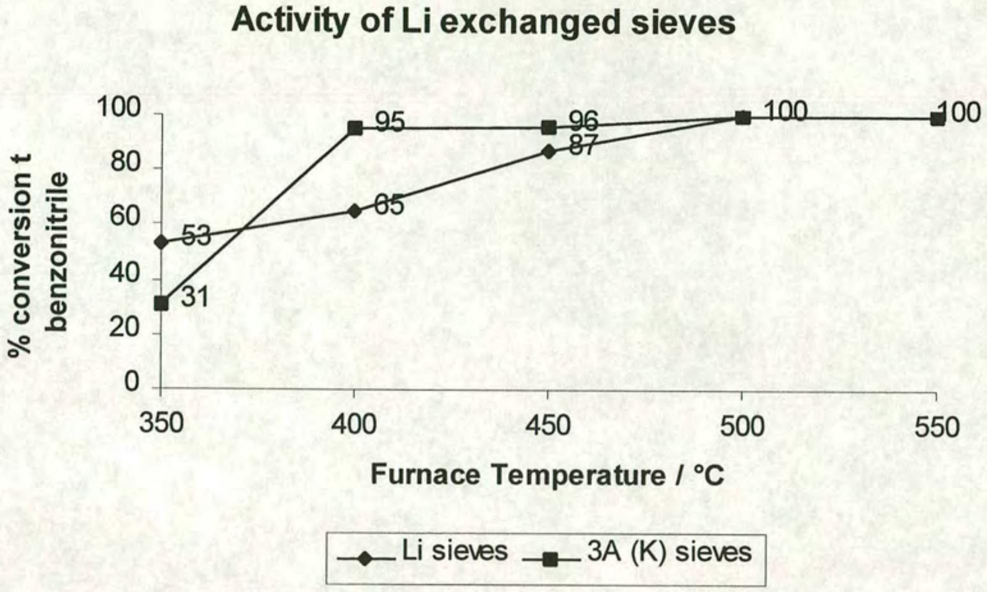


Figure 10

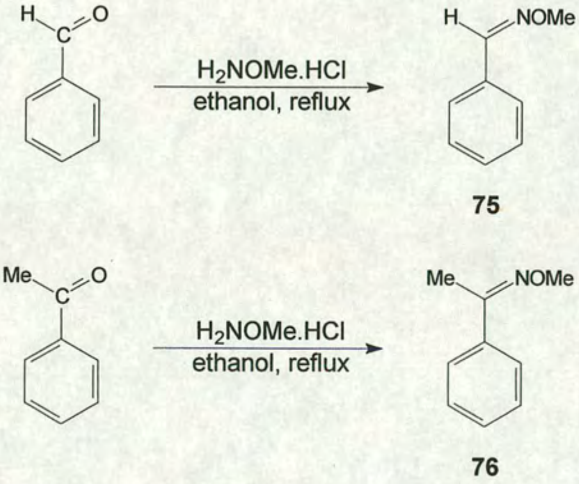
Also, the accountability for material was low in each case such that at 500 °C, only a 50% yield of benzonitrile was achieved.

Summary of other molecular sieves as dehydration catalyst

1) 5A molecular sieves are slightly less effective than 3A molecular sieves on a small scale but are vastly more robust, giving essentially no decrease in activity up to a 25 g reaction scale.
2) The 5A molecular sieve shows reduced activity at temperatures higher than 500 °C.
3) Li^+ exchanged molecular sieves offer no improvement to the process over 3A or 5A although this could be due to difficulties experienced in their preparation.

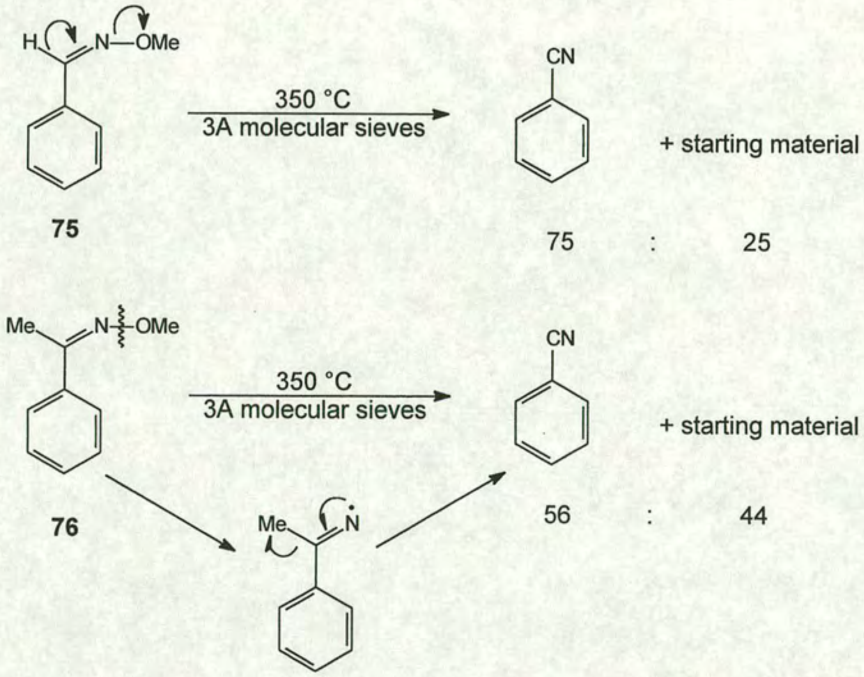
1.1.5 Elimination from *O*-methyl oximes

Although an insight has now been gained into the stability of the molecular sieves and how their activity can be altered, no information has been gained on their role in the mechanism of the dehydration. To investigate this *O*-methyl oximes **75** and **76** were prepared as shown in scheme 44.



Scheme 44

Cleavage of the N—O bond from these substrates is a standard method for the generation of nitrogen centred radicals by flash vacuum pyrolysis.[66] This process would normally occur to 100% conversion at a temperature of 650 °C in an unpacked furnace tube and indeed on carrying out this process, 100% conversion to benzonitrile was obtained from acetophenone *O*-methyl oxime **76** (scheme 45). Thus, by analogy, conversion to benzonitrile from **76** at lower temperatures over molecular sieves would suggest at least a radical element to the mechanism of dehydration. In contrast, no C—C bond cleavage is required in the reaction of benzaldehyde *O*-methyl oxime **75** and the formation of benzonitrile can be rationalised by β elimination. The results obtained from pyrolysis of **75** and **76** over 3A molecular sieves and the mechanistic details are shown in scheme **45**. It should be noted that these experiments were carried out on an NMR scale and isolated yields of products were not pursued.



Scheme 45

These results suggest two things. Firstly it appears that there may indeed be a radical element to this dehydration, indicated by conversion of **76** to benzonitrile. This presumably takes place by the relatively easy elimination of a methyl radical from the N-centred radical formed by N—O cleavage. The higher conversion obtained from **75** however, suggests that the radical pathway does not dominate.

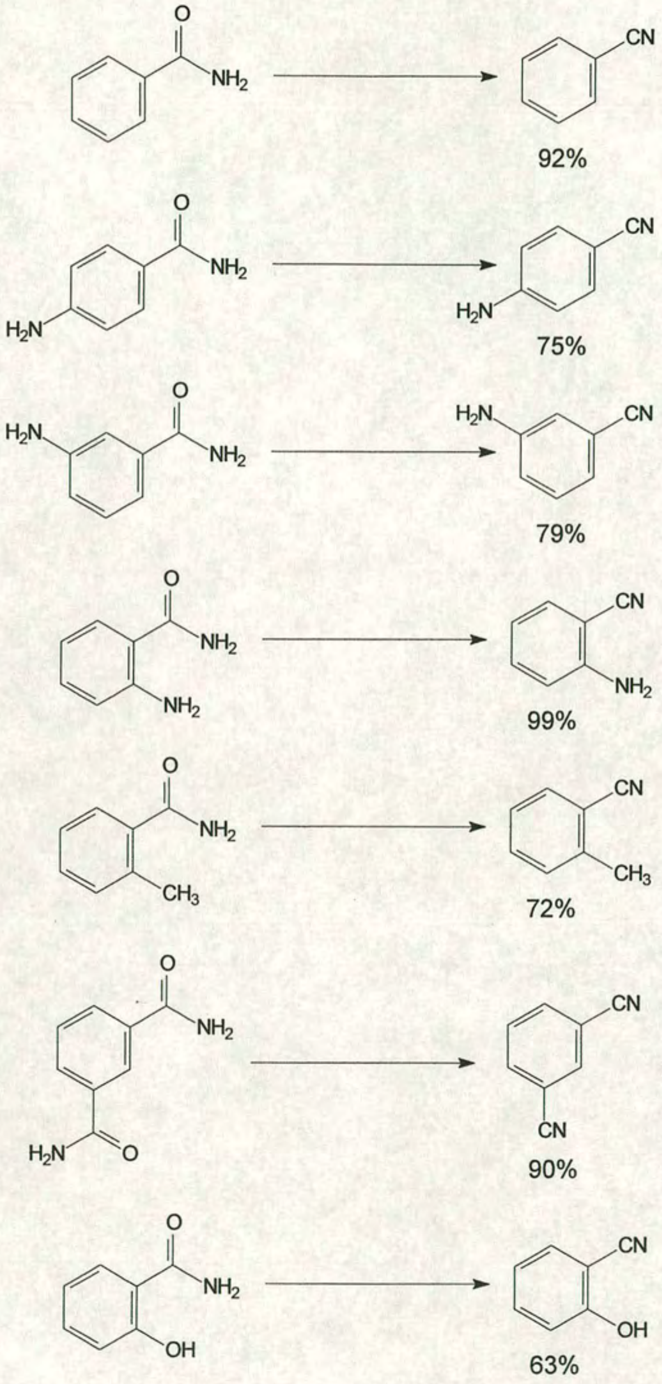
Secondly it appears that the molecular sieves catalyse this N—O cleavage. Pyrolysis of **76** over 3A sieves at an increased temperature of 450 °C gave 90% conversion to benzonitrile. Under normal FVP conditions, much higher temperatures of 600-650 °C would be required to generate this amount of the N-centred radical. These results were checked by a simple control experiment. Pyrolysis of **76** over silica beads of similar size to the 3A molecular sieve beads at 350 °C gave no conversion to benzonitrile whatsoever.

1.1.6 Preparative scale dehydration of amides by FVP

Having optimised conditions for amide dehydration by FVP and also investigated the catalyst activity using benzamide as a standard, the process was then utilised in the preparation of other aromatic, heteroaromatic and aliphatic nitriles. It should be stressed that the conditions employed for these dehydrations were those detailed earlier, optimised for benzamide. The optimisation procedure described has provided a robust, lab-scale method, with none of the toxicity or work up problems highlighted earlier for solution phase methods. It was therefore hoped that this would prove to be of general utility, although there are a large number of variables apparent in this process and there would be further scope for optimisation for each substrate.

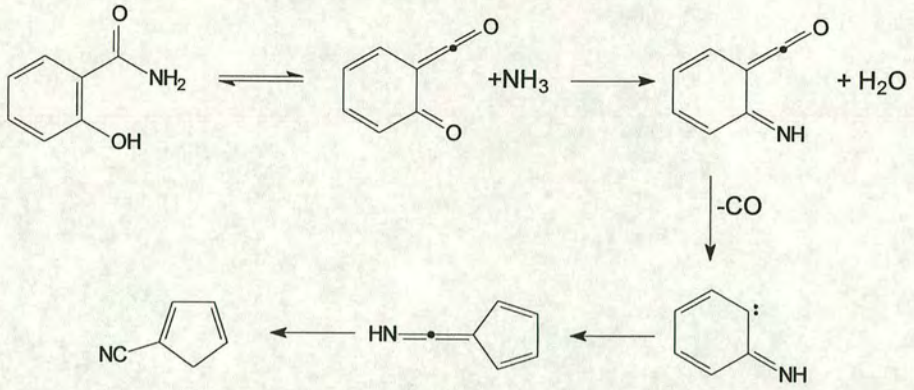
Scheme 46 shows the dehydration of a number of aromatic amides to the corresponding nitriles. All of the amides shown were commercially available. The dehydration of benzamide to benzonitrile is shown at the top, in 92% yield. *Para-* and *meta-* amino benzonitriles were also prepared in high yield. The dehydration of *ortho-* substituted derivatives was carried out to investigate the possibility of any side reactions taking place. In all but one example, no competing processes were apparent and no other components were found in the products, with the amino substituted amide dehydrating in almost quantitative yield. In the preparation of *o*-cyanophenol, the lowest yielding process and the only one in which column chromatography was required for isolation, a second component was identified. This was found to be 1-cyanocyclopentadiene **78** (3% yield) and a suggested mechanism for its formation is shown in scheme 47.

Preparation of the dinitrile, isophthalonitrile, in 90% yield further emphasises the utility of this method.



Conditions used: 10^{-2}-10^{-3} moles of substrate (< 1 g) pyrolysed at 500 °C over 10 g of 3A molecular sieves.

Scheme 46

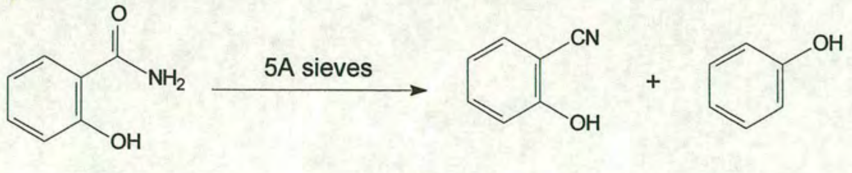


78 **77**

Scheme 47

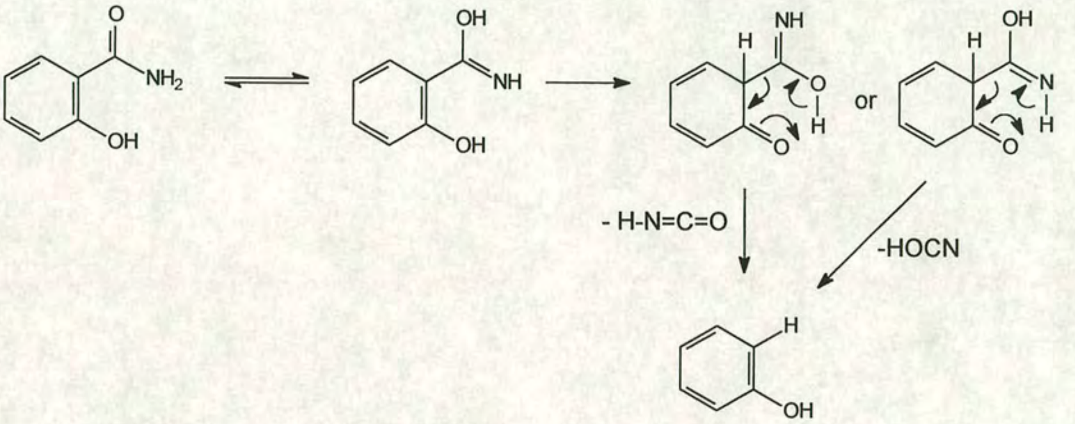
The final steps of this mechanism from the iminocarbene **77** have been proposed before[67] and it is well precedented that formation of this kind of intermediate in the gas phase leads to ring contraction to 1-cyanocyclopentadiene **78**.[68] This compound dimerises on formation and is identified as such.

Given the lower yield of *o*-cyanophenol under these conditions, its preparation was attempted using 5A molecular sieves. The conditions used were otherwise the same. As shown in scheme 48, this gave a similar yield of product (~66%) but also yielded an appreciable amount of phenol (~34%).



Scheme 48

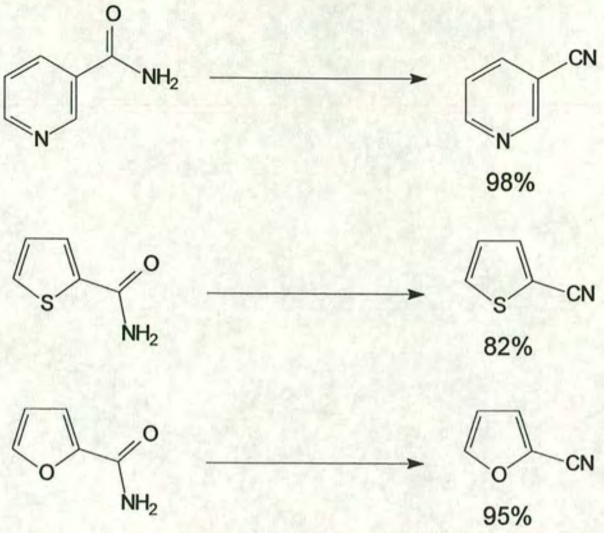
This experiment was also carried out at a lower temperature of 450 °C in an attempt to stop this phenol formation. This, however, gave an almost identical result. A suggested mechanism for the formation of phenol is shown in scheme 49.



Scheme 49

This involves the extrusion of a small molecular entity which is a highly favourable process under FVP conditions. This mechanism is supported but not proved by an experiment in which deuterium exchanged salicylamide was pyrolysed. This was first prepared by crystallisation of salicylamide from MeO[^{2}H]. When pyrolysed under the dehydration conditions, this yielded a product, the ^{2}H NMR spectrum of which exhibited a large peak at around 6.8 ppm. This is the area in which the *ortho*-hydrogens appear in phenol, supporting the mechanism proposed above.

Scheme 49 shows the preparation of some heteroaromatic nitriles which, as can be seen, were obtained in excellent yield.

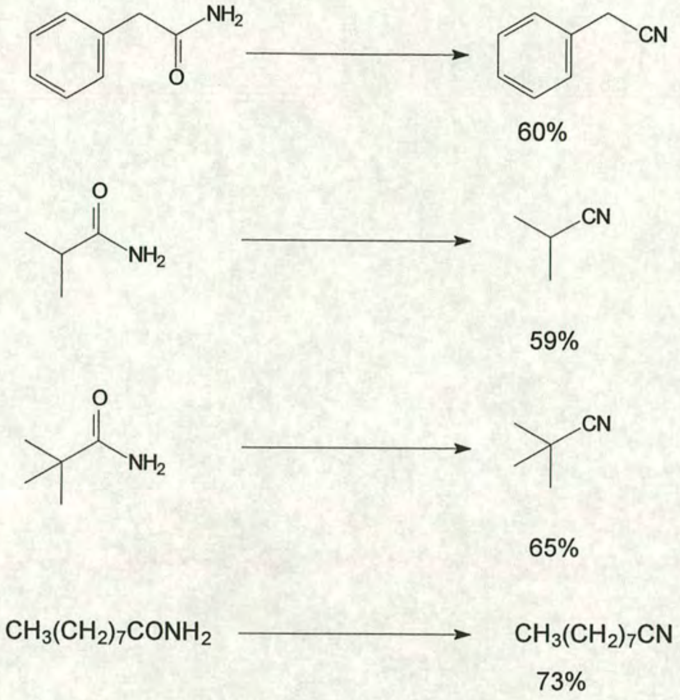


Scheme 50

Of the three amide precursors shown, the thiophene and pyridine derivatives were commercially available. The furan derivative was prepared in 81% yield by heating of 2-furoic acid with thionyl chloride and then displacement with ammonia.

Of particular note are the high yielding preparations of 2-thiophenecarbonitrile and 2-furancarbonitrile. Both can be prepared in two steps from the relatively inexpensive acid to the more valuable nitrile product in good yield.

The dehydration of aliphatic amides was also investigated, as shown in scheme 51.



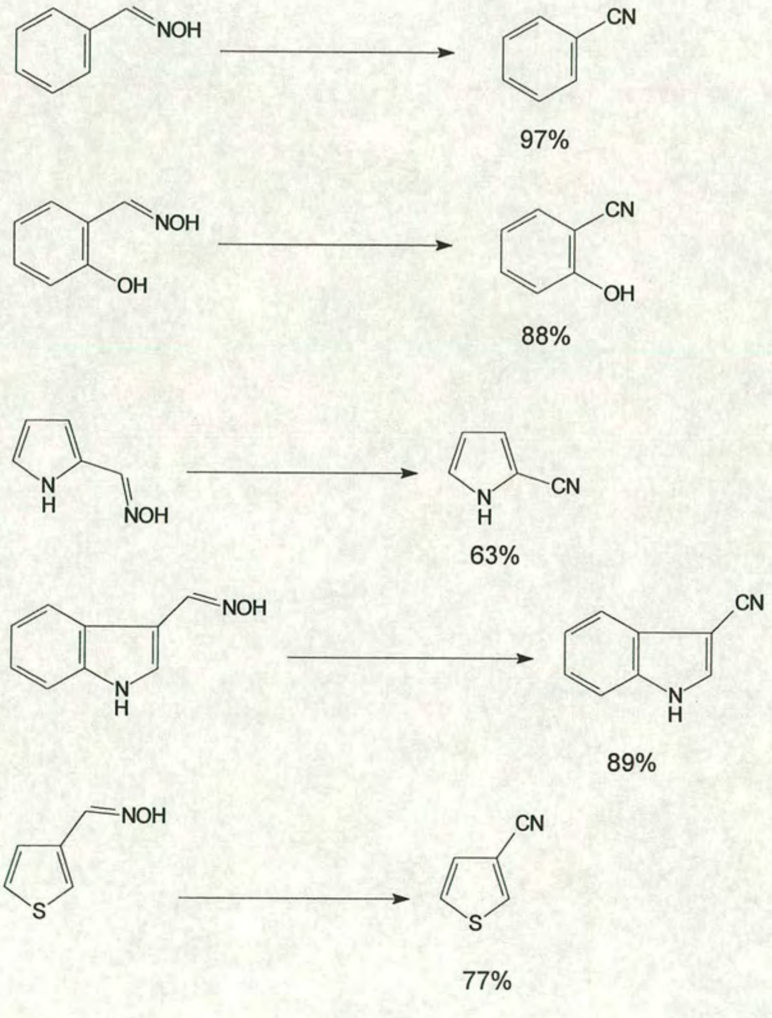
Scheme 51

All of the amide precursors shown were commercially available. The slightly lower yields apparent in this series of preparations are probably at least in part due to the difficulty of collecting these fairly volatile products, especially the di- and tri- methyl acetonitriles. In each case, no other products were detected, furthering the utility of the dehydration method to the clean preparation of aliphatic nitriles.

Overall, a general lab-scale method has been developed for the dehydration of amides to nitriles. The process is clean and efficient, involves little work up and does not suffer from the need for acidic reagents. No by-products, toxic or otherwise, are obtained. The method is both easy to carry out and does not require long reaction times.

1.1.7 Preparative scale dehydration of oximes by FVP

The optimised conditions for the dehydration of oximes [350 °C, 3A molecular sieves (10 g)] were employed in the preparation of a number of nitriles. The results obtained are shown in scheme 52.

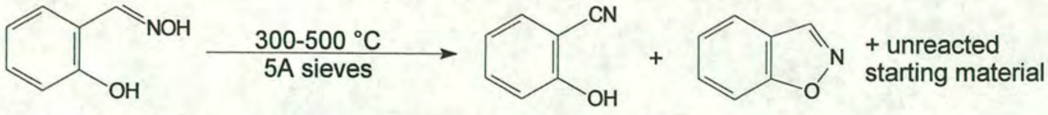


Scheme 52

It can be seen that all of the dehydrations shown were carried out in good to excellent yields. All but salicylaldoxime were unavailable commercially and were prepared by condensation of the corresponding aldehyde with hydroxylamine hydrochloride.

Salicylaldoxime was pyrolysed in an attempt to improve upon the relatively poor conversion obtained from the amide. Indeed, this works extremely well, giving a yield of 88%. Again, heteroaromatic nitriles were prepared efficiently. Since this process is effectively based upon an aldehyde precursor, this makes available different substitution patterns from the amides in the cases where the aldehyde is more readily available than the corresponding acid. In the case of the pyrrole derivative, the actual yield of the process is almost certainly much higher than that shown. The lower yield obtained was due to the comparative involatility of pyrrole-2-carbaldoxime in the FVP inlet tube.

The dehydration of salicylaldoxime was also carried out over 5A molecular sieves, to investigate whether the increased stability shown by this catalyst in the dehydration of amides also applied for oximes. In the event, this proved to be difficult to explore, as side reactions became apparent. Scheme 53 shows the problems which were encountered in these reactions.



79

Scheme 53

Formation of 1,2-benzisoxazole **79** becomes apparent, especially at lower temperatures. This was identified mainly from the ^{13}C NMR spectrum of the crude product mixture, with supporting evidence from the ^{1}H NMR spectrum At higher temperatures formation of *o*-cyanophenol predominates but recovery of material drops to around 65%. Figure 11 follows the formation of these products with changing temperature.

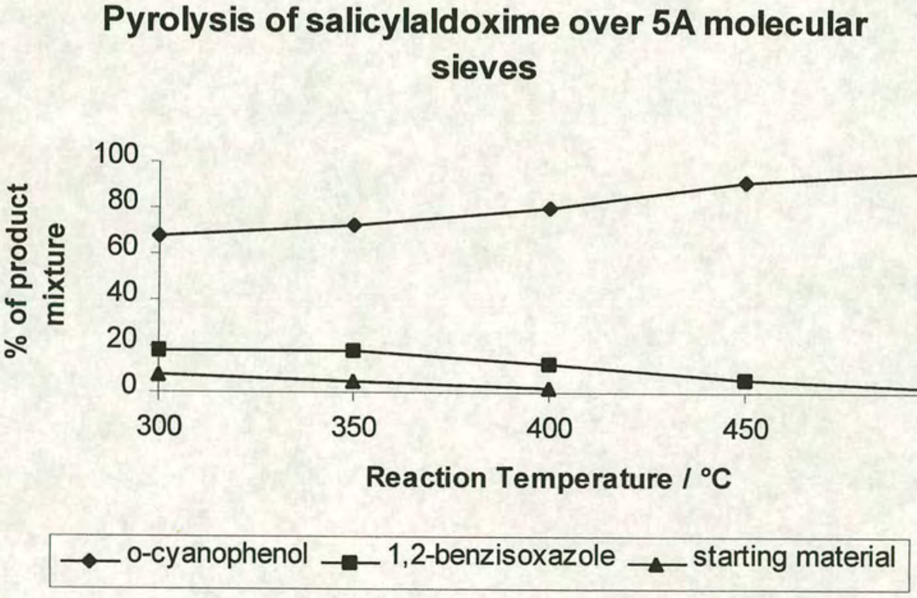


Figure 11

The graph shows the increase in conversion from starting material to products with increasing temperature. Unfortunately this coincides with a decrease in accountability for material, keeping yields relatively low. The graph also shows the decrease in the amount of 1,2-benzisoxazole **79** formed with increasing temperature.

Indeed, in a separate experiment, **79** was found to convert to *o*-cyanophenol quantitatively at 500 °C. It would seem from this that 1,2-benzisoxazole **79** lies on a possible reaction pathway from salicylaldoxime to *o*-cyanophenol but to what extent this predominates is unknown.

Summary of preparative scale dehydrations

The preparative utility of this catalytic gas phase dehydration method has been inarguably demonstrated, with the preparation of a number of example nitriles in excellent yields and selectivity. The scope of the method itself is vast: many more molecular sieves, both commercially available and synthetically prepared could be applied. For any required substrate, the number of experimental variables is large enough to warrant a scheme of optimisation specific to the target.

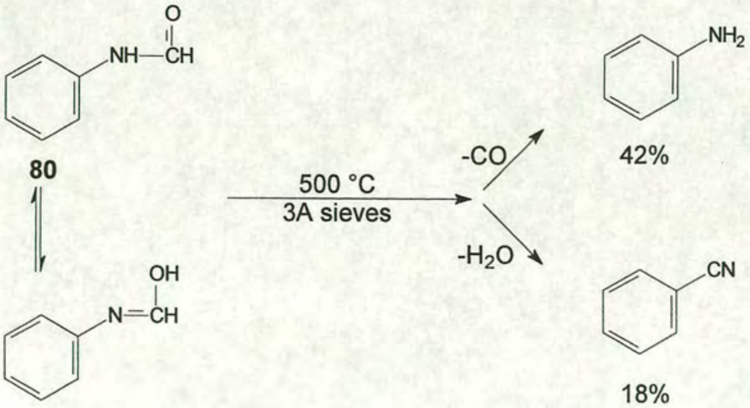
The fact that the method is applicable to both amides and oximes gives an even wider range of possible precursors and perhaps the option of less vigorous conditions in the preparation of sensitive compounds, as highlighted by the example preparation of 2-cyanopyrrole. The method is clean, reproducible and gives high yields. Few by-products are observed and both the method and work up are quick and convenient. No toxic gases are evolved and no acidic reagents are required. It would seem therefore that this gas phase method is a useful addition to the methodology available for the preparation of nitriles by dehydration.

1.2 Other eliminations mediated by FVP over molecular sieves

1.2.1 Deprotection of formylated/acetylated secondary amines

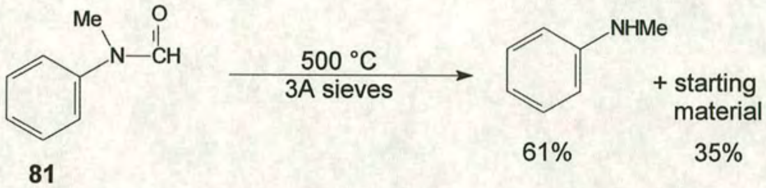
The common protection strategy for amines, that of acetylation, suffers from the relatively vigorous conditions required for subsequent deprotection. For example, one quoted cleavage protocol for acetylated amines describes reflux in 1.2M acid for 9 h, resulting in only 61-77% yields.[69] This is obviously an extremely undesirable process and yield for a deprotection step. Formylated amines are similarly difficult to cleave, with reagents such as hydrazine being necessary and yields of as low as 60% obtained.[70] The conditions developed for the gas phase preparation of nitriles potentially offer a mild and selective method for this step.

Interest in this process arose when an attempted dehydration of formanilide **80** gave an unexpected result as shown in scheme 54.



Scheme 54

Dehydration did take place, giving benzonitrile after rearrangement of the initially formed isonitrile but the major product formed was aniline, by decarbonylation. Given this result, it was attempted to block the dehydration reaction by pyrolysing *N*-methylformanilide **81**, hopefully to give a clean conversion to *N*-methylaniline. Scheme 55 shows the result of this attempt.

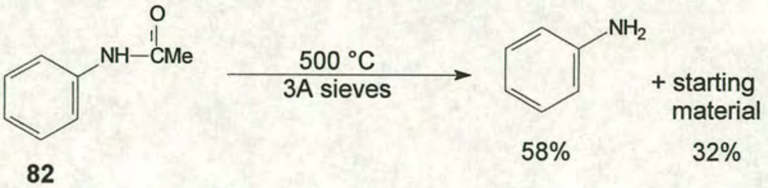


81

Scheme 55

Indeed the decarbonylation process is the only one which takes place, although an appreciable amount of starting material remains unreacted.

In the corresponding pyrolysis of acetanilide, aniline was obtained (scheme 56).

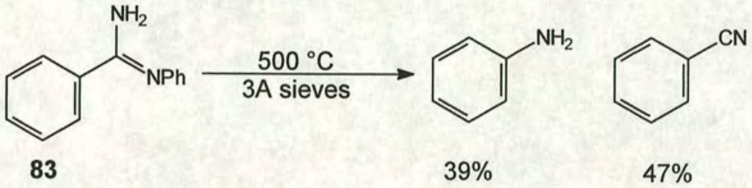


82

Scheme 56

This seems to indicate that cleavage of the N—C bond is taking place, followed by abstraction of a hydrogen atom. Although this requires extensive further investigation, a potentially useful process for the deprotection of secondary amines has been uncovered. This method has all the advantages provided by flash vacuum pyrolysis methods in general: low contact time (therefore higher selectivity), reagent/solvent free chemistry and easy collection and work up.

In this vein, the same method has also been used to cleave *N*-phenylbenzamidine to aniline and benzonitrile as shown in scheme 57.

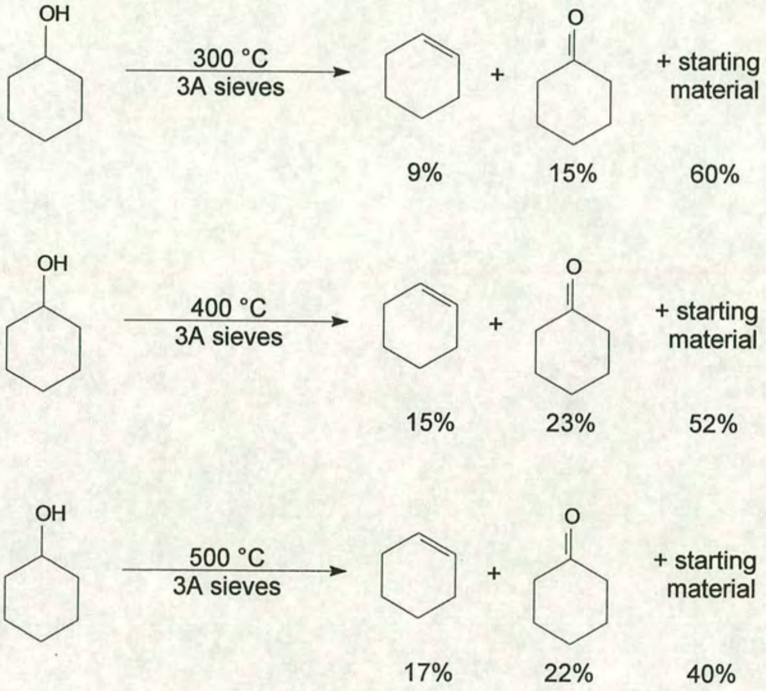


Scheme 57

Since this is the reverse of the usual preparation of amidines, this process is unlikely to be of great preparative utility, but gives further evidence of the possibilities this methodology carries.

1.2.2 Dehydration of cyclohexanols

Having found a successful dehydration protocol for the preparation of nitriles, the possibility of an extension of this method to the preparation of alkenes from alcohols was investigated. The dehydration of cyclohexanol to cyclohexene was chosen as a test reaction for this purpose. Scheme 58 shows the results obtained at differing temperatures from the pyrolysis of cyclohexanol over 3A molecular sieves (10 g).

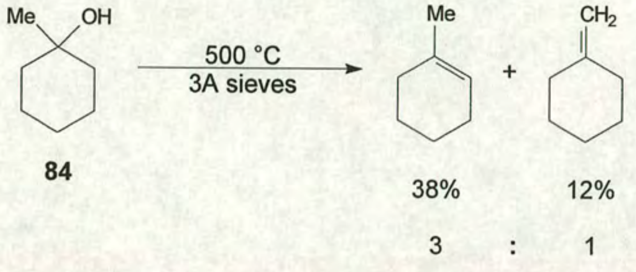


Scheme 58

The yields shown are calculated by addition of a known amount of a reference compound to the ^{1}H NMR sample and do not refer to isolated products.

Although the main component in the product mixture at all temperatures (300-500 °C) is unreacted cyclohexanol, most surprising is the formation of cyclohexanone by dehydrogenation. This also seems to be a more favourable process even than the dehydration to cyclohexene.

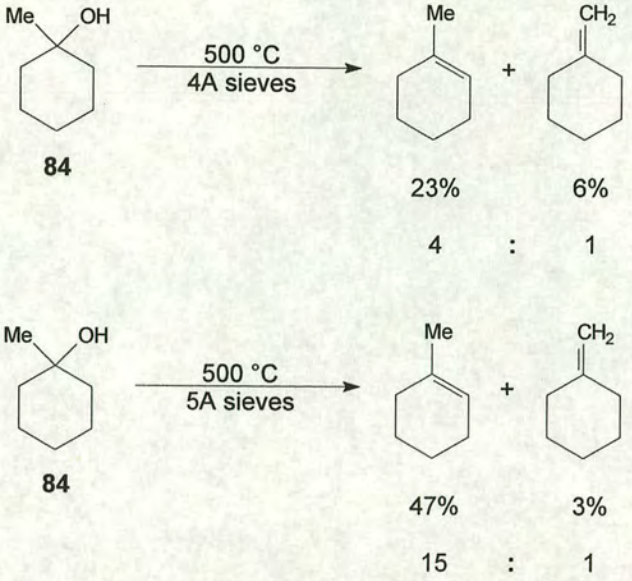
This dehydrogenation process can be blocked by using 1-methylcyclohexanol **84** as the test substrate. The result obtained by pyrolysis of **84** at 500 °C over 3A molecular sieves is shown in scheme 59.



Scheme 59

Again, yields are calculated from the ^{1}H NMR spectrum. In each case, poor accountability for material was obtained, although this could be due in part to the volatility of the products formed.

It can be seen that several things have occurred. Firstly the process leads to greater conversion – no starting material (or by-product) is found in the product mixture. Secondly, only dehydration processes have taken place. This has led to the formation of *exo* and *endo* alkene products. The reaction favours the formation of the *endo* alkene by a factor of about three. It seemed possible that this selectivity could be altered by using molecular sieves of different pore sizes and scheme 60 shows the results of such an investigation.



Scheme 60

As in the reaction shown in scheme 59, poor material recovery was obtained, thought to be due to the volatility of the products. The use of different molecular sieves makes a dramatic difference to the product distribution. With sieves of larger (~5 Å) pore size, the process is almost entirely selective for the cyclohexene product. This alteration of the reaction pathway points to an exciting possibility for the future utility of this kind of method, with selectivity perhaps being amenable to even finer control with more exotic zeolite catalysts.

In carrying out these dehydrations using solution phase methods, the Zaitsev product usually predominates, in line with our results.[71] In direct comparison with scheme 60, a ratio of 95:5 (methylcyclohexene:methylenecyclohexane) was obtained in the dehydration of 1-methylcyclohexanol using copper triflate catalyst.[72]

Summary of miscellaneous molecular sieve catalysed processes

Although most of the research carried out on this catalytic system has been directed toward the preparation of nitriles, the small number of other reactions carried out has exposed its vast potential. From a process seemingly involving bond cleavage for mild deprotection to product selectivity alteration, a number of important observations have been made which will hopefully provide a starting point for the further development of this work. In each of these latter uses for zeolites as a catalyst in gas phase chemistry, only some initial investigations have been made, highlighting some areas which may be worth further investigation, but clearly no further preparative utility has been described.

1.3 Conclusions and future work

Using flash vacuum pyrolysis (FVP) methodology and incorporating the use of solid catalysts, a preparative process for the preparation of nitriles by dehydration has been developed. This has been applied to a number of amides and oximes, aromatic, heteroaromatic and aliphatic. Research has also focussed on the role of the catalyst in this process and work has been carried out towards making this a truly catalytic process wherein the catalyst can be reused indefinitely. The fate of water produced and the catalyst deactivation pathways have been investigated extensively.

