New Pyrolytic Routes to *ortho*-Condensed Ring Systems

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Ph.D. Thesis

The University of Edinburgh

2007

Odi et amo
Quare id faciam, fortasse requiris
Nescio, sed fieri et sentio et excrucior

Catullus

Acknowledgements

Firstly I would like to thank Prof. Hamish McNab for his calming conversations and guidance in the art of chemistry.

For technical support and sympathetic chats Mr John Millar and Mr Alan Taylor.

The members of the McNab group have been the source of much entertainment over the past three years and some of them have even been helpful. Notable thanks go to Dr Rich Tyas for being The King of Chromatography and Dr Stuart Wharton for being The God of NMR. Above all I would like to thank Dr Karen Jonhston for redressing the gender balance, saving my thesis *via* the Royal Mail on several occassions and generally being optimistic on my behalf.

My parents and brother have supported me in all my adventures especially during my time at University and I know that finishing this thesis is as much of a relief to them as it is to me. Having Keith in the lab upstairs was always helpful (especially when I thought I'd broken the NMR machine or needed dry THF) and as always he looked after his wee sister. To thank them enough for all of their love and support is impossible.

My partner Tom has dealt with all of the stressed midnight phone calls for nearly three years with great valour and patience.

Finally, never has anyone consumed so much caffeine in the cause of my sanity than Craig McGowan. I can never thank him enough for being my best friend, my computer support and never letting me fall.

P.S. I should thank the girls and leaders of The 93rd City of Edinburgh Guide Unit for keeping life in perspective and ensuring that I was reminded on a weekly basis that none of this really matters.

Lectures Attended

Organic Synthesis Seminars (3 years)

Organic Synthesis Colloquia (3 years)

School Colloquia (3 years)

Researchers in Residence (Balwearie High School, 4 days)

Royal Society of Chemistry, Perkin Division (2003 and 2004)

Postgraduate Synthesis Symposium (3 years)

SCI Postgraduate Symposium (2003)

Mass Spectrometry – Dr P. Barran (2003)

History of The Aldrich Chemical Company – Dr A. Bader (2003, 2004)

International Congress on Heterocyclic Chemistry - Oral Presentation (2004)

International Symposium on Reactive Intermediates and Unusual Molecules – Poster (2004)

EastChem Thesis Writing Workshop (2005)

Organic Synthesis Firbush Seminars (2005 – Poster, 2006 – Oral Contribution; 2nd prize)

Royal Society of Chemistry – Transition Metals in Biology and Catalysis (2006)

Supramolecular Symposium (2006)

Abstract

In 2000 it was discovered that Flash Vacuum Pyrolysis (FVP) of methyl biphenyl-2-acrylate at 950 °C produced phenanthrene in good yield. Investigation of this reaction showed that the first step of the reaction was an electrocyclisation followed by a [1,5]-hydrogen shift. However the mechanism of the oxidative loss of the ester group to form phenanthrene was unknown. Pyrolysis of a number of model compounds and analysis of their products shows that ester groups in benzylic positions are prone to radical cleavage at high temperatures. This suggests that the phenanthrene is produced *via* radical cleavage of the ester group followed by loss of a hydrogen atom.

In order to demonstrate the generality of this reaction a variety of methyl biphenyl-2-acrylate precursors, substituted in the 2'-, 3'- or 4'-positions, were synthesised using a Suzuki coupling reaction between 2-formylphenylboronic acid and the appropriate aryl halide, followed by Wittig olefination. These precursors were then pyrolysed to produce 3-cyano, 3-methyl and 3-chloro substituted phenanthrenes. The synthesis of 1-cyanophenanthrene was also successful but 2-cyanophenanthrene and 4-cyanophenanthrene were produced as an equal mixture. This route was also successful in producing naphthothiophenes and naphthofurans from appropriate heteroaryl-substituted precursors.

This methodology was expanded into the synthesis of several four-ring systems. Due to the known toxicity of such compounds a nitrogen atom was included within the skeleton as this is known to reduce toxicity. This was done by using 4-chloroquinoline-3-carbaldehyde as a starting material for the Suzuki coupling reactions as this included both a nitrogen atom in the final structure and the aldehyde functionality required for the Wittig olefination. 10-Cyanobenzophenanthridine was synthesised in this way to demonstrate that it is possible to produce substituted four-ring systems. By coupling 4-chloroquinoline-3-carbaldehyde with thiophene- and furan-boronic acids followed by Wittig olefination and pyrolysis it was possible to produce two thienylphenathridines and two furanylphenanthridines.

By reacting 2,5-dibromothiophene and two equivalents of 2-formylphenylboronic acid followed by a double Wittig olefination and pyrolysis it was possible to synthesise dinaphtho[1,2-*b*-2',1']thiophene. This is the first example of a double cyclisation of this type onto a single central ring.

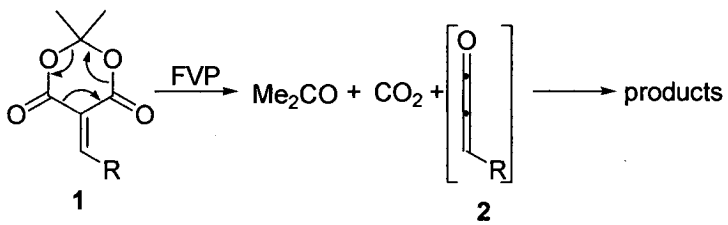
Four benzo[5]heterohelicenes were synthesised *via* a Suzuki coupling reaction of both dibenzothiopheneboronic acid and dibenzothiopheneboronic acid with both 1-bromonaphthalene-2-carbaldehyde and 4-chloroquinoline-3-carbaldehyde followed by Wittig olefination and pyrolysis. 1-Aza[5]helicene was also synthesised by a similar strategy, involving Suzuki coupling of quinoline-8-boronic acid and 1-bromonaphthalene-2-carbaldehyde followed by Wittig olefination and pyrolysis at 950 °C under FVP conditions. Using NMR spectroscopy it was possible to observe the effect of titrating aza[5]helicene with trifluoroacetic acid on the ^{1}H NMR spectrum and to show that the nitrogen within the bay region of the helicene could be protonated. These compounds possess the unusual structural feature of having a heteroatom located within the helical cavity.

It was possible to condense the 2-aryl and 2-heteroarylbenzaldehydes synthetic intermediates, with *O*-methylhydroxylamine hydrochloride to produce oxime ethers which were subjected to FVP at 700 °C to give 5-azaphenanthrenes and their heterocyclic analogues *via* iminyl radical intermediates. Using this route, eight novel compounds were synthesised. Pyrolysis of 2-(isoquinolin-4-yl)-benzaldehyde *O*-methyl oxime produced two isomeric products which provides further evidence that the cyclisation mechanism of this reaction goes *via* a spirodienyl intermediate.

1 Introduction to Project

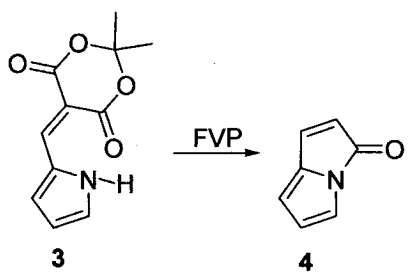
1.1 Background

It is known that flash vacuum pyrolysis (FVP) is a highly useful technique for intramolecular reactions of many types. One of the most documented FVP reactions is that of Meldrum's acid derivatives **1** which upon pyrolysis generally react to produce acetone, carbon dioxide and a methyleneketene intermediate **2** which can then rearrange to produce unsaturated ketenes which collapse to form a variety of products. [1]



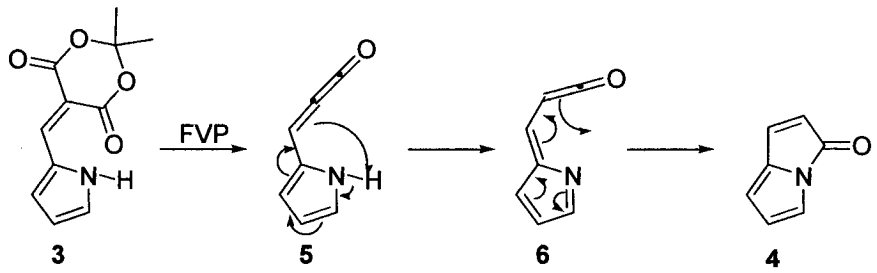
Scheme 1

In the course of a previous project it was discovered that pyrolysis of the Meldrum's acid derivative **3** at 600 °C produced the pyrrolizin-3-one **4** in good yield.[2]



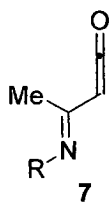
Scheme 2

The likely mechanism of this reaction involves the production of a methyleneketene **5** followed by a [1,7]-hydrogen shift of the pyrrole NH to generate a pyrrol-2-ylmethylideneketene **6** which forms the pyrrolizinone **4** by an electrocyclic ring closure.

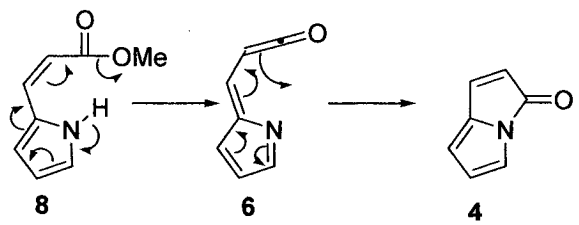


Scheme 3

This mechanism demonstrated that the key intermediate for the formation of the pyrrolizinone was **6** and that it might be possible to generate **6** from another starting material. This would be useful as there are some volatility problems associated with the Meldrum's acid derivative and would also allow a greater variation of the subsitution patterns in the final products. It had been shown by Chuche *et al.*[3] that iminoketenes **7** which are structurally similar to **6** could be generated by the thermal elimination of alcohols from enamino esters.

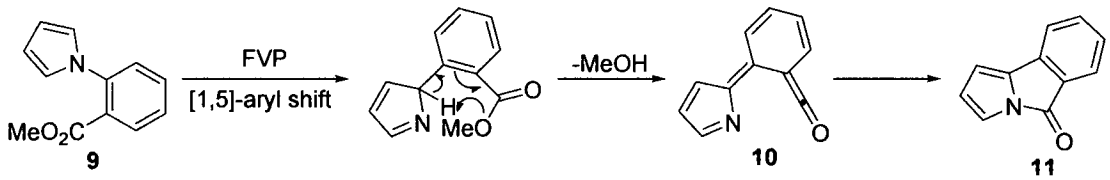


This methodology was used to synthesise **4** from a methyl acrylate starting material **8** *via* **6**. Pyrolysis of **8** at 850 °C produced **4** in 87% yield.



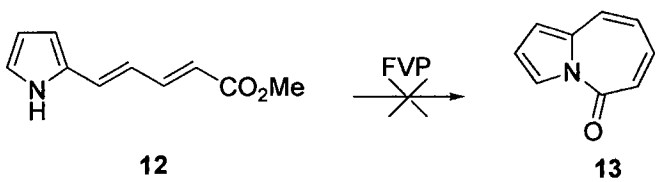
Scheme 4

Previous work had shown that 1-subsituted pyrroles underwent thermal rearrangement to 2- and 3-substituted pyrroles under FVP conditions. Combining this with the reaction in **Scheme 4** produced a novel pyrolytic cascade process which could be used to produce pyrrolo[2,1-*a*]isoindol-5-one **9** by the pyrolysis of **9**.



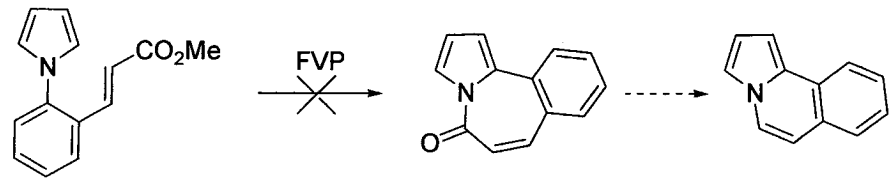
Scheme 5

The success of this route for the synthesis of pyrrolizinones led to the idea that the addition of an extra double bond into the FVP precursor **12** might generate a larger ring in the cyclisation step to produce a lactam **13**. In practise, analysis of the crude pyrolysate of **12** showed that **13** had not been produced.



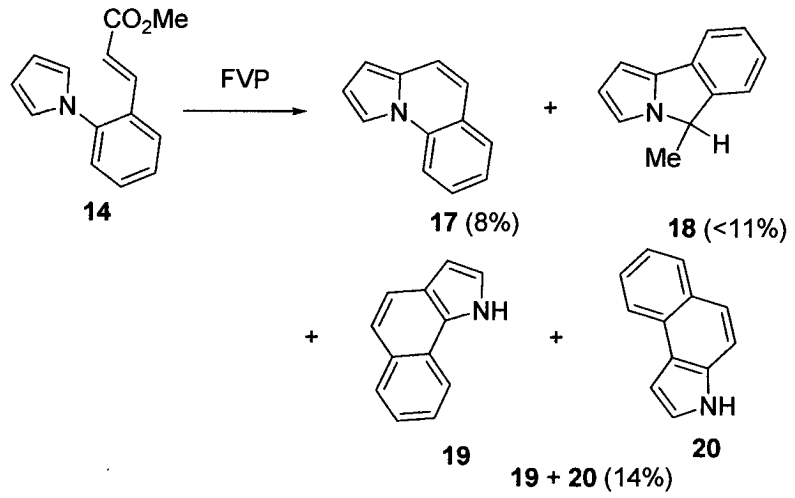
Scheme 6

This reaction was thought to be unsuccessful due to the number of rotational degrees of freedom of **12** at high pyrolysis temperatures. In an effort to decrease the number of rotational degrees of freedom a fused benzene ring was incorporated. The benzene ring was attached to the pyrrole nitrogen **14** as previous work[4] had shown that this group could migrate under FVP conditions to the 2-position before the cyclisation takes place thus forming **15** or **16** which is the potential decarbonylation product.[5]



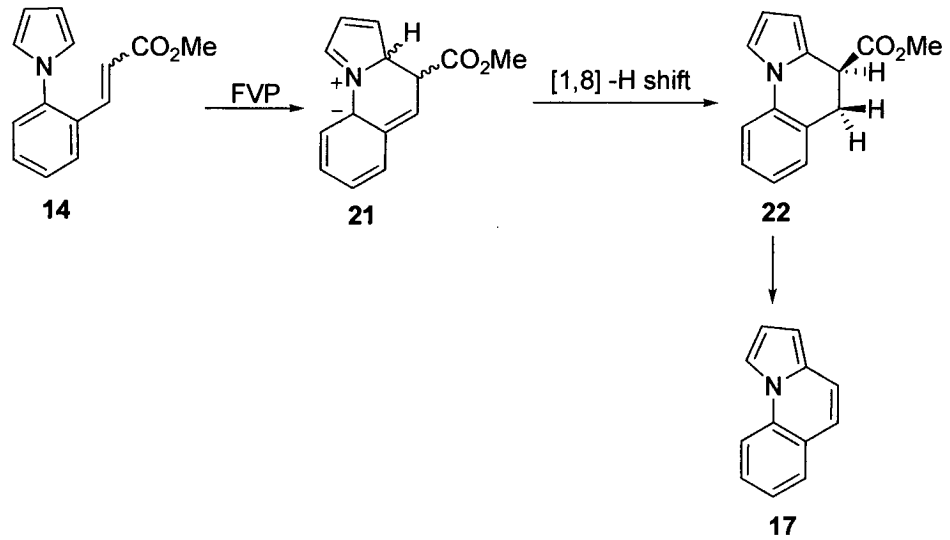
Scheme 7

When methyl 2-(pyrrol-1-yl)cinnamate **14** was pyrolysed at 850 °C four different products were isolated in low yields but none were the expected lactone **15** or the decarbonylation product **16**.



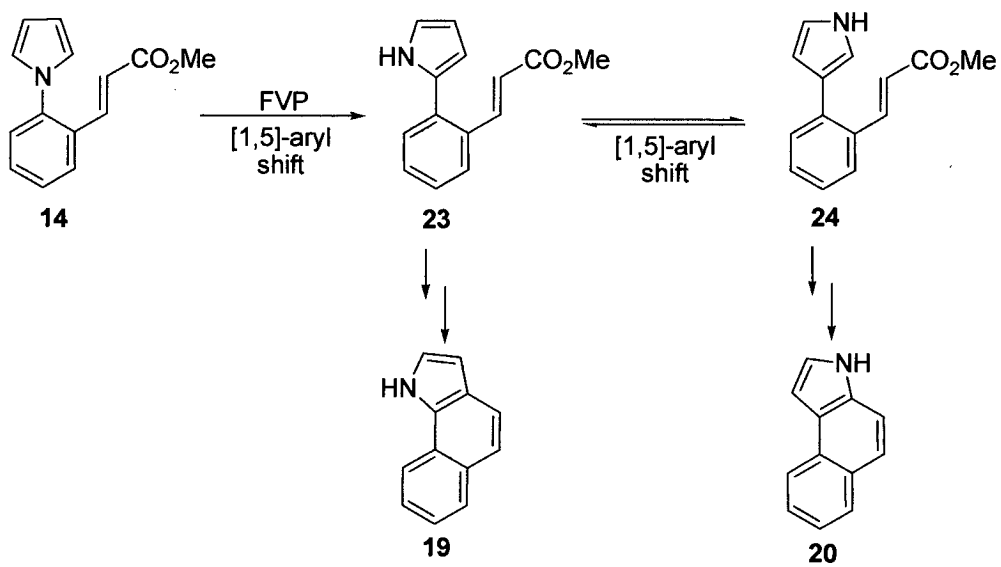
Scheme 8

The structure of the "major" product **17** (8%) suggests that under FVP conditions an unprecedented cyclisation had occurred prior to the sigmatropic shift of the aryl group which additionally resulted in the loss of the ester group. The most likely mechanism for this reaction is an electrocyclisation of **14** to produce a dipolar species **21** which then undergoes a [1,8]-hydrogen shift to form the dihydro compound **22**. The final step of the mechanism which produced the final fully aromatic system **17** is a novel oxidative elimination involving the loss of the ester group possibly *via* the concerted elimination of methanol and carbon monoxide.



Scheme 9

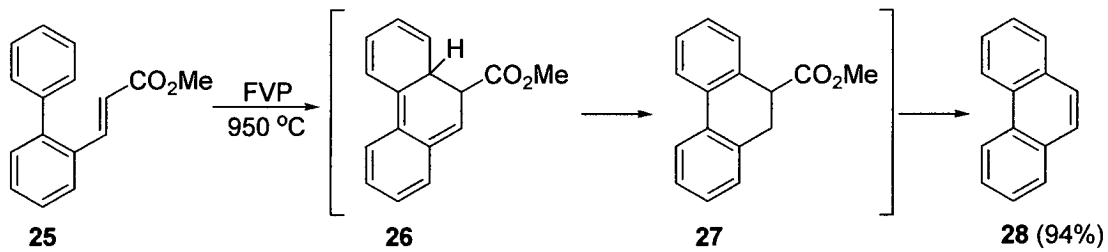
Pyrolysis of **17** showed that **19** and **20** were not formed by thermal rearrangements of the main product **17**. This suggests that they might be produced by the electrocyclisation and oxidative elimination of **23** and **24** which were generated by [1,5]-shift(s) of the aryl group.



Scheme 10

1.2 Phenanthrenes

The pyrolysis of methyl 2-(pyrrol-1-yl)cinnamate **14** gave four identifiable products, *via* competing pathways, three of which seemed to be the result of electrocyclisation followed by oxidative elimination of the ester group to yield the fully aromatic products. As formation of **21** competes with sigmatropic migration during pyrolysis it was thought that replacement of the pyrrole ring with a benzene ring would eliminate this possibility therefore allow a simpler study of this new reaction. This led to the synthesis and pyrolysis of the structurally simpler biphenylacrylic acid methyl ester **25**.



25 **26** **27** **28** (94%)

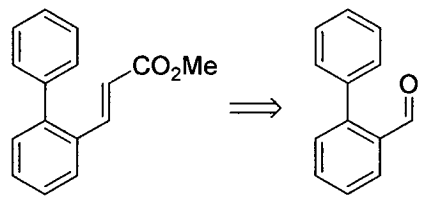
Scheme 11

Pyrolysis of **25** at 950 °C produced phenanthrene **28** in 94% yield.[6] The pyrolysis was repeated at 900 °C and 850 °C; the proton NMR spectra of these crude pyrolysates showed the presence of methyl 9,10-dihydrophenanthrene-9-carboxylate **27** as well as small amounts of unreacted starting material **25**. The presence of the intermediate **27** was good evidence that the first step of this reaction was, as in the previous case, an electrocyclisation to form **26** followed by a hydrogen shift to form **27** although at this point the mechanism of the loss of the ester group to yield the fully aromatic product was unknown.

As this new reaction was a good route to phenanthrene it was thought that it could be used to produce a variety of three-ring systems *via* FVP.

1.2.1 Synthesis of FVP Precursors

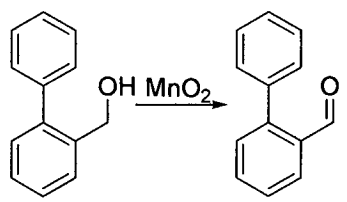
The methyl acrylate FVP precursors required for the synthesis of these three-ring systems could all be synthesised from aldehyde derivatives *via* a Wittig reaction.



25 **29**

Scheme 12

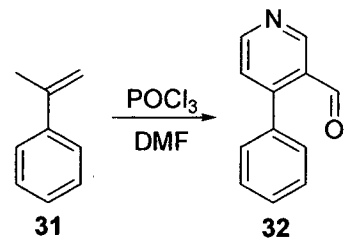
The aldehydes could be made in three different ways. The precursor **25** had been easily synthesised from the aldehyde **29** *via* a Wittig reaction. Oxidation with manganese dioxide of alcohol **30** was used to produce **29**.



30 **29**

Scheme 13

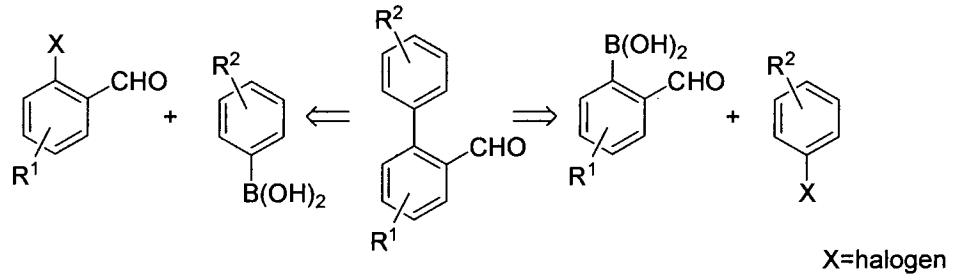
Some aldehyde precursors could be made by a Vilsmeier reaction using 2-arylprop-2-ene **31** and the normal Vilsmeier reagent to produce 4-phenylpyridine-3-carbaldehyde **32**.[7]



31 32

Scheme 14

These methods of synthesising the required aldehydes (**Scheme 13** and **Scheme 14**) are both only suitable for specific targets and a more generic route was required. The use of Suzuki reactions[8] to form this type of biphenyl system is well documented. For this route to be effective all that is required is either a halide or boronic acid with an *ortho*-aldehyde functionality.

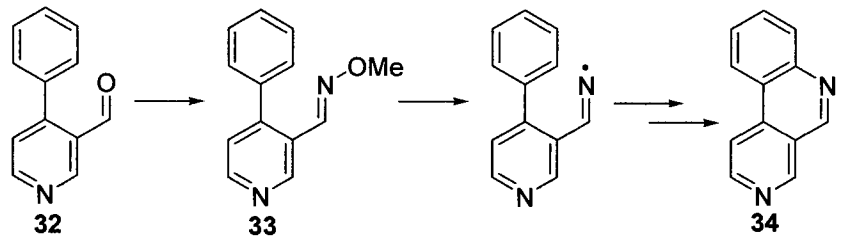


Scheme 15

This thesis will report the synthesis of a variety of aldehydes using the route in **Scheme 15** which will then be used to produce a variety of multiple-ring systems.

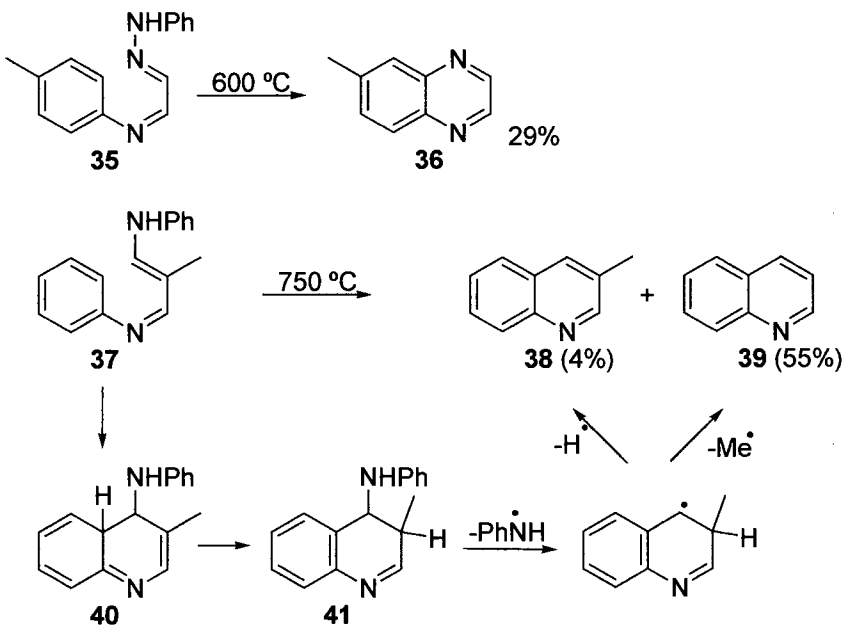
1.3 Iminyl Radicals

Using the proposed synthetic route (**Scheme 16**) it was possible to use the aldehydes **32** to produce oxime ethers **33** which were known to be iminyl radical precursors under FVP conditions. Following this route it would be possible to synthesise both a variety of condensed ring systems using the route of **Scheme 11** and their aza-analogues **34** using the iminyl route.[7]



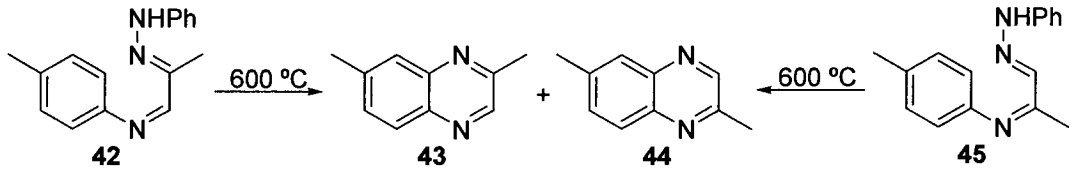
Scheme 16

In 1980 it was recorded by McNab[9] that pyrolysis of **35** produced the cyclised product **36**. At the time the proposed mechanism for this reaction involved an iminyl radical which explained the presence of the minor products in the crude pyrolysate. Under similar conditions pyrolysis of **37** produced **38** and **39** which suggested that the pyrolysis of **37** takes place *via* an electrocyclisation to form **40** followed by a hydrogen shift to produce a benzenoid intermediate **41**. It was shown that both arylamino and methyl radicals were present in the gas phase suggesting a stepwise free radical mechanism for the final aromatisation step in the formation of both **38** and **39**.[10]

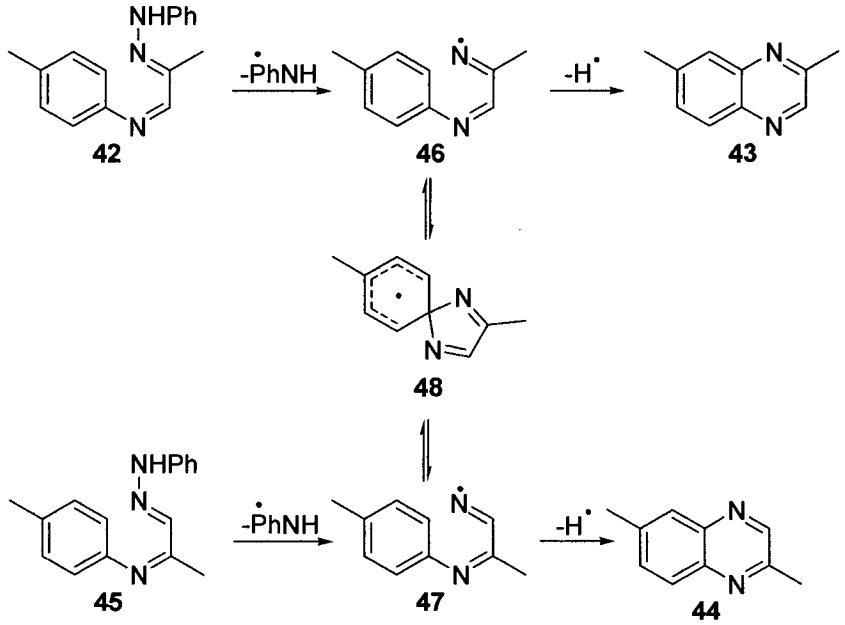


Scheme 17

A further complication was discovered in the iminyl cyclisation, when it was found that pyrolysis of disubstituted compounds like **42** produced a mixture of products including **43** (14%) and **44** (6%).[11] He then showed that **45**, an isomer of **42** also produced **43** (7%) and **44** (13%) under the same FVP conditions. [12, 13]



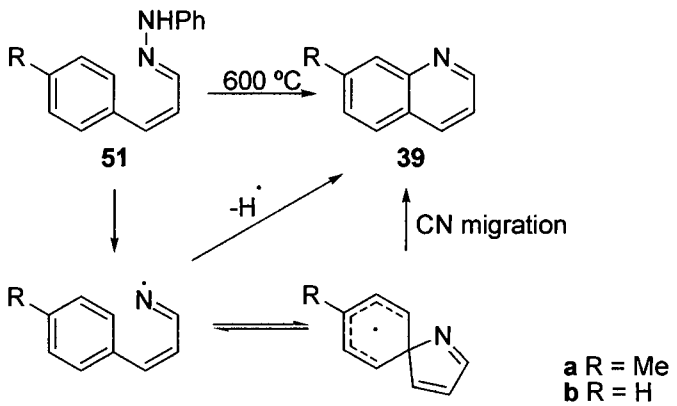
Scheme 18



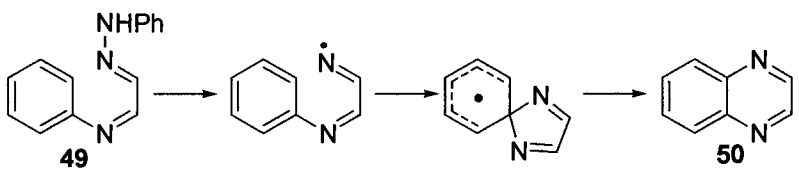
Scheme 19

As the pyrolysis of **42** produced two products, which can also be synthesised by the pyrolysis of **45**, this suggested that the iminyl radicals **46** and **47** undergoes *ipso* attack to produce a spirodienyl intermediate **48** rather than directly attacking the *ortho*-position (**Scheme 19**). Surprisingly, in view of the isomeric mixtures obtained when **42** and **45** are pyrolysed, pyrolysis of **51a** produced a single product **39a**. This could be formed by

the electrocyclisation mechanism or by direct cyclisation of the iminyl radical or by formation of the spirodienyl intermediate followed by selective migration of the C-N bond with no migration of the C-C bond. Since the methyl substituents are unlikely to influence the course of the reaction the parent hydrazone **49** is likely to cyclise to quinoxaline **50** by a spirodienyl mechanism (**Scheme 20**).



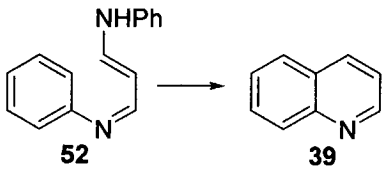
Scheme 20



Scheme 21

In much later work, McNab *et al.*[13] reported that it was possible to use the position and shape of the sigmoid curves on the temperature-conversion plots which had been used to determine the optimum furnace temperature for a reaction to provide mechanistic information about the reaction in question. Comparison of the temperature-conversion plots for the pyrolyses of the hydrazones **49** and **51b** showed that both started to react at a furnace temperature lower than 500 °C and both have similar, steep curves, **Figure 1**. It was known that **49** reacted *via* a spirodienyl intermediate and the similarity of the

curves suggests that the pyrolysis of **51b** must react in a similar way. However it is still not clear whether the iminyl derived from **51b** cyclises to provide **39a** or does so *via* a spirodienyl intermediate with exclusive C-N bond migration.



Scheme 22

The third curve refers to the pyrolysis of **52** which was thought to produce **39** by an electrocyclisation reaction as in **Scheme 17**. The plot shows that **52** is stable at above 600 °C and a much larger temperature range is required for complete conversion to products. This shows that the pyrolysis of **52** does not go by the same mechanism as both **42** and **51**.

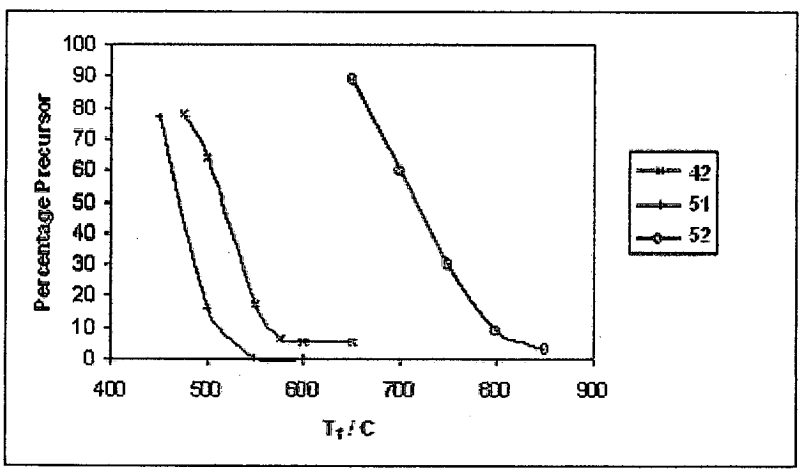


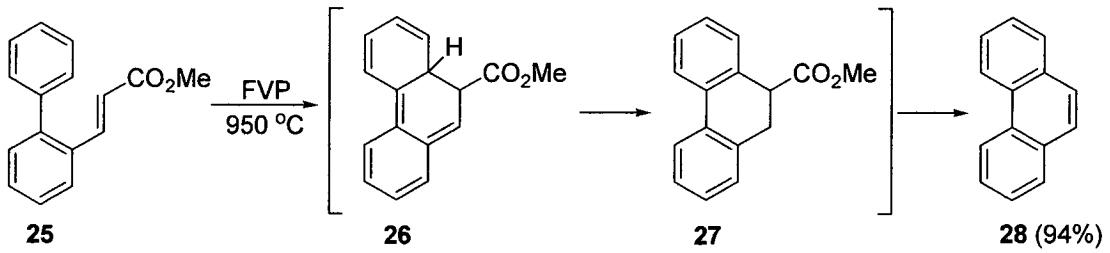
Figure 1: Correlation of percentage of unreacted precursor against furnace temperature

Synthesis of nitrogen containing three-ring systems such as **34** may divulge more information on the mechanism of these cyclisation reaction and the proposed spirodienyl intermediates and will also provide aza-analogues of the multiple-ring systems synthesised using the route in **Scheme 11**.

2 Mechanistic Studies

2.1 Introduction

The novel cyclisation of **25** was shown by Tyas[6] to be a useful route to phenanthrene **28** and it was thought that similar methyl acrylates would also cyclise when pyrolysed to produce other three-ring systems, including heterocyclic analogues.



25 **26** **27** **28** (94%)

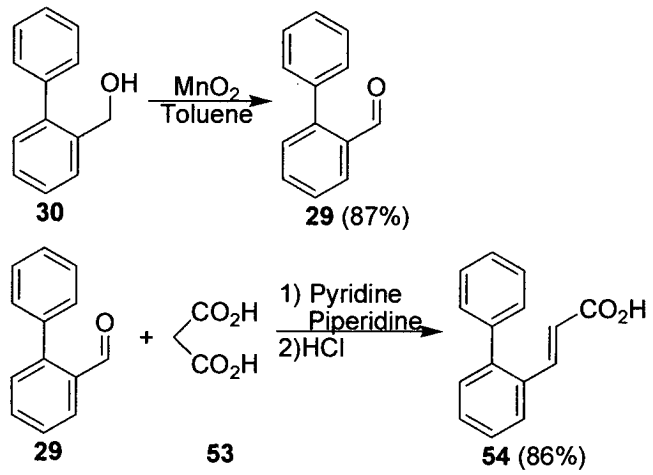
Scheme 11

A key step of this process is the final aromatisation from **27** to **28** involving formal loss of HCO_2Me. In order to investigate the importance of the leaving group on the scope and success of the reaction a variety of precursors with different leaving groups was synthesised and their effect on the reaction was assessed.

2.2 Variation of Leaving Group

2.2.1 Preparation of Precursors

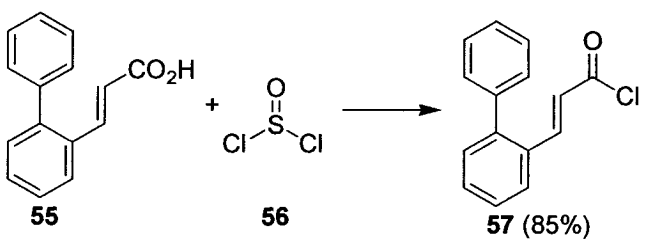
It is important to control the reaction of the leaving group. If a labile leaving group is used then it might be lost before the cyclisation can occur. Loss of the leaving group prior to cyclisation would produce the acetylene which would react as reported by Brown *et al.*[14] which will be discussed later. If a poor leaving group is used then the reaction will not work at all. Therefore at this point carboxylic acid derivatives were chosen as they were known to be lost under FVP conditions. The aldehyde **29** was then used as the starting material to produce three other precursors with different potential leaving groups.



Scheme 23

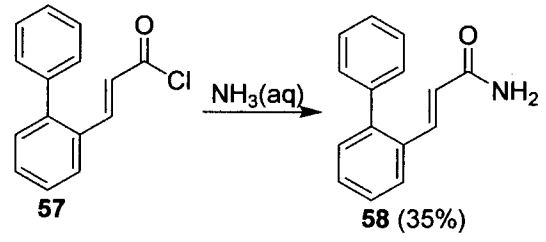
The biphenylcarbaldehyde **29** skeleton was synthesised from biphenyl-2-methanol **30** using activated manganese oxide (**Scheme 23**) and was characterised by the appearance of a sharp singlet at 10.16 ppm in the ^{1}H NMR spectrum. The carboxylic acid **54** was produced *via* a Doebner condensation from biphenylcarbaldehyde **29** and malonic acid **53** in pyridine with a few drops of piperidine (**Scheme 23**). In the ^{1}H NMR spectrum of **54** the singlet of the aldehyde had completely disappeared and a characteristic doublet due to the alkene at 6.41 ppm was observed.

The acid chloride 57 was synthesised in the normal way by reacting 2-phenylcinnamic acid **55** with thionyl chloride **56** to produce 2-phenylcinnamoyl chloride **57** (**Scheme 24**).



Scheme 24

The amide **58** was also synthesised in the normal way by reacting 2-phenylcinnamoyl chloride **57** with an excess of aqueous ammonia (**Scheme 25**).



57 **58** (35%)

Scheme 25

2.2.2 Pyrolyses

The optimum temperature for the reaction is the furnace temperature required for the pyrolysate to contain only the desired product with no intermediates or by-products present. The optimum temperature for the pyrolysis of the acrylate **25** had been shown by Tipping to be 950 °C **Figure 1**.[21] All of the precursors were pyrolysed at a range of temperatures to determine the optimum pyrolysis conditions for each leaving group to compare with the acrylate reaction. The composition of the pyrolysate was determined by analysis of the ^{1}H NMR spectra and the results used to produce a temperature profile of furnace temperature against percentage composition of pyrolysate. The characteristic peaks in the ^{1}H NMR spectra which were used to characterise the products of all of the pyrolyses in this section are shown in **Table 1**.

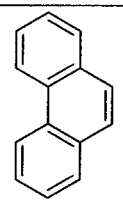
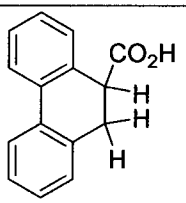
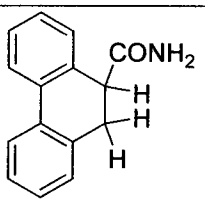
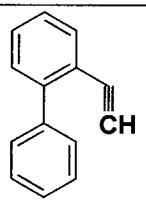
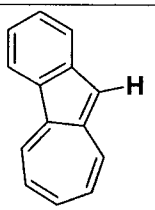
 **28**	8.75 (2H, d, *J* 8.1), 7.96 (2H, dd, *J* 1.3, 7.8) and 7.81 (2H, s)[15]
 **59**	3.23 (2H, m) and 3.84 (1H, t)[16]
 **60**	3.65 (1H, t, *J* 1.0, 6.0)[17]
 **61**	3.05 (1H, s)[14]
 **62**	6.84 (1H, d, *J* 8.5), 6.96 (1H, d, 8.3), 7.19 (1H, d, 8.5) and 7.23 (1H, s)[18]

Table 1: Characteristic peaks in ^{1}H NMR spectra of 28, 59, 60, 61 and 62

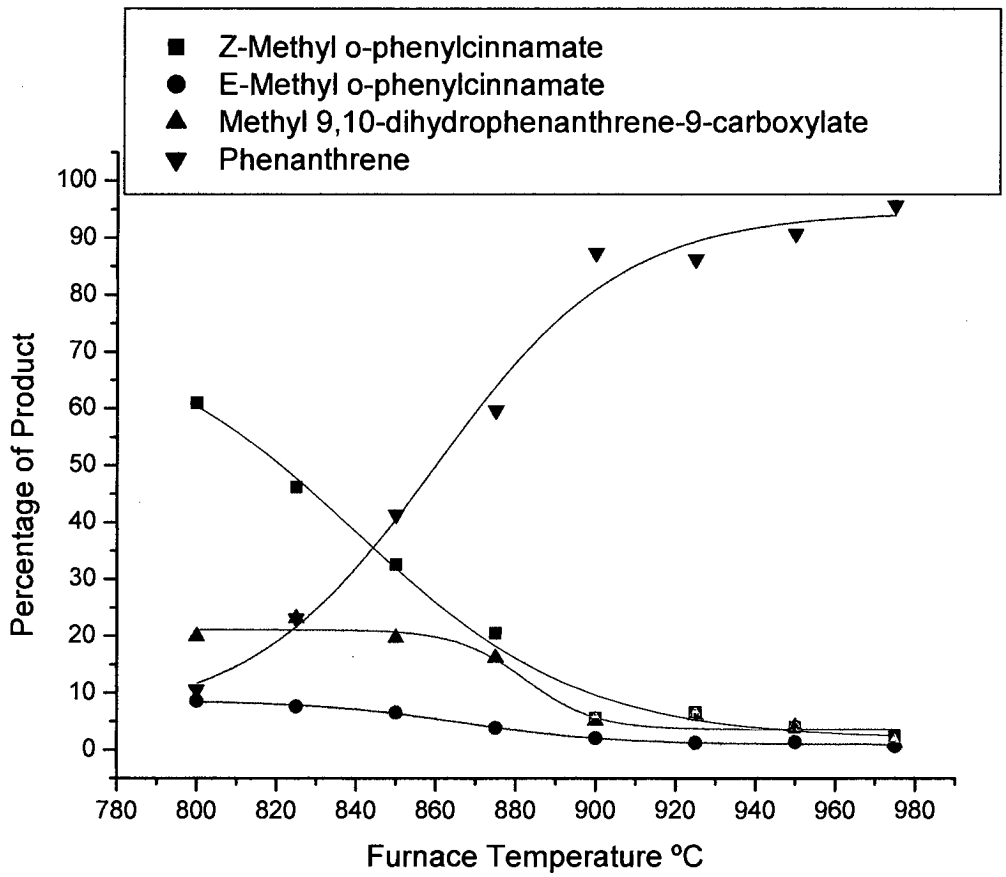
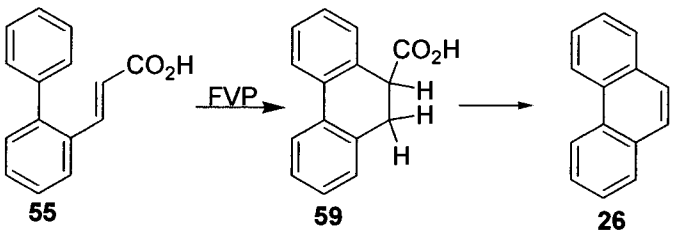


Figure 2: Correlation of percentage of product against furnace temperature plotted using Origin

Samples of 2-phenylcinnamic acid **55** were pyrolysed (**Scheme 26**) at temperatures between 750 °C and 950 °C **Figure 3**. The intermediate, 9,10-dihydrophenanthrene-9-carboxylic acid **59**, was shown to be present. As there was no evidence of any 9,10-dihydrophenanthrene intermediate this suggests that no thermal decarboxylation had occurred. The intermediate **59** was present at a low level at all temperatures up to 950 °C which suggests that the acrylate ester may be a better leaving group for this reaction than the corresponding acid.



Scheme 26

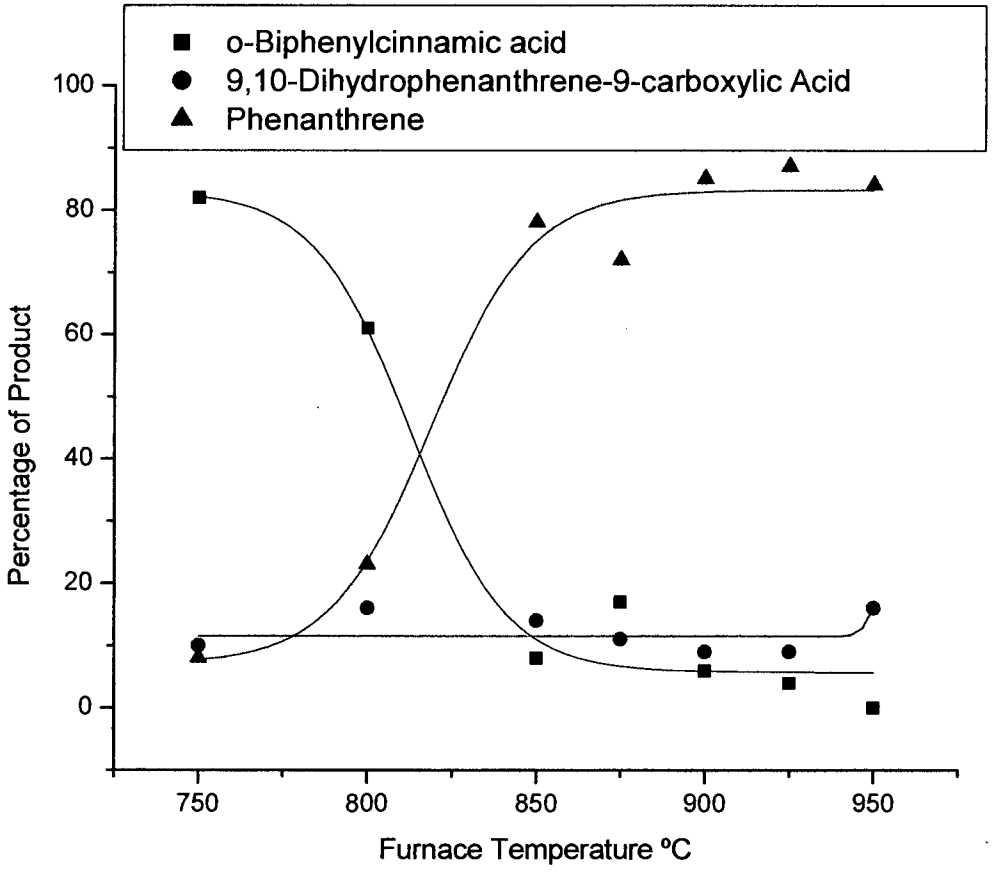


Figure 3: Correlation of percentage of product against furnace temperature plotted using Origin

Samples of 2-phenylcinnamamide **58** were also pyrolysed, (**Scheme 27**), at a range of temperatures from 650 °C to 950 °C (**Figure 4**). In this case the intermediate, 9,10-

dihydrophenanthrene-9-carboxamide **60** was only present in the pyrolysate at temperatures below 900 °C. This shows that the amide may be as good a leaving group as the acrylate but the synthesis is longer and as such there is no real advantage to producing the amide where the acrylate could be produced in less steps.

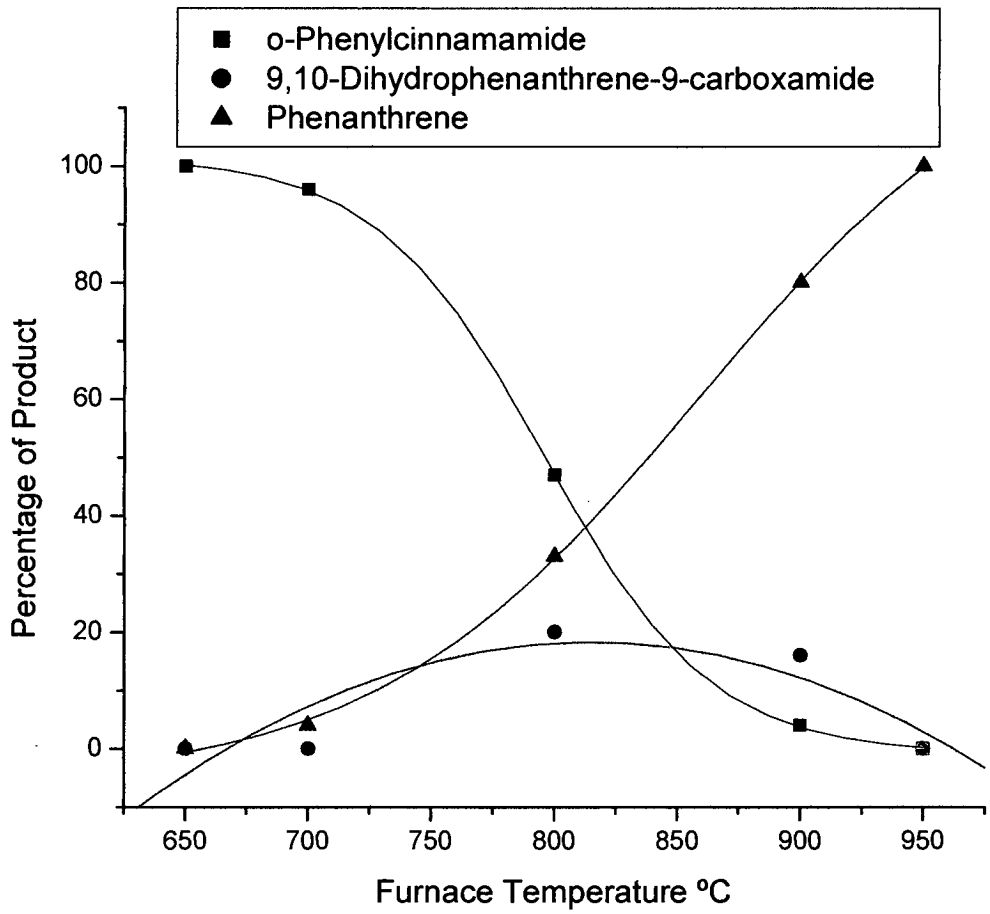
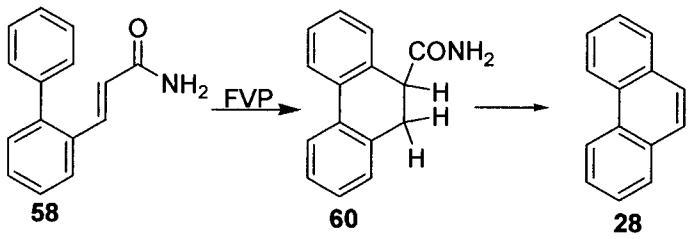
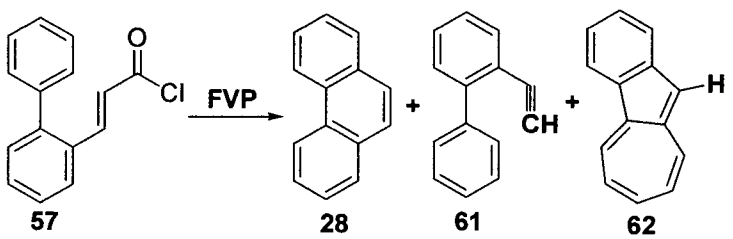


Figure 4: Correlation of percentage of product against furnace temperature plotted using Origin



Scheme 27

Finally samples of 2-phenylcinnamoyl chloride **57** were pyrolysed over a range of furnace temperatures (**Figure 5**). However the range of temperatures used was larger than that of previous examples as the starting material started to react at much lower temperatures (450 °C) and was completely consumed at *ca.* 600 °C. The pyrolysis products of the acid chloride were not as expected. At high temperatures (>900 °C) the pyrolysate was blue in colour which was unusual and at temperatures <900 °C it was green which is even more unexpected.



Scheme 28

By comparison with literature spectra it was determined that phenanthrene **28**, 2-ethynylbiphenyl **61** and benzo[*a*]azulene **62** were all present in the crude pyrolysate when the furnace temperature was between 550 °C and 900 °C (**Scheme 28**). The temperature profile, **Figure 5**, of this reaction shows that at low temperatures the pyrolysis of 2-phenylcinnamoyl chloride produces **61** as the major product with **28** and **62** being the minor products. At 700 °C the percentage of **61** in the pyrolysate reaches a maximum. At temperatures above 700 °C the percentage of **61** in the pyrolysate decreases and the percentage of **28** and **62** increase.

Therefore at high temperatures, 950 °C, the pyrolysate contains only phenanthrene **28** and benzo[*a*]azulene **62** which is why the pyrolysate is coloured as benzo[*a*]azulene is an intensely blue compound. At lower temperatures the pyrolysate was green as it was a mixture of the blue benzo[*a*]azulene **62** and the yellow 2-ethynylbiphenyl **61**.

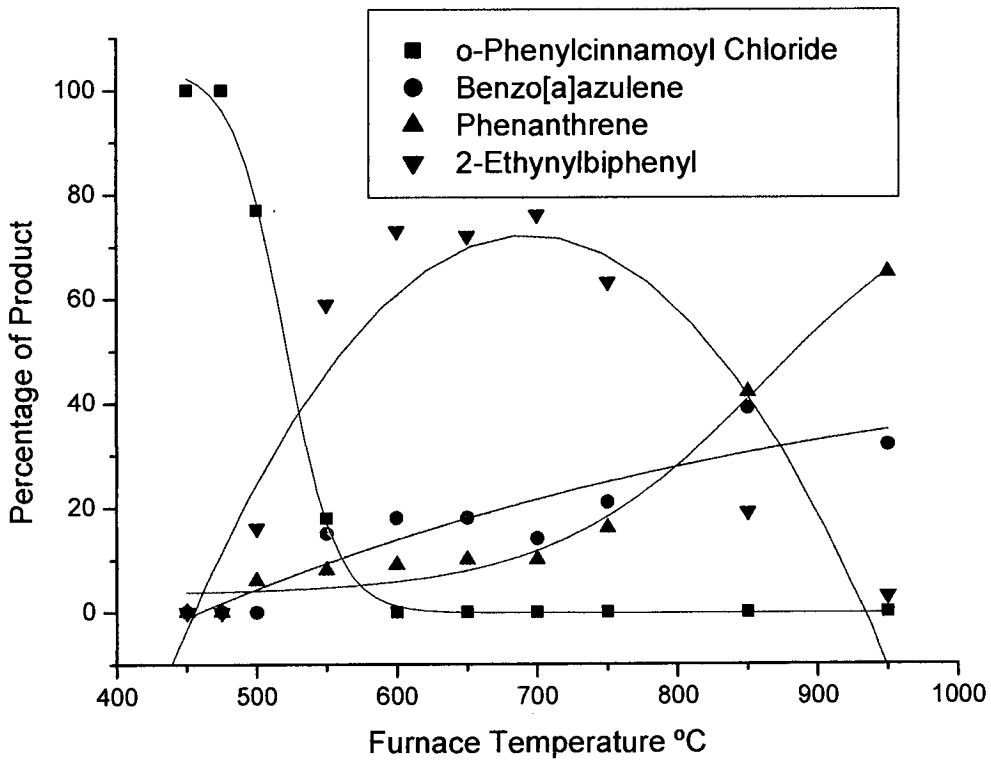
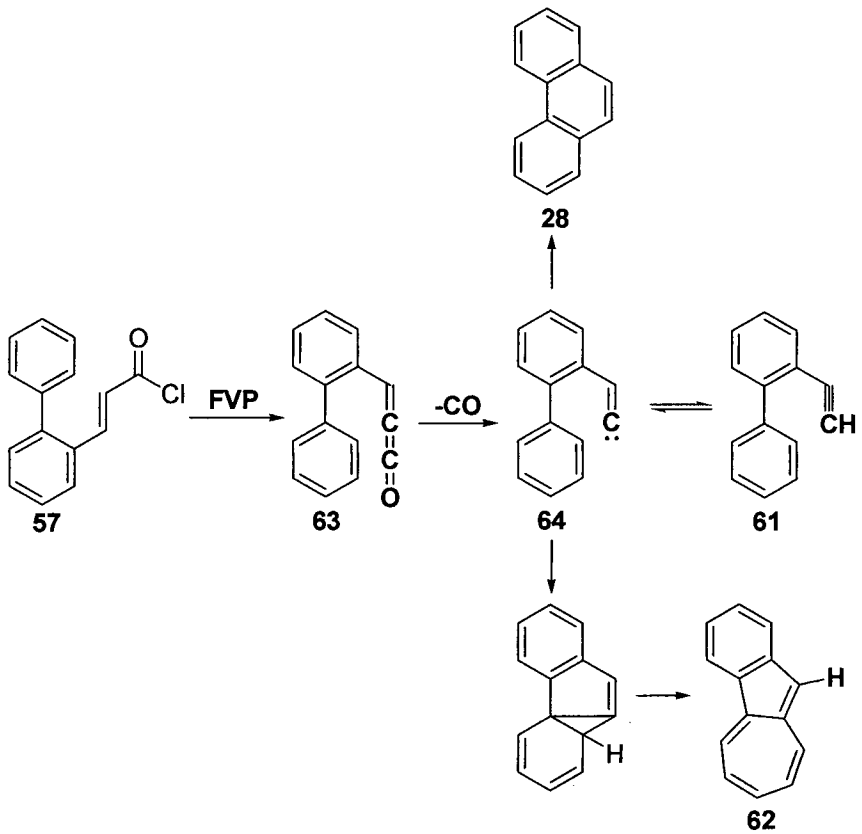


Figure 5: Correlation of percentage of product against furnace temperature plotted using Origin

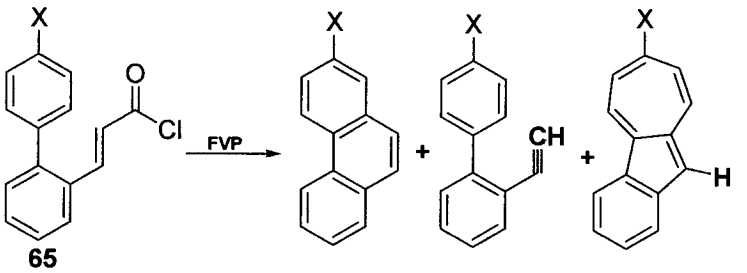
Comparison of these results with the work of Brown *et al.*[14] suggests that the pyrolysis of the acid chloride **57** is an alternative route to the methyleneketene **63** which is known to lose carbon monoxide to form the carbene **64**. In the work by Brown pyrolysis of 5-(biphenyl-2'-ylmethylene)-2,2-dimethyl-1,3-dioxan-4,6-one produced the carbene which reacts to produce **28**, **61** and **62**. Consideration of the shapes of the curves in **Figure 5** show that as the amount of acetylene **61** formed decreases the amount of both **18** and **62**

produced increases suggesting that at higher temperatures the equilibrium between **64** and **61** lies to the left resulting in the formation of less **61** and consequently the production of more **28** and **62**.



Scheme 29

This work was extended in a final year project[19] to include the pyrolyses of three different substituted acid chlorides.



Scheme 30

The pyrolyses of **65** at a variety of temperatures all produced substituted phenanthrenes, acetylenes and azulenes. The optimum temperature for the production of the phenanthrene was 850 °C which is slightly lower than the unsubsituted acid chloride. It was noted that increasing the electron donating capacity of the substituent increased the amount of phenanthrene produced and decreased the amount of acetylene seen in the crude pyrolysate. This suggested that altering the character of the substituent had an effect on the equilibrium between the methylenecarbene and the acetylene.

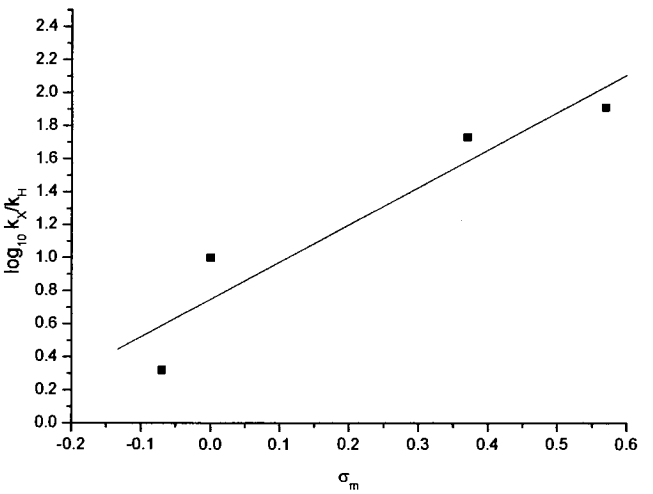


Figure 6: Hammett plot for acetylene plotted using Origin

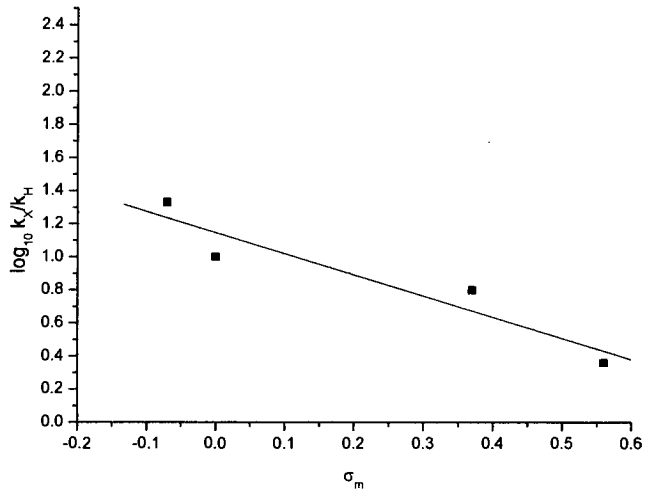


Figure 7: Hammett plot for phenanthrene plotted using Origin

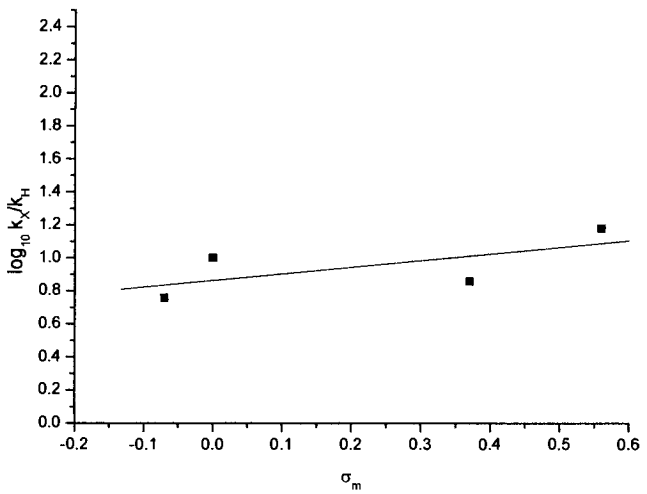


Figure 8: Hammett plot for azulene plotted using Origin

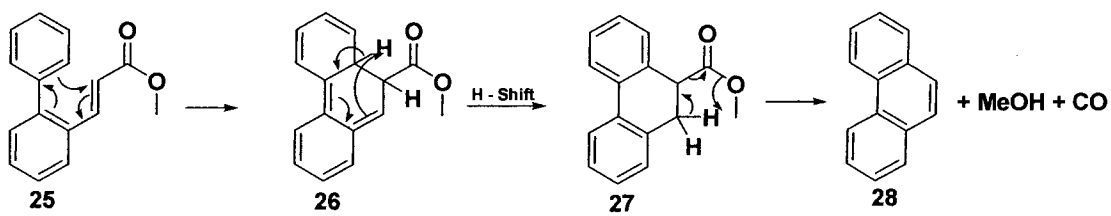
The Hammett plots of the results, **Figures 6 – 8**, showed that increasing the electron density at the *meta*-position increases the cyclisation of the electrophilic

methylenecarbene into the C-H bond of the phenyl ring at the position *meta* to the substituent.

Returning to the formation of phenanthrenes from 2-phenylcinnamic acid derivatives, overall these results have shown that acrylate was the best leaving group for this reaction as it is easy to synthesise and the desired product is obtained without any side-products. The acid group is unsuitable as the intermediate dihydro-compound could not be fully converted at a reasonable temperature. Although the amide produced the desired product there was no advantage in using the longer synthesis to produce the same results as the acrylate. The acid chloride, although not suitable for producing phenanthrenes, has the potential to be a new methylenecarbene generator, which may be applied to the synthesis of a variety of other compounds.[19]

2.3 Mechanism

When the reaction had first been discovered the mechanism was thought to involve the electrocyclisation of **25** to produce the intermediate **26** which then underwent a hydrogen shift to **27**, identified from the ^{1}H NMR data, which then formed **28** (**Scheme 31**). As there was a distinct pressure increase during the pyrolysis it was thought that a concerted elimination mechanism might produce carbon monoxide and methanol. The former is not condensed in liquid nitrogen at 0.01 Torr.



Scheme 31

This mechanism could therefore be supported by detection of methanol in the pyrolysate. However, being volatile the small amount of methanol produced would normally evaporate upon warming to room temperature. Therefore the normal pyrolysis

apparatus (see **Section 7.1**) had to be altered to provide a way of trapping the methanol (**Figure 9**). This was done by adding a second trap internally coated with acetyl chloride to trap any methanol produced as methyl acetate. Trap 1 was cooled in ice, to trap less volatile products and trap 2 was cooled in liquid nitrogen to trap the methanol as methyl acetate. One equivalent of acetyl chloride was evaporated into trap 2 prior to the pyrolysis and another equivalent after the pyrolysis. This ensured that there was an excess of acetyl chloride so that all of the methanol in trap 2 would react.

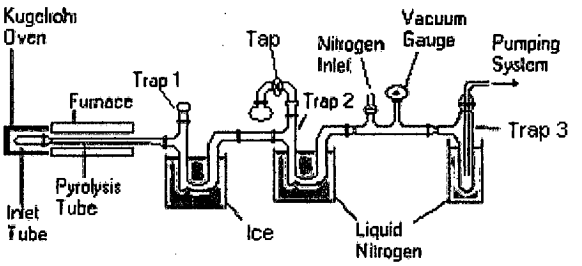
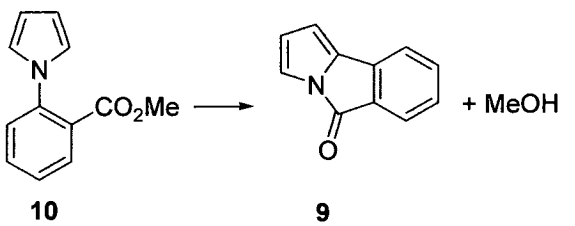


Figure 9

In order to test the system a reaction known to produce methanol was first used. As it was already known that upon pyrolysis at 925 °C *N*-(2-methoxycarbonylphenyl)pyrrole **10** produced **9** (**Scheme 32**)[20] this reaction was used to determine a method of proving the loss of methanol during pyrolysis.



10 **9**

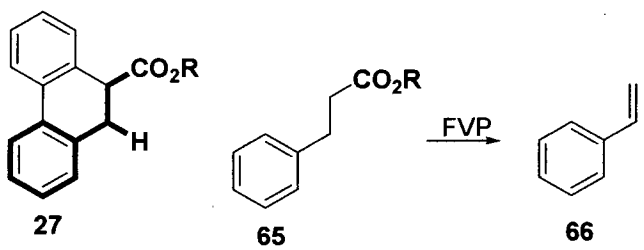
Scheme 32

After the pyrolysis the contents of trap 2 were analysed by ^{1}H NMR spectroscopy. The presence of residual acetyl chloride was shown by a singlet at 2.66 ppm which was expected as two equivalents of acetyl chloride had been used. It was expected that any methanol produced by the pyrolysis would react with the acetyl chloride and any methyl

acetate produced could be observed by peaks at 2.05 ppm and 3.66 ppm. Using this apparatus the pyrolysis of *N*-(2-methoxycarbonylphenyl)pyrrole was shown to produce methanol as methyl acetate was observed in the ^{1}H NMR spectrum. Upon pyrolysis, under the standard conditions, of **25** to produce **26** the contents of trap 2 were similarly analysed and only acetyl chloride was seen in the ^{1}H NMR spectrum. This shows that no methanol is produced and therefore that the mechanism which had been suggested, (**Scheme 31**) was not correct.

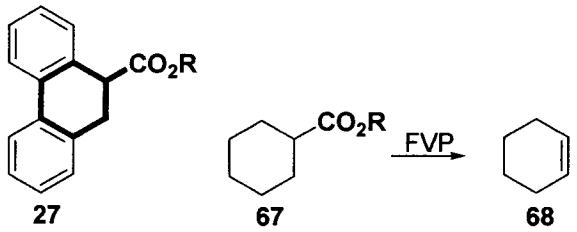
2.4 Study of Essential Structural Features for Reaction

To determine the mechanism it was necessary to examine the structural features of the intermediate required for the reaction to work.



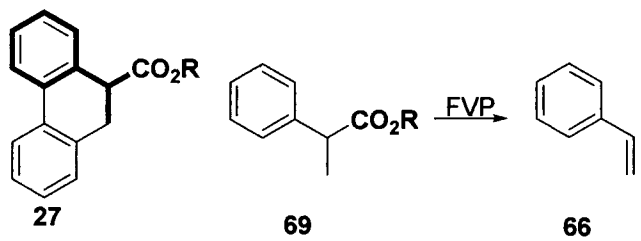
Scheme 33

If the substructure shown in bold (**Scheme 33**) was required for the reaction, with the eliminated hydrogen atom at the active benzylic position, then pyrolysis of **65** would yield styrene **66**. This pyrolysis was attempted but NMR analysis of the pyrolysate showed that there had been only a very small amount of styrene produced.[21] There were three major products observed in the crude pyrolysate. The main product was ethylbenzene **72** but there were also notable amounts of bibenzyl **71** and toluene **74**. The presence of bibenzyl **71** shows that benzyl radicals are being generated in this pyrolysis. The observation of ethylbenzene **72** suggests that the ester leaving group produces methyl radicals after cleavage from the benzyl radical (see **Section 2.4.1** for related reactions).



Scheme 34

Alternatively if it was necessary for the ester group to be held in the correct orientation for the intramolecular reaction (**Scheme 34**) then the pyrolysis of **67** would produce cyclohexene **68** which is characterised by peaks at 5.66 ppm, 1.99 ppm and 1.61 ppm. However pyrolysis of **67** did not produce any cyclohexene **68**, the NMR spectrum of the crude pyrolysate showed no major products had been formed.



Scheme 35

Finally if it was necessary for the ester group to be attached to the benzylic position, **Scheme 35**, then the pyrolysis of **69** would produce styrene **66**. Pyrolysis of **69** showed that styrene **66** was produced (**Table 2**).

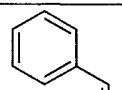
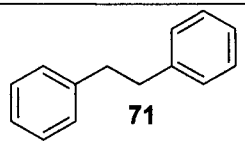
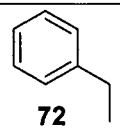
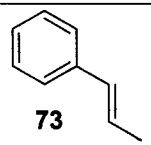
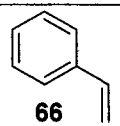
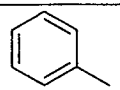
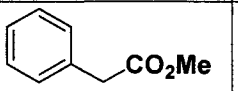
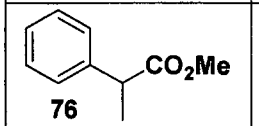
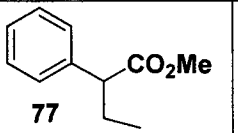
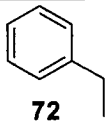
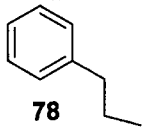
	Temp/°C	Starting Material	 70	 71	 72	 73	 66	 74
 75	975	11%	4%	8%	45%	0%	13%	19%
 76	925	8%	18%	0%	15%	0%	48%	11%
 77	925	5%	44%	0%	26%	0%	25%	0%
 72	975	57%	0%	4%	N/A	0%	17%	22%
 78	975	16%	0%	15%	22%	0%	10%	37%

Table 2: Composition of crude pyrolysates of 75 - 78

2.4.1 Synthesis and Pyrolysis of Model Compounds

To aid the determination of the mechanism of this reaction several model compounds, **75** - **78** were pyrolysed and the composition of the pyrolysate mixture analysed.

