NEW GAS-PHASE CASCADE REACTIONS OF STABILISED PHOSPHORUS YLIDES LEADING TO RING-FUSED INDOLES AND QUINOLINES

Lorna Murray

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NEW GAS-PHASE CASCADE REACTIONS OF STABILISED PHOSPHORUS YLIDES LEADING TO RING-FUSED INDOLES AND QUINOLINES

by

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B. Sc. (Hons), AMRSC

Thesis presented towards the degree of

DOCTOR OF PHILOSOPHY

University of St. Andrews

December 2009

Dedicated to the memory of:

Gran Jane Vandal (17.11.27–04.03.97) Papa Robert Vandal (05.04.27–22.02.02) Papa William Murray (05.11.32–28.06.09)

DECLARATION

I, Lorna Murray, hereby certify that this thesis, which is approximately 50000 words in length, has been written by me, that it is the record of work carried out by me and that it has not been submitted in any previous application for a higher degree.

I was admitted as a research student in October 2005 and as a candidate for the degree of Doctor of Philosophy in October 2006; the higher study for which this is a record was carried out in the University of St Andrews between 2005 and 2009.

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I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of Doctor of Philosophy in the University of St Andrews and that the candidate is qualified to submit this thesis in application for that degree.

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LECTURE COURSES ATTENDED

Organic Research Seminars	3 years attendance
School Colloquia	3 years attendance
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The Chemistry of Phosphorus and Related Elements	Dr. R. A. Aitken
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ABSTRACT

Synthesis and flash vacuum pyrolysis (FVP) of stabilised phosphorus ylides containing an *o*-amino functionalised benzene ring has been examined for the first time. Model studies using *N*-methyl-*N*-tosyl and *N*-mesyl-*N*-methyl ylides showed that the ylides could be prepared, although yields were variable, and had the expected spectroscopic properties. Upon FVP, however, the expected loss of Ph₃PO and the sulfonyl group was accompanied by unexpected transfer of the reactive site from nitrogen to carbon giving 3-substituted quinolines rather than the expected indole products.

Moving to ylides with an α -cinnamoyl group (or heterocyclic analogue) did, however, result in the originally planned tandem cyclisation leading to ring-fused carbazole products. *N*-Benzyl was also found to be a suitable thermally labile group and a series of α -cinnamoyl *N*-benzyl-*N*-methyl ylides were prepared and characterised. For their synthesis, use of *N*-cinnamoylbenzotriazoles was found to be preferable to cinnamoyl chloride, requiring only half the amount of amino-functionalised phosphonium salt. While FVP of some of these ylides led to benzo-, furo- and thienocarbazoles in good yield, others again gave quinoline-type products pointing to a fine balance between the two alternative modes of cyclisation.

It was noted that one of the furocarbazole products was very similar to a natural product, Eustifoline D, isolated from the medicinally active shrub *Murraya euchrestifolia* from Taiwan and its synthesis was planned. With a view to producing the required N-H carbazole, *N*,*N*-dibenzylamino amino ylides were prepared and were found to exhibit restricted rotation leading to broad NMR signals. Their FVP again led to both quinoline and carbazole products, with the former having usually, but not always, lost a phenyl group. Mechanistic pathways for the formation of the various products are proposed. Complete assignment of the complex ¹H NMR spectra of the various fused-ring heterocyclic products was achieved, assisted by simulations in many cases.

The ylide precursor required for Eustifoline D was prepared in five steps and 10% overall yield from 5-methylanthranilic acid. The final FVP step gave a quinoline as the major product, but the minor product was Eustifoline D, spectroscopically identical to the natural product.

SYMBOLS AND ABBREVIATIONS

AIBN	azobis(isobutyronitrile)
bp	boiling point
br, s, d, t, q	broad, singlet, doublet, triplet, quartet
Bn	benzyl
Boc	<i>t</i> -butyloxycarbonyl
δ	chemical shift in parts per million
DMA	dimethylacetimide
DMF	dimethylformamide
ES	electrospray
FVP	flash vacuum pyrolysis
h, min	hours, minutes
J	spin-spin coupling constant in Hertz
V _{max}	infra-red absorption frequency
М	mol dm ⁻³
M^+	molecular ion
mp	melting point
MS	molecular sieve
Ms	mesyl (methanesulfonyl)
<i>m/z</i> ,	mass to charge ratio
MW	microwave
NMR	nuclear magnetic resonance
NMP	N-methylpyrrolidin-2-one
NBS	N-bromosuccinimide
Tf	trifluoromethanesulfonyl
TBS	t-butyldimethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyran-2-yl
TLC	thin layer chromatography
TMS	tetramethylsilane or trimethysilyl
Ts	tosyl (<i>p</i> -toluenesulfonyl)

INTRODUCTION

A Indoles

1 Historical Background

Indoles and indole chemistry have been well documented from the mid 19th century, mainly because of the importance of indigo dye. Initial isolation of indole was from the natural indigo dye **1** by treating with oleum, and this was how indole was named; *ind*igo *ole*um. The first synthesis of indole was reported by Nobel prize winner Alfred von Baeyer in 1866. ¹ This was achieved by converting indigo dye to isatin **2** by oxidation and then reduction to oxindole **3**. Baeyer then reduced oxindole by heating with zinc dust to form indole **4**.



Since this first synthesis was published, numerous syntheses of indoles have been documented. Arguably the most famous is the Fischer indole synthesis,² which was published shortly after Baeyer's synthesis in 1883. Fischer started from phenylhydrazine and an aldehyde or ketone **5** with an acid catalyst to form 2,3-disubstituted indoles **6**.



This procedure is very useful in synthetic chemistry and is used in the synthesis of pharmaceuticals, for example indomethacin 7. Inodomethacin 7 is a non-steroidal antiinflammatory drug used to treat rheumatoid arthritis and the first step in the synthesis is the formation of the core indole structure. Starting from 4-methoxyphenylhydazine and reacting with methyl levulinate **5a** gives 2-methyl-3-methyloxycarbonylmethyl-5methoxyindole **8**, which undergoes several further steps to give **7**.^{3,4}



Due to the vast number of publications on the synthesis of indoles, this review will focus on the formation of the C-N bond *via* an *o*-alkynylarylamine and the synthesis of tetracyclic heteroaromatic molecules containing the carbazole motif.

2 Synthesis of *o*-alkynylanilines

There are many different ways in which indole can be formed from *o*-alkynylarylamines. These include transition metal catalysts, base cyclisation and radical chemistry. A fundamental step in these reactions is the formation of the *o*-alkynylarylamine which is achieved by coupling *o*-haloanilines with alkynes, and there has been extensive research into this procedure alone. Early work in this field involved the use of alkynylcopper reagents, as was shown in 1966.⁵ This work indicated that the solvent was essential in determining the nature of the product; either the coupling product **9** could be isolated by using pyridine, or indole **10** could be obtained directly in a tandem coupling/cyclisation reaction in a one-pot synthesis by using DMF.



Perhaps the most widely used method for the synthesis of *o*-alkynylanilines is the use of a palladium catalyst. Pioneering work on the use of the palladium catalyst to couple aryl halides with alkynes was undertaken by Cassar,⁶ Heck⁷ and Sonogashira⁸ around the same time, making use of different catalysts and all with the aim of finding milder reaction conditions. Cassar looked at using nickel[0] and palladium[0] triphenylphosphine as catalysts, with palladium being the most successful in forming alkynes **11**.



Heck reported similar results, however an amine base was used as the solvent and all reactions were carried out at 100 °C. Sonogahira again made use of palladium, however, cuprous iodide was also used as a catalyst to give good yields at room temperature and the catalyst was easily removed though an alumina column. This was shown to be very versatile, making use of aryl and alkyl halides to form products **11**.



The mild conditions and synthetic applications of the Sonogashira cross-coupling reaction have been widely successful, and as a result the procedure has been thoroughly investigated and developed, with the use of *o*-haloanilines of specific importance for this review. When *o*-alkynylanilines are required, Sonogashira conditions are most likely to be used, e.g. in the sythesis of the aniviral (\pm)-virantmycin, isolated from *Streptomyces nitrosporeus*.⁹



The Sonogashira reaction has also been used more recently in the synthesis and cyclistion of a bis-indole carboxamide 12^{10} which has the potential to be the basis of anti-cancer drug design.



An interesting development in the Sonogashira coupling reaction was in the use of a microwave, solvent free system.¹¹ This is important from an environmental point of view, as solvents contaminated with palladium can be difficult to recycle and dispose of. Microwave irradiation has become an important method in organic synthesis, and recently coating the reactants onto surfaces to carry out microwave reactions has been investigated.¹¹ The use of surfaces is beneficial as they absorb minimal amounts of microwave energy, allowing the active species to absorb the microwaves but with minimal rise in temperature, meaning that open beakers can be used. The application of this system to the synthesis of *o*-alkynylanilines **13** involves the use of potassium fluoride doped alumina in the presence of palladium powder, cuprous iodide and triphenylphosphine. The use of palladium powder is also more economical as many specialist palladium catalysts are very expensive.



The coupling product is not the only product that can be formed in this procedure: one pot formation of the indole product may also be observed but this will discussed in a later section. Products **13** are obtained exclusively from *o*-iodoaniline coupling with phenylacetylene and *p*-tolylacetylene.

Another modification to the Sonogashira reaction is to form alkynylarylamines 14 from the use of an iron catalyst instead of the palladium which had been previously used.¹²



Many reaction conditions were examined to optimise this procedure including time, ligand, iron source, solvent and catalyst loading. The use of iron instead of the more common copper or palladium is more economical and will perhaps be of interest in industry.

A development to the work by Castro was described in 1985, where instead of having *o*-iodoaniline, *o*-thalliated aromatic amides are used.^{13,14} It was known that exclusive *o*-thalliation occurs on aromatics with substituents capable of forming Lewis acid/base complexes with thallium(III) tris(trifluoracetate) (TTFA). This was extended to the use of aromatic amides, which again in the presence of TTFA/TFA or TTFA/TFA/ether gave the *o*-thalliated anilides.



The thalliated product **15** was then reacted with the copper derivative of phenylacetylene **16** in acetonitrile to give the desired *o*-alkynylaromatic amide **17**, however the presence of the amide motif is imperative for the success of the reaction.



Developed from the use of *o*-thalliated compounds, a different type of palladium catalysis for the synthesis of *o*-alkynylanilines **19** has been studied, making use of aryl triflates coupling with organostannanes¹⁵ which has been developed to incorporate alkynylstannanes **18**.¹⁶



The yields of the *o*-alkynylanilines ranged from 73-97% in relatively short reaction times of 1-3 h. The reaction conditions are however more severe than the Sonogashira cross-coupling and organostannanes are not prefered starting materials.

Another alternative method of synthesising o-alkynylanilines **20** is using trisubstituted aluminium.¹⁷



When R^1 = H a mixture of 2- and 4- substituted coupling products was observed. This was eliminated with the introduction of fluoro or ethyl groups at the 4-position.

3 Thermal Synthesis of Indole

The cyclisation of *o*-alkynylanilines has been carried out in many ways, mostly involving some sort of catalyst but an interesting early example is by heating alone.¹⁸ It was known that that heating aniline in the presence of ethyne gave indole *via* radical intermediates, but it was not known if the radical formed on ethyne attacked at the nitrogen (path b) or the *o*-position of the benzene ring (path a). By synthesising *o*-ethynylaniline and heating at 500-700 °C to give indole **4** it was shown that the reaction did indeed proceed by path a.



4 Synthesis of Indoles Using Transition Metal Catalysis

Many metals have been used to catalyse the cyclisation of *o*-alkynylanilines, including palladium, copper, zinc, indium, iridium, gold, mercury and molybdenum.

a Palladium Catalysis

Palladium catalysis is perhaps the most widely used method for both cross-coupling to form *o*-alkynylanilines and cyclisation to form indoles. An early example was in 1985 where *o*-phenylethynylacetanilides **21** were treated with palladium chloride in acetonitrile heated to reflux.^{14,19,20}



The synthetic versatility of this type of reaction quickly became apparent and many synthetic applications to different indoles 22 were examined. It was shown that electrophilic substitution on the 3-position was a convenient way to introduce further functionality to the indole ring with 23 being a specific example.^{21,16}



Palladium catalysed one-pot cross-coupling/cyclisation reactions have been achieved by treating *o*-iodoanilines **24** and alkynes **25** with palladium with or without triphenylphosphine and either *N*-Bu₄NCl (procedure A) or LiCl (procedure B).^{22,23}


When R^3 = TMS, this introduces further scope for modification at the 2-position. This can be achieved by desilylation/protonolysis, halogenation or the Heck reaction to give a variety of products **26**.

Palladium cyclisation has been well documented over the last 10–20 years with numerous examples of different substituted indoles.^{24–29} An interesting example is the synthesis of the indolo[2,3-*a*]carbazole **27**, the core structure known to be the basis of several biologically active compounds.³⁰



Solid supported palladium cyclisation to form functionalised indoles is synthetically useful, especially towards lead compounds. Depending on the substitution pattern, the reaction conditions subtly change. An example is shown of introducing diversity by means of the trimethylsilyl group in **28** to allow further functionalisation at the 2-position of the indole to give **29**.^{31,32} Another interesting way of introducing variation is at the 3-position, via the Mannich reaction.



Palladium modified zeolites have also been used in the synthesis of 2-substituted indoles.³³ These have been shown to have the same activity as complexes in solution, the zeolite has the potential to prevent or reduce the leaching of catalyst, and finally zeolites can stabilise the active intermediate and direct the reaction pathway. After optimisation of conditions it was found that DMF with caesium carbonate and lithium chloride resulted in the best overall yields of **30** and tolerated different functionality.



The zeolite catalyst has shown the potential to be recycled although reaction times are longer, 6–36 h, and yields drop, 82% to 65%, over 5 x catalyst recycling.

b Copper Catalysis

As has been previously mentioned, it is possible to obtain indoles **31** in a one-pot cyclistation from o-iodoaniline and alkynyl copper reagents in DMF.⁵



However, by changing the solvent to pyridine then the product changes to either pure uncyclised coupling product or a mixture of both, with the majority product uncyclised. The uncyclised product **32** can then be cyclised by treatment with cuprous iodide in DMF, however no cyclisation is observed without the copper salt. In the case of the one-pot cyclisation, this is generated *in situ*.



In some cases it is preferable to use the 2-step procedure, for example in the case of cuprous 2-pyridylacetylide which yielded only starting material in a one-pot synthesis.

Recently Lewis acids have been used in the cyclisation of *o*-alkynylanilines **33** to form the indole **30**. It was reported that previous methods for cyclisation had significant drawbacks, for example metal alkoxides cannot be used for alkaline-sensitive substrates, there are very few examples where their are no substituents on the nitrogen and there

was no cyclisation where the alkyne had an electron-withdrawing group attached.^{34,35} In an attempt to overcome these problems, the use of Lewis acids was examined.



After studying different Lewis acids, it was concluded that copper was the optimal metal catalyst and further investigation showed $Cu(OAc)_2$ to give the best yields for the shortest time, followed by $Cu(OTf)_2$.



The success of this reaction mainly appears to rest on the nature of the substituents on the nitrogen. Methanesulfonamide starting materials **34** ($R^1 = SO_2Me$) give consistently lower reaction times and higher yields than carbamates ($R^1 = CO_2Et$) or anilines ($R^1 = H$). However, in some instances Cu(OTf)₂ is a more effective catalyst, bringing carbamates and anilines to within a comparable yield and time range of methansulfonamides ($R^1 =$ CO₂Et, $R^2 = Ph$, 88%. $R^1 = H$, $R^2 = Ph$, 68%), although no conclusions have been drawn as to the compatibility of substrate and catalyst. This has demonstrated cyclisation of an unsubstituted aniline. The major effect of the nature of R^2 on the cyclisation was that bulky groups (*t*-butyl and TMS) produced significantly lower yields (22% and 9% respectively). There is also an interesting example of tandem cyclisation *via* this method to give **35**. The yields for tandem cyclisation when n = 1 or 2 are comparable, however, when n = 2 there is 14% of monocylisation product. This is not observed when n = 1.



This technique has been used in the synthesis of natural products. One such example is Happadine,³⁵ which is a lycorine alkaloid isolated from *Amaryllidaceae*, and is known to have adverse effects on fertility in male rats.



This method has been useful but where there are problems of low solubility in organic solvents and long reaction times, the use of aqueous media allows the reaction temperature to be reduced to room temperature and solubility issues to be overcome.³⁶ Yields at room temperature with a 1:1 ratio of H₂O and MeOH and Cu(OCOCF₃)₂ were excellent, allowing nitro, bromo, methyl and methoxy groups as substituents at R² and R³ of the aniline **36**, however aniline and carbamate cyclisation were not successful. When using an aqueous medium the bulky *t*-butyl at R¹ was tolerated, but TMS was eliminated to give 2-unsubstituted indole.



Another benefit of the aqueous medium is the ease of catalyst recycling. This was achieved by extracting the reaction mixture with ether, where the product was in the organic phase and the catalyst was left in the aqueous phase. To the aqueous phase, organic solvent was added along with amine and starting material and a second and third cycle was run with negligible difference in the yields; in fact in the case of the terminal alkyne the yield actually improved. This has been proved successful with *N*-mesyl and - tosyl compounds and with Ph, CH_2OH and H on the alkynyl terminal.

c Zinc Catalysis

Zinc has been used successfully to catalyse the cyclisation of *o*-alkynylanilines such as $37.^{37-39}$ This was achieved by using a strong base, butyllithium to deprotonate the amine followed by treatment with zinc chloride to give 2-substituted 3-zincioindole, which can then either be treated with NH₄Cl to give 2-substituted indole **38** or with electrophiles to give 2,3-substituted indoles **39**.



This was developed to include the synthesis of bis(indole) **40** by coupling the 3zincioindole with 1,4-diiodobenzene and 2,5-diiodothiophene in the presence of Pd(0) catalyst.



This technique has been extended to the use of Et_2Zn as the weak base for the initial deprotonation as well as incorporation into the indole intermediate **41** and this was achieved by changing the nitrogen protecting group. Several different types of protecting group were examined and sulfonamides gave the best results, in particular tosyl.



d Indium Catalysis

Other Lewis acids have been used in the synthesis of indoles, in particular those based on indium. Recently indium tribromide has proven successful, and interestingly depending on the substituent on the alkyne terminal, either an indole or a quinoline is formed.⁴⁰

The formation of the indole product **43** occurs when the alkyne terminal in **42** has either alkyl or aryl groups attached, *via* an intramolecular cyclisation. This synthesis is very versatile, as substituents on C-4 and C-5 of the aniline do not have any significant detrimental effect on the outcome of the reaction, which tolerates halide, nitro, cyano and methyl substituents. Also substituents on the nitrogen do not appear to influence the reaction: anilines give excellent yields and *N*-benzyl, acetyl and alkoxylcarbonyl derivatives all give between 70–78% yield, although the strongly electron withdrawing groups did require significantly longer reaction times (20 h compared to 1-2 h).



A very nice triple cyclisation of a trialkynyltriamine **45** to form a 1,3,5-tris(2indolyl)benzene **46** was also reported. The starting material **45** was synthesised by conventional Sonogashira coupling between *o*-iodoanilne and trialkynylbenzene **44**, which was then treated under the same reaction conditions as for the single cyclisation to give a near quantitative yield.



Quinolines can also be formed using an indium tribromide catalyst, *via* an intermolecular dimerisation. This occurred when there was TMS or no substituent on the alkynyl terminal of **47**. This reaction was again found to tolerate different substituents on the C-4 and C-5 of the aniline, with success using halide, cyano, nitro and methyl substituents.



The mechanism of these cyclisations was elucidated by conducting a labelling experiment. This involved starting with *o*-ethynylaniline **48** under standard conditions but using methanol- d_4 instead of methanol giving deuterated product **49**. This was carried out in an NMR tube and monitered by ¹H NMR. As well as showing product **49** rapid H-D exchange on the terminal carbon *in situ* was observed.



e Iridium Catalysis

Iridium catalysis has been shown to be useful as the reactions can be carried out without exclusion of air and water in almost quantitave yields, however as terminal alkynes rearrange to form vinylidene, the synthesis is limited to internal alkynes **49**.⁴¹



After an extensive mechanistic study involving Ir-*D* instead of Ir-H and monitoring by NMR it was proposed that the alkyne binds to the Ir(III) centre, activating it towards nucleophilic attack, followed by direct protonolysis of the resulting Ir-C bond.

f Gold Catalysis

Gold has been successfully shown to facilitate the cyclisation of *o*-alkynylaniline in ethanol or aqueous ethanol at room temperature.⁴² This cyclisation allows functional variation on the alkyl terminal, tolerating aryl, alkyl, vinyl and -H in good yields. When a halogen is present in the reaction mixture, then electrophilic substitution takes place to give 3-haloindoles.

Functional variation of the indole can be introduced by conjugate addition at the C-3 position, which has been shown previously to be catalysed by gold.⁴³ This has been developed to include the cyclisation/conjugate addition in a one-pot synthesis.^{44,45}

One-pot cyclisation/conjugate addition synthesis has also been used in the formation of vinyl indoles **52**. These are of synthetic importance as they are precursors of poly(*N*-vinylindoles), which can be used as semiconductors and photosensitive materials. This was achieved by reacting *o*-alkynylaniline **50** with terminal alkynes **51** in the presence of AuCl₃/AgOTf (5 mol%/15 mol%) at room temperature with no solvent.



Many different substituents were examined, including phenyl, cyclohexenyl and butyl at the alkyne substituent, R^1 . Also, variation was introduced in the nature of the terminal alkyne, R^2 with different aromatic substituents, cyclohexenyl and aliphatic chains. The reactivity was reduced for the aliphatic groups at R^2 , however, having aliphatic groups at R^1 did not appear to have a significant effect on the reactivity. Mechanistic studies of this reaction are currently underway, but a preliminary hypothesis indicates that the terminal alkyne is activated by Au(OTf)₃, which is then subject to nucleophilic attack by the aniline to form the imine. The carbon-carbon triple bond of the aniline is then activated by Au(OTf)₃ which then subsequently undergoes nucleophilic addition followed by protonation at the C-3 position to regenerate the catalyst.

Another interesting example of gold catalysed indole formation is the use of microencapsulated gold(III) (MC Au) on silicon oxide⁴⁶. The yields **53** from this reaction were excellent for a selection of aromatic, aliphatic and terminal halo, alcohol, phenyl and acetonitirile functionality, ranging from 81–95%. However, when R^1 = pyridyl, 1,4 imidazolyl or silyl groups yields dropped dramatically to 0–5%.



g Mercury Catalysis

An interesting example of cyclisation was by mercury triflate.⁴⁷ Mercury triflate was developed in 1983 as a catalyst for alkene cyclisation.⁴⁸ Different reaction conditions for the cyclisation of *o*-alkynylaniline were examined and it was shown that tosyl was the optimal protecting group for the nitrogen. Although toluene appeared to give more satisfactory results with high yields and low catalyst loading, dichloromethane was chosen as the optimal solvent, probably due to lower reflux temperatures and a possibility of solubility issues with toluene.



Cyclisation to form different 2-substituted indoles **54** usually occurred within an hour (e.g. for $R^1 = p$ -methoxybenzyl, hydroxybutyl, butyl) however the compound with $R^1 = 4$ -OTBS-butyl took 15 h and for $R^1 = p$ -nitrobenzyl and t-butyl it took 24-40 h. A recent development of the mercury catalyst has been immobilisation on a solid support.⁴⁹ This is beneficial as it can be easier to separate the products, facilitating recycling of the catalyst and handling. The principle of solid supported mercury triflate catalysis was tested by first of all replacing one of the triflate groups with phenyl which was shown to

give excellent yields at room temperature in 15 mins. Next was to attach the organomercury to the solid support. The support chosen was Silia*Bond* Phenyl which is used for column chromatography allowing a flow system to be set up for the reaction meaning that catalyst recycling could be easily examined.



The flow system was set up by mixing a 2:3 ratio of catalyst **55** to silica gel and packing in a column. Quantitative yields of **56** were found up to 20 x catalyst recycling indicating that this is an excellent system for catalytic cyclisation, with minimal mercury leakage.

h Molybdenum Catalysis

Molybenum has been shown to be an active catalyst for the cyclisation of *o*ethynylanilines. This was achieved by using 0.1 equivalents of metal catalyst with triethylamine as a base to give resonable to good yields of **57**.



5 Base-Induced Cyclisation

Bases have been used successfully in the cyclisation of *o*-ethynylanilines, and in an early example it was shown that this reaction relies on protection of the amine as in **58**. However the removal of the protecting group occurs during work-up which also removes the trimethylsilyl group when R^1 = TMS.⁵⁰



On the basis of these results, other bases have been examined for the formation of indole **59**, and it was shown that potassium *t*-butoxide in *t*-butanol was comparable with sodium ethoxide in ethanol.⁵¹



The conditions have been shown to be tolerant of different functional groups,⁵² and for this reason the use of bases in the cyclisation has been further examined. In 2000, an examination of different bases in *N*-methylpyrrolidinone (NMP) was carried out and it was shown that KH, KO^tBu and CsO^tBu bases are highly effective at room temperature and successful cyclisations have been carried out on a solid-support to give **60** and **61**.⁵³



Potassium *t*-butoxide and potassium hydride have been used in the synthesis of azaindoles at room temperature in THF,⁵⁴ 2-alkynylindoles at room temperature in NMP⁵⁵ and for polysubstituted indoles working towards the synthesis of natural products at 60-70 °C in NMP.^{56,59}

An interesting recent development of base catalysed cyclisation makes use of powdered sodium hydroxide.⁶⁰ This eliminates problematic water sensitive bases. This procedure is a one-pot synthesis starting from o-iodoanilines and, under Sonogashira conditions, coupling with acetylenes, followed by addition of sodium hydroxide giving the corresponding indole **62**.



This method is extremely versatile, allowing N-acetyl (removed under the basic conditions to form N-unsubstitured indole) or -benzyl groups to be used and halo

functionality was introduced at different positions on the benzene ring giving different halo-indoles, and also nitro and cyano functions were introduced at C-5. The terminal alkyne was also tolerent of different substituents, including aliphatic, alkenyl and aryl groups. The use of microwave irradiation in this technique is very useful for reducing the reaction times and also for reducing the amount of sodium hydroxide required for cyclisation to occur.

Cyclisations also accur under very mild conditions using tetrabutylammonium fluoride (TBAF). Under optimised conditions different substituents are tolerated at R^1 and R^2 , and depending on the nature of the substituents either indole **63** or *N*-substituted indole **64** is formed.



In most cases the only product formed was an *N*-unsubstituted indole. The ratio of *N*-substituted:unsubsituted appears to be both dependant on time and the subsitiuents. For example when $R^1 = CO_2Et$, $R^2 = Bu$ heating under reflux for 4 h gave almost a 1:1 ratio of products. However, heating the same mixture under reflux for 24 h gives 96% yield of pure *N*-unsubstituted product. This indicates that reaction proceeds by cyclisation followed by loss of substituent. This feature can be used to control which products are formed. In the case of $R^1 = Ms$, $R^2 = TMS$ and reaction at room temperature for 24 h, the *N*-substituted indole was isolated in 51% yield as the sole product but heating under reflux for 3 h gave 100% yield of the *N*-unsubstituted indole.

6 Electrophilic Cyclisation

A useful synthesis of 3-iodoindoles **66** is the iodocyclisation, which is synthetically useful as the product can undergo further cross-coupling reactions to form a wide variety of functional derivatives. In 1977 iodocyclisation was achieved by treating N,N-dimethyl-2-(p-tolylethynyl)aniline with HI in tetrachloromethane, and based on this it

was shown that *N*,*N*-dialkyl-2-(1-alkynyl)anilines form 3-iodoindoles with iodine in dichloromethane in under 2 h at room temperature, with addition of $Na_2S_2O_3$ to decompose the triiodide salt.⁶¹⁻⁶³ This procedure is very versatile, accommodating many different functional groups on both the aromatic ring and the alkyne.



Depending on the nature of substituents on the nitrogen, different ratios of products **65** and **66** are formed. In the case of $R^3 = n$ -Bu, the methyl group will preferentially leave, giving a ratio of products of about 1.7:1, depending on the nature of R^1 . When $R^3 =$ cyclohexyl, the cyclohexane will prefentially leave to give a mixture of **65** and **66** in a ration of 9:1 and finally when $R^3 =$ Ph, methyl is lost in the form of methyl iodide and only *N*-phenylindole is observed.

The subsequent synthesis of 3-substituted indoles by palladium cross-coupling reactions has also been achieved, demonstrating the extra functionality that can be introduced to **67** by this method.



Iodocyclisation has also been achieved using *N*-tosyl-alkynylanilines **68** and treating them with iodine and anhydrous potassium carbonate.⁶⁴ It was also demonstrated that *N*-Boc can be used under the same reaction conditions to give the desired indole, however the reaction times were significantly longer at 24 h.



7 Radical Cyclisation

Radical cyclisation is of particular interest, although examples of direct bond formation between nitrogen and C-2 of an alkyne have not been found. An interesting example is the cyclisation of *N*-[2-(1-alkynyl)phenyl]ketenimines *via* biradical formation ending in either quinolines and/or 5*H*-benzo[*b*]carbazoles depending on the nature of the substituent on the alkynyl terminus.^{65,66} The reaction started from *o*-alkynylanilines **69** which were reacted with PPh₃Br₂ to give iminophosphoranes **70** which in turn are treated with diphenylketene undergoing a aza-Wittig reaction to form N-[2-(1-alkynyl)phenyl]ketenimines **71**. In a one-pot synthesis, 1,4-cyclohexadiene is added and depending on the nature of the R¹ substituent either quinolines **72** and/or 5*H*-benzo[*b*]carbazoles **73** are formed.



Another method of indole synthesis *via* radical intermediates is to start from an isonitrile-alkyne 74.^{67,68} This was to give the potential of introducting further functionalisation to the indole.



The presence of TMS at the alkyl is useful as it is then possible to introduce further functional variation to the indole. The example **75** shown is important as it can form a C-3 spiro compound by exposure to 4 Å MS in the presence of aldehyde giving **76**.



An interesting example of radical cyclisation to form indoles involves treating arenediazonium salts **77** with the electron donor tetrakis(dimethylamino)ethylene (TDAE).⁶⁹ The intermediate formed undergoes a 5-exo-*trig*-cyclisation to give **78** which then either gives the exocyclic alkene **79** directly by loss of a bromine atom or by loss of bromide followed by gain of an electron. Alkene **79** then undergoes tautomerisation in trace amounts of acid to give the desired indole **80** in 68% yield.