Following this, the further utility of the method was studied. This has produced some leads for future development and has also given some important information as regards the scope of such methodology.

Future work in this area should focus upon finding further use for this method in real synthetic applications. The potential for FVP coupled with catalysis to make an impact in the realm of synthetic methodology looks promising and in the following chapters further evidence will be presented for this.

Molecular sieves and zeolites in general are a vast family of materials with widely differing properties. Although this project has essentially used the simple precept of using a drying agent for a dehydration reaction, the scope for much finer control over reactions exists.

2. Catalytic dehydrogenations under FVP conditions

2.1 Aromatisations

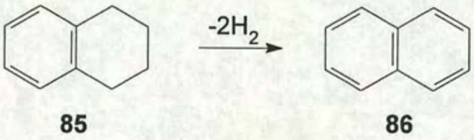
2.1.1 Introduction

The dehydrogenation of polycyclic hydrocarbons to aromatic and cyclic olefinic molecules is frequently the last step in the synthesis of polycyclic aromatic hydrocarbons and their derivatives. This topic was the subject of a review article in 1978, highlighting the general observations detailed below.[73] Traditionally, platinum group metals are used catalytically for this process requiring the use of high boiling solvents and temperatures of up to 500 °C. These forcing conditions have obvious ramifications for the dehydrogenation of sensitive substrates and loss or modification of side groups on the rings is possible. Other methods include the use of sulfur and selenium. This again requires high temperatures (generally around 250-300 °C) and has the further drawback of the formation of highly toxic and odorous by-products (H_2S and H_2Se). Quinones are also classically a popular reagent for these transformations. DDQ, the most effective of these, is sensitive to hydrolysis with evolution of hydrogen cyanide, requiring anhydrous conditions for its use. Side reactions can also take place, most commonly Diels-Alder reactions, where the quinone acts as a dienophile. The reactions generally take place at reflux in moderately high boiling solvents such as toluene or xylene and these solvents must be dried thoroughly before use.

In the introduction section of this thesis, several gas phase methods for dehydrogenation were described, some applicable to aromatisation. It is the aim of the work described here to develop a robust catalytic gas phase process for the selective dehydrogenation of polycyclic hydrocarbons.

2.1.2 Optimisation of aromatisation conditions

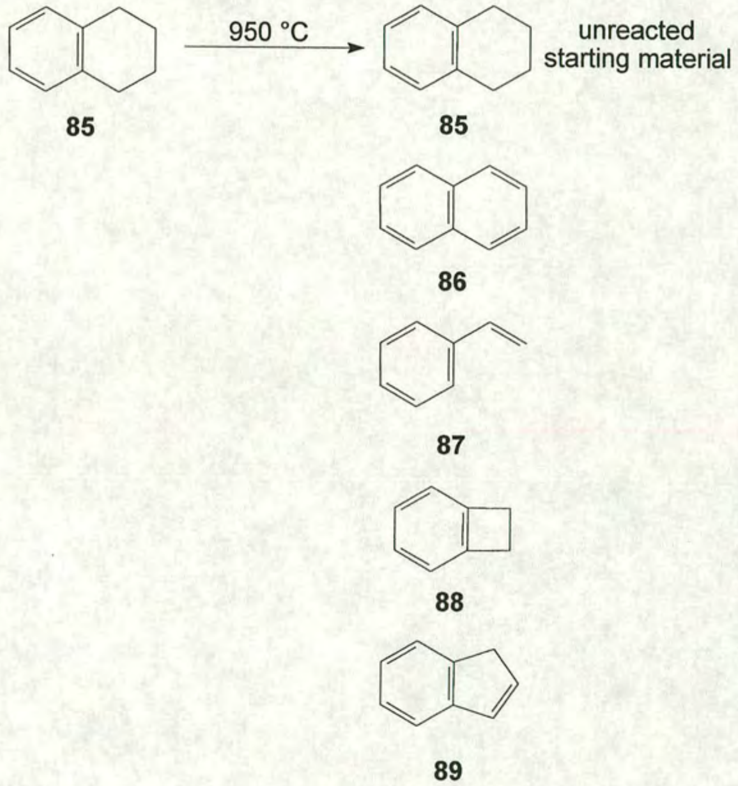
To identify, develop and optimise a general method for the preparation of aromatic compounds by dehydrogenation, the test reaction shown in scheme 61, the conversion of tetrahydronaphthalene (tetralin) **85** to naphthalene **86**, was chosen.



Scheme 61

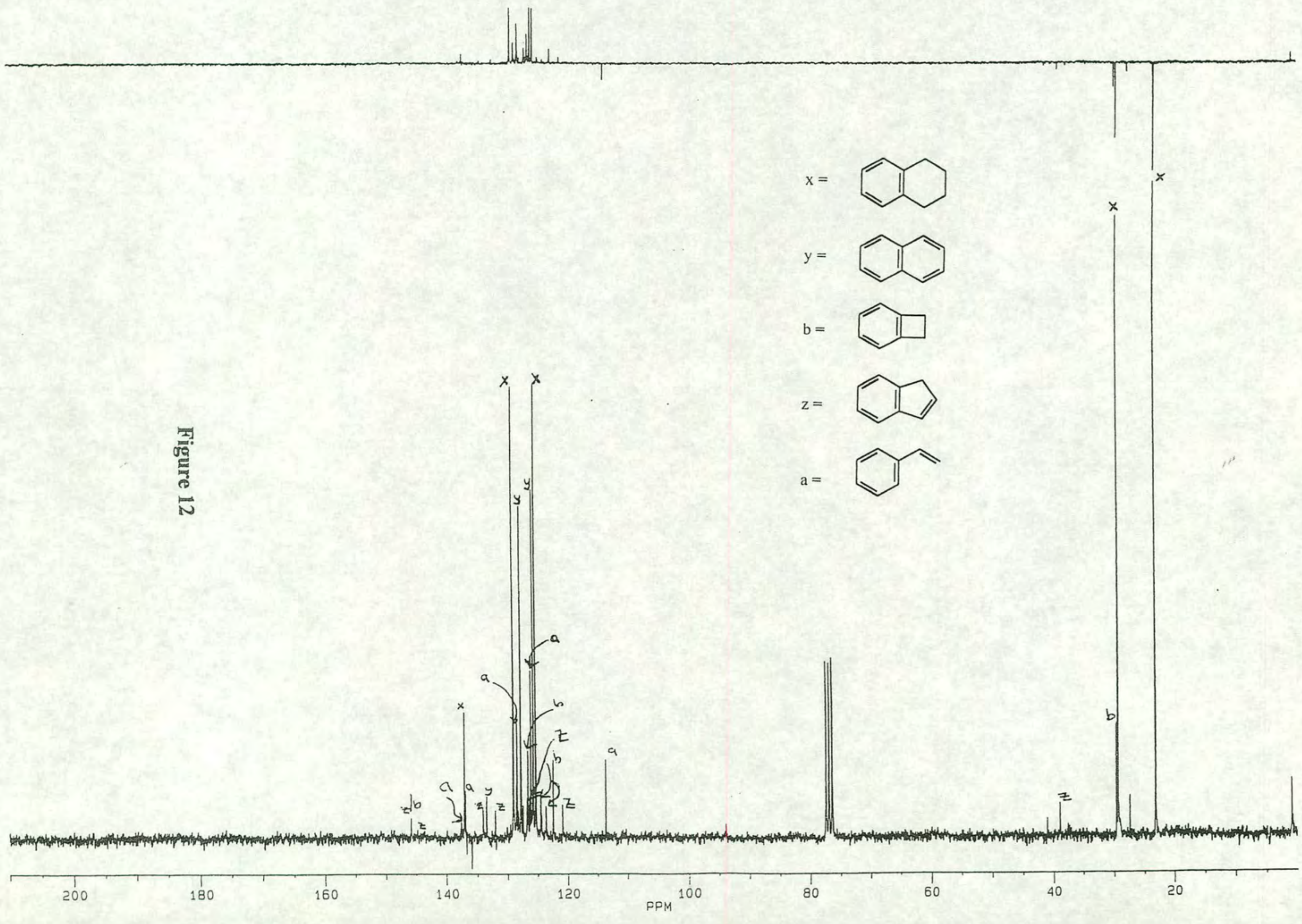
This is convenient as it utilises readily available materials for both reaction and analytical comparison. The starting material has a boiling point of 207 °C which is reasonable for carrying out an FVP experiment and most importantly, tetralin and naphthalene give distinct ^{1}H NMR spectra which allows quantitative analysis.

Firstly, the uncatalysed thermal chemistry of tetralin was investigated. Flash Vacuum Pyrolysis (FVP) (see introduction section 1.2, p5 for details) of this material was carried out at elevated temperatures to give several breakdown products. A furnace temperature of 950 °C was required to give any breakdown of the starting material whatsoever, yielding the products shown in scheme 62.



Scheme 62

The products shown are identified beyond doubt from the ^{13}C NMR spectrum of the product mixture and are listed in order of decreasing abundance. Unreacted starting material dominates the mixture – the level of abundance of the products formed can be seen in figure 12, which shows the ^{13}C NMR spectrum.



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 DEPT2CPD.AU
DATE 12-3-98
TIME 16:11

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SFO      62.900
O1     4000.000
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TD    32768
SW    17241.379
HZ/PT     1.052

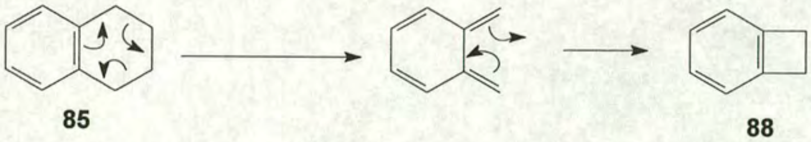
PW        3.0
RD        1.200
AQ         .950
RG      800
NS      486
TE      297