The products of these pyrolyses were analysed by observation of characteristic peaks in the ^{1}H NMR spectra of the pyrolysates **Table 3**.

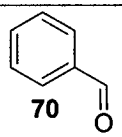
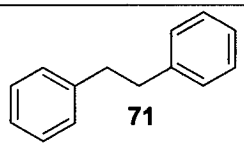
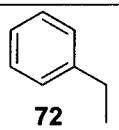
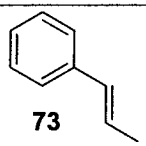
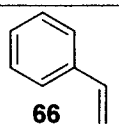
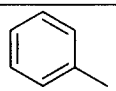
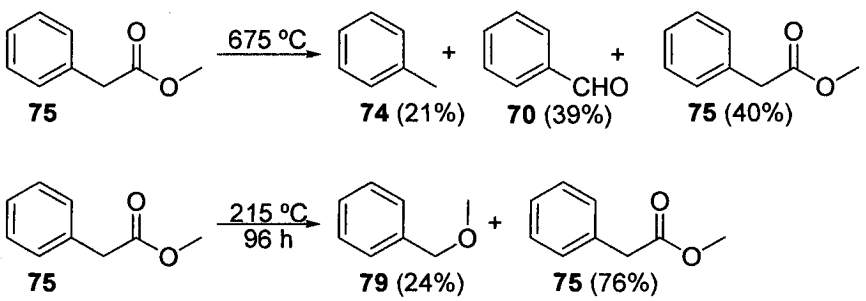
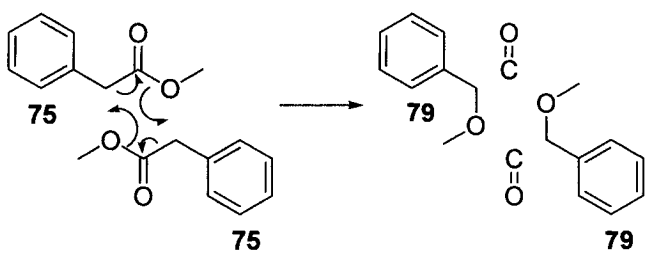
 **70**	10.02 (1H, s), 7.87 (2H, d), 7.61 (1H, t) and 7.51 (2H, dd).
 **71**	7.42 (10H, m) and 2.91 (4H, s).
 **72**	1.22 (3H, t), 2.63 (2H, q) and 7.0 – 7.45 (5H, m).
 **73**	7.20 – 7.50 (5H, m), 6.60 (1H, d), 1.30 (1H, dq) and 1.80 (3H, d).
 **66**	7.50 – 7.10 (5H, m), 6.69 (1H, dd), 5.74 (1H, d) and 5.23 (1H, d).
 **74**	7.04 – 7.13 (5H, m) and 2.32 (3H, s).

Table 3: Characteristic peaks in ^{1}H NMR spectra of 66 and 70 - 74

The thermal decomposition of **75** by flow pyrolysis has been reported previously but the products reported by Mach and Risinger [22] differ from those now obtained by FVP. Mach and Risinger proposed that **75** decomposed *via* benzyl methyl ether **79** to form toluene **74** and benzaldehyde **70** as analysed by gas chromatography (**Scheme 36**). Mach and Risinger felt that the composition of the products suggested an unsymmetrical ester intermediate. They repeated the reaction at a lower temperature for a longer period of time in an attempt to capture some of this intermediate. The small amount of **75** that reacted was found to have produced **79**. Using this result Mach and Risinger proposed that the decomposition of **75** may involve a bimolecular elimination *via* a *quasi* six-membered intermediate as shown in **Scheme 37**.



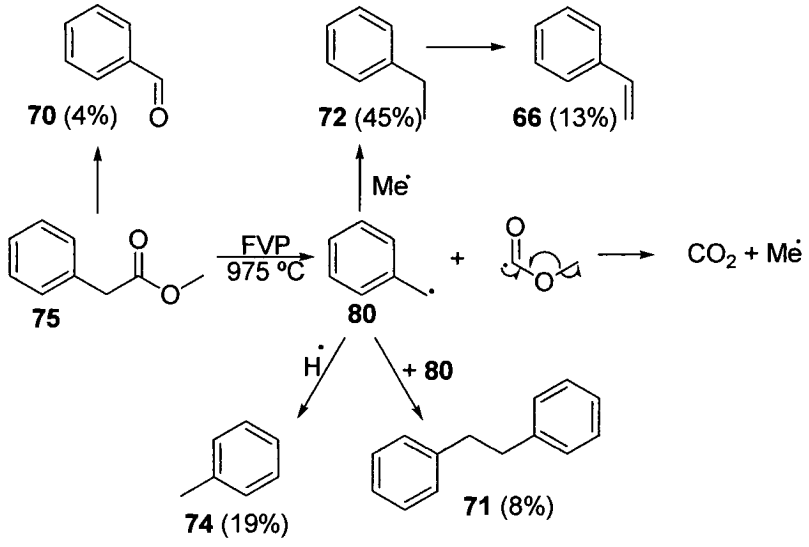
Scheme 36



Scheme 37

In the case of the pyrolysis of **75** at 975 °C under FVP conditions a high percentage of ethylbenzene **72** was produced suggesting that methyl radicals are involved in the reaction. It was thought from this result that the ester group was lost as a radical which then released carbon dioxide leaving a methyl radical which could couple with the

benzyl radical **80** to produce ethylbenzene **72** (**Scheme 38**). The presence of bibenzyl **71** suggests that the benzyl radical **80** is formed and can couple with itself. It is known that benzyl radicals are better trapped by methyl radicals than by other benzyl radicals which explains why much more ethylbenzene was prodcued than bibenzyl **71**.[7] Toluene **74** would be produced by **80** gaining a hydrogen atom. A control pyrolysis of ethylbenzene **72** produced styrene **66** which could account for the small amount of styrene **66** in the pyrolysate.

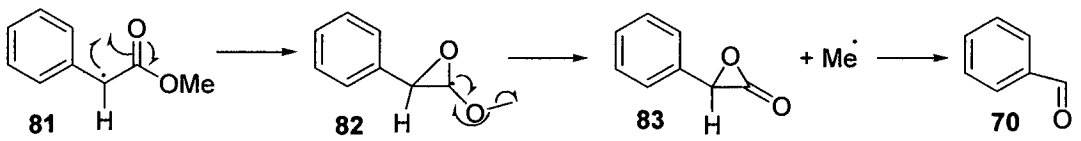


Scheme 38

To show that the benzyl radical **80** is trapped by the methyl radical produced from the ester group the deuteriated analogue of **75**, $PhCH_2CO_2CD_3$, was synthesised and pyrolysed. The pyrolysate was studied by ^2H NMR spectroscopy and it was shown that the methyl group of ethylbenzene was deuteriated. This proves that there are methyl radicals produced in the pyrolysis from the ester group.

The presence of a small amount of benzaldehyde **70** in the pyrolysate can be explained by the work of Domingo *et al.*[23] in conjunction with the proposed radical mechanism. If the radical **81** were to be produced it could react to produce the epoxide **82** which could

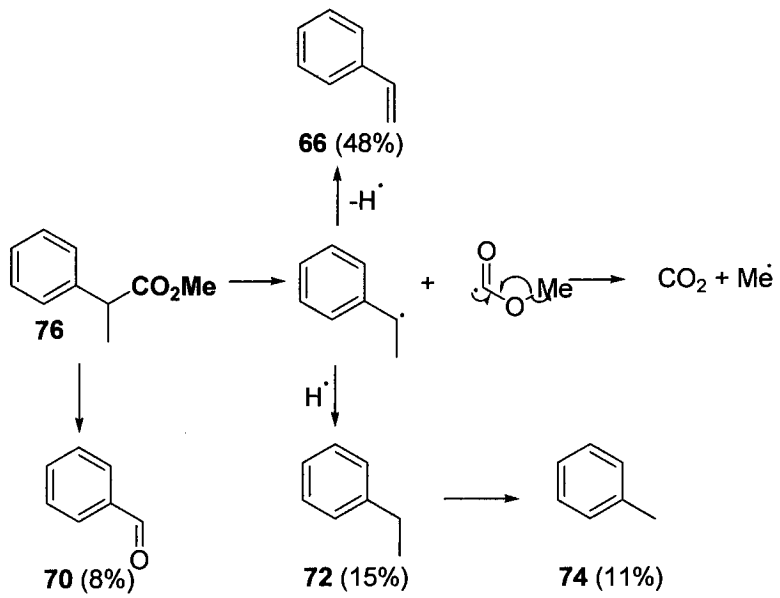
lose a methyl radical to produce **83**. It has been shown by Domingo *et al.*[23] through their computational studies that **83** is likely to decarbonylate to produce **70**.



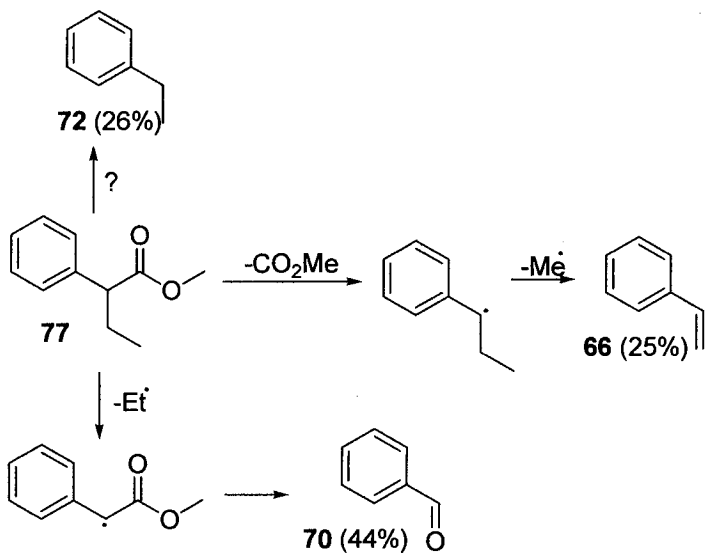
Scheme 39

The pyrolysis of **76** was carried out to investigate further the probability of this proposed radical mechanism. The furnace temperature required for the pyrolysis of **76** was lower than had been used for the pyrolysis of **75**. Pyrolysis of **75** produced a primary radical which is not as stable as the secondary radical expected to be formed by the pyrolysis of **76**. As more stable radicals are more easily formed the energy required for the production of a secondary radical is lower than that required to produce a less stable primary radical. Due to the radical cleavage of the methyl group of **76** benzaldehyde **70** was produced as previously discussed (**Scheme 40**). The radical cleavage of the ester group would produce a radical which can react in two ways, it can either lose a hydrogen atom to produce styrene **66** or it can gain a hydrogen atom to produce ethylbenzene **72**. As it is known that pyrolysis of **25** (**Scheme 11**) produces the aromatic product **28** it was expected that **66** would be the main product of this reaction and the experimental results show this to be correct. Pyrolysis of **72** showed that toluene was produced and thus the toluene which was seen to be present in the pyrolysate is possibly due to further reaction of **72**.

Analysis of the pyrolysate of **77** at 925 °C showed that the major product of the pyrolysis was benzaldehyde **70** (**Scheme 41**). In all of the other cases **70** had been a minor product as the formation of radical **81** was less favourable than formation of the ester group radical. However in the case of the pyrolysis of **77** it is more favourable to produce the ethyl radical than the ester radical as the ethyl radical is more stable.



Scheme 40

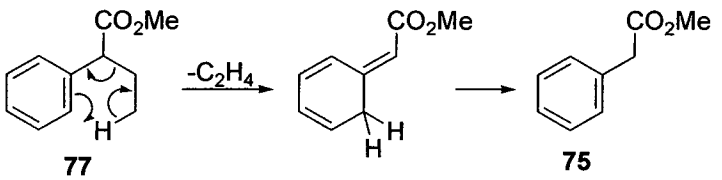


Scheme 41

In this case loss of the ester group would produce a radical which could lose a methyl radical which would result in styrene **66**. It was also proposed that if the radical were to gain a hydrogen atom then propylbenzene would be produced. However, no

propylbenzene **78** was observed in the pyrolysate. Pyrolysis of **78** was seen to produce a significant quantity of ethylbenzene **72** (22%) and a larger amount of toluene **74** (37%). As there was only a very small amount of toluene **74** present in the crude pyrolysate of **77** it is not possible that the ethylbenzene **72** in the pyrolysis of **77** is due to the formation and subsequent pyrolysis of **78**. This means that unlike the two previous model compounds the formation of the products of the pyrolysis of **77** cannot all be justified by a radical mechanism.

It is now proposed that increasing the length of the side chain in the model compounds introduces another complication, since retro-ene-type processes (**Scheme 42**), common in mass spectrometry, might be expected to compete with radical reactions. In the case of the pyrolysis of **77** this type of reaction would produce **75** and as shown in **Table 2** pyrolysis of **75** produces a large amount of **72**.

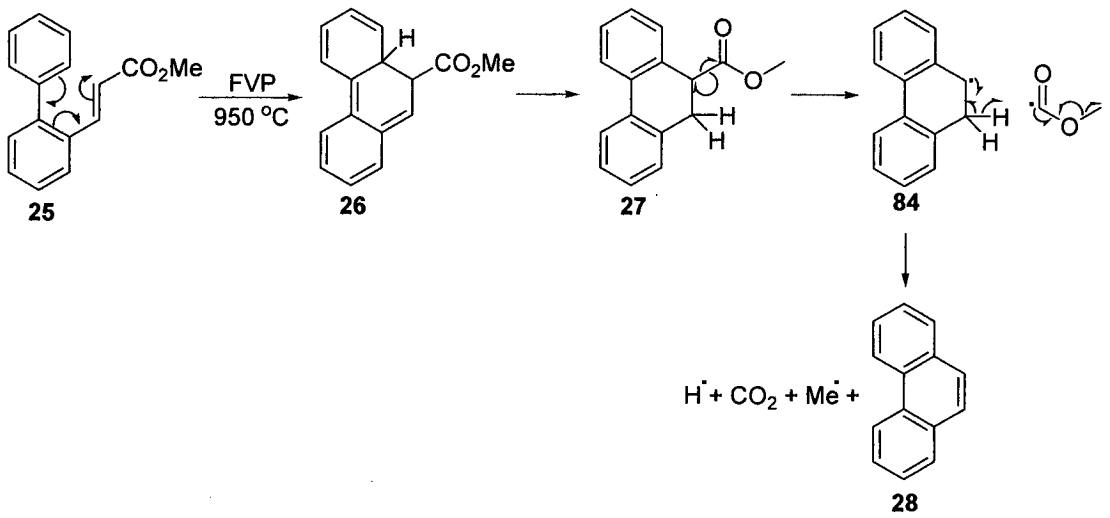


77 **75**

Scheme 42

The pyrolysis of the model compounds discussed in this chapter has led to the following proposed mechanism of the cyclisation of **25** to produce **28**.

It can now be suggested that under FVP conditions **25** undergoes an electrocyclisation reaction followed by a [1,5]-hydrogen shift to form **27**. As indicated by the pyrolysis of the model comounds it is thought that the ester group is then lost *via* radical cleavage to produce **84** and an ester radical. The ester radical then produces carbon dioxide and a methyl radical as discussed. The radical **84** then loses a hydrogen radical to produce **28** in the same way that the pyrolysis of **69** produces styrene. In this case the formation of **28** is also favoured as it is the only fully aromatic product available.



Scheme 43

As discussed previously it was observed that the pyrolysis of carboxylic acids gave similar products to the pyrolysis of methyl acrylates. However it was noted that the dihydro intermediate **59** was always present which suggests that the acid **54** may react slightly differently to the ester **25**. Compounds **85** – **87** were pyrolysed to determine if this was always the case. The compositions of the pyrolysates were analysed by ^{1}H NMR spectroscopy.

Analysis of the pyrolysates showed that the results of these pyrolyses were slightly different to those of their methyl ester analogues. This was surprising in the case of **85** as the thermal decomposition and low pressure pyrolysis of **85** has been reported and the products observed suggest a radical mechanism as in the case of the methyl esters.[24] The main products of the pyrolysis of **85** were bibenzyl **71** and toluene **74** (**Scheme 44**). This was expected as, similarly to the methyl ester case, the carboxylic acid group could be lost as a radical to produce a benzyl radical **80** and a hydrogen atom. Bibenzyl **71** could be formed from the benzyl radical **80** as discussed previously and the reaction of **80** with the hydrogen atom produced would result in toluene **74**. The origin of the small amount of ethylbenzene **72** produced is unknown.

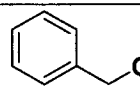
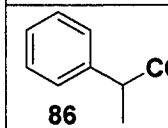
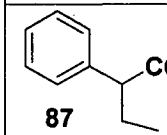
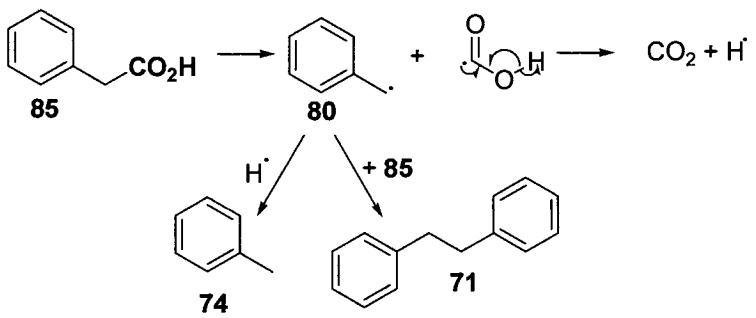
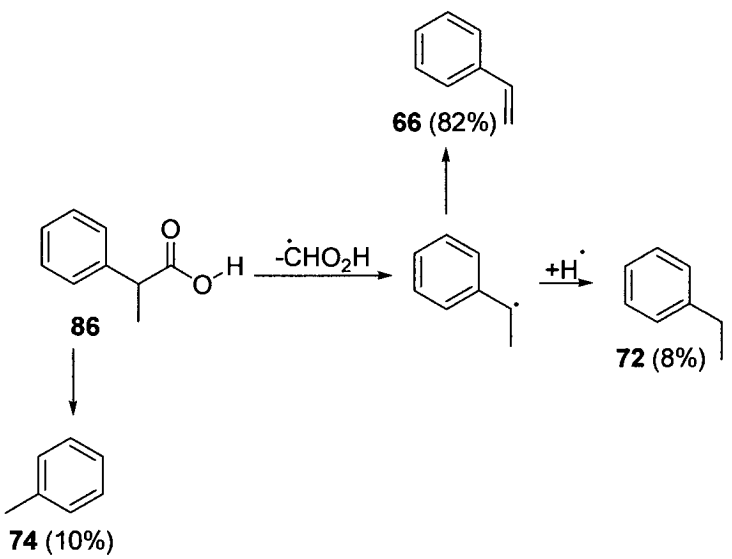
	Temp/°C	Starting Material	70	71	72	73	66	74
 85	925	41%	0%	29%	5%	0%	0%	25%
 86	975	0%	0%	0%	8%	0%	82%	10%
 87	925	0%	0%	5%	29%	31%	23%	12%

Table 4: Composition of crude pyrolysates of 85 - 87



Scheme 44

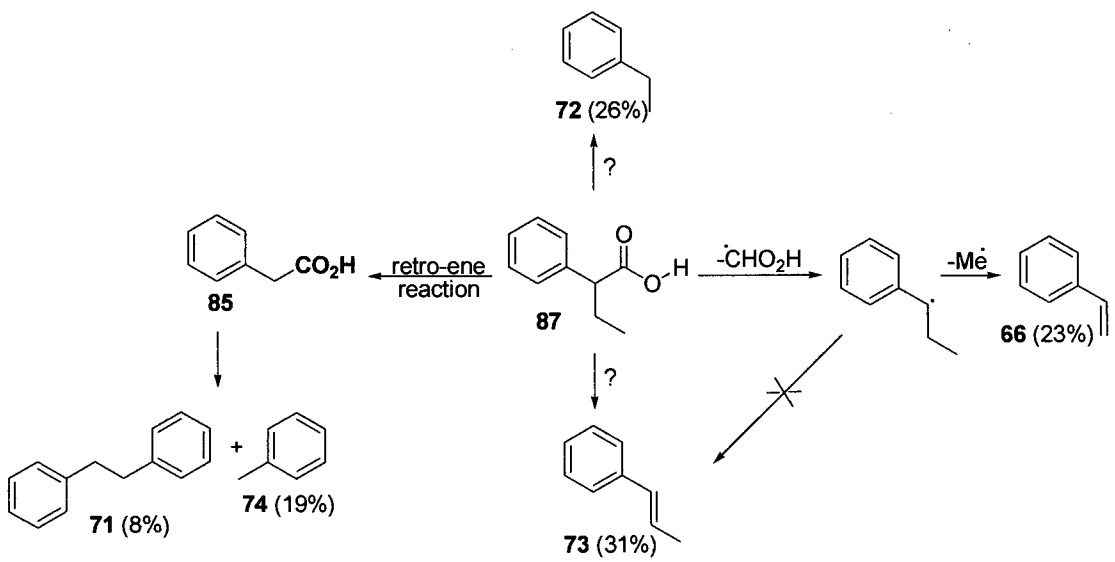
The pyrolysis of **86** produced mainly styrene **66** and toluene **74** along with a small amount of ethylbenzene **72**. It was expected that **66** would be the major product as the radical produced is the same as in **Scheme 40** and it is more likely to produce **66** than **72**.



Scheme 45

Loss of the acid group of **86** would produce a radical which could gain a hydrogen atom to yield ethylbenzene **72**. It was originally suggested that both the toluene **74** and styrene **66** present in the crude pyrolysate could be due to the further reaction of **72**. However, pyrolysis of **72** produced **74** and **66** in approximately equal quantities. This is not consistent with the product composition in **Scheme 45** so it can be assumed that decarboxylation of **86** to **72** is not the major pathway in that pyrolysis. The origin of the small amount of toluene **74** is unknown as there is more than would be expected by further decomposition of ethylbenzene **72**.

The final acid to be pyrolysed was **87** and analysis of the pyrolysate showed the presence of five products (**Scheme 46**). Loss of the acid group from **87** would produce a radical which could either lose a methyl radical to produce styrene **66.** or gain a hydrogen atom to produce propylbenzene **78**. As in the pyrolysis of **77** it is possible that **87** undergoes a retro-ene reaction to produce **85** which accounts for the presence of **71** and **74** in the crude pyrolysate.



Scheme 46

Methylstyrene **73** was the main product of this pyrolysis but this does not fit the proposed radical mechanism as cleavage of a C-C bond (to give **66**) is always more favourable than cleavage of a C-H bond (to give **73**).

2.5 Conclusions

These results suggest that although the radical mechanism is probably the main mechanism in the pyrolysis of the esters there is more than one mechanism occurring in the reaction of the carboxylic acids. This is unexpected as in **Section 2.2.2** it appeared that the carboxylic acid **55** produced phenanthrene **28** in roughly the same way as the ester **25** did. It was therefore expected that the carboxylic acid model compounds would react similarly to their ester analogues. At this point further work is required to determine the reaction mechanism of the carboxylic acid pyrolyses fully.

3 Three- Ring Systems

3.1 Introduction

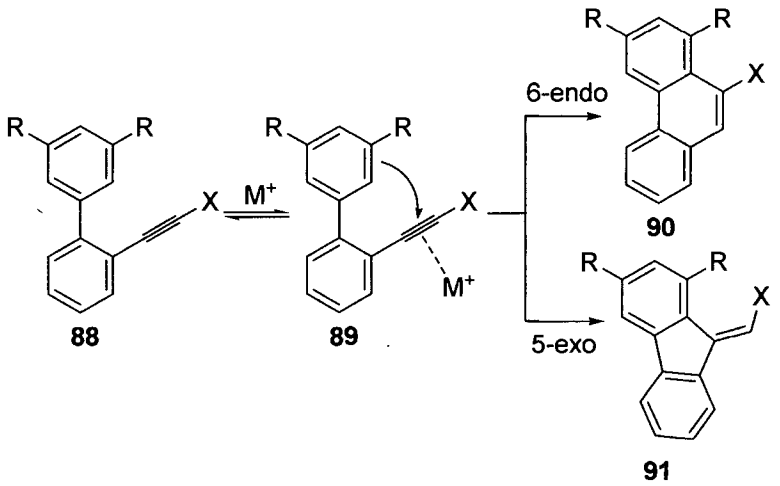
The aim of this introduction is to review briefly the existing literature available on the synthesis of three-ring fused systems covering both phenanthrenes and related naphthothiophenes and naphthofurans. The structure of phenanthrene was first determined in 1873 by Fittig and Ostermayer using a sample isolated from coal tar[25] and since then a multitude of syntheses of phenanthrene and similar compounds has been published.

3.1.1 Phenanthrenes

In 1976 a review was published by Floyd *et al.*[26] on the synthesis of phenanthrenes. As this review provides an overview of the literature prior to 1976 this chapter will only refer to work published since. There have been over 5000 papers published discussing the synthesis of three-ring systems since 1976 and as this thesis is concerned with the synthesis of compounds using intramolecular cyclisations to form the central ring the syntheses involving other reactions will not be discussed. It should be noted that phenanthrenes can be synthesised by carbocyclic ring expansions such as Wagner-Meerwein rearrangements and by intermolecular cycloadditions both of which are discussed in great depth by Floyd *et al.*[26] Analysis of the current literature shows that new routes to phenanthrenes most commonly involve intramolecular cyclisation of biphenylalkynes.

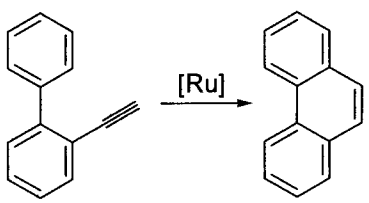
3.1.1.1 Metal Catalysed Cyclisations

The majority of the cyclisations used to synthesise phenanthrenes use a metal catalyst. It was known that addition of an electrophilic metal salt or metal complex to alkynes like **88** resulted in an equilibrium between the alkyne **88** and the corresponding metal complex **89**.[27] This complex could either follow the 6-endo pathway to form the phenanthrene **90** or the 5-exo pathway to form **91**.



Scheme 47

It was reported that for most of the alkynes studied the 6-endo pathway was favoured when the catalyst used was $PtCl_2$. In some cases (R=X=Me) only **90** was produced but this was the only example of 100% conversion to the phenanthrene. In the case where X was a strong electron-withdrawing group the 5-exo pathway was favoured in the ratio 5:95 (**90** : **91**) but this was the only exception when $PtCl_2$ was used.



[Ru] = $TpRuPPh_3(CH_3CN)_2PF_6$
Tp = tris(1-pyrazolyl)borate

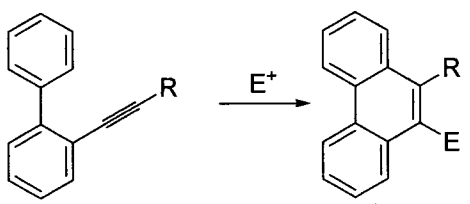
Scheme48

Screening of a variety of metal catalysts showed that other metal chlorides (Au, Ga and In) also favoured production of the phenanthrene as did cationic platinum complexes formed *in situ* from $[PtCl_2(PhCN)_2]$ and a halide sequestering agent (*e.g.* $AgBF_4$). Both $RuCl_3$ and $RhCl_3$ resulted in low yields, poor selectivity and in some cases no reaction.

This was also the case with other ruthenium complexes. This makes the results published later by Liu *et al.*[28] surprising as they reported the cyclisation of **92** to form phenanthrene **28** in good yield using a ruthenium complex in much lower quantity as the catalyst.

3.1.1.2 Electrophilic Cyclisation

The cyclisation of alkynes can also be carried out using electrophiles in place of metal catalysts as electrophilic addition to carbon-carbon triple bonds generates cationic species which can undergo intramolecular cyclisation to form phenanthrenes and other polycyclic aromatic compounds. Larock *et al.*[29] have reported the use of several electrophiles in the formation of phenanthrenes *via* the cyclisation of alkynes **(Scheme 49)**. The simplest system (R=Ph) produced the desired products at room temperature with reaction times between 0.5 – 144 hours but when more complicated alkynes where used it was noted that the reactions gave better results at -78 °C. Once again it was seen that the 6-endo pathway was favoured and the phenanthrene products were synthesised. Unfortunately this method only seems to be a useful route to phenanthrenes with bulky substituents.



93 **94**

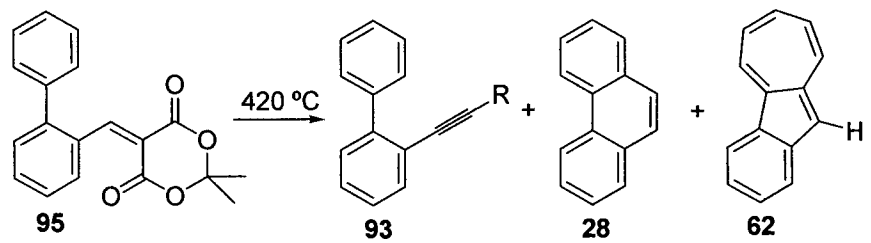
E^+ = ICl, NBS, *p*-$O_2NC_6H_4SCl$, PhSeCl

R = Ph, C_6H_9, CH_2TMS

Scheme 49

3.1.1.3 Flash Vacuum Pyrolysis

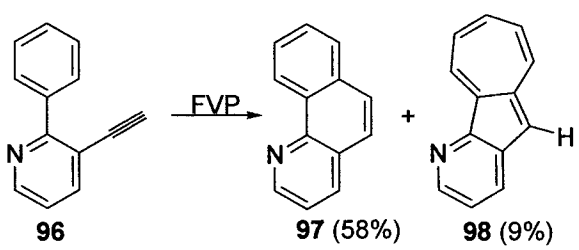
The formation of phenanthrenes by the cyclisation of alkynes is not restricted to reactions using a catalyst. Information about the cyclisation of alkynes *via* FVP was first published in 1974 by Brown *et al.*[14] but was not included in Floyd's review of phenanthrene synthesis. Brown knew that alkynes could be synthesised by the FVP of Meldrum's acid derivatives. However, when he pyrolysed **95** only a small amount of the acetylene **93** was observed along with both phenanthrene **28** and the benzazulene **62** (**Scheme 50**, *cf.* **Scheme 29**).



Scheme 50

It was found that pyrolysis at higher temperatures produced only **28** and **62** which suggested that the alkyne was an intermediate and that pyrolysis of the alkyne would produce **28** and **62**.

In 2002 Hopf *et al.*[30] used this reaction to produce an aza-analogue of phenanthrene **97**, benzo[*a*]quinoline **97** along with several larger polycyclic aromatic systems.

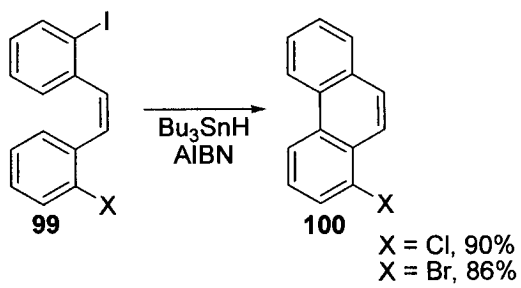


Scheme 51

Although pyrolysis of **96** also produced the aza-benzazulene product **98** the yield was low and the two products could be separated using chromatographic techniques.

3.1.1.4 Other Methods

It should be noted that there are many effective syntheses of phenanthrenes other than the cyclisation of alkynes and many that do not involve the formation of the central ring. It is common for helicenes to be synthesised from stilbene starting materials and this is also true for phenanthrenes. In the case of helicenes these cyclisations take place under photochemical conditions but it is also possible for these reactions to be done using radicals. One example of this type of reaction is the synthesis of 1-halogenophenanthrenes as reported by Harrowven *et al.*[31] in 2006 (**Scheme 52**).



Scheme 52

Using tributyltin hydride and azoisobutyronitrile (AIBN) the carbon-iodine bond was selectively homolysed to generate the aryl radical which could only attack one position on the other ring as the other possible site was protected by the halogen atom. This route works well but can only be used to synthesise 1-halophenanthrenes and other halogeno-substituted ring systems.

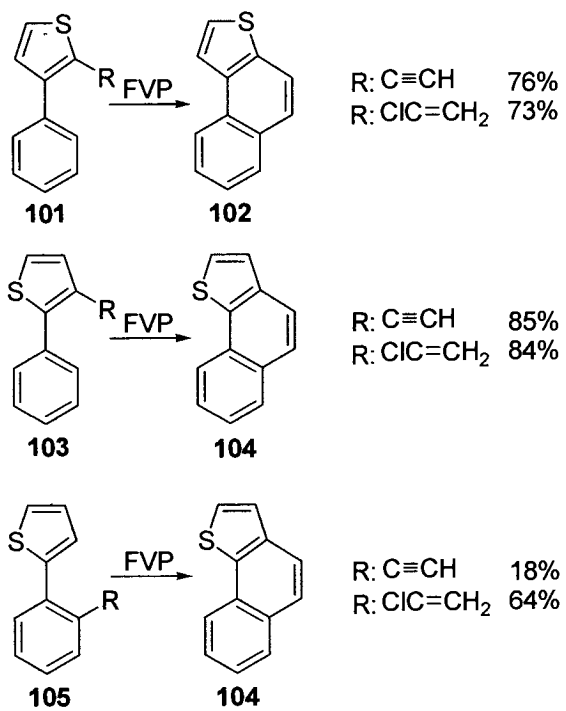
3.1.2 Heterocyclic Three-Ring Systems

Relative to the amount of data available on the synthesis of phenanthrenes the literature covering the synthesis of its thiophene and furan analogues is scarce. Unlike the phenanthrenes there have been no reviews published about the synthesis of

naphthothiophenes or naphthofurans so this thesis will provide an overview of recent literature with emphasis on high energy methods (FVP and photochemical). Some of the techniques used for the synthesis of these compounds are the same as those discussed previously.

3.1.2.1 Flash Vacuum Pyrolysis

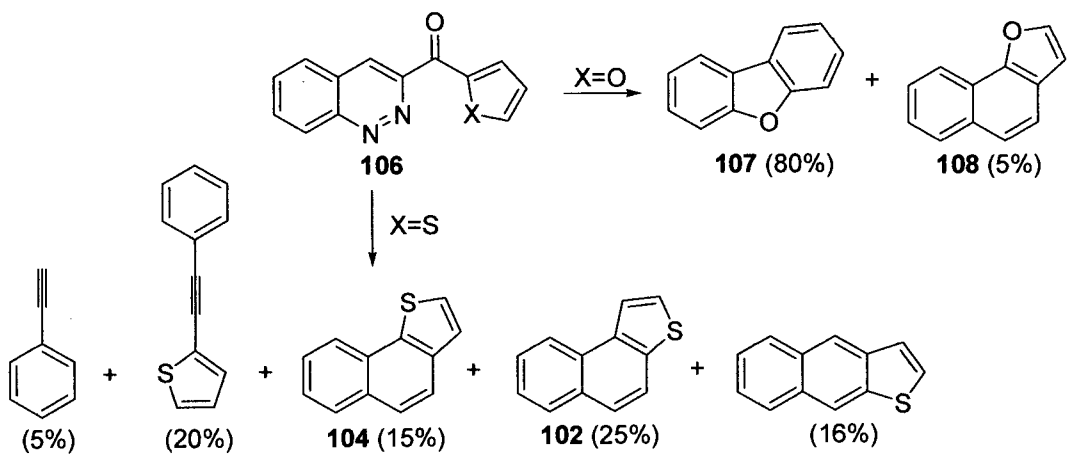
One technique used to synthesise three-ring systems is FVP. As in the synthesis of phenanthrenes and their aza-analogues it is possible to use the Brown[14] cyclisation of alkynes to synthesise these other heterocyclic systems. Using this well documented FVP reaction Otsubo *et al.*[32] synthesised a number of condensed ring systems of varying size. It is known that under FVP conditions chloroalkenes lose HCl to form alkynes. This meant that both naphthothiophenes could be synthesised from two different sets of starting materials (**Scheme 53**).



Scheme 53

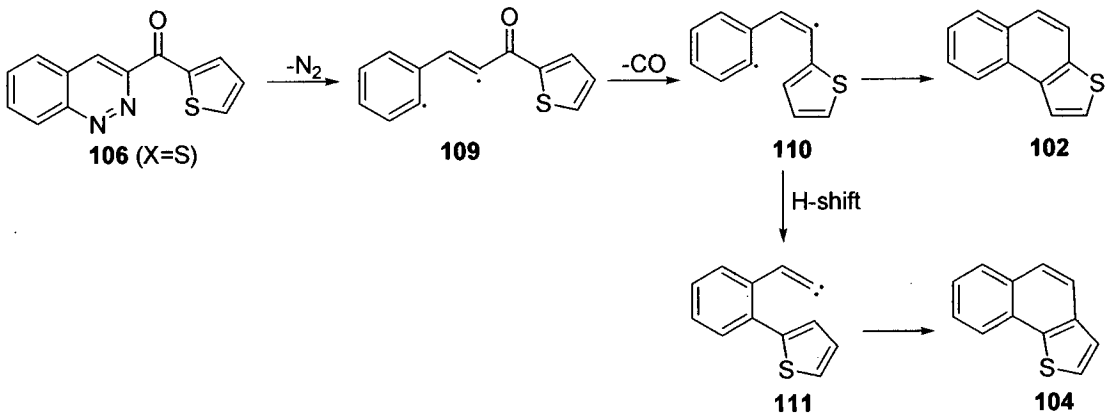
Both of these side chains form methylenecarbenes under FVP conditions and it is the carbenes which cyclise to produce the final ring systems. When the side chain is on the thiophene ring (**101** and **103**) it is the alkynes which give the higher yields. Conversely when the side chain is on the benzene ring (**105**) it is the chloroalkene that gives the higher yield. This may be because the chloroalkenes are more stable to volatilisation as acetylenes tend to polymerise at high temperatures. Following Brown's report it was expected that azulenes would also be isolated from the crude pyrolysate but Otsubo reports no azulene formation, possibly because of the strain induced by two fused 5-membered rings.

Al-Awadi *et al.*,[15] in their work pyrolysing cinnolines, discovered a new route to **102**, **104** and the furan analogue of **104** which may involve methylenecarbene intermediates. Pyrolysis of 3-(2-furanoyl)cinnoline **106** (X=O) produces dibenzofuran **107** and the side product **108** which is the furan analogue of **104**. Pyrolysis of 3-(2-thienoyl)cinnoline **106** (X=S) produces five products including **102** and **104** (**Scheme 54**).



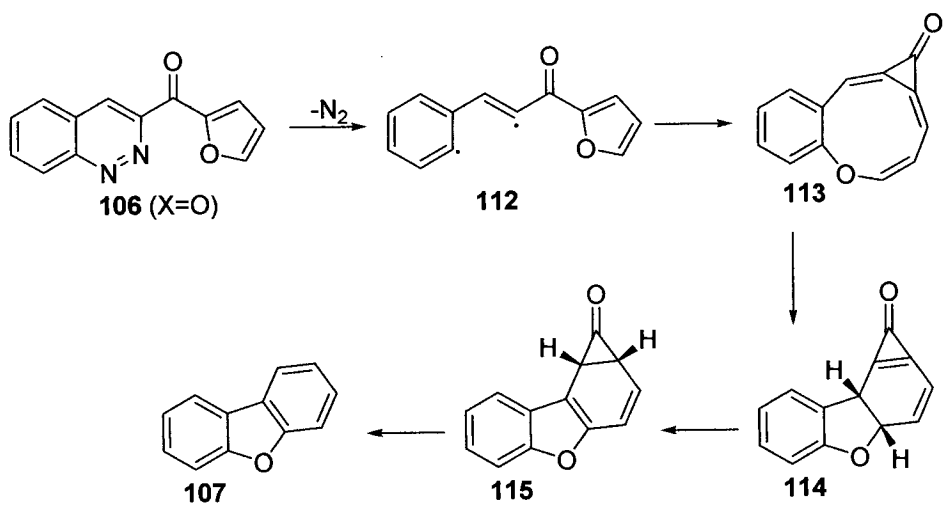
Scheme 54

Unlike the reaction in **Scheme 53** this reaction does not produce the naphthothiophenes in good yield. It was suggested that **104** may be formed by methylenecarbene cyclisation (**Scheme 55**).



Scheme 55

In the proposed mechanism the cinnoline **106** loses nitrogen to form **109** and then is thought to undergo a decarbonylation reaction. The diradical **110** then either cyclised to produce **102** or rearranged to form the methylenecarbene **111** which, as in the Brown reaction, cyclised to form **104**. No evidence for this mechanism has been provided in the paper and there are some steps which do not seem plausible. It may be the case that further mechanistic studies would show that the sequence of the mechanism in **Scheme 55** is incorrect as it seems unlikely that **109** could lose CO to produce **110**.

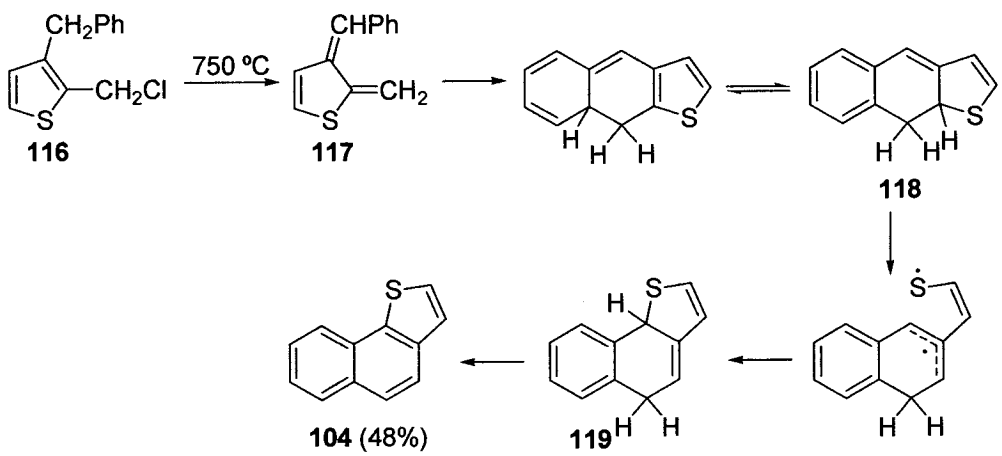


Scheme 56

As in **Scheme 54** the furan analogue of **104** (**108**) was produced but not the analogue of **102** and again the authors have suggested a mechanism which they feel provides an explanation for this (**Scheme 56**).

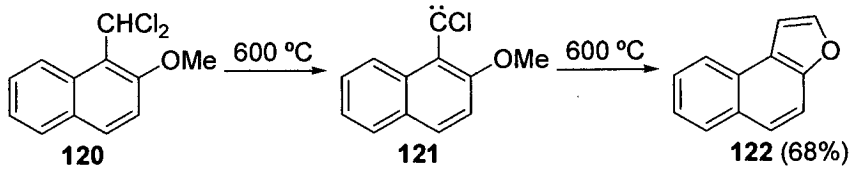
The proposed mechanism suggests that nitrogen is lost to produce a diradical **112** however in this case the diradical rearranges to produce **113**. The benzononatetraene **113** then undergoes a 6π-electrocyclisation to form **114**. To produce **107** compound **114** has to undergo two successive [1,5]-hydrogen shifts to form **115** followed by carbon monoxide extrusion to form dibenzofuran. It seems unlikely that such an unusual intermediate as **113** would be formed preferentially to all other possible intermediates and Al-Awadi has provided no evidence for this mechanism or the existence of **113**. Again further mechanistic studies are likely to show that this mechanism is incorrect.

Storr *et al.* [33] published a better synthesis of **104** by the pyrolysis of substituted thiophene **116**. Pyrolysis of **116** was thought to produce **117** which undergoes an electrocyclisation followed by a [1,5]-hydrogen shift to form **118**. The sulfur-containing ring then undergoes radical cleavage to produce a diradical which then cyclises to form **122** which rearomatises to give **104**.



Scheme 57

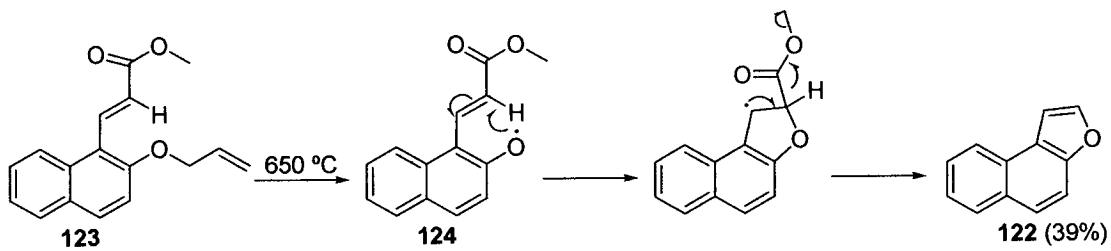
There is a final compound which has not yet been discussed. The furan analogue of **102** (**122**) can be synthesised in three ways under FVP conditions. The highest yield of **122** was achieved by Parrick *et al.*[34] by the pyrolysis of a substituted naphthalene **120**.



Scheme 58

After labeling experiments it was determined that this reaction went *via* a carbene intermediate **121**. It is possible to produce 1-naphthylcarbene which undergoes the same cyclisation reaction as **121** by the pyrolysis of a silane precursor.[35]

The third synthesis of **122** using FVP was published by McNab *et al.*[36] *via* a phenoxyl radical **124** formed by the pyrolysis of **123**. Once **124** had been formed a cyclisation took place followed by the selective cleavage of the ester group to yield **122**.

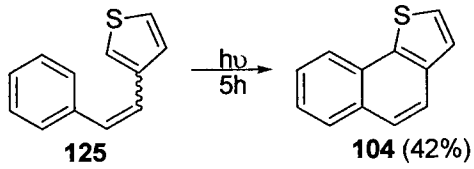


Scheme 59

3.1.2.2 Photochemistry

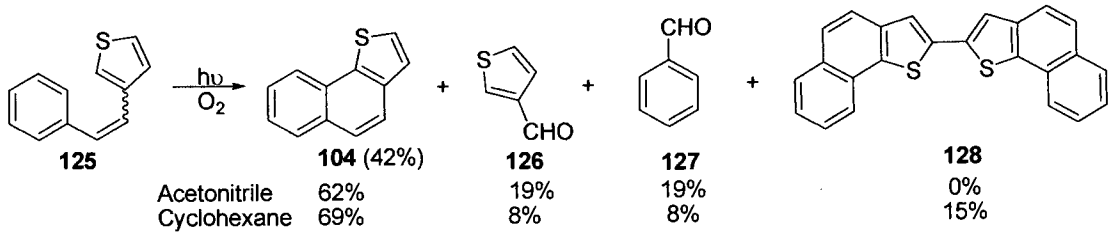
One of the most popular techniques in the synthesis of helical polycyclic aromatic compounds is photochemistry. In the case of the naphthothiophenes and naphthofurans photochemistry is not used as much as FVP but it is still one of the more prevalent techniques. As with most photochemical syntheses of helicenes the precursors are all

stilbenes. The first synthesis of the heterocyclic three-ring systems being discussed was by Castle *et al.*[37] who published the photochemical synthesis of **104**.



Scheme 60

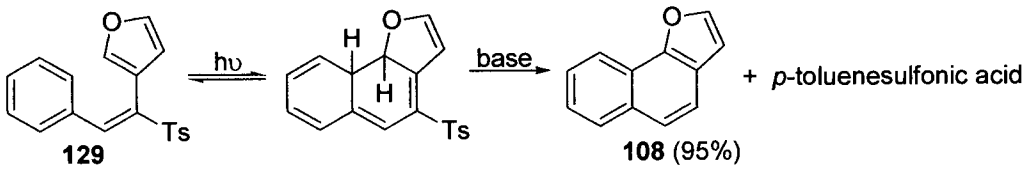
In this case the stilbene was synthesised *via* a Wittig reaction. At this point there was no discussion of the mechanism of reaction or alteration of the reaction conditions to optimise the yield. In 2000 Wu *et al.*[38] published a study of the effects of changing the solvent on the yield of the various products of the photochemical reaction of **125**. In this case an oxidant was added to ensure complete conversion to the fully aromatic product as it was possible that the dihydro-intermediate may have been trapped. It was found that if the reaction was done in acetonitrile then **104** was formed in reasonable yield along with **126** and **127**. However changing the solvent to cyclohexane resulted in a slightly increased yield of **104** and lower yields of **126** and **127** although it was then noted that the dimer **128** was also present (**Scheme 61**).



Scheme 61

Although the reaction in acetonitrile gives a slightly lower yield it is likely that separation of **104** from the aldehydes **126** and **127** would be easier than separating **104** from **128**.

The final photochemical synthesis of this type is another route to the naphthofuran **108**.[39] Again this reaction is the cyclisation of a stilbene precursor **129** under photochemical conditions (**Scheme 62**). In this case the precursor had a leaving group attached to the alkene, on the production of the dihydro compound, would, upon addition of base, undergoes an elimination to produce **108**. As a tosyl leaving group was used the cyclisation of **129** produced toluenesulfinic acid and **108** in high yield.

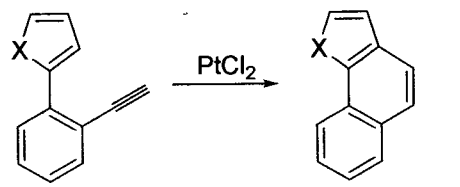


129 **108** (95%)

Scheme 62

3.1.2.3 Metal Catalysed Intramolecular Cyclisations

As in the synthesis of phenanthrenes the metal catalysed cyclisation of alkynes is an important route to the type of heterocyclic three-ring systems under consideration. The route in **Scheme 47** was also used to cyclise **130** to produce **104**[27] and **108**[40] using a platinum catalyst (**Scheme 63**).



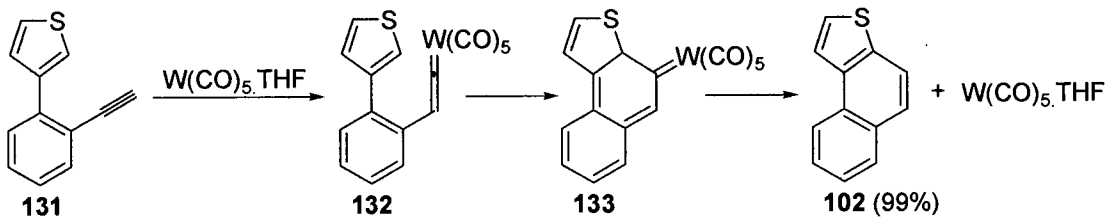
130

X=S: **104** (54%)
X=O: **108** (90%)

Scheme 63

There is one other metal catalysed route to both **104** (82%) and **108** (82%) using a tungsten catalyst.[41] This route has the advantage of also being useful for the production of **102** (**Scheme 64**). The tungsten catalyst is added to alkyne **131** and a tungsten

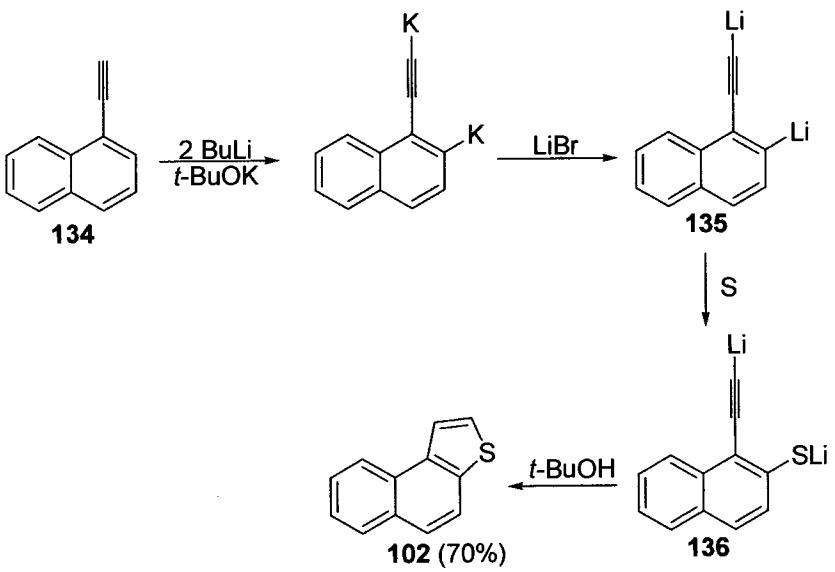
vinylidene species **132** is formed which then undergoes a 6π-electrocyclisation to form **133**. Regeneration of the catalyst then allows formation of **102**.



Scheme 64

3.1.2.4 Other Methods

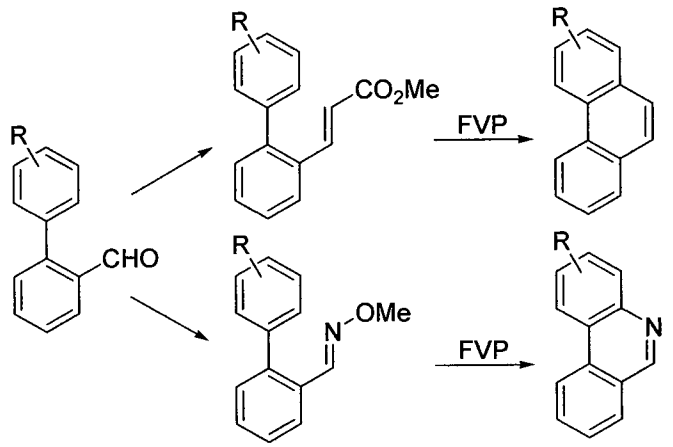
It is possible to produce compound **102** from an alkyne using a metal that is not a catalyst. Brandsma *et al.*[42] used 1-naphthylacetylene **134** in two consecutive metallation reactions to produce the dilithiated species **135**. Addition of sulfur under heating resulted in the insertion of a sulfur atom into the carbon-lithium bond at the 2-position to yield **136**. Addition of *tert*-butanol resulted in the cyclisation of **136** to form **102** in good yield.



Scheme 65

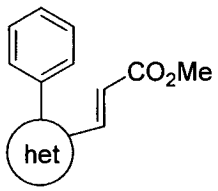
3.2 Synthetic Applications

As discussed in chapter 1, this thesis will discuss the synthesis of a variety of multiple ring systems produced using the cyclisation reactions described earlier (**Scheme 66**). This chapter will only deal with the synthesis of three-ring systems.

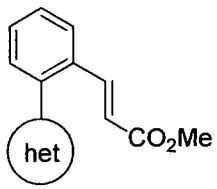


Scheme 66

It was necessary to determine both the scope and the limitations of this reaction and as such several aspects of generality have been investigated. All of the reactions were attempted using the acrylate leaving group for the reasons discussed in chapter 2. It was important to show if the reaction can be done on *ortho*-, *meta*- and *para*-substituted precursors. It was also important to determine the compatibility of the reaction with both electron withdrawing and electron donating substituents as well as with both π-excessive heterocycles, furans and thiophenes, and π-deficient heterocycles, pyridines. There are two types of possible systems to be observed. The first has the acrylate group on the heterocyclic group cyclising onto the benzene ring, **137**, whilst in the second the acrylate group attached to the benzene ring cyclises onto the heterocycle **138**. However, due to the difficulty in obtaining many heterocyclic aldehydes the majority of the work in this project is restricted to precursors of type **138**.



137



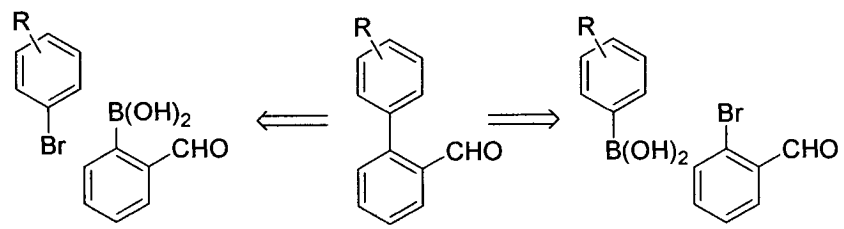
138

3.2.1 Precursor Synthesis

In order to produce these three-ring systems the precursors for the FVP had to be synthesised. These were all made in a similar fashion by initial synthesis of the biaryl unit which contained the aldehyde functionality which was then converted into the acrylate or oxime ether required for the cyclisation reaction.

3.2.1.1 Aldehydes

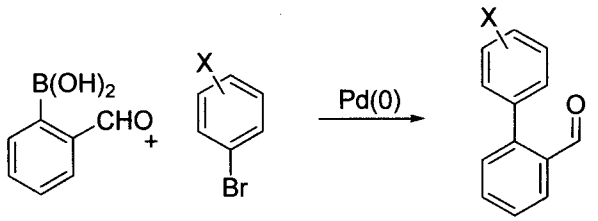
The biaryl units of all the FVP precursors were initially synthesised as aldehydes. Aldehyde **29** was synthesised in reasonably high yields as described earlier in chapter 1. All of the other aldehydes were synthesised *via* Suzuki reactions.



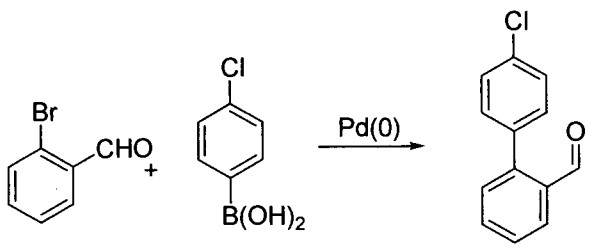
Scheme 67

The basic biaryl aldehydes can be synthesised from two different sets of starting materials. The first is 2-bromobenzaldehyde and the appropriate boronic acid. The second is 2-formylphenylboronic acid and the appropriate halide, usually bromide. Many of the boronic acids required to couple with 2-bromobenzaldehyde were not commercially available so most of the following syntheses use 2-formylphenylboronic acid. There is a wide range of different conditions for Suzuki reaction that have been reported.[43] In in the majority of cases the conditions published by Tsvetkov *et al.*[8c] were

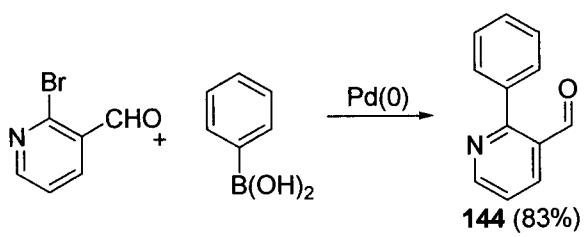
used as it had been shown in earlier work that these conditions produced better results than more traditional conditions such as those reported by Sharp *et al.*[8b] despite Tsvetkov's conditions being originally optimised for the Suzuki coupling of quinolines. In some cases the Suzuki coupling was not favoured and the self-coupling of the boronic acid was observed therefore a better set of conditions had to be found for these specific reactions. It was found that the conditions reported by Fu *et al.*[44] produced positive results where other reaction conditions had failed. It was considered that taking **142** through the next two steps might yield more information about the reaction mechanism so **142** was also synthesised *via* a Suzuki coupling reaction.



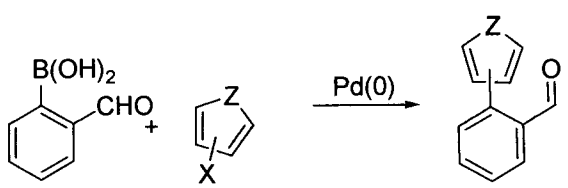
139 X = 4-CN (82%)
140 X = 3-CN (98%)
141 X = 2-CN (~ 80%)
142 X = 2-CHO (~ 90%)



143 (86%)



144 (83%)



145 Z = S, X = 2-I (66%)
146 Z = S, X = 3-Br (67%)
147 Z = O, X = 2-Br, 5-CO_2Et (~ 60%)
148 Z = O, X = 2-Br (50%)

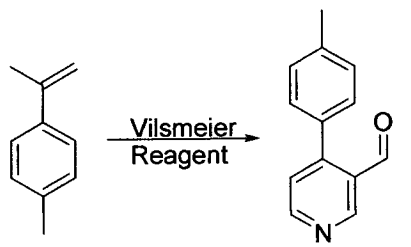
Scheme 68

Most of these aldehydes were synthesised *via* Suzuki reactions from commerically available starting materials. 2-(2-Furanyl)benzaldehyde could not be produced in this way as the synthesis of 2-bromofuran is problematic. This resulted in the synthesis of **147** anticipating that the elimination and decarboxylation of the ethyl ester under FVP conditions would produce the parent ring system.

To produce substituted three-ring systems a variety of substituted aldehydes were synthesised. The substituents were chosen for their thermal stability as many substituents are not stable under the very high temepratures needed for these cyclisations under FVP conditions. Aldehyde **149** had been previously synthesised by Milligan and the methyl substituent provided an example of a modest electron donating group.[7] It was known that both cyano groups and chloro substituents are stable under FVP conditions. The cyano substituent was chosen as an example of an electron withdrawing group and the chloro substituent was used as an example of a halogen. It would also be possible to use the final chloro-/cyano-substituted ring systems as precursors to other compounds as cyano groups can undergo a variety of functional group transformations and chloro groups can be used to form Grignard and other organometallic reagents.

To investigate the possibility of producing three-ring systems with substituents in different positions compounds **139**, **140** and **141** were also produced. The cyano substituted compounds were chosen due to the availability of starting materials and the known stablility of nitriles under FVP conditions.

Aldehyde **149** was not synthesised via Suzuki coupling reactions but by the reaction of a 2-arylprop-2-ene with the Vilsmeier reagent to produce a multiply iminoalkylated bis(iminium) salt. In the presence of ammonium acetate the salt then underwent a cyclisation followed by hydrolysis to produce the aldehyde functionality.[7]



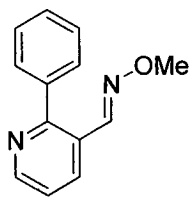
149 (12%)

Scheme 69

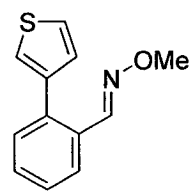
As discussed in chapter 1 aldehyde **29** was also not produced *via* a Suzuki coupling reaction.

3.2.1.2 Oxime Ethers

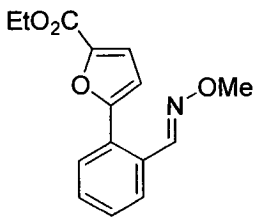
All of the oxime ethers were synthesised in the standard way by heating the aldehyde with *O*-methylhydroxylamine hydrochloride in ethanol for two hours followed by a normal work-up to produce the oxime ethers without the need for purification. The transformation of the aldehydes to the oxime ethers was observed by ^{1}H NMR spectroscopy. The characteristic aldehyde peaks at *ca.*10 ppm disappeared and both a singlet methyl peak at *ca.* 4 ppm due to the presence of the methoxy group and a singlet at *ca.* 8 ppm due to the proton on the carbon adjacent to the nitrogen appeared. There was also a loss of 31 Da in most of the mass spectra which equates to the loss of the methoxy group.



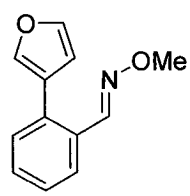
150 (92%)



151 (51%)



152 (53%)

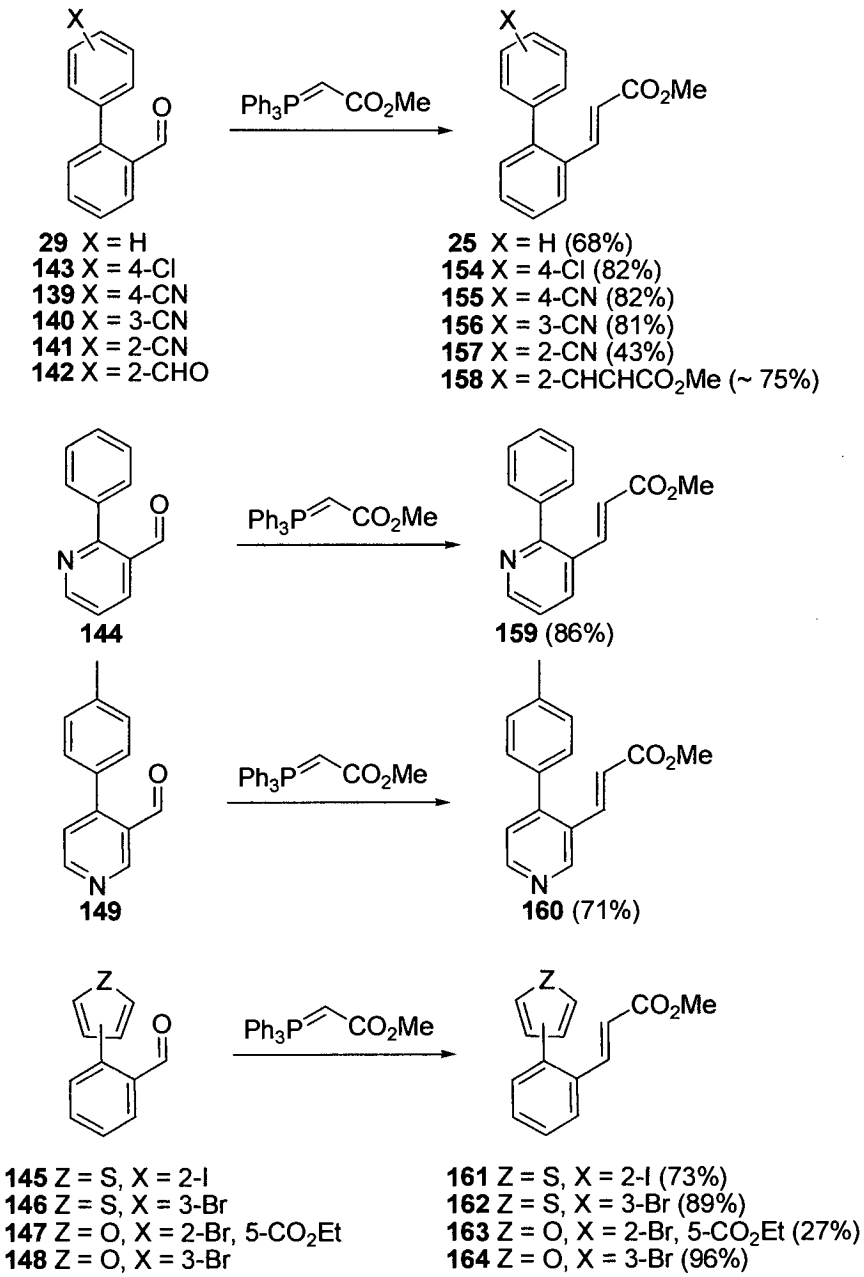


153 (71%)

Compounds **150** – **153** were synthesised in this way.

3.2.1.3 Wittig and Knoevenagel Products

The final set of functional group transformations carried out on the aldehydes involved the synthesis of two different types of alkenes. The first type, **25** and **154** – **164**, were synthesised *via* a Wittig reaction in the standard way using methyl(triphenylphosphoranylidene) acetate as the Wittig reagent.[7] The products were easily separated from the triphenylphosphine oxide by-product by dry flash chromatography. The yields of this reaction were generally greater than 60% and the *E* : *Z* ratio was, on average, 87 : 13.

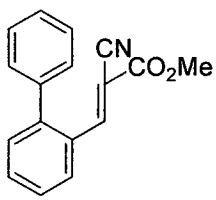


Scheme 70

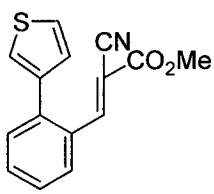
The *E*-isomers produce doublets with a coupling constant of *ca.* 16 Hz and the *Z*-isomer doublets have coupling constants of *ca.* 12 Hz. There was no attempt to separate the

isomers as it is known that they will isomerise under FVP conditions when the furnace temperature is above 650 °C.[45]

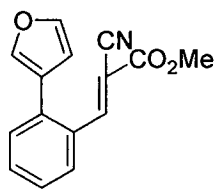
The second type of alkenes produced were cyano-esters, **165** – **167**, which were synthesised from the aldehydes *via* a Knoevenagel reaction under standard conditions using methyl cyanoacetate in toluene with catalytic amounts of piperidine and glacial acetic acid for two hours. The ^{1}H NMR spectra showed singlets at *ca.*8 ppm due to the alkene proton which is deshielded by the two electron withdrawing groups. Only one isomer was produced but the configuration was not determined.



165 (96%)



166 (40%)



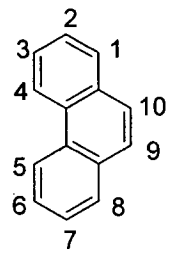
167 (24%)

3.2.2 Pyrolyses

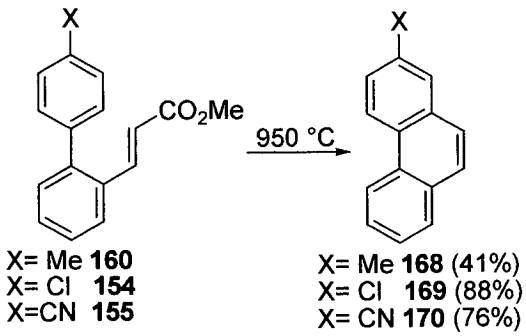
3.2.2.1 Phenanthrenes

The pyrolyses of all the methyl acrylates were carried out at 950 °C as this had been shown by Tipping[21] to be the optimum furnace temperature for this reaction. The majority of these pyrolyses were done on a very small scale using samples of *ca.* 20 mg as, in most cases, this would yield enough product for full characterisation. In some cases low yields required the repetition of the pyrolysis to gain enough product and to overcome some of the difficulties of working on such a small scale at high temperatures. These problems include contamination of the product with joint grease and decomposition of starting materials in the inlet.

The standard numbering system for the subsituted phenanthrenes produced is shown.

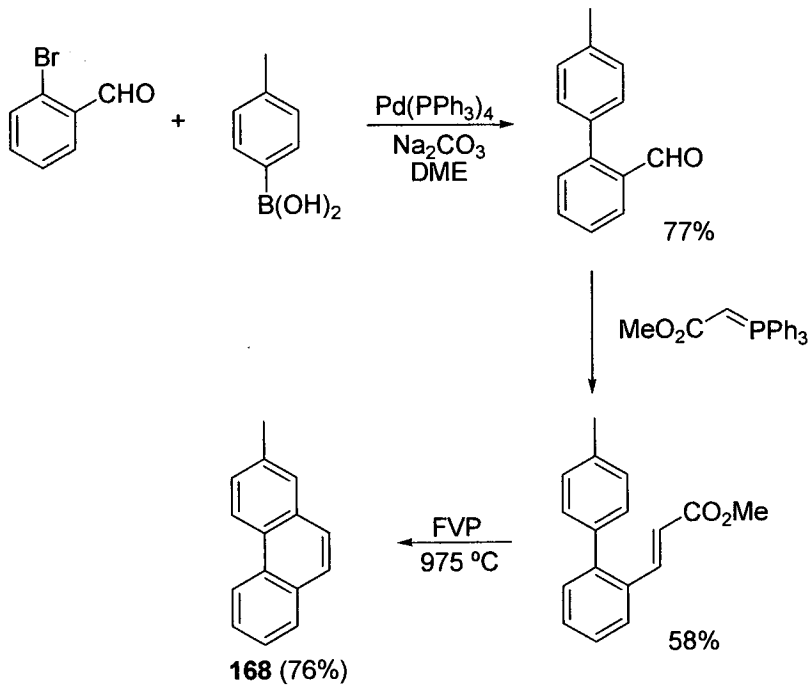


As expected the 2-substituted phenanthrene precursors **154**, **155** and **160** could only cyclise to give one product and there was no phenanthrene observed suggesting that all of the substituents are stable at high temperatures and no rearrangments or loss of substituents occur. Compounds **168**, **169** and **170** were obtained in 41%, 88% and 76% yield respectively.

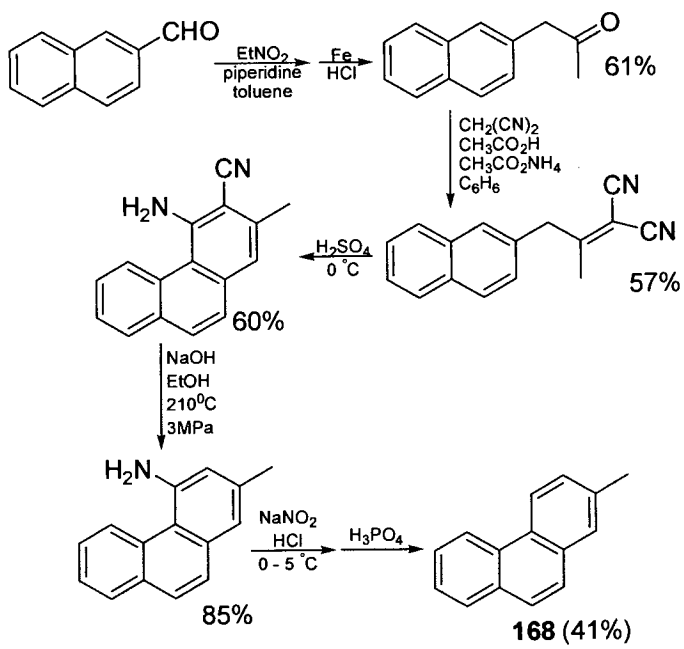


Scheme 71

The synthesis of **168** was performed by Tipping[21] in three steps from commercially available starting materials with an overall yield of 34% (**Scheme 72**).