8 Electrochemical Cyclisation

An interesting development has been the use of electrochemical technology in the synthesis of indoles.⁷⁰ This technique is particularly valuable due to the limited environmental impact. The procedure involves the use of electrogenerated bases, in particular in this case cyanomethyl anion formed from the acetonitrile used as solvent. The electroyses were carried out using a supporting electrolyte solution, tetraethylammonium tetrafluoroborate (TEATFB) [CH₃CN/0.1 M TEATFB] in a divided cell equipped with platinum electodes under galvanostatic control (J = 25 mAcm⁻²) at 0 °C. During the optimisation it was discovered that the electricity supplied during the electrolysis (Q, Q= 2.5 Fmol⁻¹) and the temperature for the following cyclisation (rt or 80 °C) had effects on the outcome of the reaction. By adding 2-alkynylanilines at the end of the electrolyses sensitive functionality can be protected.



 R^1 = H, CO₂Et R^2 = H, aromatic, α,β-unsaturated acyl groups, 4ry C

This proved to be a very versatile synthetic procedure tolerating many different functional groups and giving produts **81** in yields from 60–97%. In the cases of $R^2 = Ph$ and 4-phenylcyclohex-1-enyl, no cyclisation was observed but with the introduction of the protecting group (CO₂Et) these cases gave yields of 92 and 78% respectivly. Another interesting is example where $R^1 = R^2 = H$. When no protecting group is in place ($R^1 = H$) the triple bond is reduced to the vinyl derivative but the desired indole product is obtained in 95% yield with the protecting group.

9 Indoles in Natural Products

Derivatives of indole were of interest mainly as dyestuffs until the late 19th and early 20th centrury when the study of indoles was directed towards natural products. Although indole and indigo are both natural products it was not until the isolation of the amino acid tryptophan **82** in 1901 by the hydrolysis of casein,⁷¹ that the importance of these compounds started to be fully understood. As one the essential amino acids, tryptophan **82** plays a number of important roles in the body, one of which is in the synthesis of the neurotransmitter, serotonin **83**.⁷² Serotonin is a vital componant for the normal function of the central nervous system and is involved in the the maintenance of mood, muscle contraction and many other bodily functions. This has made the regulation of serotonin of specific interest in drug development, mainly looking at the interaction of molecules binding to specific reuptake receptors aiming to increase or decrease the quantity of serotonin in the synaptic cleft, for expamle in the treatment of depression.



Many different natural products contain the basic indole structure. One group is the indolo[2,1-*a*]isoquinolines such as cryptaustoline, which have been found in the bark of *Cryptocarya bowiei*. The synthesis of indolo[2,1-*a*]isoquinolines has been achieved by radical cyclisation of 2'-bromobenzyl-3,4-dihydroisoquinolines **84** using AIBN and Bu₃SnH, however this gave a mixture of the desired product **85** and aporphine **86**.⁷³ This was overcome be replacing radical cyclisation with base cyclisation to give exclusively **87**.



A recent development in the treatment of inflammatory pain is the antagonism of EP_1 receptors.⁷⁴ This is an area that has been investigated by Hall and a series of effective antagonistic compounds have been developed. An example of such a compound **88** is

shown, and it was thought that an internal hydrogen bond could be involved, which could be mimicked by the indole scaffold in **89**.



The most successful candidate was for $R^1 = t$ -Bu, $R^2 = Cl$.

Another interesting example of an indole-based natural product is Eustifoline-D, **90**, which has been isolated from the root bark of *Murraya euchrestifolia*⁷⁵. This shrub is found in Taiwan and has been used in folk medicine as an analgesic and local anaesthetic for a number of ailments, including eczema, rheumatism, toothache, and as an anticonvlusant.⁷⁶



It has been shown that cruciferous vegetables contain a substance called glucobrassicin which, during metabolism, forms indole-3-carbinol **91** and 3,3'-diindolylmethane **92**. These compounds have been found to cause cell apoptosis in breast cancer and are thought to have some potential as a preventive and/or cure for prostate cancer.⁷⁷



Carbazole derivatives have been reported to have interesting biological effects, including antibiotic **93**,⁷⁸ cytotoxic agent **94**,⁷⁹ antiviral compound **95**,⁸⁰ antitumour compound **96**⁸¹ and anti-HIV compound **97**.⁸²



B Quinolines

1 Historical Background

Quinolines were first discovered by Runge in 1834, who distilled coal tar and gave the substance the name Leukol.⁸³ Then in 1842 Gerhardt discovered "chinolein" or "chinolin" by alkaline distillation of quinine, cinchonine and strychnine.⁸⁴ However, it was not until 1882 that Hoogewerff and von Dorp determined that these two compounds were in fact the same. ⁸⁵ This was achieved by looking at the physical properties of the compounds and the formation of salts and derivatives. The structure of the compound was confirmed through two different syntheses. The first was by Koenigs and involved passing allylaniline, **98** over glowing lead oxide to give quinoline, **99**.⁸⁶



The second was by Baeyer, starting from nitrocinnamaldehyde, 100.87



As for the synthesis of indoles, this review will focus on the synthesis of quinolines by the formation of the C-N bond *via* an *o*-alkynylarylamine. The difference in the volume of publications in this area from the indoles is dramatic, with very few publications predating 1996 and suprisingly few thereafter.

2 Palladium Catalysis

As with indoles, quinolines can be synthesised by palladium catalysis.^{88–} 90



This is achieved by starting with an *o*-alkynylarylamine **14**, as with the indole synthesis, and using palladium-catalysed coupling with an aryl- or vinyl- halide and carbon monoxide to form the arylketone **101**. This can be synthesised and isolated as an intermediate or converted directly into **102** and **103**.⁸⁹

Another method for the synthesis of quinolines using a palladium catalyst involves ionic liquids.^{64,91} This involves a tandem hydroarylation/ cyclisation process to form 3- or 4- substituted quinolines **104** and **105**, with the major product in each case being the 3-substituted quinoline. The ionic liquid used was 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) which "immobilised" the active palladium catalyst making recycling possible. When Ar = p-iodoanisole, yields vary from 89–86% with a low of 70% over 6 cycles. Over the same duration when Ar = ethyl *p*-iodobenzoate yields drop progressively from 77–58%. The catalyst used was L= [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene], Pd(0)L complex.



3 Radical Cyclisation

Cyclisation of benzannulated enyne-ketenimines, **106** occurs at mild temperatures to form the quinoline biradicals **107**, which can undergo hydrogen atom abstraction from 1,4-cyclohexadiene to form quinolines like **108**. However, as previously mentioned, dependent on the nature of R^1 , indole formation may also be observed.^{66,92} The quinoline is preferentially formed when R^1 = H or Pr.



A similar cyclisation can also occur using isonitrile **74** and a base at room temperature.⁹³



Quinolinones can also be synthesised *via* a radical intermediate. This can be achieved by treating *o*-alkynylarylamine **14** with triphosgene in triethylamine. By exposing **109** to high temperatures, 230 °C, with γ -terpinene, quinolinone **110** was obtained.⁹²



4 Nucleophilic Addition

A versatile approach to the synthesis of quinolines is cyclisation using nucleophiles. It is possible to synthesise 2,3- and 2,4-disubstituted quinolines by way of nucleophilic addition. When an arylketone **111** is stirred with a nucleophile, a conjugated addition (enaminone) intermediate, **112**, is formed before cyclisation to give 2,4-disubstituted quinolines, **113**.^{94,95}



This can give rise to wide variety of products, particularly when the nucleophile is sodium iodide as the product can then undergo palladium cross-coupling reactions.

Typical reaction conditions called for a maximum reaction temperature of 80 °C, however when this was applied to nitrogen nucleophiles the reaction stopped at the enaminone intermediate state. When toluene was used, the higher refluxing temperature allowed the reaction to run to completion. This is a very flexible procedure, showing good results for primary amines and under acidic conditions secondary amines and *N*,*N*-unsubstituted amidines. However, when an electron withdrawing group is present on the α position of a primary amine the starting material was recovered.

When starting with *o*-alkynylisocyanobenzenes, **74**, and stirring with a nucleophile produces the 2,3-disubstituted quinoline, **114**.⁹⁶ In the case of R^1 = TMS, TMS is removed during the reaction process.



R¹= TMS, *t*-Bu, *c*-Hex, CH₂OMe, Ph, 1-*c*-hexenyl

By using a deuterated nucleophile, NuD, a mechanism for this reaction has been proposed, suggesting that the cyclisation to give **115** following from the reversible attack of the nucleophile may well be the driving force in the ordinarily unfavourable addition of alcohols and amines to isonitriles.



5 Miscellaneous Syntheses

It has recently been reported that it is possible to synthesise 2,4-dichloroquinoline, **116** *via* an acetonitrile-mediated process.⁹⁷



The mechanism for this reaction is as follows:



6 Quinolines in Natural Products

The quinoline structure is found in many natural sources and has become the basis for rational drug design. Probably the most well known of these is cinchona bark, famous for the treatment of malaria. One of the legends of the discovery was that South American Indians noticed that sick mountain lions chewing on the bark of certain trees subsequently recovered. When the bark was given to malaria patients they also recovered. The

cinchona bark was given as a treatment for malaria for hundreds of years, usually ground up into a powder and taken with wine due to the bitter taste. It was not until 1820 that the active compound, quinine, **117**, in the bark was isolated by French chemist, Joseph Pelletier⁹⁸ Since this isolation, quinine has been a model for antimalarial drugs and many different derivatives have been developed.



Chloroquine (Resochin), **118**, was developed at Bayer in Germany and became the more popular method of treatment after malarial parasites started to show resistance to quinine.⁹⁹



However, resistance to chloroquine also became a major problem¹⁰⁰ and other drugs were developed. The structures of some are shown: mefloquine, **119**^{101,102} and primaquine, **120**.^{103,104}



Quinolines are also present in many other types of drugs, for example antidepressants, such as quipazine 121,¹⁰⁵ agents to treat coccidia in animals, such as cyproquinate 122,¹⁰⁶ and antibacterials, such as the oxolinic acids, 123.¹⁰⁷



C Flash Vacuum Pyrolysis (FVP)

Pyrolysis as a technique in synthesis has been has been in use since the early 18th century when the vapour of an organic compound was passed through a red-hot porcelain or iron tube¹⁰⁸ an example being formation of phenanthridine from benzylideneaniline.¹⁰⁹ As the desire to examine the effect of pyrolysis on more complex molecules increased, balancing the high activation temperatures with low pressures was desirable and flash vacuum pyrolysis (FVP) was developed. By applying a vacuum to the pyrolysis system the contact time of the organic vapour with the hot tube was also decreased. Diagram **1** shows a typical flow system of modern FVP equipment. The organic compound to be examined is measured into the inlet tube which is then connected to the quartz tube running through the furnace. In turn the quartz tube is then connected to a U-shaped trap cooled by liquid nitrogen, which is connected to the vacuum system. A line for nitrogen gas is also available for air-sensitive materials. Once the furnace is at the desired temperature, the vacuum is applied and the inlet heater is turned on and heated slowly to the desired temperature. As the starting material sublimes it is drawn through the furnace where it reacts and the products are collected in the cold trap.



Diagram 1.

FVP has become a very useful technique in organic synthesis and has a wide range of applications.¹¹⁰ Following are some examples to hightlight the versatility of FVP.



Pyrrolone 125 can be synthesised by starting from aminoalkylidene Meldrum's acid 124 and exposing to FVP conditions at 600 $^{\circ}$ C.¹¹¹



When starting from 2,4-diphenyl-1,3-oxathiolan-5-one under the same FVP conditions described above 2,3-diphenylthiirane **127** is obtained in a good yield of 91%.¹¹²



The fully substituted benzoyl chloride **128** loses HCl to give 3,4,5,6-tetramethyl benzocyclobutenone in a good yield of 83%.¹¹³

One reaction of particular relevance to the current work is elimination of Ph_3PO from β -keto phophonium ylides.¹¹⁰



This provides a versatile synthesis of alkynes, **129**, which depending on the groups R^1 and R^2 can often undergo further transformations.

D Programme of Research

Previous work in this laboratory has focused on the synthesis of benzofurans and benzothiophenes from stabilised phosphonium ylides *via* flash vacuum pyrolysis. It was first discovered that pyrolysis of ylides **130** bearing an *o*-methoxy- or *o*-methylthiophenyl group at 700 °C led to the expected loss of Ph₃PO to give alkynes **131** but, upon increasing the pyrolysis temperature to 850 °C, this was accompanied by loss of methyl radical and cyclisation to give benzofurans and benzothiophenes **132**. ^{114,115}



For $R^1 = Ph$, the product **132** was formed with $R^2 = Ph$ by intermolecular hydrogen atom abstraction, while for simple alkyl groups R^1 , intramolecular hydrogen atom abstraction led to products **132** with $R^2 =$ methyl, ethyl and vinyl. The isomeric ylides **133** were found to behave similarly and this allowed a wider variety of groups R^1 to be used.¹¹⁶

This was exploited in later studies where an R^1 group suitable for tandem cyclisation such as styryl was incorporated and ylides such as **134** were indeed found to produce the tetracyclic product **135** upon FVP providing the first example of tandem cyclisations in these systems.^{117,118}



This approach was then extended to a wide variety of ylides **136** which were found to undergo efficient tandem cyclisation by the mechanism shown, providing access to a wide range of tetracyclic heteroaromatic products **137**.^{119–121} However, all these examples involved O or S as the cyclising atom.



The objective of the current research was to examine the extension of this approach to cyclisations involving a nitrogen atom. The would potentially lead to substituted indoles and ring-fused carbazoles, which as described in section A of this introduction are of considerably more importance and recent interest than the corresponding O- and S- containing heterocycles.

Initial studies would involve identifying a suitable protecting group for the nitrogen during the formation of the stabilised ylides, which would ideally also be a good leaving group under the FVP conditions.
EXPERIMENTAL

A Instrumental and General Techniques

1. Nuclear Magnetic Resonance (NMR) Spectroscopy

¹H NMR, ¹³C NMR, ³¹P NMR – Spectra were recorded in CDCl₃ on Bruker Avance 300 and Bruker Avance II 400 spectrometers. Chemical shifts are expressed in parts per million to high frequency of the reference, internal TMS (H and C) or external H₃PO₄ (P) and coupling constants are given in Hz.

2. Melting Points (mp)

All melting points were taken using Gallenkamp melting point apparatus.

3. Thin Layer Chromatography

This was carried out using 0.20 mm layer of silica (Merck, Kieselgel $60F_{254}$) on aluminium sheets. The components were observed under ultraviolet light.

4. Preparative Thin Layer Chromotography

This was carried out using 1.0 mm layers of silica (Merck, Kieselgel 60–80 mesh), containing 0.5% Woelm fluorescent green indicator, on glass plates. After locating the components with ultraviolet light, the bands were scraped off and the products removed from the support by soaking in dichloromethane for 20 mins.

5. Column Chromatography

The separation by column chromatography was carried out using silica gel of $33-70 \ \mu m$ particle size.

6. Kugelrohr Distillation

Thiw was carried out using a Büchi model GKR-50 apparatus.

7. Mass Spectra

Mass spectra were obtained on a Micromass GCT mass spectrometer using electrospray (ES) unless otherwise stated.

8. Infrared (IR)

Infrared spectra were recorded on a Perkin Elmer 1420 instrument. Solids were run as Nujol mulls and liquids as thin films.

9. Flash Vacuum Pyrolysis (FVP)

This was carried out in a conventional flow system by subliming the starting material through a horizontal quartz tube $(30 \times 2.5 \text{ cm})$ externally heated by a tube furnace to 700 °C or 800 °C and maintained at a pressure of $2-3 \times 10^{-2}$ torr by a rotary vacuum pump, see Diagram **1** (Page 43). Products were collected in a liquid N₂ cooled U-shaped trap and purified as noted.

10. Drying Solvents and Organic Solutions.

Tetrahydrofuran was predried with sodium wire and purified by passage through active dry silica. Organic solutions were dried using anhydrous MgSO₄.

B Synthesis of Model Ylides

1 Preparation of 2-(*N*-Methylamino)benzoic acid, 147

To a solution of sodium carbonate (7.73 g, 72.9 mmol) in water (100 cm³), 2aminobenzoic acid, **146** (20.0 g, 145.8 mmol) was added with stirring. Methyl iodide (24.83 g, 10.89 cm³, 174.9 mmol) was added to the stirred solution, which was then heated under reflux for 4 h. The solution was cooled and the product filtered off and oven dried to give the title product **147** (17.03 g, 77%) as a yellow powder, mp 167–168 °C (Lit.,¹²² 166–168 °C); $\delta_{\rm H}$ 7.99 (1H, d, *J* 8, 6-H), 7.43 (1H, t, *J* 8, 4-H), 6.70 (1H, d, *J* 8, 3-H), 6.63 (1 H, t, *J* 8, 5-H) and 2.94 (3 H, s, Me).

2 Preparation of 2-(N-Methyl-N-p-toluenesulfonylamino)benzoic acid, 148

To an aqueous solution of sodium hydroxide (2 M, 50 cm³), acid **147** (10 g, 72.9 mmol) was added while stirring at 60–70 °C. Once dissolved, *p*-toluenesulfonyl chloride (22.0 g, 115.4 mmol) was added in four equal portions while the mixture was stirred over 4 h. The mixture was filtered and the filtrate acidified using hydrochloric acid and the resulting precipitate was filtered off and dried to give **148** (13.29 g, 60%) as a yellow solid, mp 159–160 °C (Lit.,¹²³ 159 °C); $\delta_{\rm H}$ 8.01 (1 H, d, *J* 9, 6-H), 7.57(2 H, d, *J* 9, Ts), 7.47–7.44 (2 H, m, 4,5-H), 7.29 (2 H, d, *J* 9, Ts), 6.93 (1 H, d. *J* 9, 3-H), 3.28 (3H, s, NMe) and 2.42 (3H, s, ArMe).

3 Preparation of 2-(N-Methyl-N-p-toluenesulfonylamino)benzoyl chloride, 149

The acid **148** (5.00 g, 16.4 mmol) was added to thionyl chloride (10.0 cm³) which was heated under reflux for 5 h. The excess of thionyl chloride was evaporated off to give **149** (5.23 g, 99%) as a pale yellow solid, mp 93–94 °C (Lit.,¹²⁴ 88–90 °C); $\delta_{\rm H}$ 7.99 (1 H, d, *J* 8, 6-H), 7.54–7.42 (4 H, m, Ts, 5-H, 4-H), 7.28 (2 H, d, *J* 8, Ts), 6.94 (1 H, d, *J* 8, 3-H), 3.23 (3 H, s, NMe) and 2.44 (3 H, s, ArMe).

4 Preparation of [1-(2-(*N*-Methyl-*N-p*-toluenesulfonylamino)benzoyl)-1propylidene]triphenylphosphorane 154

A suspension of propyltriphenylphosphonium bromide, **150** (6.19 g, 16.1 mmol) in THF (50 cm³) was stirred under nitrogen while a solution of BuLi in hexanes (6.44 cm³, 2.5 M, 16.1 mmol) was added. The resulting brightly coloured solution was stirred for 2 h and a solution of acid chloride **149** (2.60 g, 8.1 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (50 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2×50 cm³). The combined extracts were washed with water, dried and evaporated. The resulting solid was recrystallised (Et₂O/EtOAc) to give **154** (1.58 g, 31%) as yellow crystals, mp 198–199 °C (Found:

M⁺+Na, 614.1885. C₃₆H₃₄NaNO₃PS (M^+ +Na) requires, 614.1895); v_{max} /cm⁻¹ 1493 (CO), 1377 (SO₂) and 1162 (SO₂); δ_{H} 7.86–7.76 (8 H, m, Ar), 7.59–7.45 (10 H, m, Ar) 7.32 (2 H, d, J 8, H-2 or 3 of Ts), 7.26 (1 H, d, J 8, H-6), 7.10 (1 H, td, J 8, 2, H-4), 6.65 (1 H, d, J 8, H-3), 3.26 (3 H, s, NMe), 2.46 (3 H, s, ArMe), 1.68 (2 H, q, J 7, CH₂CH₃) and 0.63 (3 H, t, J 7, CH₂CH₃); δ_{C} see Table **1** (Page 103); δ_{P} +17.8; m/z (ES⁺) 614.03 (M⁺+Na, 100 %)

5 Preparation of [1-(2-(*N*-Methyl-*N-p*-toluenesulfonylamino)benzoyl) benzylidene]triphenylphosphorane, 155

This was prepared as in 4. using benzyltriphenylphosphonium bromide, **151** (6.26 g, 16.1 mmol), BuLi in hexanes (6.44 cm³, 2.5 M, 16.1 mmol) and acid chloride **149** (2.60 g, 8.1 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **155** (2.23 g, 43%) as pale yellow crystals, mp 213–214 °C (Found: M⁺+Na, 662.1879. C₄₀H₃₄NaNO₃PS (M^+ +Na) requires, 662.1895); v_{max} /cm⁻¹ 1496 (CO), 1342 (SO₂) and 1154 (SO₂); δ_{H} 7.87–7.67 (8 H, m), 7.53–7.37 (9 H, m), 7.30 (2 H, d, *J* 8, H-2 or 3 of Ts), 7.20 (1 H, d, *J* 8, H-6 of Ar), 7.14 (2 H, d, *J* 8, H-2 or 3 of Ts), 6.99–6.88 (2 H, m), 6.87–6.74 (3 H, m), 6.43 (1 H, d, *J* 8, H-3 of Ar), 3.15 (3 H, s, NMe) and 2.46 (3 H, s, ArMe); δ_{C} see Table **1** (Page 103); δ_{P} +17.4; *m/z* (ES⁺) 662.14 (M⁺+Na, 100%).

6 Preparation of Methyl 2-(N-methyl-N-p-toluenesulfonylamino)benzoate, 159

2-(*N*-Methyl-*N*-*p*-toluenesulfonylamino)benzoic acid, **148** (10.0 g, 32.70 mmol) and potassium acetate (9.32 g, 94.9 mmol) were stirred in DMF (50 cm³) for 20 min and dimethyl sulfate (3.41 cm³, 36.0 mmol) was added. The mixture was stirred for 30 min and then heated to 60 °C and stirred for a further 30 min. The mixture was then poured into water (60 cm³) and extracted with diethyl ether (2 × 60 cm³) and the combined extracts were washed with water (100 cm³), dried and evaporated. Recrystallisation of the residue (MeOH) gave **159** (5.04 g, 48%) as a colourless solid, mp 95–96 °C (Lit.,¹²⁵ 97–98 °C); $\delta_{\rm H}$ 7.85 (1 H, d, *J* 4, 6-H), 7.53 (2 H, d, *J* 4, Ts), 7.42–7.37 (2 H, m, 4,5-H), 7.26 (2 H, d, *J* 4, Ts), 6.91 (1 H, d, *J* 4, 3-H), 3.85 (3 H, s, OMe), 3.26 (3 H, s, NMe) and 2.43 (3 H, s, ArMe).

7 Preparation of 2-(N-Methyl-N-p-toluenesulfonylamino)benzyl alcohol, 160

Under a nitrogen atmosphere, a solution of ester **159** (11.0 g, 34.4 mmol) in dry THF (100 cm³) was added dropwise to a stirred suspension of LiAlH₄ (1.44 g, 37.8 mmol) in dry THF (15 cm³) and the resulting mixture was heated under reflux for 4 h. To destroy the excess of LiAlH₄, water (1.5 cm³) in THF (10.5 cm³) was added to the mixture followed by 15% solution sodium hydroxide (1.5 cm³) and finally water (4.5 cm³). The suspension was stirred for 0.5 h and extracted using Et₂O (2 × 80 cm³) which was washed with water, dried and evaporated to give **160** (9.10 g, 90%) as colourless prisms, mp 124–125 °C; v max/cm⁻¹ 3400–3200 (OH), 1340 (SO₂) and 1172 (SO₂); $\delta_{\rm H}$ 7.59 (1 H, d, *J* 8, 6-H), 7.54 (2 H, d, *J* 8, H-2 or 3 of Ts), 7.35–7.29 (3 H, m, 5-H, H-2 or 3 of Ts), 7.14 (1 H, t, *J* 8, 4-H), 6.46 (1 H, d, *J* 8, 3-H), 4.98 (1 H, br s, CH*H*OH), 4.61 (1 H, br s, CH*H*OH), 3.21 (1 H, s, OH), 3.15 (3 H, s, NMe) and 2.46 (3 H, s, ArMe); $\delta_{\rm C}$ 144.5 (4ry, C-2), 141.6 (4ry, C-1), 139.9 (4ry, C-1 or 4 of Ts), 133.7 (4ry, C-1 or 4 of Ts), 131.5 (CH), 123.0 (2C, C-2 or 3 of Ts), 129.4 (CH), 128.8 (CH), 128.7 (2C, C-2 or 3 of Ts), 126.7 (CH), 61.6 (CH₂OH), 39.9 (NMe) and 22.0 (ArMe); *m*/z (ES⁺) 314 (M+Na⁺, 100 %).

8 Preparation of 2-(*N*-Methyl-*N-p*-toluenesulfonylamino)benzyltriphenyl phosphonium bromide, 157

A solution of alcohol **160** (9.10 g, 31.1 mmol) in toluene (100 cm³) was stirred with phosphorus bromide (1.43 cm³, 15 mmol) at room temperature for 18 h. The mixture was added to water (100 cm³) and the organic layer separated, washed with water and dried. The dried organic solution was heated under reflux with triphenylphosphine (8.26 g, 31.5 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to give **157** (13.22 g, 68%) as a colourless solid, mp 251–252 °C; (Found: C, 64.4; H, 5.9; N, 2.0. C₃₃H₃₁BrNO₂PS requires C, 64.3; H, 5.1; N, 2.3%); ν_{max}/cm^{-1} 1621, 1363 (SO₂), 1159 (SO₂), 1197 and 939; $\delta_{\rm H}$ 7.89–7.71 (3 H, m), 7.69–7.57 (6 H, m), 7.66–7.57 (6 H, m), 7.47–7.32 (1 H, m), 7.35–7.23 (4 H, m), 7.21–7.15 (2 H, m), 6.31 (1 H, m), 5.67 (1 H, t, *J* 14, CH*H*PPh₃), 5.10 (1 H, t, *J* 14, CH*H*PPh₃), 2.44 (3 H, s, NMe) and 2.26 (3 H, s, ArMe); $\delta_{\rm C}$ 144.7 (4ry, C-2 of Ar), 141.4 (4ry, d, *J* 6, C-1), 135.4 (3 C, d, *J* 3, C-4 of PPh₃), 134.3 (6 C, d, *J* 10, C-2 of PPh₃), 133.1 (d, *J* 5, CH of Ar), 131.2 (4ry, C-1 or 4 of

Ts), 130.5 (6 C, d, *J* 13, C-3 of PPh₃), 129.7 (d, *J* 4, CH of Ar), 129.5 (2C, C-2 or 3 of Ts), 129.1 (d, *J* 3, CH of Ar), 128.5 (2C, C-2 or 3 of Ts), 128.4 (4ry, C-1 or 4 of Ts), 126.5 (d, *J* 3, CH of Ar), 117.4 (3C, d, *J* 86, C-1 of PPh₃), 38.5 (NMe), 27.3 (d, *J* 49, CH₂PPh₃) and 21.6 (ArMe); δ_P +24.0; *m*/*z* (ES⁺) 536 (M⁺–Br, 100 %).

9 Preparation of [α-Benzoyl-2-(*N*-methyl-*N*-*p*-toluenesulfonylamino) benzylidene]triphenylphosphorane, 158

This was prepared as in 4. using salt **157** (2.5 g, 4.05 mmol), butyllithium in hexanes (1.78 cm³, 2.5 M, 4.46 mmol) and benzoyl chloride (0.26 cm³, 2.28 mmol). The resulting solid was recrysallised (Et₂O/EtOAc) to give the title product **158** (0.15 g, 5%) as bright yellow crystals, mp 221–222 °C (Found: C, 74.6; H, 5.2; N, 2.15. C₄₀H₃₄NO₃PS requires C, 75.1; H, 5.4; N, 2.2%); v_{max} /cm⁻¹ 1502 (CO), 1344 (SO₂), 1171 (SO₂); δ_{H} (55 °C) 7.87 (4 H, br s), 7.73–7.64 (2 H, m), 7.49–7.31 (12 H, m), 7.17 (2 H, d, *J* 8), 7.09–6.99 (3 H, m), 6.89–6.81 (1 H, m), 6.78–6.71 (2 H, m), 6.43 (1 H, d, *J* 8, H-3 of Ar), 2.39 (3 H, s, NMe) and 1.80 (3 H, s, ArMe); δ_{C} see Table **1** (Page 103); δ_{P} +17.4; *m/z* (ES⁺) 662 (M⁺+Na, 100%) and 640 (M⁺+H, 70%).

10 Preparation of Methyl 2-(N-methanesulfonylamino)benzoate, 163

Triethylamine (20.09 g, 27.67 cm³, 198.5 mmol) was added to a stirred solution of methyl 2-aminobenzoate **164** (30.00 g, 18.07 cm³, 198.5 mmol) in diethyl ether (80 cm³) cooled to 0 °C. Methanesulfonyl chloride (22.74 g, 15.36 cm³, 198.5 mmol) in ethyl acetate (110 cm³) was slowly added dropwise to the solution. After stirring at 0 °C for 0.5 h, the mixture was allowed to warm to room temperature and stirred for 8 h. Water (150 cm³) was added and the mixture was extracted with ethyl acetate (2 × 75 cm³) and the combined extracts were washed with water, dried and evaporated. Recrystallisation of the residue (MeOH) gave the title product **163** (30.77 g, 68%) as colourless crystals, mp 88–89 °C (Lit., ¹²⁶ 91–92 °C); $\delta_{\rm H}$ 10.47 (1 H, s, NH), 8.07 (1 H, d, *J* 8, H-6), 7.75 (1 H, d, *J* 8, H-3), 7.56 (1 H, t, *J* 8, H-4), 7.13 (1 H, t, *J* 8, H-5), 3.94 (3 H, s, OMe) and 3.07 (3 H, s, SO₂Me).

11 Preparation of Methyl 2-(N-methanesulfonyl-N-methylamino)benzoate, 166

Sodium hydride (60% dispersion in oil) (2.6 g, 65.4 mmol) was washed with hexane (30 cm³) and DMF (30 cm³) was added. The resulting suspension was stirred while a solution of ester **163** (10.0 g, 43.6 mmol) in DMF (100 cm³) was added. The solution was stirred for 45 min and then a solution of methyl iodide (18.9 g, 8.31 cm³, 130.8 mmol) in diethyl ether (120 cm³) was added and the mixture stirred for 72 h. The mixture was cooled and acidified with HCl. The solution was added to water (150 cm³) and extracted with diethyl ether (4×100 cm³). The combined extracts were washed with water, dried and evaporated and the resulting yellow oil was triturated with diethyl ether (150 cm³) to give **166** (5.83 g, 55%) as a colourless crystalline solid, mp 55–56 °C (Lit., ¹²⁶ 55.5–58 °C); $\delta_{\rm H}$ 7.91 (1 H, d, *J* 8, H-6), 7.56 (1 H, t, *J* 8, H-4), 7.48–7.38 (2 H, m, H-3,5), 3.93 (3 H, s, OMe), 3.31 (3 H, s, NMe) and 2.97 (3 H, s, SO₂Me).