FW    21600
O2     4100.000
DP    15H CPD

LB        2.000
GB         .500
CX       35.00
CY       18.00
F1      210.014
F2         .020
HZ/CM   377.366
PPM/CM    6.000
SR    -4031.57
```

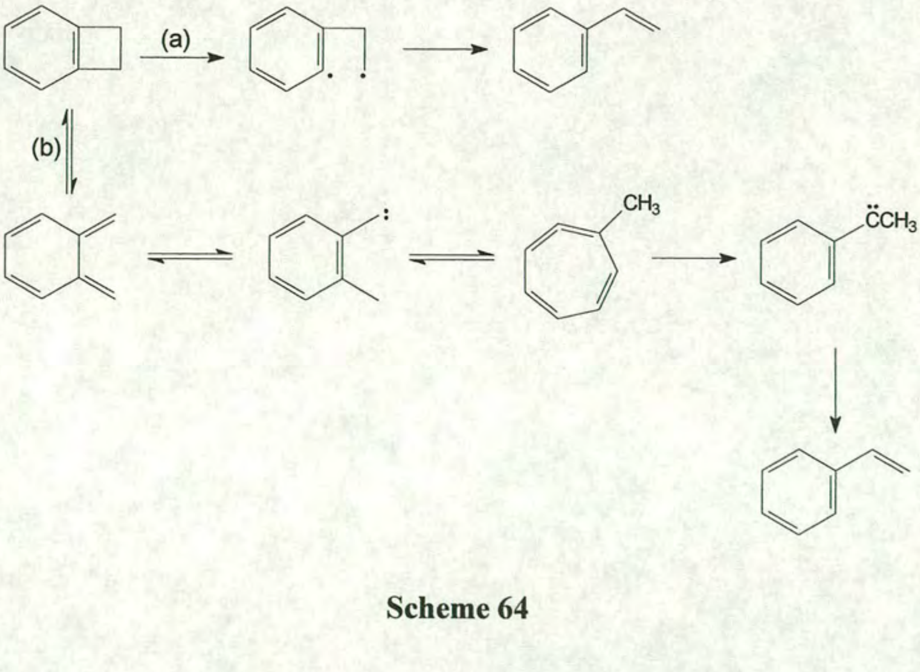
Figure 12

A similar product profile was found in a previous investigation of the pyrolysis of tetralin.[74] At 890 °C a mixture consisting of naphthalene (30%), styrene (23%), indene (15%) and benzocyclobutene (6%) was formed. The authors proposed that benzocyclobutene was formed by retro Diels-Alder reaction as shown in scheme 63.



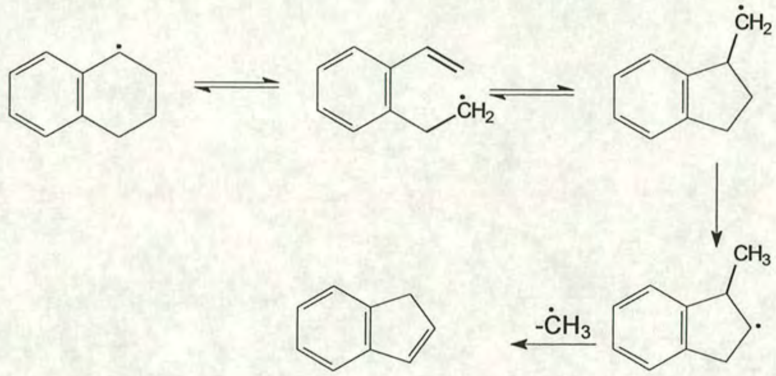
Scheme 63

It was also noted in this study that higher temperatures gave increased yields of styrene. The thermal rearrangement of benzocyclobutene to styrene is known and two alternative mechanisms have been proposed for this.[75] These are depicted in scheme 64.



Scheme 64

A possible mechanism for the formation of indene is shown in scheme 65. This is based upon work involving the pyrolytic generation of tetralinyl radicals, yielding indene in small amounts.[76]

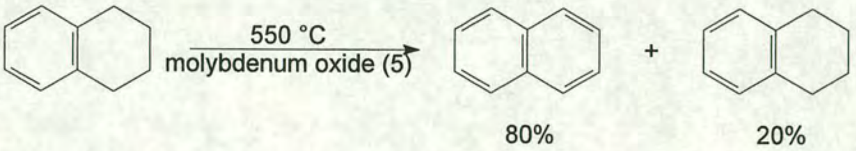


Scheme 65

It can be seen then that the pure thermal chemistry of tetralin firstly relies upon very high temperatures to break down the substrate and unsurprisingly at this temperature, leads to a number of competing processes. This makes the reaction an ideal candidate for the development of a catalytic method.

In the introduction section of this thesis, a section devoted to dehydrogenation reactions discussed the use of gas phase chemistry in this field. Several examples exist of metals and metal oxides being used and the importance of support materials was also highlighted by the examples given. To follow this methodology, a number of catalysts for dehydrogenation were supplied by Zeneca. These consisted of alumina pellets loaded with mainly molybdenum oxide. Although detailed composition data for these catalysts was not available, some information was given regarding their use. The catalysts were numbered 1-5 for identification purposes. Catalyst 5 was a doped catalyst, incorporating a small amount of cobalt oxide, and was provided in the largest quantities. A maximum working temperature of 500-550 °C was recommended for all of these catalysts due to the nature of the alumina support. These are supplied in the γ-form of alumina, which is the standard form used in catalyst supports. However at temperatures of 600 °C and above, the alumina breaks down to the more thermally stable α form. The α form of alumina has a lower surface area than the γ form and would therefore provide a less active catalyst if used as a support.[77]

A protocol similar to that described for molecular sieves was used for these catalysts. The catalyst (10 g) was packed into the centre of the furnace tube. Initially, the test dehydrogenation of tetralin to naphthalene was carried out over catalyst 5. A reaction temperature of 550 °C was used, giving the result shown in scheme 66.



Scheme 66

A clean product mixture with 80% conversion to naphthalene (by ^{1}H NMR) was obtained. This was a hugely encouraging result for several reasons. Firstly, the breakdown of tetralin to products is catalysed to the extent of a 400 °C lowering of the required temperature. Secondly, the fact that only the desired product and starting material are present is of high significance – the competing processes detailed above are not observed at all. This gives an excellent starting point from which to develop a process.

Following this, a regeneration protocol for the catalyst was developed. This was best carried out by heating the catalyst in air at 550 °C for 2 h. On carrying out the test reaction on regenerated catalyst 5, 67% conversion to naphthalene was achievable and this figure remained constant on further regeneration/testing. Heating for any further length of time gave no improvement and the use of an air stream gave poorer regeneration, possibly due to a cooling effect.

The activity of the five catalysts supplied was then evaluated and compared, the results being depicted in figure 13. The experiment consists of ~ 150 mg of tetralin pyrolysed over 10 g of catalyst at 550 °C.

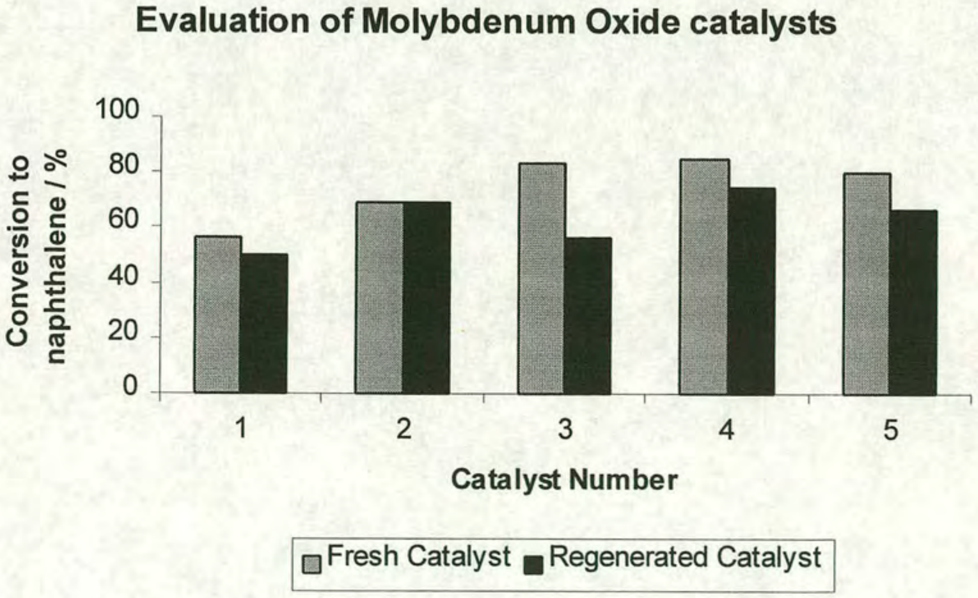


Figure 13

This showed catalyst number 4 to be the most active for the dehydrogenation of tetralin and most importantly, the most active on regeneration. From this point forward, catalyst 4 was used mainly for preparative reactions while catalyst 5 was used for investigative reactions due to its ready availability.

To confirm the catalytic activity of the molybdenum oxide, the dehydrogenation of tetralin was carried out under the same conditions over a packing of alumina pellets, supplied by Aldrich. This experiment does not give a direct comparison with the molybdenum oxide catalyst support since the Aldrich alumina is supplied in the α form (catalyst support is γ-alumina), but remarkably this still gave 33% conversion to naphthalene (25% yield), poorer than all of the molybdenum oxide catalysts, but clean, with no by products.

The applicability of this process to larger scales was investigated by pyrolysing progressively larger amounts of tetralin over regenerated catalyst 5 up to 1 g and then on a 5 g reaction scale. This gave a steady conversion to naphthalene of around 64% and at high accountability for material throughout. These results are depicted in figure 14.

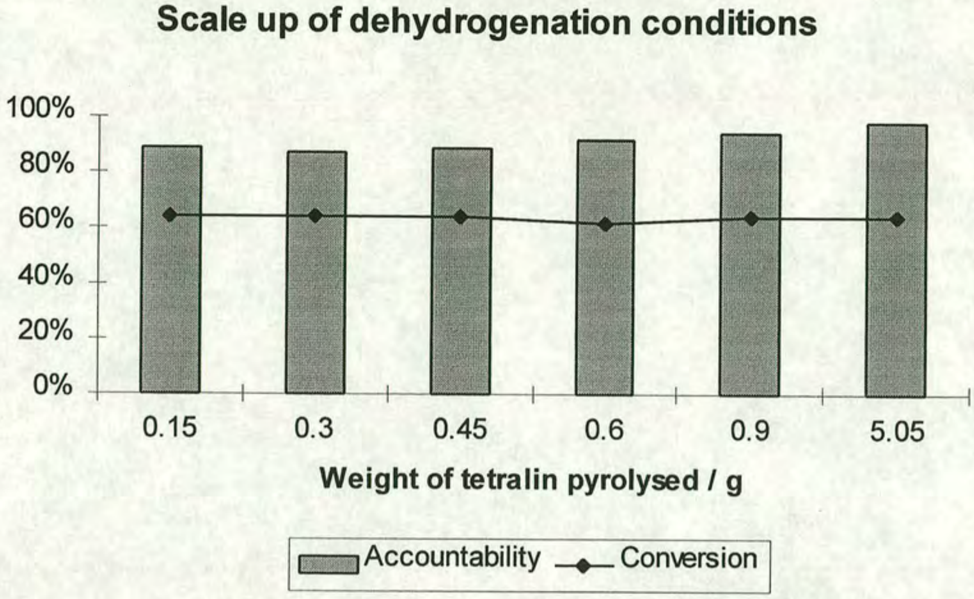


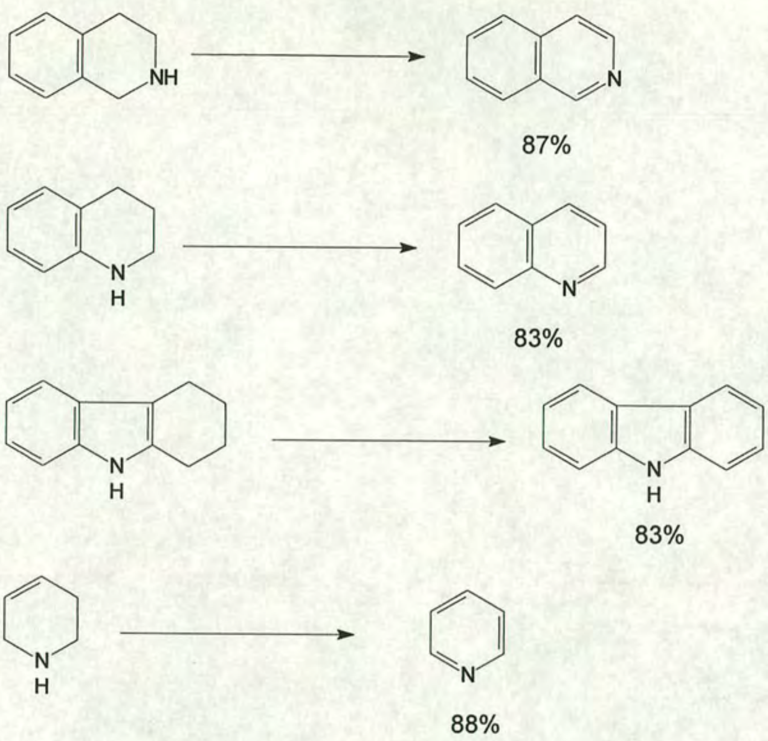
Figure 14

This result is extremely encouraging. Not only does the catalyst remain active at higher scales but also the apparent increase in accountability (presumably a function of the error inherent in product collection) gives rise to increased yields. The following section describes the applicability of the method to some more preparative examples.

In carrying out these dehydrogenations on a larger scale, some mechanistic features of the process were clarified. During the experiment, the vacuum measured in the FVP apparatus after the trapping of condensable materials was seen to deteriorate by up to two orders of magnitude. This indicates the formation of gases not condensable by liquid nitrogen and in this case must point to loss of hydrogen. Furthermore, no water was found in the pyrolysates formed. This is an important observation as it demonstrates that the catalyst does not become deactivated by loss of oxygen to allow elimination of water. This also explains the continually high activity of the catalyst on scale up, since it can presumably only be deactivated by coking. This deactivation would then be easily reversed by simply heating the catalyst in the furnace.

2.1.3 Application of aromatisation conditions

Having developed a robust method for the dehydrogenation/aromatisation of tetralin over a molybdenum oxide catalyst, the conditions were tested on other precursors, particularly heterocycles. It must again be pointed out that the conditions being used are optimised for the dehydrogenation of tetralin and are not re-optimised for each precursor. Scheme 67 depicts the results obtained using these conditions. All of the precursors shown were commercially available. Figures shown indicate crude, isolated yields of reactions on an approximately 100 mg scale, except for the preparation of carbazole (~ 0.5 g).



Conditions used: 10^{-3}-10^{-4} moles of substrate pyrolysed at 550 °C over 10 g of molybdenum oxide (4).

Scheme 67

In the dehydrogenation of tetrahydroisoquinoline, an 87% yield was obtained, with no starting material present. A trace amount of unidentified aromatic impurity was indicated by NMR spectroscopy. This shows a remarkable increase in activity for the catalyst with respect to the 80% *conversion* obtained from naphthalene to tetralin. It was thought at this stage that the basicity of the substrate may be responsible for this, involving a co-ordination to the metal oxide surface. However, the much less basic tetrahydroquinoline precursor gave a similar yield, again with no starting material (or by-products) observed. Even carbazole is prepared cleanly in excellent yield. This transformation is of particular synthetic utility since carbazoles are frequently prepared by initial generation of the tetrahydrocarbazole followed by dehydrogenation. This dehydrogenation stage is non-trivial, requiring relatively forcing conditions.[78,79]

The tetrahydropyridine, which could feasibly follow a retro Diels-Alder pathway, again yields the aromatic product in excellent yield with no starting material or by-products.

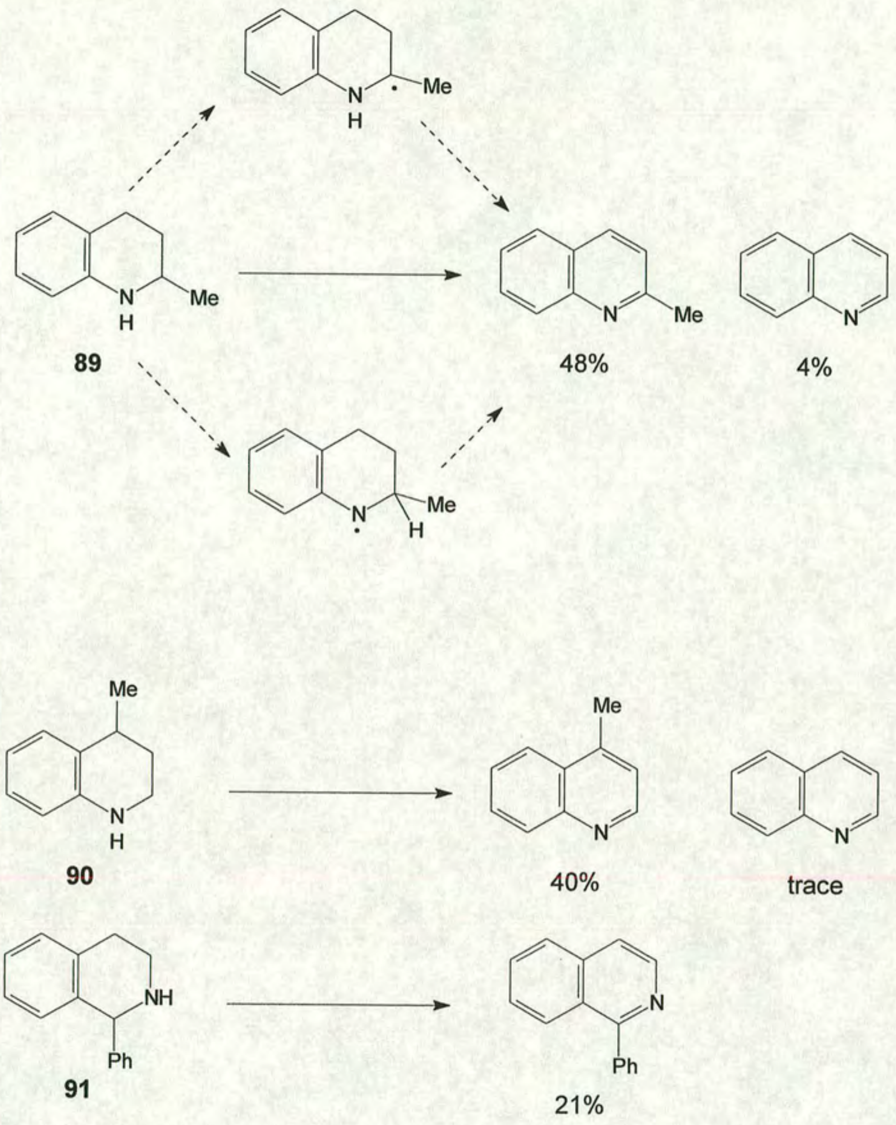
The applicability to scale up of the preparation of quinoline was tested by reacting ~ 5 g of the tetrahydro precursor over molybdenum oxide (4, 10 g). Not only was this successful (93% yield) but pyrolysis of a further 3 g portion over the same catalyst (without regeneration) gave 89% yield. The dehydrogenation of heterocyclic precursors is then equally applicable to scale up as is tetralin.

The ease of this dehydrogenation relative to non-heterocyclic precursors is highlighted further by the preparation of quinoline. This was dehydrogenated cleanly in high yield with 100% conversion of starting material at temperatures down to 400 °C. This may be of importance if faced with a potentially sensitive heterocyclic substrate – the ability to use a temperature of 150 °C lower may make the difference between a feasible or infeasible process. This result also highlights the scope for optimisation of any specific method dependent upon the substrate structure.

Still unresolved are the mechanistic implications of this increased catalytic activity observed for heterocyclic precursors. This is investigated further in the following section.

2.1.4 Investigation of dehydrogenation mechanism

The reactions shown so far have all involved relatively simple ring substrates, with no substituents present. Moreover, no positive mechanistic indication of how the reaction proceeds has been gleaned from either the products formed or catalyst deactivation, since the reactions are clean and the catalyst active throughout. A radical based mechanism may explain the increased activity observed using heterocyclic substrates due to either nitrogen centred radical stability or nitrogen stabilised carbon centred radicals. It was thought that by subjecting alkyl substituted substrates to the dehydrogenation process, otherwise similar to those shown above, the products formed may imply some mechanistic features. Scheme 68 shows the results of these experiments.



Conditions used: 10^{-3}-10^{-4} moles of substrate pyrolysed at 550 °C over 10 g of molybdenum oxide (4).

Scheme 68

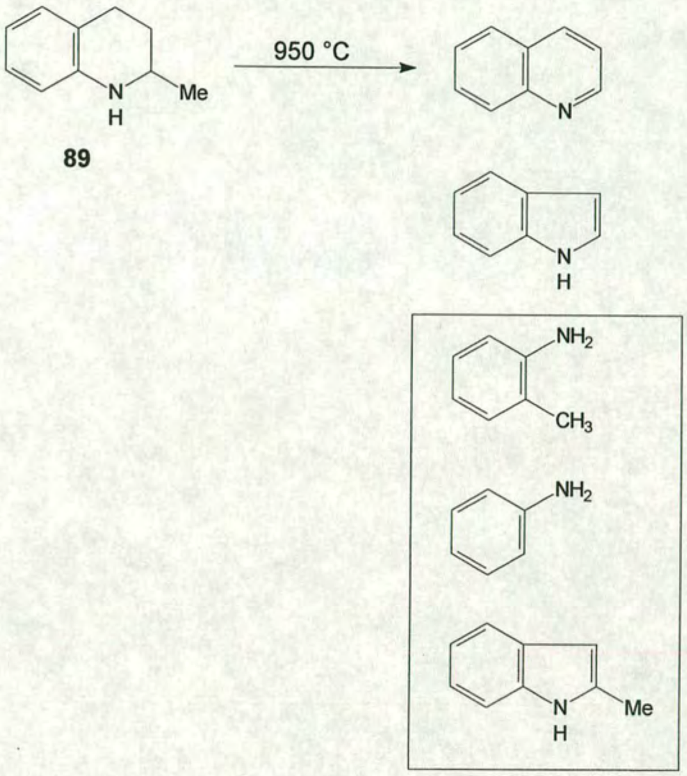
The methyl substituted tetrahydroquinoline precursors **89** and **90** were prepared by dissolving metal reduction from the corresponding quinoline. A sample of 1-phenyl-1,2,3,4-tetrahydroisoquinoline **91** was available in the laboratory.[80] The above reactions were carried out on a small scale, suitable for collection of the entire sample into an NMR tube. The yields quoted are therefore not isolated product yields but are calculated by addition of a known amount of cyclohexane to the ^{1}H NMR sample. Although the reactions are clean – no other products are formed – the apparent loss of material indicates a surprisingly poor accountability for these reactions, not observed elsewhere in this study. Reaction on a larger scale would be required to verify this apparent anomaly.

The small amount of quinoline obtained from tetrahydroquinaldine **89** rules out the nitrogen centred radical as a major intermediate in the first dehydrogenation step. This would certainly lead to higher yields of unsubstituted product since this relatively facile β-cleavage of methyl radicals under FVP conditions is well precedented.[66] Not ruled out however is the intermediacy of the stabilised carbon centred radical. This 4% of cleavage product is reduced to zero in the pyrolysis of the phenyl substituted substrate **91**, presumably due to the higher heat of formation of the phenyl radical.

It was also found that the dehydrogenation of tetrahydroquinaldine **89** could also be carried out using alumina pellets (α-form) as catalyst. This gave an 80% yield (based upon the ^{1}H NMR spectrum as above) and only a trace of cleavage product (quinoline). Again, this gives a much higher yield than the corresponding dehydrogenation of tetralin (25%). It is certainly worth further remark that simple alumina pellets can be active in some cases as a selective gas phase dehydrogenation catalyst.

The pure thermal chemistry of tetrahydroquinaldine **89** was investigated by pyrolysis over an inert packing of quartz beads. It was found that a temperature of

950 °C was required to give complete breakdown of the starting material, giving rise to a complex mixture as depicted in scheme 69.



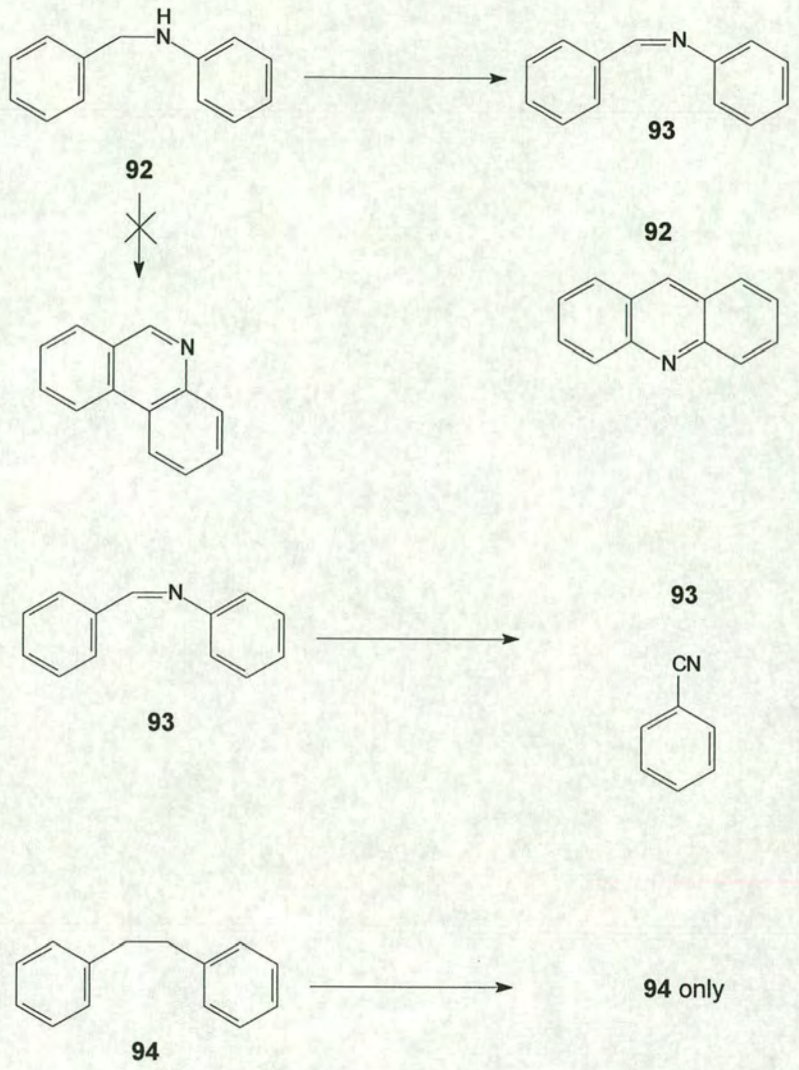
Scheme 69

The products shown are listed in approximate order of abundance and identified by their ^{13}C NMR spectra. Quinoline and indole were unambiguously identified while the compounds shown in the box, 2-toluidine, aniline and 2-methylindole are tentatively proposed as being present. Indole is presumably formed by a mechanism analogous to the formation of indene from tetralin (scheme 65). 2-Methylindole could also be formed in an analogous fashion.[76] Several other unidentified components are also present. Once again this illustrates the remarkable catalytic effect of the process. Not only does tetrahydroquinaldine break down at a temperature 400 °C lower than this under catalysis but also gives dehydrogenation product with almost total selectivity, a process which looks most unlikely given the uncatalysed thermal breakdown pathways.

2.1.5 Miscellaneous attempted dehydrogenations

Although the method described in the preceding chapters for catalytic gas phase dehydrogenation has been successfully used for aromatisation reactions, it was hoped that the method could be applied more generally to dehydrogenation (oxidation) processes. A number of trial experiments were carried out on various substrates with differing aims. In general these were carried out on a small scale (< 50 mg) and quantification and identification are mainly derived from the NMR spectra produced.

Scheme 70 shows the attempted dehydrogenations/cyclisations of some similar substrates. This work attempts to follow the dehydrocyclisations of similar substrates as described in chapter 2.3 of the introduction to this thesis.



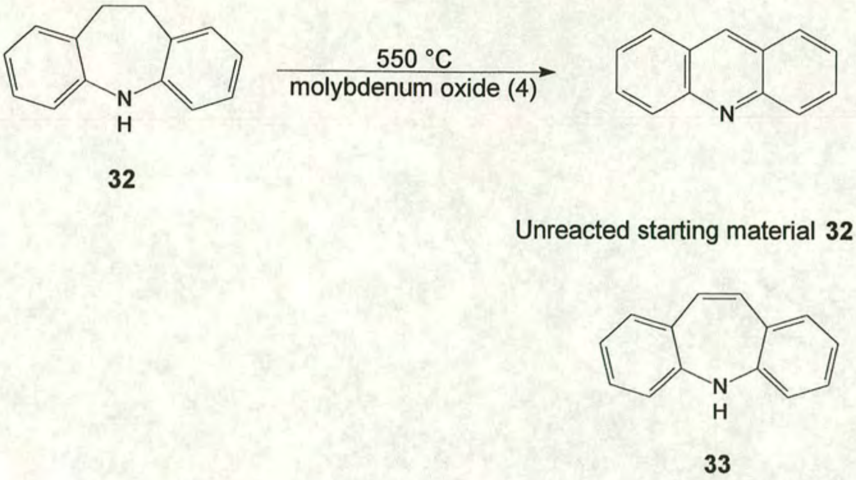
Conditions used: 10^{-3}-10^{-4} moles of substrate pyrolysed at 550 °C over 10 g of molybdenum oxide (4).

Scheme 70

The attempted dehydrogenation followed by dehydrocyclisation of *N*-phenylbenzylamine **92** to give phenanthridine gave a complex mixture of products. The components shown above were identified unambiguously from the ^{13}C NMR spectrum and are listed in order of decreasing abundance. As can be seen, the initial dehydrogenation step does take place to some degree but several other competing pathways also exist, leading to many unidentified products. The desired product, phenanthridine, is not present in the mixture. Unreacted starting material can be identified, as can acridine. This acridine formation is precedented, formed in the pyrolysis of *N*-phenylbenzylamine in the early part of the last century.[81]

N-Benzylideneaniline **93** was shown not to be an intermediate in the formation of acridine. Pyrolysis of **93** under the same conditions returned essentially only unreacted starting material, although a trace of benzonitrile is identified. This is presumably formed by a homolytic bond cleavage of the N—Ph bond followed by elimination of a hydrogen atom. Similarly, bibenzyl **94** yields only unreacted starting material, the conditions seemingly not able to dehydrogenate an alkane bond, even to give a conjugated system.

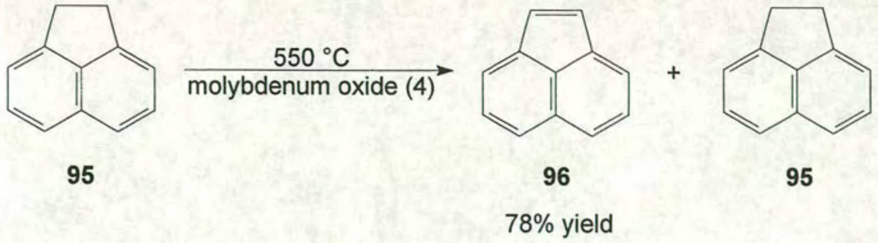
An attempt was made to convert iminodibenzyl **32** to iminostilbene **33**, a process described in chapter 2.2 of the introduction. Yields of up to 50% were quoted by the authors using palladium–charcoal catalyst and several other studies have looked at this system. The product is made commercially by pyrolysis over a mixed metal oxide catalyst consisting mainly of Fe_2O_3.[19] The yield obtained is only 61% while the remaining material is mostly unreacted starting material. Traces of acridine and 9-methylacridine are observed. Unfortunately, our conditions could offer no improvement, giving a complex mixture of products with poor recovery of material. Scheme 71 shows the products identified (from their ^{13}C NMR spectra in the main) in order of decreasing abundance.



Scheme 71

Although iminostilbene **33** is formed, it is a minor component in a messy product mixture. Acridine is again observed here and unreacted starting material is also present. This in particular is unfortunate since it proves the process to be of low selectivity: not only are many products formed but even higher temperature would be required to give high conversion.

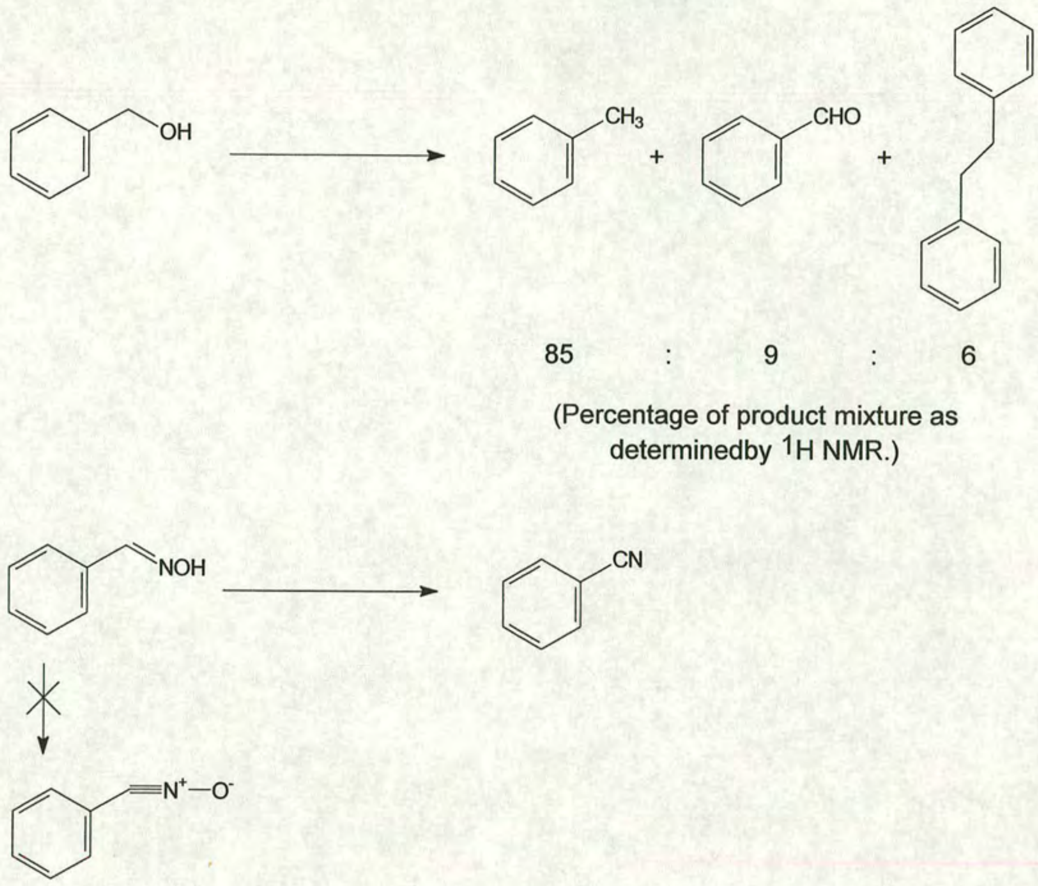
Another conversion of interest was that of acenaphthene **95** to acenaphthylene **96**. This would represent a high increase in commercial value if viable. Scheme 72 shows the initial result obtained from this system on a trial scale of ~ 100 mg.



Scheme 72

This proved successful, giving a clean mixture of only starting material and product. A conversion of 91% to product and good accountability for material result in a 78% yield of acenaphthene. The mixture was not separated and the yield quoted is based upon the measurement of the integrals in the ^{1}H NMR spectrum. However, problems were encountered on scale-up. Reaction on a scale of around 2 g gave only 69% conversion to the desired product after several attempts, and attempted re-pyrolysis of the resulting mixture proved unsuccessful. It is unclear why this should be the case. One hypothesis is that the reaction leads to polymeric side products in small amounts though large enough to deactivate the catalyst by coking. These unspecified polymeric products may not be observed by NMR. Reaction of acenaphthene under the same conditions over α-alumina pellets gives much poorer conversion to products, even on a small scale.

Other systems that proved inapplicable to the gas phase dehydrogenation conditions are shown in scheme 73.



Conditions used: 10^{-3}-10^{-4} moles of substrate
pyrolysed at 550 °C over 10 g of molybdenum oxide (4).

Scheme 73

Attempted preparation of benzaldehyde by dehydrogenation of benzyl alcohol proved unsuccessful. A gas phase method for this transformation does exist, utilising copper oxide catalyst and temperatures of 250-300 °C under flow pyrolysis.[82] Unfortunately, employment of the molybdenum oxide based conditions gave only 9% dehydrogenation while toluene is the main product formed. It is possible that this forms by cleavage of the C—O bond followed by hydrogen abstraction and this is supported by the presence of bibenzyl which would form by radical dimerisation after cleavage.

Reaction of benzaldehyde oxime does not yield the nitrile oxide shown but rather dehydrates cleanly to benzonitrile (78% yield). Pyrolysis of this substrate over α-alumina pellets gives the same result. Although this is a different, less active form of alumina than that used as the catalyst support, this result implies that the alumina support is responsible for this dehydration process.

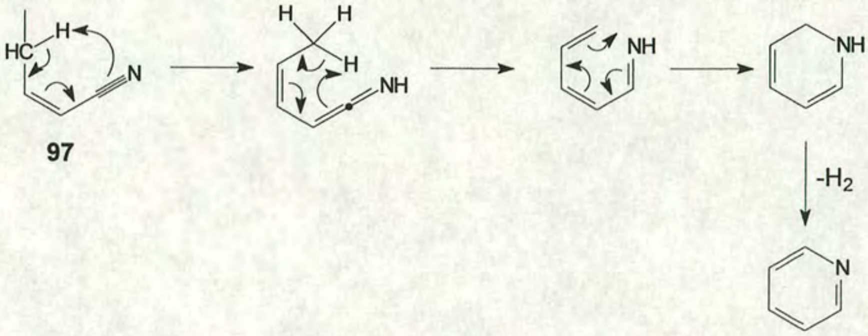
Summary of miscellaneous catalytic dehydrogenations

Having developed a robust catalytic gas phase method for aromatisations, application of this method to other dehydrogenation reactions was attempted. Although the limited number of experiments carried out did not yield a preparatively useful process, the possible future utility of this method was demonstrated further and additional experimentation is certain to prove fruitful.

2.2 The thermal chemistry of *cis*-2-pentenenitrile

2.2.1 Attempted dehydrogenation-cyclisation of *cis*-2-pentenenitrile

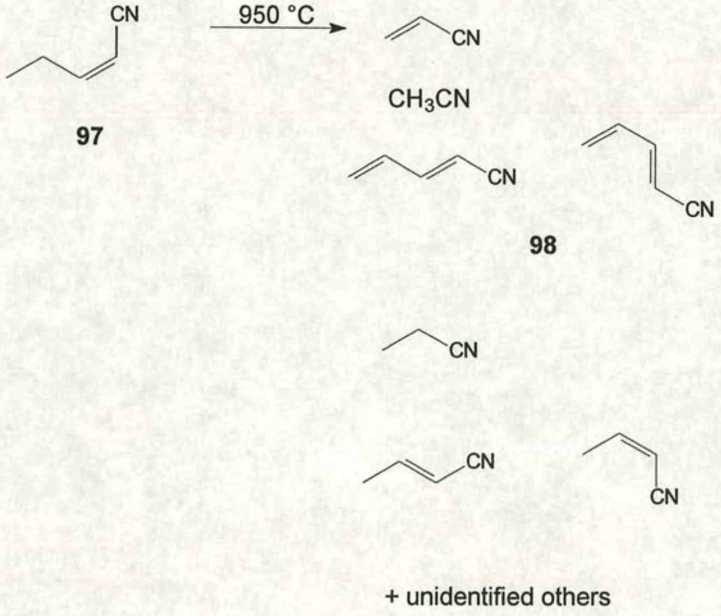
cis-2-Pentenenitrile **97** is a cheap industrial material, available in bulk and isomeric with dihydropyridine. It was thought that the catalytic method developed for aromatisations described above may be able to effect the transformation of **97** to pyridine. A possible mechanism can be written for this process, shown in scheme 74.



Scheme 74

As can be seen, whether by this mechanism or another, the transformation requires the loss of hydrogen. It was hoped therefore that our already developed dehydrogenation conditions described in the preceding sections could be successfully applied in this case.

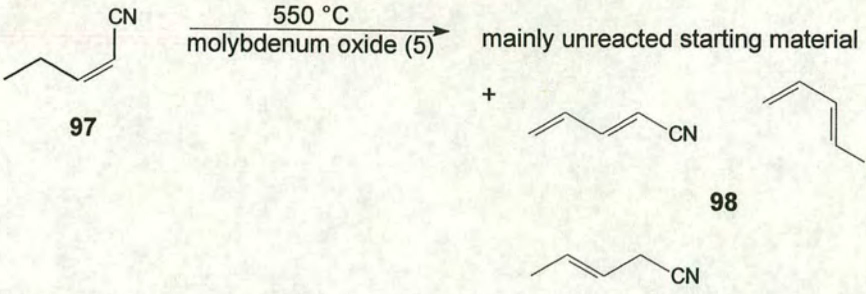
Firstly, the pure thermal chemistry of pentene nitrile **97** was investigated. This involves pyrolysis of the substrate under standard FVP conditions, with no catalyst present in the furnace tube. Full breakdown of pentenenitrile was found to occur at a temperature of 950 °C, yielding an extremely complex mixture of products as shown in scheme 75. Pyrolysis at lower temperature shows the same component mixture but also contains both isomers of pentenenitrile. This *E/Z* isomerisation under FVP conditions is well precedented, especially at these elevated temperatures.[83]



Scheme 75

The products shown are identified mainly from their ^{13}C NMR spectra and are listed in order of decreasing abundance. It can be seen that there is no one process dominating here: products are formed by cleavage of C_1, C_2 and C_3 fragments. Most importantly, no pyridine was observed at all in the product mixture. Some very minor peaks in the NMR spectra remain unaccounted for. Among these are some which by chemical shift and their DEPT $3\pi/4$ spectrum seem to belong to terminal CH_2 groups. This led us to propose that perhaps dehydrogenation to penta-2,4-dienenitrile **98** is the first step in the majority of the breakdown pathways and the investigation of this theory is described in the following section.

An attempt to catalyse the dehydrogenation of *cis*-2-pentenenitrile using the molybdenum oxide method described in the preceding sections was unsuccessful, as shown in scheme 76

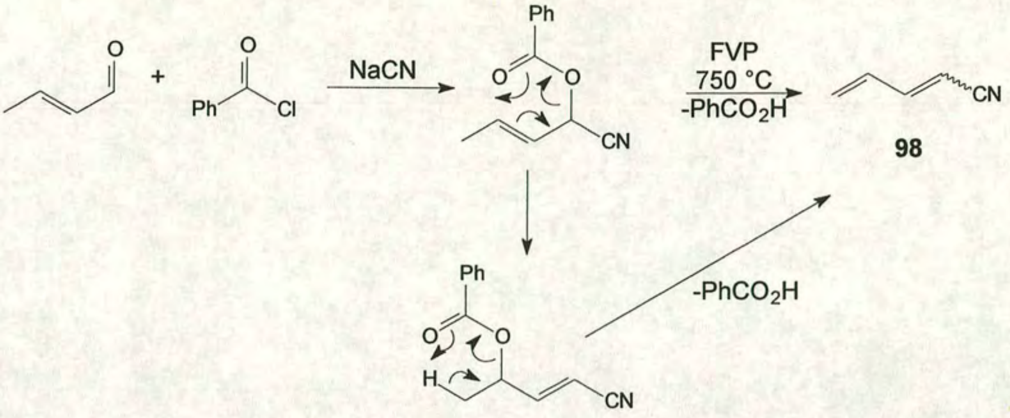


Scheme 76

The main components of the product mixture are isomers of the starting material. Both isomers of penta-2,4-dienenitrile are also present and *trans*-3-pentenenitrile is observed. No other components are present. A similar reaction over alumina pellets gave the same product profile.

2.2.2 Investigation of possible intermediate - penta-2,4-dienenitrile

The role of penta-2,4-dienenitrile **98** was investigated by first preparing a sample, both to confirm its presence in the product mixture arising from pentenenitrile pyrolysis and to provide material for subsequent reaction. This was achieved by the reactions shown in scheme 77.



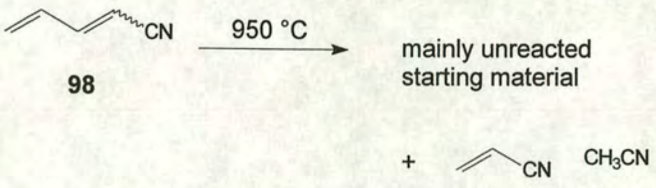
98

Scheme 77

The reaction scheme shown is a modification of a literature method for this transformation.[84] The authors detail the use of a flow pyrolysis system while it was found for this application to be quicker and more conveniently prepared by FVP. This gave pure penta-2,4-dienenitrile as a mixture of isomers in an overall yield of 33%, with purification of both the product and the intermediate by distillation.

The mechanism of this pyrolysis step is also of interest. Allylic esters are known to undergo a rearrangement step prior to elimination,[85] as shown in scheme 77.

Pyrolysis of this isomeric mixture under purely thermal conditions identical to those used for pentenenitrile gave the product mixture shown in scheme 78.



Scheme 78

Unreacted starting material accounts for ~ 80% of the products. Acrylonitrile and acetonitrile (both observed in the pyrolysis of pentenenitrile) are also present. A number of minor unidentified components are observed, these being spectroscopically identical to the unidentified components in the corresponding reaction of pentenenitrile. It would appear then that penta-2,4-dienenitrile is certainly an important intermediate in the thermal breakdown of *cis*-2-pentenenitrile by inspection of the products formed. Clearly, however, other pathways are also possible, as proven by the further products observed.

Reaction of penta-2,4-dienenitrile **98** over the molybdenum oxide catalyst at 550 °C gave no reaction, returning unchanged starting material. This is unsurprising given the thermal stability of this compound even at temperatures of 950 °C as shown in scheme 78 above.

2.3 Conclusions and future work

A dehydrogenation protocol using catalysis in the gas phase has been successfully developed and applied to a number of aromatisation reactions This incorporates the use of an alumina supported molybdenum oxide catalyst. Several such catalysts were evaluated and their regeneration optimised.

In the course of mechanistic investigation, the method has been found to be extremely selective in many cases and applicable to scale up in most of the examples tried. Trial non-aromatisation reactions involving the loss of hydrogen have proved less successful but some leads have been uncovered and there is scope for further development.

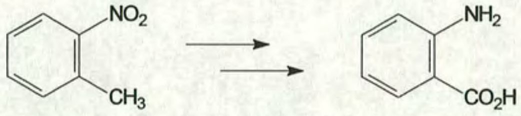
Unfortunately, this method was found to be unsuitable for the preparation of pyridine from *cis*-2-pentenenitrile. However, the thermal chemistry of this and also penta-2,4-dienenitrile has been elucidated somewhat during the study.

As with the dehydration protocol described earlier, future work should focus upon finding more real synthetic applications for this method. The remarkable selectivity shown in some reactions makes this catalytic method a worthwhile alternative to the traditional methods of dehydrogenation. The potential of this method is highlighted by the results obtained on only a small selection of transformations. Many other processes can be attempted and many other metal oxide catalysts can be used. This gives an almost limitless opportunity for experimentation to find transformations suitable to gas phase catalytic chemistry and the advantages inherent with such methodology.

This expansion will be better directed if a better understanding of the mechanism of this process can be acquired. This may then lead to the possibility of tailoring the catalysts to best suit particular situations.

3 Rearrangement of 2-nitrotoluene

2-Nitrotoluene **99** is known to rearrange *via* an oxidation-reduction rearrangement to anthranilic acid **100** as shown in scheme 79 under many different sets of conditions. Catalytic gas phase conditions have been reported for this transformation, although in low yield and the aim of the work reported here was to develop a new catalytic vapour phase method.



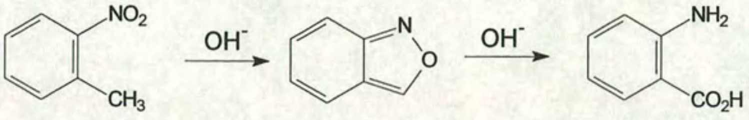
99 **100**

Scheme 79

A mechanistic awareness of the previous work carried out on this system is essential to the understanding of the work reported in this thesis. A brief summary of the relevant literature is therefore presented in the following section.

3.1 Literature methods of rearrangement of 2-nitrotoluene

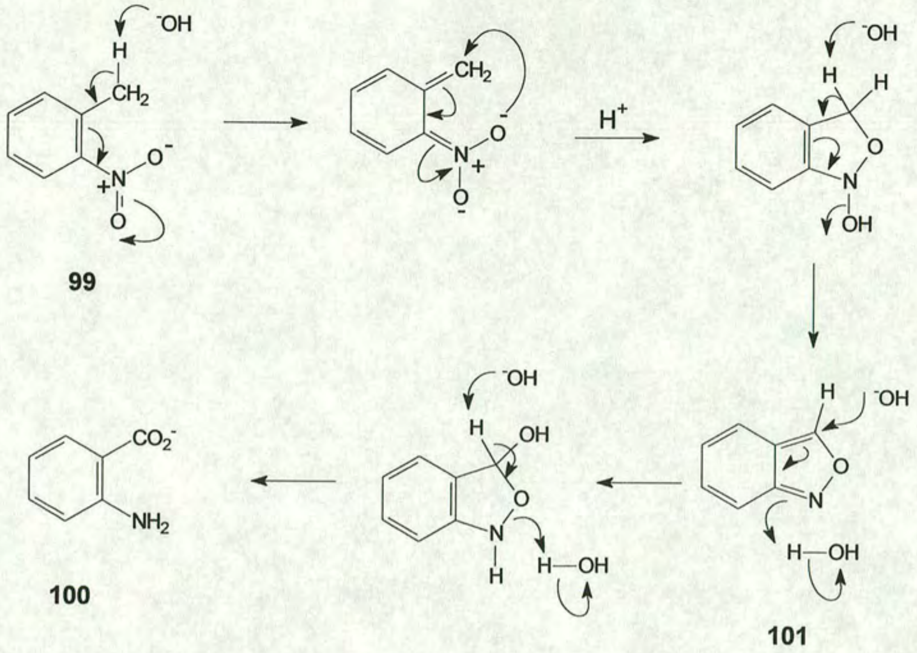
Well known is the formation of anthranilic acid **100** from 2-nitrotoluene **99** under basic conditions.[86,87] This reaction is generally assumed to proceed via anthranil (2,1-benzisoxazole) **101** as shown in scheme 80.



99 **101** **100**

Scheme 80

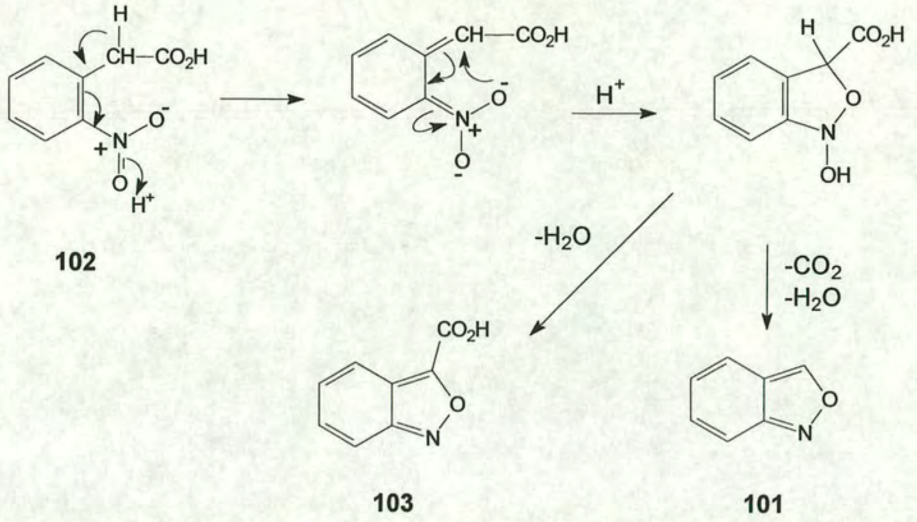
These reactions give anthranilic acid in low yield (~15%)[87] with many by-products under conditions of heating at 200 °C in 70% KOH (aq). In a labelling study,[88] the base mediated rearrangement of 2-nitrotoluene in $K^{18}OH$ (aq) gave rise to results which indicate a one oxygen transfer from the nitro group. This would correlate with the mechanism proposed by the authors and reproduced in scheme 81.



Scheme 81

This work followed an earlier report in which it had been indicated that one of the carboxylic oxygen atoms comes from the basic solution.[89]

A similar reaction has been performed in acidic media[90] in the formation of anthranil and anthranil-3-carboxylic acid **103** from *o*-nitrophenylacetic acid **102**. A similar mechanism was postulated, as shown in scheme 82.

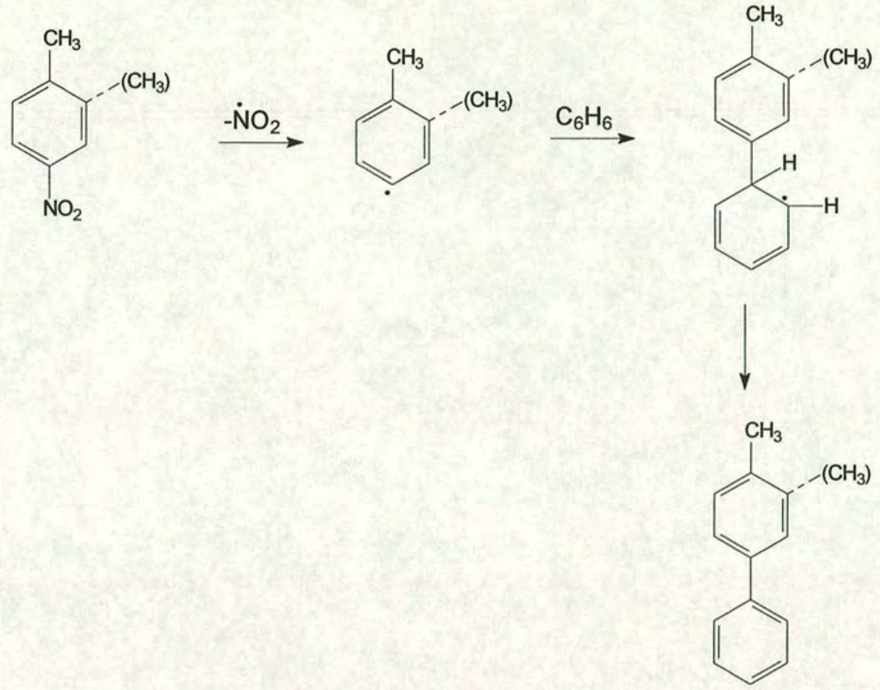


Scheme 82

This reaction is carried out in concentrated sulfuric acid at 110 °C for 15 hours. The yield of anthranil obtained is 31% while the yield of the acid **103** is 34%. Anthranil has also been prepared by reaction in 98% trifluoromethanesulfonic acid. Heating at 100 °C for 14 days gives a 50% conversion of starting material to mainly anthranil.[91]

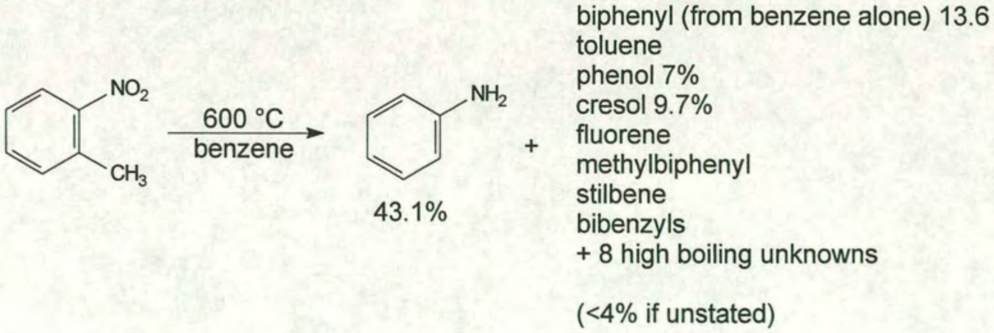
The vapour phase decomposition of 2-nitrotoluene was first reported in 1902 when Löb reacted 2-nitrotoluene **99** with water vapour on a red-hot metal wire, forming anthranilic acid **100**.[92]

Fields and Myerson however, in their studies of the thermal decomposition of nitroaromatics, expected 2-nitrotoluene to react similarly to the *meta-* and *para-* derivatives, *i.e.*, via radicals to arylate benzene and chlorobenzene to methylbiphenyls and methylchlorobiphenyls.[93] This is shown in scheme 83.



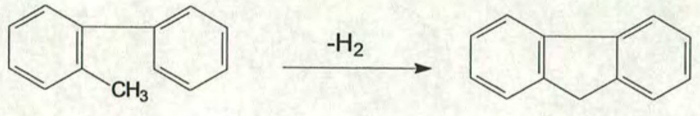
Scheme 83

However, when 2-nitrotoluene in benzene was heated at 600 °C under nitrogen, the major product formed was found to be aniline, with many other products formed, as depicted in scheme 84. The apparatus used for this and the following reactions carried out by Fields and Myerson was essentially the flow pyrolysis apparatus described in detail in the introduction to this thesis.



Scheme 84

All of these products are found in the pyrolysates of the *meta-* and *para-* isomers, except aniline and fluorene **105**, which is the dehydrogenation product of *o*-methylbiphenyl **104**.

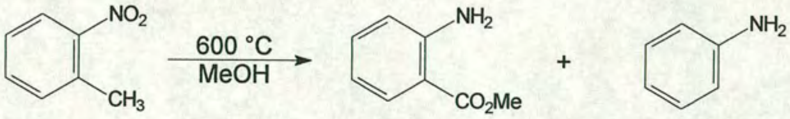


104 **105**

Scheme 85

Only aniline, therefore, arises from a pathway not predicted by Fields and Myerson in the light of their other reactions involving nitroaromatics.

Heating of 2-nitrotoluene in methanol at 600 °C under nitrogen gives methyl anthranilate **106** in 38% relative yield based upon reacted 2-nitrotoluene and approximately the same proportion of aniline, shown in scheme 86. Again, these products are absent from the pyrolysates of the *meta-* and *para-* isomers.



99 **106**

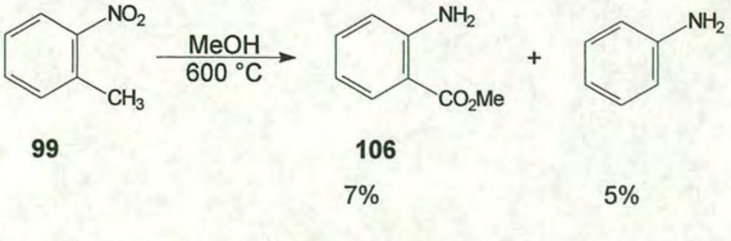
+ *o*-toluidine
o-cresol
N-methyl-*o*-toluidine
bibenzyl

Scheme 86

This led Fields and Myerson to the deduction of intramolecular oxidation and reduction to anthranilic acid, which can be trapped by methanol but will decarboxylate to aniline if not stabilised by a nucleophile. They proposed a mechanism based around the formation of a carbanion although it was noted that the same mechanism could be ascribed to a free radical. This mechanism however had several highly unlikely steps, involving the formation of intermediates with 10 electrons around a nitrogen atom.

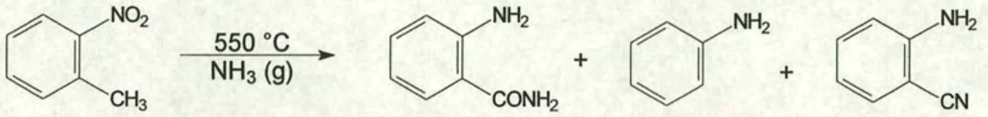
An earlier paper on the pyrolysis of nitroaromatic compounds by Janzen[94] indicated that 2-nitrotoluene produces free radicals when heated to 300°C under nitrogen. This involved heating the substrate in a sealed quartz cell in the cavity of an ESR spectrometer and monitoring for a concentration of free radicals only. No product analyses were carried out.

The most extensive investigation carried out on the pyrolysis of 2-nitrotoluene was by Bakke.[95] Repeating the Fields and Myerson experiment between 2-nitrotoluene and methanol, he achieved only 7% yield of methyl anthranilate **106** and 5% yield of aniline as shown in scheme 87.



Scheme 87

Bakke realised that if a nucleophilic mechanism was responsible for anthranilic acid derivative formation then perhaps a more efficient trapping agent could be found. 2-Nitrotoluene was then reacted in a stream of ammonia with the results shown in scheme 88.