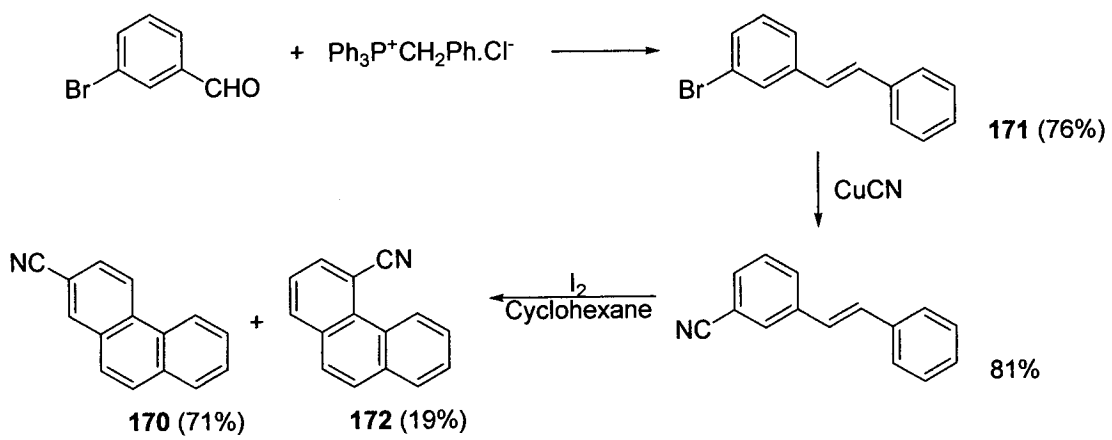
Scheme 72



Scheme 73

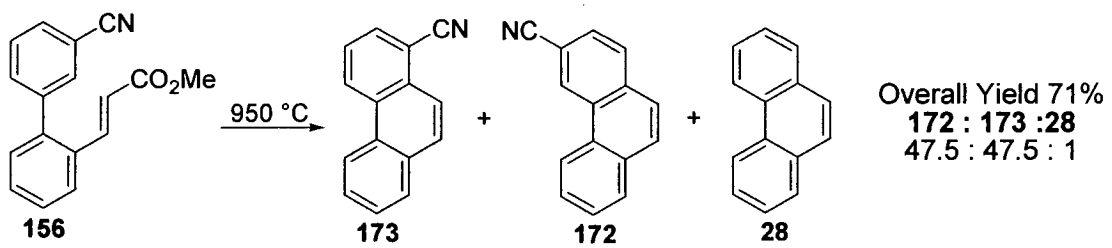
The advantages of the FVP method in synthesis can be exemplified by the cases of **168** and **170**. It was reported by Krasodomski *et al.*[46] in 2003 that **168** could be synthesised in an overall yield of 8% in five steps (**Scheme 73**). Comparison of these two syntheses shows that the FVP route produces **168** in a higher overall yield and in less steps.

Similarly the route to **170** published by Gore and Kamonah.[47] used 2-bromobenzaldehyde in a Wittig reaction to produce the bromo-substituted stilbene **171** (**Scheme 74**). The bromine atom was then exchanged for a cyano substituent using copper cyanide. The final photocyclisation step then takes place in the presence of iodine in cyclohexane to yield both **170** and **172** which required separation by preparative thin layer chromatography. Both **170** and **172** can be synthesised independently of each other using the FVP method discussed in the next section.



Scheme 74

Pyrolysis of the *meta*-substituted methyl ester precursor, **156**, could in principle produce two isomers by cyclisation *ortho* or *para* to the substituent and indeed both 1- and 3-cyanophenanthrenes, **173** and **172**, were observed in equal amounts (**Scheme 75**).



Scheme 75

Both **173** and **172** were known compounds and there were good literature data for both compounds with which to compare the ^{1}H NMR spectrum of the pyrolysate mixture so that it could be established that both compounds had been produced in equal yield (**Table 5**).

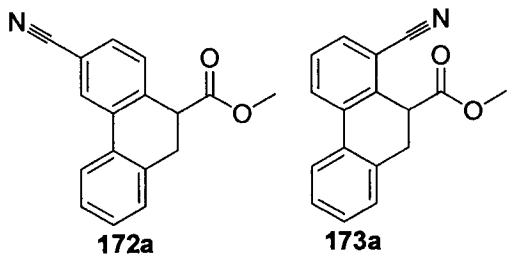
173[48] **Literature Data**	**173 Experimental Data**	**172**[48] **Literature Data**	**172 Experimental Data**
8.65 (1H, d, *J* 7.5)	8.61 (1H, d, *J* 7.3)	8.13 (1H, d, *J* 9.1)	8.07(1H, d, *J* 9.06)
9.02 (1H, s)	8.91 (1H, s,)	8.66 (1H, d, *J* 7.6)	8.53(1H, d, *J* 7.94)
		8.85 (1H, d, *J* 8.5)	8.84(1H, d, *J* 8.49)

Table 5 Comparison of Literature and Experimental ^{1}H NMR data of 142 and 143 (360 MHz in [^{2}H] chloroform)

Although the majority of the pyrolysate consisted of **172** and **173**, which could not be separated, a small amount of phenanthrene **28** was detected which suggests that some of the cyano-substituent is lost upon pyrolysis which was not seen in the case of the formation of the 2-isomer. This may occur in the final product or, more likely, at an intermediate stage.

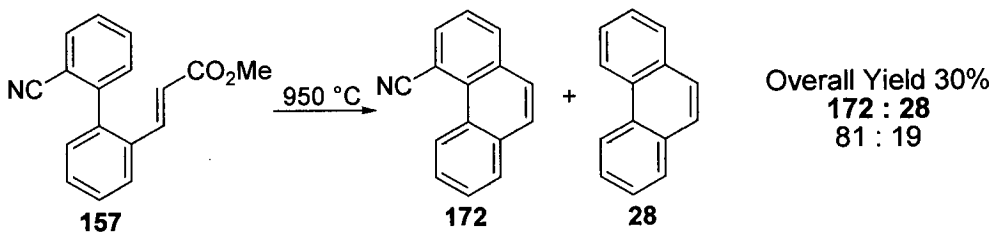
The intermediate **173a** shows that the substituent and the ester group are in close proximity whilst in **172a** the ester group is free from any steric hindrance and therefore

it was expected that **173** would be the minor isomer but as shown by the pyrolyses both **172** and **173** were produced in equal yields.



172a **173a**

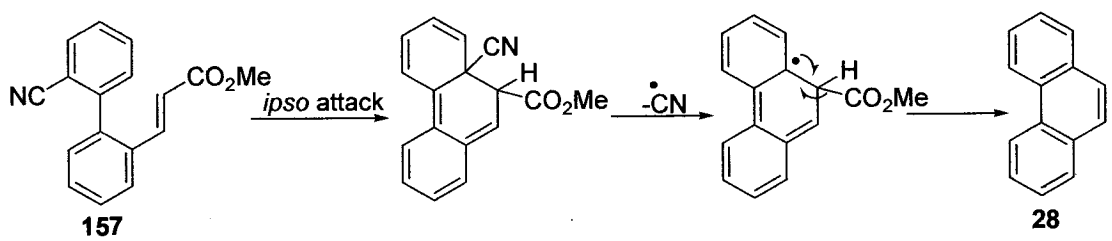
Pyrolysis of the *o*-isomer **157** was expected to produce only one product, **172**. Although no substituent migration was detected, there was a significant amount of phenanthrene **28** produced (**Scheme 76**).



157 **172** **28**

Scheme 76

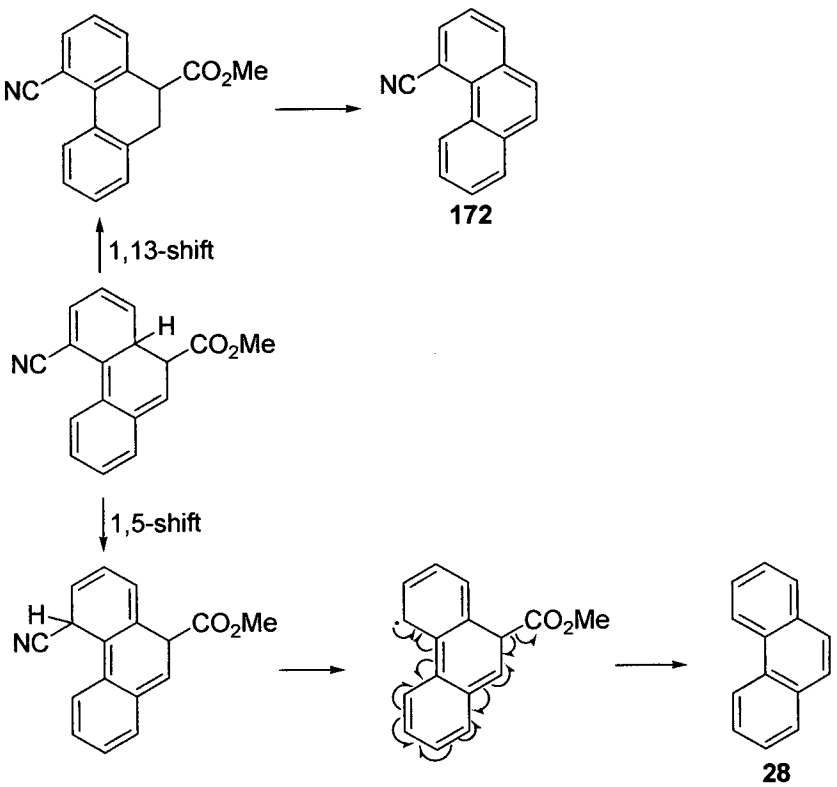
There are two possible explanations for the increased level of substituent loss in this case. One possibility is *ipso* attack and loss of the cyano group from the sp^3 site (**Scheme 77**). In this case a π-radical would be generated which is far more likely than production of a σ-radical by cleavage of CN from **172**.



157 **28**

Scheme 77

The other possibility is that one of two sigmatropic shifts might take place in the intermediate. Either a 1,5-shift would produce another intermediate which could lose the substituent as a radical. The subsequent rearrangement would result in the loss of the ester group to produce phenanthrene **28**. Alternatively, a 1,13-shift would produce an intermediate which would lose the ester group to produce **172** (**Scheme 78**).

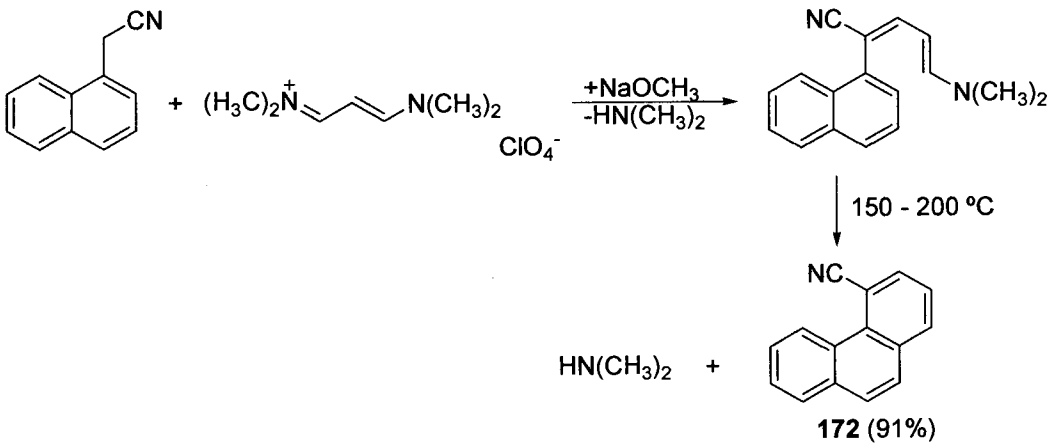


Scheme 78

There are 3 different syntheses of **172** in the literature. One of the reported syntheses produces **172** in 3% yield as a byproduct and therefore cannot be considered a useful synthesis.[49] As discussed earlier Gore and Kamonah[47] reported a route to **170** where **172** was the minor isomer produced.

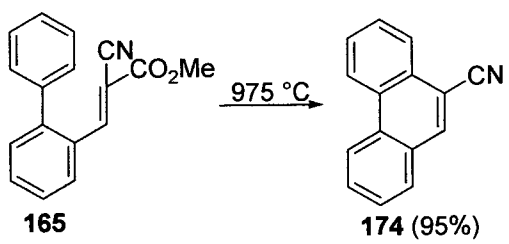
The only adequate synthesis of **172** was reported by Jutz and Wagner in 1972.[49] This synthesis relies on the cyclisation of an enamine *via* thermolysis at *ca.* 150 – 200 °C. The

enamine is produced by the reaction of 1-naphthylacetonitrile with a vinamidinium salt. Due to the formation of **28** in the FVP route this probably remains the method of choice for the synthesis of **172**.



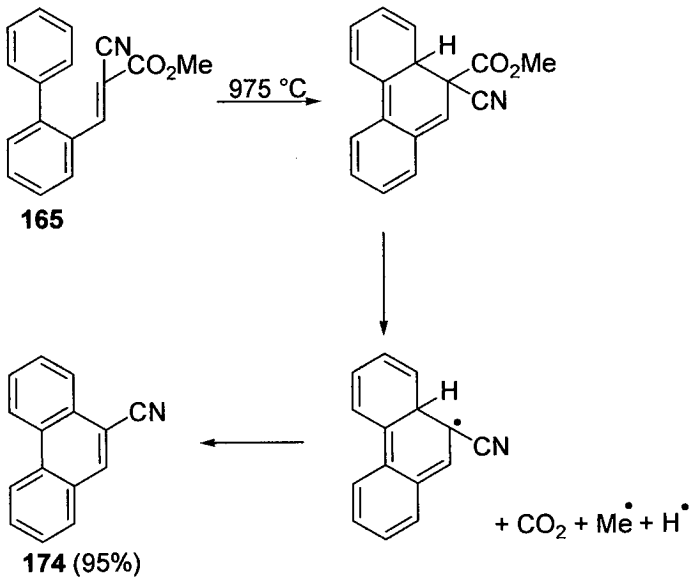
Scheme 79

Pyrolysis of the cyano-ester **165** produced a single isomer, **174**, as expected and no purification was required. Significantly there was no phenanthrene **28** or any other minor products produced in this pyrolysis (**Scheme 80**).



Scheme 80

The single product confirms the efficiency of the ester as a leaving group in these processes since, after the initial electrocyclisation, the ester group is lost *via* radical cleavage preferentially to the cyano-substituent (**Scheme 81**).

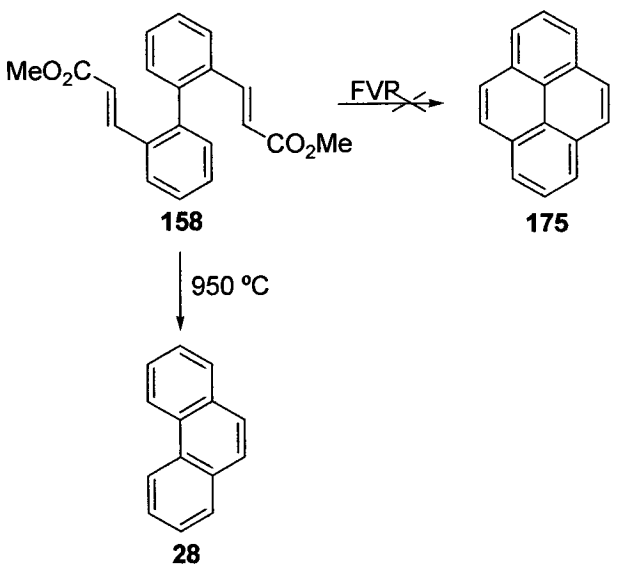


Scheme 81

Although this is a good route to **174** it should be noted that there are 178 references to **174** in the literature which include 13 original syntheses of **174**. Of these syntheses **174** is either a byproduct of negligable yield or is an intermediate which is not discussed in ten of them. The highest yielding of the remaining three syntheses was published by Goldberg *et al.*[50] who reported the bromination of phenanthrene followed by reaction with copper cyanide to yield **174** in 87% yield. However, in 1979 Gore *et al.*[51] reported a route to **174** directly from phenanthrene using cyanogen bromide with aluminium chloride as the catalyst. This new route produced **174** in 83% in one step by heating phenanthrene and the other reagents to reflux in carbon disulfide overnight. A similar route was reported by Yasuda *et al.*[52] who synthesised **174** in 78% yield *via* the photosubstitution of phenanthrene with sodium cyanide. All of these routes to **174** have reasonable yields and can be carried out simply from common starting materials. The main reason for synthesising **174** using a new FVP route as in **Scheme 81** was to determine if this type of FVP cyclisation could be used to form this type of substituted aromatic system and its use to synthesise larger and previously unknown systems will be discussed in chapters four and five.

In conclusion, this route has been shown to be an efficient synthesis of 2-cyanophenanthrenes **170** and 9-cyanophenanthrenes **174**. However, there is no selectivity in the pyrolysis of the *meta*-substituted case and therefore this is not a useful preparation of those products and the production of 5% phenanthrene **28** was a further complication.

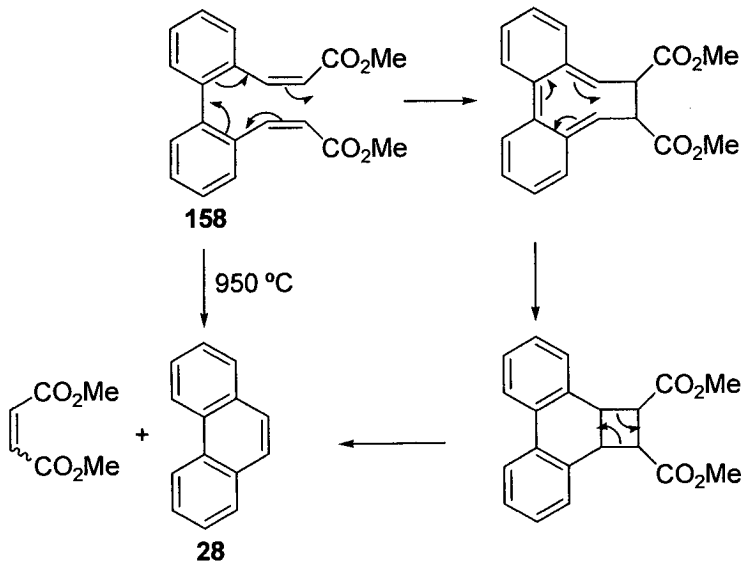
As previously discussed dialdehyde **142** had been recovered from some unsuccessful Suzuki coupling reactions where it had been formed by the self coupling of the boronic acid. The alkene **158** was produced by a Wittig reaction using two equivalents of Wittig reagent. It was thought that pyrolysis of this compound might produce pyrene **175** if both alkenes could cyclise under FVP conditions. However, the only product of the pyrolysis was phenanthrene **28** (**Scheme 82**).



Scheme 82

This unexpected result can be explained by the cyclisation to form a eight-membered ring which can rearrange to form a fixed six-membered ring and four-membered ring (**Scheme 83**). Further rearrangement would form **28** and an alkene evidence for which

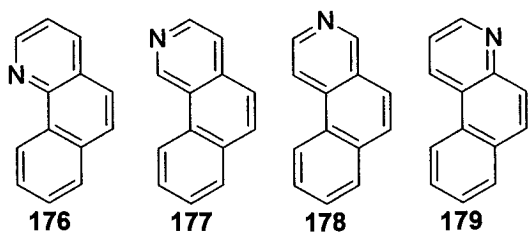
was seen in the ^{1}H NMR spectrum of the crude pyrolysate. Specifically a peak at δ_H 3.80 ppm is due to the two methyl groups of dimethyl fumarate and dimethyl maleate.[53]

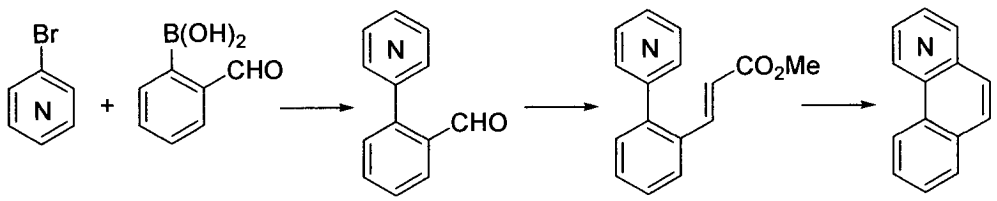


Scheme 83

3.2.2.2 Pyridines

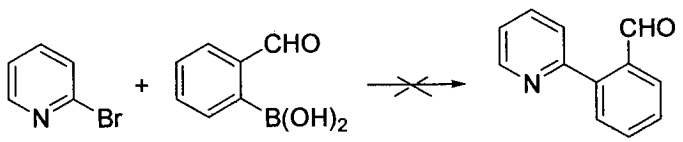
This route to phenanthrenes provides a concise method for the synthesis of benzoquinolines and benzoisoquinolines. Of the four possible benzoquinoline and benzoisoquinline isomers **176** – **179** the general route of **Scheme 84** has been used to provide access to three of the ring systems.





Scheme 84

Previous attempts to produce **176** using the route discussed involved 2-bromopyridine as the substrate for the Suzuki reaction, however this was unsuccessful, **Scheme 85**.



Scheme 85

It was discovered that Suzuki-Miyaura coupling of 2-bromopyridine with 2-formylphenylboronic acid using Sharp's conditions,[8b] which has been used successfully to to make the previous examples, gave no product which could be isolated by the usual work-up, but continuous extraction with dichloromethane over a period of 16 h gave a high yield of a single compound as a foamy solid.

The structure of this unknown product was established as 2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid **180** by the sequence of NMR experiments described below, which were carried out at 600 MHz in [$^2H_6$]acetone solution to maximize dispersion in the proton dimension (Figure 1).[54] The key features of this publication[54] are reproduced here.

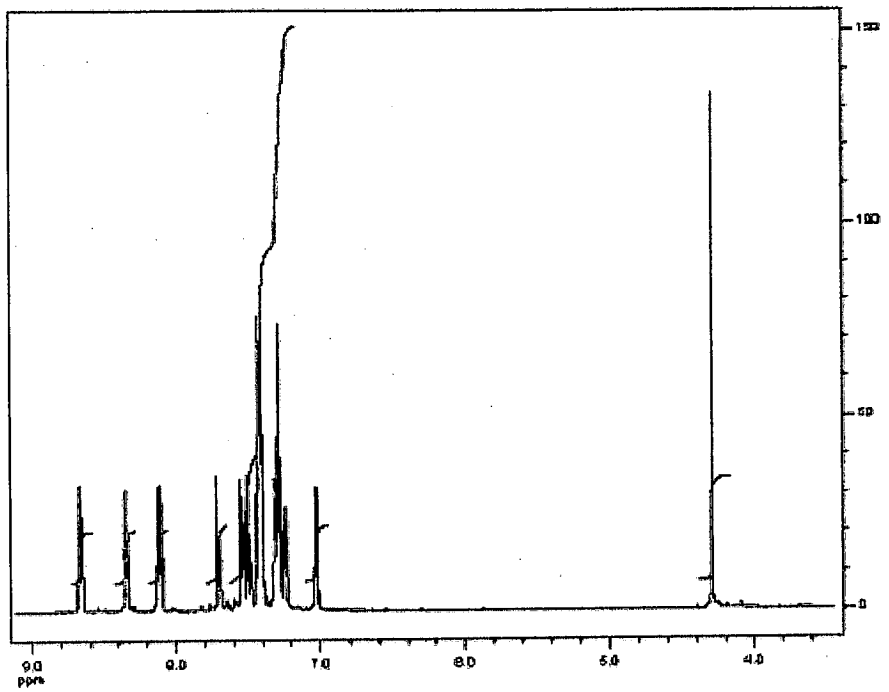
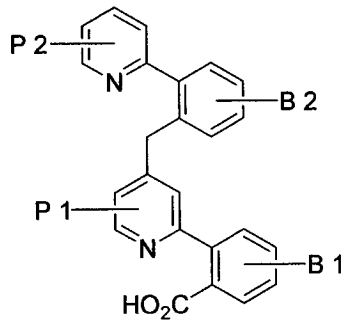


Figure 10. ^{1}H NMR spectrum (600 MHz, acetone-d_6) of 180

The correlation of ^{1}H and ^{13}C chemical shift values shown in Table 1 was obtained by a ^{1}H/^{13}C HSQC experiment. A ^{1}H TOCSY experiment permitted the grouping of the ^{1}H signals into spin systems establishing the presence of three 4-spin systems (signals K, L, M and P designated B1; signals D, G, N and R, designated P2; signals E, F, H and J, designated B2) and one 3-spin system (signals B, C and Q designated P1) in addition to the methylene group (signal A, δ_H 4.29) and that due to the carboxylic acid.

Identification of the components of the 3-spin system P1 suggested that it was likely to be due to a 2,4-disubstituted pyridine unit and a ^{1}H NOESY experiment showed that the methylene group was attached to the 4-position of this pyridine ring (*via* NOE correlations between signals A and C and also between signals A and B, thereby defining the position of the CH_2 with respect to P1). The 2-substituent of the disubstituted pyridine was identified as the 4-spin system B1, from the NOESY relation between signals C and K. Confirmation that the carboxylic acid group was attached to B1 was arrived at from a ^{1}H/^{13}C HMBC experiment, in which correlations were detected

between signals K and P (both previously designated B1) and the ^{13}C signal at δ_C 168.9 (corresponding to the carbonyl carbon atom of the carboxylic acid).



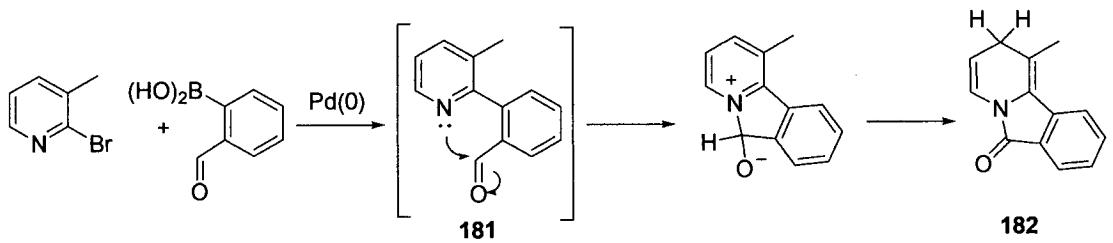
180

Close inspection of the NOESY data reveal a correlation between signals A and F, thereby establishing the P1 – CH_2 – B2 connectivity pathway. The linkage between rings P2 and B2 was confirmed from correlations present in the $^1H/^{13}C$ HMBC experiment, between a quaternary ^{13}C signal at δ_C 159.6 (due to a C2 of the pyridine ring) and ^1H signals G (from P2) and H (from B2). Therefore, having established the B1 – P1 – CH_2 – B2 – P2 linkage, along with the nature and substitution patterns of the precursors, only the 2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid structure **180** is consistent with the data.

H-1 Label	δ_H (^{1}H)	*J*/Hz	δ_H (^{13}C)	Spin system
A	4.29	S	37.8	
B	7.01	4.6	122.9	P1
C	7.27	S	123.6	P1
D	7.31	7.7, 4.9, 1.1	122.2	P2
E	7.38	6.7, 2.5	127.2	B2
F	7.40	*	128.6	B2
G	7.41	*	131.0	P2
H	7.42	*	124.3	B2
J	7.44	*	130.3	B2
K	7.48	*	130.3	B1
L	7.50	*	128.2	B1
M	7.58	7.4, 1.4	131.0	B1
N	7.80	7.7, 1.8	136.6	P2
P	7.85	7.7, 1.1	130.3	B1
Q	8.36	4.9	148.3	P1
R	8.67	4.6	148.9	P2

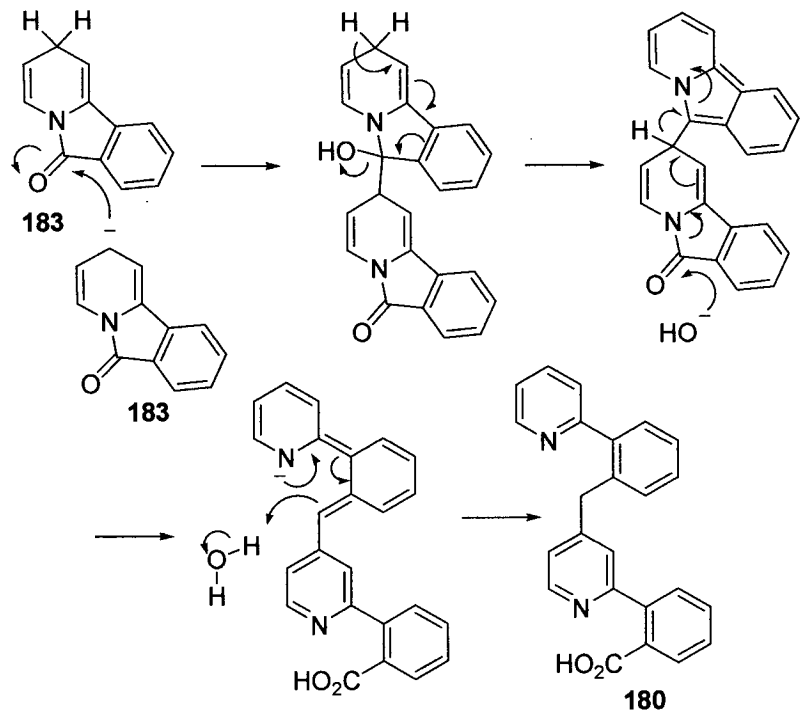
Table 6 Correlation of ^{1}H and ^{13}C NMR signals of 151 (600 MHz in [$^2H_6$]acetone) (* Complex region of overlapping signals)

In 2006 Mamane and Fort reported that anomalous products were obtained when certain 2-halogenopyridines and related heterocycles were coupled with 2-formylphenylboronic acid.[55] The initial coupling product **181** undergoes a cyclisation and formal hydride shift to provide pyrido[2,1-*a*]isoindolones **182** (**Scheme 86**). Other workers have reported very low yields of coupling products in similar reactions.[56]



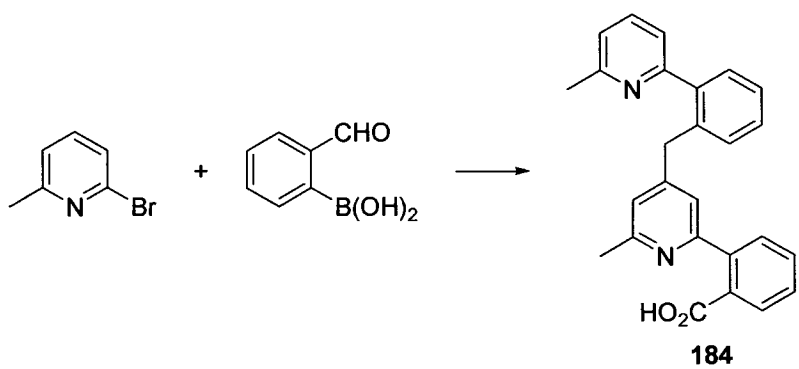
Scheme 86

This new work led to the consideration that **180** may have been produced *via* a similar mechanism. A mechanistic scheme for the formation of **180** must explain the concomitant disproportionation of two aldehyde groups and the functionalization of an unactivated pyridine ring in the 4-position by a substituted benzyl group. It is likely that the parent pyrido[2,1-*a*]isoindolone **183** (*c.f.* **182**) is an intermediate and a possible rationalization is shown in **Scheme 87**. Condensation of two molecules of **183** is possible under the basic conditions of the Suzuki-Miyaura coupling. Dehydration, hydride shift (already implicated in the formation of **182**) and rehydration complete the process.



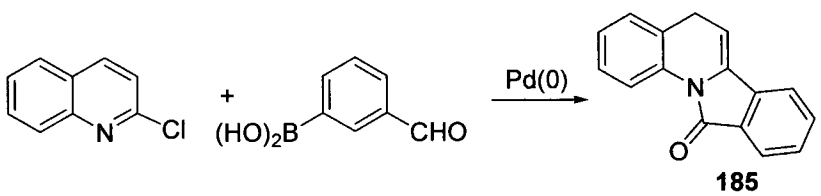
Scheme 87

As a second example of this dimerisation process, reaction of 2-formylphenylboronic acid with 2-bromo-6-methylpyridine gave the corresponding product **184** after continuous extraction of the reaction mixture.



Scheme 88

Reaction of 2-chloroquinoline under our conditions gave **185** which shows that the reaction conditions used to produce **180** can be used to give the same results as those published by Mamane and Fort (**Scheme 89**).[55]

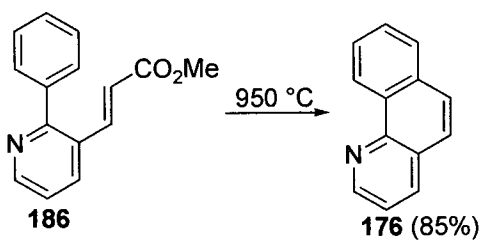


185

Scheme 89

In conclusion, unexpected products have been obtained under Suzuki-Miyaura coupling conditions when a 2-formylphenyl group is present at a site adjacent to a pyridine-type nitrogen atom. These observations complement those of Mamane and Fort[55] and provide a new, readily available pyridine scaffold for further investigation.

Compound **176** has now been synthesised from **186** using the same new route used to synthesise the phenanthrenes (**Scheme 90**).



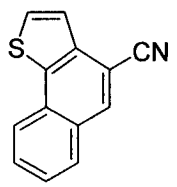
186 **176** (85%)

Scheme 90

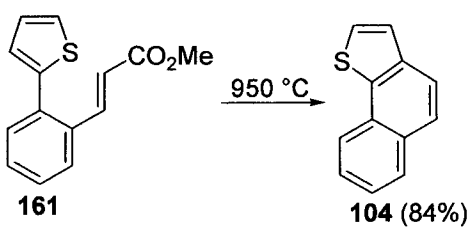
This route has now been shown to be an efficient route to benzoquinolines and benzoisoquinolines. It may also be possible to use substituted bromopyridines so that substituted benzoquinolines and benzoisoquinolines may be synthesised.

3.2.2.3 Thiophenes

This route to phenanthrenes and azaphenanthrenes can be extended to synthesise naphthothiophenes. As discussed in **Section 3.1.2** some of the cyclisation products of 2-thiophene derivatives, including **187**[57], have previously been synthesised using FVP. As expected pyrolysis of **161** produced **104**, in good yield, which in agreement with the proposed mechanism was the only possible isomer (**Scheme 91**).



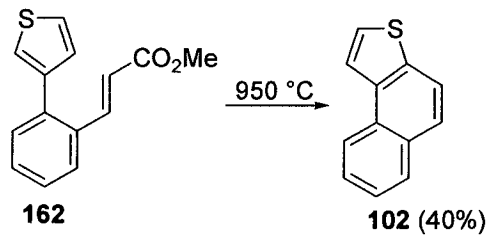
187



161 **104** (84%)

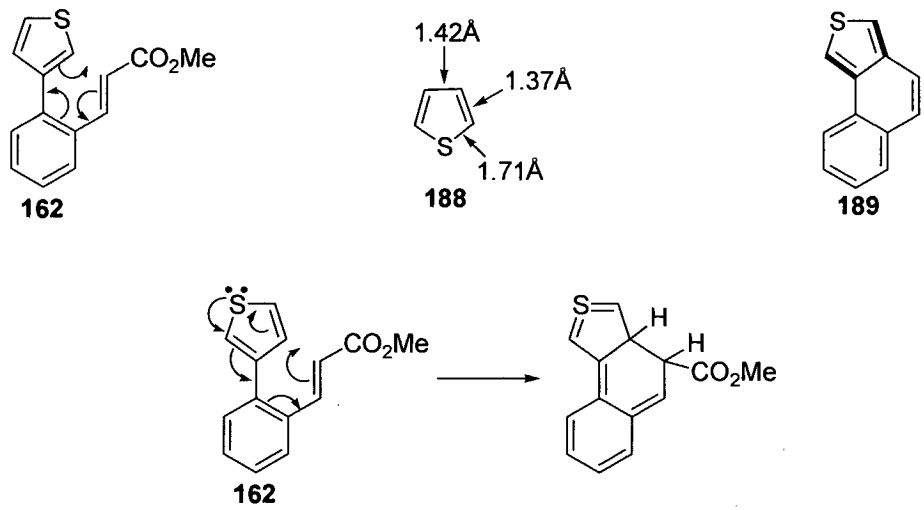
Scheme 91

Although the cyclisation reaction of the 3-thiophene derivative **162** has the potential to form two isomers, **189** and **102**, it was expected to only produce **102** (**Scheme 92**). There are three main reasons for this expectation. Firstly, and most importantly, the bonds in **161** are already perfectly positioned for the electrocyclisation to occur. If the cyclisation went to position 3 then the intermediate would be very high in energy as sulfur atom has an expanded valence shell (**Scheme 93**).



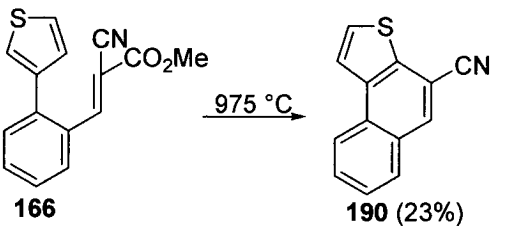
Scheme 92

Secondly the 3-4 bond, **188**, is longer than the other C-C bonds in thiophenes and therefore the structure of **189** is strained. Finally the bonds highlighted in **189** are *o*-quinonoid and thus the adjacent six-membered ring is not truly aromatic in nature. Therefore the other isomer **102** is preferentially formed by pyrolysis.



Scheme 93

The pyrolysis of **166** also produced, for the same reasons, a single isomer **190** (**Scheme 94**).



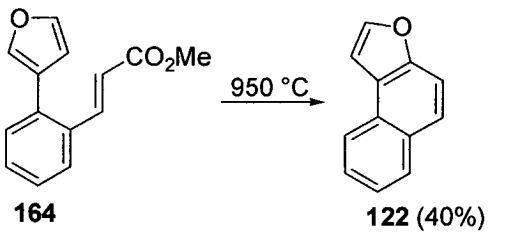
166 **190** (23%)

Scheme 94

It has now been demonstrated that the pyrolysis of these 2-thiophene precursors are a good route to naphthothiophenes. The synthesis of **190** has shown that this is also a reasonable route to substituted naphthothiophenes.

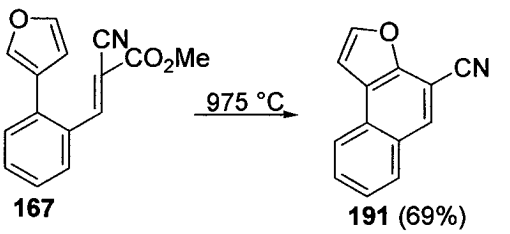
3.2.2.4 Furans

The naphthofurans produced are analogous to the thiophene compounds previously discussed.



164 **122** (40%)

Scheme 95

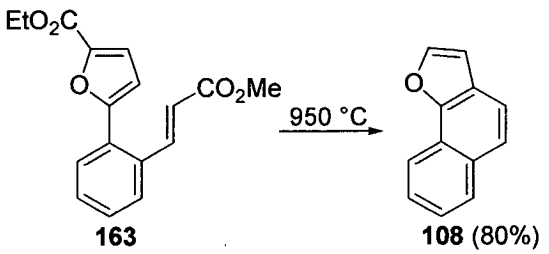


167 **191** (69%)

Scheme 96

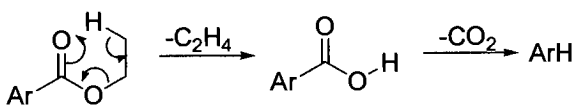
The 3-furan precursors, **164** and **167**, were pyrolysed under the same conditions as the thiophenes. Both of the pyrolysates, as in the thiophene case, contained single isomers, **122** and **191** respectively (**Scheme 95** and **Scheme 96**).

The 2-furan compounds were synthesised from readily available 5-bromofuroic acid ethyl ester. The pyrolysis of **163** produced the single isomer, **108** (**Scheme 97**).



Scheme 97

This is a new reaction as not only does the cyclisation and the oxidative de-esterification take place but the ethyl ester group is lost during the pyrolysis. There is a two-fold reason as to why the ethyl ester was lost under FVP conditions (**Scheme 98**). Firstly it is known that ethyl esters undergo ester *cis*-elimination upon pyrolysis to produce the carboxylic acid.[58] Secondly it is known that carboxylic acids decarboxylate under FVP conditions.[59]

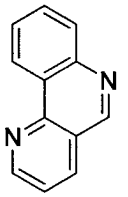


Scheme 98

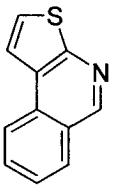
It has now been shown that this an efficient route to naphthofurans from 3-bromofurans. Moreover it has been shown that it is possible to produce naphthofurans from 2-substituted furans by using the ethyl ester **163** which is a route specific to FVP.

3.2.2.5 Oxime Ethers

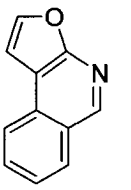
All of the oxime ethers synthesised, **150** – **153**, were pyrolysed at 700 °C as this had previously been shown to be the optimum furnace temperature for this cyclisation.[60] All of the oxime ethers, except **152**, cyclised *via* iminyl radicals to produce products as single isomers **192** – **194**; the mechanism of this reaction will be discussed in Chapter 4.



192 (78%)

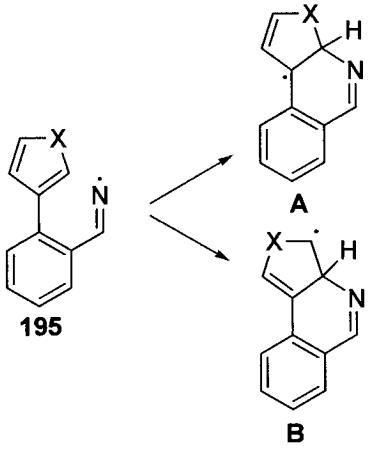


193 (65%)



194 (13%)

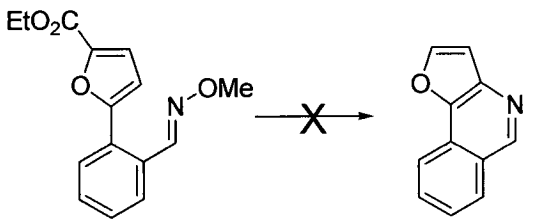
Both **193** and **194** were obtained as single products. In both cases there was no cyclisation to the 4-position observed. As discussed in chapter 1 pyrolysis of the oxime ethers results in cyclisation *via* iminyl radicals. When considering the radicals that are formed in the cyclisation reaction it is possible to rationalise the single isomers produced upon pyrolysis.



Scheme 99

If the cyclisation of **195** takes place at the 2-position radical intermediate **A** will be produced which will be resonance stabilised through the aromatic structure (**Scheme 99**). Radical **B** would be produced if the cyclisation took place at the 3-position. This radical cannot be stablised through the rest of the structure. As expected the reaction goes *via* the more stable intermediate.

Compound **152** did not give the expected product (**Scheme 100**). It was observed that the starting material had decomposed in the inlet and this was verified by the ^{1}H NMR spectrum of the residue so no further analysis was carried out.



152 **196**

Scheme 100

The pyrolysis of oxime ethers has been demonstrated to be a suitable route to benzonaphthyridines and the thiophene analogue but not the furan analogues, although the yield of **194** may be increased by repetition of the reaction.

3.3 Conclusion

In conclusion it has been proved that the reaction described in **Scheme 11** can be used to synthesise a wide variety of three-ring systems. The generality of this reaction has been shown by its ability to produce furan, thiophene and pyridine analogues of phenanthrene as well as 2- and 4-substituted phenanthrenes. The synthesis of cyano, methyl and chloro substituted systems has shown that this methodology could be used in the future to produce starting materials for other reactions.

In addition, the known cyclisation reaction of oxime ethers under FVP conditions *via* iminyl radicals has been shown to be a useful method of synthesising three-ring systems containing a nitrogen in the central ring.

Finally, the unusual reaction of 2-bromopyridine and 2-formylphenylboronic acid under Suzuki coupling condition has been noted and the structure of the unexpected product has been determined.

4 Four-Ring Systems

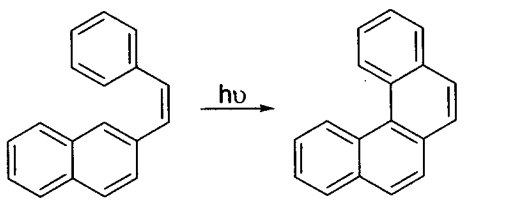
4.1 Introduction

4.1.1 Benzo[c]phenanthrene

The synthesis of benzo[*c*]phenanthrene **198** is not quite as well documented as the synthesis of phenanthrene **28**. Nevertheless, there are over one thousand papers regarding the synthesis of **198** reported in the literature of which several can be discounted as **198** is a byproduct produced in very low yield or is a degradation product from a more complicated starting material. This chapter will consider the synthesis of benzo[*c*]phenanthrene **198** and its heterocyclic analogues.

4.1.1.1 Photochemical Cyclisation

As in the synthesis of phenanthrene photochemical cyclisation can be used to produce **198**. In 1965 Mallory and Wood[61] reported that irradiation of the stilbene **197** produced **198** in good yield *via* photochemical cyclisation (**Scheme 101**).

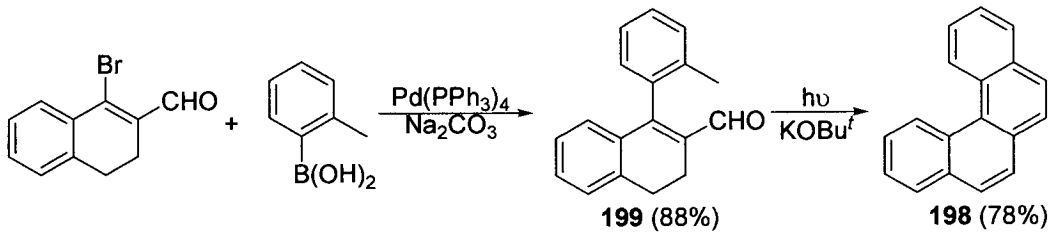


197 **198** (65 - 75 %)

Scheme 101

This reaction was later repeated by Scholz *et al.*[62] who reported similar results.

In 2000 de Koning *et al.*[63] reported that irradiation of **199**, synthesised *via* a Suzuki coupling reaction, produced **198** in the presence of a base (**Scheme 102**). Previous work had shown that using potassium ^{t}butoxide produced the highest yield.

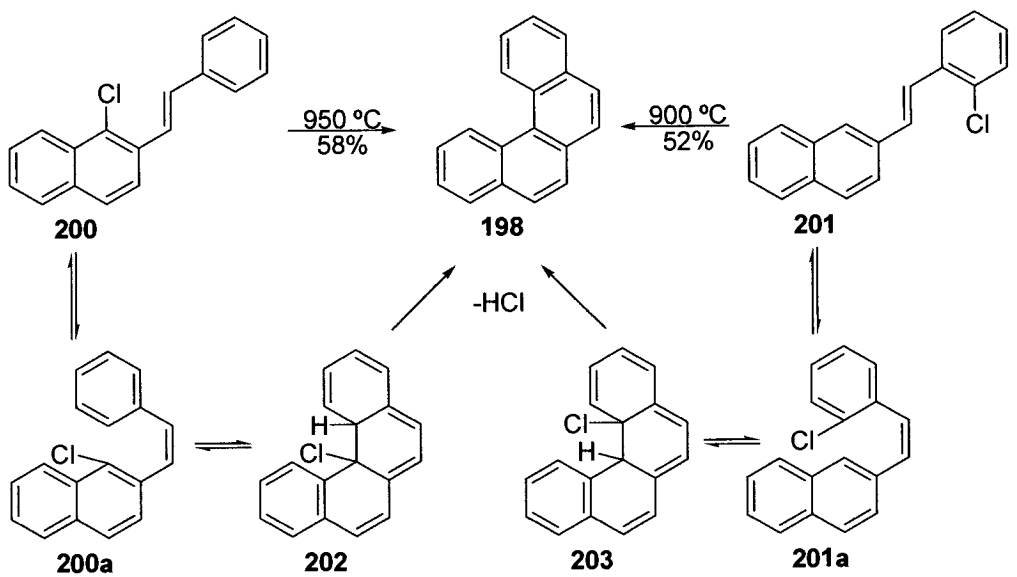


Scheme 102

The cyclisation to form **198** occurs in good yield and there are no side products reported. This synthetic methodology has been used to synthesise a variety of substituted condensed ring systems and it appears to to give high yields of the desired products in most cases. At this time the mechanism of this reaction and the reason for specifically requiring potassium ^{t}butoxide are both unknown.

4.1.1.2 Flash Vacuum Pyrolysis

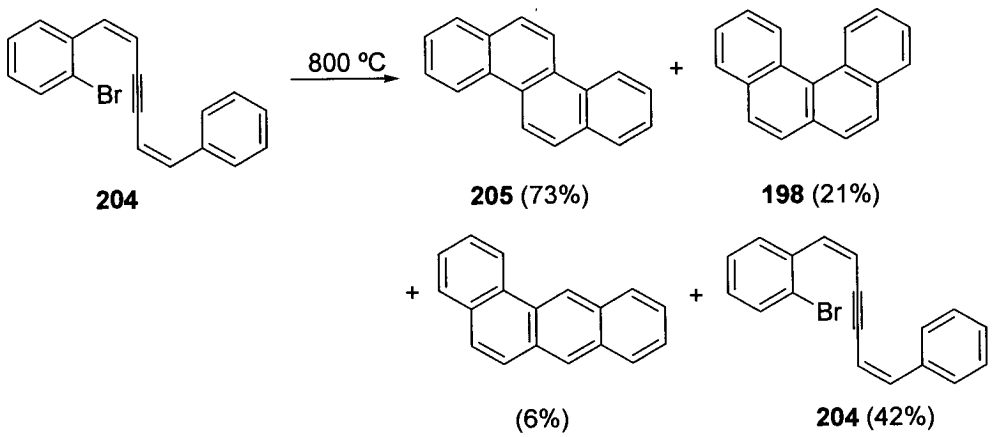
One of the other techniques used in two different ways to synthesise **198** is FVP. In 1994 Plater reported that the pyrolysis of stilbene produced phenanthrene and that the pyrolysis of 1-chlorostilbene produced phenanthrene in a much higher yield.[64]



Scheme 103

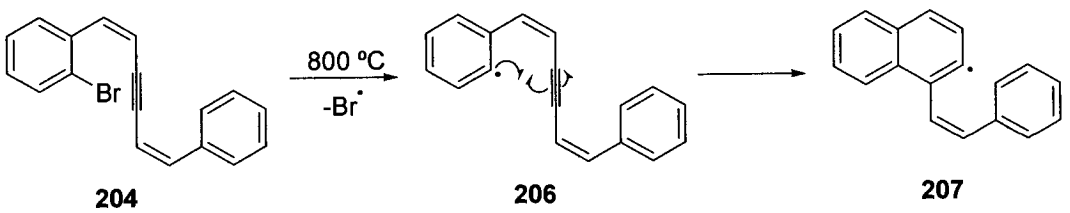
This route was extended to the synthesis of **198** by the pyrolysis of both **200** and **201** (**Scheme 103**). Under FVP conditions stilbenes undergo *cis-trans* isomerisation to form **200a** and **201a**. Gas phase electrocyclisation forms **202** and **203** which can both lose HCl to form **198**.

The only other FVP synthesis of **198** was published by Tobe *et al.*[65] in 2002 which reported tandem cyclisation of diaryldienynes under FVP conditions. Using a variety of pyrolysis temperatures it was discovered that pyrolysis of **204** at 800 °C produced the highest yield of **198** (**Scheme 104**).



Scheme 104

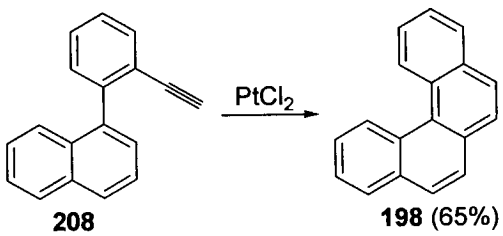
Unfortunately in this reaction **198** is only a side product and the main product is chrysene **205** and there was 42% recovery of starting material. The FVP precursor was simply synthesised from the bromostyrene *via* a Sonogashira reaction followed by a deprotection followed by a second Sonogashira coupling. It was suggested that **204** forms **198** *via* a radical reaction (**Scheme 105**). Loss of the bromine radical to form **206** followed by cyclisation would form **207** which can produce the three products shown in **Scheme 104** by rearrangement mechanisms.



Scheme 105

4.1.1.3 Metal Catalysed Cyclisation

As in the synthesis of phenanthrene, Fürstner *et al.*[27] have used the cyclisation of alkynes with a metal catalyst to synthesise **198**. Using 5 mol% of a platinum catalyst **198** was produced in good yield (**Scheme 106**).

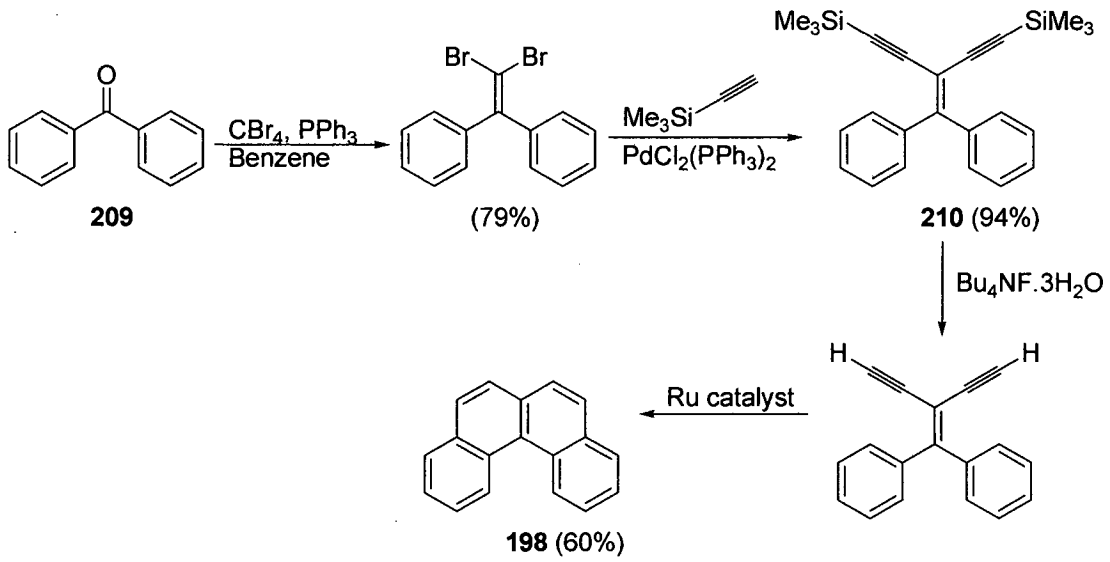


Scheme 106

As discussed in chapter 3 the metal and alkyne form a complex which can then cyclise *via* two different routes. In the case of **208** the cyclisation is reported to go *via* the 6-endo pathway.

Another route to **198** also involves a metal catalysed cyclisation as the final step of the synthesis. In 2004 Donovan and Scott[66] reported the synthesis of **198** in four steps from benzophenone **209** (**Scheme 107**).

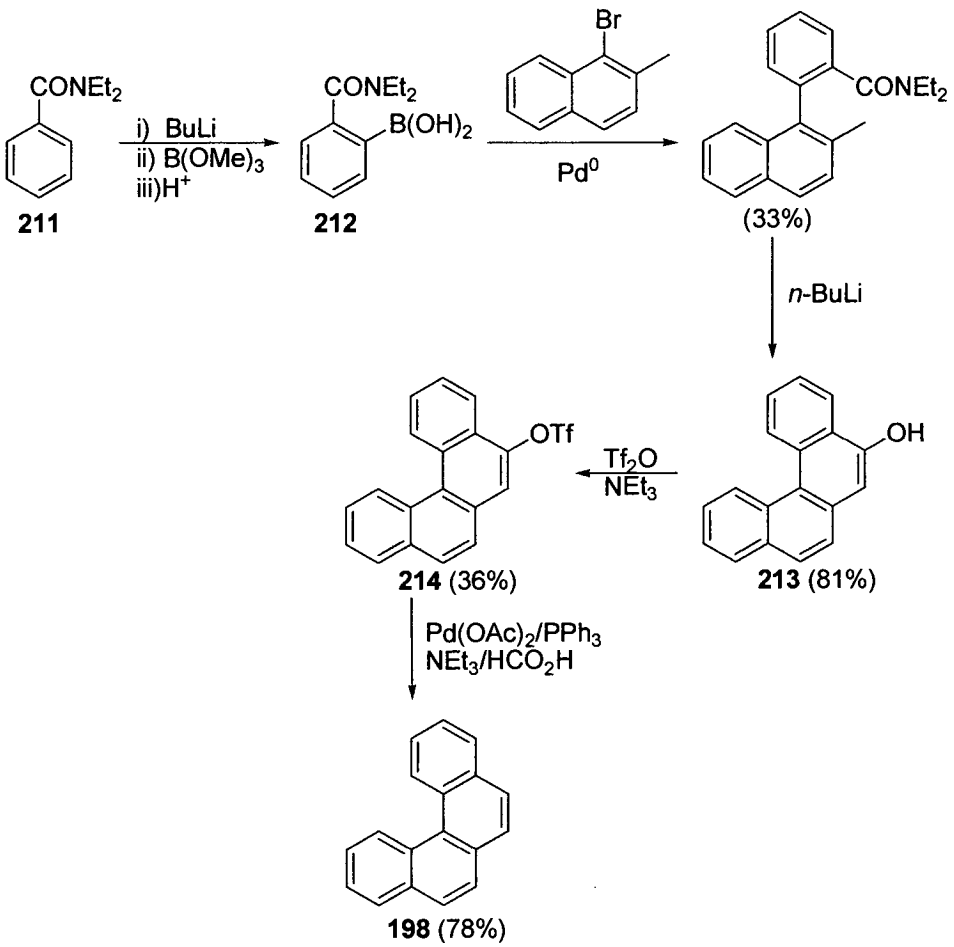
Using a Corey-Fuchs olefination reaction benzophenone was transformed into the dibromide which in turn, *via* a Sonogashira coupling reaction, produced **210** in good yield. After desilylation the final cyclisation reaction was effected using the ruthenium catalyst $RuCl_2$-(PPh_3)(η^6-cymene) producing **198** in 60% yield over the last two steps.



Scheme 107

4.1.1.4 Other Methods

The cyclisation in the final route to **198** involves the synthesis of the hydroxybenzophenanthrene **213** which was then transformed into **198** *via* the triflate **214**.[67] The basic structure required for the cyclisation was the product of a Suzuki coupling reaction between the boronic acid **212** and 1-bromo-2-methylnaphthalene. The boronic acid **212** had to be synthesised from **211** in the standard way. The next step was a remote metallation followed by cyclisation using butyllithium to produce **198** in an overall yield of 7.5% (**Scheme 108**).

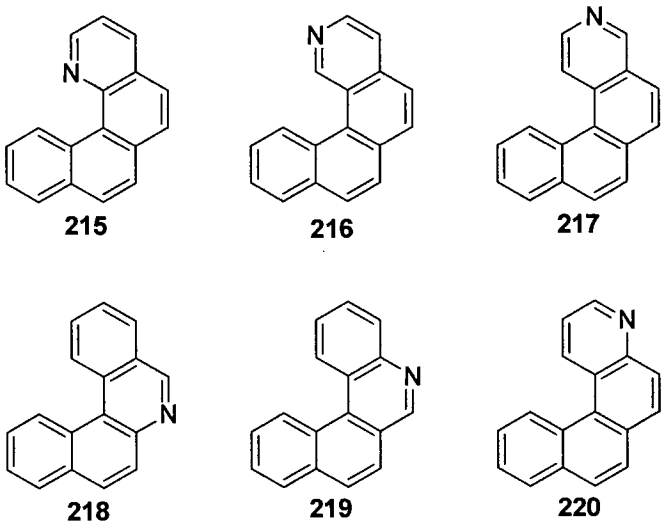


Scheme 108

4.1.2 Aza-analogues

It is known that many polycyclic aromatic hydrocarbons (PAHs) are carginogenic. However it is also known that structures which are prone to reaction are more easily metabolised and therefore more easily removed from the body.[68] If PAHs are not readily metabolised they can remain in the human body indefinitely where, as a foreign substance, they can cause damage. It is known that PAHs can be metabolised *via* oxidation by cytochrome p450.[69] Due to the mutagenicity of this particular class of compounds[70] it was felt that increasing the reactivity of the compounds synthesised for this thesis by addition of a nitrogen heteroatom would be safer. Therefore the toxicity of

these compounds may be reduced by inclusion of a nitrogen atom in the ring skeleton as this provides a point of reaction for metabolism. Due to anticipated reduced toxicity this thesis will discuss the synthesis of the aza-analogues of **198**.



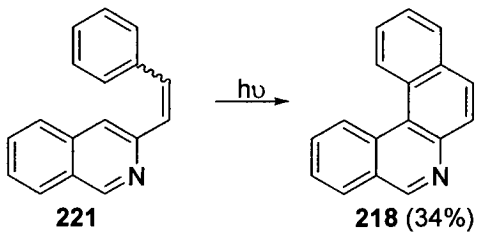
215 **216** **217**

218 **219** **220**

There are six potential aza-analogues of benzo[*c*]phenanthrene all of which are known, although the syntheses of **215**, **218** and **219**, are best discussed in the literature. As in the synthesis of **198** there are a variety of cyclisation reactions which can be used to synthesise nitrogen containing ring systems.

4.1.2.1 Photochemical Cyclisation

As in the synthesis of **104** it is possible to produce four-ring systems *via* the photochemical cyclisation of stilbene type precursors. This type of reaction has been used to synthesise 6-azabenzo[*c*]phenanthrene **218** from 3-styrylisoquinoline **221** (**Scheme 109**). The yield of this reaction is relatively high in comparison to the other photoinduced cyclisations recorded by Loader and Timmons.[71]

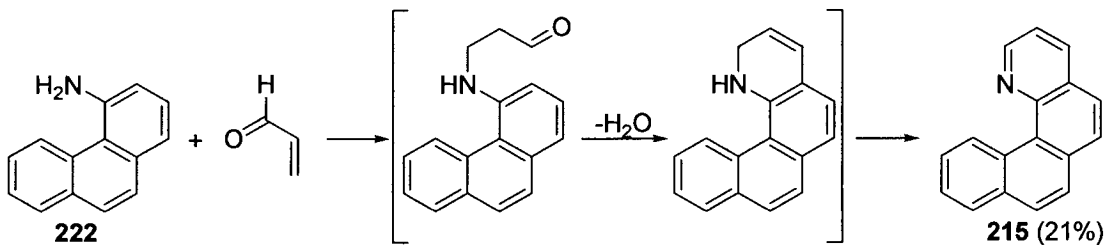


221 **218** (34%)

Scheme 109

4.1.2.2 Skraup Synthesis

One of the most common syntheses of quinolines is the Skraup synthesis which is the reaction of an amine with glycerol in the presence of concentrated sulfuric acid and a mild oxidising agent. It was reported by Cook *et al.*[72] that it was possible to synthesise 1-azabenzo[*c*]phenanthrene **215** from 4-aminophenanthrene **222** using the Skraup synthesis (**Scheme 110**).

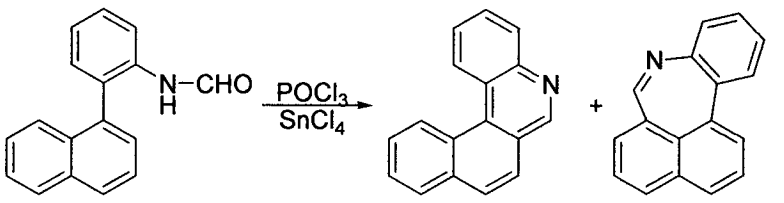


222 **215** (21%)

Scheme 110

4.1.2.3 Other Methods

The final route to monoaza four-ring systems is a unique synthesis of **219** from a formamide **223** using phosphorus oxychloride and tin (IV)chloride (**Scheme 111**). Unfortunately **219** is the minor product of this reaction as the formation of **224** seems to be favoured.



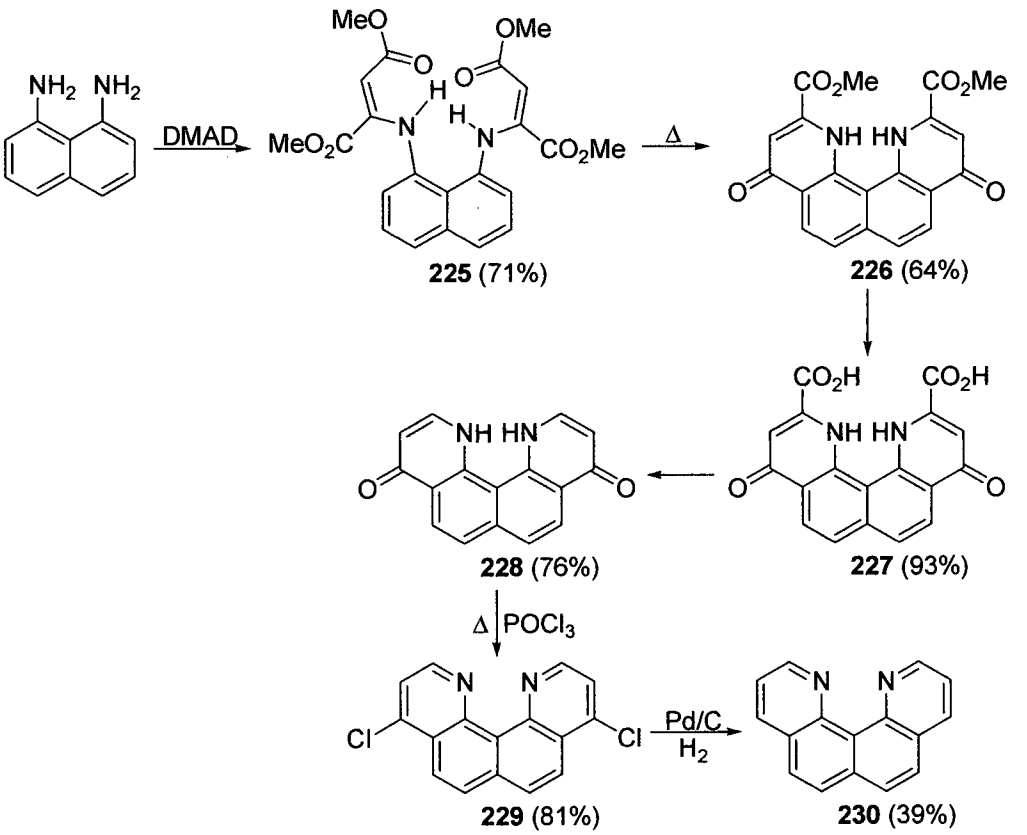
223 **219** (20%) **224** (32%)

Scheme 111

There was no discussion of the mechanism to suggest why the more strained seven-membered ring of **224** is more favoured than **219**. However it can be assumed that **224** has a slightly higher yield as reaction at a naphthalene alpha-position is often the kinetically favoured.

4.1.2.4 Diaza Analogues

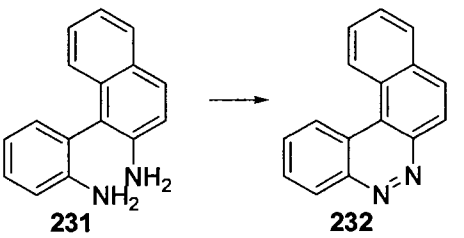
There are thirty-six possible diaza analogues of benzo[*c*]phenanthrene **198** although only seven are referenced in the literature and the synthesis of only three of those is discussed. The most widely reported diaza four-ring system is quino[7,8-*h*]quinoline **230**. The first two literature reports of **230**[73] have both now been discredited as more modern analysis of the products showed that **230** had not been produced in either case.[74] The only confirmed synthesis of **230** was reported by Staab *et al.*[75] in 1987 (**Scheme 112**). The first step of this route is the reaction of 1,8-diaminonaphthalene with dimethyl acetylenedicarboxylate (DMAD) to produce **225**. Thermal cyclisation of **225** produced **226** which upon alkaline hydrolysis produced **227**. The decarboxylation of **227** in a sublimation apparatus resulted in the dione **228**. The dione then produced **229** on heating with phosphoryl chloride. The final step of this synthesis was the catalytic hydrogenolysis of **229** to produce **230**.



Scheme 112

This synthesis, although lengthy, is relatively high yielding in all but the last step. The final product **230** was verified by NMR spectroscopy and mass spectrometry. Staab also reported the highly basic character of **230** and its ability to behave as a proton sponge.

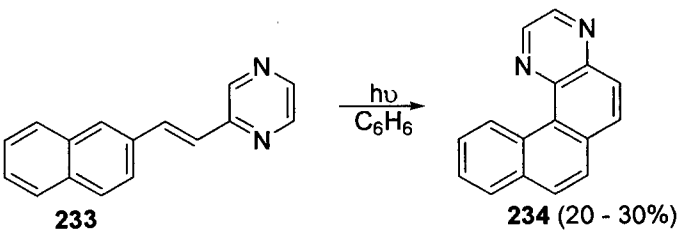
The other two isomers reported are far less discussed in the literature. The first of these was naphtho[*c,f*]cinnoline **232** as reported by Badger and Walker (**Scheme 113**).[76] The final ring-forming step in this synthesis was the oxidation of **231** with permonosulfuric acid to form **232** although the yield of the reaction was not reported. As this paper was published in 1956 **232** was characterised by the UV absorption spectrum, melting point and elemental analysis, however this reaction has since been used to synthesise similar compounds.[77]



231 232

Scheme 113

The final example of these compounds was the synthesis of **234** reported by Ohta *et al.*[78] where the final cyclisation step is, as previously discussed, a photochemical cyclisation of a stilbene type precursor **233** (**Scheme 114**).



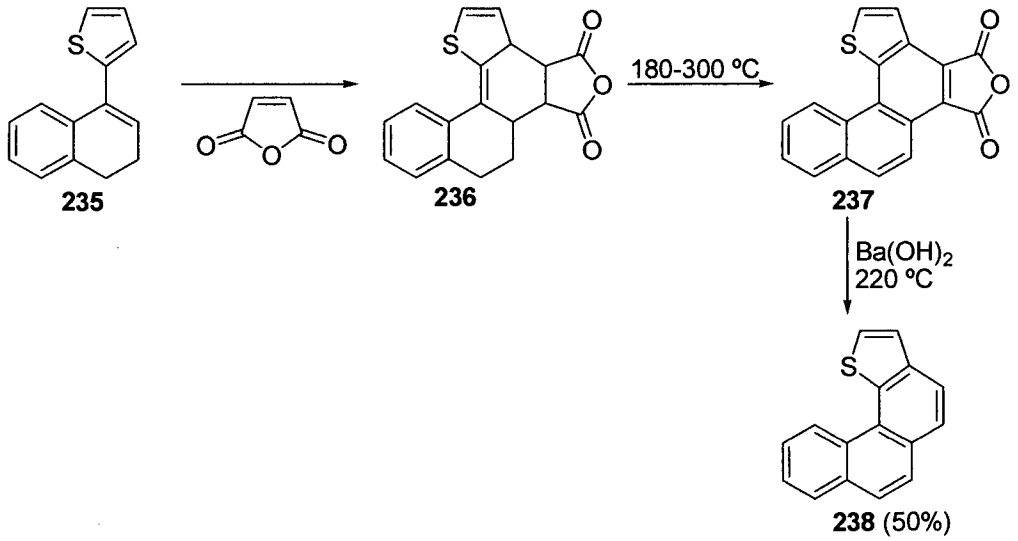
233 **234** (20 - 30%)

Scheme 114

4.1.3 Thiophene Analogues

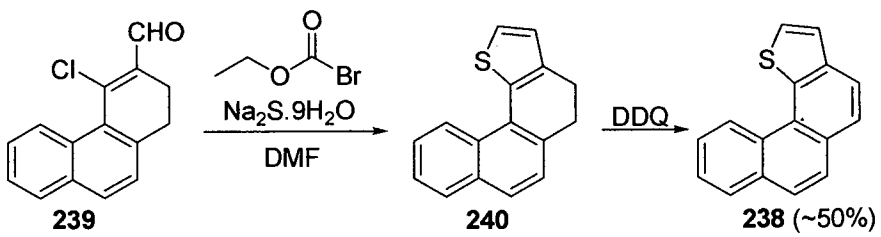
As with the three-ring systems the amount of literature about the phenanthrothiophenes and phenanthrofurans is dramatically less than their carbocyclic analogues. However both phenanthrothiophenes are referred to in studies of pollutants produced by burning coal and are commercially available in milligram quantities.

The first published synthesis of phenanthrothiophene **238** was reported in 1950 by Szmuskovicz and Modest (**Scheme 115**).[79] Cycloaddition of **235** and maleic anhydride produced **236**. Dehydrogenation of **236** followed by decarboxylation in a heated pyrex tube gave **238** in reasonable yield. In this case the yields of the intermediates were not reported so it is hard to compare this synthesis to those reported since.