12 Preparation of 2-(N-Methanesulfonyl-N-methylamino)benzyl alcohol, 167

Under a nitrogen atmosphere, a solution of ester **166** (64.13 g, 300 mmol) in dry THF (250 cm³) was added drop wise to a stirred suspension of LiAlH₄ (5.49 g, 144.5 mmol) in dry THF (50 cm³) and the resulting mixture was heated under reflux for 4 h. To destroy the excess of LiAlH₄, water (5.5 cm³) in THF (38.5 cm³) was carefully added to the mixture followed by 15% solution sodium hydroxide (5.5 cm³) and finally water (15 cm³). The suspension was stirred for 0.5 h and extracted using diethyl ether (2 × 200 cm³) and the combined extracts were washed with water, dried and evaporated to give **167** (51.74 g, 92%) as a pale yellow oil (Found: M⁺+Na, 238.0506. C₉H₁₃NaNO₃S (*M*⁺+Na) requires, 238.0514); v_{max}/cm^{-1} 3372–3198 (OH), 1345 (SO₂) and 1172 (SO₂) $\delta_{\rm H}$ 7.58 (1 H, d, *J* 8, H-6), 7.41–7.36 (2 H, m, H-4,5), 7.27 (1 H, d, *J* 8, H-3), 4.72 (1 H, br s, CH₂OH), 3.35 (1 H, br s, CH₂OH), 3.24 (3 H, s, NMe) and 2.95 (3 H, s, SO₂Me); $\delta_{\rm C}$ 140.8 (4ry, C-2 of Ar), 138.7 (4ry, C-1 of Ar), 130.0 (CH of Ar), 128.7 (CH of Ar), 128.5 (CH of Ar), 126.1 (CH of Ar), 60.4 (CH₂OH), 38.8 (NMe) and 35.3 (SO₂Me); *m/z* (ES⁺) 238.10 (M⁺+Na, 100%).

13 Preparation of 2-(*N*-Methanesulfonyl-*N*-methylamino)benzyltriphenyl phosphonium bromide, 168

A solution of alcohol **167** (14.30 g, 66.4 mmol) in toluene (100 cm³) was stirred with phosphorus tribromide (49.39 g, 14.52 cm³, 153.0 mmol) at rt for 18 h. The mixture was added to water (70 cm³) and the organic layer separated, washed with water (2×50 cm³) and dried. The dried organic solution was heated under reflux with triphenylphosphine (17.45 g, 66.5 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to give **168** (33.45 g, 93%) as a colourless solid, mp 260–261 °C (Found: C, 59.9; H, 5.1; N, 2.5. C₂₇H₂₇BrNO₂PS requires C, 60.0; H, 5.0; N, 2.6%); v_{max}/cm⁻¹ 1335 (SO₂) and 1165 (SO₂); $\delta_{\rm H}$ 7.88–7.80 (3 H, m), 7.73–7.66 (6 H, m), 7.63 (1 H, d, *J* 8), 7.60–7.51 (6 H, m), 7.47 (1 H, tt, *J* 8, 2, H-5 of Ar), 7.29–7.25 (1 H, m), 7.19 (1 H, t, *J* 8, H-4 of Ar), 5.56 (1 H, t, *J* 15, CH*H*PPh₃), 4.92 (1 H, t, *J* 15, CH*H*PPh₃), 2.95 (3 H, s, NMe) and 2.54 (3 H, s, SO₂Me); $\delta_{\rm C}$ 141.6 (4ry, d, *J* 6, C-1 of Ar), 130.7 (d, *J* 3, CH of Ar), 130.5 (6 C, d, *J* 13, C-3 of PPh₃), 129.0 (d, *J* 3, CH of Ar), 128.1 (4ry, d, *J* 8, C-2 of Ar), 127.6 (d, *J* 3, CH of Ar), 117.3 (3 C, d, *J* 86, C-1 of PPh₃), 38.7 (NMe), 34.7 (SO₂Me) and 27.4 (d, *J* 50, CH₂PPh₃); $\delta_{\rm P}$ +23.8; *m*/z (ES⁺) 460 (M⁺–Br, 100%).

14 Preparation of [α-Benzoyl-2-(*N*-methanesulfonyl-*N*- methylamino) benzylidene]triphenylphosphorane, 169

a. This preparation was attempted as in 4. using salt **168** (1.5 g, 2.8 mmol), butyllithium in hexanes (1.24 cm³, 2.5 M, 3.1 mmol) and benzoyl chloride (0.22 g, 0.18 cm³, 1.54 mmol). This procedure did not give the desired product.

b. Sodium hydride (60% dispersion in oil, 0.16 g, 4.07 mmol) was washed with hexane (10 cm³) and THF (50 cm³) was added. To the stirring suspension, salt **168** (2.00 g, 3.7 mmol) was added and the resulting brightly coloured solution was stirred for 2 h. A solution of benzoyl chloride (0.23 cm³, 0.55 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (50 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2×50 cm³). The combined extracts were washed with water, dried and evaporated. The mixture was purified by preparative TLC

(50:50 ethyl acetate:diethyl ether) to give **169** (0.07 g, 3%) as bright yellow solid, mp 221–222 °C (Found: M⁺+H, 564.1771. C₃₄H₃₁NO₃PS (M^+ +H) requires, 564.1765); v max/cm⁻¹ 1502 (CO), 1344 (SO₂) and 1171 (SO₂); $\delta_{\rm H}$ (55 °C) 8.12–8.07 (2 H, m), 7.83 (6 H, m), 7.63–7.36 (9 H, m), 7.23–7.12 (3 H, m), 7.10–7.02 (2 H, m), 6.81–6.74 (1 H, m), 6.71–6.66 (2 H, m), 2.56 (3 H, s, NMe) and 2.08 (3 H, s, SO₂Me); $\delta_{\rm C}$ see Table **2** (Page 103); $\delta_{\rm P}$ +18.3; m/z (ES⁺) 564.00 (M⁺+H, 100%).

The major product isolated was *N*-methanesulfonyl-*N*-methyl-*o*-toluidine **170** (0.28 g, 38%), as colourless crystals, mp 76–77 °C. (Found: M⁺+Na, 222.0567. C₉H₁₃NaNO₂S (M^+ +Na) requires 222.0565); v_{max}/cm^{-1} 1488, 1168, 1348 (SO₂), 1168 (SO₂), 1142, 889 and 156; $\delta_{\rm H}$ 7.32–7.23 (4 H, m, Ar), 3.24 (3 H, s, NMe), 2.97 (3 H, s, SO₂Me) and 2.42 (3 H, s, ArMe); $\delta_{\rm C}$ 139.9 (4ry), 138.5 (4ry), 131.4 (CH), 128.4 (CH), 126.83 (CH), 126.78 (CH), 38.4 (NMe), 36.6 (SO₂Me) and 18.1 (ArMe); m/z (ES⁺) 222.00 (M⁺+Na, 100%).

15 Preparation of *N*-Methanesulfonyl-*o*-toluidine

Pyridine (25 cm³) was added to a stirred solution of *o*-toluidine (5.00 g, 5.00 cm³, 46.7 mmol) in dichloromethane (100 cm³). The solution was cooled to 0 °C and methanesulfonyl chloride (8.03 g, 5.43 cm³, 70.1 mmol) was added slowly over 0.5 h. The mixture was stirred for 1 h at 0 °C then warmed to room temperature and stirred for a further 1 h. It was then poured into a saturated solution of NaHCO₃ (150 cm³) and extracted with dichloromethane (2 × 50 cm³). The combined organic extracts were washed with 5% HCl to remove excess pyridine, dried and evaporated to give the desired product (7.45 g, 86%) as colourless crystals mp 168–170 °C (Lit.,¹²⁷ 174–176 °C); $\delta_{\rm H}$ 7.35 (1 H, d, *J* 8, H-3 or 6), 7.17–7.03 (3 H, m), 2.96 (3 H, s, SO₂Me) and 2.32 (3 H, s, ArMe).

16 Preparation of N-Methanesulfonyl-N-methyl-o-toluidine, 170

Sodium hydride (60% dispersion in oil, 0.95g, 28.33 mmol) was washed with hexane (10 cm³) and DMF (80 cm³) was added. A solution of *N*-methanesulfonyl-*o*-toluidine (3.00 g, 16.19 mmol) in DMF (40cm³) was added to the suspension and it was stirred for 1 h. Methyl iodide (4.69 g, 2.06 cm³, 32.4 mmol) was added and the solution was stirred at room temperature for 18 h. The solution was neutralised using 2 M HCl and extracted

with ethyl acetate (2 × 50 cm³). The combined organic fractions were washed with water, dried and evaporated. The resulting solid was recrystalised (EtOH) to give the title product **170** (2.01 g, 62%) as colourless crystals, mp 77–78 °C; $\delta_{\rm H}$ as in B14b.

C FVP of model ylides

1 FVP of Ylide 154



Ylide **154** (0.2500 g, 0.42 mmol) was subjected to FVP at 700 °C and $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed the presence of Ph₃PO, toluene and 3ethylquinoline **172**. Purification by acid/base extraction gave 3-ethylquinoline **172** (0.0466 g, 71%) as a brown oil; $\delta_{\rm H}$ 8.63 (1 H, d, *J* 2, H-2), 7.97 (1 H, d, *J* 8, H-8), 7.81 (1 H, d, *J* 2, H-4), 7.62 (1 H, d, *J* 8, H-5), 7.51 (1 H, t, *J* 8, H-6) 7.37 (1 H, t, *J* 8, H-5) 2.67 (2 H, q, *J* 8, CH₂) and 1.18 (3 H, t, *J* 8, Me) [good agreement with Lit.¹²⁸].

2 FVP of Ylide 155



Ylide **155** (0.690 g, 1.08 mmol) was subjected to FVP at 700 °C and $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, toluene and 3-phenylquinoline, **175**. Purification by acid/base extraction gave **175** (0.0704 g, 32%) as a brown solid, mp 49–50 °C (Lit.,¹²⁹ 49–52 °C); $\delta_{\rm H}$ 9.19 (1H, d, *J* 2, H-2), 8.32 (1H, d, *J* 2, H-4), 8.15 (1H, d, *J* 8, H-8), 7.90 (1H, d, *J* 8, H-5), 7.78-7.70 (2H, m), 7.63–7.49 (4H, m) and 7.45 (1H, t, *J* 8) [good agreement with Lit.¹³⁰].

3 FVP of Ylide 158

Ylide **158** (0.0338 g, 0.0528 mmol) was subjected to FVP at 700 °C and $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, toluene and **175**. Purification by acid/base extraction gave **175** (0.0031 g, 28%) as a brown solid, mp 49–50 °C (Lit., ¹²⁹ 49–52 °C); $\delta_{\rm H}$ as in C 2.

4 FVP of Ylide 169

Ylide **169** (0.0517g, 0.09 mmol) was subjected to FVP at 700 °C and $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, toluene and **175**. Purification by acid/base extraction gave **175** (0.0065 g, 35%) as a brown solid, mp 49–50 °C (Lit., ¹²⁹ 49–52 °C); $\delta_{\rm H}$ as in C 2.

D Alternative Routes for Preparation of Ylides.

1 Preparation of 2-(*N*-*p*-toluenesulfonylamino)benzoic acid, 178

2-Aminobenzoic acid **146** (8.15 g, 59.5 mmol) was dissolved in 20 % solution of Na₂CO₃ (10 cm³) and *p*-toluenesulfonyl chloride (9.30 g, 48.8 mmol) was slowly added. The solution was stirred for 4 h at room temperature, and then filtered. The filtrate was acidified with HCl and the precipitate filtered off, washed with water (3 × 10 cm³) and dried to give the title product **178** (4.05 g, 23 %) as a colourless crystalline solid, mp 216–217 °C (Lit., ¹³¹ 217–218 °C); $\delta_{\rm H}$ 7.99 (1 H, d, *J* 8, 6-H), 7.76 (2 H, d, *J* 8, H-2 or 3 of Ts), 7.70 (1 H, d, *J* 8, 3-H), 7.49 (1 H, t, *J* 8, 4-H), 7.23 (2 H, d, *J* 8, H-2 or 3 of Ts), 7.06 (1 H, t, *J* 8, 5-H) and 2.37 (3 H, s, ArMe).

2 Preparation of 2-(*N*-methylamino)benzoic acid, 147

Potassium hydroxide (5.60 g, 100 mmol) was added to a stirred solution of 2aminobenzoic acid **146** (13.70 g, 100 mmol) in ethanol (200cm³). Methyl iodide (28.4 g, 12.6 cm³, 200 mmol) was then added and heated under reflux for 4 h. The solvent was evaporated to give the title product **147** (8.24 g, 55%), mp 167–168 (Lit.,¹²² 166–168 °C); $\delta_{\rm H}$ as for B1.

3 Preparation of *N*-Methylisotoic anhydride, 180

Sodium hydride (2.80 g, 72.33 mmol) was washed with hexane (10 cm³) and DMF (100 cm³) was added. The stirred suspension was cooled in an ice bath, keeping the temperature below 5 °C, and isotoic anhydride (10.00 g, 61.3 mmol) was added followed by methyl iodide (11.23 g, 4.90 cm³, 79.1 mmol). The solution was stirred for room temperature for 18 h. Water (50 cm³) was added and the mixture acidified with HCl (2 M). The resulting solid was filtered off and washed with water. The solid was then dissolved in dichloromethane and the solution was dried and evaporated to give the title product, **180** (10.09 g, 93 %) as a white solid, mp 178–179 °C (Lit., ¹³² 180 °C); $\delta_{\rm H}$ 8.67 (1 H, d, *J* 8, H-6), 7.79 (1 H, t, *J* 8, H-4), 7.32 (1 H, t, *J* 8, H-5), 7.20 (1 H, d, *J* 8, H-3) and 3.59 (3 H, s, Me).

4 Preparation of Methyl 2-(*N*-methylamino)benzoate, 179

N-Methylisotoic anhydride, **180** (10.00 g, 56.45 mmol) and sodium hydroxide (0.1128 g, 2.82 mmol) were added to methanol (20 cm³) and heated to 65 °C. Once all gas evolution had ceased, the methanol was evaporated. Dichloromethane (50 cm³) was added to the resulting slurry which was washed with water (2 × 30 cm³). The organic fraction was dried and evaporated to give the desired product, **179** (8.37 g, 90%) as a pale yellow oil; δ _H 7.88 (1 H, d, *J* 8, H-6), 7.75 (1 H, br s, NH), 7.35 (1 H, t, *J* 8, H-5), 6.63 (1 H, d, *J* 8, H-3), 6.56 (1 H, t, *J* 8, H-4), 3.81 (3 H, s, OMe) and 2.87 (3 H, s, NMe).

5 Preparation of Allyl 2-(*N*-allyl-*N*-methylamino)benzoate, 183

Sodium hydride (1.07g 26.8 mmol) was washed in hexane (10 cm³) and DMF (30 cm³) was added. The stirred suspension was cooled in an ice bath, keeping at 5 °C, and ester **179** (3.75 g, 22.7 mmol) was added followed by allyl bromide (3.50 g, 2.50 cm³, 29.28 mmol). The solution was stirred at room temperature for 18 h. Water was added (50 cm³), acidified with HCl (2 M) and extracted with dichloromethane (2×30 cm³). The combined organic fractions were washed with water, dried and evaporated to give an oil which was a complex mixture (¹H NMR). The oil was separated by column

chromatography (1:1 diethyl ether:hexane) to give the title product **183** (0.79 g, 11%) as a light yellow oil; (Found: M⁺+Na, 254.1161. C₁₄H₁₇NaNO₂ (M^+ +Na) requires 254.1157); (Found: M⁺+H, 232.1329. C₁₄H₁₈NO₂ (M^+ +H) requires, 232.1338); δ_H 7.68 (1 H, d, J 8, H-6), 7.34 (1 H, t, J 8, H-5), 6.98 (1 H, d, J 8, H-3), 6.86 (1 H, t, J 8, H-4), 6.11–5.97 (1 H, m, OCH₂CHCH₂), 5.97–5.84 (1 H, m, NCH₂CHCH₂), 5.45–5.24 (2 H, m, OCH₂CHCH₂), 5.24–5.14 (2 H, m, NCH₂CHCH₂), 4.79 (2 H, ddd, J 6, 1, 1, OCH₂), 3.70 (2 H, ddd, J 6, 1, 1, NCH₂) and 2.79 (3 H, s, Me); δ_C 167.9 (4ry, CO), 151.7 (4ry, C-1), 134.6 (CH), 132.3 (CH), 132.1 (CH), 131.3 (CH), 121.8 (4ry, C-2), 119.2 (CH), 118.5 (CH₂), 118.1 (CH), 117.3 (CH₂), 65.4 (OCH₂), 59.3 (NCH₂) and 39.8 (Me); m/z (ES⁺) 254.02 (M⁺+Na, 95%) and 232.05 (M⁺+H, 100%).

6 Preparation of *N*-Allylisotoic anhydride, 181

The procedure as in 3. using sodium hydride (1.43 g, 36.8 mmol, isotoic anhydride (5.00 g, 30.7 mmol) and allyl bromide (3.7 g, 2.65 cm³, 30.7 mmol), gave the title product, **181** (3.89 g, 62%) as a colourless solid, mp 94–96 °C (Lit.,¹³³ 102–104 °C); $\delta_{\rm H}$ 8.17 (1 H, d, *J* 8, H-6), 7.75 (1 H, t, *J* 8, H-4), 7.31 (1 H, t, *J* 8, H-5), 7.18 (1 H, d, *J* 8, H-3), 6.01–5.85 (1 H, m, NCH₂CH), 5.38–5.25 (2 H, m, NCH₂CHCH₂) and 4.72 (2 H, ddd, *J* 5, 2, 2, NCH₂).

7 Preparation of Methyl 2-(N-allylamino)benzoate, 182

The procedure as in 4. using *N*-allylisotoic anhydride, **181** (3.50 g, 17.2 mmol) and sodium hydroxide (0.03 g, 0.86 mmol), gave the desired product **182** (1.79 g, 53%) as a yellow oil; $\delta_{\rm H}$ 7.90 (1 H, d, *J* 8, H-6), 7.33 (1 H, t, *J* 8, H-4), 6.65 (1 H, d, *J* 8, H-3), 6.59 (1 H, t, *J* 8, H-5), 6.00–5.89 (1 H, m, NCH₂CH), 5.33–5.15 (2 H, m, NCH₂CHCH₂), 3.87 (2 H, ddd, *J* 5, 2, 2, NCH₂CHCH₂) and 3.85 (3 H, s, Me).

8 Preparation of Allylmethylamine, 184

Benzaldehyde (44.50 g, 42.58 cm³, 0.42 mol) was cooled to 0 °C with stirring and allylamine (22.80 g, 29.96 cm³, 0.39 mol) was added slowly. The mixture was allowed to

warm to room temperature and stirred for 0.5 h. Diethyl ether (150 cm³) was added, water was separated and the organic layer was dried and evaporated to give allylbenzylideneamine (50.00 g). This was stirred in a pressure bottle with methyl iodide (75.00 g, 32.89 cm³, 0.53 mol) at 80 °C for 18 h. On cooling the oil solidified. Warm water was added to the pressure bottle to dissolve the solid and the mixture was extracted with diethyl ether (3 × 100 cm³). Sodium hydroxide (50%) was added to the aqueous fraction until it was basic and the solution was saturated with sodium carbonate. Once saturated the desired product, **184** (8.95 g, 33%) separated as a dark brown oil; $\delta_{\rm H}$ 5.94– 5.83 (1 H, m, NCH₂CHCH₂), 5.21–5.06 (2 H, m, NCH₂CHCH₂), 3.20 (2 H, ddd, *J* 6, 2, 2, NCH₂CHCH₂), 2.42 (3 H, s, Me) and 1.50 (1 H, br s, NH). [good agreement with Lit.,^{134,135}]

9 Preparation of Ethyl 2-(N-allyl-N-methylamino)benzoate, 185

To chilled ethanol (1 1), 2-fluorobenzoyl chloride (100 g, 0.64 mol) was added slowly with stirring. The resulting solution was heated under reflux for 3 h and the ethanol evaporated to give ethyl 2-fluorobenzoate (105.6 g, 98%) as a pale yellow oil. A mixture of ethyl 2-fluorobenzoate (9.04 g, 44.8 mmol) and K₂CO₃ (7.44 g, 53.8 mmol) was stirred in toluene (200 cm³) while amine **184** (3.83 g, 53.8 mmol) was added. The mixture was heated under reflux for 5 days and on cooling was poured into water (100 cm³) and extracted using ethyl acetate (2×75 cm³). The combined organic fractions were extracted using 2 M HCl (100 cm³) then washed with water, dried and evaporated to give starting material ethyl 2-fluorobenzoate (1.90 g, 21%). The acid extract was brought to pH 8 using 2 M NaOH and extracted using ethyl acetate $(2 \times 75 \text{ cm}^3)$. The combined organic extracts were washed with water, dried and evaporated. The resulting oil was then distilled at 2.5 Torr at 110 °C to remove unreacted allylmethylamine leaving the pure title product **185** (9.82 g, 41%) as a pale yellow oil; $\delta_{\rm H}$ 7.63 (1 H, d, J 8, H-6), 7.30 (1 H, t, J 8, H-4), 6.99 (1 H, d, 8, H-3), 6.85 (1 H, td, J 8, 1, H-5), 5.98-5.84 (1 H, m, NCH₂CHCH₂), 5.24–5.14 (2 H, m, NCH₂CHCH₂), 4.34 (2 H, q, J 7, OCH₂Me), 3.69 (2 H, dt, J 6, 1, NCH₂CHCH₂), 2.78 (3 H, s, NMe) and 1.36 (3 H, t, J 7, OCH₂Me) [good agreement with Lit.¹³⁶]

10 Preparation of 2-(N-Allyl-N-methylamino)benzyl alcohol, 186

Under a nitrogen atmosphere, a solution of ester **185** (1.48 g, 6.7 mmol) in dry THF (20 cm³) was added drop wise to a stirred suspension of LiAlH₄ (0.2889 g, 7.4 mol) in dry THF (5 cm³) and the resulting mixture was stirred at room temp for 18 h. To destroy the excess of LiAlH₄, water (0.3 cm³) in THF (2.1 cm³) was carefully added to the mixture followed by 15% solution sodium hydroxide (0.3 cm³) and finally water (1 cm³). The suspension was stirred for 0.5 h and extracted using diethyl ether (2 × 30 cm³) and the combined extracts washed with water, dried and evaporated to give the title product **186** (1.16 g, 97%) as a pale yellow oil; (Found: M⁺+Na, 200.1053. C₁₁H₁₅NaNO (M^+ +Na) requires, 200.1051); v_{max} /cm⁻¹ 3383 (OH), 1599, 1451, 1221, 1028, 920 and 760; $\delta_{\rm H}$ 7.29–7.22 (1 H, m), 7.21–7.15 (2 H, m), 7.11–7.05 (1 H, m), 5.93–5.80 (1 H, m, NCH₂CHCH₂), 5.35 (1 H, br s, OH), 5.28–5.15 (2 H, m, NCH₂CHCH₂), 4.79 (2 H, s, CH₂OH), 3.50 (2 H, d, *J* 5, NCH₂CHCH₂) and 2.67 (3 H, s, NMe); $\delta_{\rm C}$ 150.6 (4ry, C-1), 135.3 (4ry, C-2), 134.2 (CH), 127.9 (CH), 127.4 (CH), 123.8 (CH), 120.4 (CH), 117.5 (CH₂CHCH₂), 63.0 (CH₂), 59.6 (CH₂) and 40.9 (Me); *m/z* (ES⁺) 200.07 (M⁺+Na, 100%).

11 Nitration of 3-Methylbenzoic acid

a. A stirred solution of 3-methylbenzoic acid (20.00 g, 0.15 mol) in conc. H₂SO₄ (120 cm³) was cooled to 0 °C and KNO₃ (20.00 g, 0.2 mol) in conc. H₂SO₄ (120 cm³) was added slowly. The solution was stirred for 0.5 h and poured onto ice (1 l). Once the ice had melted, the precipitate was filtered off to give a mixture of 2-nitro-3-methylbenzoic acid, **187**, and 2-nitro-5-methylbenzoic acid **188**. The mixture was separated by washing the solid with hot water (~90 °C) dissolving **188**. The undissolved solid was filtered off and oven dried to give **187** (4.08 g, 15 %) mp 203–205 °C (Lit.,¹³⁷ 218–222 °C); 7.88 (1 H, d, *J* 8, H-6), 7.53–7.43 (2 H, m, H-4 and H-5) and 2.33 (3 H, s, ArMe).

The filtrate was concentrated to 40 cm³ and left for 18 h. The resulting crystals were filtered off and oven dried to give **188** (14.11 g, 52%) mp 128–129 °C (Lit.,¹³⁷ 132–134 °C); $\delta_{\rm H}$ 7.84 (1H, d, *J* 8, H-3), 7.64 (1 H, d, *J* 1, H-6), 7.45 (1 H, d of quintets, *J* 8, 1, H-4) and 2.50 (3 H, s, Me).

b. Fuming nitric acid (67 cm³, 8.6 mmol) was cooled in an ice bath to 0 °C and 3methylbenzoic acid (25 g, 18.36 mmol) was added slowly keeping the temperature below 10 °C. The mixture was stirred at rt for 2 h, and poured into 1.5 l of crushed ice. When the ice had melted the precipitate was filtered off to give a mixture of **187** and **188** which was separated as described for a. giving **197** (17.57 g, 53%) and **188** (6.86 g, 21%); data as for D11a.

12 Preparation of 2-Amino-3-methylbenzoic acid, 189

A solution of acid **187** (10.00 g, 55.1 mmol) in conc. aqueous ammonia (250 cm³) was stirred as a suspension of FeSO₄.7H₂O (125.25 g, 425.9 mmol) in water (500 cm³) was added. The suspension was heated under reflux for 1 h. On cooling the slurry was filtered through celite and the filtrate brought to pH 7 using conc. HCl. The solution was then reduced to 40 cm³ and resulting solid was filtered off and oved dried giving the title product, **189** (5.49 g, 66%), mp 169–170 °C (Lit.,¹³⁷ 176–176 °C); $\delta_{\rm H}$ 7.59 (1 H, d, *J* 8, H-6), 7.14 (1 H, d, *J* 8, H-4), 6.45 (1 H, t, *J* 8, H-5) and 2.08 (3 H, s, ArMe).

13 Preparation of Benzyl 2-(*N*,*N*-dibenzylamino)-3-methylbenzoate, 190

Potassium carbonate (23.77 g, 172 mmol) and acid **189** (6.50 g, 43.0 mmol) were added to a stirred mixture of 5:1 methanol and water (225 cm³) and benzyl bromide (16.36 cm³, 172 mmol) was added. The mixture was heated under reflux for 3 h and the solvent mixture was removed. Water (150 cm³) was added to the resulting solid and the mixture extracted using ethyl acetate (2 × 100 cm³). The combined organic fractions were washed with water, dried and evaporated to give a dark brown oil which was triturated with ether. The solid was filtered off and the filtrate was evaporated to give a mixture of desired product, benzyl bromide and tribenzylamine by ¹H NMR. The oil was Kugelrohr distilled to give benzyl bromide (bp 90 °C/3 Torr), tribenzylamine (bp 150 °C/3 Torr) and the desired product was obtained as the residual oil **190** (7.34 g, 40%). (Found: M⁺+Na, 444.1926. C₂₉H₂₇NaNO₂ (M^+ +Na) requires, 444.1939); ν_{max} /cm⁻¹ 1712 (CO), 1581, 1368, 1119 (O-C), 955 and 735; $\delta_{\rm H}$ 7.50–7.45 (2 H, m), 7.44–7.13 (16 H, m), 6.99 (1 H, t, *J* 8), 5.38 (2 H, s, CH₂ of OBn), 4.14 (4 H, s, 2 × CH₂ of NBn) and 2.25 (3 H, s, ArMe); $\delta_{\rm C}$ 169.1 (4ry, CO), 148.4 (4ry, C-2 of Ar), 139.3 (2 C, 4ry, C-1 of NBn), 138.3 (4ry, C-1 of OBn), 135.8 (4ry, C-3 of Ar), 134.3 (CH), 131.3 (4ry, C-1 of Ar), 128.9 (4 C, C-2 or 3 of NBn), 128.8 (2 C, CH), 128.6 (CH), 128.4 (CH), 128.3 (2 C, CH), 127.9 (4 C, C-2 or 3 of NBn), 126.8 (2 C, CH), 124.4 (C-5 of Ar), 67.1 (CH₂ of OBn), 57.1 (2 C, $2 \times$ CH₂ of NBn) and 19.8 (ArMe); m/z (ES⁺) 444.09 (M⁺+Na, 100%).

14 Preparation of 2-(*N*,*N*-dibenzylamino)-3-methylbenzyl alcohol, 191

Under a nitrogen atmosphere, a solution of **190** (7.00 g, 16.6 mmol) in dry THF (25 cm³) was added dropwise to a stirred suspension of LiAlH₄ (0.68 g, 18.3 mmol) in dry THF (5 cm³) and the resulting mixture was stirred at room temperature for 18 h. To destroy the excess of LiAlH₄, water (0.7 cm³) in THF (5 cm³) was carefully added to the mixture followed by 15% solution sodium hydroxide (0.7 cm³) and finally water (2 cm³). The suspension was stirred for 0.5 h and extracted using diethyl ether (2 × 75 cm³) and the combined extracts washed with water, dried and evaporated to give the title product **191** (4.23 g, 84%) as a pale yellow oil; (Found: M⁺+Na, 340.1683. C₂₂H₂₃NaNO (*M*⁺+Na) requires, 340.1677); ν_{max} /cm⁻¹ 3309 (OH), 1593, 1360, 1189, 1025 and 756; $\delta_{\rm H}$ 7.32–7.00 (14 H, m), 4.38 (2 H, s, CH₂OH), 4.13 and 4.07 (4 H, AB pattern, *J* 13, 2 × NCH₂Ph), and 2.27 (3 H, ArMe); $\delta_{\rm C}$ 146.5 (4ry, C-2 of Ar), 140.2 (4ry, C-3 of Ar), 138.8 (2 C, 4ry, 2 × C-1 of NBn), 137.1 (4ry, C-1 of Ar), 131.3 (C-4 of Ar), 129.3 (4 C, 2 × C-2 or 3 of NBn), 128.3 (4 C, 2 × C-2 or 3 of NBn), 127.2 (2 C, 2 × C-4 of NBn), 126.6 (CH), 125.8 (CH), 62.8 (CH₂OH), 57.0 (4 C, 2 × CH₂ of NBn) and 20.1 (ArMe); *m*/*z* (ES⁺) 340.09 (M⁺+Na, 100%).