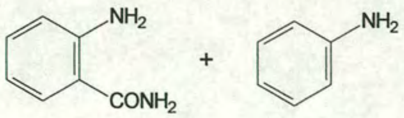


99 **107** **108**

29% 23% 1%

Scheme 88

The main product formed is anthranilamide **107**. Yields shown are based upon the amount of 2-nitrotoluene reacted, 84% in this case. To investigate the mechanism of formation of **107** (and hopefully, by correlation, **106**), anthranilic acid **100** was reacted with ammonia under the same conditions as before, yielding the products shown in scheme 89.



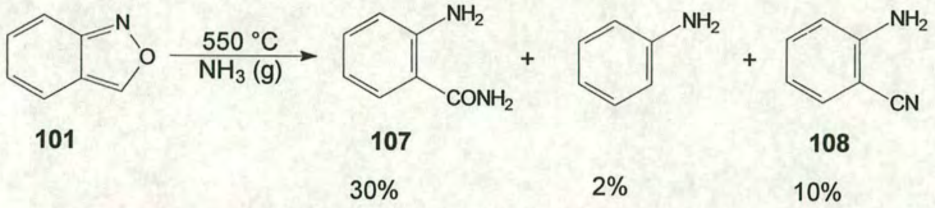
107

1 : 10

Scheme 89

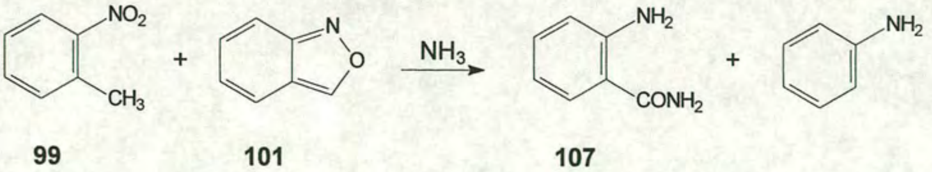
This shows that the major pathway of formation of **107** is not from anthranilic acid.

Bakke then reacted anthranil **101** with ammonia under the same conditions, the products formed shown in scheme 90.



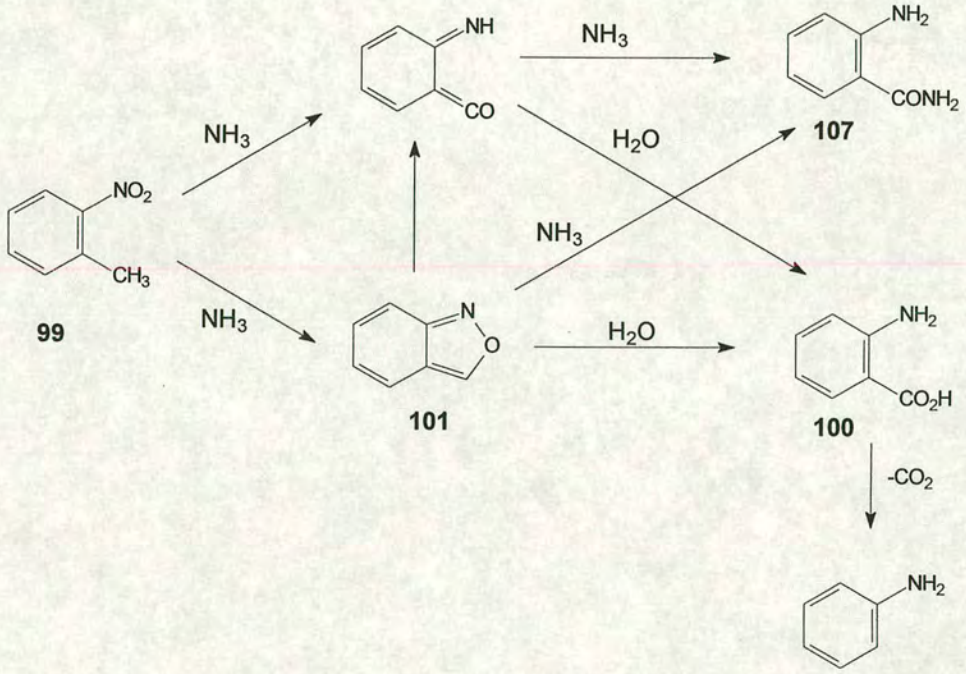
Scheme 90

The relative amounts of **107** formed indicate that anthranil (or a transformation of anthranil) is a likely intermediate in the formation of **107** while the surprise result is the increased yield of *o*-aminobenzonitrile **108**. Bakke postulated that perhaps 2-nitrotoluene or a reaction product of 2-nitrotoluene either prevented the formation of **108** or catalysed its hydrolysis to **107**. Thus, a 50:50 mixture of 2-nitrotoluene and anthranil was reacted with ammonia as shown in scheme 91.



Scheme 91

No nitrile **108** is found. Furthermore, the yields of amide **107** and aniline are of the same magnitude as the added yields of the reactions of 2-nitrotoluene and anthranil alone. Since reaction of anthranilic acid alone gave much less anthranilamide (scheme 89), anthranil is assumed to be an important link in the mechanism of anthranilic acid derivative formation, *i.e.*, the amide is not formed simply by trapping the acid. Bakke proposed several possible reaction pathways, as summarised in scheme 92.



Scheme 92

Investigating the nitrile **108** formation, 2-nitrotoluene was reacted with ammonia over silica gel, a known gas phase amide dehydration catalyst,[4] instead of the usual packing of Vycor chips. This did yield the nitrile **108** in increased yield of

30%. However, even this result is complicated by the fact that not only does silica gel catalyse the amide dehydration but also the destruction of 2-nitrotoluene. As such, a route from **99** to **108** which *does not* proceed via the amide **107** cannot be ruled out.

Summary

As can be seen, the mechanism of the transformation of 2-nitrotoluene to anthranilic acid is far from clear. A number of experiments have been described which clarify some matters and complicate others further. Although the route looked generally promising for development, it was obvious that the first task would be to gain a greater understanding of the process, as described in the following sections.

3.2 Introduction

The previous work carried out on the rearrangement of 2-nitrotoluene, as described in the preceding section, defined the goals of this research. Although the overriding objective was to provide a high yielding, clean synthetic route to anthranilic acid, other interim aims would have to be fulfilled. Firstly, a greater mechanistic understanding of the process was required to give some guidance on which of the steps involved were straightforward and which required specific catalysis. It was hoped that this would also provide information regarding the stability of the intermediates and how best to trap the desired products. Secondly, it was clear that the process would require a flow pyrolysis system, at atmospheric pressure and perhaps under reactive gas flow. This kind of apparatus incorporates far more variables than Flash Vacuum Pyrolysis and had not been developed to any great extent in the course of previous research in the laboratories. It was needed, therefore, to develop an expertise with this technique during the course of the work and to refine the apparatus throughout. This development process is outlined in the following section.

3.3 Development of flow pyrolysis apparatus

In the course of the study of the rearrangement of 2-nitrotoluene, the apparatus used for flow pyrolysis reactions was developed. As described in section 1.1 of the introduction to this thesis, the equipment consists basically of three parts: inlet, heater and outlet. However, the inlet and trapping systems are subject to extensive variation. The apparatus which ultimately evolved from this development is shown in figure 15. Various design features were adopted after early experimentation and these are highlighted here.

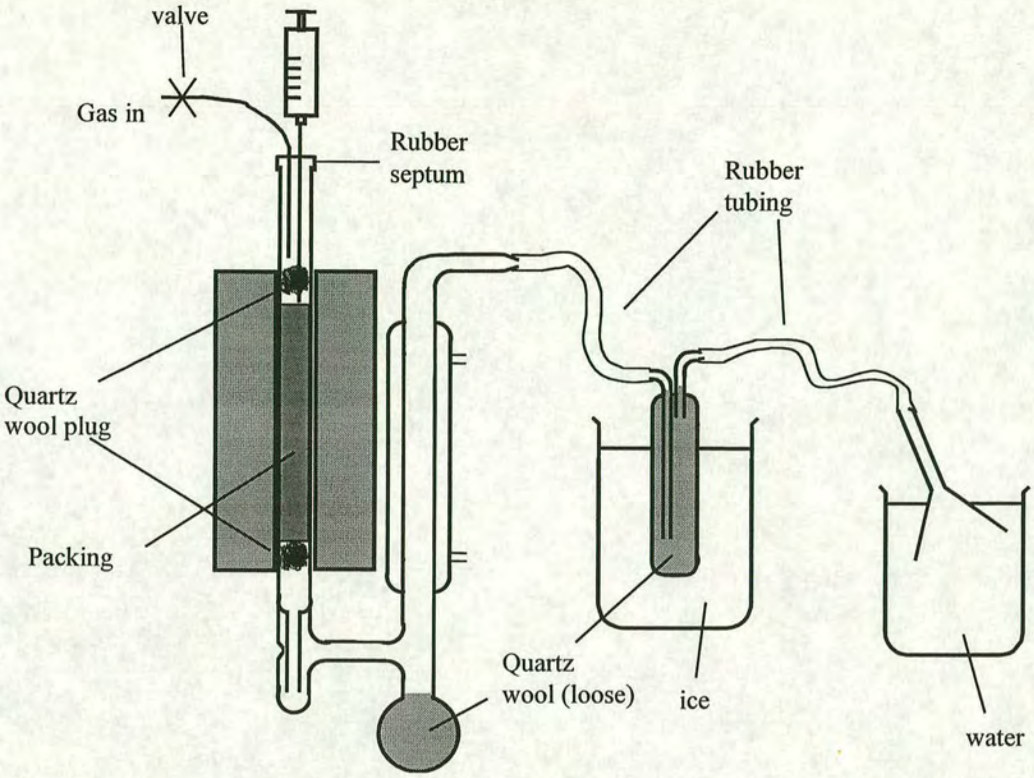


Figure 15

Inlet System

A variety of methods are described in the literature for the introduction of material to a vertically held furnace tube. Simple dropping funnels are used or adapted versions such as the Hershberg addition funnel.[96] It was found early in the development of this methodology that the simplest and most accurate delivery system for small scale work was a syringe and syringe pump arrangement. Thus an addition rate could be set on the pump and would not vary over the course of the reaction. Another important feature of the inlet is the point at which the substrate exits the needle. If the substrate is delivered in a volatile solvent, precautions must be taken to ensure that the solvent does not vaporise quickly and condense at the very top of the furnace tube, just beneath the rubber septum. This was achieved by positioning the needle such that the substrate was delivered beneath a tight plug of quartz wool, as shown in figure 15. If the carrier gas used was then delivered above the quartz wool plug, no such problems occurred.

The carrier gas itself was also delivered through a needle *via* the rubber septum. The gas flow rate was set using a needle valve. For the use of reactive carrier gases, care must be taken to ensure that the valve construction materials are compatible with the gases employed. In this case, the valve was required to be inert to ammonia and so was constructed from stainless steel with PTFE seals.

Heater

Heating was applied to the quartz furnace tube by an external electrical tube furnace. In flow pyrolysis, the furnace tube requires to be packed to aid the vaporisation of the starting material and prevent it from simply dripping straight through the tube. Although in later experiments the use of catalytic packings was attempted, most experiments were carried out using porcelain chips as an inert contact material. These were packed into the full length of the furnace tube and held in place by plugs of quartz wool. Early work used quartz wool itself as a packing material throughout the tube. Porcelain, however, was found to give slightly higher conversion of starting materials.

Outlet

As mentioned in the introduction section, the trapping of materials from flow pyrolysis reactions is a non-trivial exercise. Clearly, extreme cooling (*e.g.*, liquid nitrogen) cannot be used and depending on the carrier gas employed (*e.g.*, ammonia) even dry-ice/acetone cannot be used. The main problem encountered is the formation of mists on exiting the furnace. This is best avoided by slow cooling of the products and to this end the trap shown directly beneath the furnace in figure 15 was constructed. Figure 16 shows this more clearly.

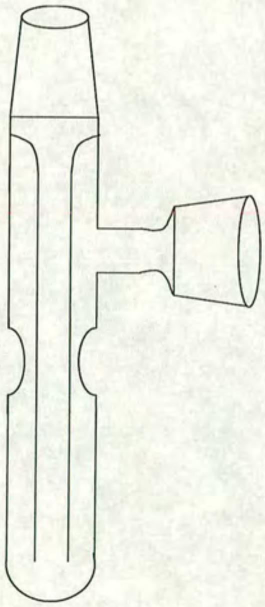


Figure 16

The design is based upon that of a preparative GC trap.[97] The main design feature is that the material exiting the furnace is slowly cooled by the gases surrounding the centre pipe which are only slightly cooler. The constriction slows down this gas flow. This trap evolved from that first used, a simpler arrangement as shown in figure 17.

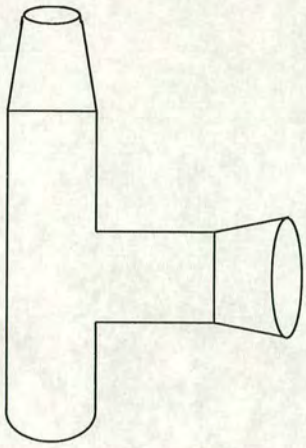


Figure 17

Further down the line, extra features for the breaking of mists were employed. Both the round-bottomed flask beneath the condenser and the Dreschel bottle were loosely packed with glass wool. This gives a larger surface area for the condensation of products. The slow cooling of products was achieved by the following:

Trap 1: beneath furnace – not externally cooled

Trap 2: condenser – water cooled

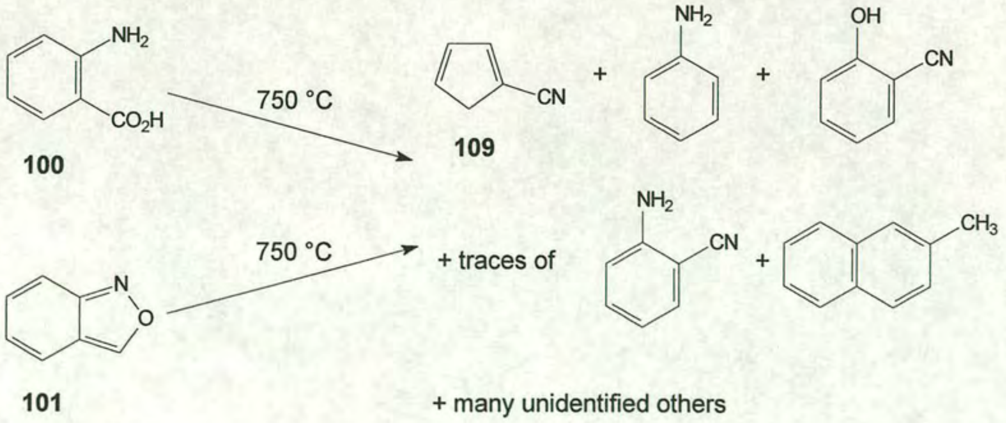
Trap 3: Dreschel bottle – ice cooled

In early experiments using nitrogen carrier gas a fourth trap, consisting of a dry-ice/acetone cooled Dreschel bottle was employed. This could not be used in conjunction with ammonia carrier gas (m.p. –33 °C, b.p. –78 °C) and in any case was found to be unnecessary.

Finally, product gases were bubbled through an upturned funnel into a water trap. This allowed a visualisation of gas flow and trapping of ammonia in cases where this was the carrier gas used. In some experiments, organic material was observed to emerge at this point and form a scum on the surface. In this event, these materials were extracted into organic solvent.

3.4 Mechanism of rearrangement

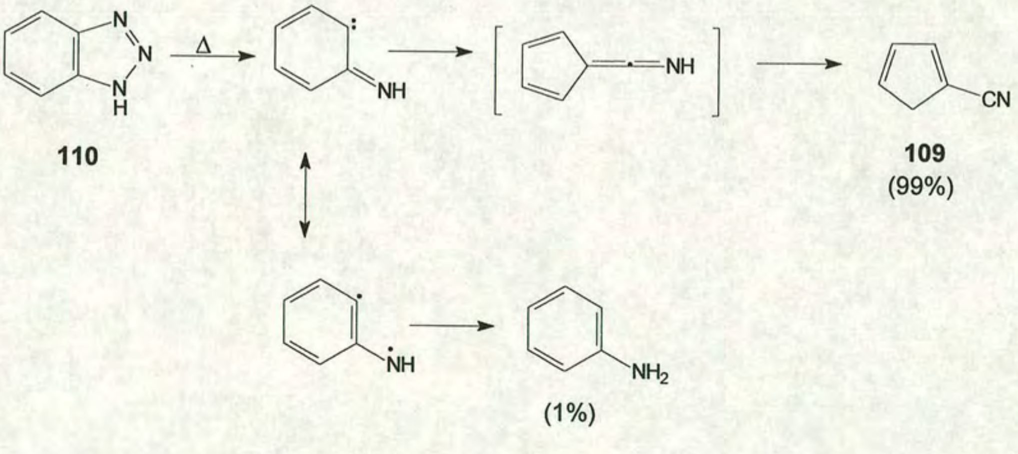
In an attempt to clarify further the possible mechanisms proposed by Bakke (scheme 92), the reactant, 2-nitrotoluene **99**, the product, anthranilic acid **100** and the proposed intermediate, anthranil **101**, were subjected to FVP conditions. It was hoped to elucidate the thermal pathways of these compounds in an environment where apparatus effects are well understood (and are therefore ruled out). A temperature of 750 °C was required to breakdown anthranilic acid fully and at this temperature the pyrolysis product mixtures of anthranilic acid and anthranil were found to be almost identical both in terms of the components present and their relative abundance. These results are shown in scheme 93.



Scheme 93

The products formed were identified firstly by NMR spectroscopy and GC-MS and confirmed and quantified by GC analysis. 1-Cyanocyclopentadiene **109** and aniline are by far the major components, accounting for approximately 70% and 10% of the mixtures respectively. Others identified are present in less than 6% abundance. 1-Cyanocyclopentadiene was tentatively identified initially due to the ^{1}H NMR spectrum being dominated by a number of aliphatic peaks, attributable to dimers of CCPD. These dimers are broken down under GC conditions which gave a correct mass of 91 in the GC-MS experiment.

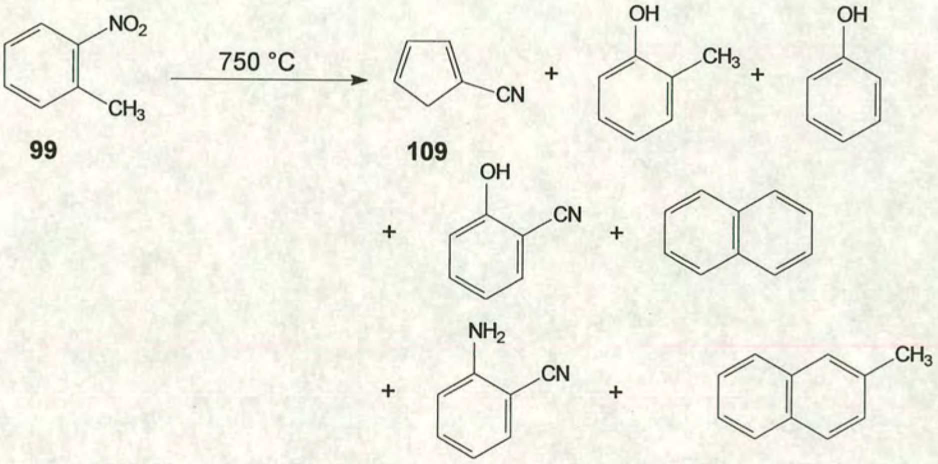
1-Cyanocyclopentadiene **109** is known to be formed, along with aniline, *via* an iminocarbene intermediate as shown in scheme 94.[68]



Scheme 94

The iminocarbene can be accessed by pyrolysis of benzotriazole **110** and indeed, on carrying this out, ^{1}H and ^{13}C NMR spectra were obtained which were identical in the aliphatic region to those obtained from the pyrolyses shown in scheme 93. However, the relative magnitudes of aniline and CCPD are not accountable by the mechanism shown in scheme 94 and therefore an alternative, perhaps decarboxylation, route to aniline must also be apparent.

A very similar set of NMR spectra were obtained from the pyrolysis of 2-nitrotoluene at 750 °C, but with some important differences. The products identified (again by GC-MS and GC) are shown in scheme 95.

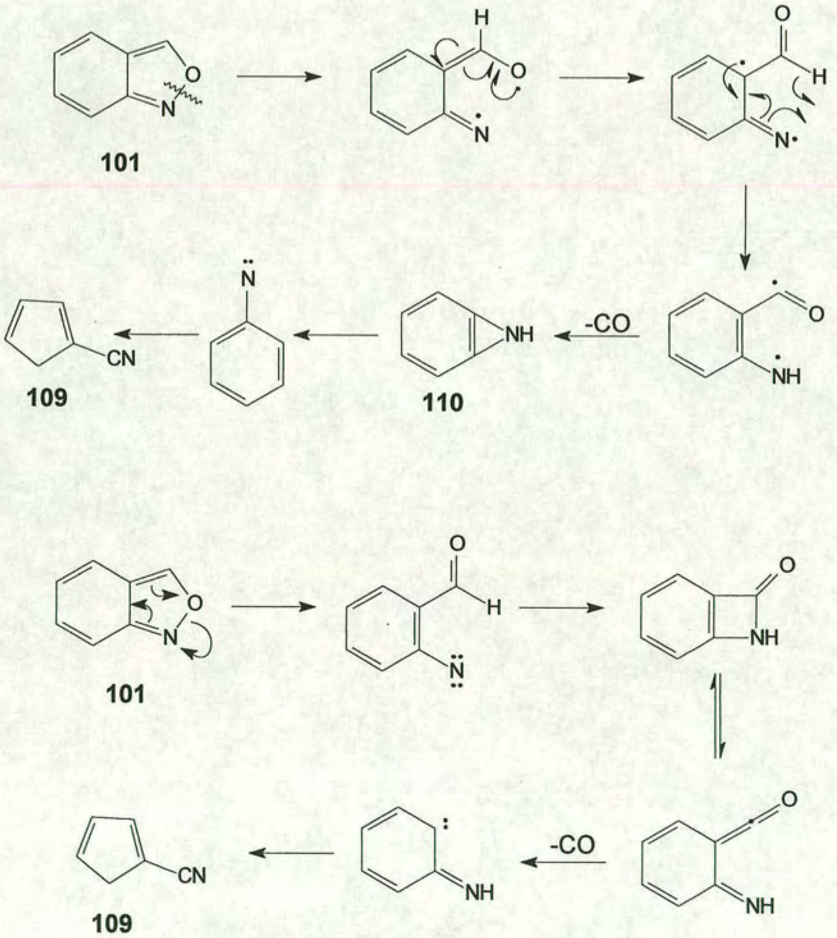


Scheme 95

Again, CCPD **109** is found to be the major component of the mixture, but accounting for only 20%. Phenol, 2-cresol and 2-cyanophenol account for around 10% of the product mixture each while the others shown are present in only trace amounts.

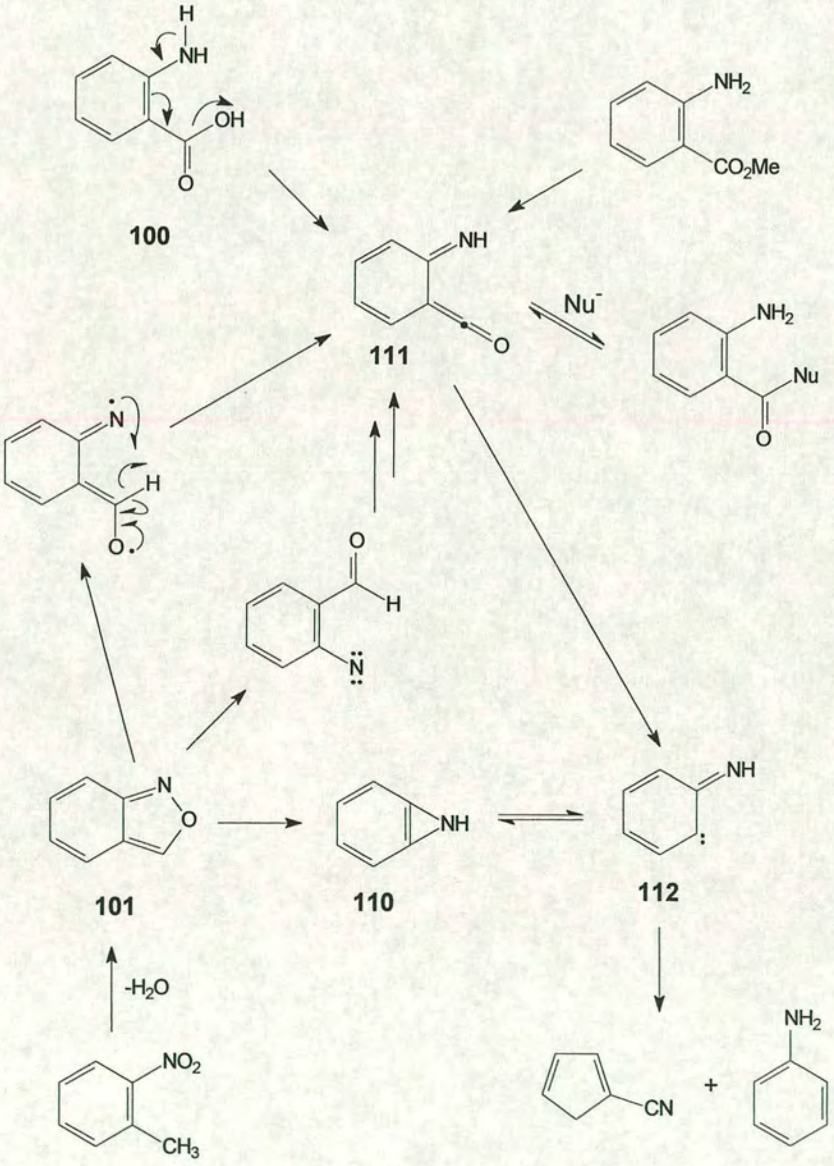
It appears from these experiments that anthranil certainly lies on a major pathway in the thermal breakdown of 2-nitrotoluene but that many other processes also occur. 1-Cyanocyclopentadiene, the major product in each case, was never described as being present in the experiments of either Fields and Myerson or those of Bakke. It is therefore presumed that under non-vacuum conditions where bimolecular reactions are possible, an intermediate in its formation is trapped in some way.

However, the occurrence of 1-cyanocyclopentadiene **109** in the pyrolysates of *o*-nitrotoluene and anthranil has been observed before.[98] The pyrolyses carried out involved single pulse shock tube experiments at 100 °C. A mechanism was proposed by the authors for the breakdown of anthranil to **109** and is reproduced in scheme 96. A possible alternative mechanism to this is proposed in the bottom half of the scheme.



Scheme 96

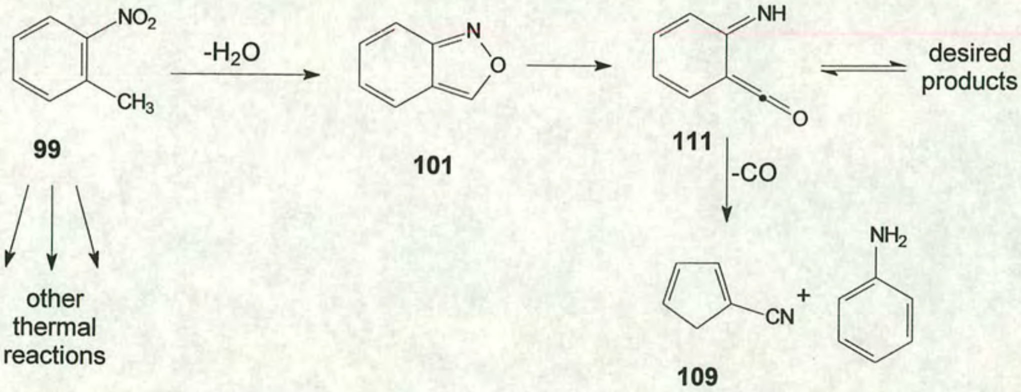
However, the pyrolyses of anthranil and anthranilic acid described earlier gave identical results and it is unclear how anthranilic acid could enter this energy surface. A mechanism is proposed to account for this, also collating mechanistic steps clarified from the literature, shown in scheme 97.



Scheme 97

The proposed mechanisms shown rely on the key intermediate iminoketene **111**. The presence of **111** has been proposed before,[99] in the pyrolysis of methyl anthranilate as shown in the scheme. This report also detailed the trapping of the iminoketene by nucleophiles such as ethanol and thiophenol. If the first mechanism proposed in scheme 96 is correct, anthranil could also enter this system *via* the benzazirine **110** as this species may be in equilibrium with the iminocarbene **112**.[68] Alternatively anthranil may approach **111** *via* the nitrene or diradical shown

This leaves us with a rather more simplified understanding of the thermal breakdown pathways of 2-nitrotoluene **99**, as depicted in scheme 98.



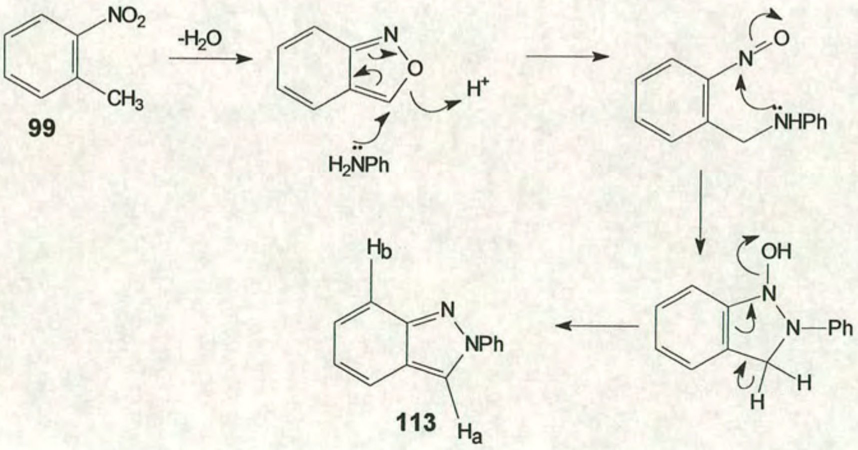
Scheme 98

This helps to identify the requirements of the development process:

1. The production of anthranil **101** versus other thermal processes must be maximised. This is, of course, a dehydration step and perhaps the investigation of dehydration catalysts could be useful.

2. A nucleophile must be found such that reversion of the anthranilic acid derivative to the iminoketene **111** (scheme 97) is minimised, as is the decarbonylation which eventually leads to 1-cyanocyclopentadiene.

In the light of the dehydration work carried out on amides (described in chapter 1) and to pursue requirement 1, 2-nitrotoluene was pyrolysed over 3A molecular sieves at 500 °C (1×10^{-2} Torr) in the hope of observing more anthranil derived products (e.g., 1-cyanocyclopentadiene) versus the many stable aromatic fragments to which 2-nitrotoluene breaks down. However this was not the case. Much of the starting material was returned unchanged along with many other components but no 1-cyanocyclopentadiene. Aniline was identified, as was 2-phenylindazole **113** after column chromatography in very low yield, possibly formed as shown in scheme 99 by nucleophilic attack of aniline produced, on anthranil.



Scheme 99

Compound **113** was identified using mass spectrometry and ^{1}H and ^{13}C NMR spectroscopy, including N.O.E. and decoupling experiments. Particularly confusing was the clear presence of a doublet at ~ δ 8.4 (*J* 1.0 Hz), but it seems that this is attributable to H_a as shown, coupling to H_b. Unfortunately, no other pure components were yielded from the column. The absence of 1-cyanocyclopentadiene and the large number of products formed would seem to indicate that thermal processes other than dehydration to anthranil are favoured in this case. This reaction is also another example of the unusual and unexpected chemistry which seems to be possible in the gas phase over molecular sieves.

In order to find a nucleophile able to satisfy the second requirement stated, that of minimising reversion from the anthranilic acid derivative, anthranilic acid, its methyl ester and its amide were pyrolysed at temperatures ranging from 600 – 750 °C. The pyrolysates were analysed by ^{1}H NMR purely to calculate the amount of unreacted starting material present. This was achieved by the addition of a known quantity of 1,4-dinitrobenzene to the NMR sample. This has a chemical shift sufficiently different from those in the spectra to be analysed and by comparison of the integral of this signal with the integral of a starting material signal, the amount unreacted could be determined. No attempt was made to identify any of the products formed - 1-cyanocyclopentadiene was identifiable from the ^{1}H NMR in each case but otherwise the spectra were too messy to comment. The results obtained are shown in figure 18.

Compound	**Temperature / °C**	**% unreacted**
acid	600	94
acid	650	71
acid	700	10
acid	750	0
amide	600	93
amide	650	92
amide	700	24
amide	750	impossible to say (if any) from ^{1}H NMR
methyl ester	600	95
methyl ester	650	91
methyl ester	700	14
methyl ester	750	10

Figure 18

Figure 19 shows these results in graphical form.

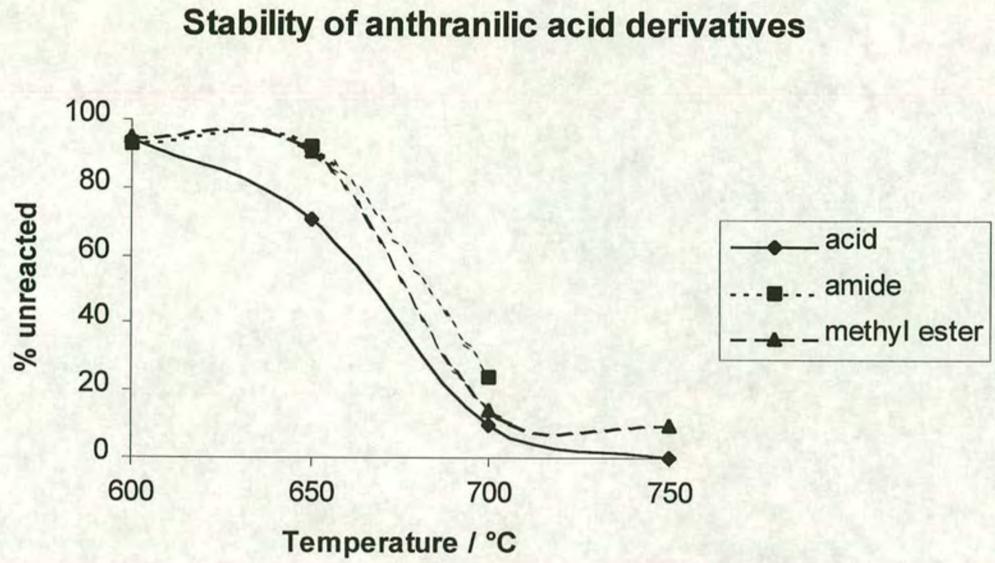
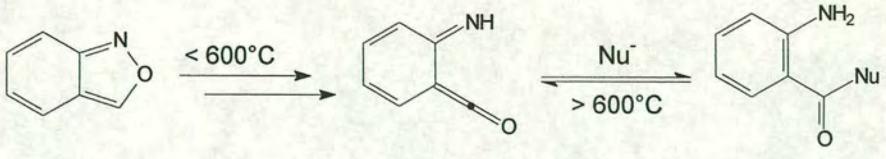


Figure 19

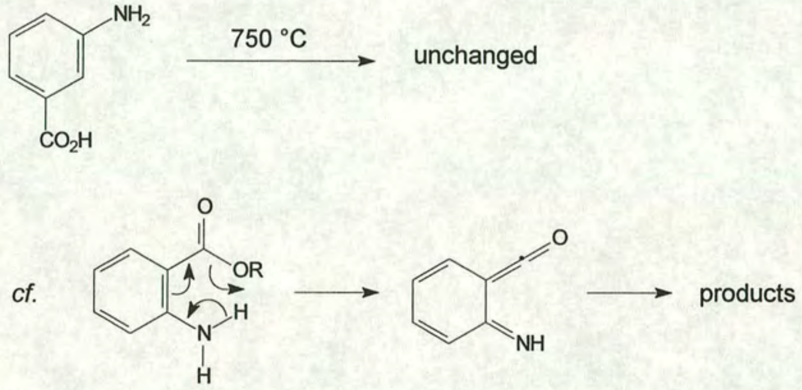
The graph shows that each compound has a very similar stability profile with only ~ 25°C between the curves at any point. It was hoped to find a larger difference between the curves in order to identify a nucleophile which would clearly be a better trapping agent than the others but this does not seem to be the case. As a reference, anthranil when pyrolysed yields some starting material at 550 °C but none at 600 °C. This means that at temperatures at which anthranil breaks down to the iminoketene intermediate **111**, the trapped anthranilic acid derivative should be stable (scheme 100).



101 **111**

Scheme 100

In order to illustrate the special thermal instability of these anthranilic derived compounds, 3-aminobenzoic acid was subjected to FVP at 750 °C, returning only unreacted starting material.



Scheme 101

Having elucidated the mechanism of the rearrangement of 2-nitrotoluene further and identified some of the other thermal pathways possible, attention can be turned to the optimisation of the reaction under flow pyrolytic conditions. Since this transformation has been shown to incorporate an intramolecular dehydration step and an intermolecular trapping step, the enormous scope for modification of variables in this area can now be regarded as an advantage to be exploited.

3.5 Flow pyrolytic reactions of 2-nitrotoluene

This section describes the results obtained from the flow pyrolysis of 2-nitrotoluene and related experiments. In many cases, the product mixture obtained from these reactions was extremely complex, with many components present, both identified and unidentified. Given this factor, the quoting of an absolute percentage yield was not always possible and indeed in some cases irrelevant in terms of depicting trends and progress. Several different protocols for illustrating the results of these experiments are used here and must be explained firstly.

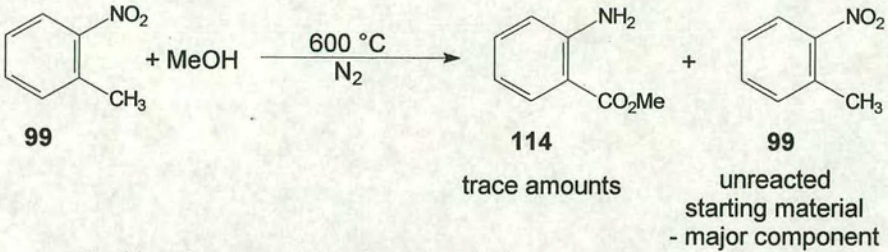
Recovery of material (also "mass balance"): this is an extremely important concept in this section. It simply describes as a percentage the amount of material collected divided by the amount reacted. As was described previously, the efficient trapping of material in flow pyrolysis reactions is an important issue and this parameter can be used to describe this. Also, polymerisation products may be formed in the furnace tube, causing a reduction in the recovery of material obtained.

Percentage of products formed: in reactions giving a complex mixture of products, this parameter indicates the preference for reaction *via* a pathway giving this product. This was generally determined by addition of a known amount of a reference compound to the ^{1}H NMR sample and calculated from the relative sizes of the integrals. Although an (unisolated) yield could be quoted instead, this parameter, together with the recovery of material, gives a better indication of the nature of the reaction.

Yield: in some cases, the reaction mixture was either clean enough to quote an isolated crude yield or a yield after further purification.

3.5.1 Trapped by methanol

The work described in this section attempts to reproduce and verify the work of Fields and Myerson in order to determine a baseline for the development of the process. This involves the flow pyrolysis of 2-nitrotoluene in the presence of methanol using the apparatus discussed in section 3.3. The initial attempt carried out is shown in scheme 102.



Packing: Quartz wool (whole tube packed)
Mass of 2-NT **99** used: 4.14 g
Methanol: 9.8 g (10 equivalents vs 2-NT)
2-NT Solution flow rate: 30 cm^3 h^{-1}
Carrier Gas flow rate: 20 cm^3 min^{-1}

+ many others

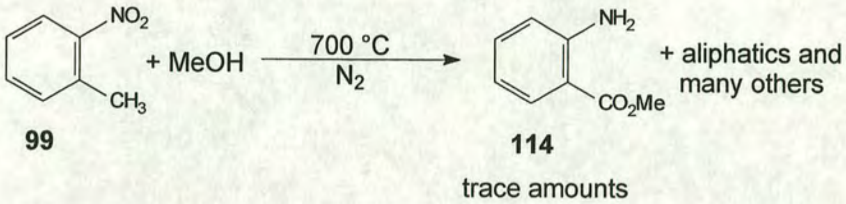
Scheme 102

As was mentioned previously, flow pyrolysis reactions require a number of variables to be defined and the values used are indicated in the scheme. This format will be used throughout this section and important changes to variables will be pointed out where necessary. In this instance, the variables shown are as close as possible to those used by Fields and Myerson. However, the amount of methyl anthranilate formed is extremely low, estimated to be less than 5% from the rather messy NMR spectra produced. Unreacted 2-nitrotoluene is by far the major component in the complex mixture formed. Clearly this result is more in line with that obtained by Bakke than with Fields' and Myerson's result. Another aspect is the poor recovery of material obtained, only 45%. This is, partly at least, certain to be due to polymerisation and tar formation but also reflects the difficulty in trapping materials in flow pyrolysis.

Using an identical system, the reaction of 2-nitrotoluene was also carried out over a packing of porcelain chips. This gave an identical product mixture in terms of the peaks in the NMR spectra but with a greater proportion of 2-nitrotoluene having reacted. The recovery of material was also higher, at 63%. The amount of unreacted 2-nitrotoluene was quantified in this case by addition of a known amount of cyclohexane to the ^{1}H NMR sample and was found to account for 12% of the products by weight.

In the light of the relatively large amounts of unreacted starting material present, the reaction temperature was increased to 700 °C. Again this gave an identical, complex mixture with poorer recovery of material (46%) and no increase in the formation of methyl anthranilate. However, no unreacted starting material remained at this temperature.

Scheme 103 shows the same reaction as described above but with a further excess of methanol. This was carried out in the hope of simplifying the product mixture and yielding more methyl anthranilate due to the increased presence of trapping material.



Packing: Porcelain chips (whole tube packed)
Mass of 2-NT used: 476 mg
Methanol: 10.18 g (100 equivalents vs 2-NT)
Solution flow rate: 30 cm^3 h^{-1}
Carrier Gas flow rate: 20 cm^3 min^{-1}

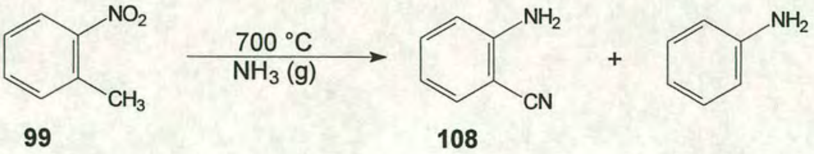
Scheme 103

Here 100 equivalents of methanol were used, a tenfold increase. This gave a product mixture which although still very complex, did seem to be cleaner in the aromatic regions of the ^{1}H and ^{13}C NMR spectra. However, a number of peaks were observed in the regions of 4-5 ppm (^{1}H NMR) and 70-90 ppm (^{13}C NMR). Although the component(s) responsible for these peaks were never identified they were tentatively attributed to breakdown or polymerisation products of methanol. Again no unreacted starting material remained and the recovery of material was low at 56%.

The disappointingly messy nature of these reactions and the resulting difficulties with analysis decreed that some way be found to simplify the product mixture. It was thought that perhaps the 2-nitrotoluene was not fully vaporised or perhaps that the vaporisation was causing local cooling in the furnace. Many descriptions of flow pyrolytic preparations describe the need for a pre-heater but the length of the furnace used (only ~30 cm) in this work does not really allow for this. An attempt was made to aid the vaporisation of 2-nitrotoluene by heating the nitrogen flow before passing it through the furnace. Thus the stainless steel tubing which delivers the nitrogen was fed through the furnace, (alongside, not within, the furnace reaction tube itself) before coupling to the reaction tube. This gave an identical product mixture to those formed in experiments carried out without this nitrogen heating. It is unclear to what extent the nitrogen heating system used was successful, as the temperature of the incoming gas was not measured.

3.5.2 Trapped by ammonia

In the work by Bakke in investigation of this anthranilate rearrangement, a higher yield of rearranged product was obtained from 2-nitrotoluene when ammonia was used as the nucleophile (scheme 88). A repeat of this in our hands gave a slightly different though related result as shown in scheme 104.



Packing: Porcelain chips (whole tube packed)
Mass of 2-NT used: 205 mg (neat)
2-NT flow rate: 0.6 cm^3 h^{-1}
Carrier Gas flow rate: 300 cm^3 min^{-1}

Scheme 104

Although this reaction gave a typically poor material recovery (47%), the product mixture was relatively clean. The NMR spectra showed the mixture to be almost entirely accounted for by anthranilonitrile **108** and aniline in an approximately 2:1 ratio. Indeed, addition of a known amount of cyclohexane to the ^{1}H NMR sample allowed anthranilonitrile to be quantified at 55% of the product mixture. Coupled with the poor material recovery obtained, this corresponds to a 26% yield. Traces of anthranilamide and unreacted starting material were indicated by t.l.c. and supported by the ^{13}C NMR spectrum though not unambiguously verified as present due to the complexity of the product mixture and the resulting identification difficulties. The result obtained by Bakke at a lower reaction temperature of 550 °C gave a 29% yield of anthranilamide (relative to the amount of starting material reacted) and only a trace of anthranilonitrile. It is presumed that the nitrile is formed by dehydration of the amide and so an appreciable amount of rearrangement must be taking place. The subsequent dehydration could be encouraged either by higher temperature or by variations inherent in the apparatus and packing used. The reaction was therefore carried out at 600 °C, giving an almost identical set of analyses. Unreacted 2-nitrotoluene was present, quantified at 17% of the product mixture by addition of cyclohexane to the ^{1}H NMR sample as before. The other products could not be quantified in this way unfortunately due to overlapping peaks, but it was noticed that anthranilamide was formed in slightly higher amount. So while there may be a temperature effect in the dehydration of anthranilamide, it appears that this is promoted primarily by the difference in the apparatus and is most likely to be due to the packing used. Chapter 1 of this discussion described how porcelain could provide a surface for the thermal dehydration of amides and although it was chosen as an inert packing, it may have a slight catalytic effect.

As was mentioned earlier, the ongoing development of a flow pyrolytic method was very much part of this work. Some difficulties had been encountered using neat 2-nitrotoluene with blockage of the addition syringe and so it was decided to use a concentrated solution of 2-nitrotoluene in methanol to circumvent this problem. This was successful in preventing blockage but led to the formation of breakdown products of methanol as mentioned previously. This was thought to be less of a problem than the practical and safety implications of syringe blockage and so this method was used frequently throughout the development process.

Ammonia flow rate

The flow rate of ammonia, used as both a reactant (nucleophilic trap) and a carrier, was varied dramatically to see whether this was likely to be an important variable. Flow rates of 30 cm^3 min^{-1} and 1200 cm^3 min^{-1} (the maximum allowed by the valve) were used. This gave very similar NMR spectra in appearance to those obtained at a flow rate of 300 cm^3 min^{-1} but with some implications for trapping of material and anthranilonitrile formation. Figure 20 depicts these results.

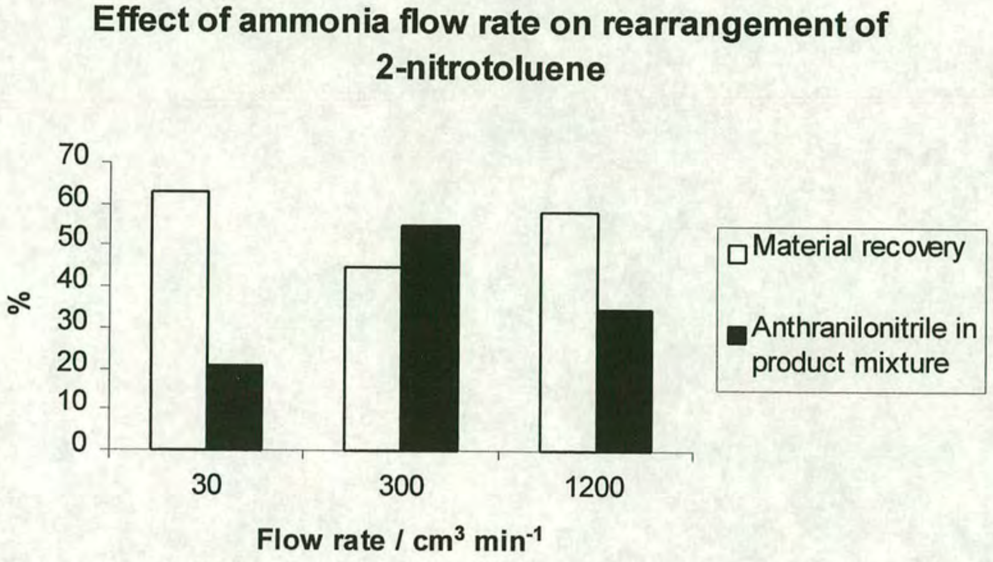


Figure 20

The graph shows that although slightly better recovery of material is obtainable at both higher and lower flow rates, the amount of rearranged product, anthranilonitrile, is reduced. The increased recovery of material is also misleading. In both these cases but especially at higher flow rate, products are distributed throughout the trapping system, rather than concentrated at the primary trap, beneath the furnace. This requires large volumes of solvent for collection and also extraction of the water trap which is used to prevent ammonia escape. The decrease in rearrangement, coupled with this collection difficulty makes the use of different flow rates disadvantageous.

Although the mechanism of the transformation of 2-nitrotoluene to the intermediate anthranil is not known, stoichiometrically it involves the loss of water. In the light of the previously described dehydration work (chapter 1), molecular sieves were used in an attempt to catalyse this apparent dehydration. 3A Molecular sieves were initially tried as these gave the highest activity for the dehydration of amides.

An initial run was carried out with 10 g of molecular sieves packed in the centre of the furnace tube, held in place with plugs of quartz wool. Porcelain packing was used to surround the zeolites as depicted in figure 21.

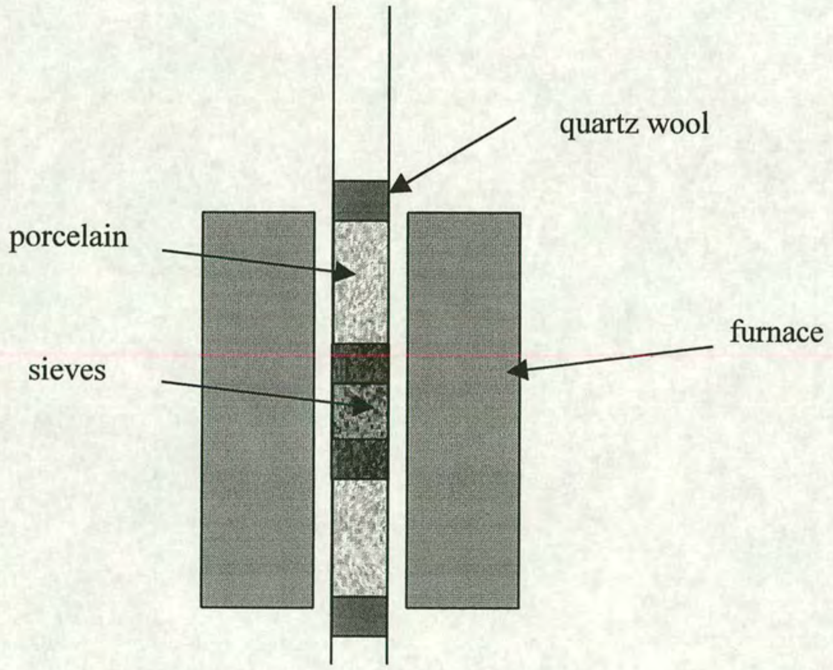
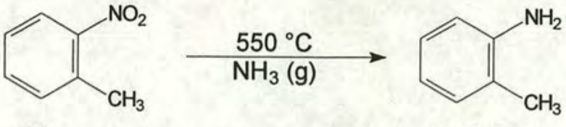


Figure 21

The reaction of 2-nitrotoluene with ammonia over 3A molecular sieves was carried out in concentrated methanol solution to prevent needle blockage as indicated previously. The reaction temperature used was limited to 550 °C due to the instability of the zeolites at temperatures higher than this. Scheme 105 shows the rather surprising result obtained.



99 **115**

Packing: Porcelain chips + Molecular sieves (centre)
Mass 2-NT used: 1.03 g in MeOH (2.94 cm^3)
2-NT (MeOH solution) flow rate: 24 $cm^3\ h^{-1}$
Carrier Gas flow rate: 300 $cm^3\ min^{-1}$

Scheme 105

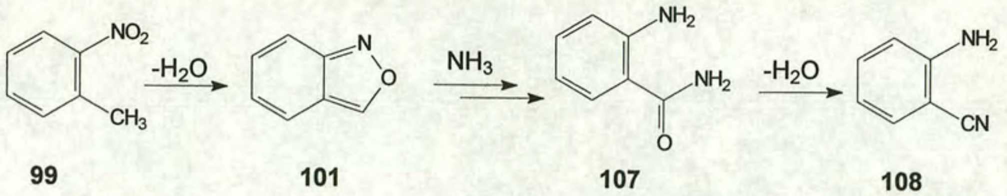
This gives a relatively clean mixture consisting predominantly of 2-toluidine **115**. No unreacted starting material is present. This is in contrast to the pyrolysis of 2-nitrotoluene over 3A molecular sieves under high vacuum which gave a complex mixture from which only unreacted starting material and 2-phenylindazole were identified. An unusually high material recovery is obtained, at 93%. While catalysing the breakdown of 2-nitrotoluene and allowing better trapping of the components formed, the molecular sieves seem to be catalysing the reduction of the nitro group. It is unclear from where the hydrogen comes for this transformation and this was investigated by the following experiment. The furnace was packed in the same way as depicted in figure 21 but ammonia was introduced *via* a long needle inserted to a position below the level of the molecular sieves. Nitrogen was introduced at the top of the furnace to carry the starting material to this point. This gave a product mixture which produced NMR spectra almost identical to those obtained when ammonia was introduced at the top of the furnace. This implies that the hydrogen required for the reduction of 2-nitrotoluene to 2-toluidine does not come from ammonia. However, little is known about the gas flows in the reactor and it could be that the thermal effects present cause a mixing of the gases throughout the furnace tube, precluding control of the ammonia flow.

A final experiment was carried out on this system in the total absence of ammonia. It was found that 2-nitrotoluene reacted at 550 °C over molecular sieves under nitrogen flow gave 2-toluidine. In this case the material recovery is poorer (51%) and the product mixture is messier. 2-Toluidine is estimated to account for ~50% of the products by observation of the NMR spectra. Hence ammonia is not required for the reduction of 2-nitrotoluene to 2-toluidine but does give a cleaner product in better yield.