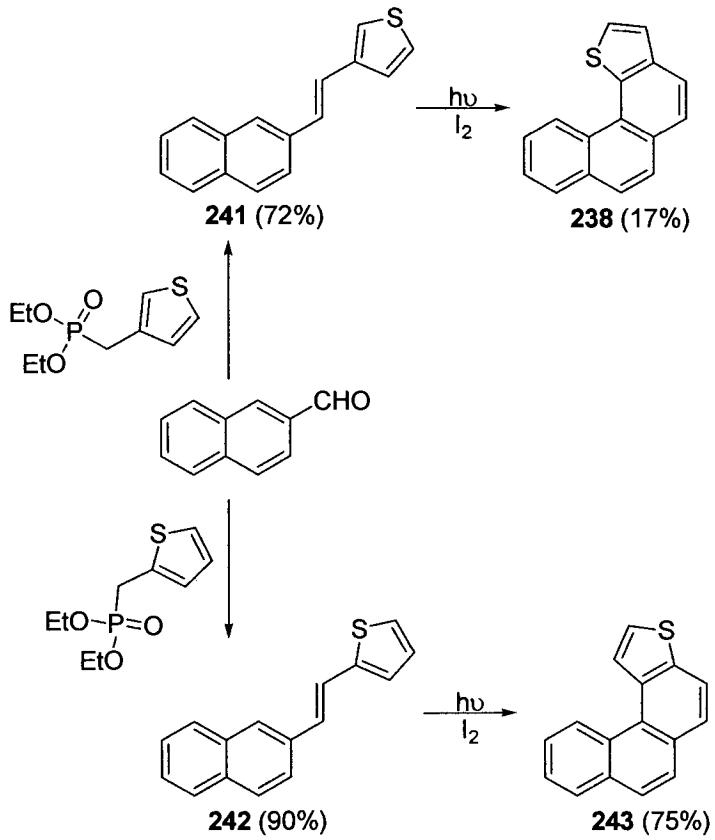
Scheme 115

The second synthesis of **238** was reported by Cagniant *et al.*[80] (**Scheme 116**) in which the basic non-aromatic structure **240** was synthesised by the condensation of $Na_2S.9H_2O$ with **239**. Oxidation with DDQ produced **238** in approximately 50% yield.



Scheme 116

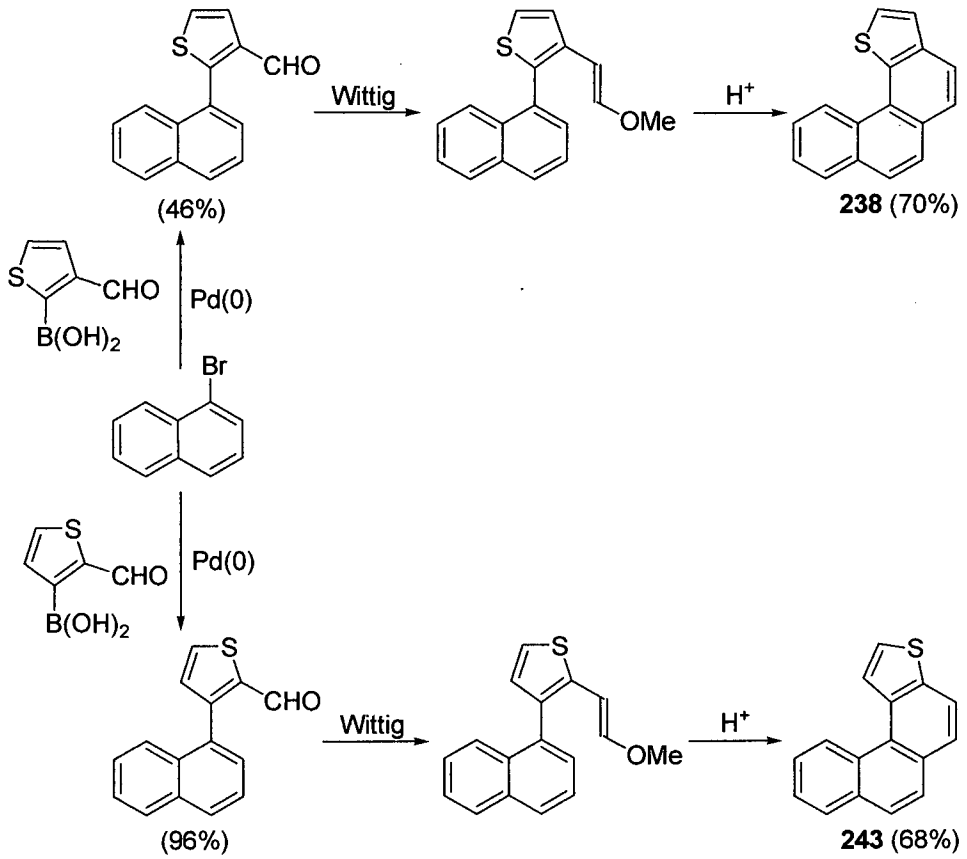
The first reported synthetic route which could be used to produce both **238** and **243** relies on a photochemical cyclisation as discussed previously (**Scheme 117**).[81] The stilbene starting materials required for this type of cyclisation were synthesised *via* a Wittig reaction of 2-naphthaldehyde with thiophene reagents. Compounds **241** and **242** cyclised in the presence of iodine to form **238** and **243** respectively.



Scheme 117

A variety of other 3-naphthylvinylthiophenes also gave low yields of their expected products upon photocyclisation. The authors suggested that the yield of **238** was low due to the explusion of thienyl radicals during the cyclisation process although no evidence was presented for this.

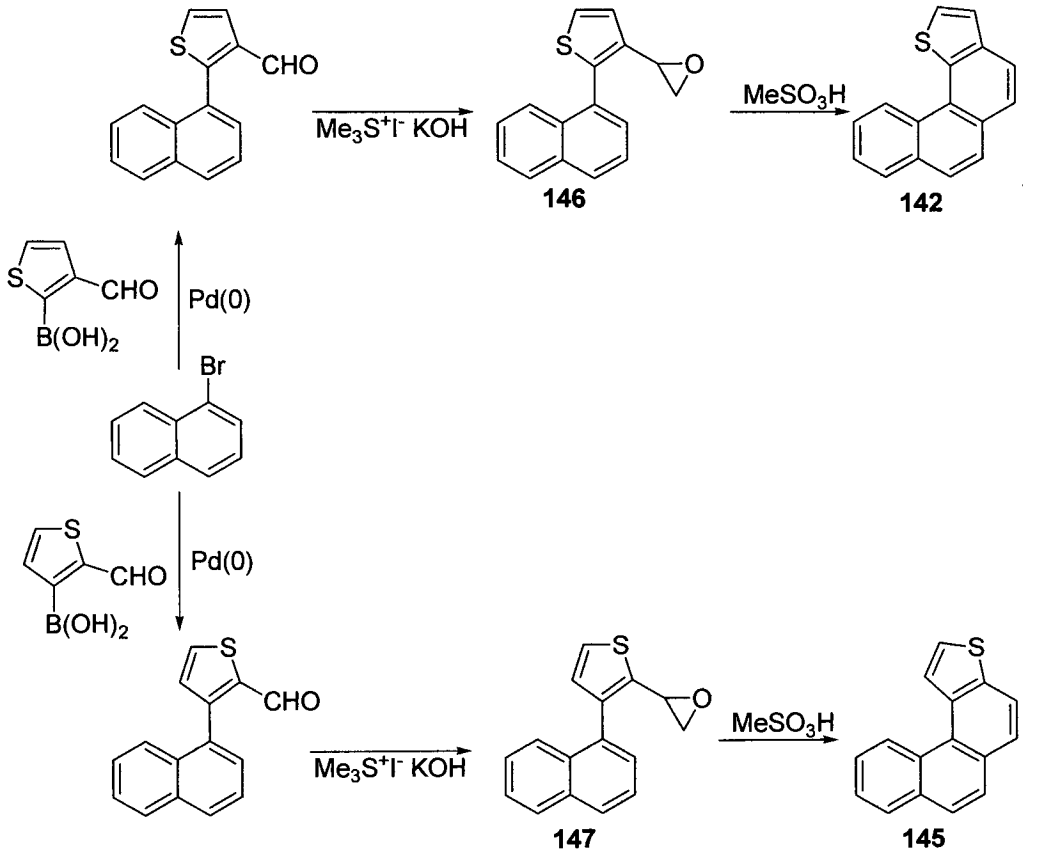
The only other synthesis of these compounds has recently been reported. This synthesis uses an acid catalysed cyclisation to produce **238** and **243** rather than a photochemical cyclisation (**Scheme 118**).



Scheme 118

The starting point for this synthetic route is the Suzuki coupling of 1-bromonaphthalene with formylthiopheneboronic acids. The aldehydes were then subjected to Wittig reactions followed by acid catalysed cyclisation to produce **238** and **243**.[82]

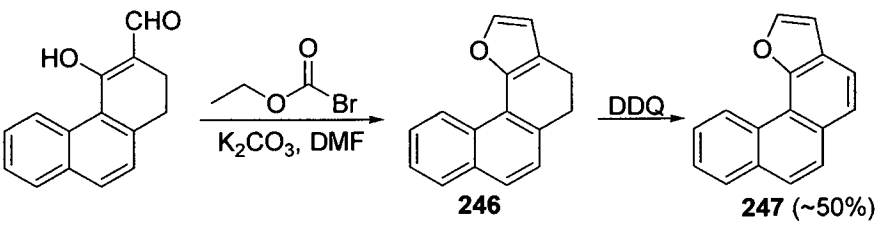
The first step of the final route to **238** and **243** are the same pair of analogous Suzuki coupling reactions shown in **Scheme 118**. Although in this case Kumar *et al.*[83] then transformed the aldehydes into the epoxides **244** and **245**. Compounds **238** and **243** were then produced by treating the epoxides with methanesulfonic acid although the yields were not reported (**Scheme 119**).



Scheme 119

4.1.4 Furan Analogues

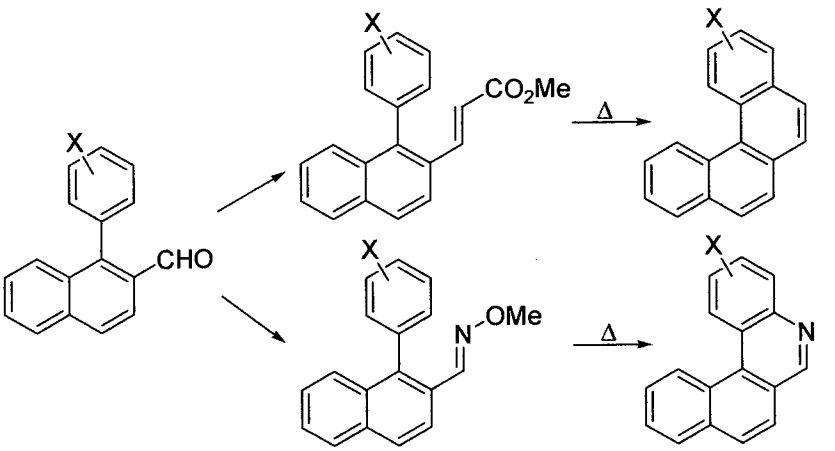
The synthesis of only one of the phenanthrofurans is reported. Using the same synthetic route as the thiophene example shown in **Scheme 116** Cagniant *et al.*[84] reported the synthesis of **247** (**Scheme 120**). As in their previous example the non-aromatic skeleton **246** was formed then oxidised with DDQ to produce the desired aromatic product **247**.



Scheme 120

4.2 Synthetic Applications

As in the route to the three-ring systems discussed in chapter 3 the precursors to the four-ring systems had to be synthesised. These were all made in a similar fashion by initial synthesis of the biaryl unit which contained the aldehyde functionality which was then converted into the acrylate or oxime ether required for the cyclisation reaction (**Scheme 121**).

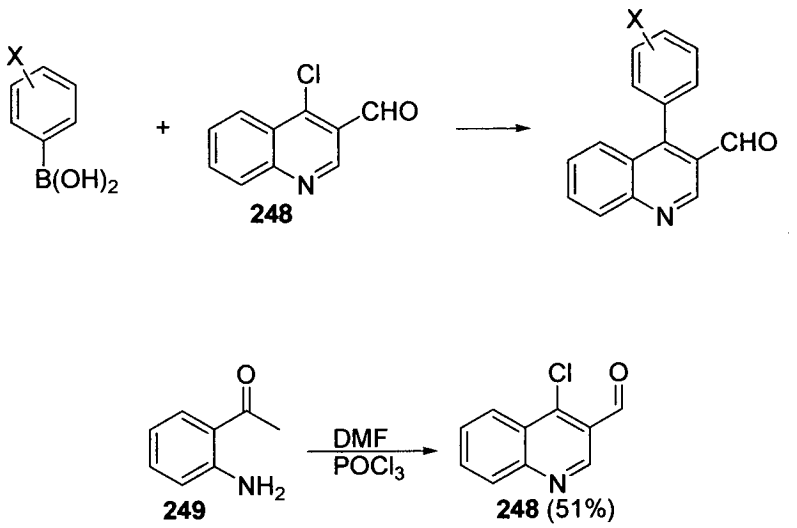


Scheme 121

4.2.1 Precursor Synthesis

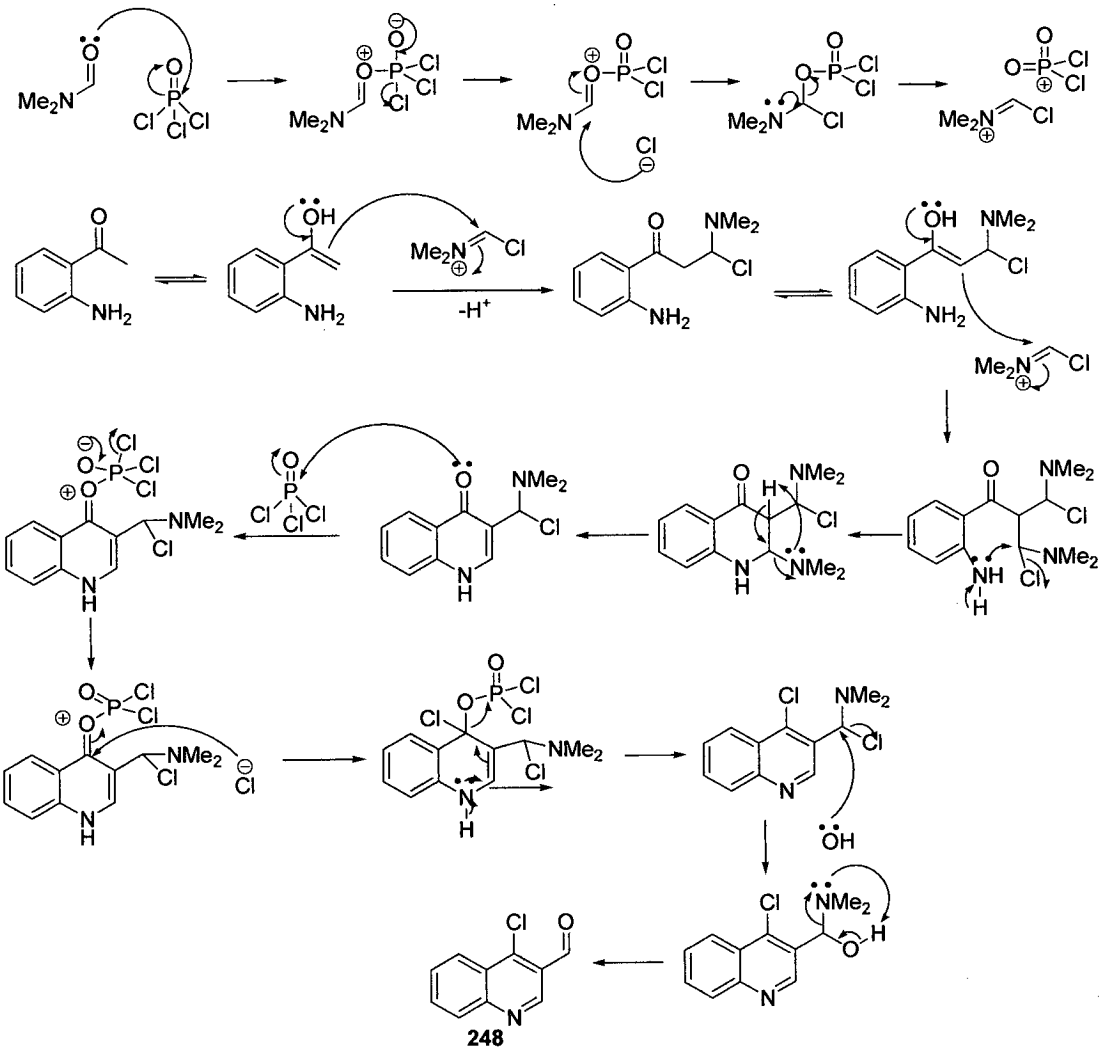
As discussed in the introduction to this chapter the toxicity of these four-ring systems can be lowered by the incorporation of a nitrogen atom into the main ring structure. The

easiest way of producing the aldehydes required for this was to couple the quinoline **248** with a phenylboronic acid as a one-step route to the quinoline was known in the literature.



Scheme 122

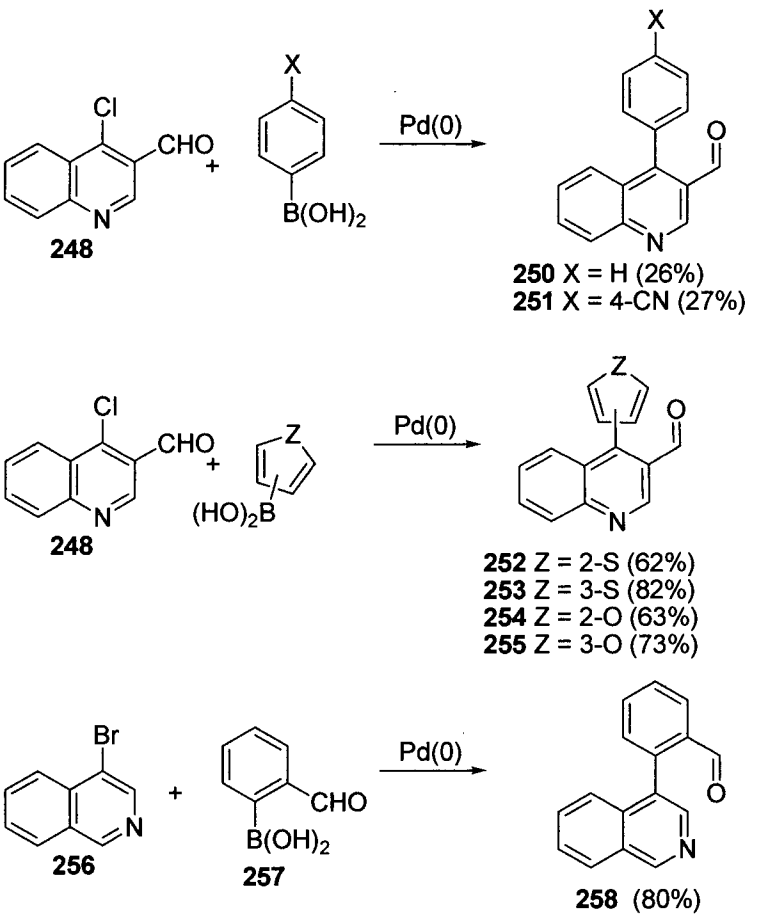
Thus, in 1997 Amaresh and Permual[85] reported the synthesis of **248** by reaction of 2-aminoacetophenone **249** with Vilsmeier reagent formed by reaction of dimethylformamide and phosphoryl chloride (**Scheme 122**). The probable mechanism of the Vilsmeier reaction to give **248** is shown below (**Scheme 123**).



Scheme 123

4.2.1.1 Aldehydes

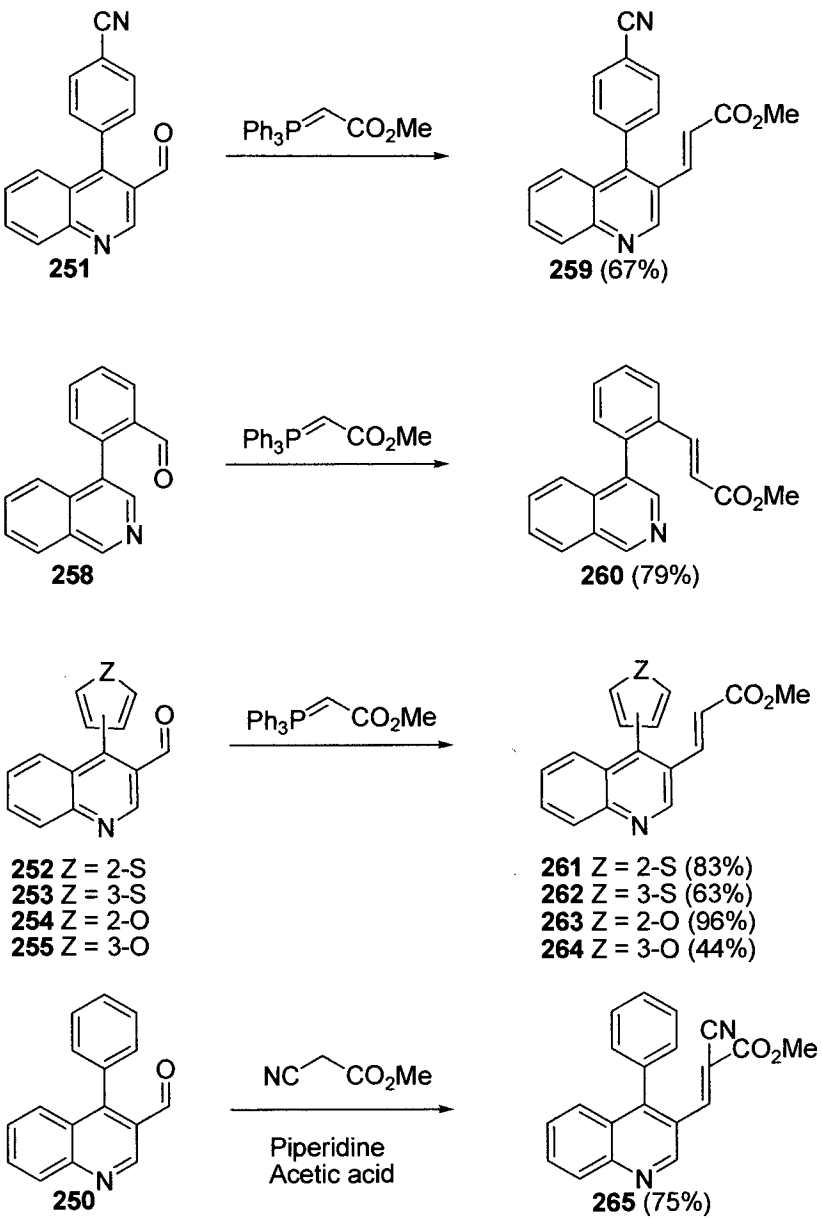
Using **248** and a selection of boronic acids it was possible to produce most of the desired aldehydes using Tsvetkov's Suzuki coupling conditions (**Scheme 124**).[8c]



Scheme 124

Arylboronic acids were used to produce **250** and **251** and thienylboronic acids and furylboronic acids were used to afford the heterocyclic examples (**252**, **253**, **254** and **255**). In the synthesis of **258** 4-bromoisoquinoline **257** was coupled with 2-formylphenylboronic acid **257** so that the nitrogen atom would be in a different position in the final product.

4.2.1.2 Wittig/Knoevenagel



Scheme 125

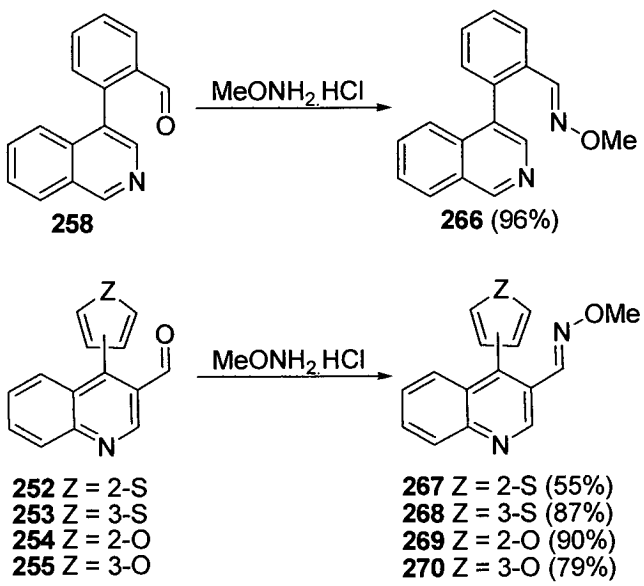
Compounds **259** – **264** were synthesised *via* a Wittig reaction, as discussed in chapter 3, using methyl(triphenylphosphoranylidene)acetate as the Wittig reagent (**Scheme 125**). The products were easily separated from the triphenylphosphine oxide by-product by dry

flash chromatography. The yields of this reaction varied but were generally >60% and the *E* : *Z* ratio was, on average, 94 : 6.

The cyano substituted ester **265** was synthesised *via* a Knoevenagel reaction under standard conditions[7] and the product was shown by ^{1}H NMR spectroscopy to be a single isomer.

4.2.1.3 Oxime Ethers

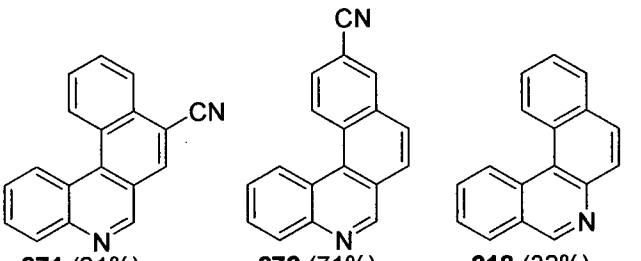
As in the synthesis of three-ring systems all of the oxime ethers were synthesised in the standard way by heating the aldehyde with *O*-methylhydroxylamine hydrochloride in ethanol for two hours followed by a normal work-up to produce the oxime ethers without the need for purification and the transformation was observed by ^{1}H NMR spectroscopy (**Scheme 126**).



Scheme 126

4.2.2 Pyrolyses

4.2.2.1 Benzophenanthridines



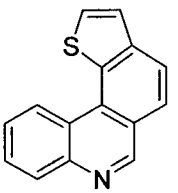
271 (21%) **272** (71%) **218** (32%)

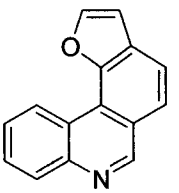
The three target benzophenanthridines were all produced *via* FVP in reasonable yield. Both **272** and **218** were produced by pyrolysis at 950 °C and **271** was produced by pyrolysis at 975 °C. The cyclisation of **265** to produce **271** shows that the cyclisation of the cyano-subsitituted methyl acrylates can also be used to produce four-ring systems.

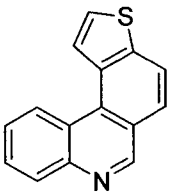
As the work discussed in chapter 3 showed that it was possible to produce ring systems with a variety of substituents in various positions only the 4-cyano substituted four-ring system was synthesised, as a proof of principle, to show that this methodology could be used.

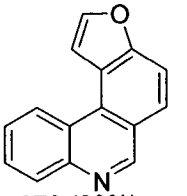
Compound **218** is a known compound as discussed in the introduction to this section. Using the FVP route reported in this thesis **218** can be produced in approximately the same yield as the literature synthesis. Although the route to **218** reported by Loader and Timmons[71] was only two steps it has one disadvantage in that only the *cis*-isomer can be used for the photocyclisation and therefore the isomers produced by a Wittig reaction must be separated. As discussed earlier the FVP cyclisation takes place with both isomers.

4.2.2.2 Thiophenes and Furans


273 (70%)


274 (43%)

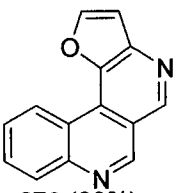

275 (95%)

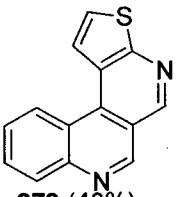

276 (88%)

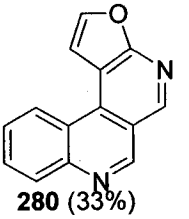
All four of these previously unknown thiophene and furan systems were produced by FVP at 950 °C under standard conditions. The yields of this reaction varied but generally were >70%.

4.2.2.3 Oxime Ethers


277 (49%)


278 (60%)


279 (43%)


280 (33%)

The four thiophene and furan containing four-ring systems produced by the pyrolysis of oxime ethers at 700 °C were all obtained as single isomers. These systems were all previously unknown compounds and no compounds of this type of architecture are known in the literature.

4.2.2.3.1 NMR Spectroscopy

It is possible, using both 1D- and 2D-NMR spectroscopy to assign the proton and carbon atom resonances in these compounds to show if changing the heteroatom effects the environment of the proton directly opposite across the bay region to alter its NMR spectra. As the analysis of 1D- and 2D-NMR spectra are routine, only one example, **277**, will be discussed in detail.

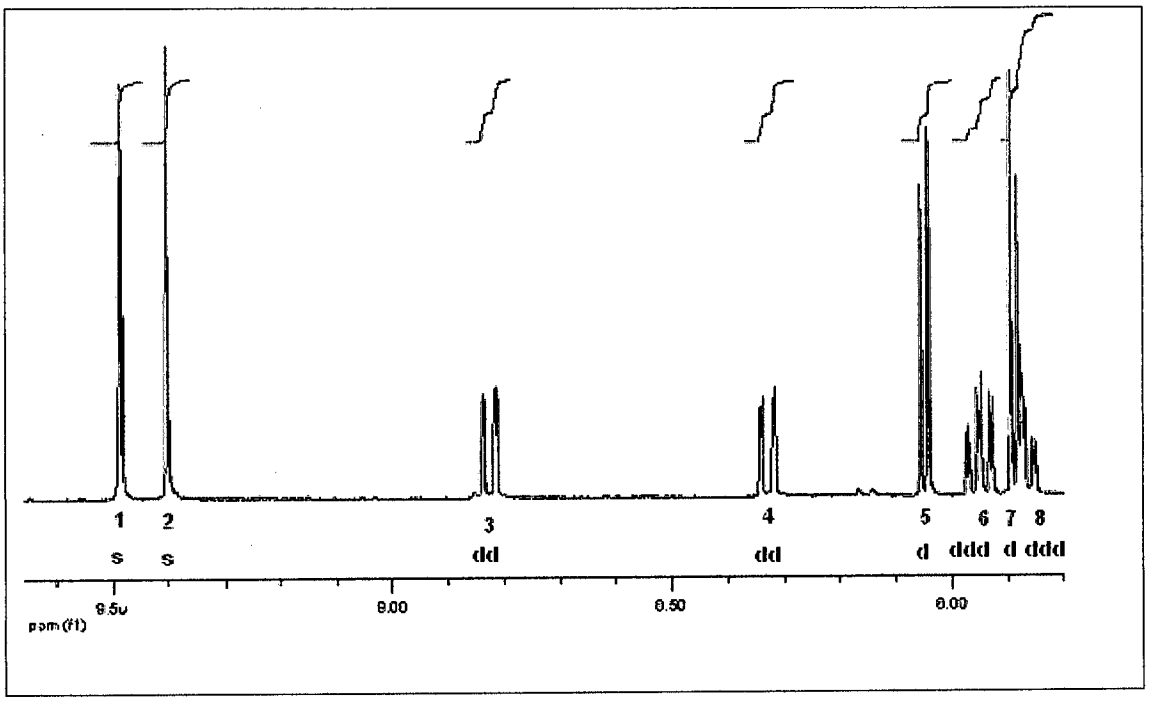
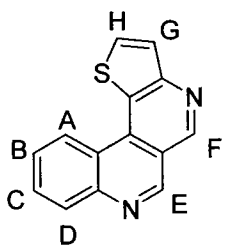


Figure 11: ^{1}H NMR spectrum of 277

The ^{1}H NMR spectrum of **277** shows that the correct number of protons are present and that the splitting patterns and coupling constants are as expected, with two doublets with a small coupling constant (*J* 5.6 Hz) due to the fused thiophene moiety suggesting that peaks 7 and 5 are due to protons G and H. The two singlets, 1 and 2, must be due to protons E and F. Peaks 3 and 4 relate to protons A and D leaving peaks 6 and 7 to be due to protons B and C.



A = dd
B = ddd
C = dd
D = dd
E = s
F = s
G = d
H = d

To confirm the connectivity of the protons and each set of peaks in the ^{1}H NMR spectrum the COSY NMR spectrum of **277** was run. As expected peaks 1 and 2 show no through bond coupling. Peak 3 shows coupling to peak 8 which in turn couples to peak 6

which couples to peak 4. This set of four peaks is due protons A, B, C and D of the benzene ring. Peaks 5 and 7 show through bond coupling which confirms the analysis that these peaks are due to protons G and H on the thiophene ring.

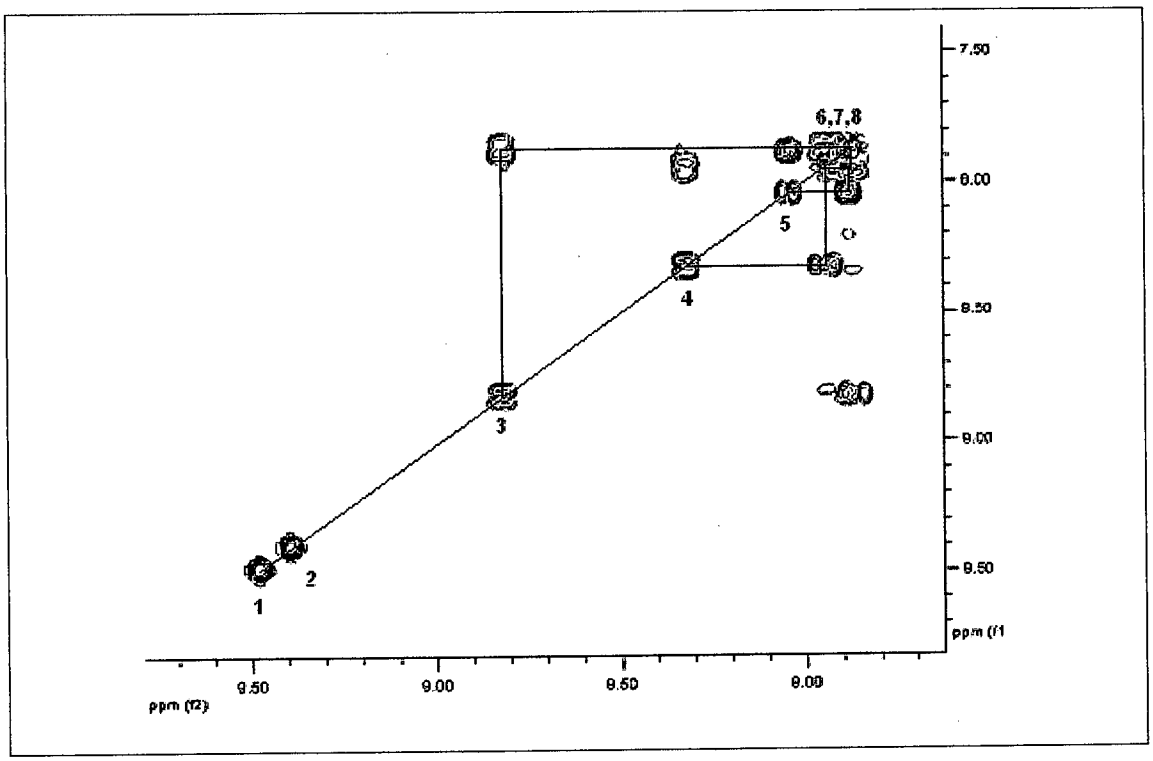
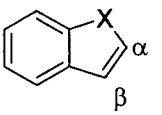


Figure 12: COSY NMR spectrum of 277

The full assignments of the ^{1}H NMR spectra of benzofuran and benzothiophene were recorded by Abraham and Reid (**Table 7**)[86]



Proton	X = O δ_H (ppm)	X = S δ_H (ppm)	$\Delta\delta_H$ (ppm)
α	7.607	7.422	0.185
β	6.758	7.325	-0.567

Table 7: Correlation between the ^{1}H NMR spectra of benzofuran and benzothiophene

The data in **Table 7** shows that changing the heteroatom X has less effect on the chemical shift of the proton in the α-position than that of the proton in the β-position. Comparison of the ^{1}H NMR spectrum of **278** with that of the furan analogue **278** (**Table 8**) suggests that peak 7 is due to proton G as changing the heteroatom moves this peak significantly whilst peak 5 is less affected. It is also the case that peak 3 moves substantially when the heteroatom is changed suggesting that this peak correlates to proton A as it is the only proton in the benzene ring close enough to be affected by the heteroatom.

After assigning all of the protons it was possible to use a proton-carbon correlation spectrum (HSQC) to assign the protonated carbons in the ring system.

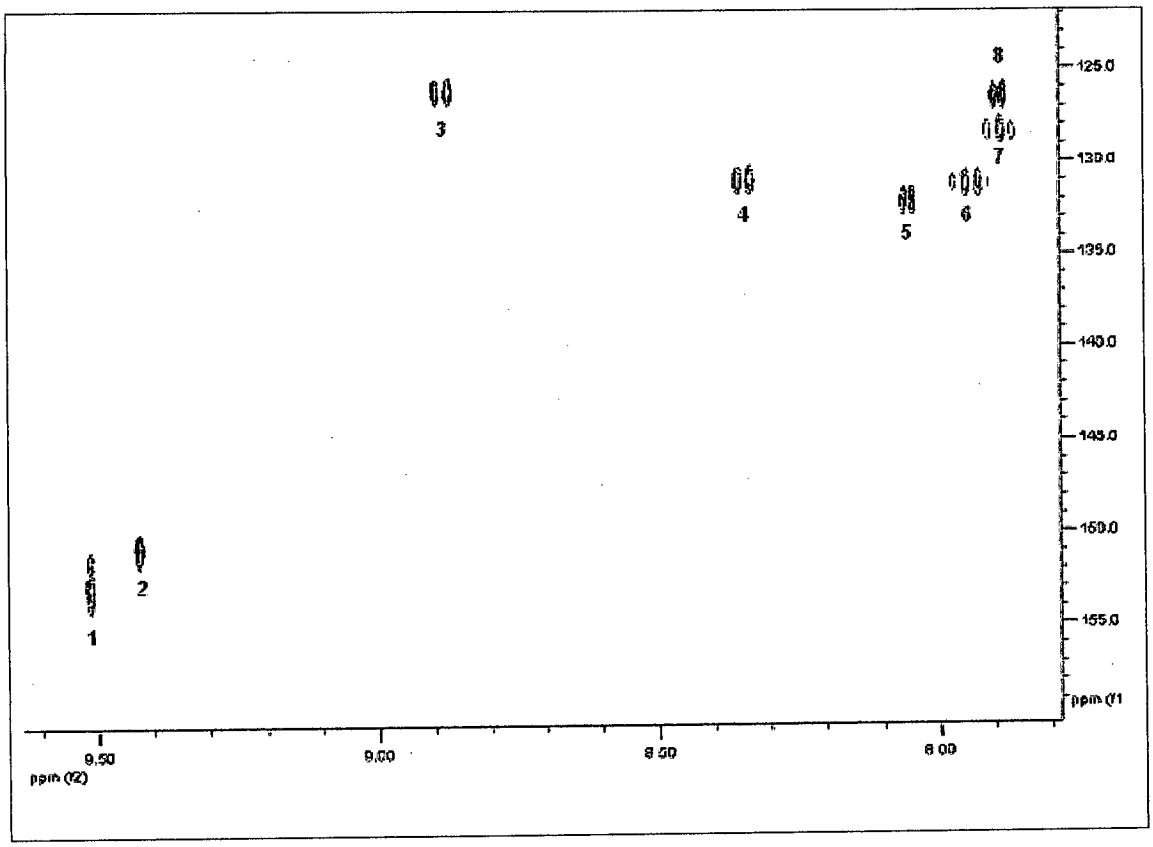


Figure 13: HSQC NMR spectrum on 277

The HSQC spectrum led to the following assignment of the protonated carbons of **277**.

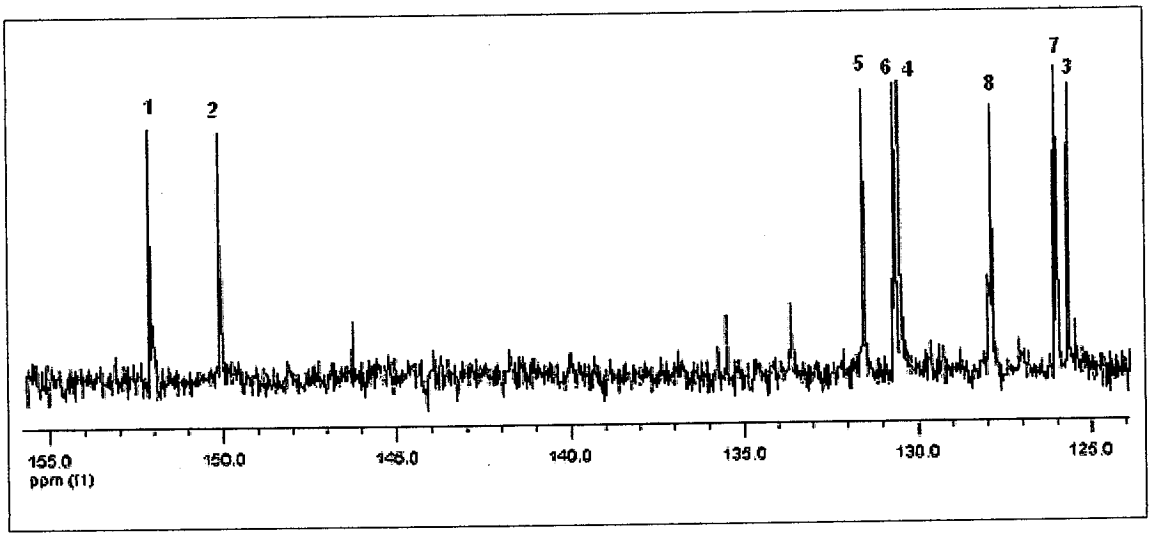
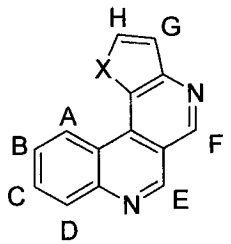


Figure 14: ^{13}C NMR spectrum of 277

Having carried out similar NMR experiments on **278** it is possible to assign both the protons and carbons A-H in both ring systems to their resulting peaks in both ^{1}H and ^{13}C NMR spectra.



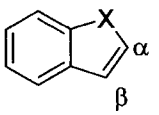
277 X=S
278 X=O

The table below lists the peaks in both the ^{1}H and ^{13}C NMR spectra of both **277** and **278** due to each position in the ring system. Rows A, G and H (in bold) are most relevant.

Proton	**277** δ_H (ppm)	**277** δ_C (ppm)	**278** δ_H (ppm)	**278** δ_C (ppm)	$\Delta\delta_H$ (ppm)	$\Delta\delta_C$ (ppm)
A	**8.83**	**125.7**	**9.27**	**128.0**	**0.44**	**2.3**
B	7.87	127.9	7.93	130.9	0.06	3.0
C	7.95	130.7	7.84	127.9	-0.11	-2.8
D	8.33	130.5	8.29	129.9	-0.04	-0.6
E/F	9.40/9.49	152.2/150.1	9.35/9.51	151.9/148.9		
G	**7.89**	**126.1**	**7.31**	**109.1**	**-0.58**	**-17.0**
H	**8.05**	**131.6**	**8.20**	**149.4**	**0.15**	**17.8**

Table 8: Correlation between the ^{1}H and ^{13}C NMR spectra of 277 and 278

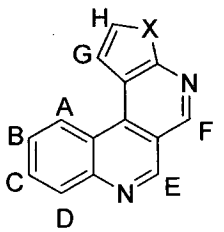
It is notable that position A is distinctly different in the ^{1}H NMR spectra of the two compounds. This is thought to be due to its proximity in space to the heteroatom within the bay region of the molecule suggesting that changing the heteroatom, X, affects the environment of proton A. It is also notable that the effect does not extend significantly to carbon A. Comparison of the ^{13}C NMR spectra of **277** and **278** shows that the chemical shifts of carbons G and H are the most affected by the change in heteroatom. Literature data for the ^{13}C NMR spectra of benzofuran and benzothiophene show that these large shifts for both the α- and β-carbons in this type of system are normal when the heteroatom is altered.[87]



Carbon	**X = O** δ_C (ppm)	**X = S** δ_C (ppm)	$\Delta\delta_C$ (ppm)
α	144.8	126.4	18.4
β	106.5	124.0	-17.5

Table 9: Correlation between the ^{13}C NMR spectra of benzofuran and benzothiophene

By analogy it is possible to assign the protons in both **279** and **280**.



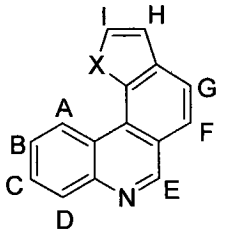
279 X = S
280 X = O

Proton	**279** δ_H (ppm)	**280** δ_H (ppm)	$\Delta\delta_H$ (ppm)
A	**8.50**	**9.00**	**0.50**
B	7.86	7.81	-0.05
C	7.93	7.91	-0.02
D	8.31	8.31	0.00
E/F	9.27/9.46	9.40/9.48	
G	**8.03**	**8.45**	**0.43**
H	7.87	7.88	0.01

Table 10: Correlation between the ^{1}H NMR spectra of 279 and 280

Again it is shown that protons A and G (shown in bold) are the most affected by the change in the heteroatom. This is surprising as the protons in position A in **277** and **278** are directly opposite the heteroatom whilst in **279** and **280** proton A is shielded from the heteratom by the rest of the five-membered ring and as these compounds are novel architectures there are not yet any literature examples to compare the data with.

By analogy it is possible to assign the protons (A-I) in compounds **273**, **274**, **275** and **276**.

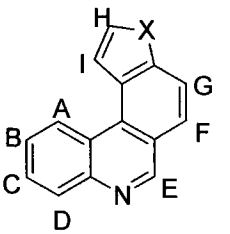


273 X = S
274 X = O

Proton	**273** δ_H (ppm)	**274** δ_H (ppm)	$\Delta\delta_H$ (ppm)
A	**9.06**	**9.39**	**0.33**
B	7.88 – 7.91	7.78	
C	7.88 – 7.91	7.80	
D	8.39	8.25	-0.14
E	9.45	9.37	-0.08
F	8.05	7.91	-0.14
G	8.19	7.91	-0.28
H	**7.70**	**7.05**	**-0.65**
I	7.90	8.04	0.14

Table 11: Correlation between the ^{1}H NMR spectra of 273 and 274

Once again proton I, adjacent to the heteroatom, is the most affected by the change in heteroatom. The only other proton whose environment is directly affected is proton A as it is opposite the heteroatom across the bay region of the compound.



275 X = S
276 X = O

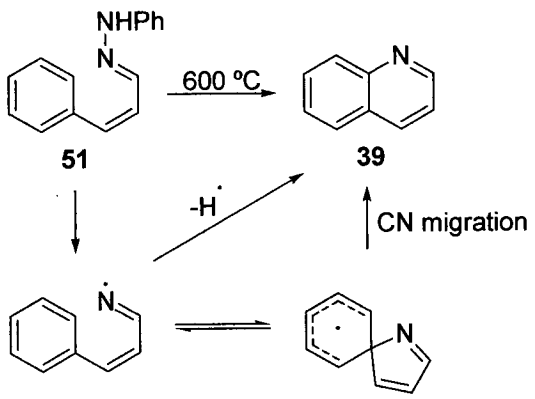
Proton	**275** δ_H (ppm)	**276** δ_H (ppm)	$\Delta\delta_H$ (ppm)
A	8.97	8.93	-0.04
B	X	X	X
C	X	X	X
D	8.22	X	X
E	9.29	9.43	0.14
F	X	X	X
G	X	X	X
H	7.92	X	X
I	8.54	X	X

Table 12: Correlation between the ^{1}H NMR spectra of 275 and 276

Due to the quality of the ^{1}H NMR spectra only protons A and E could be assigned in both **275** and **276**. This was sufficient information to show that the environment of proton A is unaffected by the change in heteroatom which is to be expected as it is no longer close to the heteroatom.

4.2.2.3.2 Mechanism

As discussed in chapter 1 it is known that pyrolysis of **51** produces iminyl radicals which cyclise to form a single product **39** but it is was not known if **39** was formed by direct cyclisation of the iminyl radical or by formation of the spirodienyl intermediate followed by selective migration of the C-N bond with no migration of the C-C bond (**Scheme 127**).

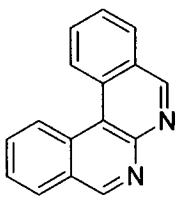


Scheme 127

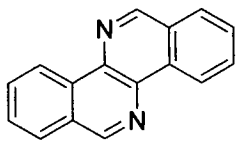
The cyclisation of iminyl radicals formed by the pyrolysis of oxime ethers discussed in chapter 3 all produced single products which, as in the case of the reaction in **Scheme 127**, did not provide any conclusive evidence for either direct cyclisation of the radical or *ipso*-attack followed by selective C-N bond migration.

It was therefore expected that the pyrolysis of **266** would produce a single product, **281**. However, pyrolysis of **266** produced two distinct products which could be separated by column chromatography. Both of the products had ^{1}H NMR spectra which fitted the expected product. Inspection of the ^{13}C NMR spectra showed that the main product had

four quaternary carbon peaks (two large peaks and two small peaks) whilst the minor product had only three (all of equal size). It follows that the main product is **281** (containing six quaternary carbons) which, due to the symmetry of the molecule, result in two peaks corresponding to two carbons each and two peaks corresponding to two single carbons each. The minor product is **282** which has only three quaternary peaks each resulting from a pair of identical quaternary carbons.

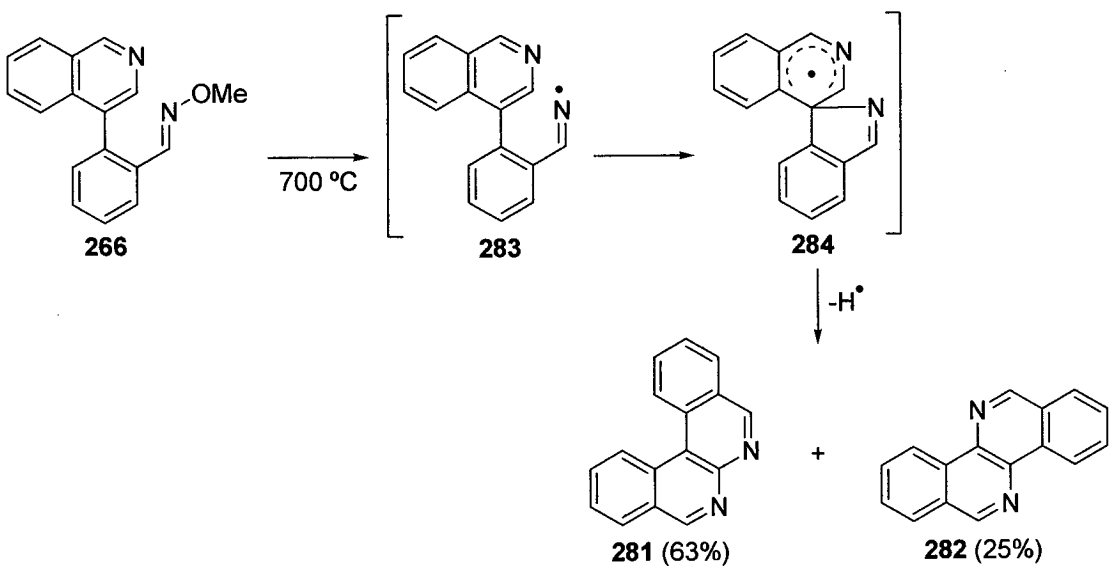


281



282

The formation of the two isomeric tetracycles can be rationalised by *ipso*-attack of the iminyl radical to produce a spirodienyl intermediate, **284**. Competitive C-N migration would form **281** while C-C migration would form **282** (**Scheme 128**).



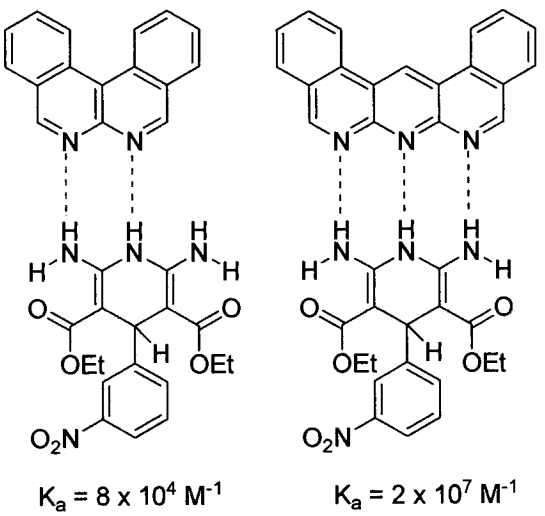
266 **283** **284**

Scheme 128

The mechanism by which a *spirodienyl* intermediate is transformed into the product in the gas phase has not been specifically addressed previously. Possibilities include a sigmatropic shift, reversion to starting materials or by a neophyl rearrangement. As discussed in chapter one the involvement of spirodienyl radicals in gas-phase iminyl chemistry is common but this is the first case where C-C migration is observed. In the past only exclusive C-N migration has been reported. It is thought that, in this case, competitive C-C migration is possible due to the steric congestion in the bay region of the transition state leading to **281**.

The route to **281** developed here was employed by Djurdjevic *et al.*[88, 89] to provide an analogous double hydrogen bond acceptor (AA) system to their novel AAA system for hydrogen bond binding studies (**Scheme 129**).

Full acknowledgement of the present author's role in developing the synthesis of **281** will be given in the full paper.[90]



Scheme 129

The work reported by Djurdjevic is an example of a good use for the type of four-ring systems discussed in this chapter. As **Scheme 129** shows **281** had to be synthesised to

provide evidence to support the theory that a complex containing three hydrogen bonds would result in a substantially higher binding constant.

During the binding studies crystals of **281** suitable for X-ray analysis were produced which, as shown, included two molecules of water.[88] This crystal structure confirms the assumption that this type of four-ring system is not flat but is twisted in the same way as a helicene.

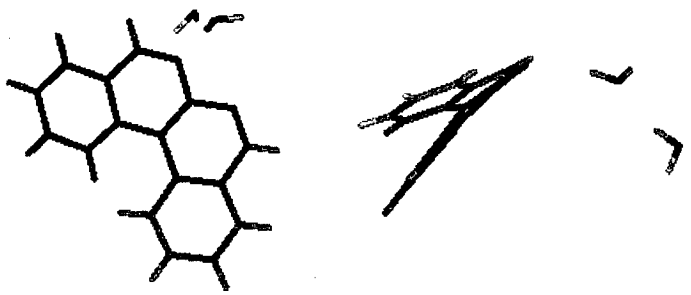


Figure 15: Crystal structure of 281, showing non-planarity and two water molecules of crystallisation.

4.3 Conclusion

In conclusion it has been proved that the reaction described in **Scheme 121** can be used to synthesise a wide variety of four-ring systems. The generality of this reaction has been shown by its ability to produce furan and thiophene analogues of benzo[*c*]phenanthridene. The synthesis of cyano substituted systems has shown that in principle this methodology could be used in the future to produce functionalised materials.

In addition, the known cyclisation reaction of oxime ethers under FVP conditions *via* iminyl radicals has been shown to be a useful method of synthesising four-ring systems containing a nitrogen in the central ring. The pyrolysis of **266** has given a deeper insight into the mechanism of this cyclisation by providing evidence of *ipso*-attack rather than

direct cyclisation. The use of **281** in a hydrogen bonding binding study has shown that the synthetic route described in this thesis can be used to produce useful compounds.

5 Five-Ring Systems

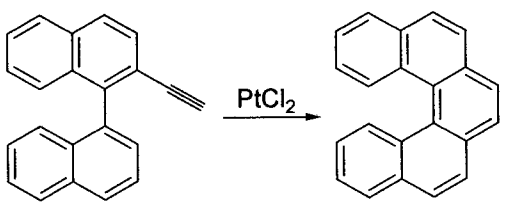
5.1 Introduction

5.1.1 [5]Helicene

There are over 250 papers which report synthetic routes to [5]helicene **286**. A number of these papers will not be discussed as they only cover the dehydrogenation of exisiting 5-ring systems,[91] variations of previously published routes[92] and many only report the synthesis of **286** in negligable yield or as a byproduct.[93] In many of the syntheses reported the final step is a cyclisation to form the central ring starting from a binaphthyl unit which is similar to the synthesis of phenanthrenes from biphenyl units.

5.1.1.1 Metal Catalysed Cyclisation

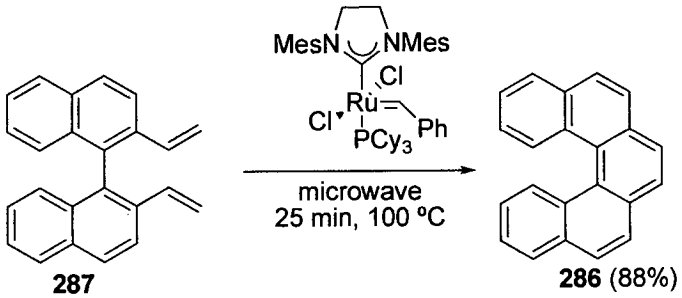
One route to **286** reported by Fürstner *et al.*[27] uses the metal catalysed cyclisation of alkynes as discussed in chapters 3 and 4.



Scheme 130

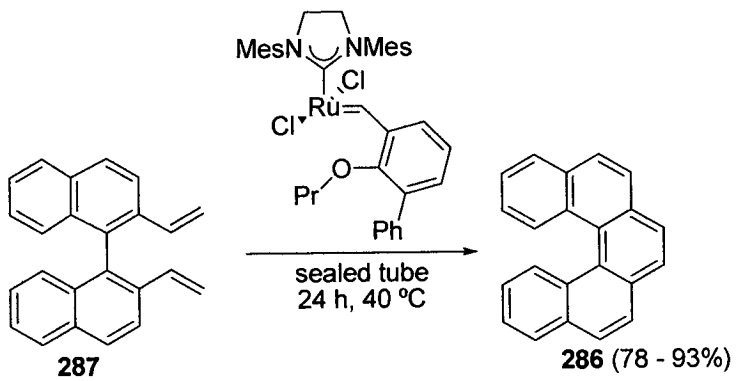
As in chapter 4 the best catalyst for this cyclisation was platinum chloride and the reaction produced **286** in reasonable yield with no reported side products (**Scheme 130**).

Another route to **286** was published recently by Collins *et al.*[94] using olefin metathesis. The reaction was attempted using the binaphthyl compound **287** and Grubbs' 2nd generation catalyst under microwave conditions at 100 °C. This reaction produced **286** cleanly and in a reproducibly good yield (**Scheme 131**).



Scheme 131

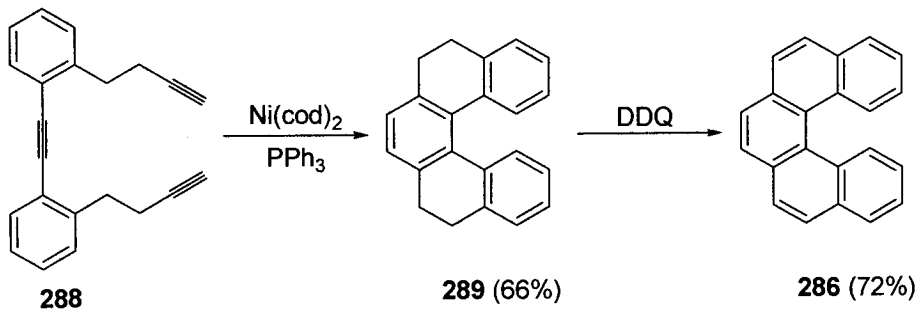
In an attempt to reduce the reaction temperature the experiment was repeated in a sealed tube at 40 °C for a longer period of time using a derivative of the Hoveyda-Grubbs 1st generation catalyst (**Scheme 132**).



Scheme 132

This reaction also produced **286** cleanly and in high yields but the yield was not consistently reproducible. Both of these reactions were then used to synthesise larger and more substituted helicenes.

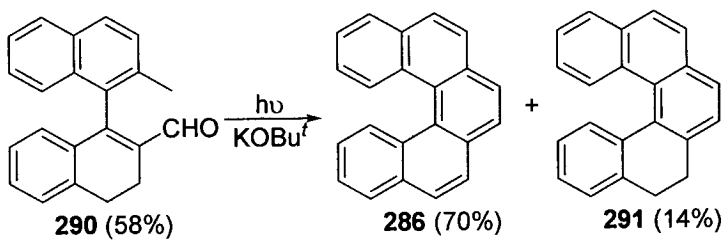
The final metal catalysed cyclisation synthesis of **286** was reported by Stara *et al.*[95] in which a nickel catalyst was used to cyclise the alkyne **288** to produce tetrahydro[5]helicene **5** which was then oxidised with DDQ (**Scheme 133**).



Scheme 133

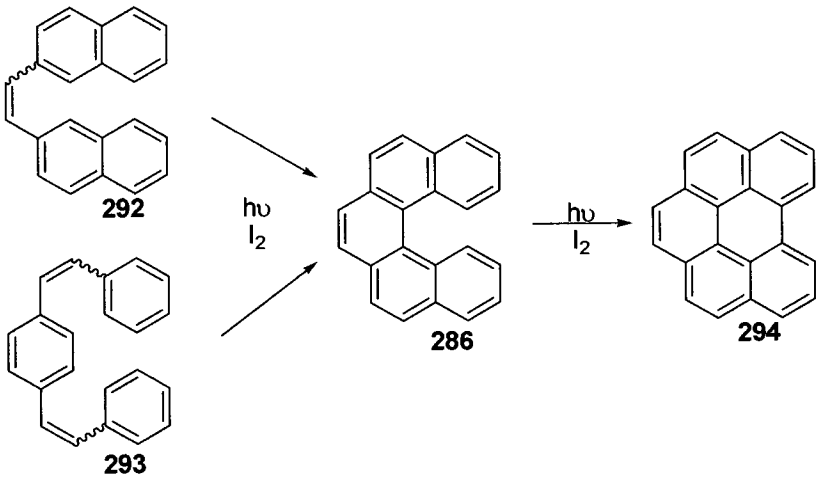
5.1.1.2 Photochemical Cyclisation

The first photochemical route involves the cyclisation of **290** in a photochemical reactor in the presence of base as discussed in chapter 4.[96] In this case the cyclisation of **290** yields two products but the helicene **286** is produced in good yield (**Scheme 134**). Although the by-product **291** is only present in low yield, due to the structural similarities it would be hard to separate the two products using traditional chromatographic methods although there is no reason why **291** could not be oxidised to **286**.



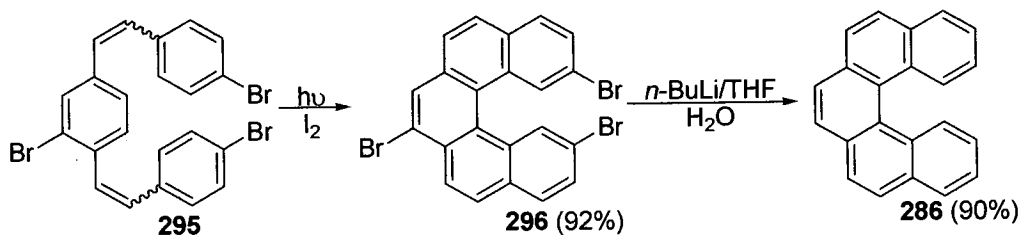
Scheme 134

It is possible to synthesise **286** from other starting materials. As discussed in chapters 3 and 4 it should be possible to synthesise these type of compounds from stilbene type starting materials under photochemical conditions. Katz and Liu[97] noted that although photochemical cyclisations of both **292** and **293** should in principle yield **286** the main product of these reactions was **294** (**Scheme 135**).



Scheme 135

It was discovered that by substituting **293** with bromine atoms the final dehydrogenation could be avoided to produce **286** after removal of the bromine atoms (**Scheme 136**).[97]

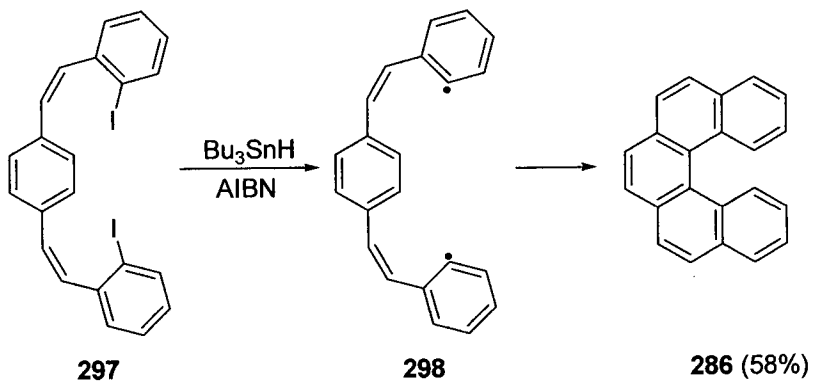


Scheme 136

It is possible that the bromine atoms on the terminal rings may prevent further reaction, as the formation of a compound like **294** would result in the bromine atoms being too close together. The reaction was repeated without the bromine atom on the central ring but the cyclisation product of this compound contained several impurities which could not be removed. This does not alter the effectiveness of this route as the overall yield of **286** was 83% which is almost as good as the syntheses which require metal catalyst although this does not take into account the synthesis of the starting materials.

5.1.1.3 Other Methods

It was shown by Harrowven *et al.*[98] that it was possible to induce the cyclisation of stilbenes *via* chemically induced radical reactions rather than photochemical cyclisations (**Scheme 137**).



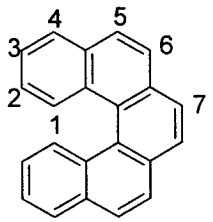
297 **298** **286** (58%)

Scheme 137

It is known that AIBN is a radical initiator which can be used to produce the diradical **298** from the diiodide **297**. The diradical then cyclises to produce **286** in reasonable yield. The main drawback of this route is that the cyclisation only works when using the (*Z,Z*)-isomer. The useful isomer is produced in equal ratio to the (*Z, E*)-isomer which means that the overall yield of [5]helicene using this route is 22% from simple starting materials.

5.1.2 Monoaza[5]helicenes

The majority of the hetero[5]helicenes that are known in the literature are aza[5]helicenes containing a single nitrogen atom. The numbering system for [5]helicene is similar to that in the smaller ring systems. Due to the symmetry of the compound there are seven possible aza[5]helicenes most of which have been reported by Caronna *et al.* since 2002.



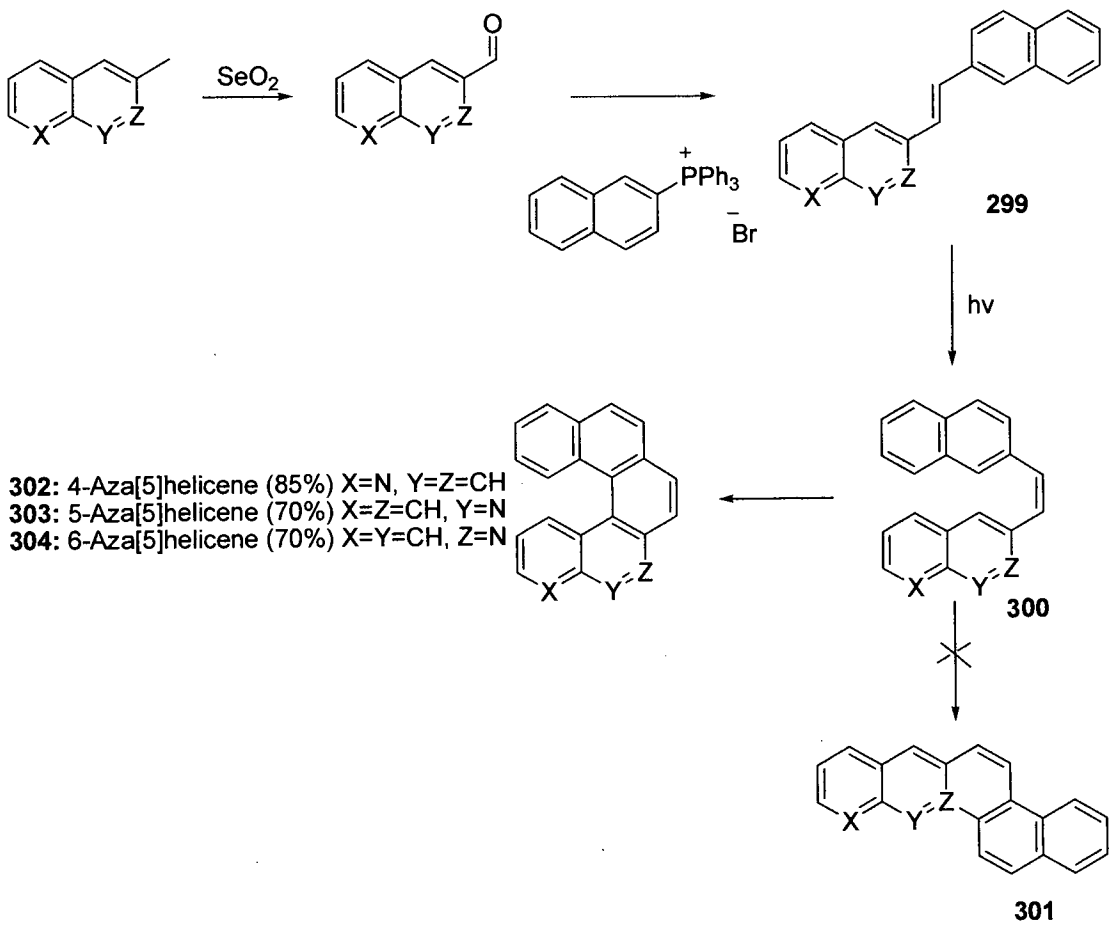
5.1.2.1 Photochemical Cyclisation

As in the syntheses of 3- and 4-ring systems one of the most common techniques used for the cyclisation step in the synthesis of aza[5]helicenes is photochemistry. Caronna *et al.*[99] first reported the photochemical synthesis of three of the monoaza[5]helicenes in 2005 (**Scheme 138**). The synthesis begins with the synthesis of the *E*-stilbene **299**. Under these photochemical reaction conditions *E*-stilbene **299** undergoes isomerisation to the *Z*-isomer **300** which then cyclises to produce the helicene (**302**, **303** and **304**).

Caronna used this reaction to produce three, previously unknown, aza[5]helicenes (**302**, **303** and **304**) in good yield.

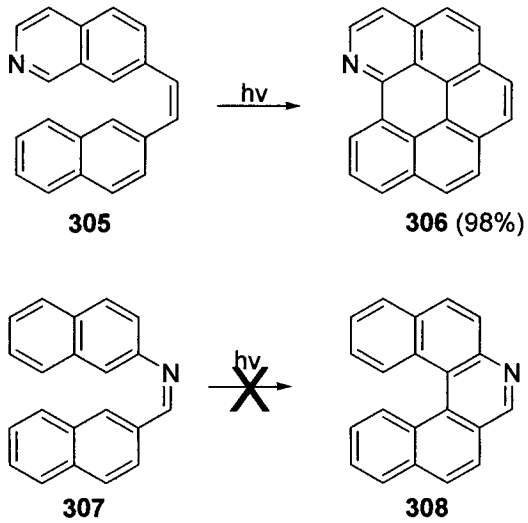
Caronna has now shown that photochemical cyclisation of these stilbenes exclusively produce the more hindered helicene, **302**, **303** and **304** rather than the less hindered dibenzanthracenes, **301**. All of the helicenes were fully characterised by NOE NMR spectroscopy and X-ray crystallography.

This photochemical methodology worked well for the synthesis of the three aza[5]helicenes **302, 303** and **304** but it was not possible to synthesise 2-aza[5]helicene **332** or 7-aza[5]helicene **308** in this way (**Scheme 139**).