15 Preparation of Diphenyliodonio-2-carboxylate, 192

Potassium persulfate (42.0 g, 156 mmol) was added over 0.5 h to a stirred solution of 2iodobenzoic acid (20.00 g, 80.7 mmol) in conc. H_2SO_4 (80 cm³) at 10 °C and stirred for a further 0.5 h. Benzene (75 cm³) was added and the solution was warmed to room temperature and stirred for 3 h. The mixture was poured onto ice and filtered when the ice melted to give 2-carboxydiphenyliodonium bissulfate. To the solution, KI (40 g, mmol) was added in the minimum water and iodonium iodide was filtered off. 2-carboxydiphenyliodonium bissulfate and iodonium iodide were combined and stirred in NaOH (200 cm³, 5 N). The precipitate was filtered off to give **192** (20.98 g, 80%), mp 218–219 °C (Lit.,¹³⁸ 223–225 °C); $\delta_{\rm H}$ 8.45 (1 H, d, *J* 8, H-6 of Ar), 7.85 (2 H, d, *J* 8, H-2 or 3 of Ph), 7.59 (1 H, t, *J* 8), 7.45–7.37 (4 H, m) and 6.78 (1 H, d, *J* 8, H-3).

16 Preparation of N-(Methanesulfonyl)aniline, 193

Under a nitrogen atmosphere, a solution of aniline (18.63 g, 18.26 cm³, 0.2 mol) and pyridine (17.40 g, 16.57 cm³, 0.22 mol) in dichloromethane (500 cm³) was cooled to 0 °C and methanesulfonyl chloride (25.20 g, 1.03 cm³, 0.22 mol) was added, ensuring the temperature did not exceed 10 °C. The solution was warmed to room temperature and stirred for 18 h. Sodium hydroxide (100 cm³, 6 M) was added followed by water (100 cm³). The organic phase was separated and the aqueous phase was cooled to 0 °C and acidified with conc. HCl. The precipitate was filtered off to give the title product, **193** (36.01 g, 96%) as a pale yellow solid, mp 99–100 °C (Lit., ¹³⁹ 99–101 °C); $\delta_{\rm H}$ 7.40–7.33 (2 H, m), 7.26–7.16 (3 H, m), 6.78 (1 H, br s, NH) and 3.02 (3 H, Me).

17 Attempted Preparation of 2-(N-Methanesulfonyl-N-phenylamino)benzoic acid

Under a nitrogen atmosphere, a solution of 2-chlorobenzoic acid (45.54 g, 0.29 mol) in 2ethoxyethanol (100 cm³) was stirred and Cu/Cu₂O (1.72 g, 63.55 mmol, 9 mol% / 1.67 g, 11.64 mmol, 4 mol%), potassium carbonate (40.20 g, 0.29 mol) and amine **193** (28.45 g, 27.80 cm³, 0.31 mol) were added. The mixture was heated under reflux for 24 h. On cooling, water (75 cm³) was added and the mixture made basic with NaOH. The mixture was filtered through celite and acidified. The product was extracted using diethyl ether (2 \times 75 cm³) and the organic fractions were extracted using saturated aqueous sodium bicarbonate (2 \times 100 cm³). The aqueous phase was acidified with 2 M HCl then extracted with diethyl ether (2 \times 125 cm³) and the combined organic fractions were washed with water, dried and evaporated. The resulting mixture was separated by column chromatography (40:60 diethyl ether:hexane) to give not the desired product but 2-(*N*phenylamino)benzoic acid **194** (40.00 g, 64%) as a colourless solid, mp 174–175 °C (Lit.,¹³⁸ 183–184 °C); $\delta_{\rm H}$ 10.48 (1 H, br s, OH), 8.15–8.10 (2 H, m, Ph), 7.94 (1 H, d, *J* 8, H-6 of Ar), 7.63 (1 H, t, J 8, H-4), 7.56–7.44 (3 H, m, Ph), 7.01 (1 H, d, J 8, H-3) and 6.94 (1 H, t, J 8, H-5).

18 Preparation of Methyl 2-N-phenylaminobenzoate

Dry HCl gas (29.5 g, 0.8 mol) was dissolved in methanol (77.7 g, 98.3 cm³, 2.4 mol) and 2-(*N*-phenylamino)benzoic acid **194** (15.00 g, 0.07 mol) was added. The solution was left to stand for 18 h. The solution was then heated under reflux for 3 h. On cooling, toluene (75 cm³) and water (100 cm³) were added and separated. The organic fraction was washed with dilute NaOH until free of acid and then washed with water (2 × 100 cm³), dried and evaporated to give the title product 15.32 g, 64%) as a pale yellow solid, mp 50–51 °C (Lit., ¹⁴⁰ 58–59 °C); $\delta_{\rm H}$ 9.49 (1 H, br s, NH), 7.94 (1 H, d, *J* 8, H-6), 7.35–7.18 (6 H, m), 7.05 (1 H, t, *J* 8, H-4), 6.69 (1 H, t, *J* 8, H-5) and 3.84 (3 H, s, Me).

E Synthesis of *N*-Methyl-*N*-mesylamino and *N*-benzyl-*N*-mesylamino ylides with α,β-unsaturated acyl groups

1 Preparation of [α-Cinnamoyl-2-(*N*-methyl-*N*-methanesulfonylamino) benzylidene]triphenylphosphorane, 195

a. A suspension of salt **168** (2.00 g, 3.7 mmol) in THF (50 cm³) was stirred under nitrogen while a solution of BuLi in hexanes (1.65 cm³, 2.5 M, 4.1 mmol) was added. The resulting brightly coloured solution was stirred for 2 h and a solution of cinnamoyl chloride (0.35 g, 2.1 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (50 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2 × 50 cm³). The combined extracts were washed with water, dried and evaporated. Recrystallisation of the residue (Et₂O/EtOAc) gave **195** (0.43 g, 20%) as a bright yellow powder, mp 215–216 °C. (Found: M⁺+H, 590.1906. C₃₆H₃₃NO₃PS (M^+ +H) requires, 590.1919); ν_{max} /cm⁻¹ 1614 (CO), 1483, 1331 (SO₂), 1164 (SO₂), 964 and 747; $\delta_{\rm H}$ (55°C) 7.71 (4 H, br s), 7.56–7.18 (18 H, m) 7.44 (1 H, half AB pattern, *J* 15, COCH=C*H*), 6.97 (2 H, d, *J* 5), 6.78 (1 H, half AB pattern, *J* 15, PhCH=C*H*), 2.92 (3 H, s, NMe) and 2.69 (3 H, s, SO₂Me); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +16.8; *m/z* (ES⁺) 590.20 (M⁺+H, 100%).

b. Sodium hydride (60% dispersion in oil) (0.16 g, 4.07 mmol) was washed with hexane (10 cm³) and THF (50 cm³) was added. To the stirred suspension, salt **168** (2.00 g, 3.7 mmol) was added and the resulting brightly coloured solution was stirred for 2 h. A solution of cinnamoyl chloride (0.34 g, 1.85 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (50 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2×50 cm³). The combined extracts were washed with water, dried and evaporated. Recrystallisation of the residue (Et₂O/EtOAc) gave **195** (0.55 g, 25%) as a bright yellow powder, mp 213–215 °C; spectroscopic data as for E1a.

2 Preparation of Methyl 2-(N-benzyl-N-methanesulfonylamino)benzoate, 196

Under a nitrogen atmosphere, sodium hydride (60% dispersion in oil, 8.80 g, 219.8 mmol) was washed with hexane (60 cm³) and DMF (100 cm³) was added. The resulting suspension was stirred while a solution of ester **163** (33.59 g, 146.5 mmol) in DMF (300 cm³) was added. The solution was stirred for 45 min and then a solution of benzyl bromide (75.17 g, 52.2 cm³, 439.5 mmol) in diethyl ether (400 cm³) was added and the mixture stirred for 72 h. The mixture was cooled and acidified with 2M HCl. The solution was added to water (300 cm³) and extracted with diethyl ether (4 × 150 cm³). The combined extracts were washed with water, dried and evaporated and the resulting yellow oil was distilled to remove excess benzyl bromide leaving **196** (41.49 g, 88%) as a yellow oil; $\delta_{\rm H}$ 7.91 (1 H, dd, *J* 8, 2), 7.42–7.33 (4 H, m), 7.26–7.18 (3 H, m), 7.09 (1 H, dd, *J* 8, 2, H-3 of Ar), 4.84 (2 H, br s, CH₂Ph), 3.92 (3 H, s, OMe) and 2.98 (3 H, s, SO₂Me) [good agreement with Lit.,¹⁴¹].

3 Preparation of 2-(N-Benzyl-N-methanesulfonylamino)benzyl alcohol, 197

Under a nitrogen atmosphere, a solution of ester **196** (10.60 g, 33.2 mmol) in dry THF (50 cm³) was added dropwise to a stirred suspension of LiAlH₄ (1.38 g, 36.5 mol) in dry THF (10 cm³) and the resulting mixture was stirred at room temp for 18 h. To destroy the excess of LiAlH₄, water (1.4 cm³) in THF (9.8 cm³) was carefully added to the mixture followed by a 15% solution of sodium hydroxide (1.4 cm³) and finally water (4 cm³). The

suspension was stirred for 0.5 h and extracted using diethyl ether $(2 \times 75 \text{ cm}^3)$ and the combined extracts washed with water, dried and evaporated. The resulting mixture was separated by column chromatography (70:30 diethyl ether:hexane) to give **197** (2.79 g, 29 %) as colouress crystals, mp 73–74 °C. (Found: M⁺+Na, 314.0835. C₁₅H₁₇NaNO₃S (M^+ +Na) requires, 314.0827); v_{max}/cm^{-1} 3529 (OH), 1655, 1319 (SO₂), 1210, 1158 (SO₂) and 1058; δ_{H} 7.50 (1 H, m), 7.38–7.34 (2 H, m), 7.28–7.20 (4 H, m), 7.18–7.14 (2 H, m), 4.97 (1 H, br d, *J* 13, CH*H*Ph), 4.52 (1H, br d, *J* 13, CH*H*Ph), 4.47 (1 H, br t, *J* 7, CH*H*OH), 4.10 (1 H, br t, *J* 7, CH*H*OH), 3.00 (3 H, s, SO₂Me) and 2.44 (1 H, br t, *J* 7, OH); δ_{C} 142.5 (4ry, C-1 of Ar), 136.8 (4ry, C-2 of Ar or C-1 of Ph), 131.5 (CH), 129.5 (2 C, C-2 or 3 of Ph), 129.4 (CH), 128.9 (CH), 128.6 (2 C, C-2 or 3 of Ph), 128.4 (CH), 127.5 (CH), 60.7 (CH₂OH), 56.3 (CH₂Ph) and 37.9 (SO₂Me); m/z (ES⁺) 314.13 (M⁺+Na, 100%).

4 Preparation of 2-(*N*-Benzyl-*N*-methanesulfonylamino)benzyl triphenylphosphonium bromide, 198

A solution of alcohol **197** (9.50 g, 32.6 mmol) in toluene (100 cm³) was stirred with phosphorus tribromide (7.04 cm³, 74.9 mmol) at rt for 18 h. The mixture was added to water (70 cm³) and the organic layer separated, washed with water (2×50 cm³) and dried. The dried organic solution was heated under reflux with triphenylphosphine (8.55 g, 32.6 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to give 198 (12.27 g, 61%) as a colourless solid, mp 234-236 °C. (Found: C, 65.0; H, 5.5; N, 2.0. C₃₃H₃₁BrNO₂PS requires C, 64.3; H, 5.1; N, 2.3%); v_{max}/cm⁻¹ 1621, 1336 (SO₂), 1147 (SO₂), 1093 and 739; δ_H 7.87–7.79 (3 H, m), 7.75–7.70 (7 H, m), 7.52– 7.40 (6 H, m), 7.27–7.07 (7 H, m), 6.86 (1 H, d, J 8, H-3 of Ar), 4.89 (1 H, half AB pattern, J 14, CHHPh), 4.79 (1 H, t, J 14, CH₂P), 4.76 (1 H, half AB pattern, J 14, CH*H*Ph), 4.59 (1 H, t, J 14, CH₂P) and 3.04 (3 H, s, SO₂Me); δ_C 147.6 (4ry, C-2 of Ar), 139.5 (4ry, d, J 8, C-1 of Ar), 135.7 (4ry, C-1 of Bn), 135.4 (3C, d, J 3, C-4 of PPh₃), 133.7 (6C, d, J 10, C-2 of PPh₃), 130.6 (6C, d, J 13, C-3 of PPh₃), 130.2 (d, J 5, C-6 of Ar), 130.4 (CH of Ar), 129.9 (2C, C-2 or C-3 of Bn), 129.2 (CH of Ar), 128.7 (2C, C-2 or C-3 of Bn), 128.4 (C-4 of Bn), 128.2 (CH of Ar), 118.0 (3C, d, J 87, C-1 of PPh₃), 56.5 (CH₂ of Bn), 38.9 (SO₂Me) and 26.7 (d, J 55, CH₂PPh₃); $\delta_{\rm P}$ +23.1; m/z (ES⁺) 536 (M⁺-Br, 100%).

5 Preparation of [α-Cinnamoyl-2-(*N*-benzyl-*N*-methanesulfonylamino) benzylidene]triphenylphosphorane, 199

Under nitrogen a atmosphere, sodium hydride (60% dispersion in oil) (0.14 g, 3.5 mmol) was washed with hexane (10 cm³) and THF (30 cm³) was added. The resulting suspension was stirred while salt **198** (2.00 g, 3.2 mmol) was added. The resulting brightly coloured solution was stirred for 2 h and a solution of cinnamoyl chloride (0.29 g, 1.76 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (50 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2 × 50 cm³). The combined extracts were washed with water, dried and evaporated. Column chromatography (50:50 EtOAc: Et₂O) of the residue gave **199** (0.42 g, 20%) mp 204–205 °C; there was severe peak broadening due to resticted rotation at room temperature; $\delta_{\rm H}$ 8.20–6.72 (31 H, m), 4.78 and 4.37 (2 H, 2 × br s, NC*H*₂Ph) and 2.97 and 2.20 (3 H, 2 × br s, SO₂Me); $\delta_{\rm P}$ +17.5 and +16.7.

6 FVP of Ylide 195



Ylide **195** (0.0201 g, 0.034 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of products. The mixture was purified by preparative TLC (15:85 hexane:diethyl ether) to give *N*-methylbenzo[*c*]carbazole **200** (0.0059 g, 75%), mp 110 °C (Lit.,¹⁴² 118–119 °C); $\delta_{\rm H}$ 8.80 (1 H, ddd, *J* 8.4, 1, 0.8, 0.8, H-1), 8.60 (1 H, ddd, *J* 8, 1.2, 0.7, H-11), 8.01 (1 H, dddd, *J* 8, 1.6, 0.8, 0.8, H-4), 7.92 (1 H, dddd, *J* 9, 8, 0.8, 0.8, H-5), 7.71 (1 H, ddd, *J* 8.4, 7, 1.6, H-2), 7.67 (1 H, d, *J* 9, H-6), 7.56 (1 H, ddd, *J* 8, 1, 0.7, H-8), 7.51 (1 H, ddd, *J* 8, 6.8, 1.2, H-9), 7.47 (1 H, ddd, *J* 8, 7,

1, H-3), 7.39 (1 H, ddd, *J* 8, 6.8, 1, H-10) and 4.02 (3 H, s, Me). [good agreement with Lit.,¹⁴³]

7 FVP of Ylide 199



Ylide **199** (0.0986 g, 0.15 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of compounds present. The mixture was purified by preparative TLC (60:40 hexane:diethyl ether) to give 7-*H*-benzo[*c*]carbazole **201** (0.0045 g, 14%); $\delta_{\rm H}$ 8.77 (1 H, dd, *J* 8, 1, H-1), 8.56 (1 H, ddd, *J* 8, 1, 0.8, H-11), 8.00 (1 H, dd, *J* 8, 1, H-4), 7.86 (1 H, d, *J* 9, H-5 or 6), 7.71 (1 H, ddd, *J* 8, 7, 1, H-2), 7.64 (1 H, d, *J* 9, H-5 or 6), 7.59 (1 H, ddd, *J* 8, 1.2, 0.8, H-8), 7.48 (1 H, ddd, *J* 8, 7, 1, H-9), 7.45 (1 H, ddd, *J* 8, 7, 1, H-3) and 7.38 (1H, ddd, *J* 8, 7, 1.2, H-10). [good agreement with Lit.,¹⁴⁴]

F Synthesis of N-Acylbenzotriazoles

1 Preparation of 1-(3-Phenylpropenoyl)benzotriazole, 205

To a stirred solution of 1*H*-1,2,3-benzotriazole, **205** (11.90 g, 100 mmol) in CH₂Cl₂ (125 cm³), thionyl chloride (2.97 g, 1.9 cm³, 25 mmol) was added dropwise. The mixture was stirred at rt for 0.5 h and cinnamic acid (3.70 g, 25 mmol) was added. The mixture was stirred for a further 3h at rt and the solid was filtered off and washed with CH₂Cl₂. The combined filtrate was washed with 2M aqueous NaOH, water and brine. Drying and evaporation followed by recrystallisation of the residue (hexane/EtOAc) gave **205** (5.2 g, 84%) as colourless needles, mp 148–149 °C (Lit.,¹⁴⁵ 152–153 °C); $\delta_{\rm H}$ 8.43 (1 H, dt, *J* 8, 1, H-7), 8.17–8.14 (3 H, m), 7.79 (2 H, m), 7.69 (1 H, ddd, *J* 8, 7, 1, H-5 or 6), 7.54 (1 H, ddd *J* 8, 7, 1, H-5 or 6) and 7.50–7.46 (3 H, m).

2 Preparation of (*E*)-3-(2-Furyl)propenic acid, 212

A mixture of malonic acid (48.25 g, 463.8 mmol), pyridine (44.60 cm³), piperidine (0.01 cm³), and furan-2-carbaldehyde (22.30 g, 231.9 mmol) was heated on a water bath (100 °C) for 4 h. After gas evolution had ceased, the cooled mixture was poured onto 1 M HCl (500 cm³). The resulting precipitate was filtered off, washed with water and dried to give the product **212** (25.95, 81%) as a pale brown powder, mp 135–136 °C (Lit.,¹⁴⁶ 139–140 °C); $\delta_{\rm H}$ 7.53 (1 H, d, *J* 16, COC*H*=CH), 7.52 (1 H, d, *J* 2, H-5 of furyl), 6.67 (1 H, d, *J* 3, H-3 of furyl), 6.49 (1 H, dd, *J* 3, 2, H-4 of furyl) and 6.32 (1 H, *J* 16, COCH=CH).

3 Preparation of 1-(3-(2-Furyl)propenoyl)benzotriazole, 206

This was prepared as in 1. using **204** (34.55 g, 290 mmol), thionyl chloride (8.65 g, 5.25 cm³, 72.5 mmol) and acid **212** (10 g, 72.5 mmol). Drying and evaporation followed by recrystallisation of the residue (hexane/CH₂Cl₂) gave **206** (9.96 g, 54%) as pale brown prisms, mp 140–141 °C (Lit.,¹⁴⁷ 142–143 °C); $\delta_{\rm H}$ 8.40 (1 H, d, *J* 8, H-7), 8.14 (1 H, d, *J* 8, H-4), 7.97 (1 H, d, *J* 15, COCH=CH), 7.87 (1 H, d, *J* 15, COCH=CH), 7.67 (1 H, t, *J* 8, H-5 or 6), 7.61 (1 H, d, *J* 2, H-5 of furyl), 7.52 (1 H, t, *J* 8, H-5 or 6), 6.87 (1 H, d, *J* 4, H-3 of furyl) and 6.54 (1 H, dd, *J* 4, 2, H-4 of furyl).

4 Preparation of (*E*)-3-(2-Thienyl)propenic acid, 213

This was prepared as in 2. using malonic acid (10.68 g, 102 mmol), pyridine (10 cm³), piperidine (0.01 cm³), and thiophene-2-carbaldehyde (4.93 g, 51 mmol) giving **213** (5.09 g, 89%); $\delta_{\rm H}$ 7.69 (1 H, br s H-5 thienyl), 7.68 (1 H, d, *J* 16, COC*H*=CH), 7.45 (1 H, br s, H-4 of thienyl), 6.62 (1 H, br s, H-3 of thienyl) and 6.17 (1 H, d, *J* 16, COCH=CH).

5 Preparation of 1-(3-(2-Thienyl)propenoyl)benzotriazole, 207

This was prepared as in 1. using **204** (15.45 g, 129.7 mmol), thionyl chloride (3.85 g, 2.35 cm³, 32.4 mmol) and acid **213** (5.00 g, 32.4 mmol). Drying and evaporation followed by recrystallisation of the residue (hexane/CH₂Cl₂) gave **207** (5.45 g, 66%) as yellow needles, mp 161–162 °C (Lit.,¹⁴⁷ 169–170 °C); $\delta_{\rm H}$ 8.41 (1 H, d, *J* 8, H-7), 8.26 (1 H, d, *J*

15, COCH=C*H*), 8.16 (1 H, d, *J* 8, H-4), 7.90 (1 H, d, *J* 15, COC*H*=CH), 7.89 (1 H, t, *J* 8, H-5 or 6), 7.57–7.47 (3 H, m) and 7.15 (1H, t, *J* 4, H-4 of thienyl).

6 Preparation of (*E*)-3-(3-Furyl)propenic acid, 214

This was prepared as in 2. using malonic acid (14.42 g, 138.6 mmol), pyridine (10 cm³), piperidine (0.01 cm³, 0.1 mmol), and furan-3-carbaldehyde (6.66 g, 69.3 mmol), giving acid **214** (4.72 g, 49%) as a pale brown powder, mp 154–155 °C (Lit.¹⁴⁸, 152.5–154 °C); δ _H 11.44 (1 H, br s, OH), 7.69 (1 H, d, *J* 16, COCH=C*H*), 7.69 (1 H, s, H-2), 7.45 (1 H, br s, H-5), 6.62 (1 H, d, *J* 2, H-4) and 6.17 (1H, d, *J* 16, COCH=CH).

7 Preparation of 1-(3-(3-Furyl)propenoyl)benzotriazole, 208

This was prepared as in 1. using **204** (17.15 g, 143.9 mmol), thionyl chloride (4.28 g, 2.61 cm³, 35.9 mmol) and acid **214** (5.00 g, 35.9 mmol). Drying and evaporation followed by recrystallisation of the residue (CH₂Cl₂) gave **208** (3.25 g, 38%) as colourless needles, mp 169–170 °C. (Found: M⁺+Na, 262.0598. C₁₃H₉NaN₃O₂ (M^+ +Na) requires, 262.0592); v_{max} /cm⁻¹ 1703, 1621 (CO), 1379, 1151 and 992; δ_{H} 8.41 (1 H, d, *J* 8, H-7), 8.15 (1 H, d, *J* 8, H-4), 8.06 (1 H, d, *J* 16, COC*H*=CH), 7.87–7.79 (2 H, m, COCH=C*H*, furyl-H), 7.68 (1 H, t, *J* 8, H-5 or 6), 7.56–7.51 (2 H, m, H-5 or 6, furyl-H) and 6.83 (1 H, d, *J* 2, H-4 of furyl); δ_{C} 163.9 (4ry, CO), 146.4 (CH), 146.2 (4ry, C-3a of Bt), 144.8 (CH), 138.6 (C-2 of furyl), 131.4 (4ry, C-7a of Bt), 130.2 (CH), 126.1 (CH), 123.0 (4ry, C-3 of furyl), 120.1 (CH), 115.7 (CH), 114.7 (CH) and 107.6 (C-4 of furyl); m/z (ES⁺) 262.04 (M⁺+Na, 100%).

8 Preparation of 1-(3-(3-Thienyl)propenoyl)benzotriazole, 209

This was prepared as in 1. using **204** (15.25 g, 128.0 mmol), thionyl chloride (3.81 g, 2.32 cm³, 32.4 mmol) and (*E*)-3-(3-thienyl)prop-2-enoic acid (5.00 g, 32.4 mmol). Drying and evaporation followed by recrystallisation of the residue (CH₂Cl₂) gave **209** (5.30 g, 65%) as yellow needles, mp 154–156 °C. (Found: M⁺+Na, 278.0370. C₁₃H₉NaN₃OS (M^+ +Na) requires, 278.0364); v_{max} /cm⁻¹ 1696 (CO), 1611, 1285, 1069, 993, 782 and 743; $\delta_{\rm H}$ 8.42 (1 H, dt, *J* 8, 1, H-7), 8.15 (1 H, dt, *J* 8, 1, H-4), 8.14 (1 H, d, *J* 15, COCH=CH), 7.93 (1 H, d, *J* 15, COCH=CH), 7.76 (1 H, dd, *J* 3, 1, H-2 of thienyl), 7.68 (1 H, td, *J* 8, 1, H-5 or 6), 7.55 (1 H, dd, *J* 5, 1, H-5 of thienyl), 7.53 (1 H, td, *J* 8, 1, H-5 or 6) and 7.43 (1 H, ddd, *J*

5, 3, 1, H-4 of thienyl); $\delta_{\rm C}$ 164.0 (4ry, CO), 146.1 (4ry, C-3a of Bt), 141.7 (CH), 137.5 (4ry, C-7a of Bt), 131.3 (4ry, C-3 of thienyl), 130.7 (CH), 130.1 (CH), 127.3 (CH), 126.0 (CH), 125.4 (CH), 120.0 (CH), 115.4 (CH) and 114.7 (CH); *m/z* (ES⁺) 277.98 (M⁺+Na, 100%).

9 Preparation of 1-(3-(2-Methylphenyl)propenoyl)benzotriazole, 210

This was prepared as in 1. using **204** (14.69 g, 123.3 mmol), thionyl chloride (3.67 g, 2.24 cm³, 30.8 mmol) and (*E*)-3-(2-methylphenyl)prop-2-enoic acid (5.00 g, 30.8 mmol). Drying and evaporation followed by recrystallisation of the residue (CH₂Cl₂) gave **210** (1.77 g, 22%) as a white powder, mp 124–125 °C (Lit.,¹⁴⁹ 127–129); $\delta_{\rm H}$ 8.47 (1 H, d, *J* 15, COC*H*=CH), 8.42 (1 H, dt, *J* 8, 1, H-4 or 7 of Bt), 8.16 (1 H, dt, *J* 8, 1, H-4 or 7 of Bt), 8.07 (1 H, d, *J* 15, COCH=CH), 7.86 (1 H, d, *J* 8), 7.69 (1 H, ddd, *J* 8, 7, 1, H-5 or 6 of Bt), 7.54 (1 H, ddd, *J* 8, 7, 1, H-5 or 6 of Bt), 7.40–7.27 (3 H, m) and 2.56 (3 H, s, Me).

10 Preparation of 1-(3-(3-Methyl-2-thienyl)propenoyl)benzotriazole, 211

This was prepared as in 1. using **204** (14.16 g, 118.9 mmol), thionyl chloride (3.53 g, 2.16 cm³, 79.7 mmol) and (*E*)-3-(3-methyl-2-thienyl)prop-2-enoic acid (5.00 g, 29.7 mmol). Drying and evaporation followed by recrystallisation of the residue (CH₂Cl₂) gave **211** (4.20 g, 60%) as pale yellow powder, mp 169–170 °C. (Found: M⁺+Na, 292.0521. C₁₄H₁₁NaN₃OS (M^+ +Na) requires, 292.0521); v_{max} /cm⁻¹ 1699 (CO), 1601, 1380, 1278 and 988; $\delta_{\rm H}$ 8.39 (1 H, dt, *J* 8, 1, H-4 or 7 of Bt), 8.32 (1 H, dd, *J* 16, 1, COCH=C*H*), 8.14 (1 H, dt, *J* 8, 1, H-4 or 7 of Bt), 7.80 (1 H, d, *J* 16, COC*H*=CH), 7.67 (1 H, ddd, *J* 8, 7, 1, H-5 or 6 of Bt), 7.52 (1 H, ddd, *J* 8, 7, 1, H-5 or 6 of Bt), 7.42 (1 H, br d, *J* 5), 6.94 (1 H, dd, *J* 5, 0.3) and 2.46 (3 H, s, Me); $\delta_{\rm C}$ 169.9 (4ry, CO), 146.2 (4ry), 144.0 (2C, 4ry), 139.2 (CH), 134.0 (4ry), 131.4 (CH), 130.1 (CH), 129.2 (CH), 126.0 (CH), 120.1 (CH), 114.7 (CH), 113.2 (CH) and 14.4 (CH₃); *m/z* (ES⁺) 292.01 (M⁺+Na, 100%).

G Synthesis of *N*-Benzyl-*N*-methylamino ylides with α,β-unsaturated acyl groups

1 Preparation of Ethyl 2-(N-benzyl-N-methylamino)benzoate, 215

To chilled ethanol (1 1), 2-fluorobenzoyl chloride (100 g, 0.64 mol) was added slowly with stirring. The resulting solution was heated under reflux for 3 h and the ethanol evaporated to give ethyl 2-fluorobenzoate (105.6 g, 98%) as a pale yellow oil. A mixture of ethyl 2-fluorobenzoate (30.0 g, 171.1 mmol) and K₂CO₃ (28.25 g, 205.32 mmol) was stirred in toluene (500 cm³) while benzylmethylamine (24.88 g, 26.50 cm³, 205.32 mmol) was added. The mixture was heated under reflux for 5 days and on cooling was poured into water (300 cm³) and the mixture then extracted using ethyl acetate (2×300 cm³). To the combined organic fractions 2 M HCl (200 cm³) was added and the layers separated. The organic fraction was washed with water, dried and evaporated to give recovered starting material ethyl 2-fluorobenzoate (8.10 g, 28%). The acid layer was then brought to pH 8 using 2 M NaOH and extracted using ethyl acetate ($2 \times 200 \text{ cm}^3$). The combined organic fractions were washed with water, dried and evaporated. The resulting oil was then distilled at 2.5 Torr and 110 °C to remove unreacted benzylmethylamine leaving the pure title product **215** (27.05 g, 68%) as a pale yellow oil; $\delta_{\rm H}$ 7.65 (1H, d, J 8, H-6), 7.34– 7.18 (6H, m), 6.97 (1 H, d, J 8), 6.88 (1 H, t, J 8), 4.36–4.28 (4 H, m, OCH₂CH₃, NCH₂Ph), 2.73 (3 H, s, NMe) and 1.34 (3 H, t, J 7, OCH₂CH₃) [good agreement with Lit.,¹³⁶].