Preliminary experiments using other commercially available molecular sieves (4A and 13X) again indicated the presence of 2-toluidine as the major product though recovery of material was poorer in each case than experiments using 3A molecular sieves.

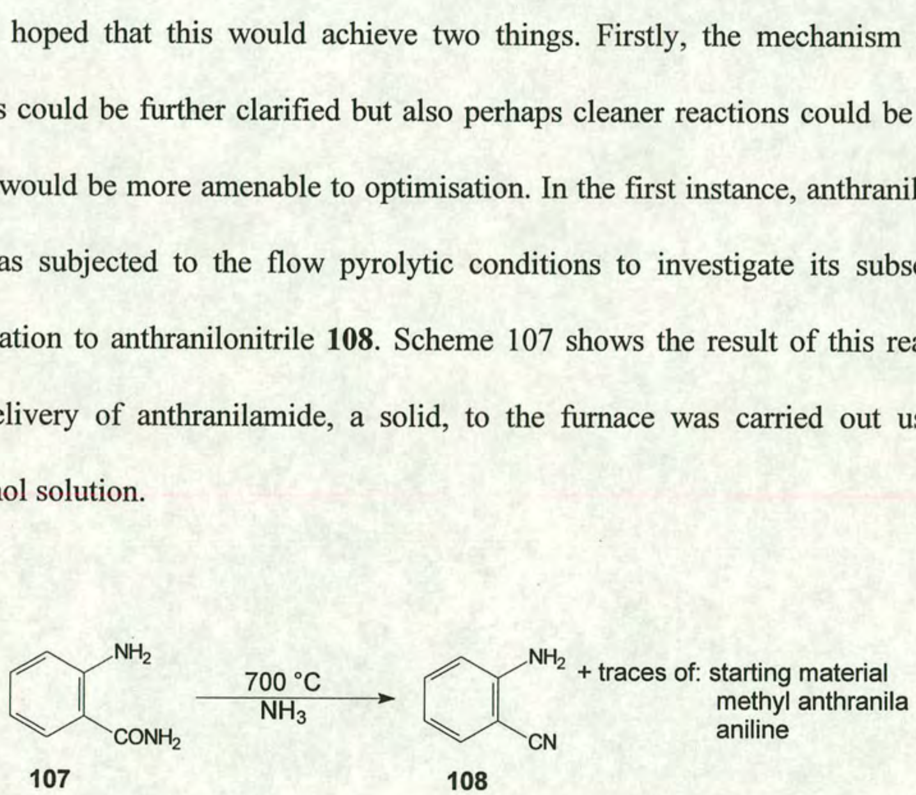
3.5.3 Flow pyrolytic reactions of anthranil and anthranilate derivatives

Given the extremely complex nature of the chemistry of 2-nitrotoluene and the resultant difficulties with analysis, it was decided to verify the mechanism of the final stages of the reaction, *i.e.*, the latter two steps shown in scheme 106.



Scheme 106

It was hoped that this would achieve two things. Firstly, the mechanism of the process could be further clarified but also perhaps cleaner reactions could be found which would be more amenable to optimisation. In the first instance, anthranilamide **107** was subjected to the flow pyrolytic conditions to investigate its subsequent dehydration to anthranilonitrile **108**. Scheme 107 shows the result of this reaction. The delivery of anthranilamide, a solid, to the furnace was carried out using a methanol solution.



Packing: Porcelain chips (whole tube packed)
Mass substrate used: 581 mg in MeOH (2.82 cm^3)
Substrate (MeOH solution) flow rate: 6 cm^3 h^{-1}
Carrier Gas flow rate: 300 cm^3 min^{-1}

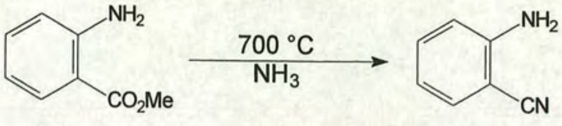
Scheme 107

This gave a reasonably clean product mixture with high material recovery (87%). Of this, the nitrile **108** was the major component, accounting for 44% of the products formed, determined by addition of a reference to the ^{1}H NMR sample. A trace of amide remained in the products. Also, some methyl anthranilate was formed presumably *via* the iminoketene intermediate as shown in scheme 97, which would be in equilibrium with the amide under thermal conditions. Aniline is observed also, perhaps formed by decarbonylation of the same intermediate.

It was found that this dehydration is independent of the carrier gas, ammonia. In conducting the same reaction under nitrogen flow, a similar set of analyses were obtained, giving anthranilonitrile **108** as the main product once more (51% of product mixture, no other identified components in appreciable amounts). Recovery of material is again high at 89%.

Furthermore, it was found that this transformation does not require a temperature of 700 °C and indeed is cleaner when carried out at lower temperature. Reaction of anthranilamide **107** at 550 °C gives a yellow oily solid (as opposed to a viscous brown oil) which when distilled, yields purified anthranilonitrile **108** in 66% isolated yield. This is the first reaction in which the flow pyrolysis apparatus, used in this system, has given a clean product in preparative yield, albeit a simple dehydration.

Having verified that anthranilonitrile can be formed from the amide under our reaction conditions, the previous step in the mechanism was investigated. Methyl anthranilate **114** was subjected to flow pyrolysis under ammonia carrier gas as shown in scheme 108.



114 **108**

Packing: Porcelain chips (whole tube packed)
Mass substrate used: 980 mg (neat)
Substrate flow rate: 1 cm^3 h^{-1}
Carrier Gas flow rate: 300 cm^3 min^{-1}

Scheme 108

The ester was delivered to the apparatus neat. This gave a relatively clean product mixture consisting predominantly of anthranilonitrile **108** (46% yield by reference in ^1H NMR). Attempted chromatographic separation yielded no further identifiable products except for a trace of starting material. This result however verifies our earlier assertion that the iminoketene intermediate is in equilibrium with its trapped derivative and in the presence of an excess of ammonia, this results in amide formation (followed by subsequent dehydration to the nitrile).

Described earlier was the effect of variation of the ammonia flow rate on the rearrangement of 2-nitrotoluene. Since reaction of methyl anthranilate is both simpler to carry out (neat substrate with no needle blockage problems) and gives a cleaner product profile, this investigation was repeated on this system. In each case the main identifiable product was anthranilonitrile. Figure 22 shows the recovery of material and yields of anthranilonitrile obtained.

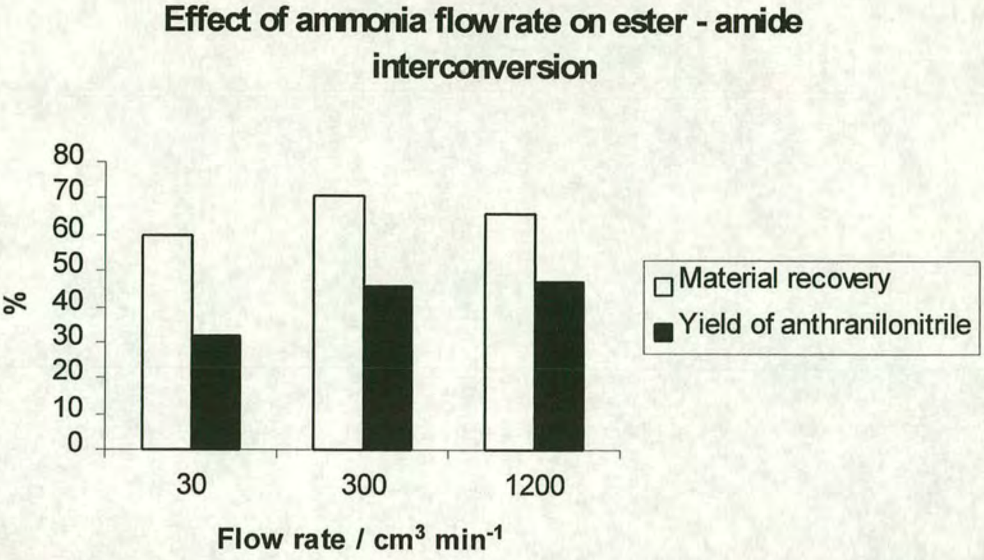
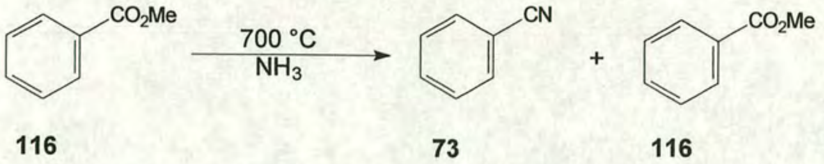


Figure 22

The graph shows that at a low flow rate a much poorer yield of anthranilonitrile is obtained. This is presumably due to the effective decrease in concentration of trapping material, allowing a greater propensity to side reactions. The profile of reaction at a very much higher ammonia flow rate shows little difference to that at standard (300 cm^3 min^{-1}) rate. This belies the difficulty in product collection however. Products were spread throughout the system, with almost a third collected by extraction from the end water trap. Again it seems that this intermediate ammonia flow rate is the best for use in this system.

As an aside, the effect of the *ortho* substituent upon the ester to nitrile transformation under ammonia was investigated by pyrolysing methyl benzoate under conditions known to convert methyl anthranilate to anthranilonitrile as shown in scheme109.

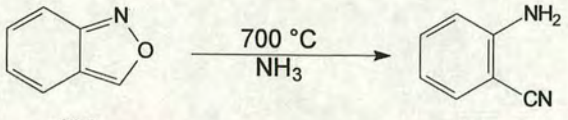


Packing: Porcelain chips　　2.8 : 1
Substrate flow rate: 1 cm^3 h^{-1}
Carrier Gas flow rate: 300 cm^3 min^{-1}

Scheme 109

This does indeed yield benzonitrile in a clean product mixture but starting material accounting for ~ 26% of the mixture remains. The recovery of material is low at 40%, perhaps partially explained by the relatively low boiling point of benzonitrile and the resulting trapping difficulties. The presence of unreacted starting material suggests that the conversion of methyl anthranilate to anthranilonitrile does indeed proceed *via* the previously proposed iminoketene intermediate, at least to some extent.

The previous step of the proposed mechanism was investigated with the reactions of anthranil **101**, a probable intermediate, under flow pyrolysis. Reactions of anthranilamide and methyl anthranilate (generating the iminoketene intermediate) have given relatively clean conversion to anthranilonitrile and it was hoped that anthranil would do the same, thus isolating the problem step in the system to the dehydration of 2-nitrotoluene. Indeed, pyrolysis of anthranil at 700 °C gave anthranilonitrile as shown in scheme 110.



101 **108**

Packing: Porcelain chips
Substrate flow rate: 1 $cm^3 h^{-1}$
Carrier Gas flow rate: 300 $cm^3 min^{-1}$

Scheme 110

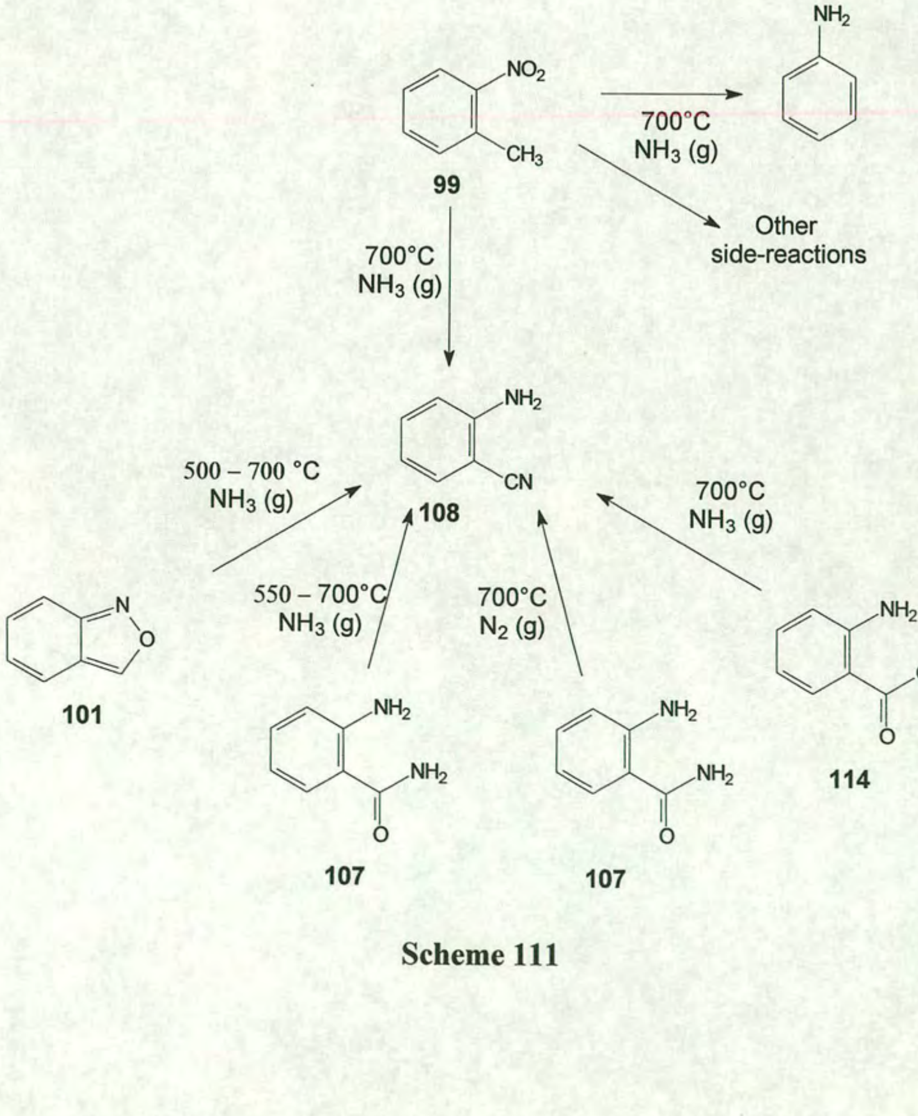
This yielded a product mixture consisting mainly of anthranilonitrile, with a 73% recovery of material. The sample was purified by distillation to give a 37% isolated yield of anthranilonitrile. The chemistry of the final steps of the rearrangement of 2-nitrotoluene, from anthranil onwards, appear to be fairly straightforward, with few side reactions occurring.

Using a lower temperature of 600 °C, the yield of nitrile from anthranil is increased to 58%. Further reduction, to 500 °C gives no further improvement (55%).

Again, blockage of the syringe needle delivering anthranil to the furnace was a problem in these reactions. Use of methanol circumvented this but it was desirable to find an alternative solvent for this process. Methanol suffers from the drawback of being reactive with the intermediates formed in the reaction and also produces unexplained peaks in the aliphatic ranges of the ^1H and ^{13}C NMR spectra. To this end, tetrahydrofuran was investigated as an alternative. Reaction of anthranil in THF under ammonia gave a high (72%) yield of anthranilonitrile, determined by reference addition to the NMR sample. However, trapping of material was extremely difficult. One third of the material collected was extracted from the water trap positioned to trap ammonia and other material was spread throughout the trapping system. Another anomaly is the apparent extra weight collected. With around 1 g pyrolysed, 1.2 g was collected, with no discrete signals observed in the NMR spectra to account for this. It is possible that some polymeric material was collected and filtered out in preparation of the NMR sample but the origin of such material remains obscure.

Summary of pyrolysis of anthranilate derivatives

By pyrolysing proposed intermediates in the rearrangement of 2-nitrotoluene, the requirements of the process have been elucidated. Scheme 111 summarises these experiments.



Scheme 111

While pyrolysis of 2-nitrotoluene **99** yields some anthranilonitrile **108**, many other side reactions take place to give a low yield of rearranged material. However, reactions of anthranil **101**, anthranilamide **107** and methyl anthranilate **114**, shown at the bottom of scheme 111, give the nitrile relatively cleanly in yields of over 50% and up to 70%. This clearly identifies the problem step as the conversion of 2-nitrotoluene to anthranil.

3.6 Conclusions and future work

The focus of the work described in this chapter shifted significantly during the course of the investigation. Initial experiments showed that the initial goal of a preparatively useful process for 2-nitrotoluene would require several other issues to be addressed first of all. It was clear that the mechanism of the rearrangement would need to be clarified and this has been achieved, though not completely. The mechanism of the conversion of 2-nitrotoluene to anthranil is not yet fully understood, although attempts to optimise this have treated the step as a dehydration. Having proposed a mechanism for the process, based upon both literature and experimental work, the efficiency of the various steps has been investigated, highlighting the generation of anthranil as the stage requiring most optimisation work. Throughout all these investigations, the requirement to develop a robust experimental apparatus and procedure for flow pyrolysis has been met. This has involved the development of delivery and trapping systems, as well as looking at different packing materials. These investigations have highlighted what appears to be a limiting constraint placed upon the research. The furnace used in this work allowed a reaction furnace tube of 30 cm long by 2.5 cm wide to be used. The hot zone of this furnace is appreciably shorter than 30 cm, nearer to 20 cm. This does not really allow sufficient space for a preheater unit to be incorporated, in order to ensure complete vaporisation of the substrate before catalysis occurs. To solve this problem a larger furnace was purchased. Time constraints allowed no more than the building of this system for future researchers but the furnace length of 90 cm should give greater flexibility in packing the reaction tube. The furnace also incorporates three separately heated zones, insulated from each other, so that either a temperature gradient or a larger uniform hot zone can be produced. It could be imagined that the top third of the furnace could be used as a preheater, the middle zone could be optimised for anthranil generation and the bottom could be solely responsible for the final stages of the reaction, which seem to require a lower temperature.

Alongside this apparatus development, it is clear that a catalytic process will be required for the conversion of 2-nitrotoluene to anthranil. The beginnings of an investigation into this were described earlier, with the use of molecular sieves proving unsuccessful. Further dehydration catalysts should be tried and perhaps alternative methods, if the mechanism of this step can be elucidated.

Experimental

ABBREVIATIONS

NMR	nuclear magnetic resonance
δ_H, δ_C	chemical shift
ppm	parts per million
s	singlet
d	doublet
t	triplet
q	quartet (^{1}H NMR)
	quaternary (^{13}C NMR)
m	multiplet
br	broad
J	coupling constant
Hz	Hertz
IR	infra-red
ν	wavenumber
m/z	mass to charge ratio
M^+	mass of molecular ion
FVP	flash vacuum pyrolysis
t.l.c.	thin layer chromatography
DMSO	dimethyl sulfoxide
mp	melting point
bp	boiling point

g	grams
mg	milligrams
mol	moles
M	molarity
s	seconds
ms	milliseconds
min	minutes
h	hours

1. Instrumentation and general techniques

1.1 Nuclear Magnetic Resonance spectroscopy

^{1}H NMR spectra were recorded on Bruker AC250, Bruker AC200 and Varian Gemini 200 spectrometers. ^{13}C NMR spectra were recorded on Bruker WH360, Bruker AC250, Bruker AC200 and Varian Gemini 200 spectrometers.

^{1}H NMR spectra were routinely recorded in [^{2}H]chloroform at 200 MHz and only at 250 MHz when specified in the text. ^{13}C NMR spectra were generally recorded on the Bruker AC250 at 63 MHz unless otherwise stated. Chemical shifts (δ_H and δ_C are quoted in ppm, relative to tetramethylsilane and coupling constants (*J*) are given in Hz.

1.2 Mass Spectrometry

All the mass spectra quoted were obtained by electron impact mass spectrometry. Low resolution electron impact mass spectra were recorded on Finnigan 4500 and Finnigan 4600 instruments. High resolution mass spectra were recorded on a Kratos MS50 Tc instrument.

1.3 Infra-red spectroscopy

IR spectra were obtained as liquid films or nujol mulls on a Perkin Elmer Paragon 1000 FT-IR spectrometer and are quoted in wavenumbers (cm^{-1}).

1.4 Chromatography

Thin layer chromatography was carried out on pre-coated aluminium sheets (0.2 mm silica gel, Merck, grade 60) impregnated with an UV fluorescent indicator.

Dry flash column chromatography was carried out on silica gel (silica gel H, Fluka, 30-250 mesh) by the method of Harwood[100] using an hexane/ethyl acetate gradient as eluent.

Gas chromatography was carried out on a Hewlett Packard HP 5890 GC apparatus. Quantitative GC analysis was carried out for three complex mixtures detailed in section 4.1. This was achieved as follows. Firstly, components believed to be present in each mixture were verified by spiking the GC sample with authentic compounds. A response factor was then calculated for each compound present by injecting each authentic sample into the chromatograph under the same conditions and at similar concentrations to the reaction mixtures. This response factor was then applied to the chromatogram obtained from the reaction mixture. Percentages quoted in the text refer to percentage of the products formed and not yield. Although not as accurate as determination by internal standard, this method gave valid results for comparison between the three mixtures subjected to the method.

1.5 Flash Vacuum Pyrolysis (FVP)

FVP experiments were conducted using the apparatus shown in figure 23, based on the design of W.D. Crow (Australian National University). The system is maintained under vacuum, typically at 10^{-2}-10^{-3} Torr, by a high capacity oil pump. The pressure is monitored between the product trap and the pump. The FVP experiment involves placing the substrate to be pyrolysed in the inlet tube and heating it with a glass Büchi oven until it volatilises. The gaseous substrate then passes through a silica tube (30 × 2.5 cm) which is heated to temperatures of 300-1100 °C by a laboratory tube furnace. The tube may contain a packing material, as discussed in section 1.7. The estimated contact time in the hot zone of an empty tube is in the order of 10 ms. Products formed are collected on exiting the furnace usually by means of a liquid nitrogen-cooled trap. Products may be collected into solvent for further work-up or directly into [^{2}H]chloroform for NMR spectroscopy in the case of small scale experiments.

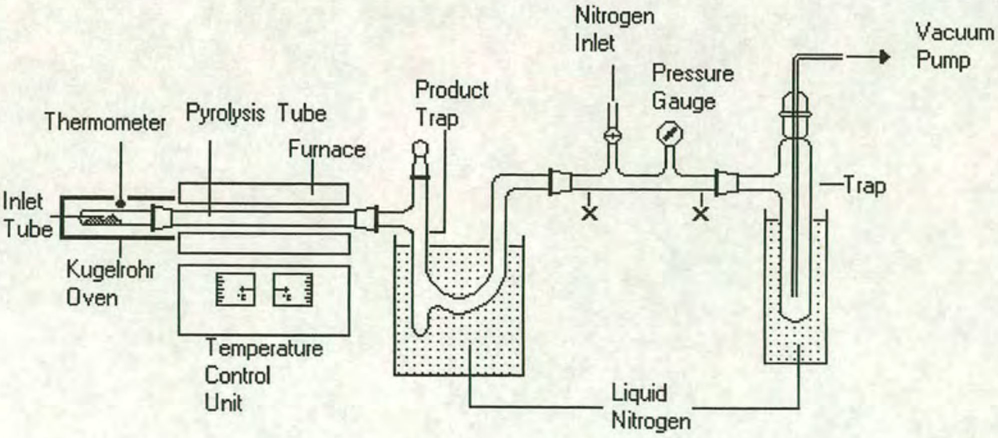


Figure 23

1.6 Flow Pyrolysis

Flow pyrolysis experiments were conducted under the following protocol, using the apparatus described in chapter 3.3 of the discussion section. The basic apparatus is shown in figure 24 below.

While the furnace is heating to the desired temperature for reaction, the carrier gas flow is adjusted to the required level. This is achieved by attaching a flow meter to the exit of the entire apparatus and adjusting the gas needle valve until the desired flow rate is reached. The flow meter is then disconnected. Coolants (ice, dry-ice/acetone) for the trapping system are then put in place.

The substrate to be pyrolysed is placed in a weighed syringe and needle assembly and the needle inserted into the pyrolysis apparatus as described in section 3.3, discussion. A syringe pump is set up around the syringe and the desired substrate flow rate is set on the pump. Switching on the pump commences the reaction.

When finished, the syringe and needle assembly is removed and weighed, determining accurately the amount of substrate which has been delivered. After allowing the apparatus to cool, products are collected by dissolution in an appropriate solvent (generally methanol) from each trap, combined and concentrated under reduced pressure. Any material observed in the water trap (see figure 15, section 3.3, discussion) is extracted into a suitable solvent, dried and concentrated under reduced pressure.

Various trapping systems were used. The primary trap, positioned at the exit of the furnace, used in each case was either A or B as depicted in figure 25. Trap B is based on the design of a preparative GC-style trap to maximise collection at this point.[97] Most of the products formed were collected here. Following this, the product gases were collected using a series of cooled traps. For reactions where nitrogen was the carrier gas, the trapping system consisted of: double surface condenser; ice-cooled Dreschel trap; dry ice/acetone-cooled Dreschel trap; bubble through water. For reactions where ammonia was the carrier gas, the trapping system consisted of: double surface condenser; ice-cooled Dreschel trap; bubble through water. In each case the Dreschel traps were loosely packed with quartz wool to aid the breakdown of mists. The products formed were collected together into methanol or dichloromethane for further analysis. The water trap was extracted into dichloromethane if necessary.

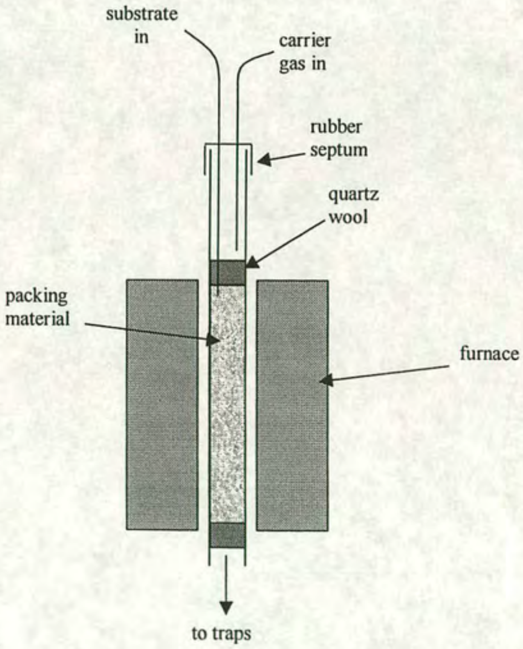
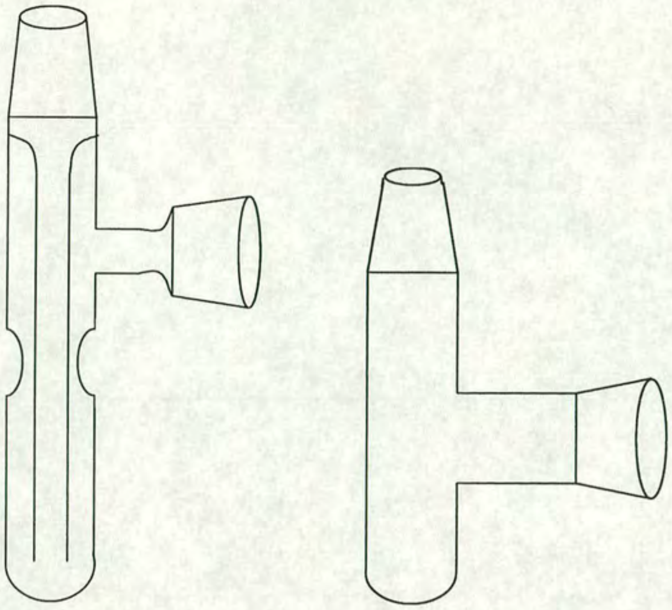


Figure 24



Trap A Trap B

Figure 25

1.7 Packing materials used in FVP and Flow Pyrolysis

Molecular sieves, when used in FVP, were prepared as follows: molecular sieves, 1-2 mm beads (Lancaster), (10 g) were held in the centre of the furnace by two plugs of quartz wool (Multilab). The tube was then heated in air for 2 h at the reaction temperature (or at 450 °C if the reaction temperature is less than 450 °C) and then heated for approximately 30 min at reaction temperature under vacuum.

Molecular sieves were also used in some flow pyrolysis reactions. These were packed into different areas of the furnace as specified in the text and held in place by plugs of quartz wool. They were prepared for use by heating in air for 2 h at 500 °C and then for 15 min under nitrogen gas flow.

A range of commercial molybdenum oxide catalysts was supplied by Zeneca for use in dehydrogenation reactions. Five samples were supplied, denoted as (1), (2), etc. throughout the report. Few details on these catalysts are available but what is known is presented below.

The catalysts were supplied in pelleted form, loaded onto alumina. A working temperature of 500-550 °C was recommended for these catalysts due to the alumina support. They are supplied in the γ-form of alumina, which is most active and which is transformed to other forms on heating at 600 °C and above. Catalyst 5 was a doped catalyst, incorporating a small amount of cobalt oxide. All of the catalysts used had similar regeneration and activity properties (see section 3.1.2).

These, where used, were prepared/regenerated as follows: pellets (1-2 mm) of alumina loaded with molybdenum oxide (10 g) were held in the centre of the furnace tube by two plugs of quartz wool (Multilab). The tube was then heated in air for 2 h at 550 °C. These conditions were found to give slightly less than full regeneration, the amount of which was dependent on the particular catalyst employed. However, the level of regeneration obtained was the same on further repetition. Other regeneration protocols were tried including heating for shorter/longer times and heating in a stream of air but these gave no improvement over the conditions described above.

Alumina pellets (Aldrich) where used are 1-2mm beads of alumina, prepared as for molybdenum oxide catalysts.

Porcelain saddles (6 mm, Aldrich) were used as a bulky packing material to effectively raise the contact time of an FVP experiment. These were packed into the full length of the furnace tube and held in place by plugs of quartz wool. They were used without any special preparation as they were found to be no more effective if heated prior to reaction.

Porcelain saddles were also used in flow pyrolysis reactions in exactly the same manner.

Quartz wool (5-30 μm, Multilab) was also used to raise the contact time of an FVP experiment and occasionally as a flow pyrolysis packing. The furnace tube would be packed fairly loosely with the wool for its full length. This packing required no special preparation for use.

The use of quartz beads is occasionally described. These are 1-2 mm beads drawn from a quartz rod and were used in control experiments to mimic the volume effects of other catalysts used. These were packed into the centre of the furnace tube in the same manner as molecular sieves and used without preparation.

2. Catalytic dehydrations under FVP

2.1 Preparation of nitriles by dehydration

2.1.1 Preparation of dehydration precursors

2-Furancarboxamide. 2-Furoic acid (2.13 g, 0.019 mol) was heated under reflux in thionyl chloride for 1 h. The excess of thionyl chloride was then removed by evaporation under reduced pressure. Concentrated ammonia solution was added until the vigorous reaction subsided. The precipitate formed was filtered off, washed with light petroleum (bp 40 – 60 °C) and dried under oil pump pressure to yield 2-furancarboxamide (1.71 g, 81%), mp 138-141 °C [lit.[101] 141-142 °C]; δ_H (250 MHz, DMSO) 7.79-7.78 (2 H, m), 7.40 (1 H, br s), 7.10 (1 H, m) and 6.59 (1 H, m); δ_C (DMSO) 159.69 (q), 148.19 (q), 145.23, 113.90 and 112.01. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[102]

Benzaldehyde oxime. Benzaldehyde (2.00 cm^3, 0.020 mol) and hydroxylamine hydrochloride (2.03 g, 0.029 mol) were heated under reflux in ethanol (20 cm^3) and pyridine (2 cm^3) for 1 h. The solvent was removed by evaporation under reduced pressure and water (20 cm^3) was added. The oily substance formed was extracted into dichloromethane (3 × 20 cm^3), dried over magnesium sulfate and the solvent was evaporated under reduced pressure. The residual clear oil was purified by distillation to yield benzaldehyde oxime (2.23 g, 92%), bp 65 °C (0.5 Torr) [lit.[103] 104 °C (6 Torr)]; δ_H 8.50 (1 H, br s), 8.09 (1 H, s) and 7.50-7.26 (5 H, m); δ_C 150.18, 131.73 (q), 129.91, 128.63 and 126.90. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Pyrrole-2-carbaldoxime. Pyrrole-2-aldehyde (2.09 g, 0.022 mol) and hydroxylamine hydrochloride (2.00 g, 0.029 mol) were heated under reflux in ethanol (20 cm^3) and pyridine (2 cm^3) for 1 h. The solvent was removed by evaporation under reduced pressure and water (20 cm^3) was added. The mixture was then stirred in an ice-bath until crystallisation occurred. The deep purple solid formed was filtered, washed with light petroleum (bp 40 – 60 °C) and then dried under oil pump pressure to yield pyrrole-2-aldoxime (both syn and anti isomers present) (2.01 g, 83%) mp 160-163 °C [lit.[104] 165-166 °C]; δ_H (250 MHz, DMSO) (major isomer) 11.15 (2 H, br s), 7.27 (1 H, s), 6.89 (1 H, m), 6.56 (1 H, m) and 6.12 (1 H, m); δ_H (250 MHz, DMSO) (minor isomer) 10.60 (2 H, br s), 7.93 (1 H, s), 6.81 (1 H, m), 6.30 (1 H, m) and 6.08 (1 H, m); δ_C (DMSO) (major isomer) 137.42, 124.13 (q), 121.19, 114.16 and 108.65; δ_C (DMSO) (minor isomer) 141.06, 125.26 (q), 120.95, 111.03 and 108.82. The ^{1}H NMR spectrum concurred with that in the literature.[105]

Thiophene-3-carbaldoxime. Thiophene-3-carboxaldehyde (4.02 g, 0.036 mol) and hydroxylamine hydrochloride (4.21 g, 0.061 mol) were heated under reflux in ethanol (40 cm^3) and pyridine (4 cm^3) for 1 h. The solvent was removed by evaporation under reduced pressure and water (40 cm^3) was added. The mixture was extracted into dichloromethane (3 × 30 cm^3), dried over magnesium sulfate and concentrated under reduced pressure. The residual yellow oily solid (1.03 g) was purified by distillation to yield thiophene-3-carbaldoxime as a mixture of *syn* and *anti* isomers (0.92 g, 90%), bp 110 °C (0.2 Torr), mp 125-128 °C [lit.[106] 111-112 °C]; δ_H (250 MHz, DMSO, major isomer) 11.04 (1 H, br s), 8.16 (1 H, s), 7.56-7.52 (2 H, m) and 7.35 (1 H, dd, *J* 5.0, 0.8); δ_C (DMSO, major isomer) 144.11, 135.58 (q), 127.53, 126.24 and 124.66; δ_H (250 MHz, DMSO, minor isomer) 11.56 (1 H, br s), 8.21 (1 H, dd, *J* 2.7, 1.4), 7.68 (2 H, m) and 7.50 (1 H, s); δ_C (DMSO, minor isomer) 139.93, 132.38 (q), 130.51, 129.60 and 125.88.

Indole-3-carbaldoxime. Indole-3-carboxaldehyde (4.00 g, 0.027 mol) and hydroxylamine hydrochloride (4.10 g, 0.059 mol) were heated under reflux in ethanol (40 cm^3) and pyridine (4 cm^3) for 1 h. The solvent was removed by evaporation under reduced pressure and water (40 cm^3) was added. The precipitated solid was filtered under suction and washed with light petroleum (bp 40-60 °C) to give a mixture of indole-3-carbaldoxime and unreacted starting material (4.72 g). The mixture (1.60 g) was recrystallised from acetic acid to give indole-3-carbaldoxime as a pale yellow solid (0.79 g, 54%), mp 193-196 °C [lit.,[107] 197-198 °C]; δ_H (DMSO) 11.56 (1 H, br s), 11.20 (1 H, br s), 8.22 (1 H, d, *J* 2.6), 7.86-7.77 (2 H, m), 7.44 (1 H, m) and 7.19-7.05 (2 H, m); δ_C (DMSO) 138.56, 135.07 (q), 130.63, 126.36 (q), 122.06, 120.09, 118.34, 111.93 and 106.48 (q). The ^1H and ^{13}C NMR spectra concurred with those in the literature.[107]

Acetophenone *O*-methyl oxime. Acetophenone (1.00 g, 8.33×10^{-3} mol) and methoxyamine hydrochloride (1.39 g, 1.67×10^{-2} mol) were heated under reflux in ethanol (50 cm^3) for 1.5 h. The solvent was removed by evaporation under reduced pressure and the residue was treated with aqueous sodium hydroxide solution (0.25 M, 40 cm^3) and extracted with ether (3 × 20 cm^3). The extracts were dried over magnesium sulfate and concentrated under reduced pressure to yield acetophenone *O*-methyl oxime as a clear oil after distillation (1.09 g, 88%), bp 90-92 °C (1.5 Torr) [lit.[108] 54-60 °C (0.5 Torr)]; δ_H 7.71-7.66 (2 H, m), 7.42-7.37 (3 H, m), 4.04 (3 H, s) and 2.26 (3 H, s); δ_C (50 MHz) 154.30 (q), 136.43 (q), 128.80, 128.17, 125.82, 61.64 and 12.20. The ^{1}H NMR spectrum concurred with that in the literature.[109]

Benzaldehyde *O*-methyl oxime. Benzaldehyde (1.05 g, 9.91×10^{-3} mol) and methoxyamine hydrochloride (1.65 g, 1.98×10^{-2} mol) were heated under reflux in ethanol (50 cm^3) for 1.5 h. The solvent was removed by evaporation under reduced pressure and the residue treated with aqueous sodium hydroxide solution (0.25 M, 40 cm^3) and extracted with ether (3 × 20 cm^3). The extracts were dried over magnesium sulfate and concentrated under reduced pressure to yield benzaldehyde *O*-methyl oxime, identified as the *E*-isomer, as a clear oil after distillation (0.96 g, 72%), bp 80-85 °C (15 Torr) [lit.[110] 79-82 °C (1.5 Torr)]; δ_H 8.09 (1 H, s) 7.63-7.58 (2 H, m), 7.41-7.36 (3 H, m) and 4.00 (3 H, s); δ_C 148.31 (q), 132.59 (q), 129.57, 128.47, 126.79, and 61.75. The ^{1}H NMR spectrum concurred with that in the literature.[111]

2.1.2 Optimisation of amide dehydration

The following experiments detail the optimisation of conditions developed to effect the dehydration of amides to the corresponding nitriles. The process was evaluated on the test dehydration of benzamide to benzonitrile. A general method follows:

Benzamide (~ 10^{-3} mol) was pyrolysed at temperatures ranging from 350 to 900 °C as detailed in section 1.5. The furnace tube was packed with various materials as stated below. These materials were prepared and used according to the methods detailed in section 1.7. The crude pyrolysate, in each case consisting of only benzamide and benzonitrile, was collected into methanol and concentrated under reduced pressure.

The product mixture was quantified as follows. The % conversion to benzonitrile was calculated as the ratio of intensity (product peak) versus intensity (reactant peak) in the ^{13}C NMR spectrum, normalised against the same intensity ratio in a standard 1:1 mixture of benzamide and benzonitrile. This process was repeated for each product peak referenced against each reactant peak and the mean average value taken. The validity of this method is confirmed by the example spreadsheet shown in table 1, where there is no more than 15% difference in the ratios to be averaged. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: % conversion to benzonitrile.

amide **Intensity A**	**GM (17.2)**	Ratio as referenced to B1	Ratio as referenced to B2	Ratio as referenced to B3	Ratio as referenced to B4	Ratio as referenced to B5	**Average Ratio**	Standard Intensities
38.9		0.649688	0.709537	0.722297	0.621905	0.689298	0.678545	39.5
30.1		0.601207	0.665068	0.678898	0.572111	0.643289	0.632115	37.6
45.7		0.661193	0.719923	0.732399	0.633808	0.700103	0.689485	44.1
101.1		0.636993	0.698002	0.711062	0.608809	0.677326	0.666438	108.5
99.4		0.639551	0.700333	0.713334	0.611445	0.679743	0.668881	105.5
	Averages:	0.637727	0.698573	0.711598	0.609616	0.677952	**0.667093**	

nitrile **Intensity B**		Ratio as referenced to A1	Ratio as referenced to A2	Ratio as referenced to A3	Ratio as referenced to A4	Ratio as referenced to A5		
27.4		0.350311	0.398792	0.338806	0.363006	0.360448	0.362272	51.6
43.5		0.290462	0.334931	0.280076	0.301997	0.299666	0.301426	107.9
40.4		0.277702	0.321101	0.267600	0.288937	0.286665	0.288401	106.7
9.4		0.378094	0.427888	0.366191	0.391190	0.388554	0.390383	15.7
9.1		0.310701	0.356710	0.299896	0.322673	0.320256	0.322047	20.5
	Averages:	0.321454	0.367884	0.310514	0.333561	0.331118	**0.332906**	

Table 1

FVP of benzamide over porcelain saddles. (148 mg, 1.22 × 10^{-3} mol), 150 °C, 500 °C, 5 × 10^{-3} Torr, 5 min, 120 mg: 18.9% conversion to benzonitrile; δ_H (DMSO) 7.74-7.43 (5 H, m); δ_C (50 MHz, DMSO) 133.55, 132.61, 128.76, 118.15 (q) and 110.66 (q). The ^1H and ^{13}C NMR spectra concurred with those in the literature.[103]

(163 mg, 1.35 × 10^{-3} mol), 150 °C, 600 °C, 5 × 10^{-3} Torr, 5 min, 130 mg: 33.3%.
(167 mg, 1.38 × 10^{-3} mol), 150 °C, 700 °C, 5 × 10^{-3} Torr, 5 min, 131 mg: 48.6%.
(180 mg, 1.49 × 10^{-3} mol), 150 °C, 800 °C, 5 × 10^{-3} Torr, 5 min, 127 mg: 64.3%.
(162 mg, 1.34 × 10^{-3} mol), 150 °C, 900 °C, 5 × 10^{-3} Torr, 5 min, 96 mg: 82.6%.

FVP of benzamide over silica tubes. 7 silica gel coated quartz tubes (5 cm × 6 mm) were prepared by dipping the tubes into a 1:1 slurry of t.l.c. grade silica gel and methanol, removing any excess adsorbent and then activating by heating in an oven at 120 °C for 30 min. These were then packed tightly in the centre of the furnace tube before pyrolysis. (354 mg, 2.93×10^{-3} mol), 150 °C, 700 °C, 5×10^{-3} Torr, 15 min, 327 mg: 27.3%.

FVP of benzamide over 3A molecular sieves. (150 mg, 1.24×10^{-3} mol), 150 °C, 350 °C, 5×10^{-3} Torr, 15 min, 88 mg: 31%.

(366 mg, 3.02×10^{-3} mol), 150 °C, 400 °C, 5×10^{-3} Torr, 15 min, 262 mg: 95%.

(429 mg, 3.55×10^{-3} mol), 150 °C, 450 °C, 5×10^{-3} Torr, 20 min, 283 mg: 96%.

(461 mg, 3.81×10^{-3} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 20 min, 359 mg: 100%.

(572 mg, 4.73×10^{-3} mol), 150 °C, 550 °C, 5×10^{-3} Torr, 20 min, 372 mg: 100%.

2.1.3 Optimisation of oxime dehydration

The following experiments detail the optimisation of conditions developed to effect the dehydration of oximes to the corresponding nitriles. The process was evaluated on the test dehydration of benzaldehyde oxime to benzonitrile. A general method follows:

Benzaldehyde oxime (~ 10^{-3} mol) was pyrolysed at temperatures ranging from 300 to 450 °C as detailed in section 1.5. The furnace tube was packed 3A molecular sieves, prepared and used according to the method detailed in section 1.7. The crude pyrolysate, in each case consisting of only benzaldehyde oxime and benzonitrile, was collected into dichloromethane, dried over magnesium sulfate and concentrated under reduced pressure.

Quantitative mixture analysis was carried out using ^{13}C NMR spectroscopy as described in section 2.1.2. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: % conversion to benzonitrile.

FVP of benzaldehyde oxime over 3A molecular sieves. (127 mg, 1.05×10^{-3} mol), 60° C, 300 °C, 1×10^{-2} Torr, 10 min, 67 mg: >90% conversion to benzonitrile.

(97 mg, 8.04×10^{-4} mol), 60 °C, 350 °C, 1×10^{-2} Torr, 10 min, 80 mg: >90%.

(109 mg, 9.01×10^{-4} mol), 60 °C, 400 °C, 1×10^{-2} Torr, 10 min, 67 mg: >90%.

(80 mg, 6.61×10^{-4} mol), 60 °C, 450 °C, 1×10^{-2} Torr, 10 min, 42 mg: 100%.

2.1.4 Role and activity of molecular sieves

The following experiments involve the pyrolysis of benzamide over molecular sieves to give benzonitrile under various conditions. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, work-up and products.

Investigation of reaction capacity of 3A molecular sieves. Benzamide was placed in the FVP inlet tube (see fig.23) and pyrolysed over molecular sieves. The reaction was stopped when unreacted benzamide began to form in the product trap and the amount which had reacted was noted. (1.35 g, 1.10×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 1 h. The pyrolysate was collected into dichloromethane and concentrated under reduced pressure to give a clear oil (1.22 g) containing water from the dehydration. The mixture was dried over magnesium sulfate and collected to give water-free benzonitrile (1.07 g, 1.04×10^{-2} mol); δ_H 7.58-7.33 (5 H, m); δ_C (50 MHz) 132.60, 131.88, 128.93, 118.60 (q) and 112.12 (q). Formation of benzonitrile (1.04×10^{-2} mol) requires that the same number of moles of water are formed. The weight of product before and after drying indicates that water (0.15 g, 8.3×10^{-3} mol, 80% recovery) was collected.

Benzamide was then pyrolysed over the same molecular sieves under the same conditions after attempted reactivation, immediately yielding unreacted starting material in the product trap.

Investigation of stability of 3A molecular sieves to prolonged heating. Benzamide was placed in the FVP inlet tube (see fig.23) and pyrolysed over molecular sieves, prepared by heating at 500 °C for 16 h. The reaction was stopped when unreacted benzamide began to form in the product trap and the amount reacted was noted. This amount was found to be much less than that reacted before starting material is observed in the normal experiment where the sieves used have not been exposed to prolonged heating, (253 mg, 2.09×10^{-3} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 20 min. The pyrolysate was collected into dichloromethane, dried over magnesium sulfate and the solvent evaporated under reduced pressure to give benzonitrile (197 mg, 92%); δ_H 7.60-7.34 (5 H, m). This result indicates that the initial activity of the molecular sieves is reduced to 19% of its normal value.

Investigation of 3A molecular sieve reaction capacity on a 5 g scale. (5.75 g, 4.76×10^{-3} mol), 180 °C, 500 °C, 10^{-2} Torr, 2 h. The pyrolysate was collected firstly into dichloromethane and the remainder into methanol. The dichloromethane fraction was dried over magnesium sulfate and concentrated under reduced pressure to give benzonitrile (4.17 g, 85%); δ_H 7.61-7.38 (5 H, m); δ_C (50 MHz) 132.50, 131.75, 128.79, 118.49 (q), 111.98 (q). The methanol fraction was concentrated under reduced pressure to give unreacted benzamide (0.67 g); mp 129-130 °C.

Portionwise investigation of 3A molecular sieve reaction capacity on a 25 g scale. Benzamide was pyrolysed in portions of ~ 5 g over 3A molecular sieves. The sieves were initially prepared as described in section 1.7 but were used without further preparation for each 5 g portion. The pyrolysate in each case was collected into dichloromethane and dried over magnesium sulfate to give benzonitrile while the unreacted benzamide was subsequently collected into methanol.

(Portion 1) (5.15 g, 4.26×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 2 h: benzonitrile (3.83 g, 87% conversion); benzamide (0.56 g).

(Portion 2) (5.01 g, 4.14×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 40 min: benzonitrile (1.25 g, 29% conversion); benzamide (3.01 g).

(Portion 3) (4.89 g, 4.04×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 2 h: benzonitrile (2.83 g, 69% conversion); benzamide (1.23 g).

(Portion 4) (5.22 g, 4.31×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 50 min:

benzonitrile (1.92 g, 45% conversion); benzamide (2.35 g).

(Portion 5) (5.35 g, 4.42 × 10^{-2} mol), 150 °C, 500 °C, 5 × 10^{-3} Torr, 1 h 45 min: benzonitrile (2.46 g, 54% conversion); benzamide (2.09 g).

As a result of different inlet tube geometry, portions 2 and 4 were introduced to the furnace at a much higher rate than in the other cases, which can be seen in the data above. This resulted in nonconformity in the amount of conversion to benzonitrile. This sensitivity to throughput rate is an interesting result in itself, not normally observed under standard FVP conditions.

To mimic the thermal conditions under which **Portion 5** was carried out, benzamide was pyrolysed over 3A molecular sieves, prepared by heating for 9 h at 500 °C. (5.07 g, 4.19 × 10^{-2} mol), 150 °C, 500 °C, 5 × 10^{-3} Torr, 2 h: benzonitrile (3.82 g, 84% conversion); benzamide (0.39 g). It was noticed that unreacted benzamide was observed in the product trap immediately on starting the reaction.

To mimic the dehydration conditions which the molecular sieves have experienced in **Portion 5**, water (1.72 g) was vaporised over sieves before benzamide was pyrolysed under otherwise identical conditions to those described for Portion 5. (5.54 g, 4.58 × 10^{-2} mol), 150 °C, 500 °C, 5 × 10^{-3} Torr, 2 h: benzonitrile (2.45 g, 47% conversion); benzamide (2.73 g). Hence the presence of water is more important than the thermal deactivation of the molecular sieves.

Investigation of water-deactivation of 3A molecular sieves. To investigate the deactivation of molecular sieves, amounts of water were passed over the sieves prior to reaction. Subsequently, benzamide was pyrolysed until unchanged starting material was observed in the product trap. In each case the water passed through the apparatus was collected and weighed, demonstrating that no water was retained in the molecular sieves. Results are quoted as follows: quantity of water passed, inlet temperature, furnace temperature, pressure, amount of benzamide reacted before its appearance in product trap: products.

(198 mg, 1.1 × 10^{-2} mol), 150 °C, 500 °C, 5 × 10^{-3} mol, (34 mg, 2.81 × 10^{-4} mol): benzonitrile (24 mg, 2.33 × 10^{-4} mol).

(146 mg, 8.11 × 10^{-3} mol), 150 °C, 500 °C, 5 × 10^{-3} mol, (112 mg, 9.26 × 10^{-4} mol): benzonitrile (82 mg, 7.96 × 10^{-4} mol).

(101 mg, 5.61 × 10^{-3} mol), 150 °C, 500 °C, 5 × 10^{-3} mol, (246 mg, 2.03 × 10^{-3} mol): benzonitrile (185 mg, 1.80 × 10^{-3} mol).

(50 mg, 2.78 × 10^{-3} mol), 150 °C, 500 °C, 5 × 10^{-3} mol, (580 mg, 4.79 × 10^{-3} mol): benzonitrile (485 mg, 4.71 × 10^{-3} mol).

Investigation of 5A molecular sieve reaction capacity on a 5 g scale. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time: work-up and products. (5.11 g, 4.22 × 10^{-2} mol), 180 °C, 500 °C, 5 × 10^{-3} Torr, 2 h: the pyrolysate was collected firstly into dichloromethane, dried over magnesium sulfate and the solvent was evaporated under reduced pressure to give benzonitrile (3.79 g, 87% conversion), δ_H 7.60-7.33 (5 H, m); the remaining white solid not dissolved by dichloromethane was collected into methanol and concentrated under reduced pressure to give unreacted benzamide (0.56 g).

It was noticed during reaction that unreacted benzamide was apparent in the product trap immediately on starting the reaction.

Portionwise investigation of 5A molecular sieve reaction capacity on a 25 g scale. Benzamide was pyrolysed in portions of ~ 5 g over 5A molecular sieves. The sieves were initially prepared as described in section 1.7 but were used without further preparation for each 5 g portion. The pyrolysate in each case was collected into dichloromethane and dried over magnesium sulfate to give benzonitrile while the unreacted benzamide was subsequently collected into methanol.

(Portion 1) (4.98 g, 4.12×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 2 h: benzonitrile (4.05 g, 94% conversion); benzamide (0.27 g).

(Portion 2) (5.10 g, 4.21×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 2 h: benzonitrile (4.11 g, 94% conversion); benzamide (0.26 g).

(Portion 3) (5.24 g, 4.33×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 1 h 45 min: benzonitrile (4.05 g, 93% conversion); benzamide (0.31 g).

(Portion 4) (5.15 g, 4.26×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 1 h 50 min: benzonitrile (3.87 g, 92% conversion); benzamide (0.32 g).

(Portion 5) (5.22 g, 4.31×10^{-2} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 1 h 50 min: benzonitrile (3.99 g, 91% conversion); benzamide (0.38 g).

Investigation of stability of 5A molecular sieves to higher temperature.

Benzamide (5.00 g, 4.13×10^{-2} mol), 165 °C, 600 °C, 10^{-2} Torr, 2 h: benzonitrile (3.52 g, 95% conversion, 77% yield); benzamide (0.18 g).

Investigation of efficiency of Li^+ exchanged molecular sieves. Molecular sieves containing Li^+ ions were prepared by heating 4A molecular sieves (50 g) in LiCl (aq) (5 M, 500 cm^3) under reflux for 2 days. The solution was then discarded and the sieves heated in LiCl (aq) as before a further twice. Care was required not to stir the refluxing solution too vigorously as this resulted in degrading the molecular sieve beads and leaving only a fine powder behind. It was therefore necessary to find a balance between excessive stirring and violent bumping of the mixture. As before, analysis of benzamide dehydration was by comparison of intensity values in the ^{13}C NMR spectrum. Yields given in these cases are therefore not based on isolated products. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: % conversion to benzonitrile. Work up method A was used in each case.

(227 mg, 1.88×10^{-3} mol), 150 °C, 350 °C, 5×10^{-3} Torr, 15 min, 161 mg: 53% conversion to benzonitrile.

(207 mg, 1.71×10^{-3} mol), 150 °C, 400 °C, 5×10^{-3} Torr, 15 min, 136 mg: 65% conversion to benzonitrile.

(206 mg, 1.70×10^{-3} mol), 150 °C, 450 °C, 5×10^{-3} Torr, 15 min, 146 mg: 87% conversion to benzonitrile.

(222 mg, 1.83×10^{-3} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 15 min, 95 mg: 100% conversion to benzonitrile.

2.1.5 Elimination from *O*-methyl oximes

The following experiments involve the preparation of benzonitrile by elimination from *O*-methyl oximes. In each case, the product mixture contains only benzonitrile and unreacted starting material. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: % conversion to benzonitrile as determined by integrals in the ^{1}H NMR spectrum.

FVP of acetophenone *O*-methyl oxime. (43 mg, 2.89×10^{-4} mol), 30 °C, 650 °C, 5×10^{-3} Torr, 5 min, 27 mg: 100% conversion to benzonitrile.

FVP of acetophenone *O*-methyl oxime over silica beads (1-2 mm). (33 mg, 2.21×10^{-4} mol), 30 °C, 350 °C, 10^{-2} Torr, 5 min, 30 mg: 0%, only starting material present by ^{1}H NMR.

FVP of acetophenone *O*-methyl oxime over 3A molecular sieves. (37 mg, 2.48×10^{-4} mol), 30 °C, 350 °C, 10^{-2} Torr, 5 min, 29 mg: 56% conversion to benzonitrile.

FVP of acetophenone *O*-methyl oxime over 3A molecular sieves. (35 mg, 2.35×10^{-4} mol), 30 °C, 400 °C, 10^{-2} Torr, 5 min, 22 mg: 80% conversion to benzonitrile.

FVP of acetophenone *O*-methyl oxime over 3A molecular sieves. (30 mg, 2.01×10^{-4} mol), 30 °C, 450 °C, 10^{-2} Torr, 5 min, 20 mg: 90% conversion to benzonitrile.

FVP of benzaldehyde *O*-methyl oxime over 3A molecular sieves. (38 mg,

2.81×10^{-4} mol), room temp., 350 °C, 10^{-2} Torr, 5 min, 28 mg: 75% conversion to benzonitrile.

2.1.6 Preparative scale dehydration of amides by FVP

The general procedure employed was as follows: the amide to be dehydrated (10^{-3}-10^{-2} mol) was pyrolysed at 500 °C as detailed in section 1.5. The furnace tube was packed with 3A or 5A molecular sieves as specified, prepared and used according to the methods detailed in section 1.7. Following FVP, two work up methods were employed. Method A involved collection into methanol followed by concentration under reduced pressure. Using this method, the nitrile formed and any unreacted amide were collected together to give not only yield information but also data as to the efficiency of the process. This method was also used to collect nitriles that were found to be insoluble in dichloromethane. Method B involved collection into dichloromethane followed by drying over magnesium sulfate and evaporation of the solvent under reduced pressure. This method was used either when no amide was apparent in the FVP product trap or when it was desirable to leave any such unreacted starting material behind.

Results are quoted as follows: catalyst used, nature and quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, work up method and a discussion of the characterisation of the products.

Benzonitrile. 3A molecular sieves, benzamide (461 mg, 3.81×10^{-3} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 20 min, method A to give benzonitrile (359 mg, 91%); δ_H (DMSO) 7.74-7.43 (5 H, m); δ_C (50 MHz, DMSO) 133.25, 132.25, 129.47, 118.91 (q) and 111.62 (q). The ^1H and ^{13}C NMR spectra concurred with those in the literature.[103]

***p*-Aminobenzonitrile.** 3A molecular sieves, *p*-aminobenzamide (855 mg, 6.29×10^{-3} mol), 225 °C, 500 °C, 5×10^{-3} Torr, 35 min, method B. The product was a colourless solid identified as *p*-aminobenzonitrile (559 mg, 75%), mp 84-86 °C [lit.[103] 83-85 °C]; δ_H 7.41-7.33 (2 H, m), 6.65-6.58 (2 H, m) and 4.21 (2 H, br s); δ_C 150.36 (q), 133.58, 120.07 (q), 114.21 and 99.66. The ^1H and ^{13}C NMR spectra concurred with those in the literature.[103]

***m*-Aminobenzonitrile.** 3A molecular sieves, *m*-aminobenzamide (824 mg, 6.06×10^{-3} mol), 180 °C, 500 °C, 5×10^{-3} Torr, 30 min, method B. This yielded *m*-aminobenzonitrile (562 mg, 79%), bp 125 °C (0.2 Torr); δ_H 7.25-6.80 (4 H, m) and 3.92 (2 H, br s); δ_C (50 MHz) 146.96 (q), 129.92, 121.71, 119.10 (2 signals), 117.27 and 112.65. The ^1H and ^{13}C NMR spectra concurred with those in the literature.[103]

Anthranilonitrile. 3A molecular sieves, anthranilamide (910 mg, 6.69×10^{-3} mol), 180 °C, 500 °C, 5×10^{-3} Torr, 40 min, method B to give a colourless solid identified as anthranilonitrile (778 mg, 99%), bp 75 °C (0.3 Torr) [lit.[103] 267 °C]; δ_H (250 MHz) 7.38-7.25 (2 H, m), 6.75-6.68 (2 H, m) and 4.42 (2 H, br s); δ_C 149.49

(q), 133.84, 132.15, 117.78, 117.48 (q), 115.00 and 95.78 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

***o*-Tolunitrile.** 3A molecular sieves, *o*-toluamide (555 mg, 4.11×10^{-3} mol), 120 °C, 500 °C, 5×10^{-3} Torr, 25 min, method B followed by distillation to give *o*-tolunitrile (348 mg, 72%), bp 95 °C (15 Torr) [lit.[103] 205 °C]; δ_H 7.62-7.09 (4 H, m) and 2.46 (3 H, s); δ_C 141.31 (q), 132.20, 131.92, 129.77, 125.78, 117.58 (q), 112.20 and 19.88. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

***o*-Cyanophenol.** 3A molecular sieves, salicylamide (476 mg, 3.47×10^{-3} mol), 180 °C, 500 °C, 5×10^{-3} Torr, 20 min, method A. A light brown solid mixture was separated by dry-flash chromatography to give *o*-cyanophenol (258 mg, 63%), mp 94-96 °C [lit.[103] 92-95 °C]; δ_H (DMSO) 11.05 (1 H, br s), 7.57-7.41 (2 H, m) and 7.00-6.84 (2 H, m); δ_C (50 MHz, DMSO) 160.41 (q), 134.93, 133.44, 119.75, 117.26 (q), 116.37 and 99.04 (q); a component unambiguously identified as 1-cyanocyclopentadiene (10 mg, 3%) according to comparison of its NMR spectra with those of an authentically prepared sample (section 4.1).[112] The ^{1}H and ^{13}C NMR spectra of *o*-cyanophenol concurred with those in the literature.[103]

The dehydration of salicylamide to *o*-cyanophenol was carried out over 5A molecular sieves in an attempt to increase the yield of this transformation.

***o*-Cyanophenol.** 5A molecular sieves, salicylamide (957 mg, 6.99×10^{-3} mol), 180 °C, 500 °C, 1×10^{-2} Torr, 30 min, the pyrolysate was collected firstly into dichloromethane and the remainder into methanol. The dichloromethane fraction was dried over magnesium sulfate and concentrated under reduced pressure to give *o*-cyanophenol: (482 mg, 58%), mp 93-95 °C [lit.[103] 92-95 °C]; δ_H (DMSO) 7.53-7.37 (2 H, m) and 6.95-6.73 (2 H, m); δ_C (DMSO) 159.10 (q), 134.64, 132.92, 120.31, 116.74 (q), 116.41 and 99.01 (q). The methanol fraction was concentrated under reduced pressure to give a two-component mixture (292 mg) containing phenol and *o*-cyanophenol in approximately 3.5:1 ratio by ^{1}H NMR integrals. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

This experiment was also conducted at a lower temperature of 450 °C in an attempt to remedy this apparent breakdown to phenol. Salicylamide (477 mg, 3.48×10^{-3} mol), 180 °C, 450 °C, 5×10^{-3} Torr, 30 min, method A. This gave a mixture of *o*-cyanophenol and phenol (380 mg) in the ratio 69:31 by comparison of intensity values in the ^{13}C NMR spectrum as described in section 2.1.2.

Nicotinonitrile. 3A molecular sieves, nicotinamide (1.011 g, 8.29×10^{-3} mol), 150 °C, 500 °C, 1×10^{-3} Torr, 40 min, method A. A colourless solid was obtained and was identified as nicotinonitrile (843 mg, 98%), bp 75 °C (10 Torr) [lit.[103] 201 °C]; mp 46-51 °C [lit.[4] 50-52 °C]; δ_H 8.80-8.72 (2 H, m), 7.90 (1 H, m) and 7.38 (1 H, m); δ_C (50 MHz) 152.73, 152.15, 139.01, 123.38, 116.23 (q) and 109.78 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

2-Thiophenecarbonitrile. 3A molecular sieves, 2-thiophenecarboxamide (998 mg, 7.86×10^{-3} mol), 180 °C, 500 °C, 5×10^{-3} Torr, method A followed by distillation gave a clear oil identified as 2-thiophenecarbonitrile (704 mg, 82%), bp 30 °C (0.6 Torr) [lit.[103] 192 °C]; δ_H (250 MHz) 7.93 (1 H, m), 7.82 (1 H, m) and 7.18 (1 H, m); δ_C 138.42, 134.37, 128.05, 114.37, and 108.66 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

2-Furancarbonitrile. 3A molecular sieves, 2-furancarboxamide (838 mg, 7.55×10^{-3} mol), 90 °C, 500 °C, 5×10^{-3} Torr, 40 min, method B to give 2-furancarbonitrile (666 mg, 95%); δ_H 7.57 (1 H, m), 7.09 (1 H, m) and 6.52 (1 H, m); δ_C 147.20, 126.10 (q), 121.84, 111.29 and 111.25. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Phenylacetonitrile. 3A molecular sieves, phenylacetamide (410 mg, 3.04×10^{-3} mol), 225 °C, 500 °C, 5×10^{-3} Torr, 20 min, method B followed by distillation. A clear oil was obtained and identified as phenylacetonitrile (214 mg, 60%), bp 80 °C (0.6 Torr) [lit.[103] 234 °C]; δ_H 7.36-7.18 (5 H, m) and 3.67 (2 H, s); δ_C 129.69 (q), 128.68, 127.57, 127.52, 117.64 (q) and 23.03. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Isophthalonitrile. 3A molecular sieves, isophthalamide (315 mg, 1.92×10^{-3} mol), 280 °C, 500 °C, 3×10^{-3} Torr, 15 min, method A. A white solid was obtained, identified as isophthalonitrile (220 mg, 90%); mp 161-163 °C [lit.[103] 163-165 °C]; δ_H 8.48 (1 H, m), 8.20 (2 H, m) and 7.79 (1 H, m); δ_C (DMSO) 136.93, 136.22, 130.81, 117.30 (q), 112.87 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Isobutyronitrile. 3A molecular sieves, isobutyramide (225 mg, 2.59 × 10^{-3} mol), 90 °C, 500 °C, 1 × 10^{-2} Torr, 15 min, method B to give a yellow oil identified isobutyronitrile (140 mg, 59%); δ_H (250 MHz) 2.69 (1 H, septet, *J* 7.0 Hz), 1.31 (6 H, d, *J* 7.0 Hz; δ_C 123.61 (q), 19.76, 19.66. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Trimethylacetonitrile. 3A molecular sieves, trimethylacetamide (299 mg, 2.96 × 10^{-3} mol), 90 °C, 500 °C, 1 × 10^{-2} Torr, 15 min, method A to give trimethylacetonitrile (159 mg, 65%); δ_H 1.34 (9 H, s); δ_C 125.70 (q), 28.18, 27.86 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Pelargononitrile. 3A molecular sieves, pelargonamide (314 mg, 2.00 × 10^{-3} mol), 90 °C, 500 °C, 5 × 10^{-3} Torr, 15 min, method B to give a yellow oil identified as pelargononitrile (203 mg, 73%), bp 65 °C (0.5 Torr) [lit.[103] 224 °C]; δ_H (250 MHz) 2.29 (2 H, t, *J* 7.0 Hz), 1.64-1.58 (2 H, m), 1.43-1.37 (2 H, m), 1.25-1.24 (8 H, m) and 0.87-0.81 (3 H, m); δ_C 119.57 (q), 31.41, 28.68, 28.44, 28.37, 25.10, 22.31, 16.80 and 13.74. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

2.1.7 Preparative scale dehydration of oximes by FVP

The general procedure employed was as follows: the oxime to be dehydrated (10^{-3}-10^{-2} mol) was pyrolysed at 350 °C as detailed in section 1.5. The furnace tube was packed with 3A or 5A molecular sieves as specified, prepared and used according to the methods detailed in section 1.7. Following FVP, two work up methods were employed as discussed in section 2.1.3. Method A involved collection into methanol followed by concentration under reduced pressure. Method B involved collection into dichloromethane followed by drying over magnesium sulfate and evaporation of the solvent under reduced pressure.

Results are quoted as follows: catalyst used, nature and quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, work up method and a discussion of the characterisation of the products.

Benzonitrile. 3A molecular sieves, benzaldoxime (97 mg, 8.04×10^{-4} mol), 60 °C, 350 °C, 1×10^{-2} Torr, 10 min, method B to give benzonitrile (80 mg, 97%); δ_H 7.74-7.43 (5 H, m); δ_C (50 MHz) 132.60, 131.91, 128.93, 118.60 (q) and 112.15 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

2-Cyanophenol. 3A molecular sieves, salicylaldoxime (808 mg, 5.90×10^{-3} mol), 180 °C, 350 °C, 5×10^{-3} Torr, 30 min, method B: a yellow solid after distillation was identified as 2-cyanophenol (621 mg, 88%), mp 90-93 °C [lit.[103] 92-95 °C]; δ_H 7.50-7.40 (2 H, m), 7.05-6.90 (2 H, m) and 6.53 (1 H, br s); δ_C 158.80 (q), 134.63, 132.87, 120.59, 116.49 (2 signals) and 99.22 (q). The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

The following experiments detail the pyrolytic dehydration of salicylaldoxime over 5A molecular sieves at temperatures ranging from 250 to 500 °C. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected, products. Work-up was by method A in each case. The percentages of each product given are a percentage of the product mixture, as determined from integrals in the ^{1}H NMR spectrum.

FVP of salicylaldoxime over 5A molecular sieves. (372 mg, 2.72×10^{-3} mol), 150 °C, 250 °C, 5×10^{-3} Torr, 20 min, 287 mg: 1,2-benzisoxazole (17%); δ_C 161.65 (q), 146.01, 130.27 (q), 123.79, 122.01, 120.62 and 109.29; 2-cyanophenol (71%); δ_C 159.51 (q), 134.45, 132.74, 119.81, 116.77 (q), 116.26 and 98.77 (q); unreacted salicylaldoxime (10%); δ_C 156.49 (q), 152.96, 130.59, 130.27, 119.46 and 116.10 (1 quaternary signal missing).

(340 mg, 2.48×10^{-3} mol), 150 °C, 300 °C, 5×10^{-3} Torr, 20 min, 291 mg: 1,2-benzisoxazole (18%); 2-cyanophenol (68%); unreacted salicylaldoxime (8%).

(344 mg, 2.51×10^{-3} mol), 150 °C, 350 °C, 5×10^{-3} Torr, 20 min, 281 mg: 1,2-benzisoxazole (18%); 2-cyanophenol (72%); unreacted salicylaldoxime (5%).

(351 mg, 2.56×10^{-3} mol), 150 °C, 400 °C, 5×10^{-3} Torr, 20 min, 294 mg: 1,2-benzisoxazole (12%); 2-cyanophenol (80%); unreacted salicylaldoxime (2%).

(299 mg, 2.18×10^{-3} mol), 150 °C, 450 °C, 5×10^{-3} Torr, 15 min, 198 mg: 1,2-benzisoxazole (6%); 2-cyanophenol (91%).

(234 mg, 1.71×10^{-3} mol), 150 °C, 500 °C, 5×10^{-3} Torr, 15 min, 164 mg: 1,2-benzisoxazole (2%); 2-cyanophenol (96%).

2-Cyanopyrrole. 3A molecular sieves, pyrrole-2-carbaldoxime (870 mg, 7.91×10^{-3} mol), 150 °C, 350 °C, 1×10^{-3} Torr, 2 h, method B giving an orange oil after distillation which was identified as 2-cyanopyrrole (457 mg, 63%) (some starting material remained unvolatilised in furnace tube entry. The yield is based on all of the starting material used and so is a low estimate. Pyrolysis at 400 °C is likely to prevent this volatility problem.) bp 80 °C (0.3 Torr) [lit.[113] 89-90 °C (1.5 Torr)]; δ_H 9.65 (1 H, br s), 6.87-6.78 (2 H, m) and 6.18 (1 H, s); δ_C (50 MHz) 123.78, 120.11, 114.77 (q), 109.84 and 100.28 (q). The ^{1}H NMR spectrum concurred with that in the literature,[114] as did the ^{13}C NMR spectrum.[115]

Indole-3-carbonitrile. 3A molecular sieves, indole-3-carbaldoxime (613 mg, 3.83×10^{-3} mol), 240 °C, 350 °C, 1×10^{-2} Torr, 25 min, method A to give an orange solid identified as indole-3-carbonitrile (484 mg, 89%), mp 177-181 °C [lit.[114] 183-184 °C]; ν_{max} (nujol) 2224; δ_H (DMSO) 8.23 (1 H, s), 7.65-7.43 (2 H, m) and 7.34-7.15 (2 H, m); δ_C 135.35 (q), 134.60, 126.87 (q), 123.54, 121.85, 118.57, 116.57 (q), 113.09 and 84.36 (q). The ^{1}H and ^{13}C NMR and IR spectra concurred with the desired product.

Thiophene-3-carbonitrile. 3A molecular sieves, thiophene-3-carbaldoxime (318 mg, 2.50×10^{-3} mol), 135 °C, 350 °C, 1×10^{-2} Torr, 15 min, method A. This yielded thiophene-3-carbonitrile after distillation as a clear oil (209 mg, 77%), bp 210 °C [lit.[116] 203-205 °C]; δ_H 9.02 (1 H, dd, *J* 3.0, 1.2), 7.40 (1 H, dd, *J* 5.1, 3.0) and 7.27 (1 H, dd, *J* 5.1, 1.2); δ_C 135.22, 128.43, 127.12, 114.90 (q) and 110.37 (q). The ^1H and ^{13}C NMR spectra concurred with those in the literature.[117]

2.2 Other eliminations mediated by FVP over molecular sieves

2.2.1 Deprotection of formylated/acetylated secondary amines

The protocol developed for the dehydration of amides to nitriles is employed here, *i.e.*, the compound to be subjected to elimination (10^{-4}-10^{-3} mol) was pyrolysed at 500 °C as detailed in section 1.5. The furnace tube was packed with 3A molecular sieves prepared and used according to the method detailed in section 1.7.

Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time: products. In each case the pyrolysate was collected directly into deuteriated solvent for NMR studies. The yield of each product in the simple mixtures obtained was determined in each case by addition of a known amount of cyclohexane to the ^{1}H NMR sample.

FVP of formanilide over 3A molecular sieves. (47 mg, 3.88×10^{-4} mol), 90 °C, 500 °C, 3×10^{-3} Torr, 15 min: aniline (42%); δ_H 7.12-6.95 (2 H, m), 6.72-6.58 (3 H, m), 3.43 (2 H, br s); δ_C 146.21 (q), 129.15, 118.42 and 114.97; benzonitrile (18%); δ_H 7.61-7.50 (3 H, m), 7.44-7.36 (2 H, m); δ_C 132.64, 132.03, 128.98, two quaternary signals not apparent. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of *N*-methylformanilide over 3A molecular sieves. (85 mg, 6.30×10^{-4}

mol), 130 °C, 500 °C, 4 × 10^{-3} Torr, 20 min: *N*-methylaniline (61%); δ_H (DMSO) 7.09-7.01 (2 H, m), 6.52-6.48 (3 H, m), 5.45 (1 H, br s); δ_C (DMSO) 150.04 (q), 128.97, 115.62, 111.78 and 29.85; recovered *N*-methylformanilide (35%); δ_H (DMSO) 8.51 (1 H, s) and 7.40-7.33 (5 H, m); δ_C (DMSO) 162.20, 142.18 (q), 129.58, 125.80, 121.68 and 31.20. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of acetanilide over 3A molecular sieves. (63 mg, 4.67 × 10^{-4} mol), 150 °C, 500 °C, 2 × 10^{-2} Torr, 5 min: aniline (58%); δ_H (250 MHz) 7.19-7.12 (2 H, m), 6.79-6.65 (3 H, m), 3.71 (2 H, br s); δ_C 146.18 (q), 129.10, 118.37 and 114.95; recovered acetanilide (32%); δ_H (250 MHz) 7.81 (1 H, br s), 7.52-7.47 (2 H, m), 7.34-7.25 (2 H, m), 7.09 (1 H, m) and 2.13 (3 H, s); δ_C 168.55 (q), 137.82 (q), 128.75, 124.07, 119.83 and 24.28. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of *N*-phenylbenzamidine over 3A molecular sieves. (65 mg, 3.32 × 10^{-4} mol), 180 °C, 500 °C, 3 × 10^{-3} Torr, 20 min: aniline (39%); δ_H 7.20-7.12 (2 H, m), 6.80-6.66 (3 H, m) and 3.20 (2 H, br s); benzonitrile (47%); δ_H 7.68-7.50 (3 H, m) and 7.48-7.43 (2 H, m); The ^{1}H NMR spectra concurred with those in the literature.[103]

2.2.2 Dehydration of cyclohexanols

The dehydration conditions developed for the conversion of amides to nitriles in the gas phase, using 3A molecular sieves as catalyst, were applied to the dehydration of alcohols to alkenes using cyclohexanol as a model system. The molecular sieves were prepared for use as described in section 1.7.

Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time: products. In each case the pyrolysate was collected directly into [^{2}H]chloroform for NMR studies. The yield was determined in each case by addition of a known amount of either cyclohexane or 1,4-dinitrobenzene to the ^{1}H NMR sample as indicated in each example.

FVP of cyclohexanol over 3A molecular sieves. (63 mg, 6.3×10^{-4} mol), 30 °C, 300 °C, 5×10^{-2} Torr, 5 min. This gave a mixture of unreacted starting material, cyclohexene and cyclohexanone. These components were identified mainly from the ^{13}C NMR spectrum of the mixture, supported by the presence of prominent peaks in the ^{1}H NMR spectrum. The yields were determined by addition of a known amount of 1,4-dinitrobenzene to the ^{1}H NMR sample. Unreacted cyclohexanol (60%); δ_C 69.90, 35.23, 25.26 and 23.97; cyclohexene (9%); δ_C 126.95, 24.88 and 22.35; cyclohexanone (15%); δ_C (quaternary at ~210 ppm not observed) 41.67, 26.76 and 24.73.

FVP of cyclohexanol over 3A molecular sieves. (62 mg, 6.2 × 10^{-4} mol), 30 °C, 400 °C, 3 × 10^{-2} Torr, 5 min. The yields were determined by addition of a known amount of 1,4-dinitrobenzene to the ^{1}H NMR sample. Unreacted cyclohexanol (52%); cyclohexene (15%); cyclohexanone (23%).

FVP of cyclohexanol over 3A molecular sieves. (52 mg, 5.2 × 10^{-4} mol), 30 °C, 500 °C, 2 × 10^{-2} Torr, 5 min. The yields were determined by addition of a known amount of 1,4-dinitrobenzene to the ^{1}H NMR sample. Unreacted cyclohexanol (22%); cyclohexene (17%); cyclohexanone (40%).

To avoid the occurrence of this unexpected dehydrogenation reaction to cyclohexanone, 1-methylcyclohexanol was subjected to the same conditions.

FVP of 1-methylcyclohexanol over 3A molecular sieves. (50 mg, 4.39 × 10^{-4} mol), 50 °C, 500 °C, 2 × 10^{-3} Torr, 15 min. This gave a mixture of 1-methylcyclohexene and methylenecyclohexane, identified mainly from the ^{13}C NMR spectrum of the mixture, supported by the presence of prominent peaks in the ^{1}H NMR spectrum. No unreacted starting material was present. The yields were determined by addition of a known amount of cyclohexane to the ^{1}H NMR sample. 1-methylcyclohexene (38%); δ_C 133.82 (q), 120.97, 29.88, 25.14, 23.75, 22.87 and 22.25; methylenecyclohexane (12%); δ_C 149.93 (q), 106.30, 35.25, 28.17 and 26.17. This then gives a ratio of ~ 3:1 in favour of *endo*-alkene formation.

The same reaction was then carried out over molecular sieves of different pore size in an attempt to vary this ratio of alkene formation and to achieve greater selectivity.

FVP of 1-methylcyclohexanol over 4A molecular sieves. (42 mg, 3.68×10^{-4} mol), 50 °C, 500 °C, 2×10^{-3} Torr, 15 min. This gave a mixture of 1-methylcyclohexene and methylenecyclohexane with no unreacted starting material present. The yields were determined by addition of a known amount of cyclohexane to the ^{1}H NMR sample. 1-methylcyclohexene (23%); δ_C 133.82 (q), 120.97, 29.88, 25.14, 23.75, 22.87 and 22.25; methylenecyclohexane (6%); δ_C 149.93 (q), 106.30, 35.25, 28.17 and 26.17. This then gives a ratio of ~ 4:1 in favour of *endo*-alkene formation.

FVP of 1-methylcyclohexanol over 5A molecular sieves. (40 mg, 3.51×10^{-4} mol), 50 °C, 500 °C, 2×10^{-3} Torr, 15 min. This gave a mixture of 1-methylcyclohexene and methylenecyclohexane with no unreacted starting material present. The yields were determined by addition of a known amount of cyclohexane to the ^{1}H NMR sample. 1-methylcyclohexene (47%); δ_C 133.82 (q), 120.97, 29.88, 25.14, 23.75, 22.87 and 22.25; methylenecyclohexane (3%); δ_C 149.93 (q), 106.30, 35.25, 28.17 and 26.17. This then gives a ratio of ~ 15:1 in favour of *endo*-alkene formation.