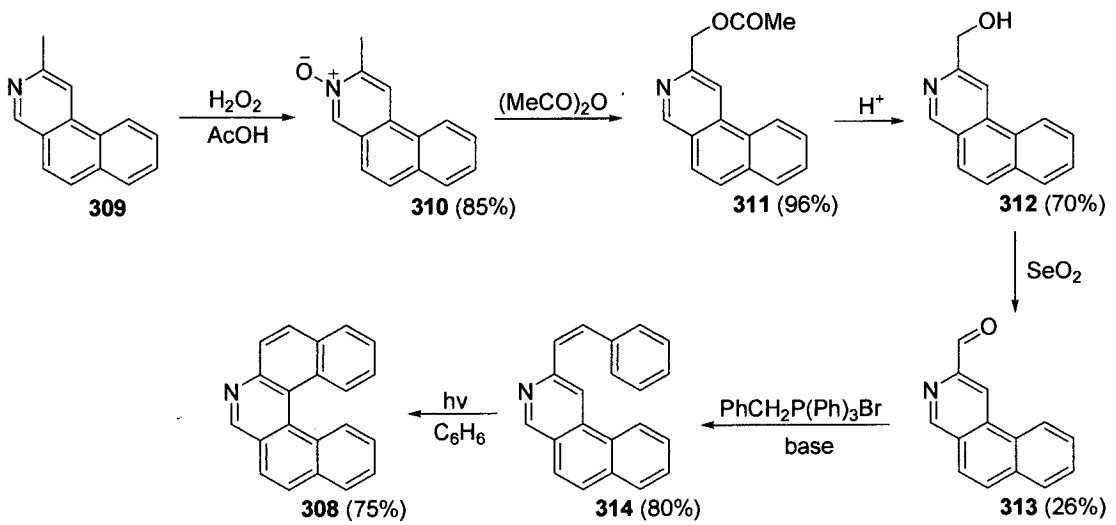
Scheme 138

The photochemical reaction of **305** produced the dehydrogenated helicene **306** and the imine **307** did not react at all under the usual conditions. Caronna *et al.*[100] therefore devised a new synthetic route to these two helicenes along with the two remaining monoaza[5]helicenes.



Scheme 139

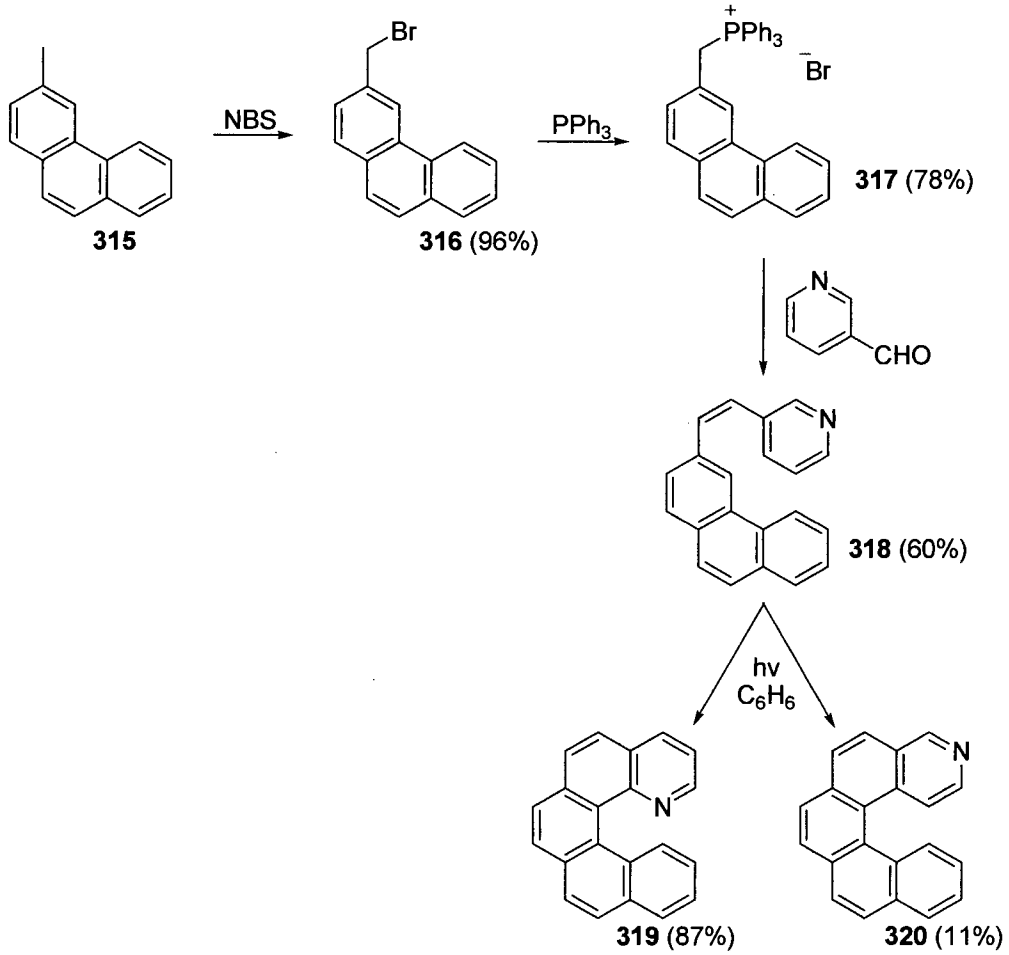
Thus, substituted benzoquinoline precursors were made which could undergo cyclisation to the helicene *via* tradational methods. There were two different routes to these substituted benzoquinolines, the first of which used methylbenzoquinoline **309** to produce the alkene precursor.



Scheme 140

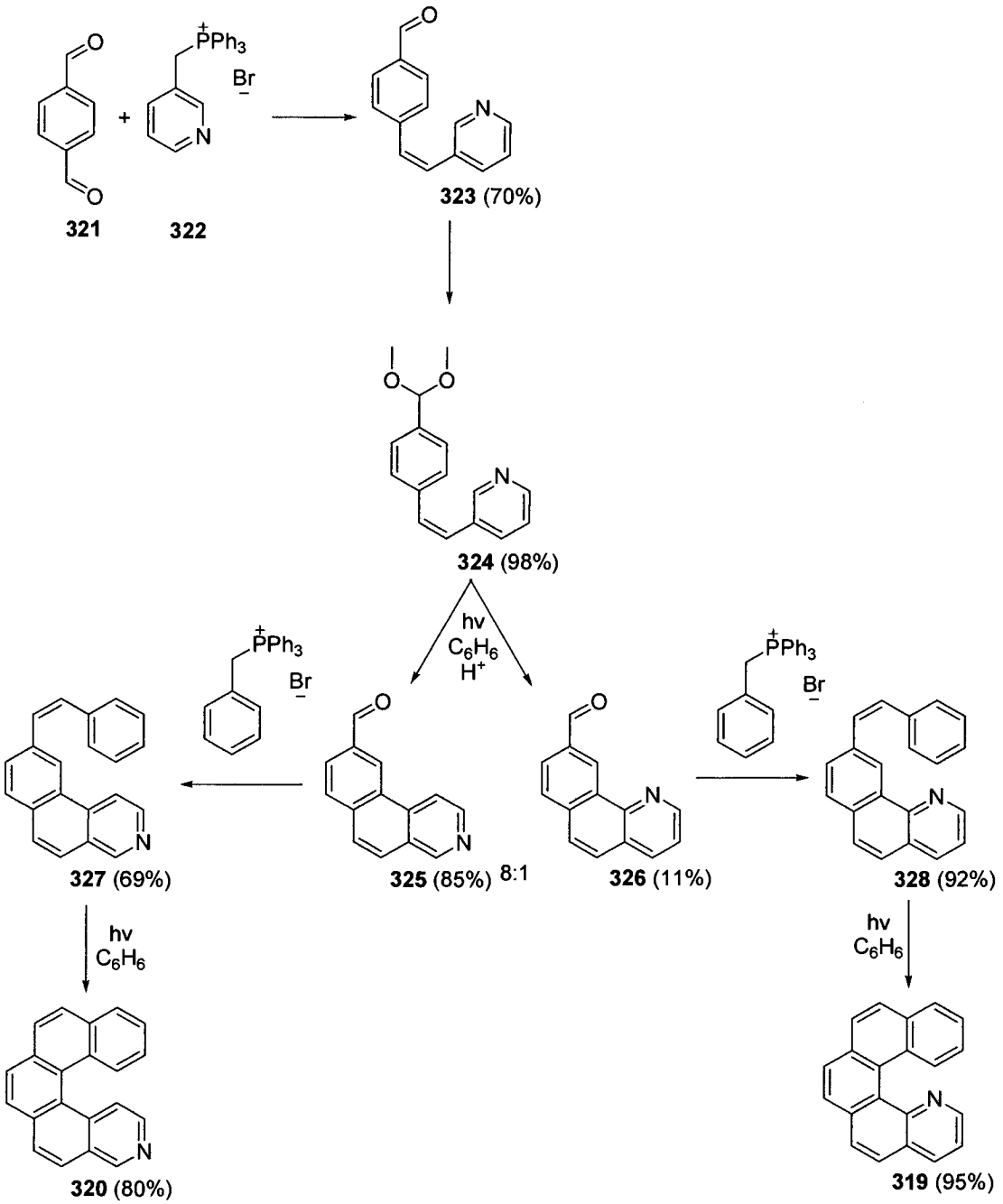
The *N*-oxide was formed to activate the methyl group so that it could be functionalised. Functionalisation of the methyl group followed by hydrolysis produced the alcohol **312** which was then oxidised to the aldehyde **313**. A Wittig reaction was used to form the alkene **314** which then cyclised under photochemical conditions to produce **308** (**Scheme 140**).

Both the final two monoaza[5]helicenes in this section can be synthesised in different yields using the photochemical method. Following the method in **Scheme 141** using the methylphenanthrene **315** as a starting material 1-aza[5]helicene **319** can be synthesised in a high yield containing a small amount of 3-aza[5]helicene **320**. However using 1,4-phenyldicarbaldehyde **321** as a starting material as in Scheme **142** 3-aza[5]helicene **320** can be synthesised in a high yield containing a small amount of 1-aza[5]helicene **319**.



Scheme 141

The Wittig reagent **317** was produced by making the phosphonium salt of **316** from the product of the bromination of **315**. Compound **317** was then tranformed into **318** by a Wittig reaction. Photochemical cyclisation of **318** produced **319** in good yield and **320** as a byproduct although the authors did not comment on the selectivity of the reaction.

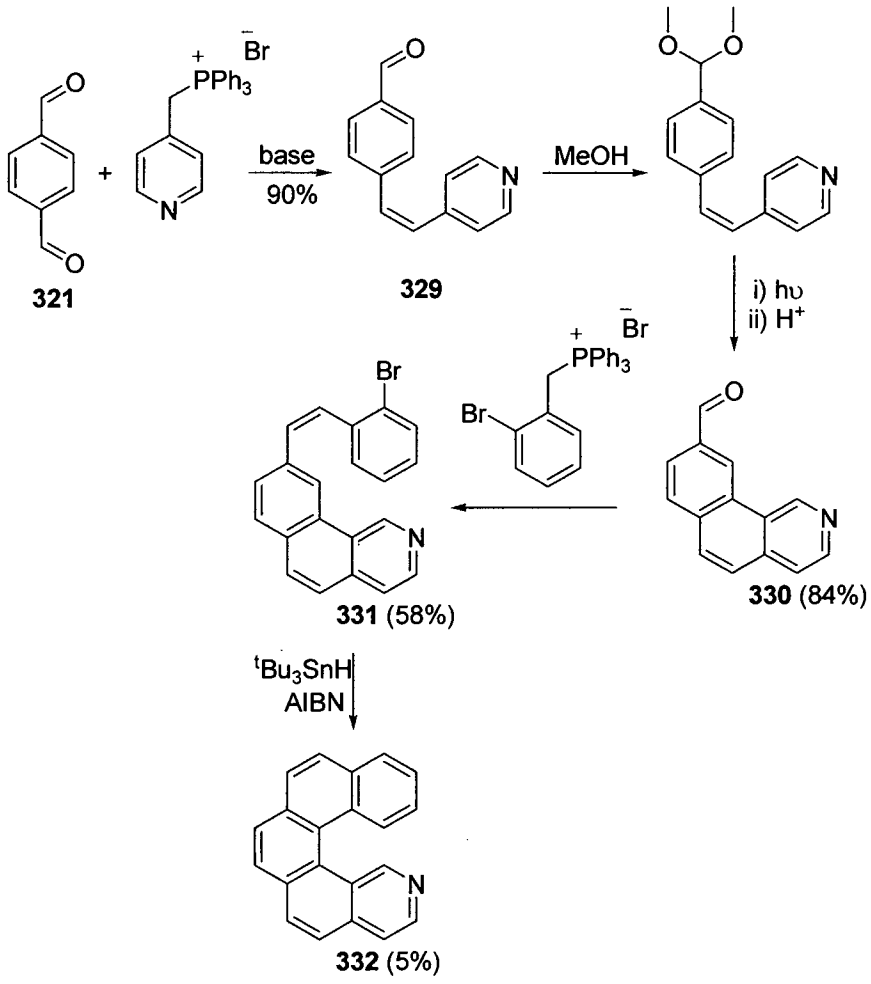

321
322
323 (70%)
324 (98%)
hv
C6H6
H+
325 (85%) 8:1
326 (11%)
327 (69%)
328 (92%)
320 (80%)
319 (95%)

Scheme 142

The other route to **319** and **320** which gave a higher yield of **320** began with the Wittig reaction of the dialdehyde **321** and the phosphonium salt **322** to produce the aldehyde **323**. The photochemical cyclisation was attempted on **323** but no reaction was observed and only starting material was recovered. The aldehyde group of **323** was transformed into the dimethylacetal **324** which cyclised under photochemical conditions immediately followed by acid hydrolysis to produce **325** in good yield with a small amount of **326** also isolated although the reason for this selectivity was not discussed. Both **325** and **326** underwent a further Wittig reaction with benzyltriphenylphosphonium bromide to produce **327** and **328** which were shown to cyclise photochemically to form **320** and **319** respectively (**Scheme 142**). Although the yields of the final cyclisation are high in both cases this route can only be considered to be a good route to **320** as the yield of **326** was very low and thus the overall yield of **319** was only 7% whilst the overall yield of **320** was 32%.

5.1.2.2 Radical Cyclisation

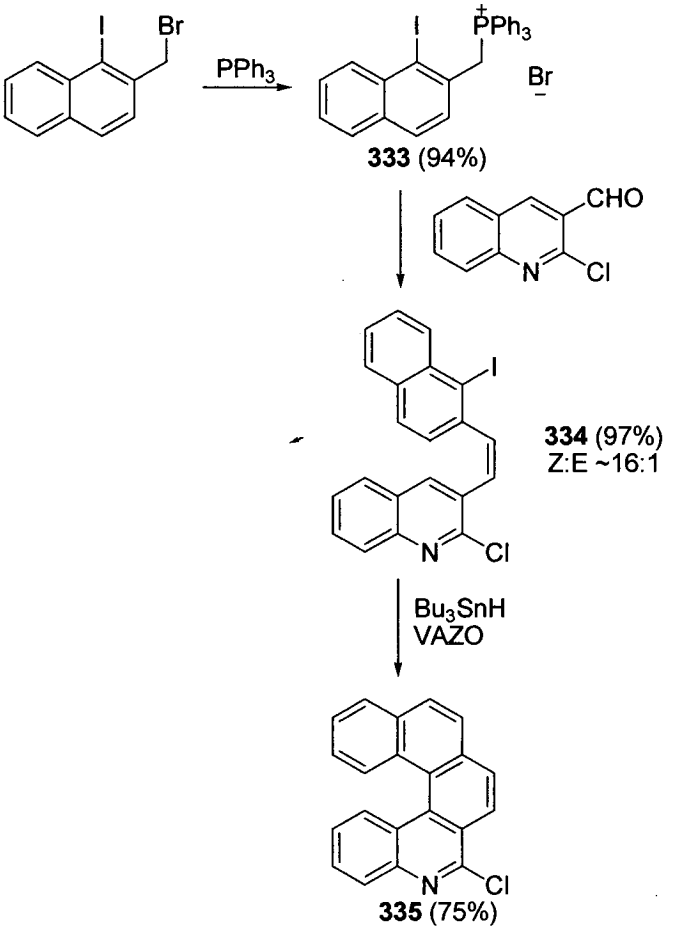
Since the photochemical cyclisation of a stilbene was not suitable for production of 2-aza[5]helicene **332** a route using a chemical-induced cyclisation had to be developed. In this case the precursor **331** underwent cyclisation using tributyltin hydride with AIBN as the radical initiator to produce **332** in low yield. As in the synthesis in **Scheme 142**, **330** was produced by the formation of the aldehyde **329** *via* a Wittig reaction which was then protected as the acetal followed by photochemical cyclisation and acid hydrolysis. A second Wittig reaction with (2-bromobenzyl)triphenylphosphonium bromide produced **331** which underwent radical cyclisation to form **332** (**Scheme 143**).



Scheme 143

It is obvious that all of the monoaza[5]helicenes can be synthesised following the work of Caronna although the synthesis of a substitued helicene has not been reported. In 2006 Harrowven *et al.*[31] reported the synthesis of a chloro-substituted 5-aza[5]helicene **335**. A substituted naphthalene starting material was transformed into the Wittig reagent **333** by reaction with triphenylphosphine. Reaction under standard Wittig conditions with 2-chloro-3-quinolinecarbaldehyde produced the alkene **334** in a high *Z*:*E* isomer ratio (~16:1) as the phosphonium salt used produced a non-stablised ylide. This selectivity was vital as the cyclisation conditions used in this synthesis only allow cyclisation of the *Z*-isomer. As in some of the previous syntheses by Caronna tributyltin

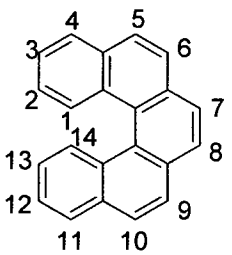
hydride was used in the cyclisation step although in this case the radical initiator VAZO [1,1'-azobis(cyclohexane)carbonitrile] was used to initiate the reaction instead of the more commonly used AIBN. As expected, the C-I bond is selectively homolysed to produce the aryl radical rather than homolysis of the C-Cl bond to produce a heteroaryl radical. This synthesis, unlike Caronna's, could only be used to produce the 6-chloro-5-aza[5]helicene **335** as any attempt to produce the parent helicene would probably result in two isomers (**Scheme 144**).



Scheme 144

5.1.3 Diaza[5]helicenes

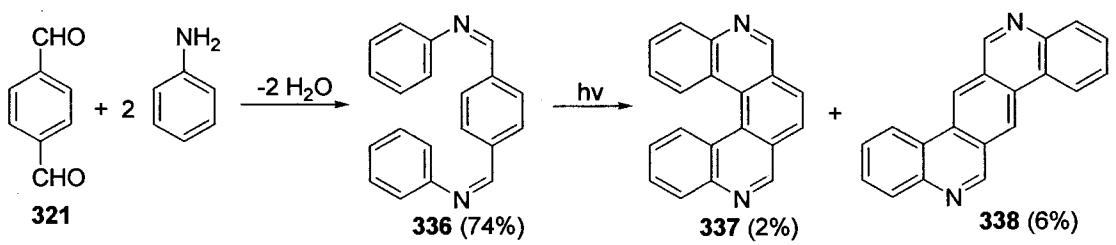
There are forty-nine possible diaza[5]helicenes which can be synthesised. However only nine are referred to in the literature but only the syntheses of eight are reported. The synthesis of the known diaza[5]helicenes are reported in three papers and have mostly been synthesised by Caronna *et al.* [99, 100, 101] using a variety of techniques.



The numbering system used for naming these compounds is shown above and is similar to that used in the four-ring systems.

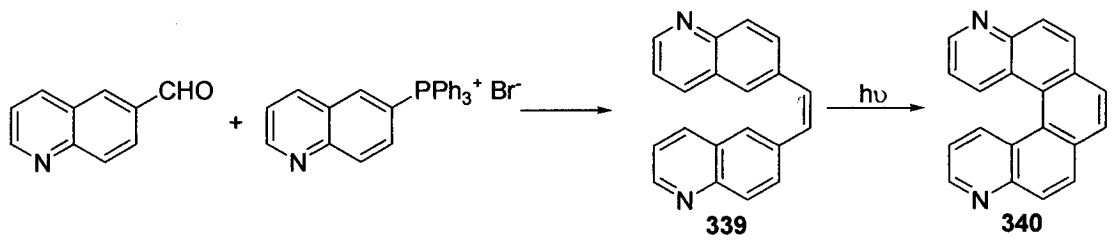
5.1.3.1 Photochemical Cyclisation

As in all of the cases discussed earlier it is possible to produce diaza[5]helicenes using a photochemical cyclisation. The first diaza[5]helicene synthesised in this way, 5,10-diaza[5]helicene, was synthesised by the condensation of the dialdehyde **321** with aniline followed by a more traditional photochemical cyclisation.[101] However using this type of cyclisation resulted in two products in very low yield with the helicene being the minor product (**Scheme 145**).

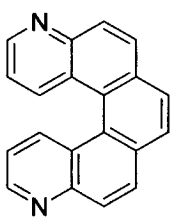


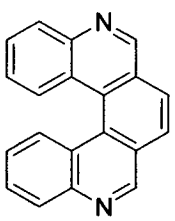
Scheme 145

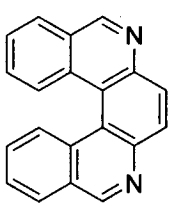
In 2005 Caronna *et al.*[99] reported a continuation of this work using photochemical cyclisations to produce six different diaza[5]helicenes, **340** - **345**, in good yield. As in the similar syntheses of the monoaza[5]helicenes Caronna used alkenes which were known to cyclise under photochemical conditions to produce single isomers. The alkenes used were produced by Wittig reactions (**Scheme 146**).

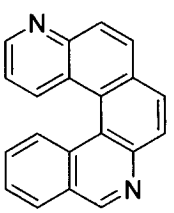


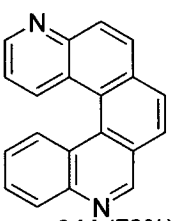
Scheme 146

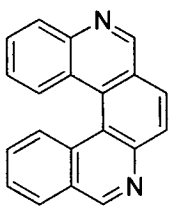

340 (78%)


341 (83%)


342 (68%)


343 (78%)

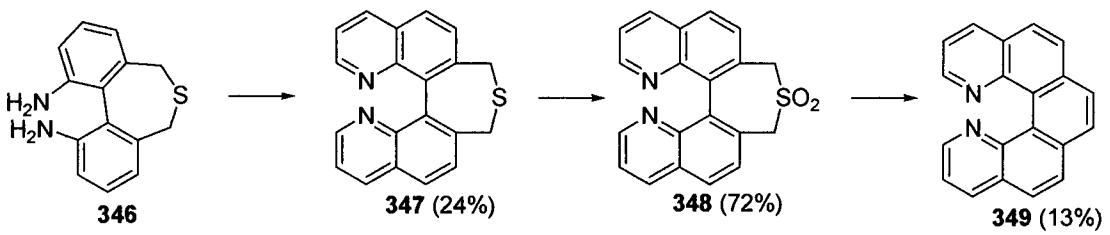

344 (72%)


345 (89%)

5.1.3.2 Other Methods

The first reported synthesis of a diaza[5]helicene did not include a phototchemical cyclisation. In 1989 Staab *et al.*[102] published the synthesis of 1,14-diaza[5]helicene **349** using traditional chemical techniques. The synthesis of **346** had previously been reported

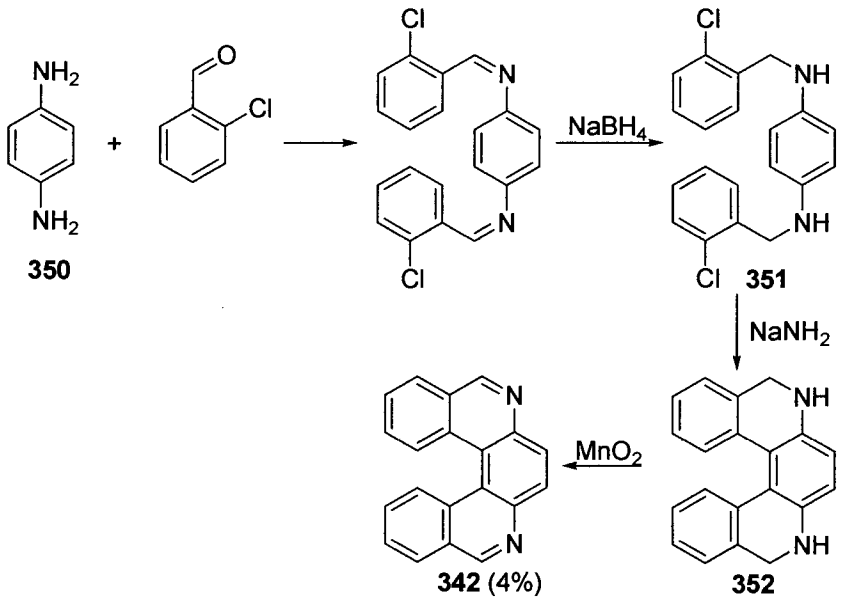
in 1986[103] and was used in a double Skraup reaction to produce **347** which was then oxidised using trifluoroperacetic acid in high yield to form **348**. The final step used a variation of the Ramberg-Bäcklund rearrangement to produce 1,14-diaza[5]helicene **349** (**Scheme 147**).



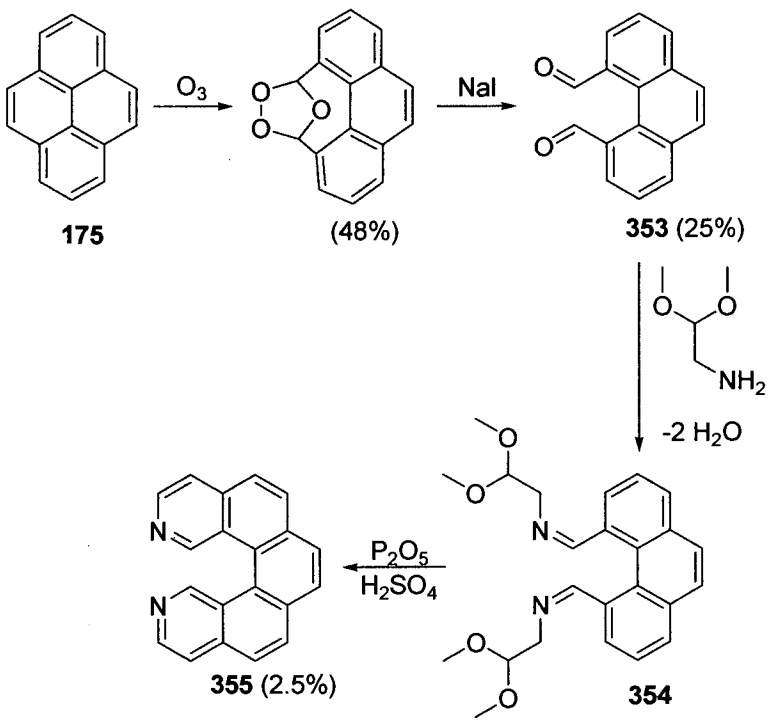
346 → **347** (24%) → **348** (72%) → **349** (13%)

Scheme 147

This work was followed by Caronna *et al.*[101] in 2002 with the synthesis of three diaza[5]helicenes, one of which was synthesised using a photochemcial cyclisation as discussed earlier. Both 2,13-diaza[5]helicene **355** and 6,9-diaza[5]helicene **342** were produced using traditional chemical cyclisations. The first of these syntheses was the route to **342** which began using a condensation reaction between the diamine **350** and 2-chlorobenzaldehyde followed by reduction of the double bond to form **351**. In this case the cyclisation was achieved by addition of sodium amide resulting in a non-aromatic five-ring system **352** which was rearomatised by oxidation with manganese dioxide to produce the helicene **342** (**Scheme 148**).



Scheme 148

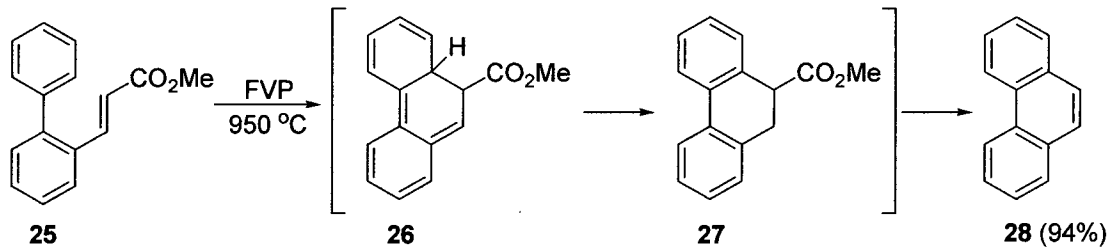


Scheme 149

The synthetic route to **355** used a very different starting material from all of the previous methods. The ozonolysis of pyrene **175** followed by treatment with sodium iodide produced the dialdehyde **353**. Reaction of the aldehyde functionalities with an amine gave the helicene precursor **354**. Using phosphorus pentoxide for the cyclisation reaction resulted in the helicene **355** in low yield (**Scheme 149**).

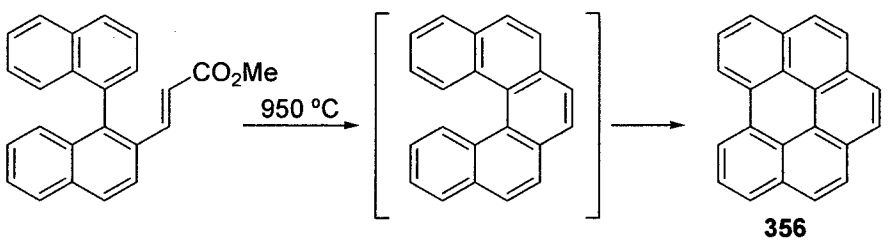
5.2 Synthetic Applications

Continuing the work discussed in previous chapters a selection of five-ring systems were synthesised. Previous work by Tipping [21] had shown that the using the binaphthyl analogue of the reaction shown in **Scheme 66** did not afford the expected product [5]helicene.



Scheme 11

It appeared from Tipping's work that the main product of the pyrolysis was the dehydrogenation product **356** (**Scheme 150**).[21] Subsequently the five-ring targets considered in this chapter all contain a heteroatom within the skeleton of the system to prevent such dehydrogenation.



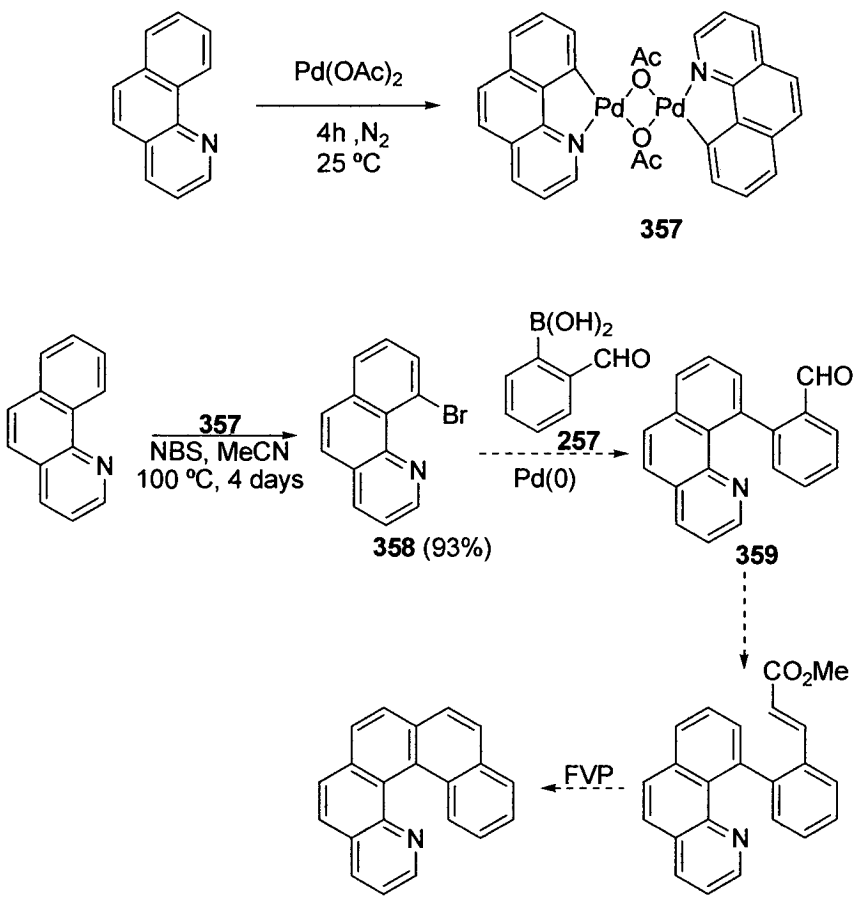
Scheme 150

The precursors synthesised are similar to those discussed in chapters 3 and 4. The intention was the produce the aldehydes which could be converted into the acrylate or oxime ether required for the cyclisation reaction. Unlike both the three and four-ring systems a number of routes to the aldehydes were explored.

5.2.1 Precursor Synthesis

5.2.1.1 Approach 1

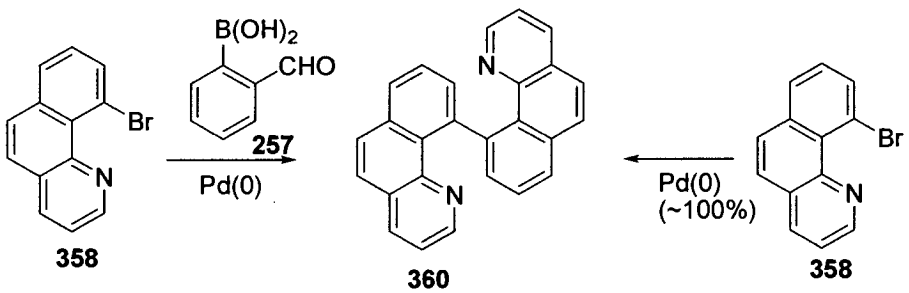
The first possible route to the five-ring systems involved starting with the coupling of a three-ring component with a single-ring component. The three-ring starting material **358** was synthesised following the work of Dick *et al.*[104]



Scheme 151

To obtain the three-ring starting material **358** catalyst **357** had to be formed by reaction of palladium acetate with benzo[*h*]quinoline. This catalyst was then added to more benzo[*h*]quinoline and *N*-bromosuccinimide in a sealed vessel; a Parr reaction vessel was used. During early attempts at this reaction it was observed that a brown solid accumulated on sides of the metal reaction vessel and the metal temperature probe of the Parr apparatus. It was for this reason that a teflon insert in the reaction vessel was used and the temperature probe was covered by a glass tube to prevent any reactions occuring with the metal of the vessel and the probe. Using these precautions this reaction then produced **358** in good yield (**Scheme 151**).

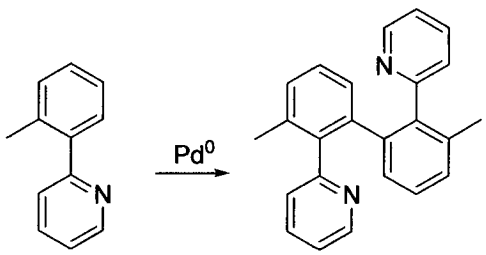
A Suzuki coupling reaction using **358** and 2-formylphenylboronic acid, **257**, under Tsvetkov's conditions[8c] produced a single product which was shown by NMR spectroscopy to contain no aldehyde moiety. Both the ^{1}H and ^{13}C NMR spectra were similar to those of **358** but the mass spectrum showed a strong molecular ion at *m/z* 356 corresponding to the dimeric species **360**, which has been previously inferred as a minor product in Bruce *et al.*'s reactions although their evidence for this structure was sparce.[105]



Scheme 152

It appeared that the boronic acid **257** had played no part in the reaction. The reaction was repeated under the same Suzuki coupling conditions in the absence of boronic acid (**Scheme 152**). Compound **360** was afforded in near quanititative yield. Although this was not a useful result in the synthesis of the desired five-ring system it is a particularly

interesting reaction which provides the novel biaryl **360** in two simple steps. Since this work was done Sanford *et al.*[106] have reported the dimerisation of *o*-tolylpyridine **361** under similar conditions (**Scheme 153**).



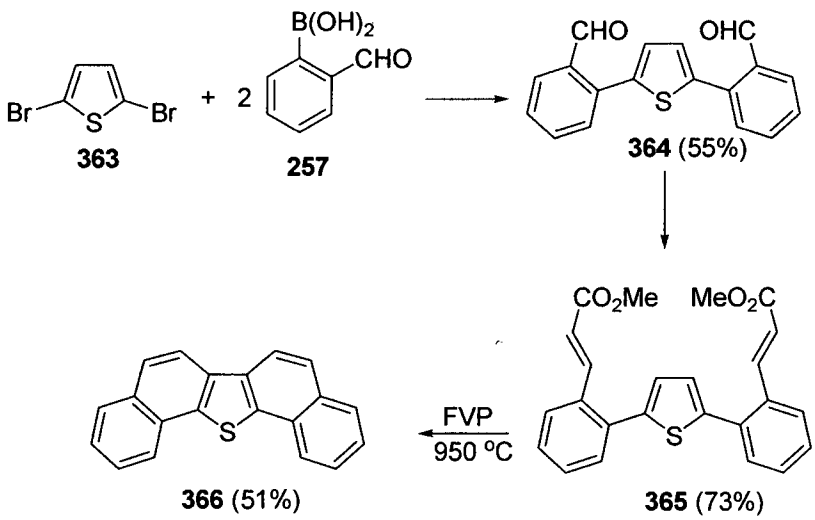
361 **362** (86%)

Scheme 153

Sanford *et al.*[106] speculate that this reaction occurs *via* a similar catalytic cycle to the Suzuki coupling reaction where both molecules of **361** oxidatively add to the palladium catalyst and are coupled to form the dimer **362** upon reductive elimination. In the case of **360** two molecules of **358** oxidatively add to the palladium catalyst which then undergo reductive elimination to form **360**.

5.2.1.2 Approach 2

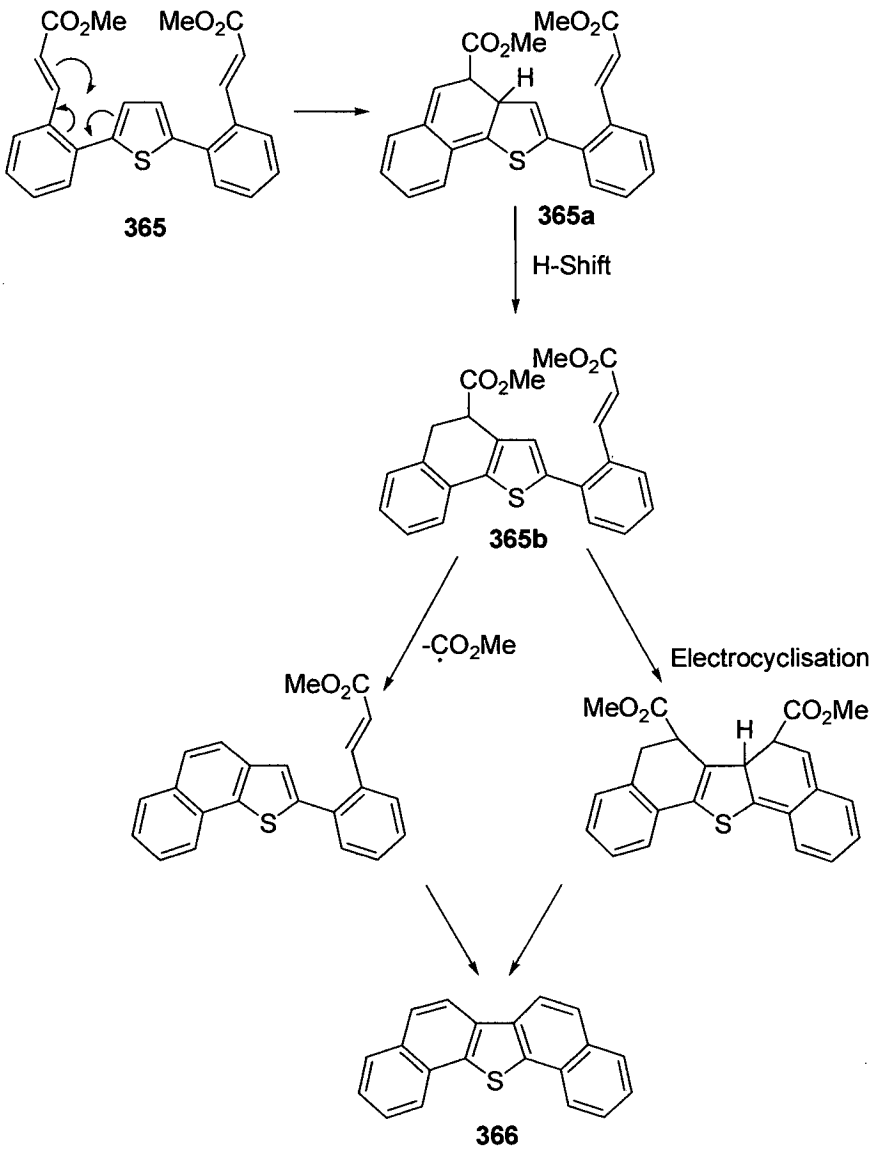
The second approach to five-ring systems involved the use of three one-ring starting materials.



Scheme 154

In this case 2,5-dibromothiophene, **363**, and two equivalents of 2-formylphenylboronic acid, **257** were coupled using Tsvetkov's Suzuki coupling conditions to give the dialdehyde **364** in reasonable yield. Following a Wittig reaction using two equivalents of Wittig reagent **365** was pyrolysed at 950 °C to afford **366** in 51% yield (**Scheme 154**).

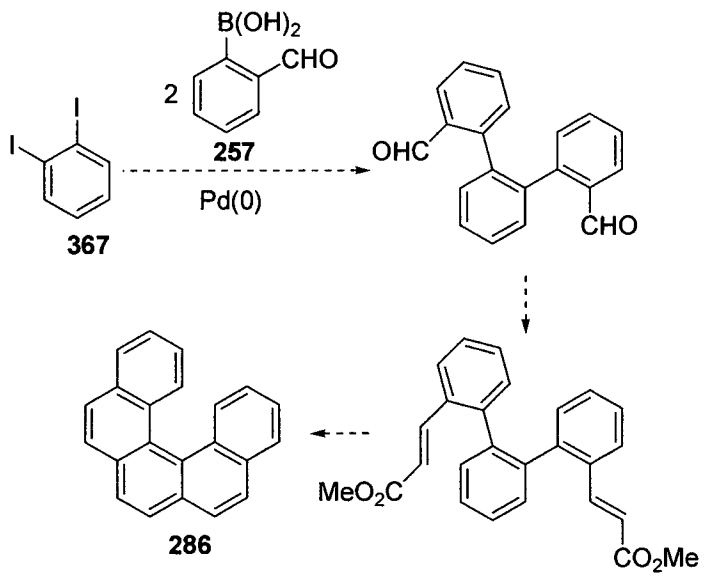
Dinaphtho[1,2-*b*:2',1'-*d*]thiophene **366** is a known compound however this synthesis was important as it was the first example of a double cyclisation of this type onto a central ring. It is possible to make some suggestions about the possible mechanism of this double cyclisation using the results discussed in chapter 2 (**Scheme 155**).



Scheme 155

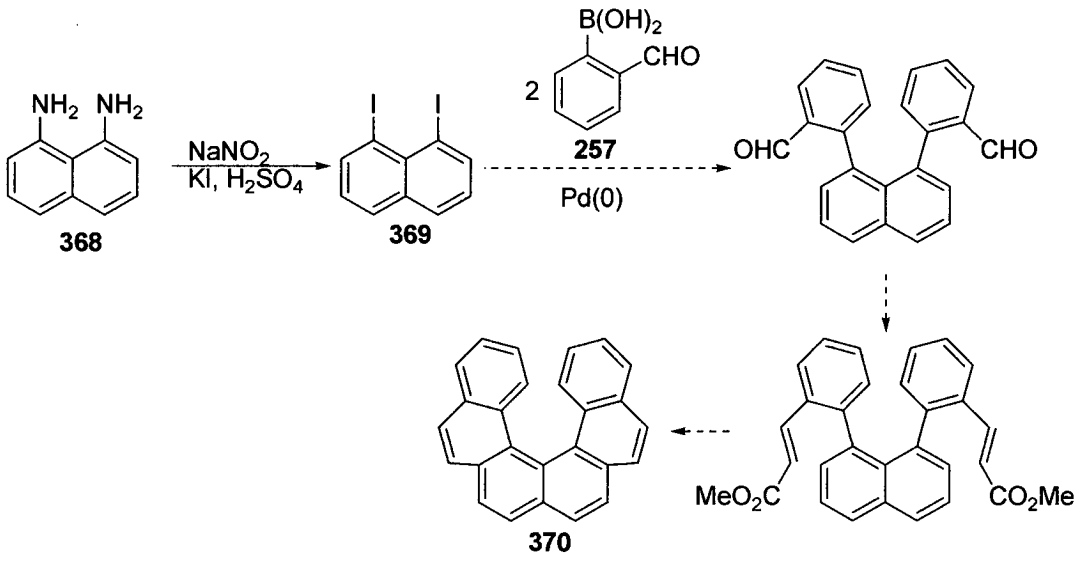
If it is assumed that both methyl acrylates do not cyclise at the same time then compound **365a** would be formed. As reported by Lewis *et al.*[107] it is known that the hydrogen-shift required to form **365b** occurs rapidly and therefore it can be assumed that this shift occurs prior to the second cyclisation. There is no evidence to suggest whether the second cyclisation would occur before or after the radical cleavage of the ester group.

Having established that this approach worked an attempt was made to transfer this methodology to a benzene based system (**Scheme 156**). The aim was to perform a double Suzuki coupling between 1,2-diiodobenzene **367** and two equivalents of 2-formylphenyl boronic acid **257** to produce a dialdehyde. The dialdehyde could then be used to produce [5]helicene **286** *via* a Wittig olefination followed by pyrolysis under standard FVP conditions.



Scheme 156

Unfortunately the Suzuki coupling reaction of **367** and **257** did not yield any useful results. It was thought that the halide atoms may be too close in space for the Suzuki reaction to take place. Similar Suzuki coupling reactions of 1,2-dihalobenzenes are known in the literature[108] although these reactions only occur in the presence of the catalyst *cis,cis,cis*-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane 1/2[$PdCl(C_3H_5)]_2$ which is currently only available *via* a seven step synthetic route.[109] The reaction was repeated using 1,8-diiodonaphthalene **369**, synthesised from 1,8-diaminonaphthalene **368**, as the iodine atoms are further apart and it was thought that this might be a suitable route to [6]helicene **370** (**Scheme 157**).

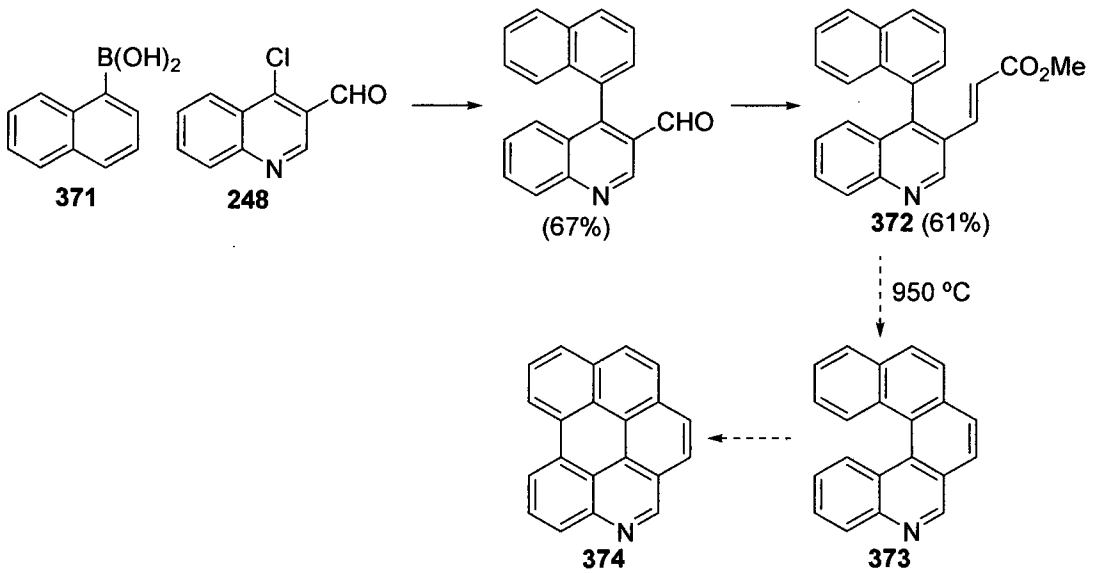


Scheme 157

1,8-Diiodonaphthalene **369** was produced from 1-8-diaminonaphthalene **368** following a literature procedure[110] and was reacted under Suzuki coupling conditions with two equivalents of **257**. The crude reaction product did not contain any identifiable products The reaction was repeated using phenylboronic acid and again there were no identifiable compounds produced. Successful application of this approach therefore awaits the development of robust catalysts which can be applied to Suzuki reactions in sterically hindered environments.

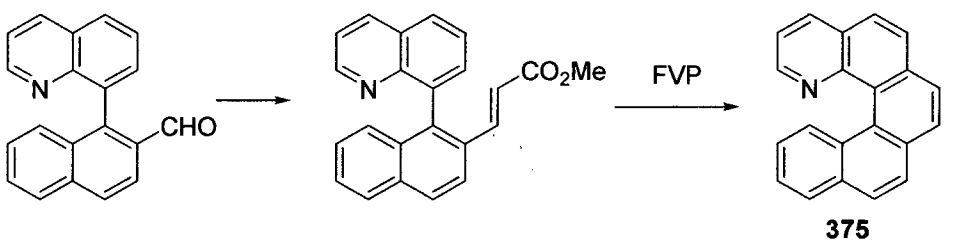
5.2.1.3 Approach 3

The third and final approach to five-ring systems involved the coupling of two two-ring starting materials. It had previously been shown that this route did not produce the desired helicene **373**. Pyrolysis of **372** produced multiple products which were not separated and identified. Comparison of this reaction with work reported by Tipping[21] suggests that dehydrogenation of the helicene **373** to form **374** (**Scheme 158**).



Scheme 158

It was therefore decided to use this methodology to produce a helicene with a heteroatom in position 1 in an attempt to prevent any dehydrogenation taking place **(Scheme 159)**.

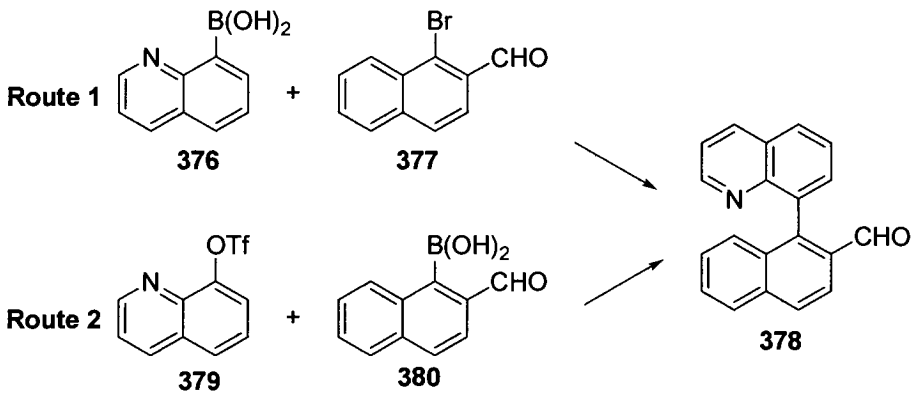


Scheme 159

The main target of this route was 1-aza[5]helicene **375** as it is analogous to [5]helicene, but five-membered heterocyclic ring, furan or thiophene, were also used to distort the overall structure of the product.

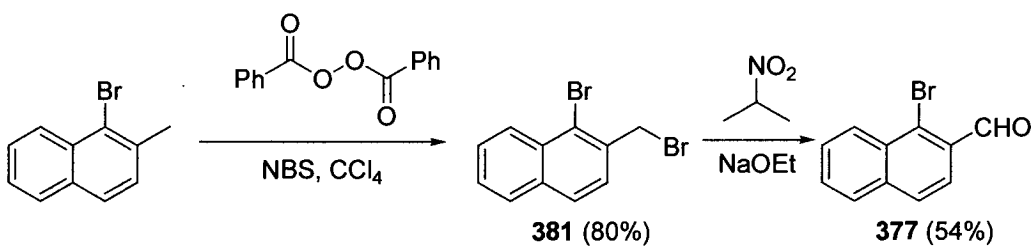
5.2.1.3.1 Aldehydes

To produce the aza[5]helicene **375** (**Scheme 159**) it was necessary to synthesise the aldehyde **378** which could be produced from two available sets of starting materials (**Scheme 160**).



Scheme 160

As 8-quinolineboronic acid **376** was commercially available and the synthesis of 1-bromo-2-formylnaphthalene was a known procedure this was the first route to **378** attempted.

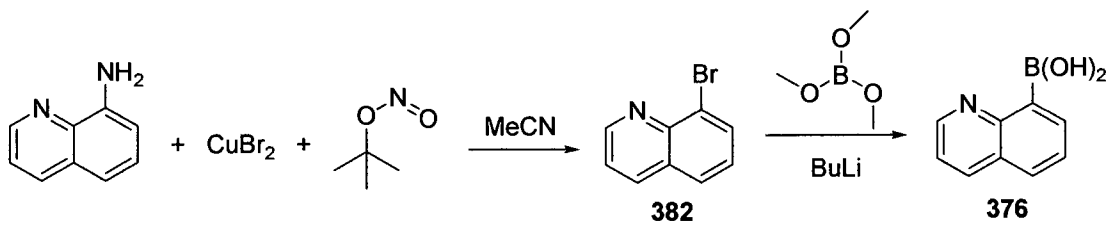


Scheme 161

Using benzoyl peroxide and *N*-bromosuccinimide it was possible to form **381** from 1-bromo-2-methylnaphthalene in good yield. The aldehyde was formed by reaction of **381** with 2-nitropropane in the presence of sodium ethoxide (**Scheme 161**). [21] Overall **377** was formed in 43% yield over two steps. A trial Suzuki coupling reaction between the

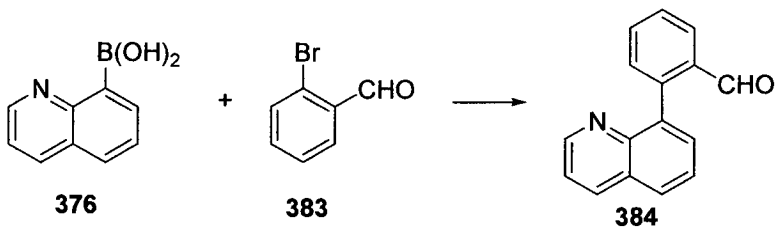
boronic acid **376** and the halide **377** under the conditions reported by Sharp and O'Shea[8b] produced the desired aldehyde **378** in reasonable yield. When the reaction was repeated on a larger scale no product was formed. The reaction was then repeated on the original scale under identical conditions and no product was obtained.

Following work by Wada *et al.*[111] it was attempted to synthesise **376**. Reaction of 8-aminoquinoline to form 8-bromoquinoline **382** appeared to be successful. It was attempted to transform the crude 8-bromoquinoline **382** into the boronic acid **376** in the normal way (**Scheme 162**). The solid produced was reacted with bromobenzene under Suzuki conditions but no reaction took place suggesting that the synthesis of **376** was unsuccessful.



Scheme 162

A number of test reactions were set up between the bought quinoline **376** and 2-bromobenzaldehyde **383** varying the catalyst, base, solvent mixture and reaction time, the results, **Table 13**, were all negative (**Scheme 163**).



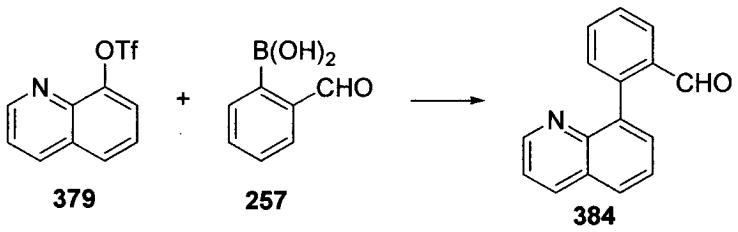
376 383 384

Scheme 163

Catalyst	Base	Solvent	Time (h)	Product (%)
$Pd(PPh_3)_4$	Na_2CO_3	Toluene/Ethanol	4	0
$Pd(PPh_3)_4$	K_2CO_3	Dioxane/Water	4	0
$Pd(PPh_3)_4$	K_2CO_3	Dioxane/Water	16	0
$PdCl_2(PPh_3)_2$	K_2CO_3	Dioxane/Water	16	0
$PdCl_2(dppf)_2$	K_2CO_3	Dioxane/Water	16	0
$Pd(PPh_3)_4$	Na_2CO_3/LiCl	Toluene	16	0

Table 13: Table of reaction conditions used for Suzuki coupling reaction of 376 and 383

Due to the irreproducibility of results route two was considered. The triflate **379** was synthesised from 8-hydroxyquinoline following Li's method.[112] The initial model reactions were done with **379** and 2-formylphenylboronic acid **257** and the conditions were varied (**Scheme 164**).



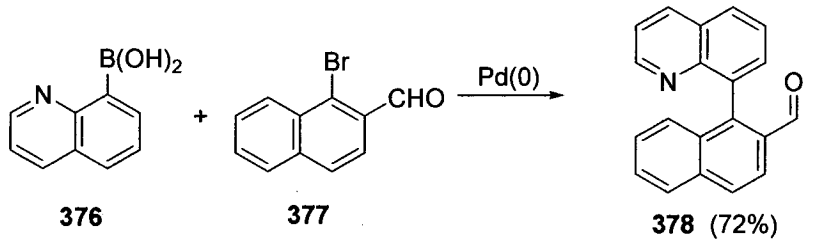
379 257 384

Scheme 164

Catalyst	Base	Solvent	Time (h)	Unreacted Triflate	Product (%)
$Pd(PPh_3)_4$	Na_2CO_3/LiCl	Toluene	16	Present	0
$Pd(PPh_3)_4$	Na_2CO_3/LiCl	Toluene	2 (OTf, Pd, tol) 16	Present	0
$Pd(PPh_3)_4$	K_2CO_3	Dioxane/Water	16	Present	0
$Pd(PPh_3)_4$	Cs_2CO_3	DME/Ethanol	16	Present	0
$PdCl_2(PPh_3)_2$	K_2CO_3	Dioxane/Water	16	Present	0
$PdCl_2(dppf)_2$	K_2CO_3	Dioxane/Water	16	Present	0

Table 14: Table of reaction conditions used for Suzuki coupling reaction of 379 and 257

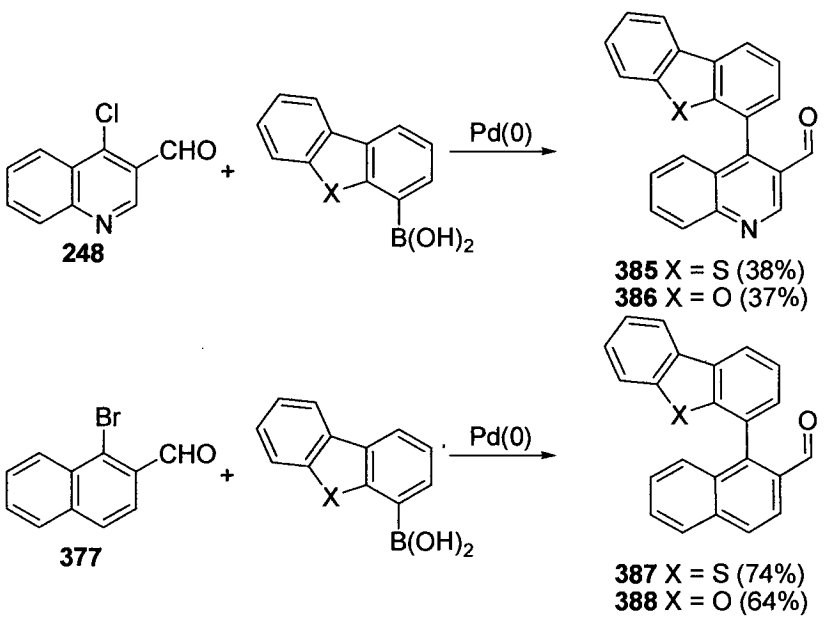
None of the conditions used produced any of the desired product. Another batch of 8-quinolineboronic acid, **376**, was purchased and the reaction with **377** was repeated under the original set of conditions. The desired product **378** was obtained. When the reaction was repeated within 24 hours the yield of the product obtained was significantly less and after 3 days there was no reaction using the same batches of reagents. As it was now recognised that this boronic acid rapidly lost activity, another batch of **376** was bought and the reaction repeated immediately on a larger scale to afford **378** in 72% yield after chromatography (**Scheme 165**).



376 **377** **378** (72%)

Scheme 165

In an attempt to produce a variety of helical systems containing a heteroatom within the cavity, to prevent any dehydrogenation upon pyrolysis, both dibenzothiopheneboronic acid and dibenzofuranboronic acid were used to produce the aldehydes **385** and **386** *via* Suzuki coupling reactions under Tsvetkov's conditions.[8c] As the final helicenes would be much less soluble it was thought that they would be less toxic therefore incorporation of a nitrogen atom into the skeleton was not necessary. Both boronic acids were coupled with **248** and **377** to produce the four aldehydes **385**, **386**, **387** and **388** (**Scheme 166**).

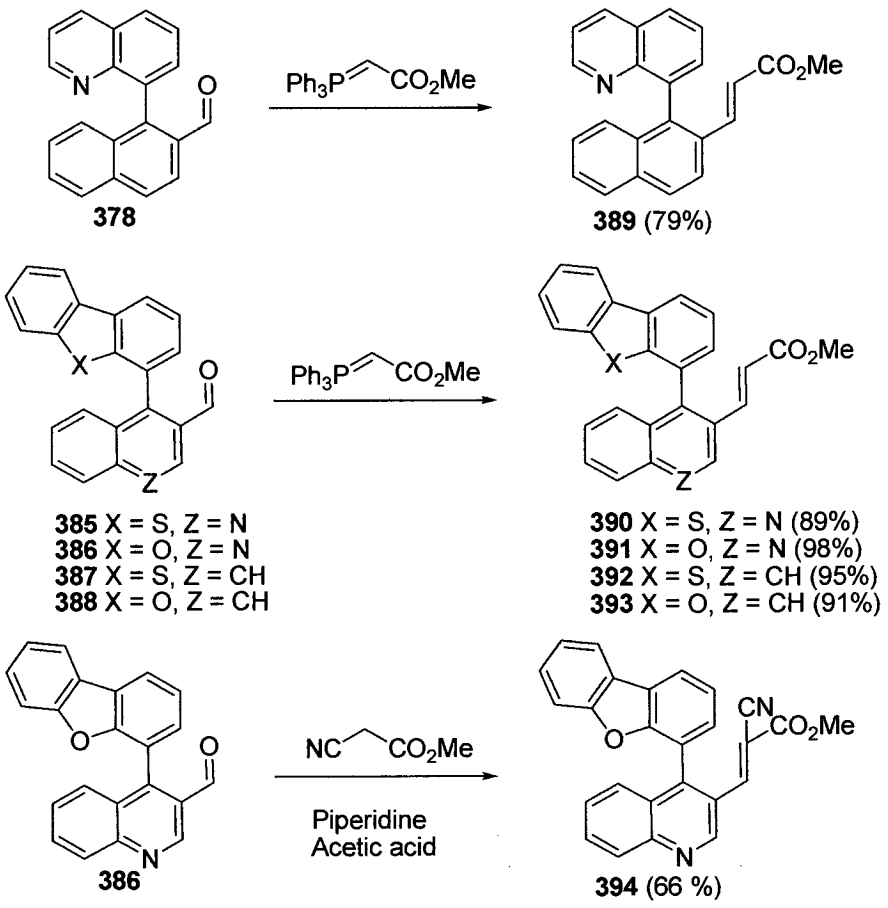


Scheme 166

5.2.1.3.2 Wittig/Knoevenagel

Compounds **389** – **393** were synthesised *via* a Wittig reaction, as discussed in chapter 3, using methyl (triphenylphosphoranylidene)acetate as the Wittig reagent (**Scheme 167**). The products were easily separated from the triphenylphosphine oxide by-product by dry flash chromatography. The yields of this reaction were all ~90% and the *E* : *Z* ratio was, on average, 81 : 19.

The cyano substituted ester **394** was synthesised *via* a Knoevenagel reaction under standard conditions and the product was shown by ^{1}H NMR spectroscopy to be a single isomer.



378

389 (79%)

385 X = S, Z = N
386 X = O, Z = N
387 X = S, Z = CH
388 X = O, Z = CH

390 X = S, Z = N (89%)
391 X = O, Z = N (98%)
392 X = S, Z = CH (95%)
393 X = O, Z = CH (91%)

386

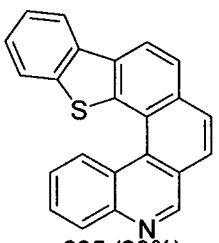
394 (66 %)

Scheme 167

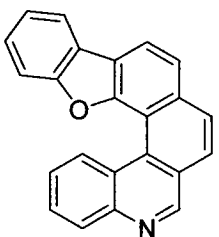
5.2.2 Pyrolyses

5.2.2.1 Dibenzothiophenes and furans

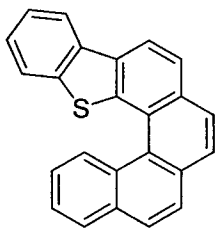
Four helical ring systems, **395** – **398**, were sucessfully produced from the methyl acrylates **390** - **393**. These compounds are not only previously unknown compounds but are a completely novel architecture.



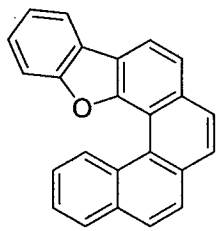
395 (23%)



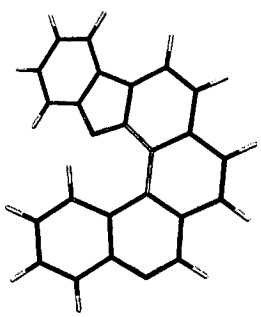
396 (90%)



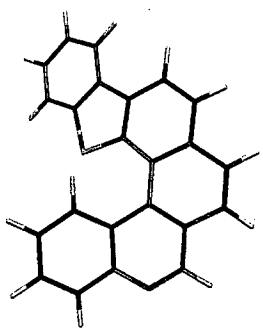
397 (33%)



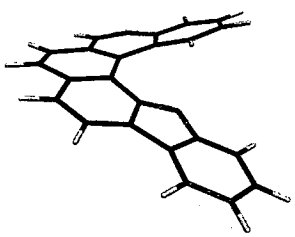
398 (41%)



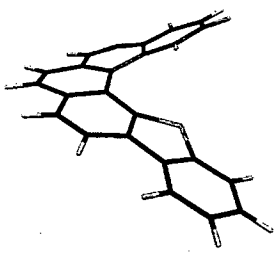
396



395

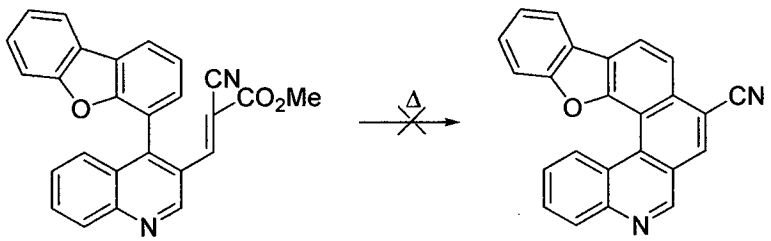


396



395

As it was not possible to produce adequate crystals of these compounds to obtain a crystal structure molecular modelling calculations were used to approximate the structure of compounds **395** and **396** (red = O, yellow = S).[113] From the calculated structures it is possible to see the helical structure of both compounds. It is notable that the pitch of the helix in the furan example, **396**, is smaller than in the thiophene example, **395**. This shows that the identity of the heteroatom within the bay of the helicene has some effect on the final structure of the compound.

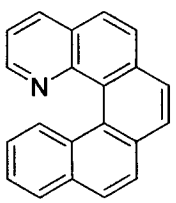


394 **399**

Scheme 168

The pyrolysis of **394** did not produce the expected product **399** (**Scheme 168**). Analysis of the crude pyrolysate of **394** showed that it contained some unreacted **394** and some decomposition products. This suggests that the product is too sterically hindered for this cyclisation to take place and that this cyclisation methodology has reached its limit.

5.2.2.2 1-Aza[5]helicene



375 (13%)

Pyrolysis of **389** produced **375** in low yield. The reaction was not repeated due to the problems with the boronic acid discussed earlier. During the course of this work, **375**

was reported by Caronna *et al.*[100] as discussed in the introduction. The helicene was identified therefore by comparison with literature ^{1}H NMR data.

Although a crystal structure could not be obtained for **375** a molecular modelling calculation was carried out to determine the theoretical structure.[114]

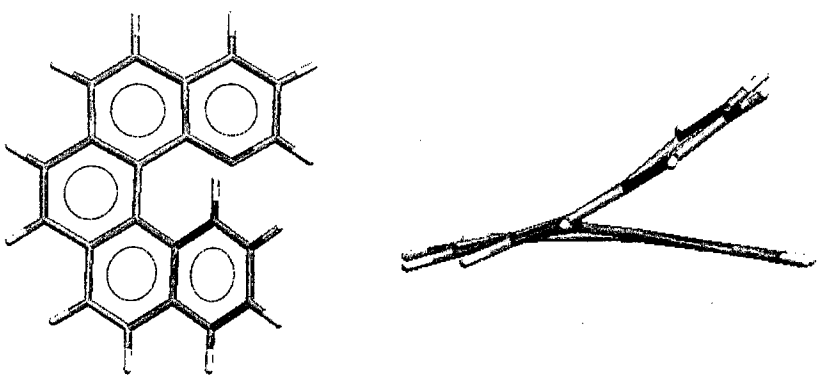
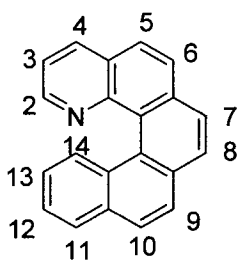
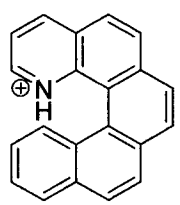


Figure 16: Calculated structure of 375

The model shows the pitch of the helix demonstrating the bay region which is available for reaction with the nitrogen lone pair of electrons.



375



400

In order to examine the potential reactivity of the lone pair of electrons on the nitrogen atom, a solution of **375** in $CDCl_3$ in an NMR tube was titrated against trifluoroacetic acid (TFA), which was expected to produce the protonated compound **400**. After each addition of acid the ^{1}H NMR spectrum of the solution was run and compared with the spectrum of **375**. In both pyridine and quinoline model systems, regular high-frequency

changes in chemical shift of C(2)-C(4) have been observed on protonation[115,116] together with an increase in coupling constant $J_{2,3}$[117] (**Table 15**).

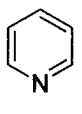
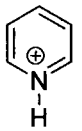
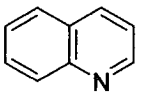
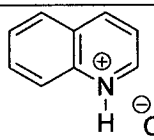
			Δ			Δ
H–2	8.60 ppm	9.23 ppm	**0.63**	9.02 ppm	9.41 ppm	**0.39**
H–4	7.64 ppm	9.04 ppm	**1.40**	7.83 ppm	9.32 ppm	**1.49**
J(2,3)	5.5 Hz	6.0 Hz	**0.5**	4.25 Hz	5.2 Hz	**0.95**

Table 15: Correlation between the ^{1}H NMR spectra of pyridine, protonated pyridine, quinoline and quinoline hydrochloride

In the spectrum of **375**, the doublet at δ_H 8.69 ppm was assigned as H-2 and the doublet at δ_H 8.28 ppm was assigned as H-4 in agreement with data reported by Caronna *et al.*[100] The chemical shifts of these protons increased by up to 0.7 ppm on addition of TFA (**Figure 9**) and these changes are comparable (though somewhat less than) the changes observed for the pyridine and quinoline model systems (**Table 15**). Although the chemical shift of some of the other peaks of **375** also altered, the changes could not be monitored unambiguously because of overlapping signals.