2 Preparation of 2-(*N*-Benzyl-*N*-methylamino)benzyl alcohol, 216

Under a nitrogen atmosphere, a solution of ester **215** (19.92 g, 73.87 mmol) in dry THF (400 cm³) was added dropwise to a stirred suspension of LiAlH₄ (3.09 g, 81.34 mmol) in dry THF (80 cm³) and the resulting mixture was stirred at room temperature for 18 h. To destroy the excess of LiAlH₄, water (3 cm³) in THF (21 cm³) was added to the mixture followed by 15% solution sodium hydroxide (3 cm³) and finally water (9 cm³). The suspension was stirred for 0.5 h and MgSO₄ was added and stirred overnight. The mixture was filtered through celite, the solid washed with ethyl acetate and the combined filtrate and washings evaporated to give **216** (14.08 g, 84%) as a yellow oil; (Found: M⁺+Na, 250.1213. C₁₅H₁₇NaNO (M^+ +Na) requires, 250.1208); v_{max} /cm⁻¹ 3387 (OH), 1597, 1446, 1209, 1029, 776 and 686; $\delta_{\rm H}$ 7.33–7.18 (8 H, m), 7.09 (1 H, t, *J* 8), 5.25 (1 H, br s, OH),

4.80 (2 H, s, CH₂OH), 4.00 (2 H, s, NCH₂Ph), 2.58 (3 H, s, NMe); $\delta_{\rm C}$ 151.2 (4ry, C-2), 137.4 (4ry), 135.7 (4ry), 128.8 (2 CH, C-2 or 3 of NCH₂Ph), 128.3 (2 CH, C-2 or 3 of NCH₂Ph), 128.3 (CH), 127.9 (CH), 127.2 (CH), 124.5 (CH), 121.2 (CH), 63.8 (CH₂OH), 61.6 (NCH₂Ph) and 41.3 (Me); *m/z* (ES⁺) 250.05 (M⁺+Na, 100%).

3 Preparation of 2-(*N*-Benzyl-*N*-methylamino)benzyltriphenylphosphonium bromide, 217

A solution of alcohol **216** (12.61 g, 55.3 mmol) in toluene (500 cm³) was stirred at 60 °C and phosphorus tribromide (12.11 cm³, 127.5 mmol) was added dropwise over 0.5 h. The solution was stirred at 60 °C for 2h, cooled to rt and stirred for 18 h. The mixture was added to water (200 cm³), stirred for 0.5 h and the organic layer separated, washed with water $(2 \times 50 \text{ cm}^3)$ and dried. The dried toluene solution was heated under reflux with triphenylphosphine (14.48 g, 55.3 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to give 217 (12.89 g, 39%) as a colourless solid, mp 206–207 °C (Found: C, 71.6; H, 5.6; N, 2.6. C₃₃H₃₁BrNP requires C, 71.7; H, 5.7; N, 2.5%); $v_{\text{max}}/\text{cm}^{-1}$ 1621, 1446, 1307, 1098, 739 and 694; δ_{H} 7.80–7.71 (5 H, m), 7.67–7.55 (14 H, m), 7.14–6.94 (5 H, m), 5.35 (2 H, br d, *J* 15, CH₂PPh₃), 3.73 (2 H, br s, NCH₂Ph) and 2.04 (3 H, br s, Me); δ_C 153.6 (4ry, d, J 5, C-2 of Ar), 137.2 (4ry, C-1 of Bn), 135.0 (3C, d, J 3, C-4 of PPh₃), 134.2 (6C, d, J 10, C-2 of PPh₃), 131.9 (d, J 5, CH of Ar), 130.1 (6C, d, J 13, C-3 of PPh₃), 129.8 (d, J 3, CH of Ar), 128.9 (2C, C-2 or C-3 of Bn), 128.1 (2C, C-2 or C-3 of Bn), 127.5 (C-4 of Bn), 125.5 (d, J 3, CH of Ar), 123.2 (4ry, d, J 8, C-1 of Ar), 122.5 (d, J 3, CH of Ar), 118.1 (3 C, d, J 85, C-1 of PPh₃), 62.1 (CH₂ of Bn), 40.6 (CH₃) and 25.5 (d, J 47, CH₂PPh₃); $\delta_{\rm P}$ +23.0; m/z (ES⁺) 472.05 (M⁺-Br, 90%) and 353.02 (M⁺–NMeBn, 100%).

4 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-phenylpropenoyl) methylene]triphenylphosphorane, 219

A suspension of salt **217** (0.30 g, 0.54 mmol) in THF (10 cm³) was stirred under nitrogen while a solution of BuLi (0.23 cm³, 2.25 M, 0.54 mmol) in hexanes was added. The resulting brightly coloured solution was stirred for 2 h and a solution of *N*-acylbenzotriazole **205** (0.135 g, 0.54 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (20 cm³) was added to the solution and the mixture was

extracted using ethyl acetate (2 × 20 cm3). The combined extracts were washed with water, dried and evaporated. Recrystallisation of the residue (Et₂O/EtOAc) gave **219** (0.24 g, 74%) as yellow crystals, mp 190–191 °C. (Found: M⁺+H, 602.2623. C₄₂H₃₇NOP (M^+ +H) requires, 602.2613); v_{max} /cm⁻¹ 1627 (C=C); δ_H 8.11–6.78 (30 H, m), 6.42 (1 H, d, *J* 8, H-3 of Ar), 4.46 (1 H, d, *J* 14, CH*H*Ph), 3.76 (1 H, d, *J* 14, CH*H*Ph) and 2.11 (3 H, s, NMe); δ_C see Table **2** (Page 122); δ_P +15.3; *m/z* (ES⁺) 602.07 (M⁺+H, 100%).

5 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl) (3-(2-furyl) propenoyl)methylene]triphenylphosphorane, 220

This was prepared as in 4. using salt **217** (1.00 g, 1.81 mmol), a solution of butyl lithium in hexanes (0.80 cm³, 2.25 M, 1.81 mmol) and *N*-acyl-benzotriazole **206** (0.43 g, 1.81 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **220** (0.45 g, 53%) as yellow crystals, mp 188–189 °C. (Found: M⁺+H, 592.2414. C₄₀H₃₅NO₂P (M^+ +H) requires, 592.2405); v_{max}/cm⁻¹ 1617 (C=C); $\delta_{\rm H}$ 7.66–7.52 (3 H, br m), 7.48–7.42 (2 H, m), 7.39–7.14 (15 H, m), 7.08–6.97 (4 H, m), 6.91 (2 H, d, *J* 8), 6.42 (1 H, d, *J* 8), 6.27 (1 H, dd, *J* 6, 3), 6.21 (1 H, br s), 4.41 (1 H, CH*H*Ph), 3.08 (1 H, CH*H*Ph) and 2.10 (3 H, NMe); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +16.8, *m*/*z* (ES⁺) 592.04 (M⁺+H, 100%).

6 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-(2-thienyl) propenoyl)methylene]triphenylphosphorane, 221

This was prepared as in 4. using salt **217** (1.00 g, 1.81 mmol) in THF (10 cm³), a solution of butyl lithium in hexanes (0.80 cm³, 2.25 M, 1.81 mmol) and *N*-acyl-benzotriazole **207** (0.41 g, 1.81 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **221** (0.48 g, 44%) as orange crystals, mp 182–183 °C. (Found: M⁺+H, 608.2156. C₄₀H₃₅NOPS (M^+ +H) requires, 608.2177); v_{max}/cm⁻¹ 1635 (C=C); $\delta_{\rm H}$ 7.60–7.57 (2 H, m), 7.50–7.27 (13 H, m), 7.19–7.15 (4 H, m), 7.09 (1 H, d, *J* 8), 7.07–6.91 (4 H, m), 6.90–6.84 (4 H, m), 6.36 (1 H, d, *J* 8, H-3 of Ar), 4.47 (1 H, d, *J* 14, CH*H*Ph), 3.75 (1 H, d, *J* 14, CH*H*Ph), 2.07 (3 H, s, NMe); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +16.6; *m/z* (ES⁺) 608.06 (M⁺+H, 100%).

7 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-(3-furyl)propenoyl) methylene]triphenylphosphorane, 222

This was prepared as in 4. using salt **217** (2.00 g, 3.62 mmol), a solution of butyl lithium in hexanes (1.60 cm³, 2.25 M, 3.62 mmol) and *N*-acyl-benzotriazole **208** (0.86 g, 3.62 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **222** (0.89 g, 41%) as yellow crystals, mp 184–185 °C; (Found: M⁺+H, 592.2411. C₄₀H₃₅NO₂P (M^{+} +H), requires 592.2405); v_{max}/cm⁻¹ 1633, 1434, 1105, 970, 748 and 692; $\delta_{\rm H}$ 7.87–7.27 (15 H, m), 7.21–7.09 (6 H, m), 7.07–6.79 (7 H, m), 6.40 (1 H, d, *J* 8, H-3 of Ar), 4.45 (1 H, d, *J* 14, CH*H*Ph) and 2.10 (3 H, s, Me); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +15.3; *m*/*z* (ES⁺) 592.09 (M⁺+H, 100%).

8 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-(3-thienyl) propenoyl)methylene]triphenylphosphorane, 223

This was prepared as in 4. using salt **217** (1.35 g, 2.44 mmol), a solution of butyl lithium (1.08 cm³, 2.25 M, 2.44 mmol) and *N*-acyl-benzotriazole **209** (0.55 g, 2.44 mmol). The resulting solid was recrystallised (Et2O/EtOAc) to give **223** (0.51 g, 35%) as orange crystals, mp 178–180 °C. (HMRS: found M⁺+H, 608.2175. C₄₀H₃₅NOPS (M^+ +H) requires, 608.2177); ν_{max} /cm⁻¹ 1624, 1492, 1197, 1101, 750 and 691; δ_{H} (+55°C) 7.68–7.54 (8 H, m), 7.45–7.33 (5 H, m), 7.30–7.21 (4 H, m), 7.19–7.11 (5 H, m), 7.09–7.02 (2 H, m), 6.99–6.89 (4 H, m), 6.52 (1 H, d, *J* 8), 4.40 (1 H, d, *J* 14, C*H*HPh), 3.84 (1 H, d, *J* 14, C*H*HPh) and 2.19 (3 H, s, Me); δ_{C} see Table **2** (Page 122); δ_{P} +15.3; *m/z* (ES⁺) 608.01 (M⁺+H, 100%).

9 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-(2-methyl) phenylpropenoyl)methylene]triphenylphosphorane, 224

This was prepared as in 4. using salt **217** (1.00 g, 1.81 mmol), a solution of butyl lithium in hexanes (0.89 cm³, 2.04 M, 1.81 mmol) and *N*-acyl-benzotriazole **210** (0.48 g, 1.81 mmol). Recrystallisation of the residue (diethyl ether/EtOAc) gave the title product **224** (0.55 g, 50%) as yellow crystals, mp 207–208 °C. (Found: M⁺+H, 616.2753. C₄₃H₃₉NOP (M^+ +H) requires, 616.2769); ν_{max} /cm⁻¹ 1634, 1433, 1172, 1086, 710 and 677; $\delta_{\rm H}$ 7.75 (1

H, d, J 15, CH=CH), 7.70–7.59 (5 H, br s), 7.51–7.31 (11 H, m), 7.24–7.16 (3 H, m), 7.12–6.93 (9 H, m), 6.55 (1 H, d, J 8, H-3 of Ar), 4.51 (1 H, d, J 14, CHHPh), 3.85 (1 H, d, J 14, CHHPh), 2.39 (3 H, s, Me) and 2.24 (3 H, s, Me); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +15.4; m/z (ES⁺) 616.08 (M⁺+H, 100%).

10 Preparation of [(2-(*N*-Methyl-*N*-benzylamino)phenyl)(3-(3-methyl-2thienyl)propenoyl)methylene]triphenylphosphorane, 225

This was prepared as in 4. using salt **217** (1.00 g, 1.81 mmol), solution of butyl lithium in hexanes (0.89 cm³, 2.04 M, 1.81 mmol) and *N*-acyl-benzotriazole **211** (0.49 g, 1.81 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give the title product **225** (0.55 g, 49%) as orange crystals, mp 197–198 °C. (Found: M⁺+H, 622.2347. C₄₁H₃₇NOPS (M^+ +H) requires, 622.2334); v_{max} /cm⁻¹ 1720, 1605, 1196, 1094, 719 and 686; $\delta_{\rm H}$ (+55°C) 7.71–7.51 (7 H, br m), 7.48–7.27 (10 H, m), 7.19–7.14 (3 H, m), 7.05–6.88 (5 H, m), 6.81 (1 H, d, *J* 15, C*H*=CH), 6.70 (1 H, d, *J* 5), 6.44 (1 H, d, *J* 8, C-3 of Ar), 4.45 (1 H, d, *J* 14, C*H*HPh), 3.72 (1 H, d, *J* 14, C*H*HPh), 2.22 (3 H, s, Me) and 2.15 (3 H, s, Me); $\delta_{\rm C}$ see Table **2** (Page 122); $\delta_{\rm P}$ +15.7; m/z (ES⁺) 622.03 (M⁺+H, 100%).

H FVP of *N*-methyl-*N*-benzylamino ylides with α,β-unsaturated acyl groups

1 FVP of Ylide 219

Ylide **208** (0.512 g, 0.85 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixure was purified by preparative TLC (1:1 CH₂Cl₂:hexane) to give *N*-methylbenzo[*c*]carbazole **200** (0.130 g, 66%) as colourless crystals, mp 110 °C (Lit.,¹⁴² 118–119 °C); $\delta_{\rm H}$ as for E 6.

2 FVP of Ylide 220



Ylide **220** (0.56 g, 0.95 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by preparative TLC (80:20 diethyl ether:hexane) to give *N*-methylfuro[2,3-*c*]carbazole **226** (0.136 g, 65%), mp 65–67 °C; (Found: M⁺+H, 222.0920. C₁₅H₁₂NO (*M*⁺+H) requires, 222.0919); $\delta_{\rm H}$ 8.20 (1 H, ddd, *J* 8.1, 1.2, 1, H-10), 7.82 (1 H, dd, *J* 2.1, 0.5, H-2), 7.66 (1 H, dd, *J* 9, 1, H-4), 7.50 (1 H, ddd, *J* 8, 6, 1, H-8), 7.47 (1 H, ddd, *J* 8, 1.7, 1.2, H-7), 7.35 (1 H, dd, *J* 9, 0.5, H-5), 7.33 (1 H, dd, *J* 2.1, 1, H-1), 7.29 (1 H, ddd, *J* 8.1, 6, 1.7, H-9), 3.92 (3 H, s, NMe); $\delta_{\rm C}$ 150.3 (4ry), 145.4 (CH), 140.7 (4ry), 137.2 (4ry), 124.9 (CH), 122.3 (4ry), 121.1 (CH), 120.6 (4ry), 118.8 (CH), 114.2 (4ry), 109.3 (CH), 108.7 (CH), 105.37 (CH), 105.32 (CH) and 29.5 (NMe); *m/z* (ES⁺) 222.09 (M⁺+H, 100%).



Ylide **221** (0.524 g, 0.86 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by preparative TLC (1:1 diethyl ether:hexane) to give *N*-methylthieno[2,3-*c*]carbazole **227** (0.123 g, 60%), mp 72–74 °C; (Found: M⁺+H, 238.0690. C₁₅H₁₂NS (*M*⁺+H) requires, 238.0691); $\delta_{\rm H}$ 8.33 (1 H, ddd, *J* 8, 1.2, 1, H-10),

8.07 (1 H, dd, *J* 5.4, 0.5, H-1), 7.96 (1 H, dd, *J* 8.8, 0.5, H-4), 7.69 (1 H, d, *J* 5.4, H-2), 7.52 (1 H, ddd, *J* 8, 4.8, 1, H-8), 7.51 (1 H, ddd, *J* 8, 1.7, 1.2, H-7), 7.49 (1 H, d, *J* 8.8, H-5) 7.33 (1 H, ddd, *J* 8, 4.8, 1.7, H-9) and 3.96 (3 H, s, Me); *m*/*z* (ES⁺) 238.07 (M⁺+H, 100%).

4 FVP of Ylide 222



Ylide **222** (0.3234 g, 0.54 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. Attempted separation by column chromatography (9:1 diethyl ether:hexane) gave significant peaks in fractions 31-end of column. There were recombined and attempted purification by preparative TLC (60:40 diethyl ether:hexane) possibly gave 9-methylphenanthridine **228**, $\delta_{\rm H}$ 9.25 (1 H, s, H-6), 8.59 (1 H, ddd, *J* 8, 1, 0.4, H-1), 8.42 (1 H, d, *J* 1, H-10), 8.20 (1 H, dd, *J* 8, 1, H-8), 8.00 (1 H, d, *J* 8, H-7), 7.75 (1 H, tdd, *J* 8, 1, 0.4, H-2 or 3), 7.68 (1 H, tdd, *J* 8, 1, 0.4, H-2 or 3), 7.56 (1 H, ddd, *J* 8, 1, 0.4, H-4) and 2.71 (3 H, ArMe) [Lit.¹⁵⁰ $\delta_{\rm H}$ (DMSO) 9.05 (1 H, s), 8.28 (1 H, dd, *J* 8.1, 1.2) and 2.41 (3 H, s).]; *m*/*z* (ES⁺) 536.08 (unknown, 100%), 301.04 (Ph₃PO+Na, 5%) and 194.09 (M⁺+H, 10%).



Ylide 223 (0.2147 g, 0.35 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was separated by column chromatography (60:40 diethyl ether:hexane) giving 3-(2-(3-thienyl)ethenyl)quinoline 234 (E, 0.0235 g, 28%. Z, 0.0126 g, 15%); (Found: M⁺+H, 238.0689. C₁₅H₁₂NS (M^+ +H) requires, 238.0690); δ_H (E) 9.09 (1 H, d, J 2, H-2), 8.14 (1 H, d, J 2, H-4), 8.09 (1 H, ddd, J 8, 1.2, 0.6, H-8), 7.81 (1 H, ddd, J 8, 1.2, 0.6, H-5), 7.67 (1 H, ddd, J 8, 7, 1.2, H-6 or 7), 7.54 (1 H, ddd, J 8, 7, 1.2, H-6 or 7), 7.43 (1 H, m, H-4'), 7.38–7.35 (2 H, m, H-2' and 5'), and 7.35 and 7.09 (2 H, AB pattern, J 16, H-a and b); δ_H (Z) 8.82 (1 H, d, J-2, H-2), 8.05 (1 H, d, J 2, H-4), 8.07 (1 H, ddd, J 8, 1.2, 0.6, H-8), 7.73 (1 H, ddd, J 8, 1.2, 0.6, H-5), 7.69 (1 H, ddd, J 8, 6, 1.2, H-6 or 7), 7.53 (1 H, ddd, J 8, 7, 1.2, H-6 or 7), 7.18–7.15 (2 H, m, H-2' and 5'), 6.86 (1 H, ddd, J 3, 2.5, 1, H-4') and 6.76 and 6.65 (2 H, AB pattern, J 12, H-a and b); m/z (ES⁺) 238.01 $(M^++H, 100\%)$. Also obtained was thieno[3,2-k]phenanthridine 235 (0.0066 g, 8%); (Found: M⁺+H, 236.0535. C₁₅H₁₀NS (M^+ +H) requires 236.0534); $\delta_{\rm H}$ 9.40 (1 H, s, H-6), 9.10 (1 H, ddd, J 6.8, 0.8, 0.3, H-11), 8.67 (1 H, ddd, J 4.6, 1, 0.3, H-3), 8.31 (1 H, ddd, J 6.8, 0.8, 0.3, H-8), 8.22 (1 H, ddd, J 6.3, 1, 0.3, H-4), 8.00 (1 H, dd, H-6.3, 0.3, H-5), 7.86 (1 H, dd, J 4.6, 0.3, H-2), 7.82 ddd, J 8.6, 5.6, 0.8, H-9) and 7.79 (1 H, ddd, J 6.8, 5.6, 0.8, H-10); m/z (ES⁺) 236.04 (M⁺+H, 100%).



Ylide **224** (0.1971 g, 0.32 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was roughly separated into two fractions by column chromatography (50:50 diethyl ether:hexane). The first fraction was purified by preparative TLC (10:90 diethyl

ether:hexane) to give 4,7-dimethylbenzo[c]carbazole 237 (0.0179g, 22%); (Found: M⁺+H, 246.1279. C₁₈H₁₆N (M^+ +H) requires, 246.1283); $\delta_{\rm H}$ 8.71 (1 H, ddd, J 8.4, 0.8, 0.5, H-1), 8.605 (1 H, ddd, J 8, 1.2, 0.5, H-11), 8.119 (1 H, dd, J 9.2, 0.5, H-5), 7.696 (1 H, d, J 9.2, H-6), 7.602 (1 H, dd, J 8.4, 6.8, H-2), 7.562 (1 H, ddd, J 8, 1.2, 0.5, H-8), 7.515 (1 H, ddd, J 8, 7.2, 1.2, H-9), 7.385 (1 H, ddd, J 8, 7.2, 1.2, H-10), 7.324 (1 H, dd, J 6.8, 0.8, H-3), 4.00 (3H, s, NMe) and 2.82 (3H, s, ArMe); δ_C 129.1 (4ry), 125.5 (CH), 123.0 (CH), 122.9 (CH), 122.1 (CH), 121.1 (CH), 120.5 (CH), 119.9 (4ry), 119.3 (4ry), 118.6 (CH), 114.6 (4ry), 113.6 (4ry), 112.8 (4ry), 109.1 (CH), 108.0 (CH), 28.2 (NMe) and 19.4 (ArMe); m/z (ES⁺) 246.08 (M⁺+H, 100%). The second fraction was purified by TLC diethyl ether:hexane) to preparative (10:90)give 3-(2-(2methylphenyl)ethenyl)quinoline 236 (E, 0.0134 g, 17%. Z, 0.0101 g, 14%); (Found: M^+ +H, 246.1291. C₁₈H₁₆N (M^+ +H) requires, 246.1283); δ_H (E) 9.13 (1 H, d, J 2, H-2), 8.18 (1 H, d, J 2, H-4), 8.10 (1 H, d, J 8, H-5 or 8), 7.84 (1 H, dd, J 8, 1, H-5 or 8), 7.69 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.66 (1 H, d, J 8), 7.56 (1 H, half of AB pattern, J 16, H-a or b), 7.55 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.29–7.20 (3 H, m), 7.15 (1 H, half of AB pattern, J 16, H-a or b) and 2.49 (3 H, s, Me); $\delta_{\rm H}(Z)$ 8.62 (1 H, d, J 2, H-2), 8.09 (1 H, d, J 8, H-5 or 6), 7.84 (1 H, d, J 2, H-4), 7.63 (1 H, ddd, J 8, 6.5, 1, H-6 or 7), 7.61 (1 H, d, J 8), 7.46 (1 H, ddd, J 8, 6.5, 1, H-6 or 7), 7.19 (1 H, br t, J 7.5), 7.12 (1 H, d, J 8), 7.04 (1 H, br t, J 7.5), 6.89 and 6.75 (2 H, AB pattern, J 12, H-a and b) and 2.32 (3 H, s, Me); m/z (ES⁺) 246.00 (M⁺+H, 100%). Also isolated form the same preparative TLC was 9methylbenzo[k]phenanthridine **238** (0.0171 g, 22%), (Found: M⁺+H, 244.1120. C₁₈H₁₅N (M^++H) requires, 244.1126); δ_H 9.37 (1 H, s, H-6), 9.07 (2 H, t, J 8, H-1 and 12), 8.38 (1 H, dd, J 8, 2, H-4), 8.25 (1 H, d, J 9, H-8), 8.00 (1 H, d, J 9, H-7), 7.81 (1 H, ddd, J 8, 7, 1, H-2 or 3), 7.74 (1 H, ddd, J 8, 7, 1, H-2 or 3), 7.67 (1 H, t, J 7, H-11), 7.59 (1 H, d, J 7, H-10) and 2.87 (3 H, s, Me); m/z (ES⁺) 244.03 (M⁺+H, 100%).


Ylide **225** (0.1072 g, 0.17 mmol) was subjected to FVP at 700 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was roughly separated into two fractions by column chromatography (50:50 diethyl ether:hexane). The combined fractions 18–36 were purified by preparative TLC (30:70 diethyl ether:hexane) to give what appeared to be impure 3-(2-(3-methyl-2-thienyl)ethenyl)quinoline **239** as a dark brown oil. Indicative peaks at $\delta_{\rm H}$ 9.09 (1 H, d, *J* 2, H-2 *E*), 8.83 (1 H, d, *J* 2, H-2 *Z*), 2.39 (3 H, s, ArMe *E* or *Z*) and 2.20 (3 H, s, ArMe, *E* or *Z*) indicated a 1:1 mixture of *E*/*Z*, however further purfication and analysis was not possible.

Ι Synthesis of *N*,*N*-dibenzylamino ylides with α,β-unsaturated acyl groups

1 Preparation of Benzyl 2-(*N*,*N*-dibenzylamino)benzoate, 240

Potassium carbonate (80.80 g, 584.0 mmol) and 2-aminobenzoic acid **136** (20.00 g, 146.0 mmol) were added to a stirred mixture of methanol:water (5:1, 750 cm³) and benzyl bromide (79.9 g, 55.50 cm³, 467.2 mmol) was added. The mixture was heated under reflux for 3 h and the solvent mixture was removed. Water (200 cm³) was added to the residue and the mixture was extracted using ethyl acetate (2×100 cm³). The combined organic fractions were washed with water, dried and evaporated to give a dark brown oil which was shown to be a mixture of desired product, benzyl bromide and tribenzylamine by ¹H NMR. The oil was Kugelrohr distilled with an oil pump vacuum. Benzyl bromide was removed at 90 °C, tribenzylamine was removed at 150 °C and **240** was obtained as the residue (45.3 g, 79%) as a light brown oil (Lit.¹⁵¹, white solid, mp 53–55 °C). $\delta_{\rm H}$ 8.12 (1 H, d, *J* 8), 7.70 (1 H, dd, *J* 8, 2), 7.43 (2 H, d, *J* 8), 7.36-7.14 (13 H, m), 6.92-6.86 (2 H, m), 5.34 (2 H, s, OCH₂Ph) and 4.17 (4 H, s, N(CH₂Ph)₂).

2 Preparation of 2-(*N*,*N*-dibenzylamino)benzyl alcohol, 241

Under a nitrogen atmosphere, a solution of ester **240** (45.00 g, 114.3 mmol) in dry THF (400 cm³) was added dropwise to a stirred suspension of LiAlH₄ (4.04 g, 125.9 mmol) in dry THF (80 cm³) and the resulting mixture was stirred at room temperature for 18 h. To

destroy the excess of LiAlH₄, water (4.5 cm³) in THF (31.5 cm³) was added to the mixture followed by 15% solution sodium hydroxide (4.5 cm³) and finally water (13.5 cm³). The suspension was stirred for 0.5 h and MgSO₄ was added and stirred overnight. The mixture was filtered through celite, the solid washed with ethyl acetate and the combined filtrate and washings evaporated to give **241** (30.00 g, 90%) as a pale yellow oil. (Found: M⁺+Na, 326.1521. C₂₁H₂₁NaNO (M^+ +Na) requires, 326.1521); v_{max} /cm⁻¹ 3325 (OH), 1601, 1483, 1197 and 898; $\delta_{\rm H}$ 7.30–7.12 (13 H, m), 7.07–7.01 (1 H, m), 4.56 (2 H, s, CH₂ of OBn), 4.01 (4 H, s, 2 CH₂ of NBn₂) and 2.94 (1 H, br s, OH); $\delta_{\rm C}$ 148.8 (4ry, C-1 of Ar), 137.3 (2 C, 4ry, C-1 of Bn), 136.7 (4ry, C-2 of Ar), 129.1 (4 C, C-2 or 3 of Bn), 128.3 (CH), 128.2 (4 C, C-2 or 3 of Bn), 127.6 (CH), 127.2 (2 C, C-4 of Bn), 124.8 (C-5 of Ar), 123.3 (C-3 of Ar), 63.2 (CH₂OH) and 58.0 (2 C, 2 CH₂ of Bn); m/z (ES⁺) 326.08 (M⁺+Na, 100%)

3 Preparation of 2-(*N*,*N*-dibenzylamino)benzyltriphenylphosphonium bromide, 242

A solution of alcohol 241 (28.86 g, 95.5 mmol) in toluene (150 cm³) was stirred and heated to 60 °C and phosphorus tribromide (10.5 g, 3.68 cm³, 390 mmol) was added dropwise over 0.5 h. The solution was stirred at 60 °C for 2 h, and cooled to rt for 16 h. The mixture was added to water (80 cm^3) and the organic layer separated, washed with water $(2 \times 70 \text{ cm}^3)$ and dried. The dried organic solution was heated under reflux with triphenylphosphine (24.50 g, 95.5 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to give 242 (25.59 g, 42%) as a white powder mp 268-269 °C (Found: C, 74.3; H, 5.9; N, 2.2. C₃₉H₃₅BrNP requires C, 74.8; H, 5.6; N, 2.2%); (Found: M⁺–Br, 548.2509. C₃₉H₃₅NP (M^+ –Br) requires 548.2507); v_{max} /cm⁻¹ 1589, 1336, 1205, 1111 and 739; δ_H 7.79 (3 H, t, J 8), 7.62 (6 H, td, J 8, 3), 7.48–7.36 (6 H, m), 7.31 (1 H, t, J 8), 7.26–7.17 (6 H, m), 7.04 (1 H, d, J 8), 6.97 (1 H, t, J 8), 6.93–6.83 (5 H, m), 4.86 (2 H, d, J 14, CH₂PPh₃) and 3.67 (4 H, s, 2 CH₂ of Bn); δ_C 151.2 (4ry, d, J 7, C-1 of Ar), 136.2 (2 C, 4ry, C-1 of Bn), 135.1 (3 C, d, J 2, C-4 of PPh₃), 133.5 (6 C, d, J 10, C-2 of PPh₃), 130.1 (6 C, d, J 12, C-3 of PPh₃), 129.9 (d, J 5, C-6 of Ar), 129.5 (d, J 3, C-4 of Bn), 128.7 (4 C, C-2 or 3 of Bn), 127.9 (4 C, C-2 or 3 of Bn), 127.2 (2 C, C-4 of Bn), 125.5 (d, J 3, C-3 or 5 of Ar), 125.4 (d, J 3, C-3 or 5 of Ar), 124.1 (4ry, d, J 7, C-2 of Ar), 117.3 (3 C, d, *J* 85, C-1 of PPh₃), 57.5 (2C, 2 CH₂ of Bn) and 24.5 (d, *J* 49, CH₂PPh₃); $\delta_{\rm P}$ +21.8; *m*/*z* (ES⁺) 548.07 (M⁺–Br⁻, 100%).

4 Preparation of [(2-(*N*,*N*-dibenzylamino)phenyl)(3-phenylpropenoyl) methylene]triphenylphosphorane, 243

A suspension of salt **242** (1.00 g, 1.59 mmol) in THF (10 cm³) was stirred under nitrogen while a solution of BuLi in hexanes (0.71 cm³, 2.25 M, 1.59 mmol) was added. The resulting brightly coloured solution was stirred for 2 h and a solution of *N*-acyl benzotriazole **205** (0.39 g, 1.59 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (20 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2 × 20 cm³). The combined extracts were washed with water, dried and evaporated. Recrystallisation of the residue (Et₂O/EtOAc) gave **243** (0.62 g, 56%) as yellow crystals, mp 199–200 °C. (Found: M⁺+H, 678.2917. C₄₈H₄₂NOP (M^+ +H) requires, 678.2926); ν_{max} /cm⁻¹ 1634, 1483, 1434, 1205 and 1087; $\delta_{\rm H}$ (+55 °C) 7.68–7.52 (3 H, m), 7.50–7.28 (8 H, m), 7.28–7.03 (19 H, m), 6.93 (1 H, tt, *J* 8, 1), 6.83–6.77 (4 H, m), 6.61 (1 H, d, *J* 8, C-3 of Ar), 4.21 (2 H, d, *J* 14, CHHPh) and 3.91 (2 H, d, *J* 14, CHHPh); $\delta_{\rm C}$ see Table **3** (Page 134); $\delta_{\rm P}$ +16.8; *m/z* (ES⁺) 678.04 (M⁺+H, 100%).