An attempt was made to further extend this process to the elimination of ammonia from cyclohexylamine using the same conditions and 3A molecular sieves as catalyst. This however yielded only unreacted starting material.

3. Catalytic dehydrogenations under FVP

3.1 Aromatisations

3.1.1 Preparation of aromatisation precursors

Tetrahydrolepidine. By the method of Oldham and Johns,[118] lepidine (3.00 g, 0.021 mol) in boiling ethanol (50 cm^3) was treated with sodium metal (3.40 g, 0.15 mol) in small portions with stirring. The resulting solution was diluted with water (100 cm^3) and acidified with hydrochloric acid. The ethanol was removed by evaporation under reduced pressure and the remainder basified with sodium hydroxide pellets. The mixture was extracted with ether (3 × 50 cm^3) and the combined extracts concentrated under reduced pressure to give a brown oil which was shown by ^{1}H NMR to contain an approximately 2:1 mixture of desired product : starting material. This mixture was treated with sodium metal and worked up exactly as before to give an orange oil which was purified by dry-flash chromatography to give tetrahydrolepidine as a yellow oil (66%); δ_H (250 MHz) 7.08 (1 H, m), 6.98 (1 H, m), 6.65 (1 H, td, *J* 7.4, 1.3), 6.49 (1 H, dd, *J* 7.9, 1.2), 3.55 (1 H, br s), 3.40-3.23 (2 H, m), 2.93 (1 H, sextet, *J* 6.4), 2.00 (1 H, m), 1.69 (1 H, m) and 1.31 (3 H, d, *J* 7.0); δ_C 144.09 (q), 128.29, 126.57, 126.44 (q), 116.78, 114.01, 38.84, 30.07, 29.71 and 22.50. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[119]

Tetrahydroquinaldine. By the method of Oldham and Johns,[118] quinaldine

(5.00 g, 0.035 mol) in boiling ethanol (50 cm^3) was treated with sodium metal (5.60 g, 0.24 mol) in small portions with stirring. The resulting solution was diluted with water (100 cm^3) and acidified with hydrochloric acid. The ethanol was removed by evaporation under reduced pressure and the remainder basified with sodium hydroxide pellets. The mixture was extracted with ether (3 × 50 cm^3) and the combined extracts evaporated under reduced pressure to give tetrahydroquinaldine as an orange oil (91%); δ_H (250 MHz) 7.07-7.01 (2 H, m), 6.68 (1 H, td, *J* 7.3, 1.2), 6.53 (1 H, dd, *J* 8.1, 1.4), 3.74 (1 H, br s), 3.44 (1 H, m), 2.98-2.74 (2 H, m), 1.99 (1 H, m), 1.70 (1 H, m) and 1.27 (3 H, d, *J* 6.3); δ_C 144.57 (q), 129.05, 126.47, 120.85 (q), 116.73, 113.79, 46.92, 29.91, 26.39 and 22.39. The ^1H and ^{13}C NMR spectra concurred with those in the literature.[119]

***N*-Benzylideneaniline.** Benzaldehyde (0.50 g, 4.72×10^{-3} mol) and aniline (0.44 g, 4.72×10^{-3} mol) were heated together at 100 °C for 10 min and then allowed to cool. The resulting solid was recrystallised from ethanol to give *N*-benzylideneaniline as a yellow solid (0.77 g, 90%), mp 51-53 °C [lit.,[103] 53 °C]; δ_H 8.47 (1 H, m) 7.94-7.90 (2 H, m), 7.51-7.38 (4 H, m) and 7.28-7.21 (3 H, m). The ^1H NMR spectrum concurred with that in the literature.[103]

3.1.2 Optimisation of aromatisation conditions

These experiments were carried out on a test dehydrogenation of tetralin → naphthalene. Tetralin was pyrolysed at temperatures ranging from 550 °C to 950 °C as detailed in section 1.5. Where specified, the furnace tube was packed with molybdenum oxide catalyst or quartz beads prepared and used according to the methods detailed in section 1.7.

The pure thermal chemistry (empty pyrolysis tube) of tetralin is first investigated followed by the results obtained when molybdenum oxide catalysts were used. In these experiments, the product mixture contained only naphthalene and tetralin starting material and conversions indicated were obtained by comparison of integrals in ^{1}H NMR spectra. Work-up involved collection into dichloromethane followed by concentration under reduced pressure. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: products.

FVP of tetralin at 800 °C. (138 mg, 9.93×10^{-4} mol), room temp., 800 °C, 10^{-2} Torr, 15 min, 125 mg: unreacted tetralin only; δ_H 6.96-6.94 (4 H, m), 2.69-2.63 (4 H, m) and 1.70-1.65 (4 H, m). The ^{1}H NMR spectrum concurred with that in the literature.[103]

FVP of tetralin at 950 °C. (88 mg, 6.33×10^{-4} mol), room temp., 950 °C, 10^{-2} Torr, 10 min, 49 mg: products were identified from ^{1}H and ^{13}C NMR and are listed in order of decreasing abundance. Unreacted tetralin; δ_H 6.97-6.95 (4 H, m), 2.70-2.63 (4 H, m) and 1.73-1.66 (4 H, m); δ_C 136.98 (q), 128.98, 125.28, 29.27 and 23.11; naphthalene; δ_H 7.77-7.71 (4 H, m) and 7.40-7.33 (4 H, m); δ_C 133.38 (q), 127.75 and 125.67; styrene; δ_C 137.38 (q), 136.80, 128.38, 127.65, 126.09 and 113.61; benzocyclobutene; δ_C 145.75(q), 126.56, 122.38 and 29.57; indene; δ_C 145.75 (q), 144.40 (q), 133.95, 131.95, 126.31, 124.42, 123.56, 120.82 and 38.91.

FVP of tetralin at 550 °C over quartz beads. (118 mg, 8.49×10^{-4} mol), room temp., 550 °C, 5×10^{-3} Torr, 15 min, 109 mg: unreacted tetralin only; δ_H 6.97-6.95 (4 H, m), 2.69-2.63 (4 H, m) and 1.72-1.65 (4 H, m).

The following experiments are an evaluation of the activity of different molybdenum oxide catalysts. The performance of previously unused catalyst is described first followed by catalyst which has been regenerated according to the method detailed in section 1.7.

FVP of tetralin over fresh molybdenum oxide catalyst (1). (165 mg, 1.25×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 138 mg: 56% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (1). (147 mg, 1.11×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 122 mg: 50% conversion to naphthalene.

FVP of tetralin over fresh molybdenum oxide catalyst (2). (152 mg, 1.15×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 135 mg: 69% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (2). (163 mg, 1.23×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 117 mg: 69% conversion to naphthalene.

FVP of tetralin over fresh molybdenum oxide catalyst (3). (150 mg, 1.14×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 115 mg: 83% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (3). (154 mg, 1.17×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 118 mg: 56% conversion to naphthalene.

FVP of tetralin over fresh molybdenum oxide catalyst (4). (158 mg, 1.20×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 119 mg: 85% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (4). (156 mg, 1.18×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 122 mg: 75% conversion to naphthalene.

FVP of tetralin over fresh molybdenum oxide catalyst (5). (104 mg, 7.88×10^{-4} mol), room temp., 550 °C, 10^{-2} Torr rising to 10^{-1} Torr during reaction, 15 min, 67 mg: 80% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (112 mg, 8.48×10^{-2} mol), room temp., 550 °C, 10^{-2} Torr rising to 10^{-1} Torr during reaction, 15 min, 102 mg: 67% conversion to naphthalene.

FVP of tetralin at 550 °C over alumina pellets. (51 mg, 3.86×10^{-4} mol), room temp., 550 °C, 3×10^{-3} Torr, 10 min, 38 mg: 33% conversion to naphthalene.

The following experiments are an evaluation of the capacity of the molybdenum oxide catalyst to scale-up. Tetralin (10^{-3}-10^{-1} mol) was pyrolysed at 550 °C as detailed in section 1.5. The furnace tube was packed in each case with molybdenum oxide catalyst (5), prepared and used in accordance with the method detailed in section 1.7. Work-up involved collection into dichloromethane followed by concentration under reduced pressure.

Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: products.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (150 mg, 1.14×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 131 mg: 64% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (300 mg, 2.27×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 25 min, 257 mg: 64% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (450 mg, 3.41×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 30 min, 392 mg: 64% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (600 mg, 4.54×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 40 min, 543 mg: 62% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (900 mg, 6.82×10^{-3} mol), room temp., 550 °C, 5×10^{-3} Torr rising to 10^{-1} Torr during reaction, 45 min, 833 mg: 64% conversion to naphthalene.

FVP of tetralin over regenerated molybdenum oxide catalyst (5). (5.05 g, 3.80×10^{-2} mol), room temp., 550 °C, 5×10^{-3} Torr rising to $>10^{-1}$ Torr during reaction, 2 h, 4.88 g: 64% conversion to naphthalene.

3.1.3 Application of aromatisation conditions

The general procedure employed was as follows: the compound to be dehydrogenated (generally 10^{-4}-10^{-3} mol, some experiments scaled up to ~10^{-1} mol) was pyrolysed at 550 °C as detailed in section 1.5. The furnace tube was packed with molybdenum oxide catalyst (4) which was found to be the most active on regeneration, prepared and used according to the methods detailed in section 1.7. Work-up involved collection into dichloromethane followed by concentration under reduced pressure.

Results are quoted as follows: nature and quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: products.

Quinoline. 1,2,3,4-Tetrahydroquinoline, (68 mg, 5.11×10^{-4} mol), 90 °C, 550 °C, 2×10^{-3} Torr rising to 10^{-1} Torr during reaction, 10 min, 55 mg: 100% conversion to quinoline; δ_H (250 MHz) 8.88 (1 H, dd, *J* 4.2, 1.7), 8.11-8.08 (2 H, m), 7.78-7.64 (2 H, m), 7.50 (1 H, m) and 7.34 (1 H, m); δ_C 150.17, 148.01 (q), 135.86, 129.25, 129.19, 128.05 (q), 127.57, 126.32 and 120.85. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

1,2,3,4-tetrahydroquinoline, (5.01 g, 3.77×10^{-2} mol), 80 °C, 550 °C, 7×10^{-3} Torr rising to 10^{-1} Torr during reaction, 2 h, 4.72 g: 96% conversion to quinoline by ^{1}H NMR integrals (remainder is starting material). A further portion of 1,2,3,4-tetrahydroquinoline was pyrolysed over the same catalyst under the same conditions without regeneration. (3.01 g, 2.26 × 10^{-2} mol) 80 °C, 550 °C, 7 × 10^{-3} Torr rising to 10^{-1} Torr during reaction, 1.5 h, 2.81 g: 92% conversion to quinoline.

The following experiments show the % conversion from 1,2,3,4-tetrahydroquinoline to quinoline obtained at lower temperatures.

FVP of 1,2,3,4-tetrahydroquinoline at 500 °C. (198 mg, 1.49 × 10^{-3} mol), 90 °C, 500 °C, 2 × 10^{-3} Torr rising to 5 × 10^{-1} Torr during reaction, 10 min, 162 mg: 98% conversion to quinoline.

FVP of 1,2,3,4-tetrahydroquinoline at 450 °C. (192 mg, 1.44 × 10^{-3} mol), 90 °C, 450 °C, 2 × 10^{-3} Torr rising to 5 × 10^{-1} Torr during reaction, 10 min, 164 mg: 97% conversion to quinoline.

FVP of 1,2,3,4-tetrahydroquinoline at 400 °C. (123 mg, 9.25 × 10^{-4} mol), 90 °C, 400 °C, 2 × 10^{-3} Torr rising to 5 × 10^{-1} Torr during reaction, 10 min, 110 mg: 99% conversion to quinoline.

Pyridine. 1,2,3,6-Tetrahydropyridine, (104 mg, 1.25 × 10^{-3} mol), room temp., 550 °C, 2 × 10^{-3} Torr rising to 5 × 10^{-1} Torr during reaction, 10 min, 87 mg: 100% conversion to pyridine; δ_H 8.56-8.53 (2 H, m), 7.61 (1 H, m) and 7.24-7.18 (2 H, m). The ^{1}H NMR spectrum concurred with that in the literature.[103]

Isoquinoline. 1,2,3,4-Tetrahydroisoquinoline, (122 mg, 9.17 × 10^{-4} mol), 120

°C, 550 °C, 3 × 10^{-3} Torr rising to 10^{-1} Torr during reaction, 10 min, 103 mg: 100% conversion to quinoline (no starting material present but a small amount of unidentified aromatic impurity observed in NMR spectra); δ_H (250 MHz) 9.20 (1 H, s), 8.48 (1 H, d, *J* 5.7), 7.92 (1 H, m), 7.89 (1 H, m) and 7.77-7.51 (3 H, m); δ_C 152.21, 142.62, 135.48 (q), 130.11, 128.38 (q), 127.34, 127.00, 126.19 and 120.23. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

Carbazole. 1,2,3,4-Tetrahydrocarbazole, (590 mg, 3.45 × 10^{-3} mol), 120 °C, 550 °C, 10^{-2} Torr rising to 3 × 10^{-1} Torr during reaction, 2 h, 477 mg: 100% conversion to carbazole, mp 242-246 °C, [lit.,[103] 246 °C]; δ_H (DMSO) 11.24 (1 H, br s), 8.09 (2 H, d, *J* 7.7), 7.48 (2 H, m), 7.36 (2 H, m) and 7.13 (2 H, m); δ_C (DMSO) 139.81 (q), 125.61, 122.49 (q), 120.26, 118.59 and 111.03. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

3.1.4 Investigation of dehydrogenation mechanism

The following experiments are small scale pyrolyses designed to test the ability of the catalyst to leave ring substituents intact during reaction. The products were collected directly into [^{2}H]chloroform and quantified by addition of a known amount of cyclohexane to the ^{1}H NMR sample. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected: products.

FVP of 1-phenyl-1,2,3,4-tetrahydroisoquinoline over regenerated molybdenum oxide catalyst (4). (31 mg, 1.48×10^{-4} mol), 100 °C, 550 °C, 6×10^{-3} Torr, 5 min, 22 mg: NMR spectra show the main product to be 1-phenylisoquinoline (21%); δ_H (250 MHz) 8.61 (1 H, d, *J* 5.7) and 7.78-7.41, (10 H, m); δ_C 160 .42 (q), 142.03, 139.38 (q), 136.77 (q), 129.94, 129.81, 128.50, 128.24, 127.50, 127.08, 126.88, 126.59 (q) and 119.83. No isoquinoline was found in the product mixture. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[120]

FVP of 1,2,3,4-tetrahydroquinaldine over regenerated molybdenum oxide catalyst (4). (100 mg, 6.80×10^{-4} mol), 40 °C, 550 °C, 6×10^{-3} Torr rising to 10^{-1} Torr during reaction, 10 min, 65 mg: quinaldine (48%); δ_H (250 MHz) 8.01-7.96 (2 H, m), 7.73-7.60 (2 H, m), 7.43 (1 H, m), 7.21 (1 H, d, *J* 8.4) and 2.70 (3 H, m); δ_C 158.74 (q), 147.61 (q), 135.96, 129.21, 128.37, 127.27, 126.25 (q), 125.45, 121.77 and 25.14; quinoline (4%); δ_H 8.88 (1 H, dd, *J* 4.2, 1.7), 8.10-8.07 (2 H, m), 7.78-7.67 (2 H, m), 7.49 (1 H, m) and 7.33 (1 H, m); δ_C150.17, 148.11 (q), 135.85, 127.57, 126.32 and 120.85, 3 signals overlapped by quinaldine. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of 1,2,3,4-tetrahydroquinaldine over alumina pellets. (142 mg, 9.93×10^{-4} mol), 50 °C, 550 °C, 3×10^{-3} Torr rising to 10^{-1} Torr during reaction, 15 min, 122 mg: quinaldine (80%); ^{1}H NMR spectrum indicates the presence of a trace amount of quinoline.

FVP of 1,2,3,4-tetrahydrolepidine over regenerated molybdenum oxide catalyst (4). (104 mg, 7.07×10^{-4} mol), 80 °C, 550 °C, 7×10^{-3} Torr rising to 5×10^{-2} Torr during reaction, 10 min, 62 mg: lepidine (40%); δ_H (250 MHz) 8.73 (1 H, d, *J* 4.4), 8.08 (1 H, m), 7.94 (1 H, m), 7.67 (1 H, m), 7.52 (1 H, m), 7.17 (1 H, m) and 2.64 (3 H, m); δ_C 149.89, 147.67 (q), 144.17 (q), 129.69, 128.92, 128.05 (q), 126.08, 123.61, 121.64 and 18.43; ^{1}H and ^{13}C NMR spectra indicate the presence of a trace amount of quinoline. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of 1,2,3,4-tetrahydroquinaldine over quartz beads to determine the total breakdown temperature under pure thermal conditions. 1,2,3,4-tetrahydroquinaldine was pyrolysed at temperatures ranging from 550-950 °C to determine the minimum temperature at which there could be found no remaining starting material in the product mixture. The experiments were carried out by pyrolysing 30-40 mg of 1,2,3,4-tetrahydroquinaldine over quartz beads, packed into the furnace to provide an inert surface of similar dimensions to the molybdenum oxide catalysts. The product mixtures collected showed extremely messy and complex NMR spectra and were analysed primarily for the presence of unreacted starting material. It was found that a temperature of 950 °C was required to give complete consumption of the substrate pyrolysed. The pyrolysis was then scaled up at 950 °C to try and identify some of the components yielded from the ^{13}C NMR spectrum of the mixture, as detailed below.

(234 mg, 1.64 × 10^{-3} mol), 50 °C, 950 °C, 3 × 10^{-3} Torr rising to 1 × 10^{-1} Torr during reaction, 30 min. The pyrolysate was collected directly into [^{2}H]chloroform for NMR analysis. Unambiguously identified from the ^{13}C NMR spectrum in approximate order of abundance were quinoline; δ_C 150.02, 147.88 (q), 135.86, 129.21, 128.97, 128.21 (q), 127.53, 126.28 and 120.80; indole; δ_C 135.64 (q), 124.07, 121.41, 120.30, 119.26, 110.88 and 101.89 (one quaternary signal overlapped by other peaks in the mixture). The presence of 2-toluidine, aniline and 2-methylindole was also strongly suggested by the NMR spectra.

3.1.5 Miscellaneous attempted dehydrogenations

FVP of benzaldehyde oxime over regenerated molybdenum oxide catalyst (4). (24 mg, 1.98 × 10^{-4} mol), 50 °C, 550 °C, 7 × 10^{-3} Torr, 10 min, 16 mg: benzonitrile (78%); δ_H 7.61-7.37 (5 H, m); δ_C 132.64, 132.03, 128.99, 118.72 (q) and 112.34. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of benzaldehyde oxime over alumina pellets. (245 mg, 2.02 × 10^{-3} mol), 30 °C, 550 °C, 2 × 10^{-3} Torr, 20 min, 203 mg: benzonitrile (74%, quantified by addition of a known amount of cyclohexane to the ^{1}H NMR sample); δ_H 7.62-7.37 (5 H, m); δ_C 132.31, 131.56, 128.64, 118.32 (q) and 111.80. One other unidentified minor component was also observed in the ^{1}H and ^{13}C NMR spectra. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of bibenzyl over regenerated molybdenum oxide catalyst (4). (82 mg, 4.51×10^{-4} mol), 120 °C, 550 °C, 7×10^{-3} Torr, 5 min, 72 mg: unreacted bibenzyl only; δ_H 7.45-7.02 (10 H, m) and 2.83 (4 H, s). The ^{1}H NMR spectrum concurred with that in the literature.[103]

FVP of *N*-benzylideneaniline over regenerated molybdenum oxide catalyst (4). (33 mg, 1.82×10^{-4} mol), 90 °C, 550 °C, 2×10^{-3} Torr, 5 min, 25 mg: a mixture of mainly unreacted *N*-benzylideneaniline with the presence of benzonitrile also indicated by ^{13}C NMR spectrum; 132.66, 132.05, 129.64, 118.81 (q) and 112.37 (q).

FVP of benzyl alcohol over regenerated molybdenum oxide catalyst (4). (104 mg, 9.63×10^{-4} mol), room temp., 550 °C, 5×10^{-3} Torr, 10 min. The products were identified mainly from the ^{13}C NMR spectrum of the product mixture, supported by the presence of prominent peaks in the ^{1}H NMR spectrum. Toluene (85% of product mixture by comparison of integrals in the ^{1}H NMR); δ_C 137.74 (q), 128.92, 128.21, 125.18 and 21.34; benzaldehyde (9%); δ_C (1 quaternary signal missing) 192.27, 134.33 129.63 and 128.92 (overlapped by toluene peak); bibenzyl (6%); δ_C (1 quaternary signal missing) 128.56, 128.32, 125.79 and 37.82. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of *N*-phenylbenzylamine over regenerated molybdenum oxide

catalyst (4). (66 mg, 3.61×10^{-4} mol), 120 °C, 550 °C, 7×10^{-3} Torr, 5 min, 49 mg: a complex mixture, products identified mainly from ^{13}C NMR and presented in order of decreasing abundance; *N*-benzylideneaniline; δ_C 160.32, 136.02 (q), 131.26, 129.14, 128.98, 128.64, 125.81 and 120.73, 1 quaternary signal missing; unreacted *N*-phenylbenzylamine; δ_C 147.82 (q), 139.35 (q), 128.90, 128.48, 127.36, 127.08, 117.40, 112.68 and 48.12; acridine, unambiguously identified from partial data resolvable from the ^{1}H and ^{13}C NMR spectra; δ_H 8.71 (1 H, s), 8.17 (2 H, d, *J* 8.8), 7.94 (2 H, d, *J* 9.1), 7.78-7.63 (2 H, m) δ_C 135.58, 130.23, 128.20 and 125.58, 2 quaternary peaks not apparent and one other peak overlapped by other components. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of acenaphthene over regenerated molybdenum oxide catalyst (4). (114 mg, 7.40×10^{-4} mol), 90 °C, 550 °C, 3×10^{-3} Torr rising to 2×10^{-2} Torr during reaction, 10 min, 96 mg: a mixture of unreacted starting material and acenaphthylene, 91% conversion to acenaphthylene; δ_H 7.88 (2 H, d, *J* 8.1), 7.76 (2 H, d, *J* 6.6), 7.65-7.58 (2 H, m) and 7.17 (2 H, s); δ_C 139.49 (q), 129.23, 127.94 (q), 127.65 (q), 127.55, 127.08 and 124.04. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of acenaphthene over regenerated molybdenum oxide catalyst (4). (1.84 g, 1.20×10^{-2} mol), 90 °C, 550 °C, 3×10^{-3} Torr rising to 2×10^{-1} Torr during reaction, 4 h, 1.62 g: 69% conversion to acenaphthylene.

FVP of iminodibenzyl over regenerated molybdenum oxide catalyst (4). (160 mg, 8.21 × 10^{-4} mol), 150 °C, 550 °C, 2 × 10^{-3} Torr, 15 min, 94 mg: a complex mixture, products identified mainly from ^{13}C NMR and presented in order of decreasing abundance; acridine; δ_H 8.60 (1 H, m), 8.15 (2 H, dd, *J* 8.8, 0.7), 7.85 (2 H, dd, *J* 8.4, 0.7), 7.75-7.61 (2 H, m) and 7.54-7.36 (2 H, m); δ_C 148.81 (q), 135.96, 130.18, 129.08, 128.04, 126.71 (q) and 125.49; unreacted iminodibenzyl; iminostilbene; δ_H 6.95-6.90 (2 H, m), 6.73-6.58 (7 H, m) and 6.18 (2 H, s); δ_C 148.20 (q), 131.93, 130.31, 129.52 (q), 129.26, 122.45 and 119.11. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

3.2 The thermal chemistry of *cis*-2-pentenenitrile

3.2.1 Preparation of pyrolysis precursors

Penta-2,4-dienenitrile. To a well stirred mixture of crotonaldehyde (15.48 g, 0.221 mol) in toluene (45 cm^3) at –10 °C was added benzoyl chloride (31.08 g, 0.242 mol) slowly with stirring. Sodium cyanide (14.45 g, 0.295 mol) in water (75 cm^3) was then added dropwise with the reaction temperature maintained at –10 °C. On completion of the addition, the reaction mixture was stirred at –10 °C for 2 h and then allowed to warm to room temperature. The organic layer was separated, washed with aqueous sodium carbonate solution (5%, 2 × 25 cm^3) and water (25 cm^3) then dried over magnesium sulfate. The toluene was removed by evaporation under reduced pressure and distilled to give crotonaldehyde cyanohydrin benzoate (29.28 g, 66%) as a pale yellow oil which solidified on standing, bp 132-134 °C (1 Torr) [lit.[84] 125 °C (1 Torr)]; δ_H 8.06-8.01 (2 H, m), 7.59 (1 H, m), 7.49-7.41 (2 H, m), 6.24 (1 H, dqd, *J* 15.3, 6.7, 1.2), 6.04 (1 H, d of quintets, *J* 6.7, 1.2), 5.69 (1 H, ddq, *J* 15.3, 6.7, 1.7) and 1.81 (3 H, ddd, *J* 6.7, 1.7, 1.2); δ_C164.37 (q), 135.55, 133.74, 129.75, 128.39, 128.10 (q), 121.20, 115.62 (q), 61.68 and 17.46.

Crotonaldehyde cyanohydrin benzoate (5.11 g, 2.54×10^{-2} mol) was pyrolysed at 750 °C, using the protocol described in section 1.5, with an inlet temperature of 90 °C at a pressure of 5×10^{-3} Torr. The pyrolysate was collected into ether (50 cm^3) and washed with aqueous sodium hydroxide solution (1 M, 2 × 25 cm^3) and water (25 cm^3). The organic fraction was then dried over magnesium sulfate and concentrated under reduced pressure to give an orange oil, which on distillation yielded penta-2,4-dienenitrile as a mixture of *cis* and *trans* isomers (1.02 g, 51%), bp 85 °C (65 Torr) [lit.[84] 49.5-53 °C (30 Torr)]; δ_H 7.00-6.63 (3 H, m), 6.46-6.26 (6 H, m) and 5.67-5.18 (1 H, m). δ_C (major isomer) 150.25, 132.20, 126.35, 117.36 (q) and 99.37; δ_C (minor isomer) 149.17, 133.71, 126.64, 115.60 (q) and 97.72.

3.2.2 Attempted dehydrogenation-cyclisation of *cis*-2-pentenenitrile

Several different sets of conditions were used in an attempt to effect the dehydrogenation-cyclisation reaction required to take *cis*-2-pentenenitrile to pyridine. These are described here. The reactions involve the pyrolysis of *cis*-2-pentenenitrile

(10^{-4}-10^{-2} mol) at temperatures of 550–950 °C according to the procedure outlined in section 1.5. Different packings were utilised for this purpose and where indicated, were prepared and used as detailed in section 1.7. Results are quoted as follows: catalyst used, quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, work up method and a discussion of the characterisation of the products.

FVP of *cis*-2-pentenenitrile under pure thermal conditions. This reaction was carried out at several different reaction temperatures to achieve full breakdown of the starting material. This was found to occur at no less than 950 °C. Only this reaction is detailed here since the reaction pathway followed at lower temperatures is identical to that at 950 °C. Porcelain saddles, (319 mg, 3.94×10^{-3} mol), 0 °C, 950 °C, 5×10^{-3} Torr rising to 3×10^{-1} Torr during reaction, 20 min. The pyrolysate was collected into [^{2}H]chloroform for NMR study. This yielded a complex mixture, products identified mainly from the ^{13}C NMR spectrum and listed in order of decreasing abundance: acrylonitrile; δ_C 137.17, 116.26 (q) and 107.07; acetonitrile; 116.61 (q) and 1.21; *cis*- and *trans*-penta-2,4-dienenitrile; δ_C (major isomer) 150.34, 132.15, 126.34 and 99.25 (quaternary signal not resolvable from NMR spectrum); δ_C (minor isomer) 149.25, 133.69, 126.66 and 97.61 (quaternary signal not resolvable from NMR spectrum); propionitrile; δ_C 120.44, 10.28 and 9.87; *cis* and *trans*-crotononitrile; δ_C (major isomer) 149.99, 99.99 and 16.96 (quaternary signal not resolvable from NMR spectrum); δ_C (minor isomer) 151.24, 100.33 and 18.57 (quaternary signal not resolvable from NMR spectrum). Other very minor components remain unidentified. The ^{13}C NMR spectra concurred with those in the literature[103] apart from that of *cis*- and *trans*-penta-2,4-dienenitrile which was identified by comparison with the spectra of an authentic sample prepared (see section 3.2.1).

This reaction was also carried out over a packing of quartz wool. This gave an identical mixture of products to those described above.

FVP of *cis*-2-pentenenitrile under catalytic conditions. Molybdenum oxide (5), (260 mg, 3.21×10^{-3} mol), 0 °C, 550 °C, 5×10^{-3} Torr rising to 8×10^{-2} Torr during reaction, 10 min. The pyrolysate was collected into [^{2}H]chloroform for NMR study. This yielded a fully resolved mixture, products listed in order of decreasing abundance: *cis*- and *trans*-2-pentenenitrile; *cis*- and *trans*-penta-2,4-dienenitrile; *trans*-3-pentenenitrile; δ_H 5.73 (1 H, m), 5.30 (1 H, m), 2.97 (2 H, m) and 1.59 (3 H, m); δ_C 130.17, 117.99, 117.14 (q), 19.74 and 17.03. The ^{1}H and ^{13}C NMR spectra concurred with those in the literature.[103]

FVP of *cis*-2-pentenenitrile under catalytic conditions. Alumina pellets, (48 mg, 5.93×10^{-4} mol), 0 °C, 550 °C, 2×10^{-3} Torr, 5 min. The pyrolysate was collected into [^{2}H]chloroform for NMR study. The NMR spectra showed and identical set of products to those obtained in the reaction over molybdenum oxide above.

3.2.3 Investigation of possible intermediate - penta-2,4-dienenitrile

Penta-2,4-dienenitrile was pyrolysed under similar conditions to those used in section 3.2.2 to verify its place in the reaction pathway of *cis*-2-pentenenitrile. Results are quoted as follows: catalyst used, quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, work up method and a discussion of the characterisation of the products.

FVP of penta-2,4-dienenitrile under pure thermal conditions. Porcelain saddles, (226 mg, 2.86×10^{-3} mol), 0 °C, 950 °C, 1×10^{-2} Torr rising to 2×10^{-1} Torr during reaction, 15 min. The pyrolysate was collected into [^{2}H]chloroform for NMR study. This yielded a mixture consisting predominantly (~ 80%) of starting material, products identified mainly from the ^{13}C NMR spectrum and listed in order of decreasing abundance: *cis*- and *trans*-penta-2,4-dienenitrile; δ_C (major isomer) 150.25, 132.20, 126.35, 117.36 (q) and 99.37; δ_C (minor isomer) 149.17, 133.71, 126.64, 115.60 (q) and 97.72; acrylonitrile; δ_C 137.08, 116.49 (q) and 107.16; acetonitrile. Other very minor components remain unidentified, these being spectroscopically identical with those unidentified in the pyrolysis of *cis*-2-pentenenitrile under the same conditions. The ^{13}C NMR spectra of acrylonitrile concurred with that in the literature[103] while that of *cis*- and *trans*-penta-2,4-dienenitrile was identified by comparison with the spectra of an authentic sample prepared (see section 3.2.1).

This reaction was also carried out over a packing of quartz wool. This gave an identical mixture of products to those described above.

FVP of penta-2,4-dienenitrile under catalytic conditions. Molybdenum oxide (5), (133 mg, 1.68 × 10^{-3} mol), 0 °C, 550 °C, 5 × 10^{-3} Torr, 10 min. The pyrolysate was collected into [^{2}H]chloroform for NMR study. The ^{1}H NMR spectrum indicated that no reaction had taken place and only starting material was present.

4. Rearrangement of 2-nitrotoluene

4.1 FVP of anthranilic acid derivatives

Anthranilic acid, anthranilamide and methyl anthranilate were pyrolysed under flash vacuum conditions at a range of temperatures. This was carried out in order to determine the relative thermal stability of these compounds and to establish which would be the best trap for anthranil. The reactions involve the pyrolysis of the anthranilate derivative (~10^{-3} mol) at temperatures from 600-750 °C according to the procedure outlined in section 1.5 and collection of the resulting pyrolysate directly into [^{2}H]chloroform. To the ^{1}H NMR sample was added a known amount of 1,4-dinitrobenzene and the amount of starting material remaining in each sample was calculated from this reference. In each case, the breakdown of starting material gave complex mixtures with messy NMR spectra and no attempt was made to resolve these mixtures beyond quantification of the amount of reaction taken place, other than for the reaction of anthranilic acid which was further investigated by GC-MS and quantified by GC as described in section 1.4. It was noted however that dimers of 1-cyanocyclopentadiene were present in every case, identified by comparison of the NMR spectra with those obtained from an authentically prepared sample.[67] Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected, % unreacted starting material.

FVP of anthranilic acid. (182 mg, 1.33×10^{-3} mol), 150 °C, 600 °C, 5×10^{-3} Torr, 10 min, 176 mg, 94%.

(150 mg, 1.09×10^{-3} mol), 150 °C, 650 °C, 5×10^{-3} Torr, 139 mg, 71%.

(148 mg, 1.08×10^{-3} mol), 150 °C, 700 °C, 5×10^{-3} Torr, 66 mg, 10%.

(1.11 g, 8.10×10^{-3} mol), 150 °C, 750 °C, 1×10^{-2} Torr, 0.58 g, 0%. The crude ^{1}H and ^{13}C NMR spectra show many aliphatic peaks. These were believed to be attributable to 1-cyanocyclopentadiene present as several dimers. This was confirmed by preparation of an authentic sample (see end of section).[67] The mixture was analysed by GC-MS and found to contain mainly 1-cyanocyclopentadiene with appreciable amounts of aniline and 2-cyanophenol. Trace amounts of anthranilonitrile and 2-methylnaphthalene were also confirmed as being present, together with many unidentified other components. Quantification of the reaction mixture obtained at 750 °C by GC analysis gave the following results: 1-cyanocyclopentadiene (72%); aniline (12%); 2-cyanophenol (7%); anthranilonitrile (1%); 2-methylnaphthalene (1%).

FVP of anthranilamide. (182 mg, 1.34×10^{-3} mol), 180 °C, 600 °C, 5×10^{-3} Torr, 177 mg, 93%.

(162 mg, 1.19×10^{-3} mol), 180 °C, 650 °C, 5×10^{-3} Torr, 155 mg, 92%.

(185 mg, 1.36×10^{-3} mol), 180 °C, 700 °C, 5×10^{-3} Torr, 125 mg, 24%.

(178 mg, 1.31×10^{-3} mol), 180 °C, 750 °C, 5×10^{-3} Torr, 81 mg, undetectable by NMR.

FVP of methyl anthranilate. (166 mg, 1.10 × 10^{-3} mol), 30 °C, 600 °C, 5 × 10^{-3} Torr, 164 mg, 95%.

(158 mg, 1.05 × 10^{-3} mol), 30 °C, 650 °C, 5 × 10^{-3} Torr, 152 mg, 91%.

(152 mg, 1.01 × 10^{-3} mol), 30 °C, 700 °C, 5 × 10^{-3} Torr, 111 mg, 14%.

(175 mg, 1.16 × 10^{-3} mol), 30 °C, 750 °C, 5 × 10^{-3} Torr, 114 mg, 10%.

Anthranil and 2-nitrotoluene were also pyrolysed at a range of temperatures to find the relative thermal stability of these compounds. The amount of reaction having taken place was not quantified as above but the main points were noted. Anthranil reacts by FVP leaving no unreacted starting material at temperatures of 600 °C and above but at temperatures of 550 °C and lower, anthranil remains in the product mixture. 2-Nitrotoluene reacts under FVP conditions to leave no starting material at temperatures above 750 °C. At 750 °C, the product mixture contains a small amount of 2-nitrotoluene but the resulting spectra are much cleaner and easier to analyse than those obtained from reaction at 800 °C. Thus anthranil and 2-nitrotoluene were pyrolysed at 750 °C for GC-MS analysis and subsequent quantification by GC. Results are quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected, products.