The graph shown in **Figure 9** displays a distinct shoulder after the addition of 4 aliquots of TFA which suggests that protonation of **375** may be complete at this stage. Confirmation that *N*-protonation had occurred was obtained by analysis of the coupling constant $J_{2,3}$. of **375**. In the neutral species the size of this parameter is 4.1 Hz which and it increased by 1.2 Hz after addition of 4 aliquots of TFA. It is known that the chemical shifts in these types of system are affected by both concentration and solvent changes and this may explain the small changes in chemical shifts observed in the case of **375** after further addition of TFA (**Figure 9**).[118,119]

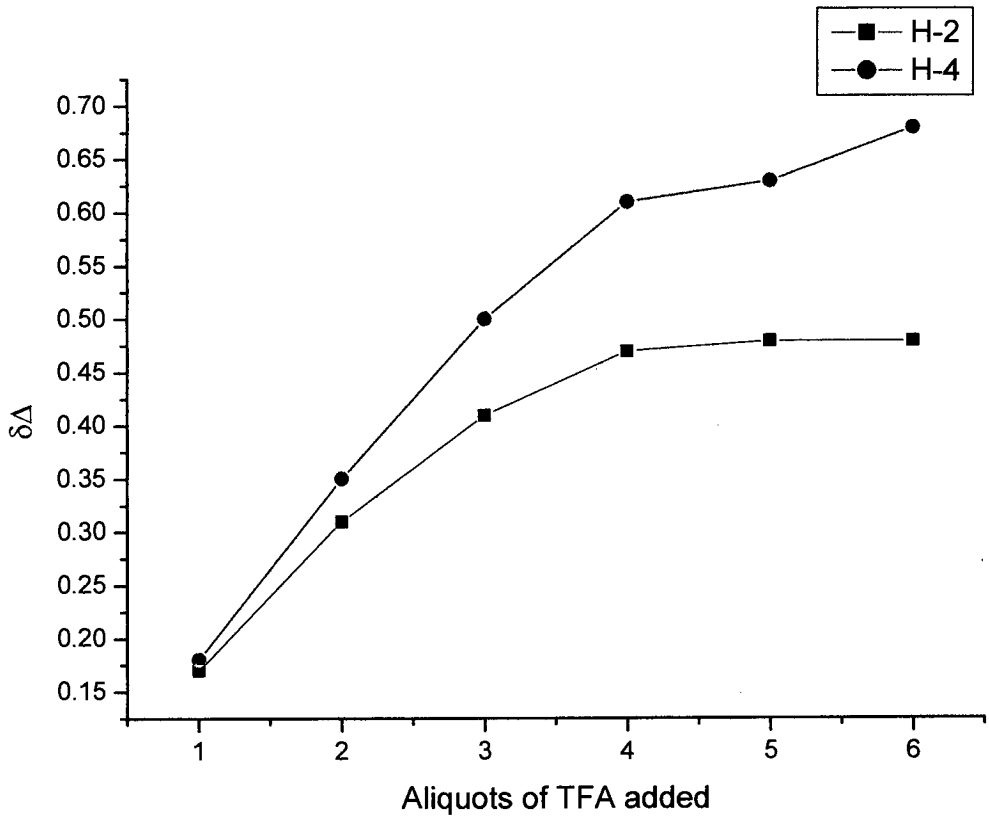


Figure 17: Change in δH of H-2 and H-4 of 375 on addition of Trifluoroacetic Acid plotted using Origin

This experiment shows that although the lone pair of electrons on the nitrogen atom is shielded by its situation in the bay region of the helicene they can still react to produce the protonated form **400**.

5.3 Conclusions

In conclusion three different routes to five-ring systems were attempted. Using first route it was discovered that under Suzuki coupling conditions 10-bromophenanthridine

underwent a self-coupling reaction to produce 10,10-biphenanthridine **360** but no five-ring system was produced.

The second route showed that it was possible to perform a double cyclisation onto a single central ring using the same cyclisation reaction discussed in the previous chapters. Although this method was used as a new route to dinaphtho[1,2-*b*:2',1'-*d*]thiophene **366** it could not be extended to the synthesis of [5]helicene due to an unsuccessful Suzuki coupling reaction.

The third and final approach, which is the same route discussed in chapter 3 and 4, was originally used in an attempt to produce [5]helicene but under the pyrolysis conditions dehydrogenation occurred. This route was then used to produce 1-aza[5]helicene **375** in which the nitrogen atom prevented any possibility of dehydrogenation under FVP conditions. This approach was also used to synthesise four new benzoheterohelicenes.

Using ^{1}H NMR spectroscopy the successful protonation of 1-aza[5]helicene **375** by trifluoroacetic acid was followed.

6 Conclusions

In conclusion it has been proved that the reaction described in **Scheme 11** can be used to synthesise a wide variety of known and unknown three-, four-and five-ring systems including four benzoheterohelicenes. The generality of this reaction has been shown by its ability to produce furan, thiophene and pyridine analogues of phenanthrene and benzo[*c*]phenanthrenes. The synthesis of cyano, methyl and chloro substituted systems has shown that this methodology could be used in the future to produce functionalised derivatives.

The possibility of performing a double cyclisation onto a single central ring has been demonstrated although this route was unsuccessful in the synthesis of a helical product.

Using ^{1}H NMR spectroscopy the protonation of 1-aza[5]helicene by trifluoroacetic acid was followed.

It has been shown that the methyl ester leaving group is the optimum leaving group for this reaction although the carboxylic acid and amides produce similar results. It was also discovered that pyrolysis of analogous acid chloride systems produced acetylene and benzazulene products *via* a methylenecarbene intermediate. The mechanistic studies suggest that the main under FVP conditions the ester group is lost *via* radical cleavage following an initial electrocyclisation and 1,5 hydrogen-shift.

In addition, the known cyclisation reaction of oxime ethers under FVP conditions *via* iminyl radicals has been shown to be a useful method of synthesising heterocyclic systems containing a nitrogen atom in the central ring of three- and four-ring systems. During this work further evidence for these cyclisations occuring *via ipso*-attack by the iminyl radical rather than direct cyclisation was obtained.

During the course of this work it was discovered that under Suzuki coupling conditions 10-bromophenanthridine underwent a self-coupling reaction to produce 10,10-biphenanthridine and the unusual reaction of 2-bromopyridine and 2-formylphenylboronic acid under Suzuki coupling condition was observed and the structure of the unexpected product has been determined.

7 Experimental

7.1 Abbreviations

δ_H, δ_C	chemical shift
DMSO	dimethyl sulfoxide
DCM	dichloromethane
THF	tetrahydrofuran
DMF	*N,N*-dimethylformamide
$MgSO_4$	anhydrous magnesium sulfate
FVP	flash vacuum pyrolysis
mol	moles
NMR	nuclear magnetic resonance
s	singlet
d	doublet
dd	doublet of doublets
t	triplet
m	multiplet
br	broad
J	coupling constant

quat	quaternary (^{13}C spectra)
MHz	megaHertz
°C	degrees Celsius
bp	boiling point
mp	melting point
lit.	literature value
m/z	mass to charge ratio
M^+	molecular ion mass
h	hours
min	minutes
cm^3	cubic centrimetres
g	grams
conc.	concentrated
aq.	aqueous solution
T_f	furnace temperature
T_i	inlet temperature
t	time taken for pyrolysis
m	mass of substrate used
P	pressure

7.2 Instrumentation and General Techniques

Nuclear Magnetic Resonance Spectroscopy

^{1}H NMR spectra were recorded on DPX360 (360 MHz), Bruker ARX250 (250 MHz) and Varian Gemini 200 (200 MHz) spectrometers.

^{13}C NMR spectra were obtained on DPX360 (90 MHz), Bruker AC250 (63 MHz) and AC200 (50 MHz) instruments.

The DPX360 was operated by Mr J. Bella, Miss F. M. McMillan, Mr J. R. A. Millar, Dr D. Reed, Dr. D. Uhrin and Dr S. I. Wharton. The Bruker AC250 was operated by Mr. J. R. A. Millar and the Varian Gemini 200 by Miss F. M. McMillan.

Spectra were recorded for solutions in [^{2}H]chloroform, unless otherwise stated. Chemical shifts (δ_H and δ_C) are quoted in ppm relative to tetramethylsilane, and all coupling constants are given in Hertz (Hz). Unless otherwise stated, ^{13}C peaks are CH resonances. ^{1}H NMR Spectra were recorded at 250 MHz and ^{13}C spectra at 63 MHz unless otherwise stated.

Mass Spectrometry

Spectra were obtained under electron impact conditions on a Kratos MS50TC instrument for both nominal and accurate masses. Spectra were recorded by Mr A. T. Taylor.

Elemental Analysis

Microanalyses were carried out on a Perkin Elmer 240 CHN Elemental Analyser by Mrs S. Djurdjevic. Some compounds synthesised during the course of this research are unstable and purification is not possible. In these cases accurate mass is recorded rather than elemental analysis.

Melting Points

Melting points were measured on a Gallenkamp capillary tube apparatus and are uncorrected.

Chromatography

Thin-layer chromatography was carried out on Merck aluminium-backed plates coated with Kieselgel GF254 (0.2 mm), impregnated with ultra violet indicator.

Dry-flash column chromatography was carried out on Kieselgel GF254 silica. The crude materials were pre-absorbed onto silica gel using DCM or methanol, and then loaded onto the column. Elution was carried out under vacuum supplied by a vacuum pump.

Solvents

All reagents were standard laboratory grade and were used as supplied, unless specifically stated in the text. Solvents for general use were standard laboratory grade and were used as supplied, unless specifically stated in the text.

Flash Vacuum Pyrolysis

Flash vacuum pyrolysis involves gaseous molecules being subjected to high temperatures for very short periods of time, usually 10^{-2}-10^{-3} seconds. In principle, the substrate is distilled or sublimed through an electrically heated tube which is connected to a cold trap and vacuum line.

Figure 18 illustrates the apparatus used in such experiments and is based on the design of W.D. Crow of the Australian National University.

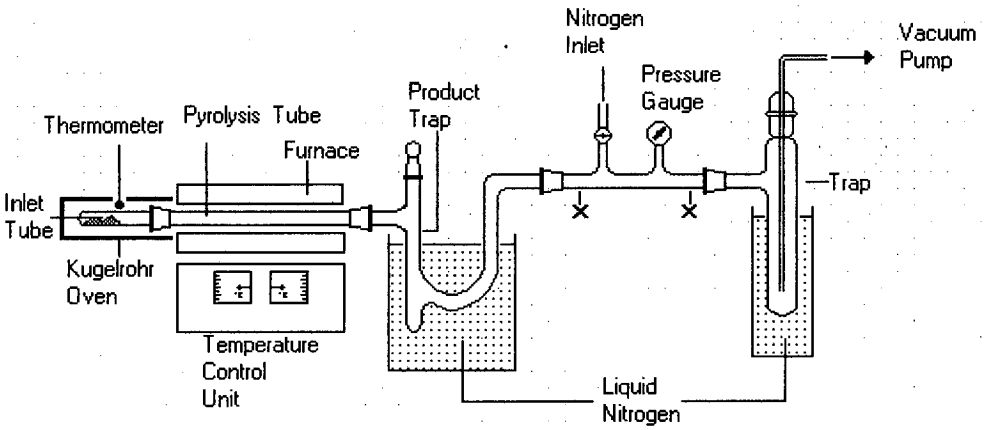


Figure 18

A glass Büchi oven, or metal Kugelrohr oven for potentially explosive azides, was used to volatilise the substrate at temperatures lower than 300°C and the gaseous substrate is then drawn through a silica tube (30 × 2.5 cm) heated by a Carbolite electronically controlled laboratory tube furnace Model No. MTF 12/38/250. The products are collected at the exit of the furnace tube in a trap surrounded by liquid nitrogen. The system was evacuated and the vacuum maintained by an Edwards Model ED100 high capacity oil pump for pressures of 1×10^{-2} Torr or suplemetned by an oil diffusion pump for pressures of 1×10^{-6} Torr. Reaction products are collected in the U-shaped product trap. Once the reaction is complete, the pump is isolated and the product trap is allowed to warm to room temperature under an atmosphere of nitrogen.The entire pyrolysate was either scraped from the trap for analysis or washed through with a suitable solvent.

Standard pyrolysis parameters used throughout this section are furnace temperature T_f, inlet temperature T_i, pressure P, time of pyrolysis t and mass of substrate m.

7.3 Mechanistic Studies

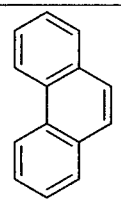
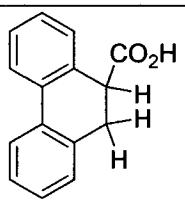
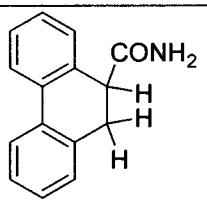
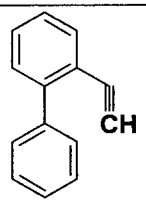
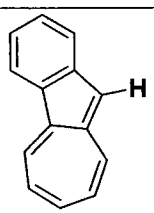
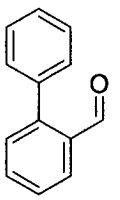
 **28**	8.75 (2H, d, *J* 8.1), 7.96 (2H, dd, *J* 1.3, 7.8) and 7.81 (2H, s)[120]
 **59**	3.23 (2H, m) and 3.84 (1H, t)[121]
 **60**	3.65 (1H, t, *J* 1.0, 6.0)[122]
 **61**	3.05 (1H, s)[14]
 **62**	6.84 (1H, d, *J* 8.5), 6.96 (1H, d, 8.3), 7.19 (1H, d, 8.5) and 7.23 (1H, s)[123]

Table 1: Characteristic peaks in ^{1}H NMR spectra of 28, 59, 60, 61 and 62

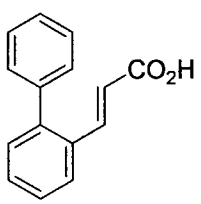
Table 1 shows the characteristic peaks used to determine the compounds present in the pyrolysates of **54**, **57** and **58**. The relative heights of the integrals of these peaks were used to determine the percentage composition of the pyrolysates of **54**, **57** and **58**.

Biphenyl-2-carbaldehyde[124] **29**



2-Biphenylmethanol **30** (3.03 g, 16.5 mmol) was added to a suspension of activated MnO_2 (17.1 g, 0.197 mol) in toluene (120 cm^3) and the mixture heated under reflux for 3 h. On cooling the mixture was filtered through celite to remove the inorganics and the filtrate dried over $MgSO_4$. The solvent was then removed under vacuum to produce biphenyl-2-carbaldehyde **29** as a yellow oil (2.62 g, 87%) bp 52 °C [lit.[124], 85 °C (0.1 Torr)]. (Found: M^+ 182.0732. $C_{13}H_{10}O$ requires *M* 182.0732); δ_H (250 MHz, $CDCl_3$): 7.52 – 7.68 (8H, m), 8.19 (1H, td, *J* 1.5, 8.0), 8.21 (1H, dd, *J* 1.5, 7.7) and 10.16 (1H, s);δ_C (250 MHz, $CDCl_3$): 127.0 (CH), 127.5 (CH),127.9 (H), 128.2 (2 CH), 129.8 (2 CH), 130.8 (CH), 133.3 (CH), 133.4 (CH), 137.4 (quat), 145.7 (quat) and 192.1 (CH); *m/z* 182 (M^+, 89%), 181 (99), 154 (70), 153 (90), 152 (100), 151 (69) and 76 (76).

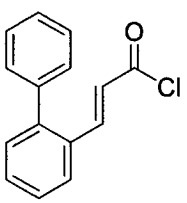
***o*-Phenylcinnamic Acid**[125] **54**



Malonic acid **53** (0.572 g, 5.49 mmol) was dissolved in pyridine (1 cm^3) and warmed to aid dissolution. Biphenyl-2-carbaldehyde **29** (1.03 g, 5.62 mmol) was added dropwise followed by a catalytic amount of piperidine (0.02 cm^3). The solution was heated to 100 °C for 3 h until CO_2 evolution had stopped. On cooling HCl (2 M, 10 cm^3) was added and the white solid produced was removed by filtration and washed with HCl (2 M), water and light petroleum (b.p. 40-60 °C). The white solid produced was recrystallised from ethanol to produce *o*-phenylcinnamic acid **54** as white crystals (1.08 g, 86%). (Found: M^+ 224.0837. $C_{15}H_{12}O_2$ requires *M* 224.0837); δ_H (250 MHz, [$^2H_6$] DMSO): 6.41 (1H, d, *J* 15.9), 6.93 – 7.45 (9H, m) and 7.83 (1H, dd, *J* 7.2, 1.7); δ_C (250 MHz, [$^2H_6$] DMSO): 119.8 (CH), 126.7 (CH), 127.4 (CH), 127.7 (CH), 128.2 (2

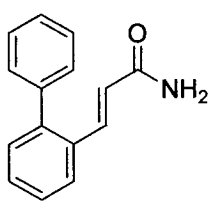
CH), 129.4 (2 CH), 129.8 (CH), 130.1 (CH), 131.5 (quat), 139.3 (quat), 141.9 (CH), 142.1 (quat) and 167.2 (quat); *m/z* 224 (M^+), 179 (100) and 178 (77).

o-Phenylcinnamoyl Chloride[126] 57



Thionyl chloride **56** (0.2 cm^3, 0.300 g, 2.50 mmol) was carefully added to *o*-phenylcinnamic acid **55** (0.566 g, 2.50 mmol) and the solution stirred at room temperature for 2 h. The solution was then heated under reflux for 20 min and heated without a condenser for 10 min. On cooling the excess thionyl chloride was removed under water pump vacuum to produce *o*-phenylcinnamoyl chloride **57** as a brown oil (0.515 g, 85 %) mp 190 °C [lit.[126], 182 °C (3 Torr)]. δ_H (250 MHz, $CDCl_3$): 6.53 (1H, d, *J* 15.8), 7.21 - 7.48 (8H, m), 7.64 (1H, d, *J* 7.8) and 7.83 (1H, d, *J* 15.8); δ_C (250 MHz, $CDCl_3$): 122.4 (CH), 126.6 (CH), 127.3 (CH), 127.4 (CH), 127.8 (2 x CH), 129.2 (2 x CH), 130.2 (CH), 130.5 (quat), 130.8 (CH), 138.6 (quat), 143.6 (quat), 149.4 (CH) and 165.5 (quat).

o-Phenylcinnamamide[126] 58



o-Phenylcinnamoyl chloride **57** (0.515 g, 2.12 mol) was melted in warm water and added dropwise to an excess of concentrated aq. ammonia solution. Fumes were produced and a white solid was formed. The solid was broken and stirred then left overnight. The solid was then removed by filtration and washed with cold water then recrystallised from hot water to produce *o*-phenylcinnamamide **58** as a white solid (0.165 g, 35%) mp 164 °C [lit.[126], 163 – 164 °C]. δ_H (250 MHz, $CDCl_3$): 5.38 (2H, br s), 6.31 (1H, d, *J* 15.7), 7.19 – 7.37 (10H, m) and 7.55 (1H, d, *J* 15.9); δ_C (250 MHz, $CDCl_3$): 120.8 (CH), 126.7 (CH), 127.5 (2 CH), 128.2 (CH), 129.5 (2CH), 129.6 (2CH), 130.5 (CH), 132.6 (quat), 139.9 (quat), 141.1 (CH), 142.7 (quat) and 167.6 (quat).

FVP of *o*-Phenylcinnamic Acid 54

Flash vacuum pyrolysis of *o*-phenylcinnamic acid **54** (0.011 g, T_f 950 °C, T_i 220 °C, P 3.8×10^{-2} - 7×10^{-2} Torr, t 15 min) gave a crude pyrolysate containing phenanthrene **28** (84%) and 9,10-dihydrophenanthrene-9-carboxylic acid **59** (16%).

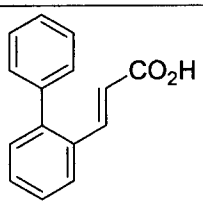
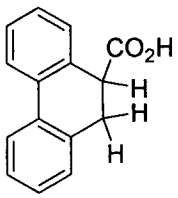
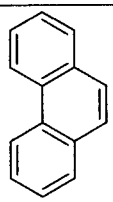
T_f	Percentage of Pyrolysate		
	 **54**	 **59**	 **28**
750	82	10	8
800	61	16	23
850	8	14	78
875	17	11	72
900	16	9	85
925	4	9	87
950	0	16	84

Table 16: Composition of Pyrolysate of 54

FVP of *o*-Phenylcinnamamide 58

Flash vacuum pyrolysis of *o*-phenylcinnamamide **58** (0.0186 g, T_f 950 °C, T_i 209 °C, P $2.3 \times 10^{-2} - 1.3 \times 10^{-1}$ Torr, t 5 min) gave phenanthrene **28** (100%).

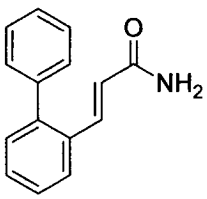
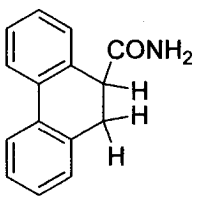
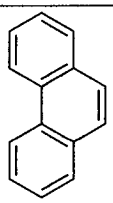
T_f	Percentage of Pyrolysate		
	 **58**	 **60**	 **28**
650	100	0	0
700	96	0	4
800	47	20	33
900	4	16	80
950	0	0	100

Table 17: Composition of Pyrolysate of 58

FVP of *o*-Phenylcinnamoyl Chloride 57

Flash vacuum pyrolysis of *o*-phenylcinnamoyl chloride **57** (0.023 g, T_f 950 °C, T_i 193 °C, P $3.4 \times 10^{-2} - 1.9 \times 10^{-2}$ Torr, t 15 min) phenanthrene **28** (65%), biphenylacetylene **61** (3%), and benzo[*a*]azulene **62** (32%).

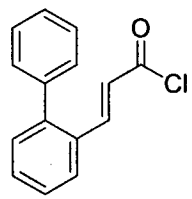
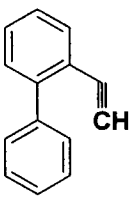
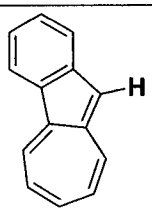
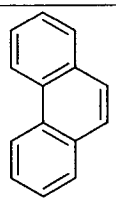
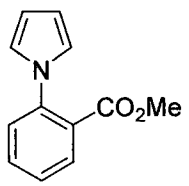
T_f	Percentage of Pyrolysate			
	 **57**	 **61**	 **62**	 **28**
450	100	0	0	0
475	100	0	0	0
500	77	16	0	6
550	18	59	15	8
600	0	73	18	9
650	0	72	18	10
700	0	76	14	10
750	0	63	21	16
850	0	19	39	42
950	0	3	32	65

Table 18: Composition of Pyrolysate of 57

N-(2-Methoxycarbonylphenyl)pyrrole[20] **10**



Methyl anthranilate (6.07 g, 44.9 mmol), 2,5-dimethoxy tetrahydrofuran (6.36 g, 48.9 mmol), dioxane (60 cm^3) and glacial acetic acid (40 cm^3) were mixed and heated under reflux for 4 h. The solvent was then removed under vacuum and the product purified by Kugelrohr distillation to produce *N*-(2-methoxycarbonylphenyl)pyrrole **10** as a yellow oil (7.40 g, 82%). δ_H (250 MHz, $CDCl_3$): 3.60 (3H, s), 6.18 (2H, t, *J* 2.1), 6.68 (2H, t, *J* 2.1), 7.26 (2H, t, *J* 5.5), 7.42 (1H, m) and 7.68 (1H, dd, *J* 2.1, 8.3).

FVP of *N*-(2-Methoxycarbonylphenyl)pyrrole **10**

Flash vacuum pyrolysis of *N*-(2-methoxycarbonylphenyl)pyrrole **10** (0.205 g, T_f 925 °C, T_i ~25 °C, P $3.2 \times 10^{-2} - 8.5 \times 10^{-2}$ Torr, t 5 min) using acetyl chloride (0.225 g) in the modified pyrolysis apparatus (**Section 2.3, Figure 9**) was shown by ^1H NMR spectroscopy to have produced methyl acetate (δ_H 3.64 ppm). This suggests that methanol was produced upon the pyrolysis of N-(2-methoxycarbonylphenyl)pyrrole **9** which reacted with the acetyl chloride.

Model Compound Synthesis and Pyrolysis

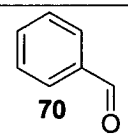
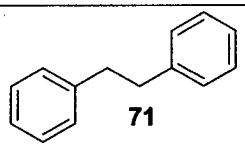
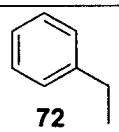
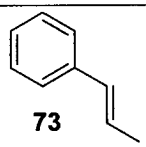
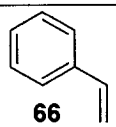
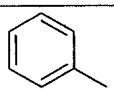
 70	10.02 (1H, s), 7.87 (2H, d), 7.61 (1H, t) and 7.51 (2H, dd).
 71	7.42 (10H, m) and 2.91 (4H, s).
 72	1.22 (3H, t), 2.63 (2H, q) and 7.0 – 7.45 (5H, m).
 73	7.20 – 7.50 (5H, m), 6.60 (1H, d), 1.30 (1H, dq) and 1.80 (3H, d).
 66	7.50 – 7.10 (5H, m), 6.69 (1H, dd), 5.74 (1H, d) and 5.23 (1H, d).
 74	7.04 – 7.13 (5H, m) and 2.32 (3H, s).

Table 3: Characteristic peaks in ^{1}H NMR spectra of 66 and 70 - 74

Table 3 shows the characteristic peaks used to determine the compounds produced upon the pyrolysis of the model compounds **72**, **75** – **78** and **85** - **87**. The relative heights of the integrals of these peaks were used to determine the percentage composition of the pyrolysates.

Methyl phenylacetate 75

Methyl iodide (0.517 g, 3.64 mmol), potassium carbonate (0.525 g, 3.80 mmol) and phenylacetic acid **85** (0.501 g, 3.68 mmol) were mixed in DMF (5 cm^3) at room temperature overnight. The mixture was then added to water (30 cm^3) and extracted with ether (3 × 25 cm^3). The combined organic layers were then washed with water and dried. The solvent was removed to produce methyl phenylacetate**75** as a yellow oil (0.484 g, 87%). δ_H (200 MHz, $CDCl_3$): 3.60 (2H, s), 3.66 (3H, s) and 7.26 (5H, m).

FVP of methyl phenylacetate 75

Flash vacuum pyrolysis of methyl phenylacetate **75** (0.0416 g, T_f 975 °C, T_i 87 °C, P 1.7 × 10^{-1} – 3.4 × 10^{-1} Torr, t 10 min) gave a yellow product which was shown, by comparison with literature ^1H NMR spectra, to contain **75** (11%), benzaldehyde **70** (4%), ethylbenzene **72** (45%), styrene **66** (13%), toluene **74** (19%) and bibenzyl **71** (8%).

Methyl phenylpropionate 76

Methyl iodide (0.499 g, 3.52 mmol), potassium carbonate (0.466 g, 3.38 mmol) and 2-phenylpropionic acid **86** (0.525 g, 3.52 mmol) were mixed in DMF (5 cm^3) at room temperature overnight. The mixture was then added to water (30 cm^3) and extracted with ether (3 × 25 cm^3). The combined organic layers were then washed with water and dried. The solvent was removed to produce methyl phenylpropionate **76** as a yellow oil (0.391 g, 68 %). δ_H (250 MHz, $CDCl_3$): 1.42 (3H, s), 1.46 (3H, s), 3.70 (1H, m) and 7.24 (5H, m).

FVP of methyl 2-phenylpropionate 76

Flash vacuum pyrolysis of methyl 2-phenylpropionate **76** (0.109 g, T_f 925 °C, T_i 89 °C, P 1.7 × 10^{-1} – 2.7 × 10^{-2} Torr, t 10 min) gave an oil containing **76** (8%), ethylbenzene **72** (15%), toluene **74** (11%), benzaldehyde **70** (18%) and styrene **66** (48%).

Methyl 2-Phenylbutyrate 77

Methyl iodide (0.435 g, 3.51 mmol), potassium carbonate (0.453 g, 3.28 mmol) and 2-phenylbutyric acid **87** (0.514 g, 3.52 mmol) were mixed in DMF (5 cm^3) at room temperature overnight. The mixture was then added to water (30 cm^3) and extracted with ether (3 × 25 cm^3). The combined organic layers were then washed with water and dried. The solvent was removed to produce methyl 2-phenylbutyrate **77** as a yellow oil (0.463 g, 74%). δ_H (200 MHz, $CDCl_3$): 0.84 (3H, t, *J* 8.0), 1.80 (1H, m), 2.04 (1H, m), 3.42 (1H, t, *J* 8.0), 3.60 (3H, s) and 7.24 (5H, m).

FVP of methyl 2-phenylbutyrate 77

Flash vacuum pyrolysis of methyl 2-phenylbutyrate **77** (0.168 g, T_f 925 °C, T_i 125 °C, P $6.5 \times 10^{-1} - 1.6 \times 10^{0}$ Torr, t 10 min) gave an oil which was shown, by comparison with literature ^{1}H NMR spectra, to contain **77** (5%), benzaldehyde **70** (44%), ethylbenzene **72** (26%) and styrene **66** (25%).

FVP of ethylbenzene 72

Flash vacuum pyrolysis of ethylbenzene **72** (0.0643 g, T_f 975 °C, T_i 20 °C, P $2.9 \times 10^{-1} - 3.8 \times 10^{-1}$ Torr, t 10 min) gave a brown oil which was shown, by comparison with literature ^{1}H NMR spectra, to contain **72** (57%), bibenzyl **71** (4%), styrene **66** (17%) and toluene **74** (22%).

FVP of propylbenzene 78

Flash vacuum pyrolysis of propylbenzene **78** (0.111 g, T_f 975 °C, T_i 25 °C, P $1.7 \times 10^{-1} - 2.1 \times 10^{-1}$ Torr, t 5 min) gave an oil which was shown, by comparison with literature ^{1}H NMR spectra, to contain **78** (16%), bibenzyl **71** (15%), ethylbenzene **72** (22%) and toluene **74** (37%).

FVP of phenylacetic acid 85

Flash vacuum pyrolysis of phenylacetic acid **85** (0.0444 g, T_f 925 °C, T_i 130 °C, P $4.8 \times 10^{-2} - 1.0 \times 10^{-1}$ Torr, t 10 min) gave a yellow product which was shown, by comparison with literature ^{1}H NMR spectra, to contain **85** (41%), ethylbenzene **72** (5%) and toluene **74** (25%).

FVP of 2-phenylpropionic acid 86

Flash vacuum pyrolysis of 2-phenylpropionic acid **86** (0.172 g, T_f 925 °C, T_i 210 °C, P $1.2 \times 10^{-1} - 1.0 \times 10^{0}$ Torr, t 10 min) gave an oil which was shown, by comparison with literature ^{1}H NMR spectra, to contain ethylbenzene **72** (8%), styrene **66** (82%) and toluene **74** (10%).

FVP of 2-phenylbutyric acid 87

Flash vacuum pyrolysis of 2-phenylbutyric acid **87** (0.0364 g, T_f 925 °C, T_i 135 °C, P $5.0 \times 10^{-2} - 2.1 \times 10^{-1}$ Torr, t 10 min) gave an oil which was shown, by comparison with literature ^{1}H NMR spectra, to contain bibenzyl **71** (5%), ethylbenzene **74** (29%), methylstyrene **73** (31%), styrene **66** (23%) and toluene **74** (12%).

7.4 Three-Ring Systems

General Method A (Suzuki)[8c]

The boronic acid (50 eq), halide (50 eq), potassium carbonate (300 eq) and tetrakis(triphenylphosphine) palladium (1 eq) were mixed in a solution of dioxane and water (3:1) and the mixture heated under reflux under a nitrogen atmosphere. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug. The solvent was removed and the residue dissolved in chloroform and the insoluble organic base was removed by filtration.

General Method B (Suzuki)[8c]

The halide (35 eq) and tetrakis (triphenylphosphine) palladium (1 eq) were stirred in ethylene glycol dimethyl ether (4 cm^3) for 20 min. Sodium carbonate (45 eq) in water (1 cm^3) and 2-formylphenylboronic acid (34 eq) were added and heated under reflux overnight. The solvent was then removed and the residue extracted from dichloromethane and the organic layers washed with water and dried over $MgSO_4$.

General Method C (Wittig)[125]

The aldehyde (1 eq) and methyl(triphenylphosphoranylidene) acetate (1.05 eq) were mixed in toluene and the solution heated to reflux under nitrogen for 4.5 h. The solvent was removed and the product was purified by dry flash chromatography using 50% ethyl acetate in hexane as eluent.

General Method D (Knoevenagel)[7]

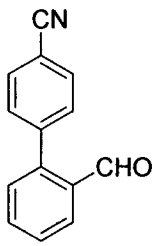
The aldehyde (1 eq) and methyl cyanoacetate (1 eq) were added to toluene (10 cm^3) followed by piperidine (2 drops) and glacial acetic acid (2 drops). The solution was left at room temperature for 2 h. The solution was then added to water (10 cm^3) and

extracted with dichloromethane (3 × 15 cm^3) and the organic extracts were washed with water (3 × 15 cm^3) and dried over $MgSO_4$ and the solvent removed.

General Method E[7]

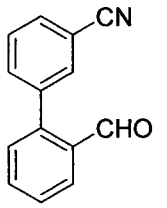
The aldehyde (1 eq) and *O*-methyhydroxylamine hydrochloride (1.5 eq) were added to ethanol and the solution heated to reflux for 2 h. The solution was then concentrated under vacuum the residue was suspended in ether (30 cm^3) and washed with NaOH (0.25 M, 10 cm^3), then with water (10 cm^3) and dried over $MgSO_4$ and then solvent was removed.

2′-Formylbiphenyl-4-carbonitrile[127] **139**



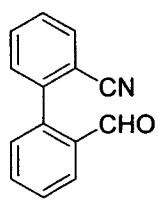
2-Formylphenylboronic acid (0.412 g, 2.75 mmol), 4-bromobenzonitrile (0.509 g, 2.79 mmol), potassium carbonate (2.286 g, 17 mmol) and tetrakis(triphenylphosphine) palladium (0.0708 g, 0.006 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce 2′-formylbiphenyl-4-carbonitrile **139** as a yellow solid (0.591 g, 82%) mp 98 – 100 °C [lit.[127], 103 – 103.5 °C]. δ_H (250 MHz, $CDCl_3$): 7.34 (1H, dd, *J* 1.6, 7.7), 7.42 (2H, d, *J* 8.4), 7.53 (1H, d, *J* 8.0), 7.61 (1H, dd, *J* 1.6, 7.7), 7.70 (2H, d, *J* 8.4), 7.97 (1H, dd, *J* 1.6, 7.7) and 9.97 (1H, s); δ_C (250 MHz, $CDCl_3$): 112.0 (quat), 118.3 (quat), 128.5 (CH), 128.8 (CH), 130.4 (CH), 130.5 (2 CH), 132.0 (2 CH), 133.4 (quat), 133.7 (CH), 142.6 (quat), 143.3 (quat) and 191.0 (CH).

2'-Formylbiphenyl-3-carbonitrile 140



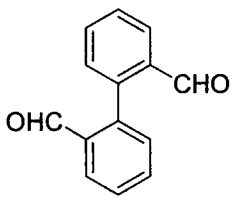
2-Formylphenylboronic acid (0.415 g, 2.77 mmol), 3-bromobenzonitrile (0.512 g, 2.81 mmol), potassium carbonate (2.279 g, 0.017 mol) and tetrakis(triphenylphosphine) palladium (0.063 g, 0.005 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce *2'-formylbiphenyl-3-carbonitrile* **140** as a yellow solid (0.570 g, 98%) mp 90 – 91 °C. (Found: M^+ 207.0686. $C_{14}H_9NO$ requires *M* 207.0684); δ_H (250 MHz, $CDCl_3$): 7.36 (1H, dd, *J* 7.6, 1.3), 7.51 – 7.66 (6H, m), 7.97 (1H, dd, *J* 7.6, 1.3) and 9.87 (1H, s); δ_C (250 MHz, $CDCl_3$): 112.8 (quat), 118.2 (quat), 128.6 (CH), 128.8 (CH), 129.1 (CH), 130.6 (CH), 131.5 (CH), 132.9 (CH), 133.5 (quat), 133.8 (CH), 134.2 (CH), 139.3 (quat), 142.9 (quat) and 191.0 (CH); *m/z* 207 (M^+, 61%), 206 (68), 183 (53), 181 (71), 156 (100), 102 (72), 76 (40) and 75 (39) .

2'-Formylbiphenyl-2-carbonitrile[128] 141



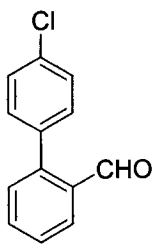
2-Formylphenylboronic acid (0.422 g, 2.82 mmol), 2-bromobenzonitrile (0.503 g, 2.76 mmol), potassium carbonate (2.322 g, 0.017 mol) and tetrakis(triphenylphosphine) palladium (0.067 g, 0.006 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce 2'-formylbiphenyl-2-carbonitrile **141** was recovered as a black solid (0.885 g) mp 110 – 112 °C [lit.[128], 117 – 118 °C]. δ_H (250 MHz, $CDCl_3$): 7.37 – 7.63 (6H, m), 7.71 (1H, dd, *J* 1.7, 8.5), 7.99 (1H, dd, *J* 1.7, 7.6) and 9.82 (1H, s); δ_C (250 MHz, $CDCl_3$): 112.4 (quat), 117.0 (quat), 128.8 (2 CH), 130.4 (CH), 130.5 (CH), 131.4 (quat), 131.8 (CH), 132.5 (CH), 133.2 (CH), 140.2 (quat), 141.5 (quat) and 190.1 (quat); *m/z* 207 (M^+, 14%), 183 (89), 181 (100), 180 (31), 179 (48), 102 (91), 76 (35) and 75 (40).

Biphenyl-2,2'-dicarbaldehyde[129] 142



2-Formylphenylboronic acid (0.5060 g, 3.10 mmol), 2-bromobenzaldehyde (0.5692 g, 3.08 mmol), potassium carbonate (2.5621 g, 0.019 mol) and tetrakis(triphenylphosphine) palladium (0.0726 g, 0.006 mmol) were mixed in a solution of dioxane (22.5 ^{cm3}) and water (7.5 ^{cm3}) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug. The solvent was removed and the residue dissolved in chloroform and the insoluble organic base was removed by filtration. The chloroform was then removed to produce crude biphenyl-2,2'-dicarbaldehyde **142** as a brown oil (0.6982 g) bp 61 °C (5.5×10^{-2} Torr) [lit.[130], 179 °C (2 Torr)] which used directly for the next step in the synthesis. δ_H (250 MHz, $CDCl_3$): 7.53 (2H, dd, *J* 1.6, 7.4), 7.77 (2H, t, *J* 7.7), 7.85 (2H, td, *J* 1.7, 7.4), 8.24 (2H, dd, *J* 1.3, 7.6) and 10.04 (2H, 2); δ_C (250 MHz, $CDCl_3$): 128.4 (2 CH), 128.7 (2 CH), 131.6 (2 CH), 133.3 (2 CH), 134.4 (2 quat), 141.1 (2 quat) and 191.0 (2 CH).

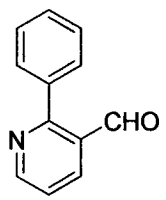
4'-Chlorobiphenyl-2-carbaldehyde[131] 143



4-Chlorophenylboronic acid (0.504 g, 3.22 mmol), 2-bromobenzaldehyde (0.644 g, 3.43 mmol), potassium carbonate (2.67 g, 0.019 mol) and tetrakis(triphenylphosphine) palladium (0.078 g, 0.007 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a brown oil which was recrystallised from hexane to produce 4'-chlorobiphenyl-2-carbaldehyde **143** as colourless crystals (0.640 g, 86%), mp 60 – 62°C [lit.[131], 63 – 65 °C]. δ_H (250 MHz, $CDCl_3$): 7.20 – 7.24 (2H, m), 7.30 – 7.42 (4H, m), 7.55 (1H, td, *J* 1.4, 7.6), 7.93 (1H, dd, *J* 1.4, 7.6) and 9.87 (1H, s); δ_C (250 MHz, $CDCl_3$): 127.8 (CH)m 128.0 (CH), 128.5 (2 CH), 130.5 (CH), 131.1 (2CH), 133.5 (quat), 133.5 (CH), 134.3

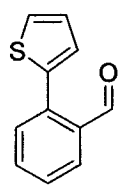
(quat), 136.1 (quat), 144.3 (quat) and 191.7 (CH). *m/z* 216 (M^+, 100%), 215 (66), 181 (84), 153 (32), 152 (97), 151 (27) and 76 (28).

2-Phenylpyridine-3-carbaldehyde[132] 144



Phenylboronic acid (1.351 g, 11.08 mmol), 2-bromopyridine-3-carbaldehyde (0.935 g, 5.02 mmol), potassium carbonate (9.207 g, 0.067 mol) and tetrakis(triphenylphosphine) palladium (0.130 g, 0.112 mmol) were mixed in a solution of dioxane (75 cm^3) and water (25 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed and the residue subjected to dry flash chromatography using 25% ethyl acetate in hexane which produced 2-phenylpyridine-3-carbaldehyde **144** as an oil (0.762 g, 83%) (Found: M^+ 183.0684. $C_{12}H_9NO$ requires *M* 183.0684); δ_H (250 MHz, $CDCl_3$): 7.39 (1H, ddd, *J* 0.8, 3.9, 4.8), 7.44 – 7.55 (5H, m), 8.24 (1H, dd, *J* 1.8, 7.9), 8.81 (1H, dd, *J* 1.8, 4.8) and 9.99 (1H,s); δ_C (250 MHz, $CDCl_3$): 122.4 (CH), 128.5 (2 CH), 129.4 (quat), 129.5 (CH), 130.2 (2 CH), 135.7 (CH), 136.9 (quat), 153.3 (CH), 162.1 (quat) and 191.5 (CH); *m/z* 183 (M^+, 83 %), 155 (96), 154 (100), 153 (42), 128 (37), 127 (63), 77 (69) and 51 (58).

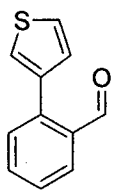
2-(2-Thienyl)benzaldehyde[8b] 145



2-Iodothiophene (0.4 cm^3, 3.68 mmol) and tetrakis(triphenylphosphine) palladium (0.118 g, 0.759 mmol) were stirred in ethylene glycol dimethyl ether (20 cm^3) for 20 min. Sodium carbonate (0.358 g) in water (5 cm^3) and 2-formylphenylboronic acid (0.508 g, 3.39 mmol) were added and heated under reflux overnight. General work-up method B was then followed to produce 2-(2-thienyl)benzaldehyde **145** as a brown oil which was purified by Kugelrohr distillation (0.799 g, 66%) bp 61 °C (3 Torr) [lit.[8b], 170 °C (0.5 Torr)]. (Found: M^+ 188.0297. $C_{11}H_8OS$ requires *M* 188.0296); δ_H (250 MHz, $CDCl_3$): 7.00 (1H, dd, *J* 1.3, 3.5), 7.06 (1H, t, *J* 4.3), 7.38 – 7.52 (6H, m), 7.93 (1H, dd, *J* 1.3, 17.7) and 10.11 (1H,s);δ_C (250 MHz, $CDCl_3$): 127.2 (CH), 127.6 (2 CH), 128.1 (CH), 129.4 (CH), 131.2

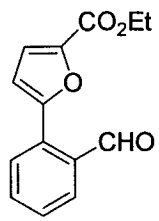
(CH), 133.4 (CH), 134.1 (quat), 137.9 (quat), 138.6 (quat) and 192.0 (CH); *m/z* 188 (M^+, 93 %), 160 (69), 144 (39), 128 (36), 115 (100), 45 (23), 41 (31) and 39 (28).

2-(3-Thienyl)benzaldehyde 146



3-Bromothiophene (1.05 cm^3, 1.827 g, 11.21 mmol) and tetrakis (triphenylphosphine)palladium (0.330 g, 0.29 mmol) were stirred in ethylene glycol dimethyl ether (60 cm^3) for 20 min. Sodium carbonate (6.870 g) in water (5 cm^3) and 2-formylphenylboronic acid (1.669 g, 11.13 mmol) were added and heated under reflux overnight. General work-up method B was then followed to produce 2-(3-thienyl)benzaldehyde **146** as a brown oil (1.403 g, 67 %) bp 43 °C (2 Torr) [lit.[8b], 160 °C (0.5 Torr)]. (Found: M^+ 188.0299. $C_{11}H_8OS$ requires *M* 188.0296); δ_H (250 MHz, $CDCl_3$): 7.47 (1H, dd, *J* 1.4, 5.1), 7.57 (1H, dd, J 1.4, 3.0), 7.72 – 7.78 (3H, m), 7.90 (1H, ddd, *J* 1.4, 7.6, 8.5), 8.28 (1H, dd, *J* 2.1, 7.6) and 10.39 (1H, s); δ_C (250 MHz, $CDCl_3$): 124.9 (CH), 126.1 (CH), 127.4 (CH), 127.7 (CH), 129.3 (CH), 130.4 (CH), 133.5 (CH), 133.8 (quat), 138.2 (quat), 140.3 (quat) and 192.3 (CH); *m/z* 188 (M^+, 94 %), 181 (76), 166 (58), 160 (100), 152 (43), 128 (55), 116 (60) and 115 (91).

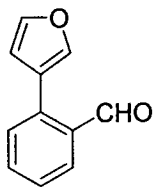
Ethyl 5-(2-formylphenyl)furan-2-carboxylate 147



2-Formylphenylboronic acid (1.032 g, 6.88 mmol), 5-bromofuroic acid methyl ester (1.512 g, 6.94 mmol), potassium carbonate (5.733 g, 0.042 mol) and tetrakis(triphenylphosphine) palladium (0.162 g, 0.15 mmol) were mixed in a solution of dioxane (112.5 cm^3) and water (35.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a black solid *ethyl 5-(2-formylphenyl)furan-2-carboxylate* **147** (2.111 g). mp 180 – 182 °C. (Found: M^+ 244.0739. $C_{14}H_{12}O_4$ requires *M* 244.0736); δ_H (250 MHz, $CDCl_3$): 1.33 (3H, t, *J* 7.1), 4.33 (2H, q, *J* 7.1), 6.65 (1H, d, *J* 3.6), 7.24 (1H, d, *J* 3.6), 7.46 – 7.57 (1H, m), 7.57 – 7.60 (1H, m), 7.69 – 7.72 (1H, m), 7.96 (1H, dd, *J* 1.4, 7.8) and 10.33 (1H, s); δ_C (250

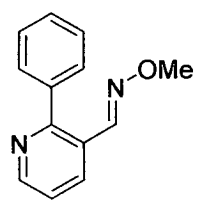
MHz, $CDCl_3$): 14.2 (CH_3), 61.1 (CH_2), 112.7 (CH), 119.2 (CH), 128.3 (CH), 129.1 (CH), 129.2 (CH), 131.8 (quat), 132.0 (quat), 133.6 (CH), 141.5 (quat), 150.8 (quat), 155.7 (quat) and 191.4 (CH); *m/z* 244 (M^+, 62%), 171 (85), 144 (72), 143 (54), 116 (53), 115 (87), 63 (50) and 29 (100).

2-Furan-3-ylbenzaldehyde 148



2-Formylphenylboronic acid (0.104 g, 0.696 mmol), 3-bromofuran (0.117 g, 0.796 mmol), potassium carbonate (0.576 g, 4.169 mol) and tetrakis(triphenylphosphine) palladium (0.017 g, 0.015 mmol) were mixed in a solution of dioxane (7.5 cm^3) and water (2.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed and the residue subjected to dry flash chromatography using 5% ethyl acetate in hexane which produced *2-furan-3-ylbenzaldehyde* **148** as a brown oil (0.0685 g, 50 %) bp 55 – 56 °C (5.5×10^{-2} Torr). (Found: M^+ 172.0525. $C_{11}H_8O_2$ requires *M* 172.0524); δ_H (250 MHz, $CDCl_3$): 6.59 (1H, dd, *J* 1.0, 1.8), 7.35 – 7.54 (5H, m), 7.91 (1H, dd, *J* 3.0, 4.8) and 10.14 (1H,s); δ_C (250 MHz, $CDCl_3$): 112.1 (CH), 122.3 (quat), 127.6 (quat), 127.7 (2 CH), 130.4 (CH), 133.7 (CH), 136.3 (quat), 141.1 (CH), 141.4 (CH) and 192.1 (CH); *m/z* 172 (M^+, 47 %), 144 (84), 116 (55), 115 (100), 89 (49), 63 (56), 39 (51) and 29 (57).

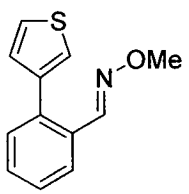
2-Phenylpyridine-3-carbaldehyde *O*-methyl oxime 150



2-Phenylpyridine-3-carbaldehyde **144** (0.203 g, 1.11 mmol) and O-methylhydroxylamine hydrochloride (0.139 g, 1.66 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *2-phenylpyridine-3-carbaldehyde O-methyl oxime* **150** as an oil (0.216 g, 92%) bp 156 °C (9 Torr). (Found: M^+ 211.0925. $C_{13}H_{12}N_2O$ requires *M* 212.0950); δ_H (250 MHz, $CDCl_3$): 3.88 (3H, s), 7.21 (1H, ddd, *J* 0.7, 4.7), 7.35 – 7.43 (5H, m), 8.00 (1H, s), 8.18 (1H, dd, *J* 1.8, 8.0) and 8.60 (1H, dd, *J* 1.7, 4.7); δ_C (250 MHz, $CDCl_3$): 62.0 (CH_3), 122.2 (CH), 125.7 (quat), 128.2

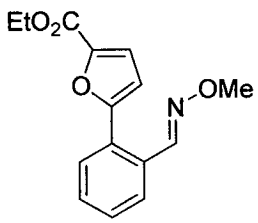
(2 CH), 128.6 (CH), 129.5 (2 CH), 134.2 (CH), 138.3 (quat), 146.3 (CH), 150.1 (CH) and 158.0 (quat); *m/z* 212 (M^+, 72%), 211 (100), 181 (96), 180 (71), 179 (33), 167 (74), 127 (66) and 78 (47).

2-Thiophen-3-yl-benzaldehyde *O*-methyl oxime 151



2-(3-Thienyl)benzaldehyde **146** (0.214 g, 1.14 mmol) and O-methylhydroxylamine hydrochloride (0.137 g, 1.64 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *2-thiophen-3-yl-benzaldehyde O-methyl oxime* **151** as an oil (0.573 g, 51%). (Found: M^+ 217.0567. $C_{12}H_{11}NOS$ requires *M* 217.0561) bp 45 °C; δ_H (250 MHz, $CDCl_3$): 4.20 (3H, s), 7.36 (1H, dd, *J* 1.2, 5.0), 7.44 – 7.46 (1H, m), 7.57 – 7.66 (2H, m), 7.89 – 7.96 (1H, m), 8.00 (1H, s), 8.18 (1H, d, *J* 6.7) and 8.42 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 61.8 (CH_3), 123.8 (CH), 126.1 (CH), 127.4 (CH), 128.0 (CH), 129.2 (CH), 129.4 (CH), 129.8 (CH) and 147.7 (CH); *m/z* 217(M^+, 52%), 216 (58), 210 (52), 188 (58), 187 (81), 186 (100), 185 (67) and 171 (69).

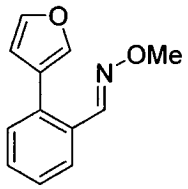
2-(5-Ethoxycarbonylfuran-2-yl)benzaldehyde *O*-methyloxime 152



Ethyl 5-(2-formylphenyl)furan-2-carboxylate **147** (0.207 g, 0.849 mmol) and *O*-methylhydroxylamine hydrochloride (0.117 g, 1.41 mmol) were added to ethanol (20 cm^3). General work-up method E was then followed to produce *2-(5-ethoxycarbonylfuran-2-yl)benzaldehyde O-methyloxime* **152** as a brown oil (0.124 g, 53%). (Found: M^+ 273.0999. $C_{15}H_{15}NO_4$ requires *M* 273.1001); δ_H (250 MHz, $CDCl_3$): 1.33 (3H, t, *J* 7.1), 3.93 (3H, s), 4.32 (2H, q, *J* 7.2), 6.48 (1H, d, *J* 3.5), 7.18 (1H, d, *J* 3.5), 7.32 – 7.42 (2H, m), 7.64 – 7.67 (1H, m), 7.82 (1H, dd, *J* 7.2, 1.7) and 8.38 (1H, s); δ_C (250 MHz, $CDCl_3$): 14.2 (CH_3), 60.9 (CH_2), 61.9 (CH_3), 111.6 (CH), 119.1 (CH), 127.1 (CH), 128.5 (CH), 128.8 (quat), 129.0

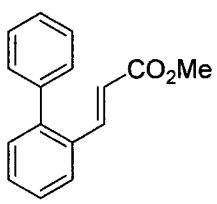
(CH), 129.5 (CH), 131.9 (CH), 132.0 (quat), 144.6 (quat), 155.1 (quat) and 158.5 (quat); *m/z* 273 (M^+, 46%), 200 (100) and 169 (52).

2-Furan-3-ylbenzaldehyde *O*-methyl oxime 153



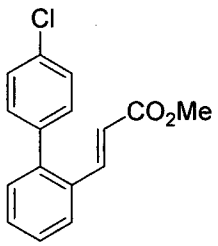
2-Furan-3-ylbenzaldehyde **148** (0.105 g, 0.608 mmol) and methoxylamine hydrochloride (0.084 g, 1.00 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *2-furan-3-ylbenzaldehyde O-methyl oxime* **153** as an oil (0.087 g, 71%) bp 133 °C (10 Torr). (Found: M^+ 201.0789. $C_{12}H_{11}NO_2$ requires *M* 201.0790); δ_H (250 MHz, $CDCl_3$): 3.89 (3H, s), 6.44 (1H, dd, *J* 0.9, 1.8), 7.25 – 7.43 (5H, m), 7.83 (1H, d, *J* 7.0) and 8.18 (1H, s); δ_C (250 MHz, $CDCl_3$): 61.9 (CH_3), 111.7 (CH), 123.8 (quat), 126.3 (CH), 127.5 (CH), 129.6 (CH), 129.7 (CH), 129.9 (quat), 132.5 (quat), 140.5 (CH), 143.0 (CH) and 147.7 (CH); *m/z* 201 (M^+, 51%), 170 (100), 142 (83) and 115 (84).

Methyl 2-Phenylcinnamate[6] 25



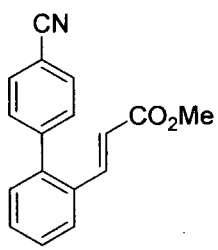
Biphenyl-2-carbaldehyde **29** (0.513 g, 2.82 mmol) and methyl(triphenylphosphoranylidene) acetate (1.160 g, 3.37 mmol) were mixed in toluene (100 cm^3) and heated under reflux for 4.5 h. General work-up method C was then followed to produce 2-phenylcinnamic acid methyl ester **25** as a yellow oil (0.546 g, 68%) bp 156 °C (11 Torr) [lit.[6], 184 °C (4 Torr)]. δ_H (250 MHz, $CDCl_3$): 3.59 (3H, s), 3.64 (3H, s), 5.83 (1H, d, *J* 12.3), 6.30 (1H, d, *J* 15.9), 6.75 (1H, d, *J* 11.9), 7.20 - 7.35 (m) and 7.58 - 7.68 (m); δ_C (250 MHz, $CDCl_3$): 51.4 (CH_3), 118.6 (CH), 127.2 (CH), 127.5 (CH), 128.2 (CH), 129.6 (3CH), 130.4 (CH), 132.4 (quat), 139.7 (quat), 140.3 (quat), 143.8 (CH) and 167.1 (quat).

Methyl 3-(4'-chlorobiphenyl-2-yl)acrylate 154



4'-Chlorobiphenyl-2-carbaldehyde **143** (0.303 g, 1.40 mmol) and methyl (triphenylphosphoranylidene) acetate (0.592 g, 1.77 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(4'-chlorobiphenyl-2-yl)acrylate* **154** as a yellow solid (0.314 g, 82%) which was an 86:14 mixture of *E* and *Z* isomers. bp 154 °C (9 Torr). (Found: M^+ 272.0604. $C_{16}H_{13}ClO_2$ requires *M* 272.0604); δ_H (250 MHz, $CDCl_3$): 3.66 (3H, s), 6.31 (1H, d, *J* 16.0), 7.15 (1H, d, *J* 6.9), 7.22 – 7.34 (6H, m) and 7.58 (2H, d, *J* 15.7); δ_C (250 MHz, $CDCl_3$): 51.5 (CH_3), 119.0 (CH), 126.8 (CH), 127.8 (CH), 128.4 (2 CH), 129.8 (CH), 130.2 (CH), 130.9 (2 CH), 132.4 (quat), 133.7 (quat), 138.1 (quat), 131.4 (quat), 143.3 (CH) and 167.0 (quat); Z-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.59 (3H, s), 5.85 (1H, d, *J* 12.1), 6.72 (1H, d, *J* 12.1) and 7.58 (2H, d, *J* 1.9); *m/z* 272 (M^+, 17%), 213 (69), 178 (100), 88 (96) and 28 (95).

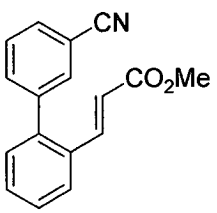
Methyl 3-(4'-cyanobiphenyl-2-yl)acrylate 155



2'-Formylbiphenyl-4-carbonitrile **139** (0.303 g, 1.46 mmol) and methyl(triphenylphosphoranylidene) acetate (0.611 g, 1.83 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(4'-cyanobiphenyl-2-yl)acrylate* **155** as a yellow solid (0.314 g, 82%) which was an 90:10 mixture of *E* and *Z* isomers. mp 95 – 97 °C (Found: M^+ 263.0941. $C_{17}H_{13}NO_2$ requires *M* 263.0946); δ_H (250 MHz, $CDCl_3$): 3.68 (3H, s), 6.34 (1H, d, *J* 15.8) and 7.19 – 7.68 (9H, m); δ_C (250 MHz, $CDCl_3$): 51.6 (CH_3), 111.4 (quat), 118.5 (quat), 119.7 (CH), 127.0 (CH), 128.6 (CH), 130.0 (CH), 130.1 (CH), 130.3 (2 CH), 132.0 (2 CH), 132.4 (quat), 140.5 (quat), 142.6 (CH), 144.5 (quat) and 166.8 (quat); *m/z* 263 (M^+, 9%), 294 (31), 131 (33),

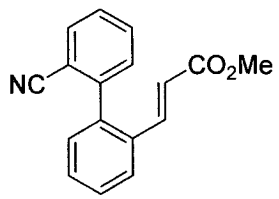
41 (100), 40 (94), 39 (84), 38 (73) and 32 (51). Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.60 (3H, s), 5.89 (1H, d, *J* 12.0) and 6.72 (1H, d, *J* 12.0).

Methyl 3-(3'-cyanobiphenyl-2-yl)acrylate 156



2'-Formylbiphenyl-3-carbonitrile **140** (0.309 g, 1.49 mmol) and methyl(triphenylphosphoranylidene) acetate (0.616 g, 1.84 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(3'-cyanobiphenyl-2-yl)acrylate* **156** as a yellow solid (0.320 g, 81%) which was an 91: 9 mixture of *E* and *Z* isomers. mp 128 – 129 °C (Found: C, 77.46: H, 4.73: N, 5.32. $C_{17}H_{13}NO_2$ requires C, 77.55: H, 5.00: N, 5.30%); δ_H (250 MHz, $CDCl_3$): 3.69 (3H, s), 6.34 (1H, d, *J* 15.9) amd 7.38 – 7.78 (9H, m); δ_C (250 MHz, $CDCl_3$): 51.6 (CH_3), 112.6 (quat), 118.4 (quat), 119.8 (CH), 127.0 (CH), 128.6 (CH), 129.1 (CH), 130.0 (CH), 130.2 (CH), 131.1 (CH), 132.5 (quat), 132.9 (CH), 134.1 (CH), 140.1 (quat), 141.1 (quat), 142.5 (CH) and 166.8 (quat); *m/z*. Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 5.90 (1H, d, *J* 12.1) and 6.72 (1H, d, *J* 12.1s).

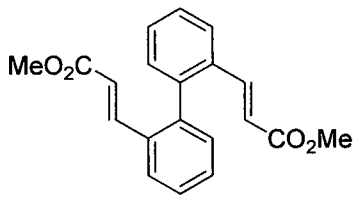
Methyl 3-(2'-cyanobiphenyl-2-yl)acrylate 157



2'-Formylbiphenyl-2-carbonitrile **141** (0.506 g, 2.44 mmol) and methyl(triphenylphosphoranylidene) acetate (1.088 g, 3.25 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(2'-cyanobiphenyl-2-yl)acrylate* **157** as a yellow solid (0.279 g, 43%) which was an 96:4 mixture of *E* and *Z* isomers. mp 90 – 92 °C (Found: M^+ 263.0950. $C_{17}H_{13}NO_2$ requires *M* 263.0946); δ_H (250 MHz, $CDCl_3$): 3.60 (3H, s), 6.26 (1H, d, *J* 15.9) and 7.23 – 7.69 (9H, m); δ_C (250 MHz, $CDCl_3$): 51.3 (CH_3), 112.7 (quat), 117.5 (quat), 119.6 (CH),

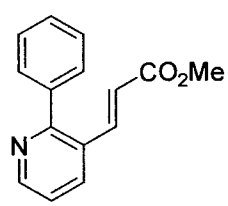
126.6 (CH), 127.6 (CH), 128.9 (CH), 129.7 (CH), 130.2 (CH), 130.8 (CH), 132.2 (CH), 132.6 (quat), 132.8 (CH), 132.9 (quat), 138.5 (CH), 143.3 (quat) and 165.7 (quat); *m/z* 263 (M^+, 74%), 232 (66), 205 (69), 204 (100), 203 (96), 202 (69), 177 (61) and 176 (66). Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.51 (3H, s), 5.78 (1H, d, *J* 12.2) and 6.71 (1H, d, *J* 12.2).

Methyl 3-(biphenyl-2,2'-yl) bisacrylate[133] 158



Biphenyl-2,2'-dicarbaldehyde **142** (0.5135 g, 2.44 mmol) and methyl (triphenylphosphoranylidene) acetate (2.0485 g, 6.13 mmol) were mixed in toluene (100 ^{cm3}) and the solution heated to reflux under nitrogen for 4.5 h. The solvent was then removed and the product was purified by dry flash chromatography using 50% ethyl acetate in hexane to produce methyl 3-(biphenyl-2,2'-yl) bisacrylate **158** as a yellow solid (0.5923 g, 75 %) mp 121 – 122 °C [lit.[133], 124 – 125 °C]; δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 6.24 (2H, d, *J* 16.2), 7.11 – 7.15 (2H, m), 7.31 – 7.37 (4H, m) and 7.63 – 7.67 (2H, m); δ_C (250 MHz, $CDCl_3$): 51.5 (CH_3), 118.0 (2 CH), 126.5 (2 CH), 129.6 (2 CH), 131.0 (2 CH), 133.2 (CH), 140.4 (CH), 142.7 (2 CH) and 167.0 (quat). Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.57 (3H, s), 5.70 (2H, d, *J* 12.3), 6.23 (2H, d, *J* 15.7) and 6.55 (2H, d, *J* 11.9).

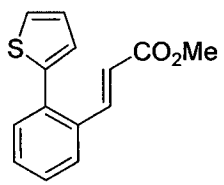
Methyl 3-(2-phenylpyridin-3-yl) acrylate 159



2-Phenylpyridine-3-carbaldehyde **144** (0.217 g, 1.18 mmol) and methyl(triphenylphosphoranylidene) acetate (0.461 g, 1.38 mmol) were mixed in toluene (40 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(2-phenylpyridin-3-yl) acrylate* **159** as a brown oil (0.2479 g, 86%) which was an 80:20 mixture of *E* and *Z* isomers. bp 149 °C (16 Torr). (Found: M^+ 239.0946. $C_{15}H_{13}NO_2$ requires *M* 239.0941); δ_H (250 MHz,

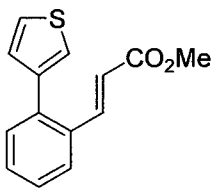
$CDCl_3$): 3.71 (3H, s), 6.38 (1H, d, *J* 16.0), 7.28 (1H, dd, *J* 5.0, 8.1), 7.39 – 7.49 (5H, m), 7.71 (1H, d, *J* 16.0), 7.91 (1H, dd, *J* 1.7, 8.1) and 8.63 (1H, dd, *J* 1.7, 5.0); δ_C (250 MHz, $CDCl_3$), 51.7 (CH_3), 120.2 (CH), 122.2 (CH), 128.0 (quat), 128.3 (2 CH), 128.8 (CH), 129.7 (2 CH), 134.8 (CH), 138.7 (quat), 142.4 (CH), 150.3 (CH), 158.9 (quat) and 166.6 (quat); Z-isomer characterised by: δ_H (250 MHz, $CDCl_3$): 3.65 (3H, s), 5.98 (1H, d, *J* 12.3) and 6.84 (1H, d, *J* 12.3); *m/z* 239 (M^+, 73 %), 208 (44), 181 (78), 180 (100), 179 (89), 178 (74), 152 (80) and 151 (51).

Methyl 3-[2-(thiophen-2-yl)phenyl]acrylate 161



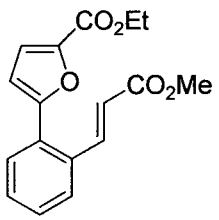
2-(2-Thienyl)benzaldehyde **145** (0.662 g, 3.51 mmol) and methyl(triphenylphosphoranylidene) acetate (1.41 g, 4.23 mmol) were mixed in toluene (300 cm^3) and the solution heated to reflux under argon for 4.5 h. General work-up method C was then followed to produce *methyl 3-[2-(thiophen-2-yl)phenyl]acrylate* **161** as a brown oil (0.628 g, 73%) which was an 80:20 mixture of *E* and *Z* isomers. bp 70 °C (1 Torr). (Found: M^+ 244.0557. $C_{14}H_{12}O_2S$ requires *M* 244.0558); *E*-isomer; δ_H (250 MHz, $CDCl_3$): 3.62 (1H, s), 6.32 (1H, d, *J* 16.0), 7.01 - 7.58 (9H, m) and 7.91 (1H, d, *J* 16.0); δ_C (250 MHz, $CDCl_3$): 51.5 (CH_3), 119.3 (CH), 126.3 (CH), 127.2 (CH), 127.5 (CH), 127.9 (CH), 128.2 (CH), 129.7 (CH), 130.7 (CH), 133.0 (quat), 134.9 (quat), 141.8 (quat), 143.7 (CH) and 167.1 (quat); *Z*-isomer; δ_H (250 MHz, $CDCl_3$): 5.93 (1H, d, *J* 12.0); *m/z* 244 (M^+, 67%), 213 (42), 187 (35), 186 (71), 185 (100), 152 (67), 141 (63) and 139 (61).

Methyl 3-[2-(thiophen-3-yl)phenyl]acrylate 162



2-(3-Thienyl)benzaldehyde **146** (0.316 g, 1.68 mmol) and methyl (triphenylphosphoranylidene) acetate (0.670 g, 2.00 mmol) were added to toluene (100 cm^3) and the solution heated to reflux under argon for 2 h. The solvent was then removed. The product was purified by dry flash chromatography using 10% ethyl acetate in hexane to produce *methyl 3-[2-(thiophen-3-yl)phenyl]acrylate* **162** as a brown oil (0.364 g, 89 %) which was an 80:20 mixture of *E* and *Z* isomers. bp 56 °C (2 Torr). (Found: M^+ 244.0554. $C_{14}H_{12}O_2S$ requires *M* 244.0558); *E*-isomer; δ_H (250 MHz, $CDCl_3$): 4.06 (1H, s), 6.26 (1H, d, *J* 12.2), 6.69 (1H, d, *J* 16.0), 7.42 (1H, dd, *J* 1.2, 4.9), 7.52 (1H, dd, *J* 1.2, 3.7), 7.67 – 7.72 (5H, m), 7.96 (1H, d, *J* 7.4) and 8.16 (1H, d, *J* 16.0); δ_C (250 MHz, $CDCl_3$): 51.5 (CH_3), 118.8 (CH), 124.1 (CH), 125.6 (CH), 126.8 (CH), 127.5 (CH), 128.9 (CH), 129.7 (CH), 130.0 (CH), 132.7 (quat), 137.2 (quat), 140.2 (quat), 143.9 (CH) and 167.1 (quat); *Z*-isomer: δ_H (250 MHz, $CDCl_3$): 4.10 (3H, s), 6.31 (1H, d, *J* 12.2), 6.70 (1H, d, *J* 16.0) and 8.31 (1H, d, *J* 16.0); *m/z* 244 (M^+, 54%), 186 (70), 185 (100), 184 (98), 162 (62), 152 (58), 139 (55), 131 (78) and 103 (69).

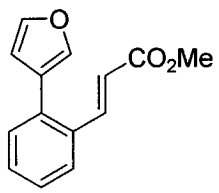
Methyl 3-[2-(2-carbethoxyfuran-5-yl)phenyl]acrylate 163



Ethyl 5-(2-formylphenyl)furan-2-carboxylate **147** (0.203 g, 0.829 mmol) and methyl(triphenylphosphoranylidene) acetate (0.373 g, 1.12 mmol) were mixed in toluene (40 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[2-(2-carboethoxyfuran-5-yl)phenyl]acrylate* **163** as a yellow oil (0.0665 g, 27%) which was an 83:17 mixture of *E* and *Z* isomers. bp 147 °C (9 Torr). (Found: M^+ 300.1009. $C_{17}H_{16}O_5$ requires *M* 300.0998); *E*-isomer; δ_H (250 MHz, $CDCl_3$): 1.32 (3H, t, *J* 7.1), 3.73 (3H, s), 4.32 (2H, q, *J* 7.1), 6.33 (1H, d, *J* 15.9), 6.49 (1H, d, *J* 3.6), 7.20 (1H, d, *J* 3.6), 7.31 – 7.39 (2H, m), 7.52 (1H, dd, *J* 1.4, 7.5), 7.75 (1H, dd, *J* 1.4, 7.5) and 8.00 (1H, d, *J* 15.9); δ_C (250

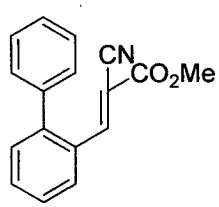
MHz, $CDCl_3$): 14.2 (CH_3), 51.6 (CH_3), 60.9 (CH_2), 112.4 (CH), 119.3 (CH), 120.4 (CH), 127.5 (CH), 128.3 (CH), 129.3 (CH), 129.7 (quat), 130.1 (CH), 132.6 (quat), 143.2 (CH), 144.5 (quat), 154.9 (quat), 158.6 (quat) and 166.9 (quat); Z-isomer: δ_H (250 MHz, $CDCl_3$): 1.18 (3H, t, *J* 7.1), 3.56 (3H, s), 4.04 (2H, q, *J* 7.1) and 6.03 (1H, d, *J* 12.1); δ_C (250 MHz, $CDCl_3$): 14.0 (CH_3), 51.2 (CH_3) and 60.2 (CH_2); *m/z* 300 (M^+, 33%), 168 (50), 139 (45), 54 (52), 42 (81), 41 (100), 40 (89) and 39 (79).

Methyl 3-[2-(furan-3-yl)phenyl]acrylate 164



2-(Furan-3-yl)benzaldehyde **148** (0.109 g, 0.635 mmol) and methyl (triphenylphosphoranylidene) acetate (0.250 g, 0.727 mmol) were mixed in toluene (20 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[2-(furan-3-yl)phenyl]acrylate* **164** as a brown oil (0.140 g, 96%) which was an 92:8 mixture of *E* and *Z* isomers. bp 144 °C (10 Torr). (Found: M^+ 228.0790. $C_{14}H_{12}O_3$ requires *M* 228.0786); δ_H (250 MHz, $CDCl_3$): 3.71 (3H, s), 6.32 (1H, d, *J* 15.2), 6.48 (1H, dd, *J* 0.9, 2.0), 7.32 – 7.45 (5H, m), 7.56 (1H, d, *J* 7.3) and 7.89 (1H, d, *J* 15.2); δ_C (250 MHz, $CDCl_3$): 52.1 (CH_3), 112.1 (CH), 119.7 (CH), 124.7 (quat), 127.4 (CH), 128.0 (CH), 130.2 (CH), 130.3 (CH), 133.3 (quat), 133.8 (quat), 141.3 (CH), 143.6 (CH), 144.32 (CH) and 167.7 (quat); Z-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.59 (3H, s), 5.93 (1H, d, *J* 12.4) and 7.03 (1H, d, *J* 12.4); *m/z* 228 (M^+, 12%), 169 (100), 168 (47), 141 (77) and 115 (39).

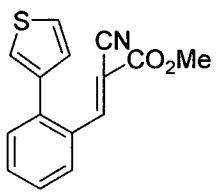
Methyl 2-cyano-[3-(2-phenyl)phenyl]acrylate 165



Biphenyl-2-carbaldehyde **29** (0.231 g, 1.27 mmol) and methyl cyanoacetate (0.126 g, 1.27 mmol) were added to toluene (10 cm^3). General work-up method D was then followed to produce *methyl 2-cyano-[3-(2-phenyl)phenyl]acrylate* **165** as an solid (0.320 g, 96%) mp 129 °C. (Found: M^+ 263.0941. $C_{17}H_{13}NO_2$ requires *M* 263.0946); δ_H (250 MHz, $CDCl_3$): 3.81 (3H, s), 7.18 – 7.22 (2H, m), 7.37 – 7.54 (6H, m)

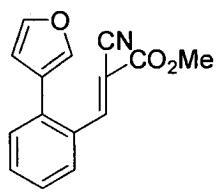
and 8.18 – 8.23 (2H, m); δ_C DEPT (250 MHz, $CDCl_3$): 53.2 (CH_3), 127.8 (CH), 128.3 (CH), 128.4 (2 CH), 128.8 (CH), 129.9 (2 CH), 130.5 (CH), 132.4 (CH) and 155.4 (CH); *m/z* 263 (M^+, 42%), 204 (100), 203 (88), 170 (59), 165 (67) and 152 (31).