5 Preparation of [(2-(*N*,*N*-Dibenzylamino)phenyl) (3-(2-furyl)propenoyl) methylene]triphenylphosphorane, 244

This was prepared as in 4. using salt **242** (2.00 g, 3.6 mmol), a solution of butyl lithium in hexanes (1.76 cm³, 2.04 M, 3.6 mmol) and *N*-acyl benzotriazole **206** (0.86 g, 3.6 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **244** (1.23 g, 51%) as yellow crystals, mp 189–190 °C; (Found: M⁺+H, 668.2708. C₄₆H₃₉NO₂P (M^+ +H) requires, 688.2718); ν_{max} /cm⁻¹ 2194, 1720, 1638, 1209, and 719; δ_{H} (+55 °C) 7.61–7.38 (7 H, br m), 7.37–6.99 (19 H, m), 6.93 (1 H, tt, *J* 7,1), 6.85–6.79 (4 H, m), 6.56 (1 H, d, *J* 8, H-3 of Ar), 6.27–6.21 (2 H, m, H-3 and 4 of furyl), 4.16 (1 H, d, *J* 14, CHHPh) and 3.94 (1H, d, *J* 14, CHHPh); δ_{C} see Table **3** (Page 134); δ_{P} +15.7; *m/z* (ES⁺) 668.00 (M⁺+H, 100%).

6 Preparation of [(2-(*N*,*N*-Dibenzylamino)phenyl)(3-(2-thienyl)propenoyl) methylene]triphenylphosphorane, 245

This was prepared as in 4. using salt **242** (2.00 g, 3.6 mmol), a solution of butyl lithium in hexanes (1.76 cm³, 2.04 M, 3.6 mmol) and *N*-acyl benzotriazole **207** (0.81 g, 3.6 mmol). The resulting solid was recrystallised (Et₂O/EtOAc) to give **245** (1.36 g, 54%) as orange crystals, mp 192–193 °C; (Found: M⁺+H, 684.2488. C₄₆H₃₉NOPS (M^+ +H) requires, 684.2490); v_{max} /cm⁻¹ 1601, 1487, 1221, 1090 and 743; δ_H 7.7–7.64 (3 H, m), 7.62–7.41 (9 H, m), 7.35–29 (4 H, m), 7.19–6.99 (11 H, m), 6.94–6.74 (9 H, m), 6.53 (1 H, d, *J* 8, C-3 of Ar), 4.12 (2 H, d, *J* 14, C*H*HPh) and 3.89 (2 H, d, *J* 14, C*H*HPh); δ_C see Table **3** (Page 134); δ_P 16.5; m/z (ES⁺) 683.97 (M⁺+H, 100%).

7 Preparation of [(2-(*N*,*N*-benzylamino)phenyl)(3-(2-methylphenyl) propenoyl)methylene]triphenylphosphorane, 246

This was prepared as in 4. using **242** (1.00 g, 1.81 mmol), a solution of butyl lithium in hexanes (0.89 cm³, 2.04 M, 1.81 mmol) and *N*-acyl benzotriazole **210** (0.4766 g, 1.81 mmol). Recrystallisation of the residue (Et₂O/EtOAc) gave **246** (0.69 g, 55%) as yellow crystals, mp 213–214 °C; (Found: M⁺+H, 692.3074. C₄₉H₄₃NOP (M^+ +H) requires, 692.3082); v_{max} /cm⁻¹ 1614, 1185, 1107, 747 and 686; δ_{H} 8.07–7.58 (7 H, m), 7.52–7.41 (4 H, m), 7.22–6.98 (13 H, m), 6.97–6.78 (8 H, m), 6.60 (1 H, d, *J* 8, C-3 of Ar), 4.24 (2 H, d, *J* 15, C*H*HPh), 3.89 (2 H, d, *J* 15, C*H*HPh) and 2.31 (3 H, s, Me); δ_{C} see Table **3** (Page 134); δ_{P} 15.9; *m/z* (ES⁺) 692.12 (M⁺+H, 100%).

J FVP of *N*,*N*-dibenzylamino ylides with α , β -unsaturated acyl groups

1 FVP of Ylide 243



Ylide 243 (0.0805 g, 0.12 mmol) was subjected to FVP at 800 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixure was purified by column chromatography (30:70 diethyl ether:hexane) to give 3-styrylquinoline **247** (*E*, 0.0096 g, 35%; *Z*, 0.0025 g, 9%); (Found: M⁺+H, 232.1131. $C_{17}H_{14}N$ (*M*⁺+H) requires, 232.1126); δ_{H} (*E*) 9.13 (1 H, d, *J* 2, H-2), 8.19 (1 H, d, *J* 2, H-4), 8.09 (1 H, dd, J 8, 1, H-8), 7.83 (1 H, dd, J 8, 1, H-5), 7.68 (1 H, ddd, J 8, 7,1, H-6 or 7), 7.61–7.57 (2 H, m), 7.55 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.44 (2 H, m), 7.35 (1 H, half of AB pattern, J 16, H-a or b), 7.34–7.29 (1 H, m) and 7.25 (1 H, half of AB pattern, J 16, H-a or b); δ_H (Z) 8.75 (1 H, d, J 2, H-2), 8.03 (1 H, dd, J 8, 1, H-8), 7.99 (1 H, d, J 2, H-4), 7.68 (1 H, d, J 8, 1, H-5), 7.66 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.50 (2 H, ddd, J 8, 7, 1, and m), 7.40–7.34 (2 H, m), 7.27–7.23 (2 H, m) and 6.84 and 6.71 (2 H, AB pattern, J 12, H-a and b) [in good agreement with literature¹⁵²]; m/z (ES⁺) 232.07 (H⁺+H, 100%). Also isolated for the same preparative TLC was benzo[k]phenanthridine 248 (0.0049 g, 18%); (Found M⁺+H, 230.0965. $C_{17}H_{12}N$ (M⁺+H) requires, 230.0970); δ_H 9.38 (1 H, s, H-6), 9.22 (1 H, dd, J 8, 2, H-1 or 12), 9.14 (1 H, dd, J 8, 2, H-1 or 12), 8.40 (1 H, d, J 8), 8.12-8.08 (2 H, m), 8.06 (1 H, d, J 9, H-7 or 8), 7.98 (1 H, d, J 9, H-7 or 8) and 7.87–7.76 (3 H, m); m/z (ES⁺) 230.06 (M⁺+H, 100%).

2 FVP of Ylide 244



Ylide **244** (0.1106 g, 0.16 mmol) was subjected to FVP at 800 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by preparative TLC (50:50 diethyl ether:hexane) to give 3-(2-(2-furyl)ethenyl)quinoline **249** (*E*, 0.0140 g, 39%; *Z*, 0.0007 g, 2%); (Found M⁺+H, 222.0911. C₁₅H₁₂NO (*M*⁺+H) requires, 222.0919); $\delta_{\rm H}$ (*E*) 9.08 (1 H, d, *J* 2, H-2), 8.12 (1 H, d, *J* 2, H-4), 8.08 (1 H, dd, *J* 8, 1, H-8), 7.81 (1 H, dd, *J* 8, 1, H-5), 7.67 (1 H, ddd, *J* 8, 7, 1, H-6 or 7), 7.54 (1 H, ddd, *J* 8, 7, 1, H-6 or 7), 7.46 (1 H, br s, 2'), 7.19 and 7.11 (2 H, AB pattern *J* 16, H-a and b), and 6.48–6.46 (2 H, m, H-3' and 4'); $\delta_{\rm H}$ (*Z*) 9.05 (1 H, d, *J* 2, H-2), 8.24 (1 H, d *J* 2, H-4), 8.11 (1 H d, *J* 8, H-8), 7.82 (1 H, d, *J* 8, H-5), 7.76–7.44 (2 H, m), 7.31 (1 H, d, *J* 2, H-2'), 6.59 and 6.52 (2 H, AB pattern, *J* 12, H-a and b) and 6.48–6.34 (2 H, m, H-3' and 4'); m/z (ES⁺) 222.07 (M⁺+H, 100%).

Also isolated was a mixture of 2-phenyl-3-(2-(2-furyl)ethenyl)quinoline **251** and 6-phenylfuro[2,3-*k*]phenanthridine **250** in varying ratios from different fractions. For **250**, (0.0186 g, 25%); (Found: M⁺+H, 296.1078. C₂₁H₁₄NO (M^+ +H) requires, 296.1075); $\delta_{\rm H}$ 8.19 (1 H, d, *J* 8, H-11), 7.82 (1 H, d, *J* 2, H-9), 7.72–7.67 (1 H, m), 7.61 (1 H, dd, *J* 8.7, 1, H-4), 7.57–7.48 (6 H, m), 7.38–7.29 (1 H, m), 7.39 (1 H, d, *J* 8.7, H-5) and 7.33 (1 H, dd, *J* 2, 1, H-1); *m*/*z* (ES⁺) 296.09 (M⁺+H, 100%). For **251** $\delta_{\rm H}$ 8.39 (1 H, s, H-4), 8.13 (1 H, d, *J* 8, H-8), 7.86 (1 H, d, *J* 8, H-5), 7.72–7.32 (8 H, m), 7.15 and 6.99 (2 H, AB pattern, *J* 15, H-a and b) and 6.43–6.38 (2 H, m, H-3' and 4').

Ylide **244** (0.0390 g, 0.06 mmol) was subjected to FVP at 500 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO and other products. The mixture was purified by preparative TLC (50:50 diethyl ether:hexane) to give 2-(4-(2-furyl)-but-1-y*N*-3-enyl)-*N*,*N*-dibenzylaniline **252** (0.0089 g, 39%) as a dark brown oil. (Found: M⁺+H, 390.1853. C₂₈H₂₄NO (*M*⁺+H) requires 390.1858); $\delta_{\rm H}$ 7.44 (1 H, dd, *J* 8, 2, H-6), 7.39–7.34 (4 H, m), 7.32–7.27 (4 H, m), 7.25–7.19 (3 H, m), 7.09 (1 H, ddd, *J* 8, 7, 2, H-5), 6.87 (1 H, t, *J* 8), 6.82 (1 H, d, *J* 8), 6.40–6.38 (1 H, m, furyl), 6.28 (1 H, d, *J* 16, half of AB pattern), 6.23 (1 H, d, *J* 3, furyl), 6.14 (1 H, d, *J* 16, half of AB pattern) and 4.48 (4 H, s, 2 × CH₂); $\delta_{\rm C}$ 143.2 (CH, C-5'), 138.7 (2 C 4ry, 2 × C-1 of Bn), 134.2 (CH, C-d or 3), 128.8 (CH, C-5), 128.3 (4 C, 2 × C-2 or 3 of Bn), 127.9 (4 C, 2 × C-2 or 3 of Bn), 127.4 (CH, C-d or 3), 126.8 (2 C, 2 × C-4 of Bn), 121.0 (CH, C-4 or 6), 111.8 (CH, C-3' or 4'), 109.7 (CH, C-3' or 4'), 106.6 (CH, C-c) and 56.0 (2 C, CH₂ of Bn); *m*/z (ES⁺) 390.09 (M⁺+H, 100%).

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Ylide **245** (0.1486 g, 0.2173 mmol) was subjected to FVP at 800 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by column chromatography (1:1 diethyl ether:hexane) to give 3-(2-(2-thienyl)ethenyl)quinoline 253 (E, 0.0181 g, 35%; Z, 0.0031 g, 6%), (Found: M⁺+H, 238.0690. C₁₅H₁₂NS (*M*⁺+H) requires, 238.0691); δ_H (*E*) 9.08 (1 H, d, *J* 2, H-2), 8.14 (1 H, d, J 2, H-4), 8.08 (1 H, dd, J 8, 1, H-8), 7.80 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.68 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.47 (1 H, d, J 16, half of AB pattern), 7.28–7.26 (1 H, m), 7.17 (1 H, d, J 3, thienyl), 7.06 (1 H, d, J 16, half of AB pattern), 7.07–7.04 (1 H, m, thienyl) and 6.99 (1 H, d, J 7, thienyl); δ_H (Z) 8.88 (1 H, d, J 2, H-2), 8.16 (1 H, d, J 2, H-4), 8.10 (1 H, dd, J 8, 1, H-8), 7.78 (1 H, dd, J 8, 1, H-5), 7.72 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.55 (1 H, ddd, J 8, 7, 1, H-6 or 7), 7.10 (1 H, m, thienyl), 7.02 (1 H, m, thienyl), 6.92-6.90 (1 H, m, thienyl) and 6.91 and 6.66 (2 H, AB pattern, J 12, H-a and b). Fractions 5-12 was combined and purified by preparative TLC (35:65 diethyl ether:hexane) to give thieno[2,3-c]carbazole **254** (0.0073 g, 15%), (Found: M⁺, 222.0372. $C_{14}H_8NS$ (M^+) requires 222.0377); $\delta_H 8.31$ (1 H, dd, J 8, 1, H-10), 8.07 (1 H, dd, J 6, 1, H-4), 7.91 (1 H, dd, J 8, 1, H-1), 7.70 (1 H, d, J 5, H-5), 7.56–7.49 (1 H, m, H-7), 7.51 (1 H, d, J 8, H-2), 7.58 (1 H, ddd, J 8, 7, 1, H-8 or 9) and 7.34 (1 H, ddd, J 8, 7, 1, H-8 or 9); m/z (ES⁻) 222.02 (M⁺, 100%). Also isolated was thieno[2,3-k]phenanthridine 255 (0.0026 g, 5%) as a black tar (Found: M⁺+H, 236.0529. C₁₅H₁₀NS (M⁺+H) requires, 236.0534); δ_H 9.46 (1 H, s, H-6), 9.09 (1 H, ddd, J 9.2, 1.2, 0.8, H-11), 8.39 (1 H, ddd, J 9.2, 1.2, 0.8, H-8), 8.22 (1 H, d, J 8, H-4 or 5), 8.08 (1 H, d, J 8, H-4 or 5), 7.91 (1 H, d, J 5.6, H-2 or 3), 7.90 (1 H, ddd, J 9.2, 7.6, 1.2, H-9 or 10), 7.88 (1 H, ddd, J 9.2, 7.6, 1.2, H-9 or 10) and 7.71 (1 H, d, J 5.6, H-2 or 3); m/z (ES⁺) 235.94 (M⁺+H, 100%).



Ylide **246** (0.2197 g, 0.32 mmol) was subjected to FVP at 800 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by column chromatography (10:90 diethyl ether:hexane) to give 3-(2-(2-methylphenyl)ethenyl)quinoline **236** (*E*, 0.0241 g, 31%. *Z*, 0.0164 g, 21%); $\delta_{\rm H}$ as for H6.

K Total Synthesis of Eustifoline D

1 Preparation of 5-Methyl-2-aminobenzoic acid, 257

This was prepared as in D12. using acid **188** (7.89 g, 3.9 mmol) in ammonia (200 cm³) with FeSO₄.7H₂O (98.63 g, 335.3 mmol) to give the desired product **257** (3.35 g, 50%) as a pale brown solid mp 170–171 °C (Lit.,¹⁵³ 175 °C); $\delta_{\rm H}$ 7.48 (1 H, d, *J* 1, H-6), 7.04 (1 H, d, *J* 8, 1, H-4), 6.64 (1 H, d, *J* 8, H-3) and 2.87 (3 H, s, Me).

2 Preparation of Benzyl 2-(*N*,*N*-dibenzylamino)-5-methylbenzoate, 258

Potassium carbonate (23.77 g, 171.9 mmol) and amino acid **257** (6.50 g, 43.0 mmol) were added to a stirred mixture of methanol:water (5:1, 240 cm³) and benzyl bromide (23.53 g, 16.36 cm³, 137.7 mmol) was added. The mixture was heated under reflux for 3 h and the solvent mixture was removed. Water (150 cm³) was added to the residue and the mixture was extracted using ethyl acetate ($2 \times 100 \text{ cm}^3$). The combined organic fractions were washed with water, dried and evaporated to give a dark brown oil which was triturated with ether. The solid was filtered off and found to be 2-(*N*,*N*-dibenzylamino)-5-methylbenzoic acid (4.39 g, 31%) mp 141–142 °C; $\delta_{\rm H}$ 7.07 (1 H, d, *J* 8, H-3), 7.34 (2 H, m), 7.29–7.25 (6 H, m), 7.19–7.17 (4 H, m), 4.15 (4 H, s, 2 × CH₂ of Bn) and 2.36 (3 H,

s, Me). The filtrate was evaporated to give a mixture of desired product, benzyl bromide and tribenzylamine by ¹H NMR. The oil was Kugelrohr distilled to give benzyl bromide (bp 90 °C/3 Torr), tribenzylamine (bp 150 °C/3 Torr) and the desired product **258** was obtained as the residue (6.95 g, 39%). (Found: M⁺+H, 422.2110. C₂₉H₂₈NO₂ (M^+ +H) requires, 422.2120); v_{max} /cm⁻¹ 1721 (CO), 1487, 1364, 1126 (O-C), 1066, 952 and 689; $\delta_{\rm H}$ 7.48 (1 H, d, *J* 2, H-6), 7.47–7.17 (15 H, m), 7.06 (1 H, dd, *J* 8, 2, H-4) 6.82 (1 H, d, *J* 8, H-3), 5.34 (2 H, s, CH₂ of OBn), 4.13 (4 H, s, 2 × CH₂Ph) and 2.23 (3 H, s, Me); $\delta_{\rm C}$ 168.3 (4ry, CO), 148.44 (4ry, C-1 of Ar), 138.1 (2 C, 4ry, C-1 of NBn), 135.9 (4ry, C-1 of OBn), 132.4 (CH), 131.3 (CH), 130.7 (4ry, C-2 of Ar), 128.5 (CH), 128.4 (2 C, CH), 128.3 (4 C, C-2 or 3 of NBn), 128.2 (CH), 128.1 (4 C, C-2 or 3 of NBn), 126.8 (2 C, CH), 125.6 (4ry), 121.7 (2 C, CH), 66.7 (CH₂ of OBn), 57.2 (2 C, 2 × CH₂ of NBn) and 20.4 (Me); *m*/z (ES⁺) 422.05 (M⁺+H, 100%).

3 Preparation of 2-(*N*,*N*-dibenzylamino)-5-methylbenzyl alcohol, 259

Under a nitrogen atmosphere, a solution of **258** (8.00 g, 18.98 mmol) in dry THF (70 cm³) was added dropwise to a stirred suspension of LiAlH₄ (0.7918 g, 20.88 mmol) in dry THF (10 cm^3) and the resulting mixture was stirred at room temperature for 18 h. To destroy the excess of LiAlH₄, water (0.80 cm³) in THF (5.6 cm³) was added to the mixture followed by 15% solution sodium hydroxide (0.80 cm³) and finally water (2.40 cm³). The suspension was stirred for 0.5 h and MgSO₄ was added and stirred overnight. The mixture was filtered through celite, the solid washed with ethyl acetate and the combined filtrate and washings evaporated to give 259 (4.69 g, 82%) as a pale yellow oil. (Found: M⁺, 317.1783. $C_{22}H_{23}NO(M^+)$ requires, 317.1780); v_{max}/cm^{-1} 3379 (OH), 1601, 1501, 1358, 1191 and 1036; δ_H 7.29–7.18 (10 H, m), 7.13 (1 H, d, J 8, H-4 of Ar), 7.03 (1 H, dd, J 8, 2, H-3 of Ar), 6.97 (1 H, d, J 2, H-6 of Ar), 4.60 (2 H, CH₂OH); 4.26 (1 H, br s, CH₂OH), 4.03 (4 H, s, $2 \times CH_2$ of NBn) and 2.28 (3 H, s, Me); δ_C 146.6 (4ry, C-1 of Ar), 137.6 (2 C, 4ry, C-1 of Bn), 136.8 (4ry, C-5 of Ar), 134.8 (4ry, C-2 of Ar), 129.4 (4 C, C-2 or 3 of Bn), 129.3 (C-4 or 6 of Ar), 128.5 (C-4 or 6 of Ar), 128.4 (4 C, C-2 or 3 of Bn), 127.4 (2 C, C-4 of Bn), 123.5 (C-3 of Ar), 63.9 (CH₂OH), 58.7 (2 C, 2 × CH₂ of NBn) and 20.9 (Me); m/z (EI) 317.18 (M⁺, 5%) and 226.11 (M⁺-Bn, 100%).

4 Preparation of 2-(*N*,*N*-dibenzylamino)-5-methylbenzyl triphenylphosphonium bromide, 260

A solution of alcohol **259** (4.00 g, 12.6 mmol) in toluene (50 cm³) was stirred and heated to 60 °C and phosphorus tribromide (1.19 g, 0.42 cm³, 4.4 mmol) was added dropwise over 0.5 h. The solution was stirred at 60 °C for 2 h, and cooled to rt for 16 h. The mixture was added to water (30 cm³) and the organic layer separated, washed with water $(2 \times 20 \text{ cm}^3)$ and dried. The dried organic solution was heated under reflux with triphenylphosphine (3.30 g, 12.6 mmol) for 8 h. The precipitate was filtered off, washed with diethyl ether and oven dried to 260 (4.5 g, 67%) as a white powder, mp 201–203 °C. (Found: C, 74.5; H, 6.45; N, 2.2. C₄₀H₃₇BrNP requires C, 74.8; H, 5.8; N, 2.2%); (Found: M⁺-Br, 562.2675. C₄₀H₃₇NP (M^+ -Br) requires, 562.2664); v_{max}/cm^{-1} 1430, 1373, 1107, 739 and 690; δ_H 7.79 (3 H, t, J 8), 7.63 (6 H, td, J 8, 3), 7.48–7.38 (6 H, m), 7.56–7.17 (6 H, m), 7.11 (1 H, br dd, J 8, 2, H-3 of Ar), 6.94 (1 H, d, J 8, H-4 of Ar), 6.89-6.85 (4 H, m), 6.56 (1 H, br d, J 2, H-6 of Ar), 4.75 (2 H, d, J 14, CH₂PPh₃Br), 3.65 (4 H, s, 2 × CH₂) of NBn) and 2.05 (3 H, s, Me); δ_C 148.9 (4ry, d, J 7, C-1 of Ar), 137.0 (4ry, C-5 of Ar), 136.7 (2 C, 4ry, C-1 of Bn), 135.4 (3 C, d, J 2, C-4 of PPh₃), 135.3 (CH of Ar), 134.1 (CH of Ar), 134.0 (6 C, d, J 9, C-2 of PPh₃), 130.4 (6 C, d, J 12, C-3 of PPh₃), 129.1 (4 C, C-2 or 3 of Bn), 128.2 (4 C, C-2 or 3 of Bn), 127.5 (2 C, C-4 of Bn), 125.4 (CH of Ar), 124.1 (4ry, d, J 7, C-2 of Ar), 117.9 (3 C, 4ry, J 86, C-1 of PPh₃), 57.9 (2 C, 2 × CH₂ of NBn), 25.0 (d, J 50, CH_2PPh_3) and 20.9 (ArMe); δ_P +21.7; m/z (ES⁺) 562.15 (M⁺-Br, 100%).

5 Preparation of [(2-(*N*,*N*-Dibenzylamino)-5-methylphenyl) (3-(2furyl)propenoyl)methylene]triphenylphosphorane, 256

A suspension of salt **260** (3.00 g, 4.67 mmol) in THF (10 cm³) was stirred under nitrogen while a solution of BuLi in hexanes (0.29 cm³, 2.04 M, 4.67 mmol) was added. The resulting brightly coloured solution was stirred for 2 h and a solution of *N*-acyl benzotriazole **206** (1.12 g, 4.67 mmol) in THF (5 cm³) was added and the mixture was stirred for a further 18 h. Water (20 cm³) was added to the solution and the mixture was extracted using ethyl acetate (2×20 cm³). The combined extracts were washed with water, dried and evaporated. The resulting solid was recrystallised (Et₂O/EtOAc) to give

256 (1.49 g, 44%) as yellow crystals, mp 203–204°C; (Found: M⁺+H, 682.2888. C₄₇H₄₁NO₂P (M^+ +H) requires, 682.2875); v_{max}/cm^{-1} 1724, 1630, 1540, 1339, 1090 and 739; δ_H 7.75–7.28 (13 H, m), 7.23–7.06 (12 H, m), 7.02 (1 H, d, *J* 15, *CH*=CH), 6.87-6.79 (4 H, m), 6.47 (1 H, d, *J* 8, H-3 of Ar), 6.25 (1 H, dd, *J* 3, 2, H-4 of furyl), 6.23 (1 H, d, *J* 3, H-3 of furyl), 4.11 (2 H, d, *J* 14, *CH*HPh), 3.94 (2 H, d, *J* 14, *CH*HPh), and 2.19 (3 H, s, Me); δ_C see Table **3** (Page 134); δ_P +16.5; m/z (ES⁺) 682.02 (M⁺+H, 100%).

6 FVP of Ylide 256



Ylide **256** (0.1540 g, 0.32 mmol) was subjected to FVP at 800 °C at $2-3 \times 10^{-2}$ torr. NMR analysis of crude product showed a mixture of Ph₃PO, bibenzyl and other products. The mixture was purified by preparative TLC (50:50 diethyl ether:petrolium ether) to give 3-(2-(2-furyl)ethenyl)-6-methylquinoline **261** (E, 0.0244 g, 46%) as dark brown oil. (Found: M⁺+H, 236.1068. C₁₆H₁₄NO (*M*⁺+H) requires 236.1075); $\delta_{\rm H}$ 9.00 (1 H, d, *J* 2, H-2), 8.01 (1 H, d, *J* 2, H-4), 7.96 (1 H, d, *J* 8, H-8), 7.55 (1 H, br s, furyl), 7.49 (1 H, dd, *J* 8, 2, H-7), 7.44 (1 H, d, *J* 2, H-5), 7.16 and 7.09 (2 H, AB pattern, *J* 16, H-a and b), 6.67–6.43 (2 H, m, furyl) and 2.53 (3 H, s, Me); 236.07 (M⁺+H, 100%) Also isolated was natural product Eustifoline D, **90**, as a dark brown oil (0.0095 g, 19%); $\delta_{\rm H}$ 8.12 (1 H, br s, NH), 7.97 (1 H, br s, H-10), 7.81 (1 H, d, *J* 2, H-2), 7.58 (1 H, dd, *J* 9, 1, H-4), 7.40 (1 H, d, *J* 8, H-7), 7.36 (1 H, d, *J* 9, H-5), 7.33 (1 H, dd, *J* 2, 1, H-1), [under chloroform, from Lit.,⁷⁵ 7.26 (1 H, dd, *J* 8, 1, H-8)] and 2.58 (3 H, s, Me).

DISCUSSION

A General Synthesis of Keto Stabilised Ylides

The standard method for the synthesis of the keto stabilised ylides is the Bestmann procedure,¹⁵⁴ where two equivalents of phosphonium salt **138** are treated with two equivalents of butyllithium to form the intermediate ylide **139**. To this one equivalent of acid chloride is added, which results in acylation to form the intermediate phosphonium salt **140**. This is immediately deprotonated by the second equivalent of **139**, to give a 1:1 mixture of **141** and **142**.



For this project, ylides with an *o*-aminophenyl substituent would be required and the amine nitrogen should have one thermally labile group as well as a second group that would be retained in the product.

It was initially thought that the *N-p*-toluenesulfonyl group might be a suitable precursor to generate the aminyl radical under FVP conditions, although surprisingly no systematic study of the pyrolysis behaviour of acyclic sulfonamides seems to have been made.¹⁵⁵ A number of cyclic sulfonamides are however known to eliminate SO_2 thermally, including **143**,¹⁵⁶ **144**¹⁵⁷ and **145**.¹⁵⁸



B Synthesis of Model Ylides

Commercially available 2-aminobenzoic acid **146** was methylated to give 2-(*N*-methylamino) benzoic acid **147**,¹²² followed by tosylation¹⁵⁹ to give 2-(*N*-methyl-*N*-*p*-toluenesulfonylamino) benzoic acid, **148**. This was then treated with thionyl chloride to give 2-(*N*-methyl-*N*-*p*-toluenesulfonylamino) benzoyl chloride, **149**.¹⁵⁹ Treatment of stable phosphonium salts **150** and **151**, which had previously been prepared in the Aitken group, with butyllithium gave dark red intermediate ylides **152** and **153** to which **149** was added to obtain the stabilised ylides **154** and **155** in 31% and 43% yields respectively. See Table **1** (Page 103) for ¹³C NMR data.



Due to the restrictions on the availability of suitable phosphonium salts, a more versatile route is to prepare ylides **156** with the position of the carbonyl and ylide functionality reversed. This can be achieved by synthesising the complex phosphonium salt **157** and reacting with a range of acid chlorides, which are more easily accessable both commercially and synthetically.



Synthesis of a simple example, **158**, was achieved by converting **148** into its methyl ester **159** using dimethyl sulfate and potassium acetate¹²⁵ and then reducing to the alcohol **160** with lithium aluminium hydride. Stirring **160** with phosphorus tribromide gave the intermediate 2-(*N*-methyl-*N*-*p*-toluenesulfonylamino)benzyl bromide **161** which was treated directly with triphenylphosphine to form 2-(*N*-methyl-*N*-*p*-toluenesulfonylamino) benzyltriphenylphosphonium bromide **157**. Salt **157** was then treated with butyllithium to generate **162** and benzoyl chloride was added to give stabilised ylide **158** in 5% yield.



The fully assigned 13 C NMR spectrum of this is also presented in Table 1 (Page 103).

The dramatic reduction in the yield of this preparation led to a consideration of the steric bulk of this molecule and to shed more light on this aspect the crystal structure was obtained. The structure is shown in Figure **1** (Page 99).



Figure 1. X-ray structure of ylide **158**. Selected bond lengths, angles and torsion angle: P(7)–C(7) 1.7459(15), C(7)–C(8) 1.408(2), C(8)–O(8) 1.2631(18) Å; P(7)–C(7)–C(2) 124.50(10), P(7)–C(7)–C(8) 109.17(11), C(7)–C(8)–O(8) 121.04(13) °; P(7)–C(7)–C(8)–O(8) -8.99(17) °.

From this it can be concluded that there is limited steric hindrance within this molecule. However, more importantly the relative positions of the phosphorus and oxygen have been highlighted. They are forced to lie on the same plane which is required for the elimination of PPh₃O during the FVP, indicating that the initial step in the FVP cascade will proceed according to plan. Although the crystal structure did not indicate too much in the way of steric hindrance, it was still decided to exchange the tosyl group for the less bulky mesyl group.