FVP of anthranil at 750 °C. (524 mg, 4.40 × 10^{-3} mol), 30 °C, 750 °C, 1 × 10^{-2} Torr, 20 min, 256 mg. The pyrolysate was collected into dichloromethane and the solvent was evaporated under reduced pressure to yield a dark brown oil. The crude ^{1}H and ^{13}C NMR spectra and GC trace were identical with those described for anthranilic acid above. Quantification of the reaction mixture by GC analysis gave the following results: 1-cyanocyclopentadiene (68%); aniline (10%); 2-cyanophenol (6%); anthranilonitrile (3%); 2-methylnaphthalene (1%).

FVP of 2-nitrotoluene. (566 mg, 4.13×10^{-3} mol), 90 °C, 750 °C, 1×10^{-2} Torr, 20 min, 288 mg. The pyrolysate was collected into dichloromethane and the solvent was evaporated under reduced pressure to yield a dark brown oil. The crude ^{1}H and ^{13}C NMR spectra showed many aliphatic peaks. These were believed to be attributable to 1-cyanocyclopentadiene present as several dimers. This was confirmed by preparation of an authentic sample.[67] The crude pyrolysate was analysed by GC-MS giving evidence of appreciable amounts of 1-cyanocyclopentadiene, 2-cresol, phenol and 2-cyanophenol and trace amounts of naphthalene, 2-methylnaphthalene and anthranilonitrile. Quantification of the reaction mixture by GC analysis gave the following results: 1-cyanocyclopentadiene (20%); 2-cresol (14%); phenol (11%); 2-cyanophenol (10%); naphthalene (2%); 2-methylnaphthalene (1%); anthranilonitrile (1%).

In order to confirm the special thermal instability of these anthranilate derivatives, 3-aminobenzoic acid was pyrolysed at 750 °C.

FVP of 3-aminobenzoic acid. (506 mg, 3.69×10^{-3} mol, 135 °C, 750 °C, 5×10^{-3} Torr, 20 min, 464 mg. The pyrolysate was collected into methanol and concentrated under reduced pressure to yield unchanged starting material, mp 181-183 °C [lit.[103] 178-180 °C]. The ^{1}H and ^{13}C NMR spectra confirmed the presence of only starting material.

FVP of 2-nitrotoluene over 3A molecular sieves. For this reaction the furnace tube was packed with 3A molecular sieves (10 g), prepared and used according to the methods detailed in section 1.6. (383 mg, 2.80×10^{-3} mol), 90 °C, 500 °C, 1×10^{-2} Torr, 15 min, 243 mg. The pyrolysate was collected into dichloromethane and the solvent evaporated under reduced pressure to yield a brown oil. The product mixture was shown by t.l.c. to contain aniline and was thus dissolved in dichloromethane (25 cm^3), subjected to acid extraction with aqueous hydrochloric acid (2 M, 2 × 5 cm^3) and washed with water (5 cm^3). The combined aqueous extracts were basified with aqueous sodium hydroxide (2 M, 12 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried over magnesium sulfate and concentrated under reduced pressure to give a brown oil (85 mg) which showed two spots by t.l.c. However, on attempted separation of this mixture by dry-flash column chromatography, no single components could be isolated, with each fraction obtained containing several products by t.l.c.

The organic fraction remaining after acid extraction was also separated by dry-flash column chromatography yielding two identifiable products: unreacted 2-nitrotoluene; δ_H 7.87 (1 H, m), 7.46-7.21 (3 H, m) and 2.51 (3 H, s); 2-phenyl indazole; δ_H (250 MHz) 8.41 (1 H, d, *J* 1.0), 7.93-7.87 (2 H, m), 7.81-7.69 (2 H, m), 7.56-7.48 (2 H, m), 7.43-7.28 (2 H, m) and 7.14-7.07 (1 H, m); δ_C (90 MHz) 149.33 (q), 140.01 (q), 129.09, 127.44, 126.35, 122.30 (q), 121.99, 120.55, 119.90, 117.48 and 29.21. The ^1H and ^{13}C NMR spectra concur with those in the literature.[121]

Preparation of 1-cyanocyclopentadiene. By a modification of the method described by Wentrup and Crow,[67] benzotriazole was subjected to FVP over porcelain saddles yielding a mixture of dimers of 1-cyanocyclopentadiene and aniline. The result is quoted as follows: quantity of substrate, inlet temperature, furnace temperature, pressure, pyrolysis time, weight collected, products. (4.90 g, 4.12×10^{-2} mol), 210 °C, 750 °C, 1×10^{-2} Torr, 2 h. This yielded a pyrolysate, the NMR spectra of which are dominated by a distinctive pattern of many peaks in the ranges 1.5-3.9 ppm and 5.4-7.4 ppm (^{1}H NMR) and also 35-60 ppm and 115-155 ppm (^{13}C NMR). The ^{1}H NMR spectrum concurred with that in the literature.[112]

4.2 Flow Pyrolytic reactions of 2-nitrotoluene

4.2.1 Trapped by methanol

This section will detail the reactions of 2-nitrotoluene under flow pyrolysis conditions, as discussed in section 1.6. Packing material was used as indicated, the material in question being prepared for use according to section 1.7. A general procedure follows.

The flow pyrolysis apparatus, packed as indicated for each experiment, (figure 24, p172) was heated to reaction temperature and allowed to equilibrate under carrier gas flow (nitrogen). 2-Nitrotoluene (0.5-4 g) was added in methanol solution *via* syringe through a rubber septum to the top of the apparatus, the rate of addition controlled by a syringe pump. The needle itself was positioned as shown in figure 24 unless otherwise stated. After complete addition of the starting material, the apparatus was allowed to cool down under nitrogen flow and the products formed collected from the traps. The primary trap used, positioned directly beneath the furnace, was either trap A or B as depicted in figure 25, p173 and most of the products formed were trapped here. Further traps were used as indicated in section 1.6. The products were combined from each trap into a suitable solvent depending on their solubility and the solution concentrated under reduced pressure. The carrier gas was bubbled through water as a final trap and where this trap was seen to contain material, it was extracted with a suitable solvent.

In most cases the product mixture obtained was complex and gave very messy NMR spectra. Products were identified mainly from the ^{13}C NMR spectrum and in relevant cases were quantified by addition of a known amount of cyclohexane to the ^{1}H NMR sample.

Results are quoted as follows: quantity of substrate, solvent, rate of addition, carrier gas (flow rate), packing used, primary trap used, furnace temperature, work-up and products.

Flow pyrolysis of 2-nitrotoluene over quartz wool. (4.14 g, 3×10^{-2} mol), methanol (9.8 g, 0.310 mol), 30 cm^3 h^{-1}, nitrogen (20 cm^3 min^{-1}), quartz wool, trap B, 600 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (1.85 g). The crude ^{1}H and ^{13}C NMR spectra show unreacted 2-nitrotoluene to be the predominant component; δ_C (250 MHz) 149.31(q), 133.13 (q), 132.70, 132.39, 126.52, 124.23 and 20.04. Methyl anthranilate was also observed though in very small amount; δ_C 168.54(q), 150.18(q), 133.75, 131.05, 115.81, 115.11, 110.66 and 51.21.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles at 600 °C. (4.10 g, 3×10^{-2} mol), methanol (9.90 g, 0.31 mol), 30 cm^3 h^{-1}, nitrogen (20 cm^3 min^{-1}), porcelain saddles, trap B, 600 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (2.57 g). The crude ^1H and ^{13}C NMR spectra were identical with those described above but with a greater proportion of 2-nitrotoluene having reacted. The amount of 2-nitrotoluene remaining in the product mixture was quantified and found to be 0.31 g.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles at 700 °C. In order to determine the temperature at which 2-nitrotoluene is completely consumed, the reaction was carried out at 700 ° C. (4.02 g, 2.9×10^{-2} mol), methanol (9.12 g, 0.32 mol), 30 cm^3 h^{-1}, nitrogen (20 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (1.86 g). The crude ^1H and ^{13}C NMR spectra were similar to those described for reaction at 600 °C but no 2-nitrotoluene was present in the product mixture.

Flow pyrolysis of 2-nitrotoluene in high methanol excess over porcelain saddles . The proportion of methanol used was increased to investigate if the presence of more trapping material resulted in the formation of more methyl anthranilate. (476 mg, 3.47×10^{-3} mol), methanol (10.18 g, 0.32 mol), 30 cm^3 h^{-1}, nitrogen (20 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (267 mg). The crude ^1H and ^{13}C NMR spectra indicated that no 2-nitrotoluene was present in the reaction mixture and the amount of methyl anthranilate present was not increased by the use of more methanol. The reaction mixture appeared to be cleaner in the aromatic regions of both the ^1H and ^{13}C NMR spectra though a number of peaks were present in the regions 2-5 ppm (^1H NMR) and 50-90 ppm (^{13}C NMR), thought to be accountable to breakdown and polymerisation products of methanol.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles using pre-heated nitrogen. Here, the nitrogen used was pre-heated by passing the gas line up through the furnace, alongside the reaction tube (see figure 2, p7), to see if this could clean up the product mixture by aiding vaporisation of the starting material. (440 mg, 3.21×10^{-3} mol), methanol (10.24 g, 0.32 mol), 30 cm^3 h^{-1}, hot nitrogen (20 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (258 mg). The crude ^1H NMR spectrum shows an identical product mixture to that found under these conditions without pre-heating of the carrier gas as described in the previous experiment.

4.2.2 Trapped by ammonia

This section will detail the reactions of 2-nitrotoluene under flow pyrolysis conditions, as discussed in section 1.6. Packing material was used as indicated, the material in question being prepared for use according to section 1.7. A general procedure follows.

The flow pyrolysis apparatus, packed as indicated for each experiment, (figure 24, p172) was heated to reaction temperature and allowed to equilibrate under carrier gas flow (ammonia). 2-Nitrotoluene was added, either neat or in solution, *via* syringe through a rubber septum to the top of the apparatus, the rate of addition controlled by a syringe pump. A solvent was occasionally used to prevent blockage of the syringe needle. The needle itself was positioned as shown in figure 24 unless otherwise stated. After complete addition of the starting material, the apparatus was allowed to cool down under nitrogen flow and the products formed collected from the traps. The primary trap used, positioned directly beneath the furnace, was either trap A or B as depicted in figure 25, p173 and most of the products formed were trapped here. Further traps were used as indicated in section 1.6. The products were combined from each trap into a suitable solvent depending on their solubility and the solution concentrated under reduced pressure. The carrier gas was bubbled through water as a final trap and where this trap was seen to contain material, it was extracted with a suitable solvent.

In most cases the product mixture obtained was complex and gave very messy NMR spectra. Products were identified mainly from the ^{13}C NMR spectrum and in relevant cases were quantified by addition of a known amount of cyclohexane to the ^{1}H NMR sample.

Results are quoted as follows: quantity of substrate, solvent/neat, rate of addition, carrier gas (flow rate), packing used, primary trap used, furnace temperature, work-up and products.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles at 700 °C. (205 mg, 1.50×10^{-3} mol), neat, 0.6 $cm^3 h^{-1}$, ammonia (300 $cm^3 min^{-1}$), porcelain saddles, trap B, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (96 mg). The presence of unreacted 2-nitrotoluene, anthranilamide, anthranilonitrile and aniline was indicated by t.l.c. The ^1H and ^{13}C NMR spectra showed a relatively clean product mixture, almost entirely accounted for by two main products: anthranilonitrile; δ_C 149.52 (q), 133.83, 132.10, 117.66, 117.55 (q), 114.97 and 95.51 (q); aniline; δ_C 145.97 (q), 129.06, 118.48 and 115.06. The ^{13}C NMR spectrum indicates that anthranilonitrile and aniline were present in an approximately 2:1 ratio. The presence of 2-nitrotoluene in trace amount was supported by peaks at δ_H 2.49 and δ_C 149.10 and 20.22 though the aromatic regions of both the ^1H and ^{13}C NMR spectra were too crowded to characterise this product fully. Similarly, peaks at δ_C 171.89 (q), 114.69 and 113.66 (q) supported the presence of a trace of anthranilamide. All products were confirmed by comparison with literature spectra[103] apart from anthranilonitrile which was further confirmed by addition of an authentic to the NMR sample.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles at 600 °C. The pyrolysis of 2-nitrotoluene was run at a lower temperature of 600 °C in an attempt to prevent the dehydration of anthranilamide to anthranilonitrile occurring. (830 mg, 6.06×10^{-3} mol), neat, 1 $cm^3 h^{-1}$, ammonia (300 $cm^3 min^{-1}$), porcelain saddles, trap B, 600 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (265 mg). The presence of unreacted 2-

nitrotoluene, anthranilamide, anthranilonitrile and aniline was again indicated by t.l.c. The ^{1}H and ^{13}C NMR spectra showed a relatively clean product mixture, almost entirely accounted for by starting material plus the two main products as for reaction at 700 °C: anthranilonitrile; δ_C 149.54 (q), 133.78, 132.04, 118.42 (q), 117.58, 114.95 and 95.46 (q); aniline; δ_C 146.07 (q), 129.03, 118.34 and 114.95. The presence of anthranilamide, in slightly increased proportion at this temperature, was supported by peaks at δ_C 171.83 (q), 130.18, 127.90, 116.23, 114.77 and 113.68 (q). The amount of 2-nitrotoluene present was found to be 44 mg, 17% of the product mixture, by addition of a known amount of cyclohexane to the ^{1}H NMR sample. The quantification of other products was not possible due to overlapping peaks.

The water trap was extracted into dichloromethane and dried over magnesium sulfate to give a dark oil (75 mg) with a similar ^{1}H NMR spectrum to that of the bulk product mixture.

Flow pyrolysis of 2-nitrotoluene in methanol solution over porcelain saddles. 2-nitrotoluene was reacted in concentrated methanolic solution to prevent blockage of the syringe needle which had become a problem with these reactions. (516 mg, 3.77×10^{-3} mol), methanol (2.95 cm^3), 6 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap A, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (230 mg). Both the ^{1}H and ^{13}C NMR spectra showed a messy aromatic region and the ^{1}H NMR spectrum in particular was dominated by a number of peaks in the aliphatic region, attributed to breakdown products of methanol. The presence of anthranilonitrile as the main product was confirmed by the ^{13}C NMR spectrum; δ_C 149.51 (q), 133.85, 132.21, 118.13 (q), 117.83, 115.02 and 95.89 (q). The presence of aniline is supported by a large peak at δ_C 129.42 while the other peaks are overlapped by other peaks in the spectrum. The ^{13}C NMR spectrum of anthranilonitrile in particular is concentration dependent and in this case causes overlap with aniline peaks. Anthranilonitrile (126 mg) was found to be present by addition of a known amount of cyclohexane to the ^{1}H NMR sample.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles with variation of ammonia flow rate. The effect of variation of the ammonia flow rate was investigated by reaction under vastly higher and lower flow rates, as allowed by the needle valve. **Lower flow rate.** (535 mg, 3.90×10^{-3} mol), methanol (2.95 cm^3), 6 cm^3 h^{-1}, ammonia (30 cm^3 min^{-1}), porcelain saddles, trap A, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (335 mg). The resulting ^{1}H NMR spectrum is very similar to that obtained from reaction under the conventional ammonia flow rate of 300 cm^3 min^{-1}. Anthranilonitrile (72 mg) was found to be present by addition of a known amount of cyclohexane to the ^{1}H NMR sample.

Higher flow rate. (564 mg, 4.12×10^{-3} mol), methanol (2.98 cm^3), 6 cm^3 h^{-1}, ammonia (1200 cm^3 min^{-1}), porcelain saddles, trap A, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to give a dark oil (326 mg). A feature of this higher flow rate was that the collection of products was much more difficult, with products distributed throughout the trapping system and not concentrated mainly at the primary trap which is the norm. Again, the resulting ^1H NMR spectrum is very similar to that obtained from reaction under the conventional ammonia flow rate of 300 cm^3 min^{-1}. Anthranilonitrile (113 mg) was found to be present by addition of a known amount of cyclohexane to the ^1H NMR sample.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles and 3A molecular sieves. The furnace tube was packed with porcelain saddles as described in section 1.7, p174, except for the middle 2-3 cm which was packed with 3A molecular sieves (10 g). The use of sieves limits the working temperature to 550 °C. The system was then prepared for use by heating as described in section 1.7, p174 also. The needle delivering the 2-nitrotoluene was positioned at the top of the furnace, as depicted in figure 24, p172. (1.03 g, 7.52×10^{-3} mol), methanol (2.94 cm^3), 24 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles + 3A molecular sieves, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to give a brown oil (883 mg). The ^1H and ^{13}C NMR spectra showed the product mixture to be reasonably clean, consisting predominantly of 2-toluidine: δ_H 6.99-6.92 (2 H, m), 6.71-6.57 (2 H, m) and 2.08 (3 H, s); δ_C 144.32 (q), 130.02, 126.54, 121.88 (q), 118.08, 114.50 and 16.90. No unreacted starting material was present among the trace components observed in the NMR spectra.

The water trap was extracted into dichloromethane and dried over magnesium sulfate to give a dark oil (72 mg) with a similar ^1H NMR spectrum to that of the bulk product mixture, *i.e.*, mainly consisting of 2-toluidine.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles and 3A molecular

sieves. This experiment was carried out with both nitrogen and ammonia carrier gases. The nitrogen was introduced at the top of the furnace while the ammonia was introduced below the level of the molecular sieves, to ascertain which element of the system is responsible for the reduction to 2-toluidine. The furnace tube was packed with porcelain saddles as described in section 1.7, p174, except for the middle 2-3 cm which was packed with 3A molecular sieves (10 g). The system was then prepared for use by heating as described in section 1.7, p174 also. The needle delivering the 2-nitrotoluene was positioned at the top of the furnace, as depicted in figure 2, p7. (1.02 g, 7.45×10^{-3} mol), methanol (2.99 cm^3), 24 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}) + nitrogen (300 cm^3 min^{-1}), porcelain saddles + 3A molecular sieves, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to give a brown oil (607 mg). Again, the ^{1}H and ^{13}C NMR spectra showed the product mixture to consist predominantly of 2-toluidine: δ_H 7.11-7.05 (2 H, m), 6.83-6.63 (2 H, m) and 2.20 (3 H, s). No unreacted starting material was present among the trace components observed in the NMR spectrum.

Flow pyrolysis of 2-nitrotoluene over porcelain saddles and 3A molecular sieves. This experiment was carried out under nitrogen carrier gas only in a further attempt to eliminate the reduction to 2-toluidine. The reaction was carried out exactly as above excepting the presence of ammonia. (1.17 g, 8.54×10^{-3} mol), methanol (3.11 cm^3), 24 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles + 3A molecular sieves, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to give a brown oil (600 mg). The ^{1}H and ^{13}C NMR spectra showed a much more complex mixture than those obtained from reactions of 2-nitrotoluene over molecular sieves under ammonia. The main component, accounting for ~ 50% of the product mixture was again 2-toluidine.

Flow pyrolysis of 2-nitrotoluene over 4A molecular sieves. The furnace tube was packed with 4A molecular sieves for its full length. The system was then prepared for use by heating as described in section 1.7, p174. The needle delivering the 2-nitrotoluene was positioned at the top of the furnace, as depicted in figure 24, p172. (1.02 g, 7.45×10^{-3} mol), methanol (2.95 cm^3), 24 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), 4A molecular sieves, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to give a brown oil (340 mg). The ^1H NMR spectrum of the product mixture appears similar to that produced from reaction over 3A molecular sieves, *i.e.*, the presence of 2-toluidine as the main product is strongly supported by the presence of a large peak at δ 2.10.

Flow pyrolysis of 2-nitrotoluene over 13X molecular sieves. The furnace tube was packed with 13X molecular sieves for its full length. The system was then prepared for use by heating as described in section 1.7, p174. The needle delivering the 2-nitrotoluene was positioned at the top of the furnace, as depicted in figure 24, p172. (1.02 g, 7.45×10^{-3} mol), methanol (3.02 cm^3), 24 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), 13X molecular sieves, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to give a brown oil (291 mg). The ^1H NMR spectrum of the product mixture appears similar to that produced from reaction over 3A molecular sieves, *i.e.*, the presence of 2-toluidine as the main product is strongly supported by the presence of a large peak at δ 2.05.

4.2.3 Flow pyrolytic reactions of anthranil and anthranilate derivatives

This section will detail the reactions of anthranil, methyl anthranilate and anthranilamide under flow pyrolysis conditions, as discussed in section 1.6. Packing material was used as indicated, the material in question being prepared for use according to section 1.7. A general procedure follows.

The flow pyrolysis apparatus, packed as indicated for each experiment, (figure 24, p172) was heated to reaction temperature and allowed to equilibrate under carrier gas flow (ammonia or nitrogen). The substrate was added, either neat or in solution, *via* syringe through a rubber septum to the top of the apparatus, the rate of addition controlled by a syringe pump. A solvent was occasionally used to prevent blockage of the syringe needle or to dissolve the solid amide precursor. The needle itself was positioned as shown in figure 24 unless otherwise stated. After complete addition of the starting material, the apparatus was allowed to cool down under nitrogen flow and the products formed collected from the traps. The primary trap used, positioned directly beneath the furnace, was either trap A or B as depicted in figure 15, p173 and most of the products formed were trapped here. Further traps were used as indicated in section 1.6. The products were combined from each trap into a suitable solvent depending on their solubility and the solution concentrated under reduced pressure. The carrier gas was bubbled through water as a final trap and where this trap was seen to contain material, it was extracted with a suitable solvent.

Results are quoted as follows: quantity of substrate, solvent/neat, rate of addition, carrier gas (flow rate), packing used, primary trap used, furnace temperature, work-up and products.

Flow pyrolysis of anthranilamide over porcelain saddles at 700 °C. (581 mg, 4.27×10^{-3} mol), methanol (2.82 cm^3), 6 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (503 mg). The ^{13}C NMR spectrum shows anthranilonitrile to be the main product with traces of starting material, aniline and methyl anthranilate also present. By addition of a known amount of cyclohexane to the ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (222 mg, 44%).

Flow pyrolysis of anthranilamide over porcelain saddles in the absence of ammonia. In order to investigate the role of the carrier gas in the dehydration of anthranilamide, the reaction was carried out under nitrogen flow. (673 mg, 4.95×10^{-3} mol), methanol (2.97 cm^3), 6 cm^3 h^{-1}, nitrogen (300 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (598 mg). The ^{1}H and ^{13}C NMR spectra are very similar to those obtained for reaction of anthranilamide under ammonia flow. By addition of a known amount of cyclohexane to the ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (297 mg, 51%).

Flow pyrolysis of anthranilamide over porcelain saddles at 600 °C. The reaction was carried out at lower temperature to investigate the ease of dehydration of anthranilamide under these conditions. (1.10 g, 8.09×10^{-3} mol), methanol (4.53 cm^3), 36 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap A, 550 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a yellow oily solid (0.99 g). The crude product was distilled under reduced pressure to yield anthranilonitrile as a white solid (0.63 g, 66%), bp 85 °C (1 Torr).

Flow pyrolysis of methyl anthranilate over porcelain saddles at 700 °C. (980 mg, 6.49×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (677 mg). The ^{13}C NMR spectrum shows the mixture to predominantly consist of anthranilonitrile. Attempted separation by dry-flash column chromatography yielded no other products but some unreacted starting material (27 mg, 3%) was found to be present. Anthranilonitrile could not be separated cleanly but by addition of a known amount of cyclohexane to the ^1H NMR sample, the mixture was found to contain anthranilonitrile (431 mg, 44%). On extraction with dichloromethane of the water trap used at the exit point of the apparatus, a further portion of pure anthranilonitrile was obtained (19 mg, 2%).

Flow pyrolysis of methyl anthranilate over porcelain saddles with variation of ammonia flow rate. The effect of variation of the ammonia flow rate was investigated by reaction under vastly higher and lower flow rates, as allowed by the needle valve. This investigation was carried out on this reaction since this is the cleanest transformation found so far in this study under flow pyrolysis conditions. **Lower flow rate.** (520 mg, 3.44×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (30 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (314 mg). The ^1H and ^{13}C NMR spectra show the product mixture to predominantly consist of anthranilonitrile with other unidentified aromatic components present. By addition of a known amount of cyclohexane to the ^1H NMR sample, the mixture was found to contain anthranilonitrile (131 mg, 32%).

Higher flow rate. (498 mg, 3.30×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (1200 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (238 mg). A feature of this higher flow rate, noticed previously in the pyrolysis of 2-nitrotoluene was that the collection of products was much more difficult, with products distributed throughout the trapping system and not concentrated mainly at the primary trap which is the norm. The ^1H and ^{13}C NMR spectra show the main component in the product mixture to be anthranilonitrile. By addition of a known amount of cyclohexane to the ^1H NMR sample, the mixture was found to contain anthranilonitrile (133 mg, 34%). On extraction with dichloromethane of the water trap used at the exit point of the apparatus, a yellow oily solid (92 mg) was obtained. By addition of a known amount of cyclohexane to this ^1H NMR sample, the mixture was found to contain anthranilonitrile (51 mg, 13%).

Flow pyrolysis of anthranil over porcelain saddles at 700 °C. (852 mg, 7.16×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap B, 700 °C. The crude products were collected into methanol and concentrated under reduced pressure to yield a brown oil (161 mg). The delivery needle blocked after addition of 220 mg of starting material and the reaction was stopped at this point. The ^1H and ^{13}C NMR spectrum show the product mixture to predominantly consist of anthranilonitrile. The sample was purified by distillation under reduced pressure to yield anthranilonitrile as a yellow oil (81 mg, 37%) which solidified on standing.

Flow pyrolysis of anthranil over porcelain saddles at 600 °C. The pyrolysis of anthranil was carried out at a lower temperature of 600 °C to investigate whether this would be sufficient to effect the transformation to the anthranilate derived products. (783 mg, 6.58×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap B, 600 °C. The crude products were collected into methanol and concentrated under reduced pressure to yield a brown oil (223 mg). The delivery needle blocked after addition of 360 mg of starting material and the reaction was stopped at this point. The ^1H and ^{13}C NMR spectrum show the mixture to predominantly consist of anthranilonitrile. The sample was partially dissolved in dichloromethane and a polymeric material filtered off. The filtrate was evaporated to yield anthranilonitrile as a brown solid (207 mg, 58%).

Flow pyrolysis of anthranil over porcelain saddles at 500 °C. Anthranil was pyrolysed in concentrated methanol solution to circumvent the problem observed involving blockage of the delivery needle. The temperature was lowered to 500 °C to further investigate the thermal requirements of this reaction. (1.12 g, 9.41×10^{-3}

mol), methanol (5.01 g), 12 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap A, 500 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (476 mg). No blockage of the delivery needle occurred. The ^{1}H and ^{13}C NMR spectrum show the product mixture to predominantly consist of anthranilonitrile. By addition of a known amount of cyclohexane to the ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (375 mg, 34%). The water trap was observed to contain an appreciable amount of organic material and so was extracted with dichloromethane and evaporated to give a brown solid (305 mg). By addition of a known amount of cyclohexane to this ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (232 mg, 21%). (Total yield of anthranilonitrile of 55%).

Flow pyrolysis of anthranil in THF solution over porcelain saddles. Anthranil was pyrolysed in concentrated tetrahydrofuran solution as an alternative to methanol. (1.02 g, 8.57×10^{-3} mol), tetrahydrofuran (5.04 g), 12 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap A, 500 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield a brown oil (803 mg). No blockage of the delivery needle occurred. The ^{1}H and ^{13}C NMR spectrum show the product mixture to consist mainly of anthranilonitrile. By addition of a known amount of cyclohexane to the ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (459 mg, 45%). The water trap was observed to contain an appreciable amount of organic material and so was extracted with dichloromethane and evaporated to give a brown solid (405 mg). By addition of a known amount of cyclohexane to this ^{1}H NMR sample, the mixture was found to contain anthranilonitrile (270 mg, 27%). Total yield of anthranilonitrile is 72%. The extra weight apparently produced from this reaction is surprising, especially as the NMR spectra show no discrete signals to account for this. It is possible that some polymerisation of solvent had taken place, resulting in this extra weight, and was filtered out in the preparation of the NMR samples.

Flow pyrolysis of methyl benzoate over porcelain saddles at 700 °C. To investigate what effect the absence of the *ortho* substituent has upon the ester to nitrile transformation under ammonia, methyl benzoate was pyrolysed under conditions known to convert methyl anthranilate to anthranilonitrile. (497 mg, 3.65×10^{-3} mol), neat, 1 cm^3 h^{-1}, ammonia (300 cm^3 min^{-1}), porcelain saddles, trap A, 700 °C. The crude products were collected into dichloromethane and concentrated under reduced pressure to yield an orange oil (198 mg). The mixture was identified as containing only two components, benzonitrile and unreacted starting material (2.8:1), the abundance of which were calculated from the respective integrals in the ^{1}H NMR spectrum: benzonitrile; δ_H 7.61-7.19 (5 H, m); δ_C 132.59, 131.95, 128.92, 118.66 (q) and 112.21 (q); methyl benzoate; δ_H 7.98-7.94 (2 H, m), 7.61-7.19 (3 H, m) and 3.84 (3 H, s); δ_C 166.92 (q), 132.73, 129.93 (q), 129.35, 128.16 and 51.90. The ^{1}H and ^{13}C NMR spectra concur with those in the literature.[103]

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