Methyl 2-cyano-[3-(2-thiophen-3-yl)phenyl]acrylate 166



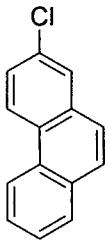
2-(3-Thienyl)benzaldehyde **145** (0.207 g, 1.10 mmol) and methyl cyanoacetate (0.105 g, 1.06 mmol) were added to toluene (10 cm^3). General work-up method D was then followed to produce *methyl 2-cyano-[3-(2-thiophen-3-yl)phenyl]acrylate* **166** as an oil (1.463 g) bp 64 °C (2.5 Torr). (Found: M^+ 269.0501. $C_{15}H_{11}NO_2S$ requires *M* 269.0511); δ_H (250 MHz, $CDCl_3$): 3.84 (3H, s), 7.06 (1H, dd, *J* 1.1, 4.9), 7.12 (1H, dd, *J* 1.1, 2.9), 7.36 – 7.48 (3H, m), 7.92 (1H, d, *J* 6.6), 8.16 (1H, d, *J* 7.8) and 8.50 (1H, s); δ_C (250 MHz, $CDCl_3$): 53.2 (CH_3), 103.8 (quat), 115.3 (quat), 125.4 (CH), 126.4 (CH), 127.7 (CH), 128.8 (2 CH), 130.0 (CH), 132.4 (CH), 133.3 (quat), 139.1 (quat), 139.4 (quat), 155.3 (CH) and 162.7 (quat); *m/z* 269 (M^+, 34%), 211 (60), 210 (100), 209 (84), 187 (60), 171 (68), 166 (72) and 156 (59).

Methyl 2-cyano[3-(2-furan-3-yl)phenyl]acrylate 167



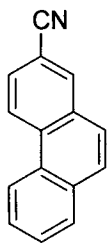
2-Furan-3-yl-benzaldehyde **148** (0.120 g, 0.695 mmol) and methyl cyanoacetate (1.13 cm3, 0.581 mmol) were added to toluene (5 cm^3). General work-up method D was then followed to produce *methyl 2-cyano[3-(2-furan-3-yl)phenyl]acrylate* **67** as a yellow oil (0.0419 g, 24%) bp 51 °C (3.4×10^{-2} Torr). (Found: M^+ 253.0731. $C_{15}H_{11}NO_3$ requires *M* 253.0739); δ_H (250 MHz, $CDCl_3$): 3.86 (3H, s), 6.48 (1H, dd, *J* 0.9, 1.8), 7.34 – 7.53 (5H, m), 8.14 (1H, d, *J* 7.8) and 8.43 (1H, s); δ_C (250 MHz, $CDCl_3$): 53.3 (CH_3), 104.2 (quat), 111.3 (CH), 115.1 (quat), 123.8 (quat), 127.7 (CH), 128.9 (CH), 129.5 (quat), 129.6 (CH), 132.5 (CH), 135.1 (quat), 141.4 (CH), 143.6 (CH), 154.8 (CH) and 162.7 (quat); *m/z* 253 (M^+, 8%), 195 (24), 194 (100), 193 (39), 166 (62), 139 (46), 69 (37) and 57 (47).

FVP of Methyl 3-(4′-chlorobiphenyl-2-yl)acrylate 154



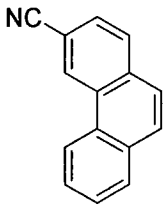
Flash vacuum pyrolysis of methyl 3-(4′-chlorobiphenyl-2-yl)acrylate **154** (0.060 g, T_f 950 °C, T_i 170 °C, P 6 × 10^{-2} – 2.2 × 10^{-1} Torr, t 10 min) gave 2-chlorophenanthrene **169** as a brown oil (0.0409 g, 88%) mp 78 – 80 °C [lit.[134], 82 – 85 °C] δ_H (250 MHz, $CDCl_3$): 7.54 – 7.73 (4H, m), 7.77 (1H, d, *J* 8.9), 7.85 – 7.92 (2H, m), 8.60 (1H, d, *J* 8.9) and 8.62 (1H, dd, *J* 8.9); δ_C (250 MHz, $CDCl_3$): 122.4 (CH), 124.2 (CH), 125.7 (CH), 126.7 (CH), 126.9 (2 CH), 127.4 (CH), 128.1 (CH, (128.5 (quat), 128.6 (CH), 129.8 (quat), 131.8 (quat), 132.2 (quat) and 132.9 (quat); *m/z* 212 (M^+, 100%), 178 (17), 177 (11), 176 (29), 152 (15), 151 (11) and 88 (13).

FVP of Methyl 3-(4′-cyanobiphenyl-2-yl)acrylate[135] 155

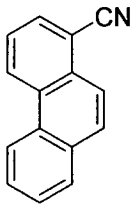


Flash vacuum pyrolysis of methyl 3-(4′-cyanobiphenyl-2-yl)acrylate **155** (0.091 g, T_f 950 °C, T_i 197 °C, P 3.2 × 10^{-2} – 2.2 × 10^{-1} Torr, t 15 min) gave a yellow oil which was purified by dry flash chromatography (hexane) to produce phenanthrene-2-carbonitrile **170** as a yellow solid (0.029 g, 41%) mp 106 – 107 °C [lit.[136], 108 – 109.5 °C]. δ_H (250 MHz, $CDCl_3$): 7.61 – 7.66 (3H, m), 7.72 – 7.79 (2H, m), 7.86 (1H, d, *J* 7.6), 8.14 (1H, d, *J* 1.6), 8.59 (1H, d, *J* 8.6) and 8.66 (1H, d, *J* 8.6); δ_C (250 MHz, $CDCl_3$): 109.8 (quat), 118.2 (quat), 123.1 (CH), 123.7 (CH), 125.8 (CH), 127.3 (CH), 127.8 (CH), 128.2 (CH), 128.8 (2 CH), 129.1 (quat), 131.3 (quat), 132.7 (quat), 132.8 (quat) and 133.5 (CH).

FVP of Methyl 3-(3′-cyanobiphenyl-2-yl)acrylate 156



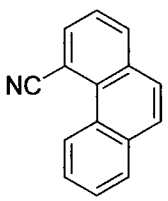
172



173

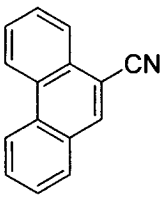
Flash vacuum pyrolysis of methyl 3-(3′-cyanobiphenyl-2-yl)acrylate **156** (0.045 g, T_f 950 °C, T_i 212 °C, P $4.0 \times 10^{-2} - 4.0 \times 10^{-1}$ Torr, t 15 min) gave a brown oil which was purified by dry flash chromatography (hexane) to produce a mixture of phenanthrene-3-carbonitrile[135] **172** and phenanthrene-1-carbonitrile[51] **173** as a yellow oil (0.025 g, 71%) which was shown by comparison with literature data[51,135] to consist of equal amounts of **172** and **173** which could not be separated. Phenanthrene was also produced (0.001 g, 3%). δ_H (250 MHz, $CDCl_3$): 7.61 – 7.71 (7H, m), 7.80 – 7.89 (6H, m), 8.07 (1H, d, *J* 9,1, **171**), 8.53 (1H, d, *J* 7.9, **171**), 8.61 (1H, d, *J* 7.3, **172**), 8.84 (1H, d, *J* 8.5, **171**) and 8.91 (1H, s, **172**); *m/z* 203 (M^+, 100%), 202 (10), 201 (8), 176 (6), 175 (5), 101 (5) and 88 (6).

FVP of Methyl 3-(2′-cyanobiphenyl-2-yl)acrylate 157



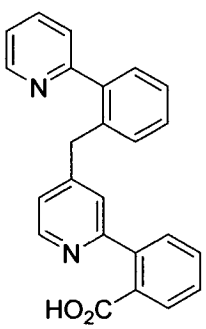
Flash vacuum pyrolysis of methyl 3-(2′-cyanobiphenyl-2-yl)acrylate **157** (0.086 g, T_f 950 °C, T_i 200 °C, P $6.0 \times 10^{-2} - 2.9 \times 10^{-1}$ Torr, t 15 min) gave a blue oil which was purified by dry flash chromatography (hexane) to produce phenanthrene-4-carbonitrile[47] **172** as a yellow oil (0.019 g, 30%) and phenanthrene **28** (0.005g, 9%). The two products were sucessfully separated and **28** was identified by comparison with the literature data discussed in **Section 7.3** (**Table 1**). Phenanthrene-4-carbonitrile was identified by the following spectroscopic data: δ_H (250 MHz, $CDCl_3$): 7.55 (1H, t, *J* 7.9), 7.63 – 7.69 (3H, m), 7.34 (1H, d, *J* 7.9), 7.85 (1H, dd, *J* 2.3, 7.0), 7.97 (1H, dd, *J* 1.4, 7.4), 8.05 (1H, dd, *J* 1.4, 7.9) and 9.73 (1H, d, *J* 7.0); δ_C (250 MHz, $CDCl_3$): 14.2 (quat), 107.8 (quat), 123.1 (quat), 125.2 (CH), 126.0 (CH), 127.1 (CH), 127.7 (CH), 128.5 (CH), 129.2 (quat), 129.3 (CH), 129.5 (CH), 133.5 (2 quat), 134.5 (CH) and 136.3 (CH); *m/z* 203 (M^+, 100%), 202 (16), 201 (8), 191 (7), 190 (5), 176 (6), 175 (6) and 88 (8).

FVP of Methyl 2-cyano-[3-(2-phenyl)phenyl]acrylate 165



Flash vacuum pyrolysis of methyl 2-cyano-[3-(2-phenyl)phenyl]acrylate **165** (0.040 g, T_f 975 °C, T_i 192 °C, P 2.3×10^{-2} – 2.6×10^{-1} Torr, t 10 min) gave a brown oil (0.2643 g) which was purified by dry flash chromatography (1:4 EtOAc/hexane) to produce phenanthrene-9-carbonitrile[137] **174** as a yellow oil (0.0578 g, 95%) mp 100 – 102 °C [lit.[138], 103 – 104 °C]. (Found: M^+ 263.0941. $C_{15}H_9N$ requires *M* 263.0941) δ_H (250 MHz, $CDCl_3$): 7.54 – 7.75 (4H, m), 7.86 (1H, dd, *J* 1.4, 7.2), 8.20 (1H, s), 8.21 – 8.27 (1H, m) and 8.62 – 8.67 (2H, m); δ_C (250 MHz, $CDCl_3$): 122.8 (CH), 123.0 (CH), 126.0 (CH), 127.5 (CH), 128.0 (CH), 128.1 (CH), 129.4 (CH), 129.7 (CH) and 135.6 (CH); *m/z* 263 (M^+, 42%), 204 (100), 203 (88), 170 (59), 165 (67) and 152 (31).

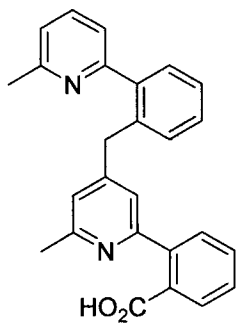
2-[4-(2-Pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid[54] 180



A solution of 2-bromopyridine (0.30 cm^3, 3.16 mmol) and tetrakis(triphenylphosphine) palladium (0.102 g, 0.09 mmol) in ethylene glycol dimethyl ether (15 cm^3) was stirred under nitrogen for 20 min. Sodium carbonate (0.437 g, 4.12 mmol), water (15 cm^3) and 2-formylphenylboronic acid (0.470 g, 3.14 mmol) were added and the reaction mixture was heated under reflux in the absence of light for 20 h. The solvent was removed from the solution under reduced pressure. The residue was added to water (25 cm^3) and small amounts of starting materials were removed by extraction into dichloromethane. After 16 h of continuous extraction of the aqueous phase with dichloromethane a yellow foam was obtained by concentration of the organic extracts which was identified as *2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid* **180**. The yield was dependent on the continuous extraction conditions, but recoveries of up to 94% (0.546 g) have been obtained; [Found: $(M+H)^+$ 367.1446. $C_{24}H_{19}N_2O_2$ requires *M* 367.1447] δ_H (250 MHz, $CDCl_3$): 4.19 (2H, s), 6.92 (1H, d, *J* 4.7), 7.23 – 7.45 (4H, m), 7.30 – 7.33 (4H, m), 7.40 (2H, ddd, *J* 1.6, 6.8), 7.61 (1H, ddd, *J* 1.8, 7.4), 8.00 (1H, dd, *J* 1.8, 7.4), 8.24 (1H, d, *J*

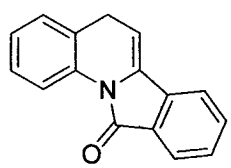
5.5), 8.56 (1H, d, *J* 4.4) and 9.95 (1H, br s); δ_C (63 MHz, $CDCl_3$): 38.7 (CH_2), 122.0 (CH), 123.4 (CH), 124.1 (CH), 124.9 (CH), 127.3 (CH), 128.8 (CH), 129.1 (CH), 129.1 (quat), 130.2 (CH), 130.5 (CH), 130.8 (CH), 131.0 (CH), 132.6 (CH), 133.0 (quat), 136.0 (quat), 136.7 (CH), 140.2 (quat), 145.6 (CH), 148.7 (CH), 153.8 (quat), 156.9 (quat), 159.2 (quat) and 169.9 (quat); other data are shown in Table 6; *m/z* (FAB) 367 [$(M+H)^+$, 100%].

2-{6-Methyl-4-[2-(6-methylpyridin-2-yl)-benzyl]-pyridin-2-yl}benzoic acid[54] 184



Using the same reactions conditions used to produce **180** using 2-bromo-6-methylpyridine in place of 2-bromopyridine, *2-{6-methyl-4-[2-(6-methylpyridin-2-yl)-benzyl]-pyridin-2-yl}benzoic acid* **184** was obtained in 8% yield, (Found: M^+ 394.1670. $C_{26}H_{22}N_2O_2$ requires *M* 394.1676) δ_H (360 MHz, $CDCl_3$): 2.51 (6H, s), 4.24 (2H, s), 6.91 (1H, s), 7.06 (2H, d, *J* 7.8), 7.18 (1H, s), 7.27 – 7.59 (9H, m) and 8.22 (1H, m); δ_C DEPT (90 MHz, $CDCl_3$): 23.7 (2 CH_3), 39.0 (CH_2), 122.1 (CH), 122.6 (CH), 123.6 (CH), 124.8 (CH), 128.5 (CH), 129.8 (CH), 130.5 (CH), 131.3 (CH), 131.6 (CH), 132.0 (CH), 132.4 (CH), 135.0 (CH) and 137.9 (CH). *m/z* (EI) 394 (M^+, 61%), 349 (59), 278 (51), 259 (86), 199 (51), 55 (79) and 43 (100).

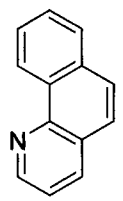
5H-Isoindolo[2,1-a]quinolin-11-one[55] 185



Using the same reactions conditions used to produce **180** 2-chloroquinoline and 2-formylphenylboronic acid **2** provided 5*H*-isoindolo[2,1-*a*]quinolin-11-one **185** as a yellow solid (13%). δ_H (360 MHz, $CDCl_3$): 3.80 (2H, d, *J* 4.0), 6.03 (1H, t, *J* 4.0, 8.2), 7.09 – 7.19 (2H, m), 7.30 (1H, ddd, *J* 1.9, 7.2, 8.6), 7.50 (1H, ddd, *J* 1.0, 7.2, 8.6), 7.59 (1H, ddd, *J* 1.0, 7.2, 8.2), 7.68 (1H, ddd, *J* 0.9, 1.9, 7.6), 7.90 (1H, ddd, *J* 0.9, 2.0, 7.6) and 9.00 (1H, dd, *J* 0.9, 8.6); δ_C (90 MHz, $CDCl_3$): 27.7 (CH_2), 103.6 (CH), 117.8 (CH), 119.1 (CH), 121.9 (quat), 123.2 (CH), 124.6 (CH), 127.5 (CH), 128.9 (CH), 129.1 (CH),

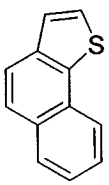
130.1 (quat), 131.9 (CH), 133.3 (quat), 133.9 (quat), 135.1 (quat) and 165.1 (quat). The data are consistent with literature values.[55]

FVP of Methyl 3-(2-phenylpyridin-3-yl) acrylate 159



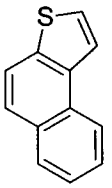
Flash vacuum pyrolysis of methyl 3-(2-phenylpyridin-3-yl) acrylate **159** (0.170 g, T_f 950 °C, T_i 195 °C, P $6.0 \times 10^{-2} - 8.0 \times 10^{-1}$ Torr, t 15 min) gave an oil (0.1248 g) which was purified by Kugelrohr distillation to produce benzo[*h*]quinoline[139] **176** as an oil (0.109 g, 85%) bp 164 °C (4 Torr) [lit.[140], 135 – 141 °C (0.2 Torr)]. (Found: M^+ 179.0738. $C_{13}H_9N$ requires *M* 179.0735); δ_H (250 MHz, $CDCl_3$): 7.46 (1H, dd, *J* 4.5, 8.0), 7.58 – 7.82 (5H, m), 8.12 (1H, dd, *J* 1.7, 8.0), 8.93 (1H, dd, *J* 1.7, 4.5) and 9.31 (1H, dd, *J* 1.7, 7.8); δ_C (250 MHz, $CDCl_3$): 121.6 (CH), 124.3 (CH), 125.0 (CH), 126.4 (quat), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.3 (CH), 130.7 (quat), 133.5 (quat), 136.3 (CH), 148.1 (CH) and 162.4 (quat); *m/z* 179 (M^+, 100%), 178 (76), 177 (60), 153 (41), 152 (53), 151 (58), 150 (47) and 89 (60).

FVP of Methyl 3-(2-thiophen-2-yl)phenylacrylate 104



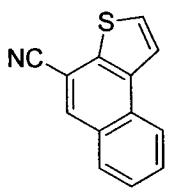
Flash vacuum pyrolysis of methyl 3-(2-thiophen-2-yl)phenylacrylate **161** (0.354 g, T_f 950 °C, T_i 179 °C, P $3.6 \times 10^{-2} - 6.5 \times 10^{-2}$ Torr, t 10 min) gave naphtho[1,2-*b*]thiophene[27] **104** as a brown oil (0.224 g, 84%). δ_H (250 MHz, $CDCl_3$): 7.54 (1H, d, *J* 5.8), 7.58 (1H, d, *J* 5.8), 7.59 (1H, dd, *J* 3.2, 7.2), 7.65 (1H, dd, *J* 3.2, 7.2), 7.81 (1H, d, *J* 8.6), 7.90 (1H, d, *J* 8.6), 8.00 (1H, dd, *J* 1.4, 8.6) and 8.23 (1H, dd, *J* 1.4, 8.6); δ_C (250 MHz, $CDCl_3$): 122.5 (CH), 124.1 (CH), 125.6 (2 CH), 125.8 (CH), 126.1 (CH), 127.1 (CH), 129.3 (CH), 129.5 (quat), 131.2 (quat) and 137.9 (2 quat).

FVP of Methyl 3-[2-(thiophen-3-yl)phenyl]acrylate 162



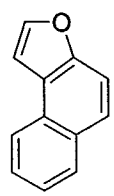
Flash vacuum pyrolysis of methyl 3-[2-(thiophen-3-yl)phenyl]acrylate **162** (0.182 g, T_f 950 °C, T_i 200 °C, P 5.5 × 10^{-2} – 5.0 × 10^{-1} Torr, t 5 min) gave a brown oil (0.1046 g) which was purified by dry flash chromatography (100% hexane) to produce naphtho[2,1-*b*]thiophene[41] **102** as a yellow oil (0.063 g, 40%). δ_H (250 MHz, $CDCl_3$): 7.63 – 7.48 (4H, m), 7.76 (1H, d, *J* 8.8.), 8.01 – 7.89 (2H, m) and 8.35 (1H, d, *J* 8.1); δc (250 MHz, $CDCl_3$): 120.5 (CH), 121.9 (CH), 123.4 (CH), 124.9 (CH), 125.1 (CH), 125.7 (CH), 126.3 (CH), 128.4 (CH), 129.2 (quat), 130.8 (quat), 135.8 (quat) and 137.2 (quat).

FVP of Methyl 3-[2-cyano(2-thiophen-3-yl)]phenylacrylate 166



Flash vacuum pyrolysis of methyl 3-[2-cyano(2-thiophen-3-yl)]phenylacrylate **166** (0.0274 g, T_f 950 °C, T_i 195 °C, P 2.6 × 10^{-2} – 1.7 × 10^{-1} Torr, t 5 min) gave a brown oil (0.0798 g) which was purified by dry flash chromatography (1:4 EtOAc/hexane) to produce naphtho[2,1-*b*]thiophene-4-carbonitrile[141] **190** as a yellow oil (0.018 g, 23%). δ_H (250 MHz, $CDCl_3$): 7.62 (1H, ddd, *J* 0.8, 6.2), 7.74 (1H, d, *J* 3.9), 7.76 (1H, ddd, *J* 0.8, 6.2), 7.98 (1H, dt, *J* 0.8, 5.4), 8.00 (1H, d, *J* 5.4), 8.16 (1H, s) and 8.33 (1H, dd, *J* 0.8, 6.2); δ_C (250 MHz, $CDCl_3$): 61.8 (quat), 104.8 (quat), 117.3 (quat), 122.2 (CH), 123.7 (CH), 126.5 (CH), 127.6 (CH), 129.1 (CH), 129.5 (CH), 129.6 (quat), 130.4 (quat), 131.9 (CH) and 136.7 (quat).

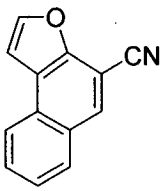
FVP of Methyl 3-(2-furan-3-yl)phenylacrylate 164



Flash vacuum pyrolysis of methyl 3-(2-furan-3-yl)phenylacrylate **164** (0.082 g, T_f 950 °C, T_i 220 °C, P 4.0 × 10^{-2} – 3.1 × 10^{-1} Torr, t 10 min) gave a yellow product which was purified by dry flash chromatography (10% EtOAc in hexane) to produce naphtho[2,1-*b*]furan[142] **122** as a yellow oil (0.0244 g, 40%). δ_H (250 MHz, $CDCl_3$): 7.44 (1H, dd, *J* 0.7, 2.1), 7.66–7.77

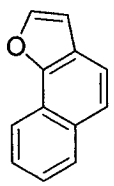
(3H, m), 7.87 (1H, d, *J* 7.7), 7.94 (1H, d, *J* 2.1), 8.11 (1H, d, *J* 7.7) and 8.31 (1H, d, *J* 8.1); δ_C (250 MHz, $CDCl_3$): 105.5 (CH), 112.4 (CH), 122.2 (quat), 123.3 (CH), 124.4 (CH), 125.0 (CH), 126.2 (CH), 126.3 (quat), 127.7 (quat), 128.6 (CH), 130.4 (quat) and 144.1 (CH).

FVP of Methyl 3-[2-cyano(2-furan-3-yl)]phenylacrylate 167



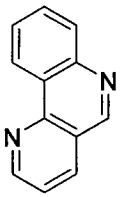
Flash vacuum pyrolysis of methyl 3-[2-cyano(2-furan-3-yl)]phenylacrylate **167** (0.028 g, T_f 975 °C, T_i 167 °C, P 2.0×10^{-2} – 1.7×10^{-1} Torr, t 10 min) gave naptho[2,1-*b*]furan-4-carbonitrile **191** as a brown oil (0.0149 g, 69%). (Found: M^+ 193.0529. $C_{13}H_7NO$ requires *M* 193.0528); δ_H (250 MHz, $CDCl_3$): 7.32 (1H, d, *J* 2.1), 7.59 (1H, ddd, *J* 1.2, 8.2), 7.74 (1H, ddd, *J* 1.2, 8.2), 7.89 (1H, d, *J* 2.1), 7.99 (1H, d, *J* 8.3), 8.12 (1H, s) and 8.13 (1H, dd, *J* 0.7, 8.3); δ_C (250 MHz, $CDCl_3$): 97.2 (quat), 105.9 (CH), 115.2 (quat), 123.5 (CH), 123.9 (quat), 125.9 (CH), 129.1 (quat), 129.3 (2 CH), 129.4 (quat), 131.2 (CH), 145.7 (CH) and 149.4 (quat). *m/z* 193 (M^+, 100%), 181 (11), 176 (16), 165 (12), 164 (22), 152 (12) and 88 (10).

FVP of Methyl-5-(2-carbethoxyfuran-5-yl)phenylacrylate 163



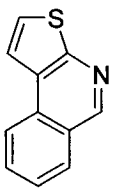
Flash vacuum pyrolysis of methyl-5-(2-carbethoxyfuran-5-yl)phenylacrylate[15] **163** (0.151 g, T_f 950 °C, T_i 282 °C, P 5.5×10^{-2} – 5.5×10^{-1}Torr, t 10 min) gave naphtho[1,2-*b*]furan **108** as a brown oil which was purified by dry flash chromatography (5% ethyl acetate in hexane (0.068 g, 80%). δ_H (360 MHz, $CDCl_3$): 6.99 (1H, d, *J* 2.2), 7.49 – 7.64 (2H, m), 7.67 (2H, s), 7.78 (1H, d, *J* 2.2), 7.99 (1H, d, *J* 8.3) and 8.32 (1H, d, *J* 8.3).

FVP of 2-Phenylpyridine-3-carbaldehyde *O*-methyl oxime 150



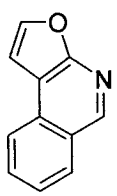
Flash vacuum pyrolysis of 2-phenylpyridine-3-carbaldehyde *O*-methyl oxime **150** (0.057 g, T_f 700 °C, T_i 191 °C, P $2.9 \times 10^{-2} - 2.4 \times 10^{-1}$ Torr, t 10 min) gave a brown oil which was purified by Kugelrohr distillation to produce *benzo[1,6]naphthyridine* **192** as a yellow oil (0.038 g, 78%) bp 138 °C (7 Torr). (Found: M^+ 180.0688. $C_{12}H_8N_2$ requires *M* 180.0688); δ_H (250 MHz, $CDCl_3$): 7.56 (1H, dd, *J* 5.2, 8.1), 7.70 – 7.79 (2H, m), 8.16 (1H, dd, *J* 1.2, 8.5), 8.28 (1H; dd, *J* 1.8, 8.1), 9.07 (1H, dd, *J* 2.0, 8.5), 9.10 (1H, dd, *J* 1.8, 4.4) and 9.25 (1H, s); δ_C (250 MHz, $CDCl_3$): 120.6 (quat), 122.7 (CH), 123.6 (CH), 125.1 (quat), 127.7 (CH), 129.0 (CH), 130.3 (CH), 136.0 (CH), 145.9 (quat), 148.4 (quat), 152.3 (CH) and 153.4 (CH); *m/z* 180 (M^+, 47%), 179 (22), 41 (100), 40 (60) and 39 (26).

FVP of 2-(Thiophen-3-yl)benzaldehyde *O*-methyl oxime 151



Flash vacuum pyrolysis of 2-(thiophen-3-yl)benzaldehyde *O*-methyl oxime **151** (0.068 g, T_f 700 °C, T_i 190 °C, P $1.6 \times 10^{-2} - 1.1 \times 10^{-2}$ Torr, t 10 min) gave a brown oil which was purified by dry flash chromatography (1:2 EtOAc/hexane) to produce *thieno[2,3-c]isoquinoline* **193** as an oil (0.056 g, 65%). δ_H (360 MHz, $CDCl_3$): 7.62 (1H, d, *J* 5.8), 7.64 (1H, m), 7.82 (1H, dd, *J* 1.6, 6.5), 7.86 (1H, d, *J* 5.8), 8.10 (1H, d, *J* 6.8), 8.27 (1H, d, *J* 6.8) and 9.13 (1H, s); δ_C (250 MHz, $CDCl_3$): 119.6 (CH), 122.6 (CH), 125.6 (quat), 125.8 (CH), 126.1 (CH), 128.4 (CH), 130.6 (CH), 131.7 (quat), 149.8 (CH), 155.8 (quat) and 161.4 (quat); *m/z* 185 (M^+, 100%), 179 (4), 158 (6), 141 (7), 140 (7), 114 (4), 93 (5) and 79 (5).

FVP of 2-(Furan-3-yl)benzaldehyde *O*-methyl oxime 153



Flash vacuum pyrolysis of 2-(furan-3-yl)benzaldehyde *O*-methyl oxime **153** (0.047 g, T_f 700 °C, T_i 192 °C, P $4.2 \times 10^{-2} - 1.8 \times 10^{-1}$ Torr, t 10 min) gave a brown product which was purified by dry flash chromatography (2:1 EtOAc/hexane) to produce *furo[2,3-c]isoquinoline*

194 as a yellow oil (0.005 g, 13%). (Found: M^+ 168.9779. $C_{11}H_7NO$ requires *M* 169.0528); δ_H (250 MHz, $CDCl_3$): 7.24 (1H, d, *J* 1.7), 7.60 (1H, dd, *J* 0.9, 5.1), 7.78 (1H, dd, *J* 0.9, 5.1), 7.81 (1H, d, *J* 1.7), 8.10 (1H, d, *J* 5.5), 8.13 (1H, d, *J* 5.5) and 8.97 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 104.7 (CH), 122.6 (CH), 125.5 (CH), 128.6 (CH), 131.0 (CH), 143.1 (CH) and 147.8 (CH); *m/z* 169 (M^+, 100%), 168 (72), 141 (78), 115 (43), 70 (34) and 41 (81).

7.5 Four-Ring Systems

General Method A (Suzuki)[8c]

The boronic acid (50 eq), halide (50 eq), potassium carbonate (300 eq) and tetrakis(triphenylphosphine) palladium (1 eq) were mixed in a solution of dioxane and water (3:1) and the mixture heated under reflux under a nitrogen atmosphere. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug. The solvent was removed and the residue dissolved in chloroform and the insoluble organic base was removed by filtration.

General Method B (Suzuki)[8c]

The halide (35 eq) and tetrakis (triphenylphosphine) palladium (1 eq) were stirred in ethylene glycol dimethyl ether (4 cm^3) for 20 min. Sodium carbonate (45 eq) in water (1 cm^3) and 2-formylphenylboronic acid (34 eq) were added and heated under reflux overnight. The solvent was then removed and the residue extracted from dichloromethane and the organic layers washed with water and dried over $MgSO_4$.

General Method C (Wittig)[125]

The aldehyde (1 eq) and methyl(triphenylphosphoranylidene) acetate (1.05 eq) were mixed in toluene and the solution heated to reflux under nitrogen for 4.5 h. The solvent was removed and the product was purified by dry flash chromatography using 50% ethyl acetate in hexane as eluent.

General Method D (Knoevenagel)[7]

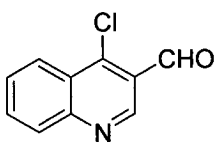
The aldehyde (1 eq) and methyl cyanoacetate (1 eq) were added to toluene (10 cm^3) followed by piperidine (2 drops) and glacial acetic acid (2 drops). The solution was left at room temperature for 2 h. The solution was then added to water (10 cm^3) and

extracted with dichloromethane (3 × 15 cm^3) and the organic extracts were washed with water (3 × 15 cm^3) and dried over $MgSO_4$ and the solvent removed.

General Method E[7]

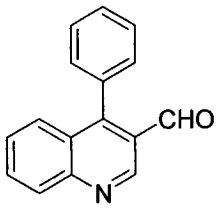
The aldehyde (1 eq) and *O*-methyhydroxylamine hydrochloride (1.5 eq) were added to ethanol and the solution heated to reflux for 2 h. The solution was then concentrated under vacuum the residue was suspended in ether (30 cm^3) and washed with NaOH (0.25 M, 10 cm^3), then with water (10 cm^3) and dried over $MgSO_4$ and then solvent was removed.

4-Chloroquinoline-3-carbaldehyde[126] **248**



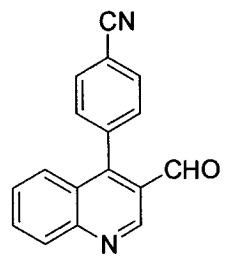
A solution of 2-aminoacetophenone **151** (7.853 g, 0.06 mol) in DMF (36 cm^3) was cooled with stirring to 0 °C. Phosphoryl chloride (22 cm^3, 0.24 mol) was added dropwise. The yellow suspension was left at room temperature for 1 h, after which it was heated to 90 °C and allowed to reflux for 4 h. The brown solution was then neutralised by the addition of ice containing sodium acetate and then the reaction mixture was left overnight. The solid was then removed by filtration and dried under vacuum resulting in 4-chloroquinoline-3-carbaldehyde **248** (5.703 g, 51%) as a beige solid. δ_H (250MHz, $CDCl_3$): 7.69 (1H, td, *J* 1.4, 6.9), 7.86 (1H, td, *J* 1.4, 6.9), 8.17 (1H, d, *J* 8.5), 8.35 (1H, dd, *J* 1.4, 8.5), 9.21 (1H, s) and 10.65 (1H, s, CHO); δ_C (250MHz, $CDCl_3$): 124.3 (quat), 125.0 (CH), 125.6 (quat), 128.7 (CH), 128.7 (quat), 129.7 (CH), 133.4 (CH), 148.2 (CH), 150.2 (quat) and 188.8 (CH).

4-Phenylquinoline-3-carbaldehyde 250



Phenylboronic acid (0.647 g, 5.31 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.105 g, 0.55 mmol), potassium carbonate (0.444 g, 3.22 mmol) and tetrakis(triphenylphosphine) palladium (0.017 g, 0.015 mmol) were mixed in a solution of dioxane (7.5 cm^3) and water (2.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce *4-phenylquinoline-3-carbaldehyde* **250** as a yellow oil (0.128 g, 80%) mp 104 – 105 °C. (Found: C, 81.8; H, 4.8; N, 5.8. $C_{16}H_{11}NO$ requires C, 82.3; H, 4.8; N, 6.0%): δ_H (250 MHz, $CDCl_3$): 7.65 – 7.69 (2H, m), 7.79 – 7.85 (4H, m), 7.95 (1H, dd, *J* 0.9, 8.5), 8.10 (1H, dd, *J* 1.4, 7.0), 8.47 (1H, d, *J* 8.5), 9.68 (1H, s) and 10.20 (1H, s); δ_C (250 MHz, $CDCl_3$): 125.3 (quat), 126.5 (quat), 127.4 (CH), 127.7 (CH), 128.6 (2 CH), 129.2 (CH), 129.9 (CH), 130.2 (2 CH), 132.2 (CH), 132.4 (quat), 148.2 (CH), 150.1 (quat), 153.4 (quat) and 191.6 (CH); *m/z* 233 (M^+, 100%), 232 (100), 205 (22), 204 (79), 177 (17), 176 (36), 155 (16) and 102 (16).

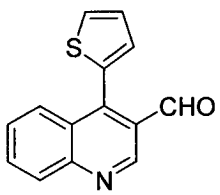
4-(3-Formylquinolin-4-yl)benzonitrile 251



4-Cyanophenylboronic acid (0.387 g, 2.63 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.503 g, 2.63 mmol), potassium carbonate (2.172 g, 0.016 mol) and tetrakis(triphenylphosphine) palladium (0.060g, 0.005 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed. The product was then purified by dry flash chromatography using 50% ethyl acetate in hexane to produce *4-(3-formylquinolin-4-yl)benzonitrile* **251** as a solid (0.186 g, 27%) mp 142 – 144 °C (Found: C, 78.2; H, 4.1; N, 10.4. $C_{17}H_{10}N_2O$ requires C, 79.1; H, 3.9; N, 10.9%). δ_H (250 MHz, $CDCl_3$): 7.43 – 7.52 (4H, m), 7.79 – 7.85 (3H, m), 8.16 (1H, d, *J* 8.6), 9.35 (1H, s) and 9.83 (1H, s); δ_C (250 MHz, $CDCl_3$): 113.5 (quat), 117.9 (quat), 124.9 (quat), 125.7

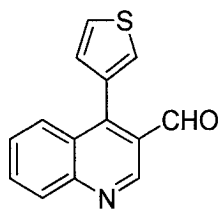
(quat), 126.7 (CH), 128.2 (CH), 130.2 (CH), 130.9 (2 CH), 132.4 (2 CH), 132.7 (CH), 137.7 (quat), 148.3 (CH), 150.0 (quat), 150.7 (quat) and 190.1 (CH); *m/z* 258 (M^+, 30%), 257 (34), 231 (51), 230 (94), 229 (100), 228 (68), 204 (45) and 119 (94).

4-(Thiophen-2-yl)quinoline-3-carbaldehyde 252



2-Thiopheneboronic acid (0.506 g, 3.96 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.750 g, 3.91 mmol), potassium carbonate (3.710 g, 0.03 mol) and tetrakis(triphenylphosphine) palladium (0.108 g, 0.094 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce *4-(thiophen-2-yl)quinoline-3-carbaldehyde* **252** as a brown oil (0.580 g, 62%). (Found: M^+ 239.0405. $C_{14}H_9NOS$ requires *M* 239.0405); δ_H (250 MHz, $CDCl_3$): 7.12 – 7.18 (2H, m), 7.43 – 7.57 (2H, m), 7.72 (1H, ddd, *J* 1.3, 7.0), 7.83 (1H, dd, *J* 1.7, 8.5), 8.07 (1H, d, *J* 8.5), 9.27 (1H, s) and 9.96 (1H, s); δ_C (250 MHz, $CDCl_3$): 123.7 (quat), 124.3 (quat), 126.4 (quat), 127.0 (CH), 127.6 (CH), 127.9 (CH), 128.9 (CH), 129.9 (CH), 131.2 (CH), 132.2 (CH), 145.0 (quat), 148.0 (CH), 150.0 (quat) and 191.1 (CH); *m/z* 239 (M^+, 81%), 238 (82), 211 (95), 210 (100), 209 (44), 195 (73), 166 (75) and 139 (53).

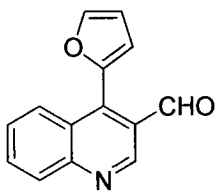
4-(Thiophen-3-yl)quinoline-3-carbaldehyde 253



3-Thiopheneboronic acid (0.368 g, 2.87 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.752 g, 3.92 mmol), potassium carbonate (3.260 g, 0.02 mol) and tetrakis(triphenylphosphine) palladium (0.091 g, 0.078 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed and the product was then purified by Kugelrohr distillation produce *4-(thiophen-3-yl)quinoline-3-carbaldehyde* **253** as a yellow solid (0.566 g, 82%); (Found: M^+

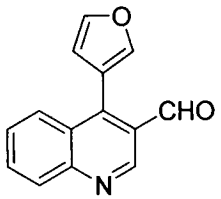
239.0406. $C_{14}H_9NOS$ requires *M* 239.0405). δ_H (250 MHz, $CDCl_3$): 7.18 (1H, dd, *J* 1.3, 4.9), 7.40 (1H, dd, *J* 1.3, 3.0), 7.48 (1H, ddd, *J* 1.3, 6.9), 7.53 (1H, dd, *J* 3.0, 5.0), 7.74 (1H, d, *J* 6.9), 7.77 (1H, dd, *J* 1.3, 6.9), 8.10 (1H, dd, *J* 1.3, 9.0), 9.30 (1H, s) and 9.94 (1H, d, *J* 0.4); δ_C (250 MHz, $CDCl_3$): 125.7 (quat), 126.8 (CH), 127.0 (CH), 127.2 (CH), 127.5 (CH), 128.3 (quat), 128.4 (quat), 129.6 (CH), 129.7 (CH), 132.0 (CH), 147.9 (CH), 148.4 (quat), 149.8 (quat) and 191.4 (CH); *m/z* 239 (M^+, 19%), 211 (100), 210 (95) and 166 (100).

4-(Furan-2-yl)quinoline-3-carbaldehyde 254



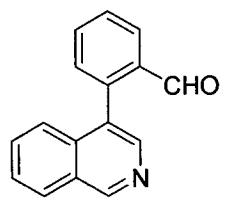
2-Furanboronic acid (0.500 g, 4.47 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.600 g, 3.13 mmol), potassium fluoride (0.796 g, 0.014 mol), *t*-tributyl phosphine tetrafluoroborate (0.014 g, 0.047 mmol) and dibenzylideneacetone palladium (0.021 g, 0.022 mmol) were mixed. The flask was flushed with argon then THF (10 cm^3) was added with stirring and the solution was heated under reflux under argon for 3 d. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug and the solvent removed to produce a solid (0.265 g) which was shown by ^1H NMR spectroscopy to contain product and starting materials. More solid was washed through the silica plug with acetone (0.258 g) which was shown by ^1H nmr to be product. The impure solid (0.265 g) was purified by dry flash chromatography using 25% ethyl acetate in hexane as eluent. A solid was isolated and combined with the previously isolated product (0.258 g) to produce a pure sample of *4-(furan-2-yl)quinoline-3-carbaldehyde* **254** (0.440 g, 63%) mp 154 – 155 °C. (Found: M^+ 223.0632. $C_{14}H_9NO_2$ requires *M* 223.0633); δ_H (250 MHz, $CDCl_3$): 6.68 (1H, ddd, *J* 0.7, 1.9, 3.4), 6.81 (1H, dd, *J* 0.7, 3.4), 7.58 (1H, m), 7.75 (1H, dd, *J* 0.7, 1.9), 7.80 (1H, m), 8.13 (2H, ddd, *J* 0.7, 2.6, 8.9), 9.32 (1H, s) and 10.10 (1H, s); δ_C (250 MHz, $CDCl_3$): 112.0 (CH), 116.6 (CH), 125.2 (quat), 125.7 (quat), 127.1 (CH), 128.1 (CH), 130.1 (CH), 132.0 (quat), 132.1 (CH), 140.3 (quat), 145.5 (CH), 148.4 (CH), 150.3 (quat) and 191.4 (CH); *m/z* 223 (M^+, 41%), 195 (100), 167 (52), 166 (51), 140 (19) and 139 (29).

4-(Furan-3-yl)quinoline-3-carbaldehyde 255



3-Furanboronic acid (0.870 g, 7.78 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.501 g, 2.61 mmol), potassium carbonate (3.804 g, 0.03 mol) and tetrakis(triphenylphosphine) palladium (0.105 g, 0.091 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce *4-(furan-3-yl)quinoline-3-carbaldehyde* **255** as a brown oil (0.736 g, 73%). The product could not be purified. (Found: M^+ 223.0634. $C_{14}H_9NO_2$ requires *M* 223.0633); δ_H (250 MHz, $CDCl_3$): 6.65 (1H, s), 7.54 – 7.68 (3H, m), 7.80 (1H, ddd, *J* 1.0, 6.0), 7.94 (1H, d, *J* 8.5), 8.13 (1H, d, *J* 8.5), 9.33 (1H, s) and 10.14 (1H, s); δ_C (250 MHz, $CDCl_3$): 113.1 (CH), 116.7 (quat), 126.1 (quat), 126.9 (CH), 127.8 (CH), 128.5 (quat), 130.1 (CH), 132.3 (CH), 143.0 (CH), 144.1 (CH), 144.5 (quat), 148.3 (CH), 150.0 (quat) and 191.5 (CH); *m/z* 279 (M^+, 14%), 133 (75), 196 (55), 195 (84), 167 (76), 166 (100), 165 (69) and 140 (63).

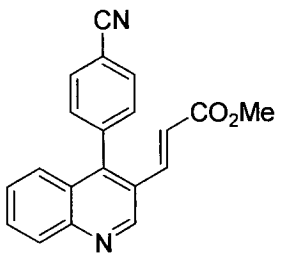
2-(1-Phenylisoquinoline-4-yl) carbaldehyde 258[143,90]



2-Formylphenylboronic acid **257** (0.510 g, 3.40 mmol), 4-bromoisoquinoline **256** (0.700 g, 3.36 mmol), potassium carbonate (2.778 g, 0.020 mol) and tetrakis(triphenylphosphine) palladium (0.077 g, 0.067 mmol) were mixed in a solution of dioxane (24 cm^3) and water (8 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a yellow oil which was purified by dry flash chromatography in 20% ethyl acetate in hexane to produce *2-(1-phenylisoquinoline-4-yl) carbaldehyde* **258** as a yellow oil (0.631 g, 80%). (Found: M^+ 233.0841. $C_{16}H_{11}NO$ requires *M* 233.0852); δ_H (250 MHz, $CDCl_3$): 7.54 – 7.86 (6H, m), 8.17 (1H, m), 8.23 (1H, ddd, *J* 0.5, 1.6, 7.7), 8.57 (1H, s), 9.43 (1H, s) and 9.75 (1H, s); δ_C (250 MHz, $CDCl_3$): 124.9 (CH), 128.1 (CH), 128.2

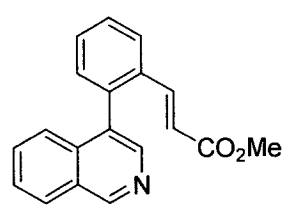
(CH), 128.4 (CH), 129.3 (CH), 129.6 (quat), 131.8 (CH), 132.3 (CH), 132.5 (quat), 134.4 (CH), 135.4 (quat), 135.7 (quat), 140.5 (quat), 143.9 (CH), 153.4 (CH) and 191.7 (CH); *m/z* 233 (M^+, 10%), 84 (13), 43 (24), 42 (16), 41 (100), 40 (60), 39 (27) and 38 (17).

Methyl 3-[4-(4-cyanophenyl)quinolin-3-yl]acrylate 259



4-(3-Formylquinolin-4-yl)benzonitrile **251** (0.1011 g, 0.39 mmol) and methyl (triphenylphosphoranylidene) acetate (0.1668 g, 0.50 mmol) were mixed in toluene (50 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. The solvent was then removed and the product was purified by dry flash chromatography using 50 % ethyl acetate in hexane as eluent to produce *methyl 3-[4-(4-cyanophenyl)quinolin-3-yl]acrylate* **259** as a yellow solid (0.0818 g, 67%) in 95:5 *E*:*Z* ratiomp 288 – 290 °C (Found: C, 75.5; H, 4.7; N, 7.9. $C_{20}H_{14}N_2O_2$ requires C, 76.4; H, 4.5; N, 8.9%); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.69 (3H, s), 6.51 (1H, d, *J* 16.0), 7.33 – 7.75 (7H, m), 7.80 (1H, d, *J* 8.2), 8.09 (1H, d, *J* 8.1) and 9.14 (1H, s); δ_C (250 MHz, $CDCl_3$): 52.7 (CH_3), 113.4 (quat), 118.7 (quat), 121.7 (CH), 125.5 (quat), 126.9 (CH), 128.6 (CH), 129.1 (quat), 129.4 (quat), 130.5 (CH), 131.5 (CH), 131.6 (2 CH), 133.0 (2 CH), 139.9 (CH), 140.4 (quat), 146.5 (quat), 148.7 (CH) and 167.1 (quat); *m/z* 314 (M^+, 14%), 278 (67), 277 (84), 257 (50), 231 (55), 130 (92), 229 (100) and 228 (76); *Z*-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 6.00 (1H, d, *J* 12.3) and 6.64 (1H, d, *J* 12.3).

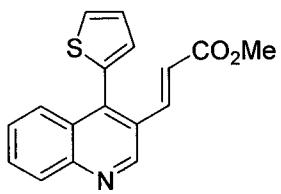
Methyl 2-(1-phenylisoquinoline-4-yl)acrylate 260



2-(1-Phenylisoquinoline-4-yl)carbaldehyde **258** (0.202 g, 0.866 mmol) and methyl (triphenylphosphoranylidene) acetate (0.360 g, 1.076 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 2-(1-*

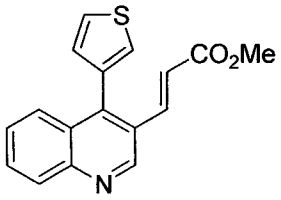
phenylisoquinoline-4-yl)acrylate **260** as a yellow solid (0.197 g, 79%) in 84:6 *E*:*Z* ratio mp 104 - 106 °C; (Found: C, 78.1; H, 5.0; N, 4.7. $C_{19}H_{15}NO_2.0.2\ H_2O$ required C, 77.9; H, 5.3; N, 4.8%); δ_H (250 MHz, $CDCl_3$): (*E*-isomer)3.52 (3H, s), 6.29 (1H, d, *J* 16.4), 7.18 – 7.28 (2H, m), 7.34 – 7.44 (3H, m), 7.53 (2H, dd, *J* 3.1, 6.4), 7.71 – 7.75 (1H, m), 7.91 – 8.00 (1H, m), 8.30 (1H, s) and 9.23 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 50.6 (CH_3), 118.4 (CH), 123.9 (CH), 125.6 (CH), 126.4 (CH), 127.0 (CH), 127.8 (CH), 129.0 (CH), 129.9 (CH), 130.8 (CH), 141.4 (CH), 142.5 (CH) and 151.7 (CH); *Z*-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.58 (3H, s), 5.60 (1H, d, *J* 12.1), 6.52 (1H, d, *J* 12.1), 8.33 (1H, s) and 9.18 (1H, s); *m/z* 289 (M^+, 6%), 162 (60), 131 (100), 103 (53), 94 (58), 77 (43), 51 (27) and 43 (42).

Methyl 3-[4-(thiophen-2-yl)quinoline]acrylate 261



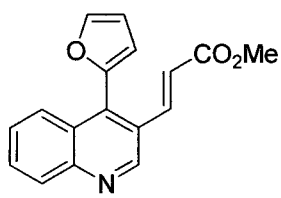
4-(Thiophen-2-yl)quinoline-3-carbaldehyde **252** (0.185 g, 0.77 mmol) and methyl (triphenylphosphoranylidene) acetate (0.347 g, 1.04 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(thiophen-2-yl)quinoline]acrylate* **261** as a yellow solid (0.189 g, 83%) in 85:15 *E*:*Z* ratio mp 157 – 159 °C (Found: M^+ 295.0667. $C_{17}H_{13}NO_2S$ requires *M* 295.0667); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.70 (3H, s), 6.49 (1H, d, *J* 16.6), 7.05 (1H, d, *J* 3.3), 7.18 (1H, t, *J* 3.3, 9.0), 7.43 (2H, t, *J* 7.5, 15.7), 7.53 (1H, d, *J* 5.7), 7.62 – 7.84 (3H, m) and 9.10 (1H, s); δ_C (250 MHz, $CDCl_3$): 51.9 (CH_3), 120.6 (CH), 126.8 (CH), 126.9 (quat), 127.6 (CH), 127.8 (quat), 128.2 (CH), 128.3 (CH), 129.5 (quat), 129.7 (CH), 130.2 (CH), 134.2 (quat), 140.4 (CH), 140.6 (CH), 141.1 (quat), 148.2 (CH) and 166.8 (quat); *Z*-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 6.00 (1H, d, *J* 12.3), 6.82 (1H, d, *J* 12.3) and 8.97 (1H, s); *m/z* 295 (M^+, < 1%).

Methyl 3-[4-(thiophen-3-yl)quinoline]acrylate 262



4-(Thiophene-3-yl)quinoline-3-carbaldehyde **253** (0.211 g, 0.88 mmol) and methyl (triphenylphosphoranylidene) acetate (0.363 g, 1.09 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(4-(thiophen-3-yl)quinoline)acrylate* **262** as a yellow solid (0.165 g, 63%) in 86:4 *E*:*Z* ratio mp 140 – 142 °C (Found: C, 69.0; H, 4.4; N, 4.8. $C_{12}H_{13}NO_2S$ required C, 69.1; H, 4.4; N, 4.7%); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.68 (3H, s), 6.46 (1H, d, *J* 16.1), 7.04 (1H, dd, *J* 1.3, 4.9), 7.26 (1H, dd, *J* 1.3, 3.0), 7.36 – 7.42 (1H, m), 7.47 (1H, dd, *J* 3.0, 5.0), 7.59 – 7.64 (3H, m), 8.03 (1H, dd, *J* 1.0, 8.6) and 9.08 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 51.6 (CH_3), 1119.9 (CH), 126.2 (CH), 126.4 (CH), 126.7 (CH), 127.2 (CH), 129.3 (CH), 129.4 (CH), 130.0 (CH), 140.6 (CH) and 148.1 (CH); *Z*-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 5.95 (1H, d, *J* 12.2), 6.75 (1H, d, *J* 12.2), 7.07 (1H, dd, *J* 1.1, 4.9), 7.29 (1H, dd, *J* 1.1, 3.3) and 8.85 (1H, s); *m/z* (*E*- and *Z*-isomer) 295 (M^+, 18%), 212 (53), 211 (83), 210 (100), 209 (80), 184 (41), 166 (21) and 139 (49).

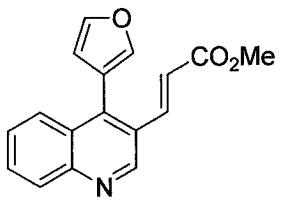
Methyl 3-[4-(furan-2-yl)quinoline]acrylate 263



4-(Furan-2-yl)quinoline-3-carbaldehyde **254** (0.201 g, 0.90 mmol) and methyl (triphenylphosphoranylidene) acetate (0.304 g, 0.91 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(furan-2-yl)quinoline]acrylate* **263** as a yellow solid (0.241 g, 96%) in 92:8 *E*:*Z* ratio mp 125 - 127 °C (Found: M^+ 279.0895. $C_{17}H_{13}NO_3$ requires *M* 279.0895); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.71 (3H, s), 6.47 (1H, d, *J* 16.2), 6.57 – 6.60 (2H, m), 7.44 (1H, ddd, *J* 1.4, 6.9), 7.60 – 7.65 (2H, m), 7.77 (1H, d, *J* 16.2), 7.94 (1H, ddd, *J* 0.6, 1.4, 8.5),

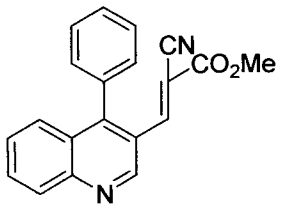
8.02 (1H, dd, *J* 0.9, 8.5) and 9.04 (1H, s); δ_C (250 MHz, $CDCl_3$): 51.7 (CH_3), 111.7 (CH), 115.5 (CH), 120.4 (CH), 125.6 (quat), 125.8 (quat), 126.5 (CH), 127.5 (CH), 129.6 (CH), 130.1 (CH), 135.8 (quat), 140.8 (CH), 144.2 (CH), 146.9 (quat), 148.3 (quat), 148.3 (CH) and 166.6 (quat); Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.58 (3H, s), 6.04 (1H, d, *J* 11.6) and 8.82 (1H, s); *m/z* 279 (M^+, 14%), 220 (36), 108 (100), 107 (82), 106 (19), 105 (20), 79 (48) and 77 (30).

Methyl 3-[4-(furan-3-yl)quinoline]acrylate 264



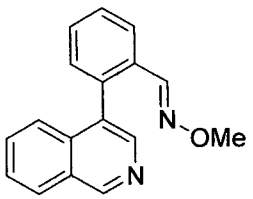
4-(Furan-3-yl)quinoline-3-carbaldehyde **255** (0.181 g, 0.81 mmol) and methyl (triphenylphosphoranylidene) acetate (0.374 g, 1.18 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-(4-(furan-3-yl)quinoline)acrylate* **264** as a yellow solid (0.100 g, 44%) in 86:4 *E*:*Z* ratio mp 163 – 165 °C; (Found: M^+ 279.0893. $C_{17}H_{13}NO_3$ requires *M* 279.0895); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.73 (3H, s), 6.52 (1H, d, *J* 16.3), 6.51 – 6.52 (1H, m), 7.42 – 7.51 (2H, m), 7.62 – 7.74 (3H, m), 7.80 – 7.85 (1H, m), 8.05 (1H, d, *J* 8.5) and 9.09 (1H, s); δ_C (250 MHz, $CDCl_3$): 51.9 (CH_3), 112.8, (CH), 118.6 (quat), 120.3 (CH), 126.0 (quat), 126.5 (CH), 127.2 (quat), 127.5 (CH), 129.6 (quat), 129.7 (CH), 130.2 (CH), 139.7 (quat), 140.7 (CH), 142.4 (CH), 143.8 (CH), 148.2 (CH) and 167.0 (quat); *Z*-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.63 (3H, s), 6.02 (1H, d, *J* 12.0), 6.93 (1H, d, *J* 12.0) and 8.85 (1H, s); *m/z* 279 (M^+, 45%), 220 (99), 219 (47), 195 (99), 191 (33), 166 (100), 165 (35) and 139 (51).

Methyl 2-cyano-3-(4-phenylquinolin-3-yl)acrylate 265



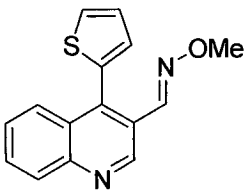
4-Phenylquinoline-3-carbaldehyde **250** (0.146 g, 0.626 mmol) and methyl cyanoacetate (0.051 g, 0.517 mmol) were added to toluene (5 cm^3). General work-up method D was then followed to produce *methyl 2-cyano-3-(4-phenylquinolin-3-yl)acrylate* **265** as a yellow oil (0.148 g, 75%) mp 158 – 160 °C; (Found: M^+ 314.1057. $C_{20}H_{14}N_2O_2$ requires *M* 314.1055); δ_H (250 MHz, $CDCl_3$): 3.77 (3H, s), 7.10 (1H, dd, *J* 7.4, 17.6), 7.18 – 7.23 (1H, m), 7.46 – 7.49 (4H, m), 7.57 (1H, m), 7.72 (1H, ddd, *J* 1.6, 1.7, 6.8), 8.0 (1H, s), 8.1 (1H, d, *J* 8.5) and 9.59 (1H, s); δ_C (250 MHz, $CDCl_3$): 60.9 (CH_3), 112.5 (quat), 130.6 (quat), 132.6 (quat), 133.8 (quat), 134.7 (CH), 135.1 (CH), 136.1 (2 CH), 136.9 (CH), 137.2 (CH), 137.6 (2 CH), 139.1 (CH), 141.3 (quat), 155.5 (CH), 156.6 (quat), 158.9 (quat), 159.4 (CH) and 169.6 (quat); *m/z* 314 (M^+, 24%), 278 (75), 277 (94), 262 (72), 238 (66), 237 (100), 201 (61) and 152 (72).

2-(1-Phenylisoquinolin-4-yl) *O*-methyloxime[89] 266



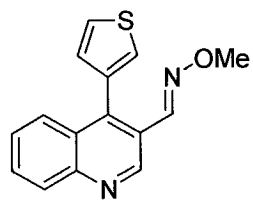
2-(1-Phenylisoquinolin-4-yl) carbaldehyde **258** (0.173 g, 0.741 mmol) and *O*-methylhydroxylamine hydrochloride (0.110 g, 1.32 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *2-(1-phenylisoquinolin-4-yl) O-methyloxime* **266** as a white solid (0.187 g, 96%) mp 108 – 110 °C. (Found: C, 77.9; H, 5.2; N, 10.7. $C_{17}H_{14}N_2O$ required C, 77.9; H, 5.4; N, 10.7%); δ_H (250 MHz, $CDCl_3$): 3.75 (3H, s), 7.23 (1H, ddd, *J* 0.5, 3.7, 6.0), 7.40 (3H, dd, *J* 3.7, 5.7), 7.49 – 7.57 (3H, m), 7.94 (1H, ddd, *J* 1.8, 4.8, 6.5), 8.00 (1H, dd, *J* 3.7, 5.5), 8.32 (1H, s) and 9.21 (1H, s); δ_C (250 MHz, $CDCl_3$): 60.9 (CH_3), 123.9 (CH), 124.7 (CH), 126.4 (CH), 126.9 (CH), 127.6 (CH), 128.6 (CH), 130.0 (CH), 130.3 (CH), 130.4 (quat), 133.9 (quat), 135.5 (quat), 142.3 (quat), 142.3 (CH), 145.8 (CH), 151.6 (CH) and 151.6 (quat); *m/z* 262 (M^+,100%), 261 (76), 231 (77), 204 (98), 203 (58), 73 (53), 57 (53) and 43 (72).

4-(Thiophen-2-yl)quinoline-3-carbaldehyde *O*-methyloxime 267



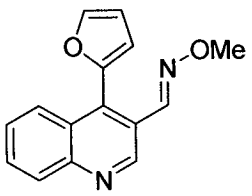
4-(Thiophen-2-yl)quinoline-3-carbaldehyde **252** (0.2681 g, 1.12 mmol) and *O*-methylhydroxylamine hydrochloride (0.0888 g, 1.06 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *4-(thiophen-2-yl)quinoline-3-carbaldehyde O-methyloxime* **267** as a brown solid (0.165 g, 55%) mp 98 – 100 °C. (Found: M^+ 168.0670. $C_{15}H_{12}N_2OS$ requires *M* 268.0671); δ_H (250 MHz, $CDCl_3$): 3.90 (3H, s), 7.00 (1H, d, *J* 2.6), 7.11 (1H, t, *J* 3.5), 7.37 (1H, t, *J* 7.3, 15.4), 7.46 (1H, d, *J* 4.7), 7.57 – 7.67 (2H, m), 7.96 (1H, s), 8.04 (1H, d, *J* 8.5) and 9.37 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 62.2 (CH_3), 126.1 (CH), 127.2 (CH), 127.3 (CH), 127.7 (CH), 129.5 (CH), 129.7 (CH), 129.8 (CH), 145.4 (CH) and 147.6 (CH); *m/z* 268 (M^+, 4%), 221 (100), 193 (77), 192 (52), 166 (67) and 139 (54).

4-(Thiophen-3-yl)quinoline-3-carbaldehyde *O*-methyloxime 268



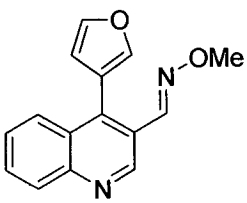
4-(Thiophen-3-yl)quinoline-3-carbaldehyde **252** (0.205 g, 0.85 mmol) and *O*-methylhydroxylamine hydrochloride (0.082 g, 0.98 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *4-(thiophen-3-yl)quinoline-3-carbaldehyde O-methyloxime* **268** as a yellow oil (0.201 g, 87%) mp 135 – 136 °C (Found: M^+ 268.0672. $C_{15}H_{12}N_2OS$ requires *M* 268.0670); δ_H (360 MHz, $CDCl_3$): 3.89 (3H, s), 7.00 (1H, dd, *J* 1.3, 4.9), 7.22 (1H, dd, *J* 1.3, 3.0), 7.31 – 7.37 (1H, m), 7.41 (1H, dd, *J* 3.0, 4.9), 7.52 – 7.60 (2H, m), 7.89 (1H, s), 8.02 (1H, d, *J* 8.3) and 9.35 (1H, s); δ_C (360 MHz, $CDCl_3$): 62.2 (CH_3), 123.2 (quat), 125.8 (CH), 126.2 (CH), 126.4 (CH), 127.0 (CH), 128.3 (quat), 129.2 (CH), 129.4 (CH), 129.7 (CH), 131.8 (quat), 133.9 (quat), 142.0 (quat), 145.5 (CH) and 147.7 (CH); *m/z* 269 (M^+, 6%), 237 (51), 212 (49), 211 (95), 210 (100), 209 (60), 166 (74) and 139 (48).

4-(Furan-2-yl)quinoline-3-carbaldehyde *O*-methyloxime 269



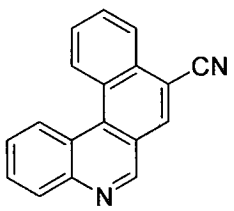
4-(Furan-2-yl)quinoline-3-carbaldehyde **254** (0.204 g, 0.92 mmol) and *O*-methylhydroxylamine hydrochloride (0.113 g, 1.35 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *4-(furan-2-yl)quinoline-3-carbaldehyde O-methyloxime* **269** as an orange solid (0.208 g, 90%) mp 87 – 89 °C. (Found: M^+ 252.0890. $C_{15}H_{12}N_2O_2$ requires *M* 252.0899); δ_H (250 MHz, $CDCl_3$): 3.96 (3H, s), 6.56 (1H, dd, *J* 1.9, 3.3), 6.60 (1H, dd, *J* 0.6, 3.3), 7.45 (1H, ddd, *J* 1.9, 6.9), 7.61 – 7.66 (2H, m), 7.89 (1H, dd, *J* 0.6, 8.5), 8.05 (1H, d, *J* 8.5), 8.11 (1H, s) and 9.37 (1H, s); δ_C (250 MHz, $CDCl_3$): 62.3 (CH_3), 111.4 (CH), 114.4 (CH), 123.5 (quat), 126.0 (quat), 126.1 (CH), 127.4 (CH), 129.7 (CH), 129.9 (CH), 135.0 (quat), 144.1 (CH), 145.8 (CH), 146.7 (quat), 148.1 (quat) and 148.2 (CH); *m/z* 252 (M^+, 42%), 221 (60), 205 (100), 183 (60), 91 (50), 86 (57) and 84 (83).

4-(Furan-3-yl)quinoline-3-carbaldehyde *O*-methyloxime 270



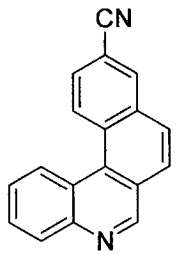
4-(Furan-3-yl)quinoline-3-carbaldehyde **255** (0.252 g, 1.13 mmol) and *O*-methylhydroxylamine hydrochloride (0.150 g, 1.79 mmol) were added to ethanol (10 cm^3). General work-up method E was then followed to produce *4-(furan-3-yl)quinoline-3-carbaldehyde O-methyl oxime* **270** as a brown oil (0.225 g, 79%). (Found: M^+ 252.0905. $C_{15}H_{12}N_2O_2$ requires *M* 252.0899); δ_H (250 MHz, $CDCl_3$): 3.95 (3H, s), 6.48 (1H, m), 7.34– 7.67 (4H, m), 7.76 (1H, d, *J* 8.6), 8.05 (1H, d, *J* 8.6), 8.08 (1H, s) and 9.35 (1H, s); δ_C DEPT(250 MHz, $CDCl_3$): 62.2 (CH_3), 112.7 (CH), 126.0 (CH), 128.3 (CH), 128.5 (CH), 129.6 (CH), 129.8 (CH), 131.9 (CH), 145.7 (CH) and 147.8 (CH); *m/z* 252 (M^+, 6%), 240 (58), 239 (50), 238 (64), 237 (84), 236 (64), 210 (70) and 166 (100).

FVP of Methyl 2-cyano-3-(4-phenylquinolin-3-yl)acrylate 265



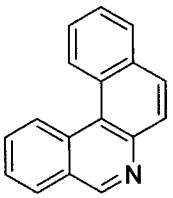
Flash vacuum pyrolysis of methyl 2-cyano-3-(4-phenylquinolin-3-yl)acrylate **265** (0.083 g, T_f 975 °C, T_i 275 °C, P 5.0×10^{-2} – 4.0×10^{-1} Torr, t 5 min) gave a brown oil which was purified by dry flash chromatography using 30% ethyl acetate in hexane as eluent to yield *benzo[k]phenanthridine-8-carbonitrile* **271** as a brown oil (0.014 g, 21%). (Found: M^+ 254.0840. $C_{18}H_{10}N_2$ requires *M* 254.0844) δ_H (250 MHz, $CDCl_3$): 7.73 (1H, ddd, *J* 1.7, 6.9, 8.3), 7.81 (1H, dd, *J* 2.0, 4.0), 7.84 (1H, d, *J* 2.9), 7.86 (1H, t, *J* 1.7), 8.28 (1H, dd, *J* 1.7, 8.3), 8.36 (1H, s), 8.41 – 8.45 (1H, m), 8.96 (1H, d, *J* 8.3), 9.11 – 9.15 (1H, m) and 9.26 (1H, s); *m/z* 254 (M^+, 26%), 231 (21), 230 (100), 229 (33), 202 (18), 176 (14), 101 (14) and 88 (17).

FVP of Methyl 3-[4-(4-cyanophenyl)quinolin-3-yl]acrylate 259



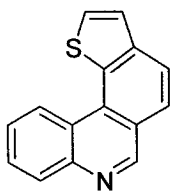
Flash vacuum pyrolysis of methyl 3-[4-(4-cyanophenyl)quinolin-3-yl]acrylate **259** (0.038 g, T_f 950 °C, T_i 241 °C, P 1.0×10^{-1} – 2.2×10^{-1} Torr, t 5 min) gave *benzo[k]phenanthridine-10-carbonitrile* **272** as a yellow oil (0.022 g, 71%).(Found: M^+ 254.0846. $C_{18}H_{10}N_2$ requires *M* 254.0844) δ_H (250 MHz, $CDCl_3$): 7.81 – 7.92 (3H, m), 7.97 (1H, dd, *J* 1.8, 8.9), 8.10 (1H, d *J* 4.6), 8.41 (1H, dd, *J* 1.8, 8.9), 8.47 (1H, d, *J* 1.2), 9.00 (1H, d, *J* 8.9), 9.30 (1H, dd, *J* 1.2, 8.9) and 9.43 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 126.4 (CH), 126.9 (CH), 127.6 (CH), 127.8 (CH), 128.1 (CH), 128.9 (CH), 129.1 (CH), 130.4 (CH), 134.0 (CH) and 152.1 (CH); *m/z* 254 (M^+, 16%), 231 (23), 230 (100), 229 (99), 228 (36), 227 (21) and 119 (38).

FVP of Methyl 2-(1-phenylisoquinoline-4-yl)acrylate 260



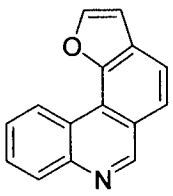
Flash vacuum pyrolysis of methyl 2-(1-phenylisoquinoline-4-yl)acrylate **260** (0.166 g, T_f 950 °C, T_i 186 °C, P $6.0 \times 10^{-2} - 8.5 \times 10^{-1}$ Torr, t 10 min) gave a brown oil which was then purified by dry flash chromatography using 10% ethyl acetate in hexane to produce benzo[*a*]phenanthridine[144] **218** as a brown solid (0.042 g, 32%). δ_H (250 MHz, $CDCl_3$): 7.60 (3H, m), 7.78 (1H, m), 7.91 – 7.96 (2H, m), 8.03 (1H, d, *J* 8.6), 8.05 (1H, dd, *J* 1.1, 8.0), 8.96 – 9.01 (2H, m) and 9.26 (1H, s); δ_C (250 MHz, $CDCl_3$): 121.1 (quat), 126.8 (CH), 126.9 (CH), 127.0 (CH), 127.1 (CH), 127.9 (CH), 128.1 (quat), 128.7 (CH), 129.1 (CH), 129.2 (CH), 130.0 (CH), 130.2 (quat), 131.2 (CH), 133.0 (quat), 133.6 (quat), 144.6 (quat) and 153.2 (CH); *m/z* 229 (M^+, 100%), 205 (49), 204 (29), 203 (38), 114 (19), 101 (25), 100 (21) and 43 (25).

FVP of Methyl 3-[4-(thiophen-2-yl)quinoline]acrylate 261



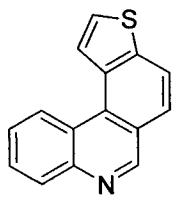
Flash vacuum pyrolysis of methyl 3-[4-(thiophen-2-yl)quinoline]acrylate **261** (0.045 g, T_f 950 °C, T_i 274 °C, P $2.8 \times 10^{-2} - 3.8 \times 10^{-1}$ Torr, t 10 min) gave *1-thia-7-azacyclopenta[c]phenanthrene* **273** a yellow oil (0.025 g, 70%) (Found: M^+ 235.0454. $C_{15}H_9NS$ requires *M* 235.0456); δ_H (360 MHz, $CDCl_3$): 7.70 (1H, d, *J* 5.5), 7.88 – 7.91 (3H, m), 8.05 (1H, d, *J* 8.6), 8.19 (1H, d, *J* 8.6), 8.36 – 8.39 (1H, m), 9.05 – 9.08 (1H, m) and 9.45 (1H, s); δ_C (360 MHz, $CDCl_3$): 123.3 (quat), 123.9 (CH), 124.2 (quat), 124.6 (CH), 125.2 (CH), 125.4 (CH), 127.3 (CH), 128.5 (CH), 129.1 (quat), 129.2 (CH), 130.1 (CH), 133.3 (quat), 142.3 (quat), 144.8 (quat) and 153.3 (CH); *m/z* 235 (M^+, 100%), 234 (10), 133 (7), 209 (5), 163 (5), 118 (10), 117 (5) and 104 (5).

FVP of Methyl 3-[4-(furan-2-yl)quinoline]acrylate 263



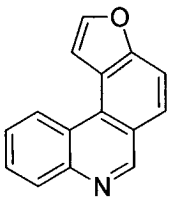
Flash vacuum pyrolysis of methyl 3-[4-(furan-2-yl)quinoline]acrylate **263** (0.052 g, T_f 950 °C, T_i 274 °C, P $5.0 \times 10^{-2} - 6.5 \times 10^{-1}$ Torr, t 10 min) gave *1-oxa-7-azacyclopenta[c]phenanthrene* **274** as a yellow oil (0.060 g) which was then purified by dry flash chromatography using ethyl acetate as eluent to produce a brown solid (0.018 g, 43%) (Found: M^+ 219.3038. $C_{15}H_9NO$ requires *M* 219.0684); δ_H (360 MHz, $CDCl_3$): 7.05 (1H, d, *J* 2.2), 7.67 – 7.81 (2H, m), 7.91 (2H, s), 8.04 (1H, d, *J* 2.2), 8.25 (1H, dd, *J* 2.2, 7.2) and 9.37 – 9.39 (2H, m); δ_C DEPT (250 MHz, $CDCl_3$): 107.4 (CH), 121.1 (CH), 123.7 (CH), 127.0 (CH), 127.3 (CH), 128.8 (CH), 129.3 (CH), 146.6 (CH) and 153.1 (CH); *m/z* 219 (M^+, 100%), 193 (12), 192 (8), 191 (9), 190 (17), 110 (8), 96 (8) and 82 (8).