For the synthesis of methyl 2-*N*-mesylaminobenzoate **163**, the literature procedure called for reaction of two equivalents of readily available methyl 2-aminobenzoate **164** with mesyl chloride,¹⁶⁰ allowing for one equivalent of **164** to deprotonate the intermediate salt and form a 1:1 mixture of the desired product **163** and **165**. Although this method was successful with a yield of 45%, the method was improved by treating **164** with one equivalent of mesyl chloride and one equivalent triethylamine. This gave a higher yield of 68% and did not waste the starting material.



Methyl (2-*N*-mesylamino)benzoate **163** was then treated with sodium hydride and methyl iodide added to give methyl 2-(*N*-methyl-*N*-mesylamino)benzoate **166**.¹⁴¹ The procedure called for a reaction time of 1 h, however, in the case of **166** it was possible by ¹H NMR to establish the presence of a small amount of product which was difficult to isolate by triturating as described in the literature procedure or column chromatography. As this was a standard starting material and required in adequate quantities, it was decided to try increasing the reaction time to improve the yield. This proved to be successful and after 72 h the product was obtained in a moderate yield of 55%. Ester **166** was reduced to the alcohol using lithium aluminium hydride to give **167** which was subsequently reacted with phosphorus tribromide followed by triphenylphosphine to obtain the corresponding phosphonium salt **168**.



When the synthesis of ylides from **168** was attempted it was apparent that the reactions did not behave in the expected manner. The initial target was the analogue of test ylide **156**, compound **169**. When this preparation was carried out under standard conditions, however, the crude ³¹P NMR indicated that none of the desired product was present.

It was observed that after treating **168** with butyllithium, there appeared to be more solid in the mixture than expected, since when the salt is deprotonated it should become fully soluble. As an alternative to butyllithium, sodium hydride was tried. There did not appear to be much change in the solubility of the salt, however after addition of benzoyl chloride, the crude ³¹P NMR spectrum indicated a small amount of the correct product. However, on examination of the ¹H NMR spectrum a mixture of products was observed: the desired ylide plus a second compound with three methyl peaks, two of which were in a similar position to the ylide and the third at 2.42 ppm. After several attempts it was apparent that recrystallisation in this case was not going to be effective, and so column chromatography was attempted. Due to the potential of the ylides to break down on silica, chromatography is not ideal, however ylide **169** was isolated in 3% yield (see Table **1** for ¹³C NMR data, Page 103) and the other compound was found to be the hydrolysis product *N*-methyl-*N*-mesyl-*o*-toluidine **170** in 38% yield.



This was confirmed by an alternative synthesis involving mesylating *o*-toluidine to give N-mesyl-*o*-toluidine¹⁶¹ and then methylating to give **170** and comparing the ¹H NMR data and melting points.



As the yield for ylide **169** is comparable with ylide **158**, it could be that the *N*-sulfonyl functionality is problematic for ylide formation.



Table 1. ¹³C NMR spectra [$\delta_C(J_{P-C})$] of the ylides.

	P-Phenyl				o-NMeTs(Ms)-C ₆ H ₄							
	C=O	C=P	C-1	C-2	C-3	C-4	C-1	C-2				
154	185.1	69.8	126.7	133.7	128.5	131.3	145.4	143.0	128.6	127.6	127.5	126.8
	(7)	(99)	(91)	(10)	(12)	(3)	(13)					
155	184.2	74.0	126.8	133.8	128.6	131.5	144.1	142.9	130.7*	128.5	127.5	126.4
	(6)	(107)	(90)	(10)	(12)	(3)	(12)					
158	184.2	70.2	127.5	134.5	128.2	131.2	132.0	143.5	136.5	126.5	125.7	128.0*
		(109)	(89)	(br s)	(br s)	(3)	(10)	(7)	(3)	(2)	(2)	
169	184.4	70.1	126.5	134.7	128.3	131.5	142.1	144.1	136.6	126.3	126.6	127.8
	(6)	(110)	(91)	(br s)	(12)	(3)	(12)	(7)	(3)	(2)	(2)	

	NMe	NTs(Ms)			Ph or Et signa	Ph or Et signals				
		C-1, C-4	C-2, C-3	Me	C-1	C-2	C-3	C-4		
154	40.9	138.9 136.8	129.3 128.2	21.5	20.9 (13)	18.3				
155	40.9	139.6 136.2	129.4 128.2	21.5	137.4 (12)	134.6 (5)	126.9	124.2*		
158	37.5	143.0 134.3	128.9 128.2	21.4	139.6 (12)	$128.8^{\#}$	$127.2^{\#}$	128.3*		
169	36.9 [*]	-	-	38.8^*	138.4 (11)	$128.3^{\#}$	$127.5^{\#}$	127.1		

* # assignments may be interchanged

C FVP of model ylides

Based on previous work,¹¹⁹ a temperature of 700 °C was chosen for the initial FVP experiments. The first compound to be examined was **154**. Based on what has previously been observed,¹¹⁵ the expected product was 1-methyl-2-vinylindole **171**. However, the spectra of the crude product proved conclusively that what was actually obtained was 3-ethylquinoline **172**. Once this was realised, acid/base extraction allowed its ready separation from toluene and Ph₃PO to give the pure product in 71% yield.

This was demonstrated by two fine doublets at an unusually high chemical shift, which is indicative of a 3-substituted quinoline. A possible explanation of this is that the reaction proceeds as expected to form aminyl radical **173**, however this can then undergo a 1,2-hydrogen atom shift from the methyl group to form **174**, allowing 6-membered ring formation. According to Baldwin's rules this 6-*endo-dig* cyclisation, giving **172**, is just as probable as the 5-*endo-dig* process to give **171**.



When ylides **155**, **158** and **169** were exposed to FVP conditions the same cyclisation was observed, with the final product in each case being 3-phenylquinoline, **175**.



As noted in the Introduction, Section B, cyclisation of *o*-aminophenyl compounds to give quinolines is relatively rare. A series of studies by Creencia *et al*,¹⁶²⁻¹⁶⁴ has however shown that pyrolysis of suitable substrates **176** and **177** over calcium oxide can give mixtures of indole and quinoline products, probably arising from the same sort of C to N transfer of the reactive site as observed here.



D Alternative Preparations

The procedures described so far have been the successful routes to each of the target compounds, however there were many attempts *via* different methods to the target compounds already described and to future targets which will now to be described. The key challenge in this area turned out to be selective functionalisation of the amine or carboxylic acid functions in *o*-aminobenzoic acid derivatives without interference from the other group. Many of these deceptively simple compounds were not previously known.



As 2-aminobenzoic acid, **146**, was already in use as a standard starting material this was a logical place to start. Acid **146** was dissolved in a 20% solution of sodium carbonate and *p*-toluenesulfonyl chloride was added to give 2-(*N*-*p*-toluenesulfonylamino)benzoic acid, **178**,¹⁶⁵ in a low yield of 23%. An attempt was then made to methylate on both the nitrogen and oxygen in one step by treating acid **178** with sodium hydride and adding dimethyl sulfate, however only starting material was recovered.¹⁶⁶

Another attempt at the same idea using two equivalents of methyl iodide to one equivalent acid 146, was also unsuccessful. The only product found was the monomethylated acid 147 and further attempts at converting this to the methyl ester 179 by treating with conc. H_2SO_4 and methanol were not successful.

In a completely different approach, we attempted to attach the desired substituent to the nitrogen of the readily available isotoic anhydride with the intention of using methanol to open the ring with the loss of CO_2 giving the *N*-substituted methyl 2-aminobenzoate.^{167,168} Unfortunately the initial tosylation was unsuccessful. However, methylation of isotoic anhydride to give *N*-methylisotoic anhydride, **180** proceeded in 93% yield and the ring opening gave methyl 2-*N*-methylaminobenzoate, **179**. Tosylation of this was attempted by deprotonating the amine using sodium hydride and adding *p*-

toluenesulfonyl chloride, however only starting material was recovered.

Allyl has also previously been shown to be a good leaving group under FVP conditions, and so we attempted to synthesise ylides with an *N*-allylamino group. *N*-allylisotoic anhydride, **181**, was synthesised in the same manner as anhydride **180** followed by ring opening to give methyl 2-*N*-allylaminobenzoate, **182**. However, when ester **182** was treated with sodium hydride and methyl iodide added only starting material was recovered, as was observed in the previous experiment using **179**. Another approach was to take the previously prepared ester **179** and treat it with allyl bromide. Instead of the expected methyl 2-(*N*-allyl-*N*-methylamino)benzoate, a low yield, 11%, of allyl 2-(*N*-allyl-*N*-methylamino)benzoate **183** was obtained along with starting material.

A different approach to the synthesis of *N*-allylamino ylides was then investigated. It was found that coupling a substituted amine with ethyl 2-fluorobenzoate is very efficient.¹³⁶ The substituted amine chosen in this instance was allylmethylamine **184**. This is a commercially available compound, however it is very expensive and so it was decided to synthesise it. This was a very difficult procedure, and the correct compound was only obtained by combining two different techniques.^{135,134} The imine was formed from benzaldehyde and allylamine and this was heated for 18 h in a pressurised bottle with methyl iodide. It took several attempts and a considerable amount of time to isolate the desired product, **184**. Amine **184** was then coupled with ethyl 2-fluorobenzoate to give ethyl 2-(*N*-allyl-*N*-methylamino)benzoate, **185**, which was reduced to the alcohol, **186**. The attempted preparation of the phosphonium salt from this however gave many phosphorus containing products and attempts at recrystallisation were not successful (see Section G). Due to time constraints and difficulty of preparing amine **184** it was decided not to continue down this route.



As will be discussed later, there was interest in preparing ylides having a methyl group on the aromatic ring and two thermally labile groups on the nitrogen to give *N*-unsubstitured indole products after FVP. The synthesis of the starting material for such compounds was achieved by nitrating 3-methylbenzoic acid. This was done *via* two different routes giving different ratios of products. Route a. involved nitration by dissolving 3-methylbenzoic acid in conc. sulphuric acid and adding a solution of potassium nitrate in conc. sulphuric acid.¹⁶⁹ This gave 2-nitro-3-methylbenzoic acid, **187** and 2-nitro-5-methylbenzoic acid, **188**, in a ratio of 1:3.5. Route b. involved adding 3-methylbenzoic acid to fuming nitric acid¹⁷⁰ giving acid **187** and acid **188** in a ratio of 1:0.4.

2-Amino-3-methylbenzoic acid, **189** was obtained by reducing acid **187** with ferrous sulfate heptahydrate.¹⁶⁹ As will be discussed later, benzyl was found to be a good leaving group under FVP conditions and so benzyl 2-(N,N-dibenzylamino)-3-methylbenzoate, **190**, was prepared in one step by treating one equivalent of acid **189** with three equivalents of benzyl bromide. Ester **190** was then reduced to give alcohol **191.** Unfortunately all attempts to convert this into the required phosphonium salt failed in the same way as for **186**.



In an attempt to favour the indole product, it was decided to block the capability of the 1,2-hydrogen atom shift by replacing the *N*-methyl with *N*-phenyl. From the literature¹⁷¹ it was known that diphenyliodonio-2-carboxylate **192** can react directly with sulfonylanilines and it was expected that the use of *N*-methanesulfonylaniline **193** would give 2-(*N*-methanesulfonyl-*N*-phenylamino)benzoic acid. The synthesis of **192**¹⁷¹ and **193**¹⁷² proceeded as described, however the coupling reaction yielded none of the desired product. By following an alternative procedure involving cuprous catalysis,¹⁷¹ the amino group was installed but this was accompanied by loss of *N*-methanesulfonyl to give **194** and attempts to put it back on failed. Although **194** was successfully convered to the methyl 2-(*N*-phenylamino)benzoate using HCl(g) in methanol, attempts to reattach methanesulfonyl group failed.



E Synthesis and FVP of *N*-Methyl-*N*-mesylamino and *N*-benzyl-*N*-mesylamino ylides with α,β-unsaturated acyl groups

Previously prepared salt **168** was treated with butyllithium and cinnamoyl chloride giving ylide **195** in a yield of 20%. As the synthesis of ylide **169** required sodium hydride to give the desired product it was decided to try the same method for the cinnamoyl derivative. By treating salt **168** with sodium hydride and cinnamoyl chloride the yield of ylide **195** was improved slightly to 25% (see Table **2** for ¹³C NMR data, Page 122).



Ylides with different substituents on the nitrogen were also examined at this stage. Previously prepared methyl (2-N-mesylamino)benzoate 163 was treated with sodium hydride and benzyl bromide was added to give methyl 2-(N-benzyl-Nmesylamino)benzoate 196^{141} in 88% yield with the same increased reaction time that was required in the case of ester 166. Ester 196 was treated with lithium aluminium hydride to give 2-(N-benzyl-N-mesylamino)benzyl alcohol 197 which was subsequently reacted with phosphorus tribromide followed by triphenylphosphine to obtain the corresponding phosphonium salt 198.



By treating salt **198** with sodium hydride and adding cinnamoyl chloride a product was obtained for which the crude ³¹P NMR spectrum indicated a peak in the correct ylide region along with many other peaks. Through column chromatography the ylide **199** was isolated, and the ¹H NMR spectrum appeared to give peaks in the expected regions, however the ¹³C NMR spectrum gave extremely broad peaks which made interpretation almost impossible, even at higher temperatures. Although there was no conclusive proof that the compound had been made, it was decided to continue with the FVP.



Despite the earlier formation of quinolines, the FVP of ylide **195** at 700 °C surprisingly gave the originally anticipated indole-based tetracyclic structure, 7-*N*-methylbenzo[*c*]carbazole **200**.



Full assignment of the ¹H NMR spectrum of this product was possible by simulating the spectrum using iNMR. This is done by entering the chemical shift and the coupling constant between each atom (taken from COSY NMR). By adjusting the coupling constants to get a perfect match (Figure **2**, Page 115) the full assignment was possible.

Following this encouraging result, the *N*-benzyl-*N*-mesyl ylide **199** was subjected to FVP. In this case the product was identified as 7H-benzo[c]carbazole, **201**.



Again assignment of the spectrum was possible using simulation (Figure 3, Page 116). The fact that the N-benzyl group had also been lost here led on to the idea of using N-benzyl as the thermally labile group in general.

Experimental ¹H NMR spectrum



Figure 2. Experimental and simulated ¹H NMR spectra of **200** using iNMR.

Experimental ¹H NMR spectrum



Figure **3**. Experimental and simulated ¹H NMR spectra of **201** using iNMR.

In view of the synthetic problems and low yields in preparing *N*-tosyl and *N*-mesyl ylides, which could be avoided by moving to *N*-benzyl as the thermally labile group, it was decided to synthesise ylides with *N*-benzyl-*N*-methylamino functionality.

F Synthesis of N-Acylbenzotriazoles

A recent paper by Katritzky and coworkers¹⁷³ reported the reaction of $Ph_3P=CHCO_2Et$ with amino acid-drived *N*-acylbenzotriazoles, **202** under microwave conditions to give the keto ylides **203**. As far as we are aware this is the first report of the use of *N*-acylbenzotriazoles in place of acid chlorides to bring about ylide acylation.



R¹ = L-Ala, L-Val, L-Phe, L-Asp(OMe), L-Trp R² = t-butoxycarbonyl, benzyloxycarbonyl

It was decided to look at the use of *N*-acylbenzotriazoles as a synthetic equivalent to acid chlorides in our work. It was hoped that this would result in an improvement on the Bestmann procedure, in that only one equivalent of **138** and base would be necessary as the released benzotriazole could deprotonate the intermediate **140** (refer to scheme on Page 95).



Based on this, it was decided to examine the synthesis of stabilised ylides from the corresponding *N*-acylbenzotriazoles, **205–211**.¹⁴⁷ These were all synthesised in the same manner by treating benzotriazole, **204**, with thionyl chloride followed by the corresponding 3-arylpropenoic acid.¹⁴⁵ In most cases the acids were available commercially or from previous work, however for selected acids, reaction of the corresponding aromatic aldehyde **212–214** with malonic acid in pyridine with piperidine catalyst gave the desired products.


G Synthesis of *N*-Benzyl-*N*-Methylamino Ylides with α,β-Unsaturated Acyl Groups

Based the resuls of the FVP of ylide 199 to give 7*H*-benzo[*c*]carbazole 201, it was decided to syngthesis ylides with the benzyl group as the thermally labile group. Ylides bearing an N-benzyl-N-methylamino group were synthesised by starting with readily available 2-fluorobenzoyl chloride and heating under reflux in ethanol to give ethyl 2fluorobenzoate, as for the synthesis of ethyl 2-(N-allyl-N-methylamino)benzoate, 185.¹³⁶ This was coupled with benzylmethylamine to give a mixture of ethyl 2-fluorobenzoate, benzylmethylamine and ethyl 2-(N-benzyl-N-methylamino)benzoate, 215, which was purified in the same manner as for 185 giving a residue of 215 in 68% yield. This was then reduced using lithium aluminium hydride give 2-(N-benzyl-Nto methylamino)benzyl alcohol, 216.



The formation of salt **217** was problematic, as when phosphorus tribromide was added a white solid precipitated and after heating to reflux with triphenylphosphine none of the desired product was obtained. On treatment of the white precipitate with 2 M sodium hydroxide and adding ethyl acetate, the solid dissolved in the organic layer. After drying and concentrating the organic fraction, **216** was recovered. This could be due to the intermediate **218** precipitating. This was overcome by warming **216** in toluene to 60 °C while adding phosphorus tribromide slowly. This is perhaps the same problem that was seen when treating alcohol **186** and **191** with PBr₃.



From **217**, the ylide **219**, was synthesised *via* the Bestmann procedure (route a) in 23% yield and isolated by recrystallisation with no indication of hydrolysis product. It was decided to attempt synthesis of **219** using 1-(3-phenylpropenoyl)benzotriazole **205** with a 1:1:1 ratio of salt **217**, butyl lithium and **205**. This was successful, giving a yield of 74% of **219**, again isolated by recrystallisation. Its ¹³C NMR data are presented in Table **2** (Page 122).



Stabilised ylides **220–225** were then synthesised from salt **217** using butyl lithium and the corresponding *N*-acylbenzoltriazoles. They were all highly crystalline and obtained in reasonable yields. Their identity was again confirmed by the highly consistent and informative pattern of the ¹³C NMR data (Table **2**, Page 122).



Bt = benzotriazol-1-yl

Table 2. ¹³C NMR spectra [$\delta_C(J_{P-C})$] of the ylides.

	P-Phenyl o-NN				o-NM	leBn(Ms)-C	$_{6}H_{4}$							
	C=O	C=P	C-1	C-2	C-3	C-4	C-1	C-2	C-3*	C-4	C-5*	C-6	C=C	C=C
195	180.1	71.0	126.8	134.2	128.5	131.6	137.2	145.0	137.8	126.7	127.0	128.2	126.7	127.5
	(6)	(112)	(91)	(10)	(12)	(3)	(11)	(6)	(4)				(12)	(2)
219	178.2	75.3	127.3	133.8	128.4	131.3	132.1	154.1	121.2	127.9	122.7	138.4	126.4	135.1
	(5)	(106)	(90	(10)	(13)	(3)	(10)	(4)	(2)	(3)	(2)	(5)	(11)	(1)
220	178.8	74.5	127.0	133.7	128.2	131.2	132.1	154.1	121.2	127.5	122.7	138.5	124.9	122.3
	(6)	(108)	(91)	(10)	(12)	(3)	(10)	(4)	(2)	(3)	(2)	(5)	(13)	(2)
221	178.5	74.5	127.5	133.8	128.3	131.4	131.7	154.0	121.5	127.9	122.9	138.3	126.1	127.8
	(5)	(108)	(91)	(10)	(12)	(2)	(10)	(4)	(2)			(5)	(13)	
222	178.9	75.3	126.7	133.8	128.3	131.4	131.8	154.1	121.3	127.7	122.8	138.4	126.3	124.7
	(6)	(107)	(91)	(10)	(12)	(2)	(10)	(4)	(2)	(3)	(2)	(5)	(12)	
223	179.1	75.7	126.7	133.8	128.3	131.4	131.8	154.2	121.3	127.8	122.8	138.4	126.4	129.1
	(5)	(108)	(91)	(10)	(12)	(3)	(10)	(4)	(2)	(3)	(2)	(5)	(12)	(1)
224	179.7	72.8	127.4	133.8	128.2	131.1	132.3	154.3	121.0	128.4	122.6	138.8	128.5	132.2
	(7)	(109)	(90)	(10)	(12)	(3)	(10)	(4)	(2)		(2)	(5)	(12)	
225	179.1	72.9	127.2	133.8	128.2	131.2	132.1	153.9	121.3	127.4	122.6	138.5	128.4	126.1
	(6)	(108)	(92)	(10)	(12)	(2)	(10)	(4)	(2)	(2)		(5)	(12)	(1)
								_ 1						
	NMe	NBn((Ms)					R						
		CH ₂	C-1	C-2	,6* C-	3,5*	C-4	C-1						
195	38.1 [#]	38.8#	-	-		-	-	136.8 (1)	128.5,	128.3, 12	7.6			
219	39.5	60.0	137.0) 129	9.5 12	27.8	126.8	137.1	128.3,	127.8, 12	7.5			
220	39.6	60.0	136.9) 129	9.6 12	27.7	126.8	153.4 (1)	142.5,	111.5, 11	0.8			
221	39.4	60.1	136.7	7 129	9.7 12	27.8	126.9	142.4 (1)	127.8,	127.5, 12	5.3			
222	39.6	60.1	136.9) 129	9.5 12	27.8	126.9	143.3	142.7,	124.1, 10	7.9			
223	36.6	60.1	137.0) 129	9.5 12	27.8	126.9	139.8 (1)	126.0,	125.6, 12	4.6			
224	39.5	60.0	137.0) 129	9.5 12	27.8	126.8	137.3	136.3,	126.3, 13	0.3, 125.	7, 127.6	20.	0 Me
225	39.3	60.0	136.8	3 129	9.7 12	27.7	126.7	136.5 (1)	136.5,	123.6, 13	0.7, 126.	0	14.	0 Me

* # assignments may be interchanged

H FVP of *N*-Benzyl-*N*-Methylamino Ylides with α,β-Unsaturated Acyl Groups

The FVP of **219** proceeded as expected to give 7-*N*-methyl-benzo[*c*]carbazole **220**, as did FVP of **220** and **221** to give *N*-methylfuro[2,3-*c*]carbazole **226** and *N*-methylthieno[2,3-*c*]carbazole **227** respectivly.



To aid in the peak allocation for **226** and **227** the ¹H NMR spectra were again simulated (Figure **4** and **5**, Pages 124 and 125).

Experimental ¹H NMR spectrum



Figure 4. Experimental and simulated ¹H NMR spectra of **226** using iNMR.

Experimental ¹H NMR spectrum



Figure 5. Experimental and simulated ¹H NMR spectra of **227** using iNMR.

In particular ylide **226** was of interest as the ring system involved occurs in the natural product Eustifoline-D, **90**, which has been isolated from the root bark of *Murraya euchrestifolia*.⁷⁵ It was decided to attempt to synthesise this compound, as an isomer of ylide **226**, and this will be described later.



The pattern of pyrolysis behaviour observed up to now can be understood by proposing an equilibrium between the *N*-centred and C-centred radicals as shown below. Both of these can cyclise onto the triple bond but only where R^1 is a styryl group or its heterocyclic analogue is the tandem cyclisation possible to give ring-fused carbazole products following irreversible loss of a hydrogen atom. Where this is not possible, as is the case for simpler R^1 groups such as Et or Ph, the quinoline products are formed by irreversible hydrogen loss from six-membered ring cyclisation product.



The FVP of **222** and **223** was more complicated and involved a departure from this pattern. In the case of **222** it was difficult to come to any definite conclusions. Within a very complex product mixture it was believed that 9-methylphenanthridine **228** had been obtained. The ¹H NMR spectrum for this in CDCl₃ was compared with the literature ¹H NMR spectrum in DMSO¹⁵⁰ and two peaks appeared to have switched places, otherwise there was good agreement.



This was not fully identified until FVP of later ylides showed undisputedly quinoline formation, which would be the initial stage in the cascade leading to **228**. When this is compared to what was observed in the test reactions where the aminyl radical **173** abstracted a hydrogen atom from the methyl group to give **174**, it can be concluded that a similar hydrogen atom transfer is occurring in the aminyl radical **229** to give **230**. This can then undergo tandem cyclisation, to give intermediate **231**. Intermediate **220** can then lose a hydrogen radical and hydrogen gas to give **232**, which subsequently breaks the C-O bond followed by decarbonylation to give **228**. It might be noted here that the expected product from pyrolysis of **222**, the furo[3,2-*c*]carbazole **233**, apears in a Japanese patent where it is claimed to have applications in light-emitting devices.¹⁷⁴



In the case of 223, the main product was a mixture of E and Z 3-(2-(3-thienyl)ethenyl)quinoline 234, which was not fully identified until FVP of later ylides also undisputedly showed quinoline formation. A small amount of 235 was also isolated.



To aid in the peak allocation for 235 the ¹H NMR spectrum was again simulated (Figure 6, Page 131). The isolation of 235 is a good indication that the proposed mechanism for formation of 228 is correct.

The FVP of **224** gave a mixture of products, including a mixture of *E* and *Z* 3-(2-(2-methylphenyl)ethenyl)quinoline **236** and corresponding benzo[c]carbazole**237** and a trace of 9-methylbenzo[*k*]phenanthridine **238**.



The spectra obtained on the products from FVP of **225** indicated that *E* and *Z* 3-(2-(3-methyl-2-thienyl)ethenyl)quinoline, **239** had been formed, however further purification and analysis was not possible.



Experimental ¹H NMR spectrum



I Synthesis of *N*,*N*-Dibenzylamino Ylides with α,β-Unsaturated Acyl Groups

Starting from 2-amino benzoic acid **146**, benzyl 2-(*N*,*N*-dibenzylamino)benzoate **240** was obtained in one step by treating with four equivalents of benzyl bromide. The literature procedure called for purification by chromatography,¹⁵¹ however distilling under an oil pump vacuum at 90 °C removed excess benzyl bromide leaving the desired product as the residue. Ester **240** was then reduced using lithium aluminium hydride to give 2-(*N*,*N*-dibenzylamino)benzyl alcohol **241**. Since in this case the alcohol bi-product was benzyl alcohol as opposed to methanol or ethanol as in previous examples, distillation was required to remove this leaving the product **241** as the residue. 2-(*N*,*N*-Dibenzylamino)benzyl triphenylphosphonium bromide **242** was obtained by treating **241** with phosphorus tribromide at 60 °C followed by addition of triphenylphosphine.



From salt **242** a selection of ylides **243–236** were formed using the appropriate *N*-acyl benzotriazoles (see Table **3** for ¹³C NMR data, Page 134). Although yields are high and the compounds were highly crystalline, it was evident from the ¹³C NMR spectra there was an element of restricted rotation around the triphenylphosphine group which caused broadening of the signals due to C-2 and C-3 of the PPh groups.





				P-Phe	nyl				o-NMeTs	$s-C_6H_4$				
	C=O	C=P	C-1	C-2	C-3	C-4	C-1	C-2	C-3*	C-4	C-5*	C-6	C=C	C=C
243	179.3	75.5	126.6	133.8	128.4	131.7	132.1	154.1	122.5	127.7	122.7	138.9	126.5	135.6
	(6)	(107)	(90)	(br s)	(br s)	(br s)	(10)	(5)	(2)	(2)	(2)	(5)	(12)	(1)
244	179.3	74.3	127.0	133.9	128.4	131.5	132.1	154.0	122.6	127.4	122.5	138.8	125.0	124.4
	(6)	(108)	(91)	(br s)	(br s)	(br s)	(10)	(5)	(2)	(2)	(2)	(5)	(12)	
245	178.9	73.8	127.0	133.8	128.3	131.5	132.1	154.0	122.6	127.3	122.6	138.9	126.3	127.9
	(6)	(106)	(92)	(br s)	(br s)	(br s)	(10)	(5)	(2)	(2)	(2)	(5)	(12)	
246	180.0	72.5	127.4	133.9#	128.3#	131.4#	131.8	154.2	122.2	127.3	122.4	139.2	128.3	132.6
	(6)	(109)	(91)	(10)	(12)	(3)	(10)	(5)	(2)	(2)	(2)	(5)	(12)	(1)
256	179.2	74.3	127.1	133.9#	128.3#	131.5#	132.2	151.4	122.5	127.9	122.6	139.2	125.5	124.3
	(6)	(107)	(90)	(10)	(12)	(3)	(10)	(5)	(2)	(2)	(2)	(5)	(13)	
	ND						D							
	NBr	1					R ⁻							
	CH	₂ C	C-1	C-2,6*	C-3,5*	C-4	- C-1							
243	54.3	3 13	36.9	129.4	127.9	126.	8 136	5.8	128.3, 12	27.6, 128.	0			
244	54.2	2 13	36.9	129.5	127.8	126.	7 153	3.3	142.6, 11	11.5, 111.	0			
245	54.1	l 13	36.8	129.5	127.8	126.	7 142	2.5	127.7, 12	27.3, 125.	2			
246	54.2	2 13	37.2	129.5	127.8	126.	7 137	7.2 (1)	137.0, 12	26.3, 130.	1, 125.6,	127.6	19.9 Me	

153.4

142.5, 111.5, 111.0

20.4 Me

Table 3. ¹³C NMR spectra [$\delta_C(J_{P-C})$] of the ylides.

256

[#] broad doublet* assignments may be interchanged

54.5

137.1

129.6

127.7

126.3

J FVP of *N*,*N*-Dibenzylamino Ylides with α,β-Unsaturated Acyl Groups

When **243** was exposed to FVP conditions, the major product was found to be 3-styrylquinoline **247** in a mixture of *E* and *Z* isolmer, along with benzo[k]phenanthridine, **248**.



From the FVP of ylide **244** at 800 °C, two definate compounds were isolated, *E* and *Z* isomers of $3-(2-(2-\text{furyl})\text{ethenyl})\text{quinoline$ **249**and 6-phenylfuro[2,3-*k*]phenanthridine**250.**The isolation of**250**provides a clue as to the mechanism involved in quinoline formation with loss of a benzene ring in these systems. A ¹H NMR spectrum was obtained indicative of 2-phenyl-3-(2-(2-furyl)ethenyl)quinoline**251**, however further analysis of this minor product was not possible.



Ylide **244** was also exposed to FVP at a lower temperature of 500 °C, and 2-(4-(2-furyl)-but-1-y*N*-3-enyl)-*N*,*N*-dibenzylaniline **252** was isolated in 39% yield.



The FVP of ylide **245** at 800 °C gave a mixture of *E* and *Z* isomers of 3-(2-(2-thienyl))ethenyl)quinoline **253**, thieno[2,3-*c*]carbazole **254** and a trace of thieno[2,3-*k*]phenanthridine **255**.