FVP of Methyl 3-[4-(thiophen-3-yl)quinoline]acrylate 262



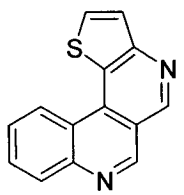
Flash vacuum pyrolysis of methyl 3-[4-(thiophen-3-yl)quinoline]acrylate **262** (0.047 g, T_f 700 °C, T_i 253 °C, P $5.5 \times 10^{-2} - 2.3 \times 10^{-1}$ Torr, t 10 min) gave *3-thia-7-azacyclopenta[c]phenanthrene* **275** as a yellow oil (0.037 g, 95%). (Found: M^+ 235.0451. $C_{15}H_9NS$ requires *M* 235.0456); δ_H (250 MHz, $CDCl_3$): 7.65 – 7.76 (3H, m), 7.87 (1H, d, *J* 8.6), 8.10 (1H, d, *J* 8.6), 8.22 (1H, dd, *J* 1.8, 7.3), 8.54 (1H, d, *J* 5.2), 8.97 (1H, d, *J* 7.3) and 9.29 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 123.1 (CH), 125.2 (CH), 125.7 (CH), 126.0 (CH), 127.4 (CH), 128.1 (CH), 128.9 (CH), 130.8 (CH) and 153.8 (CH); *m/z* 235 (M^+, 26%), 211 (40), 210 (37), 147 (60) and 73 (100).

FVP of Methyl 3-[4-(furan-3-yl)quinoline]acrylate 264



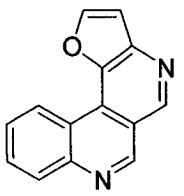
Flash vacuum pyrolysis of methyl methyl 3-[4-(furan-3-yl)quinoline]acrylate **264** (0.035 g, T_f 950 °C, T_i 250 °C, P 2.7 × 10^{-2} – 2.3 × 10^{-1} Torr, t 10 min) gave *3-oxa-7-azacyclopenta[c]phenanthrene* **276** as a yellow oil (0.024 g, 88%) (Found: M^+ 219.0683. $C_{15}H_9NO$ requires *M* 219.0684); δ_H (360 MHz, $CDCl_3$): 7.80 – 7.89 (3H, m), 7.96 – 8.07 (3H, m), 8.34 (1H, d, *J* 7.9), 8.93 (1H, d, *J* 1.8, 7.9) and 9.43 (1H, s); δ_C (360 MHz, $CDCl_3$): 108.2 (CH), 113.4 (CH), 121.1 (quat), 123.5 (quat), 124.7 (CH), 126.1 (CH), 127.0 (CH), 128.1 (quat), 128.6 (CH), 129.8 (CH), 135.6 (quat), 144.5 (quat), 145.8 (CH), 153.2 (CH) and 156.3 (quat); *m/z* 219 (M^+, 100%), 193 (21), 192 (12), 191 (35), 190 (32), 179 (35), 164 (18) and 163 (15).

FVP of 4-(Thiophen-2-yl)quinoline-3-carbaldehyde *O*-methyloxime 267



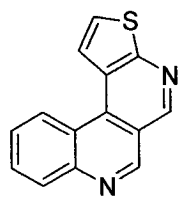
Flash vacuum pyrolysis of 4-(thiophen-2-yl)quinoline-3-carbaldehyde *O*-methyloxime **267** (0.088 g, T_f 700 °C, T_i 245 °C, P 2.3 × 10^{-2} – 2.9 × 10^{-1} Torr, t 10 min) gave a yellow oil (0.060 g) which was then purified by dry flash chromatography using 75% ethyl acetate in hexane as eluent to produce *1-thia-4,7-diazacyclopenta[c]phenanthrene* **277** as a brown solid (0.038 g, 49%) (Found: M^+ 236.0407. $C_{14}H_8N_2S$ requires *M* 236.0408); δ_H (360 MHz, $CDCl_3$): 7.87 (1H, ddd, *J* 1.4, 7.1, 8.2), 7.89 (1H, d, *J* 5.6), 7.95 (1H, d, *J* 1.4, , 7.1, 8.2), 8.05 (1H, d, *J* 5.6), 8.33 (1H, dd, *J* 1.6, 8.0), 8.83 (1H, dd, *J* 1.6, 8.0), 9.40 (1H, s) and 9.49 (1H, s); δ_C (360 MHz, $CDCl_3$): 118.0 (quat), 121.6 (quat), 135.8 (CH), 126.1 (CH), 128.0 (CH), 130.5 (CH), 130.7 (CH), 131.6 (CH), 133.7 (quat), 135.6 (quat), 146.3 (quat), 150.2 (CH), 152.1 (CH) and 156.3 (quat); *m/z* 236 (M^+, 100%), 235 (11), 210 (11), 209 (11), 180 (11), 164 (11), 118 (11) and 91 (11).

FVP of 4-(Furan-2-yl)quinoline-3-carbaldehyde *O*-methyloxime 269



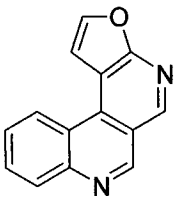
Flash vacuum pyrolysis of 4-(furan-2-yl)quinoline-3-carbaldehyde *O*-methyloxime **269** (0.059 g, T_f 700 °C, T_i 270 °C, P $3.0 \times 10^{-2} - 2.9 \times 10^{-1}$ Torr, t 10 min) gave a brown oil which was then purified by dry flash chromatography using 100% ethyl acetate to produce *1-oxa-4,7-diazacyclopenta[c]phenanthrene* **278** as a brown solid (0.031 g, 60%) (Found: M^+ 220.0638. $C_{14}H_8N_2O$ requires *M* 220.0637); δ_H (360 MHz, $CDCl_3$): 7.31 (1H, d, *J* 2.1), 7.84 (1H, ddd, *J* 1.3, 7.1, 15.3), 7.93 (1H, ddd, *J* 1.3, 7.1, 15.3), 8.20 (1H, d, *J* 2.1), 8.29 (1H, dd, *J* 1.3, 8.0), 9.27 (1H, ddd, *J* 0.5, 1.3, 8.0), 9.35 (1H, s) and 9.51 (1H, s); δ_C DEPT (360 MHz, $CDCl_3$): 109.1 (CH), 127.9 (2 CH), 129.8 (CH), 130.9 (CH), 148.8 (CH), 149.4 (CH) and 151.9 (CH); *m/z* 220 (M^+, 100%), 192 (12), 165 (12) and 164 (15).

FVP of 4-(Thiophen-3-yl)quinoline-3-carbaldehyde *O*-methyloxime 268



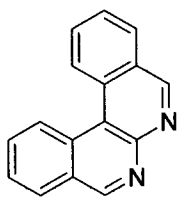
Flash vacuum pyrolysis of 4-(thiophen-3-yl)quinoline-3-carbaldehyde *O*-methyloxime **268** (0.059 g, T_f 700 °C, T_i 215 °C, P $3.4 \times 10^{-2} - 1.8 \times 10^{-1}$ Torr, t 10 min) gave *3-thia-4,7-diazacyclopenta[c]phenanthrene* **279** as a brown oil (0.052 g, 43%). (Found: M^+ 236.0408. $C_{14}H_8N_2S$ requires *M* 236.0408); δ_H (250 MHz, $CDCl_3$): 7.81 (1H, ddd, *J* 1.4, 7.1, 8.3), 7.88 (1H, *J* 6.1), 7.91 (1H, ddd, *J* 1.4, 7.1, 8.3), 8.31 (1H, dd, *J* 1.2, 8.2), 8.45 (1H, d, *J* 6.1), 9.00 (1H, dd, *J* 1.2, 8.2), 9.27 (1H, s) and 9.46 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$) 123.2 (CH), 125.3 (CH), 125.7 (CH), 126.0 (CH), 127.6 (CH), 129.0 (CH), 130.7 (CH) and 153.7 (CH); *m/z* 236 (M^+, 92%), 235 (51), 211 (100), 209 (33), 205 (39), 204 (43) and 166 (52).

FVP of 4-(Furan-3-yl)quinoline-3-carbaldehyde *O*-methyloxime 270



Flash vacuum pyrolysis of 4-(furan-3-yl)quinoline-3-carbaldehyde *O*-methyloxime **270** (0.053 g, T_f 700 °C, T_i 233 °C, P 3.0 × 10^{-2} – 9.5 × 10^{-2} Torr, t 10 min) gave a brown oil (0.1233 g) which was purified by dry flash chromatography in ethyl acetate to produce *3-oxa-4,7-diazacyclopenta[c]phenanthrene* **280** as a yellow oil (0.0235 g, 33%) (Found: M^+ 220.0634. $C_{14}H_8N_2O$ requires *M* 220.0637); δ_H (360 MHz, $CDCl_3$): 7.86 (1H, ddd, *J* 1.6, 7.0, 8.6), 7.87 (1H, d, *J* 5.5), 7.93 (1H, ddd, *J* 1.6, 7.0, 8.6), 8.03 (1H, d, *J* 5.5), 8.31 (1H, dd, *J* 1.6, 8.6), 8.50 (1H, dd, *J* 1.6, 8.6), 9.40 (1H, s) and 9.48 (1H, s); *m/z* 220 (M^+, 5%), 219 (20), 201 (15), 183 (15), 167 (12), 164 (11), 118 (11), 77 (20) and 57 (20).

FVP of 2-(1-Phenylisoquinoline-4-yl) *O*-methyl oxime[89] 266



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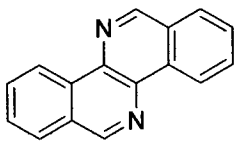


282

Flash vacuum pyrolysis of 2-(1-phenylisoquinoline-4-yl) *O*-methyl oxime **266** (0.089 g, T_f 700 °C, T_i 182 °C, P 4.8 × 10^{-2} – 1.1 × 10^{-1} Torr, t 10 min) gave a brown oil which was then purified by dry flash chromatography using a solvent gradient of 50% - 100% ethyl acetate in hexane to produce dibenzo[*c,h*][1,5]naphthyridine **282** as a yellow solid (0.019 g, 25%) mp 166 – 167 °C and dibenzo[*c,f*][1,8]naphthyridine **281** as a brown solid (0.049 g, 63%) mp 169 – 170 °C.

Dibenzo[*c,f*][1,8]naphthyridine 281

(Found: M^+ 230.0844. $C_{16}H_{10}N_2$ requires *M* 230.0834) δ_H (360 MHz, $CDCl_3$): 7.71 (2H, ddd, *J* 1.3, 7.0, 8.0), 7.87 (2H, ddd, *J* 1.3, 7.0, 8.5), 8.13 (2H, dd, *J* 1.3, 8.0), 9.01 (2H, d, *J* 8.5) and 9.43 (2H, s); δ_C (360 MHz, $CDCl_3$): 114.2 (quat), 126.8 (2 CH), 127.8 (2 CH), 128.3 (2 quat), 129.4 (2 CH), 131.6 (2 CH), 133.3 (2 quat), 151.8 (quat) and 155.0 (2

CH); *m/z* 230 (M^+, 29%), 229 (100), 228 (25), 227 (13), 201 (17), 133 (15), 100 (16) and 73 (17).

Dibenzo[*c,h*][1,5]naphthyridine 282

(Found: M^+ 230.0849. $C_{16}H_{10}N_2$ requires *M* 230.0834); δ_H (250 MHz, $CDCl_3$): 7.83 (2H, t, *J* 7.2, 7.9), 7.99 (2H, t, *J* 7.2, 8.5), 8.27 (2H, d, *J* 7.9), 9.16 (2H, d, *J* 8.5) and 9.55 (2H, s); δ_C (250 MHz, $CDCl_3$): 123.5 (CH), 127.8 (CH), 128.2 (CH), 128.4 (quat), 131.3 (CH), 134.0 (quat), 135.0 (quat), 152.6 (CH); *m/z* 230 (M^+, 83%), 229 (81), 228 (20), 221 (17), 201 (13), 147 (28), 74 (14) and 73 (100).

7.6 Five-Ring Systems

General Method A (Suzuki)[8c]

The boronic acid (50 eq), halide (50 eq), potassium carbonate (300 eq) and tetrakis(triphenylphosphine) palladium (1 eq) were mixed in a solution of dioxane and water (3:1) and the mixture heated under reflux under a nitrogen atmosphere. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug. The solvent was removed and the residue dissolved in chloroform and the insoluble organic base was removed by filtration.

General Method B (Suzuki)[8c]

The halide (35 eq) and tetrakis (triphenylphosphine) palladium (1 eq) were stirred in ethylene glycol dimethyl ether (4 cm^3) for 20 min. Sodium carbonate (45 eq) in water (1 cm^3) and 2-formylphenylboronic acid (34 eq) were added and heated under reflux overnight. The solvent was then removed and the residue extracted from dichloromethane and the organic layers washed with water and dried over $MgSO_4$.

General Method C (Wittig)[125]

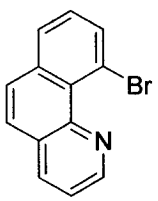
The aldehyde (1 eq) and methyl(triphenylphosphoranylidene) acetate (1.05 eq) were mixed in toluene and the solution heated to reflux under nitrogen for 4.5 h. The solvent was removed and the product was purified by dry flash chromatography using 50% ethyl acetate in hexane as eluent.

General Method D (Knoevenagel)[7]

The aldehyde (1 eq) and methyl cyanoacetate (1 eq) were added to toluene (10 cm^3) followed by piperidine (2 drops) and glacial acetic acid (2 drops). The solution was left at room temperature for 2 h. The solution was then added to water (10 cm^3) and

extracted with dichloromethane (3 × 15 cm^3) and the organic extracts were washed with water (3 × 15 cm^3) and dried over $MgSO_4$ and the solvent removed.

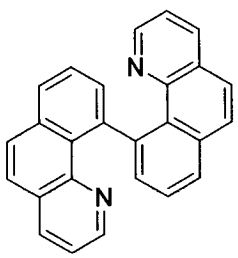
10-Bromobenzo[*h*]quinoline[104] 358



Benzo[*h*]quinoline (0.057 g, 0.319 mmol) and palladium (II) acetate (0.072 g, 0.322 mmol) were stirred in methanol (5 cm^3) under a nitrogen atmosphere for 4 h at room temperature. A yellow precipitate was filtered and washed with hexane. The yellow solid was shown to be **357** by comparison with literature data.[104]

Benzo[*h*]quinoline (0.640 g, 3.572 mmol), *N*-bromosuccinimide (0.797 g, 4.479 mmol) and **357** (0.016 g) were dissolved in acetonitrile (30 cm^3) and heated at 100 °C in a sealed vessel (ensuring no contact with any external source of any metal) for 1.5 days. The solvent was removed to produce a brown solid (1.417 g). The solid was purified by dry flash chromatography using 25% ethyl acetate in hexane as eluent to remove the succinimde. 10-Bromobenzo[h]quinoline **358** was produced as a brown solid (0.854 g, 93%) which was then used in further reactions unpurified.

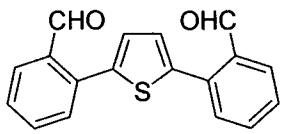
[10,10']Bibenzo[*h*]quinolinyl 360



10-Bromobenzo[*h*]quinoline **358** (0.205 g, 0.80 mmol), potassium carbonate (0.658 g, 4.76 mmol) and tetrakis(triphenylphosphine) palladium (0.018 g, 0.015 mmol) were mixed in a solution of dioxane (15 cm^3) and water (5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug. The solvent was removed and the residue dissolved in ether and the insoluble organic base was removed by filtration to produce a brown solid which was purified by dry flash chromatography using ethyl acetate as eluent to produce [10,10']bibenzo[*h*]quinolinyl **360** as a brown solid (0.1816 g , ~100%). (Found: M^+ 355.1243. $C_{26}H_{16}N_2$ requires *M* 355.1230); δ_H (250 MHz, $CDCl_3$): 7.30 (2H, t, *J* 8.0,

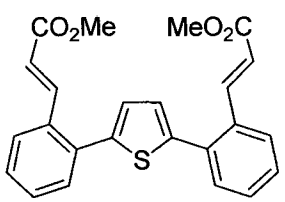
15.7), 7.40 (2H, dd, *J* 4.4, 8.0), 7.55 (4H, dd, *J* 8.9, 19.6), 7.71 (2H, dd, *J* 1.3, 8.0), 7.98 (4H, ddd, *J* 1.8, 5.2, 6.5) and 8.98 (2H, dd, *J* 1.8, 4.2);δ_C (250 MHz, $CDCl_3$): 119.9 (quat), 122.3 (CH), 127.0 (CH), 127.7 (quat), 128.3 (CH), 128.5 (CH), 128.7 (quat), 128.8 (CH), 135.9 (CH), 136.0 (CH), 136.7 (quat), 146.4 (quat) and 147.4 (CH); *m/z* 356 (M^+, 9%), 259 (97), 257 (99), 179 (24), 178 (100), 177 (29), 151 (21) and 150 (25).

2,5-Bis(2-formylphenyl)thiophene[145] 364



2-Formylphenylboronic acid **257** (0.2497 g, 1.67 mmol), 2,5-dibromothiophene **363** (0.2425 g, 1.00 mmol), potassium carbonate (1.3918 g, 0.01 mol) and tetrakis(triphenylphosphine) palladium (0.0222 g, 0.019 mmol) were mixed in a solution of dioxane (15 cm^3) and water (5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. After cooling to room temperature the solution was diluted with ether and filtered through a silica plug and the solvent was removed. The product was then purified by dry flash chromatography using 10% ethyl acetate in hexane as eluent to produce 2,5-bis(2-formylphenyl)thiophene **364** as a yellow solid (0.1623 g, 55%) mp 138 – 140 °C [lit.[145], 98 – 99 °C]. δ_H (250 MHz, $CDCl_3$): 7.05 (2H, s), 7.46 – 7.63 (6H, m), 7.97 (2H, dd, *J* 1.4, 7.7) and 10.23 (2H, s); δ_C (250 MHz, $CDCl_3$): 128.2 (2 CH), 128.6 (2 CH), 130.0 (2 CH), 131.2 (2CH), 133.7 (2 CH), 134.1 (2 quat), 137.1 (2 quat), 140.8 (2 quat) and 191.7 (2 CH); *m/z* 292 (M^+, 8%), 237 (85), 181 (100), 162 (39), 153 (19), 152 (38), 151 (16) and.76 (18).

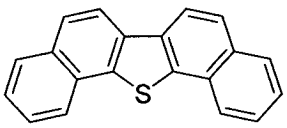
Methyl 3-(2-{5-[2-(2-methoxycarbonylvinyl)phenyl]thiophen-2-yl}phenyl)acrylate 365



2,5-Bis(2-formylphenyl)thiophene **364** (0.160 g, 0.55 mmol) and methyl (triphenylphosphoranylidene) acetate (0.3763 g, 1.13 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. The solvent was then removed and the product was purified by dry flash

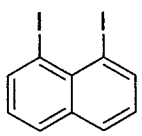
chromatography using 50% ethyl acetate in hexane as eluent to produce *methyl 3-(2-{5-[2-(2-methoxycarbonylvinyl)phenyl]thiophen-2-yl}phenyl)acrylate* **365** as a yellow solid (0.1624 g, 73%) mp 116 – 118 °C (Found: C, 71.1; H, 5.2. $C_{24}H_{20}O_4S$ requires C, 71.3; H, 5.0%); δ_H (250 MHz, $CDCl_3$): 3.71 (6H, s), 6.34 (2H, d, *J* 15.5), 6.95 (2H, s), 7.30 (4H, m), 7.46 (2H, dd, *J* 2.1, 7.2), 7.57 (2H, dd, *J* 1.8, 7.2) and 8.00 (2H, d, *J* 15.5); δ_C (250 MHz, $CDCl_3$): 51.7 (CH_3), 119.8 (CH), 127.5 (CH), 128.2 (CH), 128.9 (CH), 129.9 (CH), 130.8 (CH), 133.0 (quat), 134.7 (quat), 142.4 (quat), 143.8 (CH) and 167.2 (quat); *m/z* 404 (M^+, > 1%).

FVP of Methyl 3-(2-{5-[2-(2-methoxycarbonylvinyl)phenyl]thiophen-2-yl}phenyl)acrylate 364



Flash vacuum pyrolysis of methyl 3-(2,5-bis(2-phenyl)thiophene) acrylate **364** (0.050 g, T_f 950 °C, T_i 292 °C, P 5.5 × 10^{-2} – 3.4 × 10^{-1} Torr, t 10 min) gave dinaphtho[1,2-*b*:2',1'-*d*]thiophene[146] **366** as a yellow oil (0.017 g, 51%). δ_H (360 MHz, $CDCl_3$): 7.57 (2H, t, *J* 8.3), 7.64 (2H, t, *J* 8.3), 7.89 (2H, d, *J* 8.3), 7.98 (2H, d, *J* 8.3), 8.20 (2H, d, *J* 8.3) and 8.22 (2H, d, *J* 8.3); δ_C (360 MHz, $CDCl_3$): 119.8 (2CH), 124.3 (2CH), 125.6 (2CH), 126.1 (2CH), 126.8 (2CH) and 128.9 (2CH); *m/z* 279 (M^+, 45%), 220 (99), 219 (47), 195 (99), 191 (33), 166 (100), 165 (35) and 139 (51).

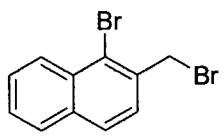
1,8-Di-iodonaphthalene[147] 369



1,8-Diaminonaphthalene **368** (5.1700 g, 0.033 mol) was distilled from zinc dust (0.25 g) at 150 °C (0.04 Torr) to yield pure 1,8-diaminonaphthalene **368** (3.713 g, 0.023 mol). A solution of sodium nitrite (5.492 g, 0.0800 mol) in water (20 cm^3) was added, dropwise, to a solution of 1,8-diaminonaphthalene **368** (3.713 g, 0.023 mol) in sulfuric acid (49 cm^3, 6.9 M) cooled to -20 °C. The reaction mixture was then kept between –15 °C and -20 °C. A solution of potassium iodide (26.990 g, 0.163 mol) in water (23 cm^3) was added

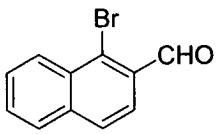
dropwise and with stirring, using a mechanical stirrer, whilst keeping the solution between -15 °C and -20 °C and adding conc. Sulfuric acid to prevent the solution freezing. The mixture was then heated to 80 °C rapidly and with stirring then cooled to 20 °C and made alkaline by the addition of solid sodium hydroxide. The mixture was filtered and the black residue was collected, pulverised and extracted with several portions of boiling ether. The ether solution was washed with aqueous hydrochloric acid (10%), saturated sodium sulfite and dilute aqueous sodium hydroxide. The ether layer was then dried and the solvent removed under vacuum to produce 1,8-di-iodonaphthalene[148] **369** as a black solid. δ_H (250 MHz, $CDCl_3$): 6.96 (2H, dd, *J* 7.3, 8.1), 7.73 (2H, dd, *J* 1.3, 8.1) and 8.32 (2H, dd, *J* 1.3, 7.3); δ_C (250 MHz, $CDCl_3$): 127.5 (2 CH), 131.5 (2 CH) and 144.5 (2 CH); *m/z* 380 (M^+, 61%), 270 (19), 254 (54), 253 (37), 128 (17), 127 (75), 126 (100) and 115 (34).

1-Bromo-2-bromomethylnaphthalene 382



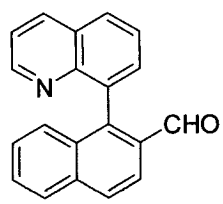
1-Bromo-2-methylnaphthalene **381** (13.588 g, 0.062 mol), *N*-bromosuccinimide (10.997 g, 0.062 mol) and benzoyl peroxide (0.299 g, 1.23 mmol) were added to carbon tetrachloride (136 cm^3) and the solution heated under reflux under a nitrogen atmosphere for 5.5 h. The solution was then cooled and washed with sodium bicarbonate solution (3 × 20 cm^3), dried with magnesium sulfate and the solvent removed. The resulting solid was recrystallised from petroleum ether (bp 60 – 80 °C) and 1-bromo-2-bromomethylnaphthalene **382** was collected as yellow crystals (14.778 g, 80%) mp 104 – 106 °C [lit.[149], 107 °C]. δ_H (250 MHz, $CDCl_3$): 5.09 (2H, s), 7.73 – 7.87 (3H, m), 8.04 (2H, t, *J* 6.4, 14.5) and 8.56 (1H, d, *J* 7.7).

1-Bromo-2-formylnaphthalene 377



Sodium (0.895 g, 0.039 mol) was added to ethanol (38 cm^3). Once the sodium had dissolved 2-nitropropane (3.66 cm^3, 0.040 mol) was added and a white precipitate formed. 1-Bromo-2-bromomethylnaphthalene **382** (10.203 g, 0.034 mol) was added and the solution was heated under reflux for 6 h. The solution was cooled to room temperature, water (30 cm^3) was added and the ethanol removed under vacuum. The residue was extracted with ether, washed with sodium hydroxide (1M, 10 × 20 cm^3) and water (2 × 20 cm^3) and dried over magnesium sulfate. The solvent was removed and the yellow solid produced was recrystallised from ethyl acetate to produce 1-bromo-2-formylnaphthalene **377** as yellow crystals (4.314 g, 54%) mp 115 – 117 °C [lit.[150], 116 – 118 °C]. δ_H (250 MHz, $CDCl_3$): 7.55 – 7.62 (2H, m), 7.73 – 7.75 (3H, m), 8.37 – 8.47 (1H, m) and 10.59 (1H, d, *J* 0.8).

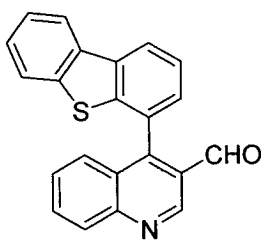
1-(Quinoline-8-yl)naphthalene-2-carbaldehyde 378



1-Bromonaphthalene-2-carbaldehyde **377** (0.144 g, 0.612 mmol) and tetrakis(triphenylphosphine) palladium (0.027 g, 0.023 mmol) were stirred under nitrogen in ethylene glycol dimethylether (11.2 cm^3) for 20 min. Quinoline-8-boronic acid **376** (0.100 g, 0.576 mmol), sodium carbonate (0.083 g, 0.780 mmol) and water (2.8 cm^3) were added to the reaction mixture and the solution heated under reflux overnight. General work-up method B was then followed and the crude product was purified by dry flash chromatography using 5% ethyl acetate in hexane as eluent to yield a mixture of **378** and triphenylphosphine. The mixture was purified by dry flash chromatography using 40% ethyl acetate in hexane as eluent to produce *1-(quinoline-8-yl)naphthalene-2-carbaldehyde* **378** as a a yellow oil (0.118 g, 72%) bp 73 °C (6 × 10^{-2} Torr). (Found: M^+ 283.0999. $C_{20}H_{13}NO$ requires *M* 283.0997) δ_H (250 MHz, $CDCl_3$): 7.30 – 7.42 (3H, m), 7.56 (1H, t, *J* 7.1), 7.67 – 7.75 (2H, m), 7.94 (1H, d, *J* 8.2), 7.99 – 8.03 (2H, m), 8.16 (1H, d, *J* 8.6), 8.27 (1H, dd, *J* 1.6, 8.2), 8.77 (1H, dd, *J* 1.6, 4.2) and 9.67 (1H, s); δ_C

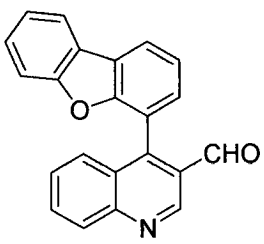
(250 MHz, $CDCl_3$): 121.4 (CH), 122.0 (CH), 125.7 (CH), 126.5 (CH), 127.5 (CH), 128.1 (2 quat), 128.2 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 131.7 (quat), 132.5 (CH), 132.8 (quat), 134.7 (quat), 136.2 (CH), 144.3 (quat), 147.6 (quat), 150.9 (CH) and 192.4 (CH); *m/z* 282 (M^+, 3%), 254 (100), 213 (5), 155 (3), 127 (20), 84 (9) and 43 (5).

4-(Dibenzothiophen-1-yl)quinoline-3-carbaldehyde 385



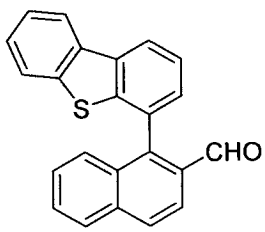
1-Dibenzothiopheneboronic acid (0.426 g, 2.22 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.426 g, 2.22 mmol), potassium carbonate (1.855g, 0.01 mol) and tetrakis(triphenylphosphine) palladium (0.053 g, 0.046 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a brown solid which was purified by dry flash chromatography using 75% ethyl acetate in hexane as eluent to produce *4-(dibenzothiophen-1-yl)quinoline-3-carbaldehyde* **385** as a yellow solid (0.280 g, 38%) mp 179 – 181 °C. (Found: M^+ 339.0718. $C_{22}H_{13}NOS$ requires *M* 339.0718); δ_H (250 MHz, $CDCl_3$): 7.29 – 7.39 (4H, m), 7.41 – 7.50 (1H, m), 7.53 – 7.60 (2H, m), 7.74 (1H, ddd, *J* 1.4, 6.8, 15.3), 8.10 – 8.19 (2H, m), 8.23 (1H, dd, *J* 1.4, 8.0), 9.44 (1H, s) and 9.75 (1H, s); δ_C (250 MHz, $CDCl_3$): 121.9 (CH), 122.3 (CH), 122.7 (CH), 124.6 (CH), 124.9 (CH), 124.9 (quat), 125.6 (quat), 126.7 (CH), 127.3 (quat), 127.3 (CH), 127.8 (CH), 128.3 (CH), 129.9 (CH), 132.5 (CH), 134.9 (quat), 136.1 (quat), 139.1 (quat), 140.2 (quat), 148.1 (CH), 150.3 (quat), 151.0 (quat) and 190.7 (CH); *m/z* 339 (M^+, 9%), 311 (37), 277 (29), 201 (53), 200 (100), 184 (64), 172 (70) and 171 (88).

4-(Dibenzofuran-1-yl)quinoline-3-carbaldehyde 386



1-Dibenzofuranboronic acid (0.502 g, 2.37 mmol), 4-chloroquinoline-3-carbaldehyde **248** (0.450 g, 2.35 mmol), potassium carbonate (1.964 g, 0.01 mol) and tetrakis(triphenylphosphine) palladium (0.057 g, 0.049 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a brown solid which was purified by dry flash chromatography using 75% ethyl acetate in hexane as eluent to produce *4-(dibenzofuran-1-yl)quinoline-3-carbaldehyde* **386** as a brown oil (0.286 g, 37%) bp 58 °C (4.2×10^{-2} Torr). (Found: M^+ 323.0936. $C_{22}H_{13}NO_2$ requires *M* 323.0946); δ_H (250 MHz, $CDCl_3$): 7.58 – 7.79 (6H, m), 7.87 (1H, d, *J* 8.1), 8.05 (1H, t, *J* 7.7, 15.3), 8.24 (1H, d, *J* 8.1), 8.31 (1H, d, *J* 7.7), 8.50 (1H, d, *J* 8.1), 9.78 (1H, s) and 10.15 (1H, s); δ_C (250 MHz, $CDCl_3$): 111.8 (CH), 116.3 (quat), 120.8 (CH), 122.0 (CH), 122.8 (CH), 123.2 (CH), 124.7 (quat), 125.5 (quat), 126.3 (quat), 126.9 (CH), 127.6 (CH), 127.8 (CH), 129.0 (CH), 129.9 (CH), 132.1 (CH), 147.7 (quat), 148.0 (CH), 150.0 (quat), 150.2 (quat), 153.7 (quat), 156.0 (quat) and 190.0 (CH); *m/z* 323 (M^+, 24%), 322 (10), 308 (7), 269 (17), 268 (71), 267 (100), 266 (91), 265 (85) and 264 (24).

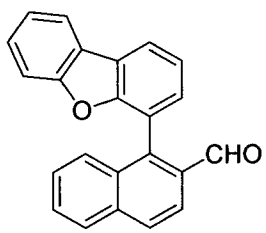
4-(Dibenzothiophen-1-yl)naphthalene-3-carbaldehyde 387



1-Dibenzothiopheneboronic acid (0.501 g, 2.20 mmol), 2-bromo-2-formylnaphthalene **377** (0.526 g, 2.24 mmol), potassium carbonate (1.825 g, 0.01 mol) and tetrakis(triphenylphosphine) palladium (0.052 g, 0.045 mmol) were mixed in a solution of dioxane (37.5 cm^3) and water (12.5 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a brown solid which was purified by dry flash chromatography using 10% ethyl acetate in hexane

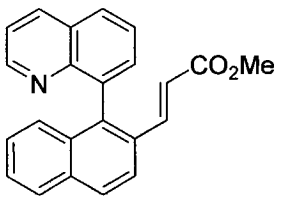
as eluent to produce *4-(dibenzothiophen-1-yl)naphthalene-3-carbaldehyde* **387** as a yellow solid (0.562 g, 74%) mp 187 – 189 °C. (Found: M^+ 338.0768. $C_{23}H_{14}OS$ requires *M* 338.0765) δ_H (250 MHz, $CDCl_3$): 7.41 (8H, m), 8.02 (1H, d, *J* 8.1), 8.10 (1H, d, *J* 8.6), 8.25 (1H, d, *J* 8.6), 8.29 (1H, d, *J* 1.2, 7.8), 8.37 (1H, dd, *J* 1.2, 7.8) and 9.92 (1H, d, *J* 0.9); δ_C (250 MHz, $CDCl_3$): 122.0 (CH), 122.3 (CH), 122. 6 (CH), 123.2 (CH), 125.0 (CH), 125.1 (CH), 127.3 (CH), 127.5 (2 CH), 128.8 (CH), 129.5 (CH), 129.6 (CH), 129.7 (CH), 130.4 (quat), 131.4 (quat), 131.9 (quat), 136.2 (quat), 136.8 (quat), 140.0 (quat), 141.8 (quat), 141.9 (quat), 144.5 (quat) and 192.6 (CH); *m/z* 338 (M^+, 22%), 201 (25), 200 (100), 172 (35), 171 (71), 128 (22), 127 (28) and 86 (19)

4-(Dibenzofuran-1-yl)naphthalene-3-carbaldehyde 388



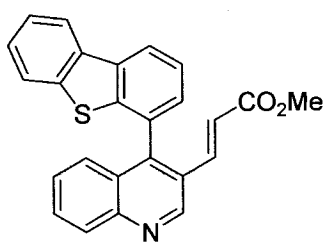
1-Dibenzofuranboronic acid (1.021 g, 4.82 mmol), 2-bromo-2-formylnapthalene **377** (1.103 g, 4.69 mmol), potassium carbonate (3.913 g, 0.03 mol) and tetrakis(triphenylphosphine) palladium (0.112 g, 0.096 mmol) were mixed in a solution of dioxane (75 cm^3) and water (25 cm^3) and the mixture heated under reflux under a nitrogen atmosphere for 4 h. General work-up method A was then followed to produce a brown solid which was purified by dry flash chromatography using 10% ethyl acetate in hexane as eluent to produce *4-(dibenzofuran-1-yl)naphthalene-3-carbaldehyde* **388** as a yellow solid (0.987 g, 64%) mp 180 – 181 °C. (Found: M^+ 322.0992. $C_{23}H_{14}O_2$ requires *M* 322.0994); δ_H (250 MHz, $CDCl_3$): 7.58 – 7.90 (8H, m), 8.22 (1H, d, *J* 8.6), 8.29 (2H, d, *J* 8.6), 8.38 (1H, dd, *J* 1.6, 7.3), 8.43 (1H, d, *J* 8.6) and 10.4 (1H, d, *J* 0.9); δ_C (250 MHz, $CDCl_3$): 111.9 (CH), 119.1 (quat), 120.8 (CH), 121.1 (CH), 122.2 (CH), 122.6 (CH), 123.0 (CH), 123.8 (quat), 124.4 (quat), 127.0 (CH), 127.3 (CH), 127.6 (CH), 128.3 (CH), 128.8 (CH), 129.0 (CH), 129.9 (CH), 131.5 (quat), 132.3 (quat), 136.2 (quat), 140.7 (quat), 154.5 (quat), 154.5 (quat) and 192.3 (CH); *m/z* 322 (M^+, 5%), 185 (31), 184 (100), 156 (28), 155 (37), 128 (34), 127 (47) and 92 (18).

Methyl 3-[1-(quinolin-8-yl)naphthalen-2-yl]acrylate 389



1-(Quinolin-8-yl)naphthalene-2-carbaldehyde **378** (0.127 g, 0.44 mmol) and methyl (triphenylphosphoranylidene) acetate (0.186 g, 0.55 mmol) were mixed in toluene (60 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce a yellow solid (0.133 g) which was shown by ^1H NMR spectroscopy to contain the aldehyde starting material so an excess of methyl (triphenylphosphoranylidene) acetate was added and the solution heated under reflux overnight. The product was then purified by dry flash chromatography using 50% ethyl acetate in hexane as eluent to produce *methyl 3-[1-(quinolin-8-yl)naphthalen-2-yl]acrylate* **389** as a yellow solid (0.074 g, 49%) in 1:1 *E*:*Z* ratio mp 203 – 204 °C; (Found: M^+ 339.1258. $C_{23}H_{17}NO_2$ requires *M* 339.1259); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.61 (3H, s), 6.45 (1H, d, *J* 16.0), 6.48 (1H, d, *J* 16.0), 7.13 – 7.76 (6H, m), 7.86 – 7.99 (4H, m), 8.24 (1H, d, *J* 8.6) and 8.74 (1H, dd, *J* 1.3, 4.1); δ_C DEPT (250 MHz, $CDCl_3$): 51.7 (CH_3), 118.1 (CH), 121.1 (CH), 122.7 (CH), 126.1 (CH), 126.2 (CH), 126.7 (CH), 127.4 (CH), 127.9 (CH), 128.3 (CH), 128.6 (CH), 132.2 (CH), 136.2 (CH), 143.6 (CH) and 150.7 (CH); *Z*-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.67 (3H, s), 5.69 (1H, d, *J* 12.6), 6.70 (1H, d, *J* 12.6) and 8.77 (1H, dd, *J* 1.3, 4.1); *m/z* 339 (M^+, 10%), 278 (35), 277 (43), 254 (25), 77 (27), 45 (42), 44 (30), 43 (81) and 41 (100).

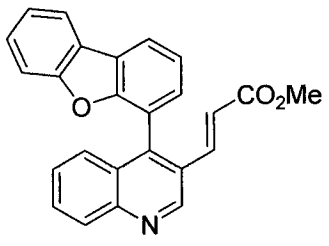
Methyl 3-[4-(Dibenzothiophen-1-yl)quinoline]acrylate 390



4-(Dibenzothiophen-1-yl)quinoline-3-carbaldehyde **385** (0.201 g, 0.59 mmol) and methyl (triphenylphosphoranylidene) acetate (0.253 g, 0.76 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(Dibenzothiophen-1-yl)quinoline]acrylate* **390** as a yellow solid (0.209 g, 89%) in 86:14

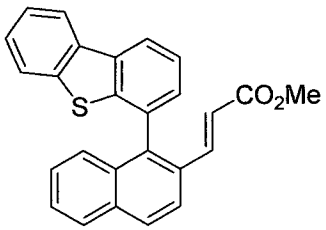
E:*Z* ratio mp 136 °C. (Found: M^+ 395.0983. $C_{25}H_{17}NO_2S$ requires *M* 395.0980); δ_H (250 MHz, $CDCl_3$): 3.56 (3H, s), 6.51 (1H, d, *J* 16.0), 7.25 – 7.42 (3H, m), 7.46 – 7.67 (6H, m), 8.10 – 8.17 (2H, m), 8.22 (1H, dd, *J* 1.0, 8.1) and 9.24 (1H, s); δ_C DEPT (250 MHz, $CDCl_3$): 51.6 (CH_3), 120.6 (CH), 121.9 (CH), 122.7 (CH), 124.6 (CH), 124.8 (CH), 126.5 (CH), 127.1 (CH), 127.5 (CH), 127.9 (CH), 129.6 (CH), 130.4 (CH), 139.6 (CH), 148.2 (CH) and 166.5 (CH); Z-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.61 (3H, s), 5.81 (1H, d, *J* 12.4), 6.67 (1H, d, *J* 12.4) and 8.99 (1H, s); *m/z* 395 (M^+, 11%), 336 (28), 311 (69), 310 (26), 200 (100), 17 1(48) and 149 (52).

Methyl 3-[4-(Dibenzofuran-1-yl)quinoline]acrylate 391



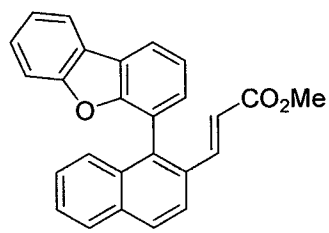
4-(1-Dibenzofuran)quinoline-3-carbaldehyde **386** (0.168 g, 0.52 mmol) and methyl (triphenylphosphoranylidene) acetate (0.223 g, 0.67 mmol) were mixed in toluene (100 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(Dibenzofuran-1-yl)quinoline]acrylate* **391** as a yellow solid (0.194 g, 98%) in 85:15 *E*:*Z* ratio mp 184 - 184 °C; δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.57 (3H, s), 6.52 (1H, d, *J* 16.8), 7.24 – 7.36 (5H, m), 7.42 (2H, t, *J* 3.5, 7.8), 7.47 (1H, d, *J* 4.8), 7.60 – 7.67 (1H, m), 7.93 (1H, dd, *J* 1.2, 7.8), 8.04 (1H, dd, *J* 1.2, 7.8), 8.12 (1H, d, *J* 8.3) and 9.24 (1H, s); δ_C (250 MHz, $CDCl_3$): 51.6 (CH_3), 111.8 (CH), 118.8 (quat), 120.4 (CH), 120.9 (CH), 121.5 (CH), 123.1 (2 CH), 123.6 (quat), 123.8 (quat), 124.7 (quat), 125.9 (quat), 126.1 (quat), 126.7 (CH), 127.3 (CH), 127.6 (CH), 128.7 (CH), 129.6 (CH), 130.3 (CH), 140.2 (CH), 143.2 (quat), 148.2 (CH), 153.6 (quat), 156.2 (quat) and 166.5 (quat); Z-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.60 (3H, s), 5.82 (1H, d, *J* 12.4), 6.72 (1H, d, *J* 12.4) and 8.99 (1H, s); *m/z* 379 (M^+, 30%), 321 (27), 320 (100), 295 (39), 200 (32), 184 (36), 160 (22) and 132 (23).

Methyl 3-[4-(Dibenzothiophen-1-yl)napthalen-2-yl]acrylate 392



4-(Dibenzothiophen-1-yl)napthalene-3-carbaldehyde **387** (0.306 g, 0.90 mmol) and methyl (triphenylphosphoranylidene) acetate (0.326 g, 0.97 mmol) were mixed in toluene (150 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(Dibenzothiophen-1-yl)napthalen-2-yl]acrylate* **392** as a yellow solid (0.338 g, 95%) in 72:28 *E*:*Z* ratio. (Found: M^+ 394.1034. $C_{26}H_{18}O_2S$ requires *M* 394.1028); δ_H (250 MHz, $CDCl_3$): (*E*-isomer) 3.53 (3H, s), 6.42 (1H, d, *J* 15.0), 7.09 – 7.66 (7H, m), 7.75 – 7.88 (4H, m) and 8.11 – 8.20 (3H, m); δ_C DEPT (250 MHz, $CDCl_3$): 51.5 (CH_3), 119.1 (CH), 121.2 (CH), 121.8 (CH), 122.7 (CH), 122.8 (CH), 124.3 (CH), 124.7 (CH), 126.8 (2 CH), 127.1 (CH), 128.0 (CH), 128.7 (CH), 129.0 (CH), 142.5 (CH) and 167.1 (CH); *Z*-isomer characterised by ^1H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.59 (3H, s) and 5.67 (1H, d, *J* 12.0); *m/z* 394 (M^+, 73%), 336 (42), 335 (100), 334 (78), 200 (34), 167 (27), 166 (23) and 43 (42).

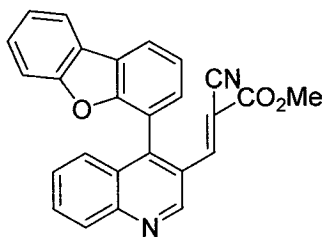
Methyl 3-[4-(Dibenzofuran-1-yl)napthalen-2-yl]acrylate 393



4-(Dibenzofuran-1-yl)naphthalene-3-carbaldehyde **388** (0.303 g, 0.94 mmol) and methyl (triphenylphosphoranylidene) acetate (0.395 g, 1.15 mmol) were mixed in toluene (150 cm^3) and the solution heated to reflux under nitrogen for 4.5 h. General work-up method C was then followed to produce *methyl 3-[4-(Dibenzofuran-1-yl)napthalen-2-yl]acrylate* **393** as a yellow solid (0.323 g, 91%) in 80:20 *E*:*Z* ratio mp 240 °C. (Found: M^+ 378.1252. $C_{26}H_{18}O_3$ requires *M* 378.1256); δ_H (250 MHz, $CDCl_3$): 3.49 (3H, s), 6.38 (1H, d, *J* 15.9), 7.16 – 7.38 (8H, m), 7.49 (1H, d, *J* 15.9), 7.71 – 7.88 (4H, m) and 7.94 (1H, dd, *J* 1.0, 7.7); δ_C (250 MHz, $CDCl_3$): 51.4

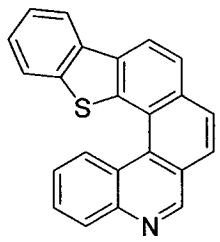
(CH_3), 111.7 (CH), 118.8 (CH), 120.6 (CH), 120.7 (CH), 121.3 (quat),122.7 (2 CH), 122.8 (CH), 124.0 (quat), 124.3 (quat), 126.7 (CH), 126.9 (CH), 127.0 (CH), 127.1 (CH), 127.9 (CH), 128.8 (CH), 129.6 (CH), 130.6 (quat), 132.5 (quat), 133.9 (quat), 135.8 (quat), 143.0 (CH), 154.2 (quat), 156.1 (quat) and 167.1 (quat); Z-isomer characterised by ^{1}H NMR spectrum: δ_H (250 MHz, $CDCl_3$): 3.54 (3H, s), 5.64 (1H, d, *J* 12.3), 6.70 – 6.81 (2H, m) and 8.05 (1H, d, *J* 8.6); *m/z* 378 (M^+, 37%), 319 (100), 318 (46), 292 (42), 291 (57), 290 (46), 289 (60) and 287 (45).

Methyl 2-cyano-3-[4-(dibenzofuran-1-yl)naphthalene]acrylate 394



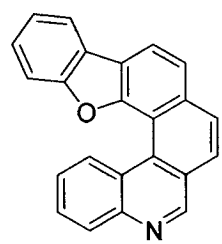
4-(Dibenzofuran-1-yl)quinoline-3-carbaldehyde **386** (0.104 g, 0.323 mmol) and methyl cyanoacetate (0.03 cm^3, 0.313 mmol) were added to toluene (5 cm^3). General work-up method D was then followed to produce a yellow solid (0.138 g). The product was purified by recrystallisation from ether to produce *methyl 2-cyano-3-[4-(dibenzofuran-1-yl)naphthalene]acrylate* **394** as a yellow solid (0.086 g, 66%) mp 200 – 201 °C. (Found: C, 74.7; H, 2.7; N, 6.2. $C_{26}H_{16}N_2O_3$ required C, 77.2; H, 4.0; N, 6.9%) δ_H (360 MHz, $CDCl_3$): 3.69 (3H, s), 7.26 – 7.50 (7H, m), 7.75 (1H, ddd, *J* 1.7, 6.7, 8.3), 7.96 (1H, dd, *J* 1.7, 8.3), 8.01 (1H, s), 8.09 (1H, dd, *J* 1.2, 7.7), 8.19 (1H, d, *J* 8.3) and 9.71 (1H, s); δ_C (360 MHz, $CDCl_3$): 52.5 (CH_3), 104.7 (quat), 111.0 (CH), 114.0 (quat), 117.0 (quat), 120.0 (CH), 121.5 (CH), 122.2 (CH), 122.4 (CH), 122.7 (quat), 123.3 (quat), 124.2 (quat), 125.6 (quat), 126.3 (CH), 127.0 (2 CH), 128.0 (CH), 129.0 (CH), 130.9 (CH), 145.6 (quat), 147.2 (CH), 148.3 (quat), 150.7 (CH), 152.6 (quat), 155.3 (quat) and 161.2 (quat); *m/z* 404 (M^+, 27%), 345 (63), 344 (24), 306 (37), 296 (21), 295 (93), 294 (41) and 184 (36).

FVP of Methyl 3-[4-(Dibenzothiophen-1-yl)quinoline]acrylate 390



Flash vacuum pyrolysis of methyl 3-[4-(dibenzothiophen-1-yl)quinoline]acrylate **390** (0.072 g, T_f 950 °C, T_i 296 °C, P 3.0 × 10^{-2} – 2.1 × 10^{-1} Torr, t 10 min) gave a yellow oil (0.028 g) which was then purified by dry flash chromatography using 50% hexane, 15% ethyl acetate and 35% dichloromethane as eluent to produce *benzothiophenyl[1,2]-11,12-benzo[k]phenanthridine* **395** as a brown solid (0.014 g, 23%) (Found: M^+ 335.0767. $C_{23}H_{13}NS$ requires *M* 335.0769); δ_H (360 MHz, $CDCl_3$): 7.46 – 7.63 (2H, m), 7.79 – 7.86 (2H, m), 7.92 (1H, d, *J* 8.5), 8.07 (1H, d, *J* 6.6), 8.09 (1H, d, *J* 6.6), 8.21 – 8.29 (2H, m), 8.35 (1H, d, *J* 8.5), 8.49 (1H, d, *J* 8.5), 8.75 (1H, d, *J* 8.5) and 9,38 (1H, s); δ_C DEPT (360 MHz, $CDCl_3$): 121.2 (CH), 121.9 (CH), 124.3 (CH), 124.4 (2 CH), 124.8 (CH), 125.5 (CH), 127.0 (CH), 127.7 (CH), 128.6 (CH), 128.9 (CH), 129.2 (CH), 129.3 (CH); *m/z* 335 (M^+, 11%), 312 (26), 311 (100), 310 (41), 155 (33), 149 (17), 59 (12) and 43 (17).

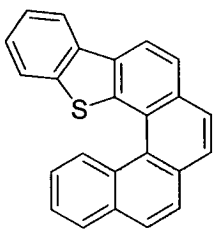
FVP of Methyl 3-[4-(dibenzofuran-1-yl)quinoline]acrylate 391



Flash vacuum pyrolysis of methyl 3-[4-(dibenzofuran-1-yl)quinoline]acrylate **391** (0.043 g, T_f 950 °C, T_i 283 °C, P 4.6 × 10^{-2} – 2.5 × 10^{-1} Torr, t 10 min) gave a yellow oil (0.052 g) which was then purified by dry flash chromatography using 20% ethyl acetate in hexane to produce *benzofuryl[1,2]-11,12-benzo[k]phenanthridine* **396** as a yellow foam (0.032 g, 90%). (Found: M^+ 319.0996. $C_{23}H_{13}NO$ requires *M* 319.0997); δ_H (360 MHz, $CDCl_3$): 7.44 (1H, ddd, *J* 1.1, 7.6, 8.7), 7.52 (1H, ddd, *J* 1.3, 7.6, 8.7), 7.63 (1H, d, *J* 8.7), 7.66 (1H, ddd, *J* 1.1, 7.0, 8.3), 7.85 (1H, ddd, *J* 1.3, 7.0, 8.3), 7.94 (1H, d, *J* 8.7), 8.00 (1H, d, *J* 8.3), 8.08 (1H, dd, *J* 1.3, 7.6), 8.13 (1H, d, *J* 8.7), 8.31 (1H, d, *J* 8.3), 8.36 (1H, dd, *J* 1.3, 8.4), 8.74 (1H, dd, *J* 1.1, 8.3) and 9.38 (1H, s); δ_C DEPT (360 MHz, $CDCl_3$): 111.8 (CH), 120.4 (CH), 121.2 (CH), 123.3 (CH), 124.0 (CH), 124.8 (CH), 124.9 (CH), 127.2

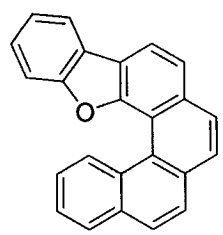
(CH), 128.5 (CH), 128.9 (CH), 129.0 (CH), 129.2 (CH) and 151.3 (CH); *m/z* 319 (M^+, 100%), 295 (19), 160 (22), 159 (14), 132 (12), 59 (10) and 43 (17).

FVP of Methyl 3-[4-(dibenzothiophen-1-yl)napthalene]acrylate 392



Flash vacuum pyrolysis of methyl 3-[4-(dibenzothiophen-1-yl)napthalene]acrylate **392** (0.252 g, T_f 950 °C, T_i 250 °C, P 1.8 × 10^{-2} – 3.0 × 10^{-1} Torr, t 10 min) gave a yellow oil which was then purified by dry flash chromatography using 2% ethyl acetate in hexane to produce *benzothiophenyl[1,2]-11,12-benzo[k]phenanthrene* **397** as a brown solid (0.070 g, 33%). (Found: M^+ 334.0817. $C_{24}H_{14}S$ requires *M* 334.0816) δ_H (360 MHz, $CDCl_3$): 7.42 (1H, ddd, *J* 1.6, 5.0, 7.4), 7.46 – 7.52 (2H, m), 7.64 (1H, ddd, *J* 1.0, 7.0, 8.0), 7.73 – 7.81 (3H, m), 7.92 – 8.02 (4H, m), 8.19 (1H, dd, *J* 1.6, 6.2), 8.34 (1H, d, *J* 8.4) and 8.64 (1H, d, *J* 8.4); δ_C DEPT (360 MHz, $CDCl_3$): 120.6 (CH), 121.7 (CH), 122.5 (CH), 124.8 (2 CH), 125.9 (CH), 126.4 (CH), 126.7 (CH), 127.1 (2 CH), 128.2 (CH), 128.5 (2 CH) and 130.4 (CH); *m/z* 334 (M^+, 100%),332 (26), 167 (24), 166 (21), 131 (11), 86 (28) and 84 (42).

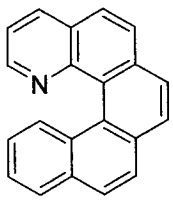
FVP of Methyl 3-[4-(dibenzofuran-1-yl)napthalene]acrylate 393



Flash vacuum pyrolysis of methyl 3-[4-(dibenzofuran-1-yl)napthalene]acrylate **393** (0.218 g, T_f 950 °C, T_i 290 °C, P 1.8 × 10^{-2} – 4.2 × 10^{-1} Torr, t 10 min) gave a yellow oil which was then purified by dry flash chromatography using 2% ethyl acetate in hexane to produce *benzofuryl[1,2]-11,12-benzo[k]phenanthrene* **398** as a brown solid (0.076 g, 41%). (Found: M^+ 318.1039. $C_{24}H_{14}O$ requires *M* 318.1045); δ_H (360 MHz, $CDCl_3$): 7.42 (1H, ddd, *J* 1.3, 7.4, 8.7), 7.49 (1H, ddd, *J* 1.3, 7.4, 8.7), 7.59 - 7.63 (2H, m), 7.69 (1H, ddd, *J* 1.3, 7.0, 8.0), 7.86 (2H, dd, *J* 5.7, 8.3), 7.98 (1H, d, *J* 8.0), 8.01 – 8.04 (2H, m), 8.07 (1H, dddd, *J* 0.6, 1.3, 2.2, 7.6), 8.20 (1H, d, *J* 8.3) and 8.64 (2H, ddd, *J* 0.6, 1.3, 8.3); δ_C DEPT (360 MHz, $CDCl_3$): 111.6 (CH), 117.0 (CH), 120.0 (CH), 122.8 (CH), 123.8 (CH), 124.1 (CH),

126.0 (CH), 126.2 (CH), 126.6 (2 CH), 127.3 (CH), 127.7 (CH), 128.2 (CH) and 129.7 (CH); *m/z* 318 (M^+, 73%), 159 (12), 131 (12), 125 (13), 58 (43) and 43 (100).

FVP of Methyl 3-[1-(quinolin-8-yl)naphthalen-2-yl]acrylate 389



Flash vacuum pyrolysis of *methyl 3-[1-(quinolin-8-yl)naphthalen-2-yl]acrylate* **389** (0.043 g, T_f 950 °C, T_i 276 °C, P 2.7 × 10^{-2} – 2.2 × 10^{-1} Torr, t 5 min) gave a brown oil which was then purified by dry flash chromatography using a solvent gradient of 5% - 100% ethyl acetate in hexane as eluent to produce 1-aza[5]helicene **375**[100] as a brown solid (4.6 mg, 13%). (Found: M^+ 279.1045. $C_{21}H_{13}O$ requires *M* 279.1048) δ_H (360 MHz, $CDCl_3$): 7.25 (2H, m), 7.49 – 7.55 (2H, m), 7.85 – 8.00 (6H, m), 8.15 (1H, d, *J* 8.6), 8.29 (1H, dd, *J* 1.6, 8.3) and 8.69 (1H, dd, *J* 1.4, 4.3); δ_C DEPT (360 MHz, $CDCl_3$): 122.3 (2 CH), 124.0 (CH), 126.1 (2 CH), 126.4 (CH), 126.9 (CH), 127.0 (CH), 128.0 (CH), 129.1 (CH), 130.6 (CH), 136.7 (CH) and 146.8 (CH); *m/z* 279 (M^+, 29%), 167 (32), 149 (75), 71 (32), 57 (67), 55 (56), 43 (100) and 41 (73).

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Appendix

F. M. McMillan, H. McNab and D. Reed, *Tetrahedron Lett.*, 2007, **48**, 2401 – 2403.

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Tetrahedron Letters 48 (2007) 2401–2403

Suzuki–Miyaura coupling of 2-bromopyridine with 2-formylphenylboronic acid

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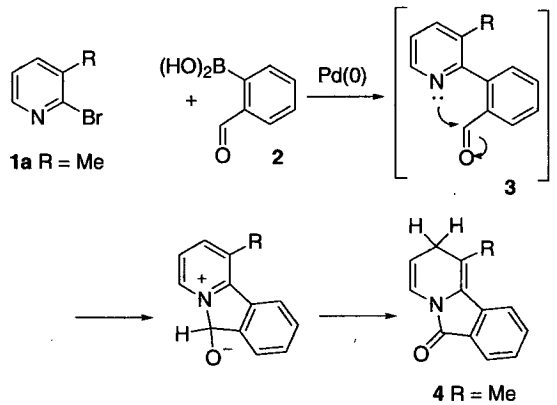
Received 19 December 2006; accepted 18 January 2007
Available online 24 January 2007

Abstract—Suzuki–Miyaura coupling of 2-bromopyridine **1b** with 2-formylphenylboronic acid **2** under standard conditions, gives 2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid **5b**. A similar reaction is observed for 2-bromo-6-methylpyridine **1c**. A mechanistic rationale for these unusual observations is suggested.

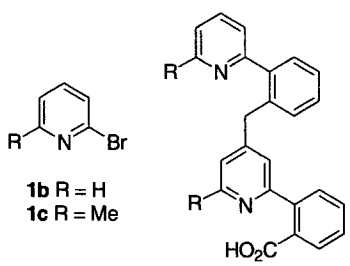
Application of the Suzuki–Miyaura coupling reaction has revolutionized synthetic routes to arylated heterocyclic compounds.[1,2] Although the reaction outcome is usually highly predictable, Mamane and Fort have reported that anomalous products are obtained when certain 2-halogenopyridines [e.g., **1a** (R = Me)] and related heterocycles are coupled with 2-formylphenylboronic acid **2**.[3] The initial coupling product **3** undergoes a cyclization and formal hydride shift to provide pyrido[2,1-*a*]isoindolones **4** (Scheme 1). Other workers have reported very low yields of coupling products in similar reactions.[4]

Here, we show that the palladium-catalyzed reaction of 2-bromopyridine **1b** itself with 2-formylphenylboronic acid **2** produces an unusual dimeric species **5b** whose formation can be rationalized by the involvement of pyrido[2,1-*a*]isoindolone intermediates. A similar reaction is observed for 2-bromo-6-methylpyridine **1c**.



Scheme 1.

Thus, Suzuki–Miyaura coupling of 2-bromopyridine **1b** with 2-formylphenylboronic acid **2** under the conditions, which were used to make the 3-isomer[5] gave no product, which could be isolated by the usual work-up, but continuous extraction with dichloromethane over a period of 16 h gave a high yield of a single compound as a foamy solid.[6] Its mass spectrum (FAB conditions) showed a molecular ion (M+1) at *m/z* 367 Da indicating that the product bears a dimeric relationship to both aldehyde **3** (R = H) and pyrido[2,1-*a*]isoindolone **4** (R = H). Its NMR spectra ($CDCl_3$) showed that a CH_2 group was present (δ_H 4.19, δ_C 38.7) and a broad signal at δ_H 9.95 was observed due to a carboxylic acid function, supported by the presence of a quaternary signal at δ_C 169.9 in the ^{13}C NMR spectrum.



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doi:10.1016/j.tetlet.2007.01.108

The structure of this unknown product was established as 2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid **5b** by the sequence of NMR experiments described below, which were carried out at 600 MHz in [$^2H_6$]acetone solution, the combination of spectrometer frequency and solvent helping to maximize dispersion in the proton dimension (Fig. 1).

The correlation of ^1H and ^{13}C chemical shift values shown in Table 1 was obtained by a $^1H/^{13}C$ HSQC experiment. A ^1H TOCSY experiment permitted the grouping of the ^1H signals into spin systems establishing the presence of three 4-spin systems (signals K, L, M and P designated B1; signals D, G, N and R, designated P2; signals E, F, H and J, designated B2) and one 3-spin system (signals B, C and Q designated P1) in addition to the methylene group (signal A, δ_H 4.29) and that due to the carboxylic acid.

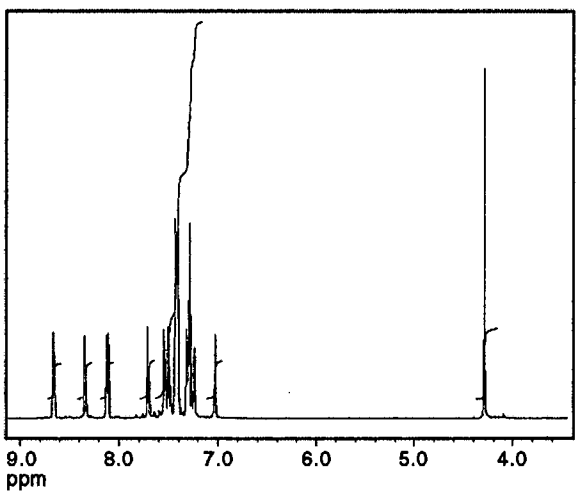
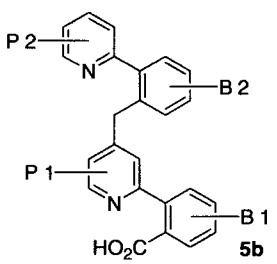


Figure 1. ^1H NMR spectrum (600 MHz, acetone-d_6) of **5b**.

Table 1. Correlation of ^1H and ^{13}C NMR signals of **5b** (600 MHz in [$^2H_6$]acetone)



5b

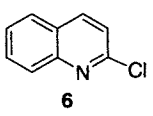
H-1 Label	δ_H (^1H)	*J*/Hz	δ_C (^{13}C)	Spin system
A	4.29	s	37.8	
B	7.01	4.6	122.9	P1
C	7.27	s	123.6	P1
D	7.31	7.7, 4.9, 1.1	122.2	P2
E	7.38	6.7, 2.5	127.2	B2
F	7.40	[a]	128.6	B2
G	7.41	[a]	131.0	P2
H	7.42	[a]	124.3	B2
J	7.44	[a]	130.3	B2
K	7.48	[a]	130.3	B1
L	7.50	[a]	128.2	B1
M	7.58	7.4, 1.4	131.0	B1
N	7.80	7.7, 1.8	136.6	P2
P	7.85	7.7, 1.1	130.3	B1
Q	8.36	4.9	148.3	P1
R	8.67	4.6	148.9	P2

[a] Complex region of overlapping signals.

Identification of the components of the 3-spin system P1 suggested that it was likely to be due to a 2,4-disubstituted pyridine unit and a ^1H NOESY experiment showed that the methylene group was attached to the 4-position of this pyridine ring (via NOE correlations between signals A and C and also between signals A and B, thereby defining the position of the CH_2 with respect to P1). The 2-substituent of the disubstituted pyridine was identified as the 4-spin system B1, from the NOESY relation between signals C and K. Confirmation that the carboxylic acid group was attached to B1 was arrived at from a $^1H/^{13}C$ HMBC experiment, in which correlations were detected between signals K and P (both previously designated B1) and the ^{13}C signal at δ_C 168.9 (corresponding to the carbonyl carbon atom of the carboxylic acid).

A close inspection of the NOESY data reveals a correlation between signals A and F, thereby establishing the P1–CH_2–B2 connectivity pathway. The linkage between rings P2 and B2 was confirmed from correlations present in the $^1H/^{13}C$ HMBC experiment, between a quaternary ^{13}C signal at δ_C 159.6 (due to a C2 of the pyridine ring) and ^1H signals G (from P2) and H (from B2). Therefore, having established the B1–P1–CH_2–B2–P2 linkage, along with the nature and substitution patterns of the precursors, only 2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid **5b** is consistent with the data.

As a second example, of this dimerization process, reaction of 2-formylphenylboronic acid **2** with 2-bromo-6-methylpyridine **1c** gave the corresponding product **5c** after continuous extraction of the reaction mixture. Reaction of 2-chloroquinoline **6** under our conditions gave **7** as found by Mamane and Fort.[3]



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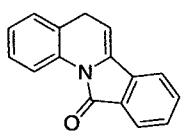

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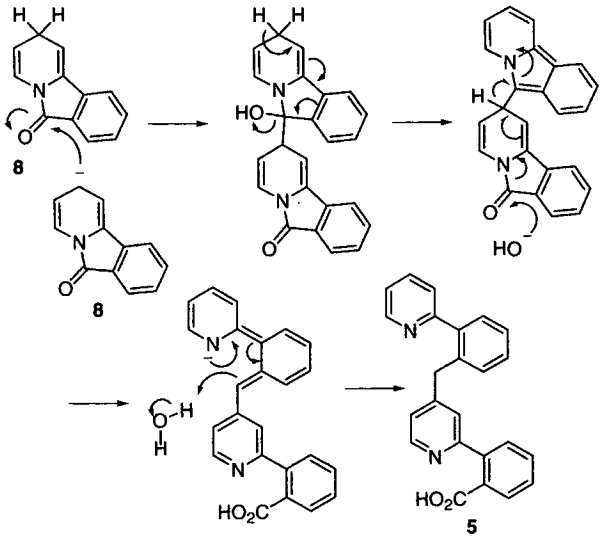
A mechanistic scheme for the formation of **5** must explain the concomitant disproportionation of two aldehyde groups and the functionalization of an unactivated pyridine ring in the 4-position by a substituted benzyl group. It is likely that parent pyrido[2,1-*a*]isoindolone **8** (cf. **4**) is an intermediate and a possible rationalization is shown in Scheme 2. Condensation of two molecules of **8** is possible under the basic conditions of the Suzuki–Miyaura coupling. Dehydration, hydride shift (already implicated in the formation of **4**) and rehydration complete the process.



Scheme 2.

In conclusion, we have obtained unexpected products under Suzuki–Miyaura coupling conditions when a 2-formylphenyl group is present at a site adjacent to a pyridine-type nitrogen atom. These observations complement those of Mamane and Fort[3] and provide a new, readily available pyridine scaffold for further investigation.

Acknowledgement

We are grateful to the EPSRC (UK) for a Research Studentship (to F.M.M.) and for the provision of the 600 MHz NMR spectrometer.

References and notes

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6. *Experimental*: A solution of 2-bromopyridine **1b** (0.30 cm^3, 3.16 mmol) and tetrakis(triphenylphosphine)palladium (0.102 g, 0.09 mmol) in ethylene glycol dimethyl ether (15 cm^3) was stirred under nitrogen for 20 min. Sodium carbonate (0.437 g, 4.12 mmol), water (15 cm^3) and 2-formylphenylboronic acid **2** (0.470 g, 3.14 mmol) were added and the reaction mixture was heated under reflux in the absence of light for 20 h. The solvent was removed from the solution under reduced pressure. The residue was added to water (25 cm^3) and small amounts of starting materials were removed by extraction into dichloromethane. After 16 h of continuous extraction of the aqueous phase with dichloromethane a yellow foam was obtained by concentration of the organic extracts, which was identified as *2-[4-(2-pyridin-2-yl-benzyl)-pyridin-2-yl]benzoic acid* **5b**. The yield was dependent on the continuous extraction conditions, but recoveries of up to 94% (0.546 g) have been obtained; [found $(M+H)^+$ 367.1446. $C_{24}H_{19}N_2O_2$ requires *M* 367.1447] δ_H (250 MHz, $CDCl_3$): 4.19 (2H, s), 6.92 (1H, d, *J* 4.7), 7.23–7.45 (4H, m), 7.30–7.33 (4H, m), 7.40 (2H, m), 7.61 (1H, td, *J* 1.8, 7.4), 8.00 (1H, dd, *J* 1.8, 7.4), 8.24 (1H, d, *J* 5.5), 8.56 (1H, d, *J* 4.4) and 9.95 (1H, br s); δ_C (63 MHz, $CDCl_3$): 38.7 (CH_2), 122.0 (CH), 123.4 (CH), 124.1 (CH), 124.9 (CH), 127.3 (CH), 128.8 (CH), 129.1 (CH), 129.1 (quat), 130.2 (CH), 130.5 (CH), 130.8 (CH), 131.0 (CH), 132.6 (CH), 133.0 (quat), 136.0 (quat), 136.7 (CH), 140.2 (quat), 145.6 (CH), 148.7 (CH), 153.8 (quat), 156.9 (quat), 159.2 (quat) and 169.9 (quat); other data obtained from a [$^2H_6$] acetone solution, are shown in Table 1; *m/z* (FAB) 367 [$(M+H)^+$, 100%].
When these reaction conditions and work-up were repeated using 2-bromo-6-methylpyridine **1c** in place of 2-bromopyridine, *2-{6-methyl-4-[2-(6-methylpyridin-2-yl)-benzyl]-pyridin-2-yl}benzoic acid* **5c** was obtained in 8% yield (found M^+ 394.1670. $C_{26}H_{22}N_2O_2$ requires *M* 394.1676) δ_H (360 MHz, $CDCl_3$): 2.51 (6H, s), 4.24 (2H, s), 6.91 (1H, s), 7.06 (2H, d, *J* 7.8), 7.18 (1H, s), 7.27–7.59 (9H, m) and 8.22 (1H, m); δ_C DEPT (90 MHz, $CDCl_3$): 23.7 ($2CH_3$), 39.0 (CH_2), 122.1 (CH), 122.6 (CH), 123.6 (CH), 124.8 (CH), 128.5 (CH), 129.8 (CH), 130.5 (CH), 131.3 (CH), 131.6 (CH), 132.0 (CH), 132.4 (CH), 135.0 (CH) and 137.9 (CH). *m/z* (EI) 394 (M^+, 61%), 349 (59), 278 (51), 259 (86), 199 (51), 55 (79) and 43 (100).
Under similar conditions, 2-chloroquinoline **6** and 2-formylphenylboronic acid **2** provided 5*H*-isoindolo[2,1-*a*]quinolin-11-one[3] **7** as a yellow solid (13%).δ_H (360 MHz, $CDCl_3$): 3.80 (2H, d, *J* 4.0), 6.03 (1H, t, *J* 4.0, 8.2), 7.09–7.19 (2H, m), 7.30 (1H, ddd, *J* 1.9, 7.2, 8.6), 7.50 (1H, ddd, *J* 1.0, 7.2, 8.6), 7.59 (1H, ddd, *J* 1.0, 7.2, 8.2), 7.68 (1H, ddd, *J* 0.9, 1.9, 7.6), 7.90 (1H, ddd, *J* 0.9, 2.0, 7.6) and 9.00 (1H, dd, *J* 0.9, 8.6); δ_C (90 MHz, $CDCl_3$): 27.7 (CH_2), 103.6 (CH), 117.8 (CH), 119.1 (CH), 121.9 (quat), 123.2 (CH), 124.6 (CH), 127.5 (CH), 128.9 (CH), 129.1 (CH), 130.1 (quat), 131.9 (CH), 133.3 (quat), 133.9 (quat), 135.1 (quat) and 165.1 (quat).