When **246** was subjected to FVP, the only product obtained was a mixture of E and Z isomers of 3-(2-(2-methylphenyl)ethenyl)quinoline **236**.



The surprisingly diverse behaviour of the *N*,*N*-dibenzylamino ylides **243–246** is summarised in the scheme below. Why only the thienyl ylide **245** give a carbazole product and only the furyl ylide **244** gives quinoline products with retention of the phenyl group is unclear.



K Total Synthesis of Eustifoline D

The shrub *Murraya euchrestifolia* Hayata occurs in Taiwan and extracts from its leaves and root bark have been used in folk medicine to treat a wide variety of conditions including eczema, rheumatism, abdominal pain, toothache, diarrhoea, oedema, thrombosis and convulsions. This activity may be due to the presence of a wide variety of carbazole alkaloids in the plant and over 30 of these have been isolated and identified. Representative examples shown below include Murrayaline A,¹⁷⁵ Pyrayafoline E,¹⁷⁶ Murrayaquinone E,¹⁷⁶ and Euchrestine C.¹⁷⁷



Useful biological activity has been reported for some examples including anticancer activity for Murrayaquininone A and Murrayafoline A,¹⁷⁸ and inhibition of blood platelet aggregation for Murrayafoline A, Murrayamine M and Girinimbine,¹⁷⁹ with the last compound acting as a cyclooxygenase inhibitor.¹⁸⁰



Our attention was drawn to the structure of Eustifoline D since it contains the furo[2,3-c]carbazole structure potentially accessible *via* our cascade cyclisation strategy. This was isolated from *M. euchrestifolia*, along with an isomer Furostifoline with the furo[3,2-a]carbazole structure, and identified by spectroscopic methods.⁷⁵



There have only been two previous syntheses of Eustifoline D both reported in 2007 (see Page 139). Knölker and coworkers (Route A) started by Pd-catalysed coupling of *p*-toluidine with *p*-bromoanisole to form the carbazole and then built on the furan ring to give the product in five steps and 20% overall yield.¹⁸¹ The approach of Kerr (Route B) involved an involved an initial Diels Alder reaction and a longer sequence of eleven steps but gave a higher overall yield of 26%.¹⁸²

In contrast to these approaches where the carbazole is first constructed and the furan ring then attached, our approach would involve a starting ylide with only benzene and furan rings present and the central two rings would be formed simultaneously in the cascade cyclisation process upon FVP.



For the synthesis of the required precursor **256**, 5-methyl-2-aminobenzoic acid **257** was required. This was prepared by nitration of 3-methylbenzoic acid which, as previously described, gave a mixture of 5-methyl and 3-methyl isomers but these were easily separated. The appropriate nitro compound **188** was reduced with ferrous sulfate heptahydrate in aqueous ammonia to give **257** in 50% yield. Acid **257** was then benzylated using three equivalents of benzyl bromide to give benzyl 2-(*N*,*N*-dibenzylamino)-5-methylbenzoate **258** which was in turn reduced with lithium aluminium hydride, to give 2-(*N*,*N*-dibenzylamino)-5-methylbenzyl alcohol **259**. The phosphonium salt **260** was synthesised by treating alcohol **259** with phosphorus tribromide at 60 °C, followed by triphenylphosphine. The target ylide **256** was prepared by treating salt **260** with butyllithium followed by addition of 1-(3-(2-furyl)propenoyl)benzotriazole **206**. The ¹³C NMR data for **256** are included in Table **3** (Page 134).



Upon FVP, ylide **256** behaved in the manner expected from the *N*,*N*-dibenzyl ylides of the previous section to give 3-(2-(2-furyl)ethenyl)-6-methylquinoline **261** as the main product. However, pleasingly and in contrast to the behaviour of analogue **244** lacking the ring methyl group, this was accompanied by the natural product Eustifoline-D.



Unfortunately the desired product was only formed in 19% yield but its ¹H NMR spectroscopic data were an exact match with those reported for Eustifoline D (Figure 7, Page 143, Table 4).⁷⁵ The overall yield for the five step synthesis from 257 was 2%. Further work is required to see whether the balance between carbazole and quinoline products might be controlled by altering the pyrolysis temperature or other parameters.

	Literature	Experimental
H-1	7.23 (dd, 2.0, 0.7)	7.33 (dd, 2,1)
H-2	7.81 (d, 2.0)	7.81 (d, 2)
H-4	7.58 (dd, 8.7, 0.7)	7.58 (dd, 9,1)
H-5	7.35 (d, 8.7)	7.36 (d, 9)
H-7	7.40 (d, 8.4)	7.40 (d, 8)
H-8	7.26 (dd, 8.4, 1.7)	-
H-10	7.97 (br s)	7.97 (br s)
NH	8.12	8.12
CH ₃	2.58 (3H, s)	2.58 (3H, s)
	1	

Table 4. Comparison of literature and experimental ¹H NMR

Experimental ¹H NMR spectrum



Figure 7. Experimental and simulated ¹H NMR spectra of Eustifoline-D using iNMR.

i Conclusions, Summary and Future Work

In conclusion, the aim to continue the investigation into how β -keto ylides behave under FVP conditions has been successful, culminating in the synthesis of the natural product Eustifoline D. It has been discovered that the nature of the substituent on the nitrogen as well as the substituent at the keto end of the ylide has an important impact on the products obtained.

Initial model ylides with tosyl/mesyl and methyl on the nitrogen yielded simple 3-substituted quinolines, but when α,β -unsaturated acyl groups were introduced full cyclisation was observed to give carbazoles. When moving to methyl and benzyl on the nitrogen, it was difficult to predict which products would be obtained. When R^1 = phenyl, 2-furyl and 2-thienyl the expected carbazole products were formed, however, when R^1 = 2-methylphenyl a mixture of 3-substituted quinoline, phenanthridine and carbazole were found. The 3-substituted quinoline and phenanthridine were formed when R^1 = 3-thienyl and the breakdown product 9-methyl phenanthridine was obtained when R^1 = 3-furyl.



When the substituents on the nitrogen were changed to two benzyl groups, the products obtained changed too. In all examples the major product was the 3-substituted quinoline, and in most cases phenanthridine was also found. When $R^1 = 2$ -furyl, 6-phenylfuro[2,3-k]phenanthridine was isolated, giving a good indication to the mechanism of the cyclisation process. Interestingly when $R^1 = 2$ -thienyl, the equivalent benzocarbazole was obtained which is consistent with the previous example with methyl and benzyl on the nitrogen. In the case where $R^1 = 2$ -methylphenyl, only the 3-substituted quinoline was found as opposed the mixture of products in the previous example. Based on these observations, there is not a clear pattern for the prediction of products to be obtained from each ylide, although it was apparent that the substituents on the nitrogen are a major influencing factor. See scheme for summary of all major products obtained.



R¹ = Ph, 2, furyl, 2-thienyl, 2-methylphenyl

Further study on the effect of the substituents on the nitrogen is required to gain sufficient insight to allow confident prediction of the products in a given case. It would be useful to attempt to synthesise a variety of ylides with methyl and allyl on the nitrogen. This should now be possible after overcoming the problems of the formation of the phosphonium salt from the alcohol **205**. It would also be interesting to synthesise two other series of ylides, one with two allyl groups on the nitrogen and the other with an allyl and a benzyl. Using these three new sets of ylides it would be possible to track trends in the products observed and also to compare allyl and benzyl. For example, would the benzyl leave first giving rise to the benzocarbazole or would allyl leave first allowing the radical transfer resulting in quinoline formation?

APPENDIX

A. Publication During Research Period

R. A. Aitken and L. Murray, J. Org. Chem., 2008, 73, 9781–9783.

B. Crystal Data for Ylide 158

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B. Crystal Data for Ylide 158

Crystal data and structure refinement for 158

Identification code	lmaa1	
Empirical formula	C40 H34 N O3 P S	
Formula weight	639.71	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 10.055(2) Å	$\alpha = 90^{\circ}$.
	b = 18.021(3) Å	$\beta = 99.928(5)^{\circ}.$
	c = 18.125(4) Å	$\gamma = 90^{\circ}.$
Volume	3234.9(11) Å ³	
Z	4	
Density (calculated)	1.313 Mg/m ³	
Absorption coefficient	0.190 mm ⁻¹	
F(000)	1344	
Crystal size	0.1000 x 0.1000 x 0.100	00 mm ³
Theta range for data collection	1.61 to 25.40°.	
Index ranges	-9<=h<=12, -20<=k<=2	21, -21<=l<=21
Reflections collected	19659	
Independent reflections	5805 [R(int) = 0.0220]	
Completeness to theta = 25.00°	98.7 %	
Absorption correction	Multiscan	
Max. and min. transmission	1.0000 and 0.3088	
Refinement method	Full-matrix least-square	es on F ²
Data / restraints / parameters	5805 / 0 / 418	
Goodness-of-fit on F ²	1.008	
Final R indices [I>2sigma(I)]	R1 = 0.0333, wR2 = 0.0)792
R indices (all data)	R1 = 0.0383, wR2 = 0.0)827
Largest diff. peak and hole	0.322 and -0.393 e.Å ⁻³	

	Х	У	Z	U(eq)
S(1)	3082(1)	4399(1)	1527(1)	14(1)
O(1)	3929(1)	3807(1)	1354(1)	18(1)
O(2)	1642(1)	4331(1)	1336(1)	19(1)
N(1)	3415(1)	4524(1)	2446(1)	15(1)
C(1)	4837(2)	4560(1)	2758(1)	15(1)
C(2)	5552(1)	3906(1)	3009(1)	15(1)
C(3)	6941(2)	3988(1)	3273(1)	18(1)
C(4)	7584(2)	4669(1)	3285(1)	21(1)
C(5)	6844(2)	5306(1)	3061(1)	23(1)
C(6)	5478(2)	5247(1)	2803(1)	20(1)
C(7)	4870(1)	3180(1)	3006(1)	14(1)
P(7)	5396(1)	2372(1)	2609(1)	13(1)
C(8)	3705(2)	3024(1)	3312(1)	16(1)
O(8)	3101(1)	2410(1)	3193(1)	20(1)
C(9)	3188(2)	3544(1)	3845(1)	16(1)
C(10)	1801(2)	3605(1)	3817(1)	21(1)
C(11)	1291(2)	4028(1)	4341(1)	23(1)
C(12)	2160(2)	4378(1)	4913(1)	23(1)
C(13)	3543(2)	4317(1)	4951(1)	24(1)
C(14)	4052(2)	3909(1)	4414(1)	20(1)
C(15)	2532(2)	5064(1)	2744(1)	20(1)
C(16)	3598(2)	5213(1)	1113(1)	16(1)
C(17)	2748(2)	5827(1)	987(1)	19(1)
C(18)	3202(2)	6467(1)	685(1)	22(1)
C(19)	4496(2)	6506(1)	510(1)	21(1)
C(20)	5328(2)	5885(1)	645(1)	23(1)
C(21)	4897(2)	5241(1)	944(1)	20(1)
C(22)	5006(2)	7204(1)	199(1)	28(1)
C(23)	6990(1)	2542(1)	2299(1)	15(1)
C(24)	6999(2)	3021(1)	1694(1)	18(1)
C(25)	8207(2)	3196(1)	1467(1)	22(1)
C(26)	9415(2)	2901(1)	1844(1)	24(1)

Table 5 Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)for Imaa1. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor. **158**

	Х	У	Z	U(eq)
C(27)	9413(2)	2417(1)	2437(1)	22(1)
C(28)	8203(2)	2234(1)	2667(1)	18(1)
C(29)	5687(1)	1636(1)	3304(1)	17(1)
C(30)	5916(2)	1831(1)	4062(1)	22(1)
C(31)	6118(2)	1284(1)	4609(1)	26(1)
C(32)	6113(2)	543(1)	4406(1)	26(1)
C(33)	5919(2)	346(1)	3659(1)	24(1)
C(34)	5697(1)	890(1)	3107(1)	19(1)
C(35)	4317(1)	1996(1)	1781(1)	15(1)
C(36)	4868(2)	1495(1)	1329(1)	17(1)
C(37)	4056(2)	1160(1)	725(1)	21(1)
C(38)	2704(2)	1341(1)	548(1)	24(1)
C(39)	2159(2)	1861(1)	975(1)	23(1)
C(40)	2957(2)	2185(1)	1594(1)	19(1)

Table 5 (contd) Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)for Imaa1. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor. **158**

Table 6 Bond lengths [Å] and a	angles [°] for 158
S(1)-O(1)	1.4329(11)
S(1)-O(2)	1.4345(11)
S(1)-N(1)	1.6563(13)
S(1)-C(16)	1.7662(15)
N(1)-C(1)	1.4462(19)
N(1)-C(15)	1.4809(19)
C(1)-C(6)	1.393(2)
C(1)-C(2)	1.413(2)
C(2)-C(3)	1.404(2)
C(2)-C(7)	1.478(2)
C(3)-C(4)	1.386(2)
C(3)-H(3A)	0.9500
C(4)-C(5)	1.390(2)

C(4)-H(4A)	0.9500
C(5)-C(6)	1.376(2)
C(5)-H(5A)	0.9500
C(6)-H(6A)	0.9500
C(7)-C(8)	1.408(2)
C(7)-P(7)	1.7459(15)
P(7)-C(23)	1.8129(15)
P(7)-C(29)	1.8192(15)
P(7)-C(35)	1.8242(15)
C(8)-O(8)	1.2631(18)
C(8)-C(9)	1.501(2)
C(9)-C(10)	1.391(2)
C(9)-C(14)	1.394(2)
C(10)-C(11)	1.383(2)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.387(2)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.385(2)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.386(2)
C(13)-H(13A)	0.9500
C(14)-H(14A)	0.9500
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.392(2)
C(16)-C(21)	1.393(2)
C(17)-C(18)	1.388(2)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.393(2)
C(18)-H(18A)	0.9500
C(19)-C(20)	1.393(2)
C(19)-C(22)	1.505(2)
C(20)-C(21)	1.383(2)

Table 6 (contd) Bond lengths [Å] and angles [°] for 158

				0					
Table 6	(contd)	Bond	lengths	[A]	and	angles	[°]	for	158

C(20)-H(20A)	0.9500
C(21)-H(21A)	0.9500
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-C(24)	1.397(2)
C(23)-C(28)	1.400(2)
C(24)-C(25)	1.385(2)
C(24)-H(24A)	0.9500
C(25)-C(26)	1.392(2)
C(25)-H(25A)	0.9500
C(26)-C(27)	1.384(2)
C(26)-H(26A)	0.9500
C(27)-C(28)	1.391(2)
C(27)-H(27A)	0.9500
C(28)-H(28A)	0.9500
C(29)-C(34)	1.392(2)
C(29)-C(30)	1.397(2)
C(30)-C(31)	1.388(2)
C(30)-H(30A)	0.9500
C(31)-C(32)	1.385(2)
C(31)-H(31A)	0.9500
C(32)-C(33)	1.380(2)
C(32)-H(32A)	0.9500
C(33)-C(34)	1.390(2)
C(33)-H(33A)	0.9500
C(34)-H(34A)	0.9500
C(35)-C(40)	1.393(2)
C(35)-C(36)	1.396(2)
C(36)-C(37)	1.386(2)
C(36)-H(36A)	0.9500
C(37)-C(38)	1.381(2)
C(37)-H(37A)	0.9500
C(38)-C(39)	1.386(2)

				0					
Table 6	(contd)	Bond	lengths	[A]	and	angles	[°]	for	158

C(38)-H(38A)	0.9500
C(39)-C(40)	1.391(2)
C(39)-H(39A)	0.9500
C(40)-H(40A)	0.9500
O(1)-S(1)-O(2)	119.82(6)
O(1)-S(1)-N(1)	107.23(6)
O(2)-S(1)-N(1)	105.91(6)
O(1)-S(1)-C(16)	107.27(7)
O(2)-S(1)-C(16)	109.05(7)
N(1)-S(1)-C(16)	106.90(7)
C(1)-N(1)-C(15)	116.24(12)
C(1)-N(1)-S(1)	114.49(9)
C(15)-N(1)-S(1)	115.23(10)
C(6)-C(1)-C(2)	121.19(14)
C(6)-C(1)-N(1)	118.65(13)
C(2)-C(1)-N(1)	120.15(13)
C(3)-C(2)-C(1)	116.32(13)
C(3)-C(2)-C(7)	121.85(13)
C(1)-C(2)-C(7)	121.82(13)
C(4)-C(3)-C(2)	122.13(14)
C(4)-C(3)-H(3A)	118.9
C(2)-C(3)-H(3A)	118.9
C(3)-C(4)-C(5)	120.15(14)
C(3)-C(4)-H(4A)	119.9
C(5)-C(4)-H(4A)	119.9
C(6)-C(5)-C(4)	119.24(14)
C(6)-C(5)-H(5A)	120.4
C(4)-C(5)-H(5A)	120.4
C(5)-C(6)-C(1)	120.85(14)
C(5)-C(6)-H(6A)	119.6
C(1)-C(6)-H(6A)	119.6
C(8)-C(7)-C(2)	126.33(13)
C(8)-C(7)-P(7)	109.17(11)

Table 6 (contd) Bond lengths A and angles ° for 158				- ?			4 - 0
	Table 6 (d	contd) Bon	d lengths	A and	angles	° for	158

C(2)-C(7)-P(7)	124.50(10)								
C(7)-P(7)-C(23)	109.50(7)								
C(7)-P(7)-C(29)	110.22(7)								
C(23)-P(7)-C(29)	106.99(7)								
C(7)-P(7)-C(35)	118.06(7)								
C(23)-P(7)-C(35)	103.91(7)								
C(29)-P(7)-C(35)	107.50(7)								
O(8)-C(8)-C(7)	121.04(13)								
O(8)-C(8)-C(9)	116.55(13)								
C(7)-C(8)-C(9)	122.20(13)								
C(10)-C(9)-C(14)	118.84(14)								
C(10)-C(9)-C(8)	118.83(13)								
C(14)-C(9)-C(8)	122.02(13)								
C(11)-C(10)-C(9)	120.44(14)								
C(11)-C(10)-H(10A)	119.8								
C(9)-C(10)-H(10A)	119.8								
C(10)-C(11)-C(12)	120.24(15)								
C(10)-C(11)-H(11A)	119.9								
C(12)-C(11)-H(11A)	119.9								
C(13)-C(12)-C(11)	119.91(15)								
C(13)-C(12)-H(12A)	120.0								
C(11)-C(12)-H(12A)	120.0								
C(12)-C(13)-C(14)	119.74(15)								
C(12)-C(13)-H(13A)	120.1								
C(14)-C(13)-H(13A)	120.1								
C(13)-C(14)-C(9)	120.79(14)								
C(13)-C(14)-H(14A)	119.6								
C(9)-C(14)-H(14A)	119.6								
N(1)-C(15)-H(15A)	109.5								
N(1)-C(15)-H(15B)	109.5								
H(15A)-C(15)-H(15B)	109.5								
N(1)-C(15)-H(15C)	109.5								
H(15A)-C(15)-H(15C)	109.5								
H(15B)-C(15)-H(15C)	109.5								
				0					
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Table 6 🛛	(contd)	Bond	lengths	[A]	and	angles	[°]	for	158
	(001100)	20110	10 mg cmb	L J		- Bres	L J		

C(17)-C(16)-C(21)	120.53(14)
C(17)-C(16)-S(1)	120.86(11)
C(21)-C(16)-S(1)	118.56(11)
C(18)-C(17)-C(16)	119.39(14)
C(18)-C(17)-H(17A)	120.3
C(16)-C(17)-H(17A)	120.3
C(17)-C(18)-C(19)	121.00(14)
C(17)-C(18)-H(18A)	119.5
C(19)-C(18)-H(18A)	119.5
C(18)-C(19)-C(20)	118.43(14)
C(18)-C(19)-C(22)	121.28(14)
C(20)-C(19)-C(22)	120.28(15)
C(21)-C(20)-C(19)	121.60(15)
C(21)-C(20)-H(20A)	119.2
C(19)-C(20)-H(20A)	119.2
C(20)-C(21)-C(16)	119.04(14)
C(20)-C(21)-H(21A)	120.5
C(16)-C(21)-H(21A)	120.5
C(19)-C(22)-H(22A)	109.5
C(19)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(19)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(24)-C(23)-C(28)	119.67(13)
C(24)-C(23)-P(7)	118.23(11)
C(28)-C(23)-P(7)	122.05(11)
C(25)-C(24)-C(23)	119.95(14)
C(25)-C(24)-H(24A)	120.0
C(23)-C(24)-H(24A)	120.0
C(24)-C(25)-C(26)	120.16(15)
C(24)-C(25)-H(25A)	119.9
C(26)-C(25)-H(25A)	119.9
C(27)-C(26)-C(25)	120.27(14)

Tabla 6	(contd)	Rond	longthe	٢Å٦	and	anglas	roi	for	159
	(conta)	Dona	lenguis	լոյ	anu	angies	LJ	101	130

C(27)-C(26)-H(26A)	119.9
C(25)-C(26)-H(26A)	119.9
C(26)-C(27)-C(28)	120.01(14)
C(26)-C(27)-H(27A)	120.0
C(28)-C(27)-H(27A)	120.0
C(27)-C(28)-C(23)	119.93(14)
C(27)-C(28)-H(28A)	120.0
C(23)-C(28)-H(28A)	120.0
C(34)-C(29)-C(30)	119.17(14)
C(34)-C(29)-P(7)	122.29(12)
C(30)-C(29)-P(7)	118.54(12)
C(31)-C(30)-C(29)	120.20(15)
C(31)-C(30)-H(30A)	119.9
C(29)-C(30)-H(30A)	119.9
C(32)-C(31)-C(30)	120.06(16)
C(32)-C(31)-H(31A)	120.0
C(30)-C(31)-H(31A)	120.0
C(33)-C(32)-C(31)	120.13(15)
C(33)-C(32)-H(32A)	119.9
C(31)-C(32)-H(32A)	119.9
C(32)-C(33)-C(34)	120.15(15)
C(32)-C(33)-H(33A)	119.9
C(34)-C(33)-H(33A)	119.9
C(33)-C(34)-C(29)	120.25(15)
C(33)-C(34)-H(34A)	119.9
C(29)-C(34)-H(34A)	119.9
C(40)-C(35)-C(36)	119.22(13)
C(40)-C(35)-P(7)	121.88(11)
C(36)-C(35)-P(7)	118.89(11)
C(37)-C(36)-C(35)	120.39(14)
C(37)-C(36)-H(36A)	119.8
C(35)-C(36)-H(36A)	119.8
C(38)-C(37)-C(36)	120.10(14)
C(38)-C(37)-H(37A)	119.9

Table 6 (contd) Bond lengths [Å] and angles [°] for 158

C(36)-C(37)-H(37A)	119.9
C(37)-C(38)-C(39)	119.96(14)
C(37)-C(38)-H(38A)	120.0
C(39)-C(38)-H(38A)	120.0
C(38)-C(39)-C(40)	120.30(14)
C(38)-C(39)-H(39A)	119.9
C(40)-C(39)-H(39A)	119.9
C(39)-C(40)-C(35)	119.94(14)
C(39)-C(40)-H(40A)	120.0
C(35)-C(40)-H(40A)	120.0

Table 7Torsion angles [°] for 158

O(1)-S(1)-N(1)-C(1)	47.38(11)
O(2)-S(1)-N(1)-C(1)	176.41(10)
C(16)-S(1)-N(1)-C(1)	-67.40(11)
O(1)-S(1)-N(1)-C(15)	-173.87(10)
O(2)-S(1)-N(1)-C(15)	-44.84(12)
C(16)-S(1)-N(1)-C(15)	71.35(12)
C(15)-N(1)-C(1)-C(6)	-48.90(18)
S(1)-N(1)-C(1)-C(6)	89.41(14)
C(15)-N(1)-C(1)-C(2)	131.31(14)
S(1)-N(1)-C(1)-C(2)	-90.38(14)
C(6)-C(1)-C(2)-C(3)	-2.5(2)
N(1)-C(1)-C(2)-C(3)	177.25(12)
C(6)-C(1)-C(2)-C(7)	176.35(13)
N(1)-C(1)-C(2)-C(7)	-3.9(2)
C(1)-C(2)-C(3)-C(4)	-0.4(2)
C(7)-C(2)-C(3)-C(4)	-179.26(14)
C(2)-C(3)-C(4)-C(5)	2.8(2)
C(3)-C(4)-C(5)-C(6)	-2.4(2)

C(4)-C(5)-C(6)-C(1) -0.5(2) C(2)-C(1)-C(6)-C(5) 3.0(2) N(1)-C(1)-C(6)-C(5) -176.75(13) C(3)-C(2)-C(7)-C(8) 127.95(16) C(1)-C(2)-C(7)-C(8) -50.9(2) C(3)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) -123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-C(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-		
CQ:-C(1)-C(6)-C(5) 3.0(2) N(1)-C(1)-C(6)-C(5) -176.75(13) C(3)-C(2)-C(7)-C(8) 127.95(16) C(1)-C(2)-C(7)-C(8) -50.9(2) C(3)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) 112.26(12) C(2)-C(7)-P(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(9)-C(10) 145.41(14) O(8)-C(9)-C(10) 174.32(14) C(7)-C(8)-C(9)-C(11) 0.7(2) C(8)-C(9)-C(10)-C(11) <td>C(4)-C(5)-C(6)-C(1)</td> <td>-0.5(2)</td>	C(4)-C(5)-C(6)-C(1)	-0.5(2)
N(1)-C(1)-C(6)-C(5) -176.75(13) C(3)-C(2)-C(7)-C(8) 127.95(16) C(1)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -55.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.28(14) C(1)-C(1)-C(12)-C(13) 1.3(2) C(1)-C(1)-C(12)-C(13) 1.3(2) C(1)-C(C(2)-C(1)-C(6)-C(5)	3.0(2)
C(3)-C(2)-C(7)-C(8) 127.95(16) C(1)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 0.7(2) C(14)-C(9)-C(11)-C(12) -1.9(2) C(14)-C(9)-C(11)-C(12) -1.9(2) C(10)-C(11)-C(12)-C(13) 1.3(2) C(10)	N(1)-C(1)-C(6)-C(5)	-176.75(13)
C(1)-C(2)-C(7)-C(8) -50.9(2) C(3)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-C(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(8) -15.0(2) P(7)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 0.7(2) C(14)-C(9)-C(10)-C(11) 0.7(2) C(8)-C(9)-C(10)-C(11) 1.3(2) C(14)-C(9)-C(13)-C(14) 0.4(2) C(10)-C(11)-C(12)-C(13) 1.1(2) C(10)-C(10)-C(11)-C(13) 1.1(2) C(8)-C(9)-C(C(3)-C(2)-C(7)-C(8)	127.95(16)
C(3)-C(2)-C(7)-P(7) -52.62(18) C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 145.41(14) O(8)-C(9)-C(10)-C(11) 0.7(2) C(8)-C(9)-C(10)-C(11) 1.74.32(14) C(9)-C(10)-C(11) 1.74.32(14) C(9)-C(10)-C(11)-C(12) -1.9(2) C(10	C(1)-C(2)-C(7)-C(8)	-50.9(2)
C(1)-C(2)-C(7)-P(7) 128.56(13) C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 0.7(2) C(14)-C(9)-C(10)-C(11) 0.7(2) C(3)-C(10)-C(11) 174.32(14) C(9)-C(10)-C(11) 0.7(2) C(10)-C(1)-C(12)-C(13) 1.3(2) C(10)-C(1)-C(12)-C(13) 1.3(2) C(10)-C(1)-C(13)-C(14) 0.4(2) C(10)-C(1)-C(13)-C(14) 0.4(2) C(10)-C(14)-C(13)	C(3)-C(2)-C(7)-P(7)	-52.62(18)
C(8)-C(7)-P(7)-C(23) -174.21(10) C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) -56.77(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 0.7(2) C(14)-C(9)-C(10)-C(11) 0.7(2) C(14)-C(9)-C(10)-C(11) 174.32(14) C(9)-C(10)-C(11) 1.3(2) C(11)-C(12)-C(13) 1.3(2) C(10)-C(11)-C(12)-C(13) 1.3(2) C(11)-C(12)-C(13) 1.1(2) C(10)-C(11)-C(12) -1.6(2) C(10)-C(14)-C(13)	C(1)-C(2)-C(7)-P(7)	128.56(13)
C(2)-C(7)-P(7)-C(23) 6.28(14) C(8)-C(7)-P(7)-C(29) 123.72(12) C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-C(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-O(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 0.7(2) C(14)-C(9)-C(10)-C(11) 0.7(2) C(14)-C(9)-C(10)-C(11) 174.32(14) C(9)-C(10)-C(11)-C(12) -1.9(2) C(10)-C(11)-C(12)-C(13) 1.3(2) C(11)-C(12)-C(13)-C(14) 0.4(2) C(10)-C(11)-C(13) 1.1(2) C(10)-C(14)-C(13) 1.1(2) C(10)-C(14)-C(13) -172.38(14) O(1)-S(1)-C(16)-C(17) 160.83(12) O(2)-S(1)-C(16)-C(17) 29.66(14) N(1)-S(1)-C(16)-C(17	C(8)-C(7)-P(7)-C(23)	-174.21(10)
C(8)-C(7)-P(7)-C(29) $-56.77(12)$ C(2)-C(7)-P(7)-C(29)123.72(12)C(8)-C(7)-P(7)-C(35) $-7.25(12)$ C(2)-C(7)-P(7)-C(35) $-112.26(12)$ C(2)-C(7)-C(8)-O(8) $170.51(13)$ P(7)-C(7)-C(8)-O(8) $-8.99(17)$ C(2)-C(7)-C(8)-C(9) $165.49(11)$ O(8)-C(9)-C(10) $-39.88(19)$ C(7)-C(8)-C(9)-C(10) $145.41(14)$ O(8)-C(8)-C(9)-C(10) $145.41(14)$ O(8)-C(8)-C(9)-C(10) $145.41(14)$ O(8)-C(8)-C(9)-C(14) $133.58(15)$ C(7)-C(8)-C(9)-C(14) $-41.1(2)$ C(14)-C(9)-C(10)-C(11) $0.7(2)$ C(8)-C(9)-C(10)-C(11) $174.32(14)$ C(9)-C(10)-C(11)-C(12) $-1.9(2)$ C(10)-C(11)-C(12)-C(13) $1.3(2)$ C(11)-C(12)-C(13)-C(14) $0.4(2)$ C(12)-C(13)-C(14)-C(19) $-1.6(2)$ C(10)-C(9)-C(14)-C(13) $-172.38(14)$ O(1)-S(1)-C(16)-C(17) $29.66(14)$ N(1)-S(1)-C(16)-C(17) $-21.88(14)$ O(2)-S(1)-C(16)-C(21) $-21.88(14)$ O(2)-S(1)-C(16)-C(21) $-21.88(14)$	C(2)-C(7)-P(7)-C(23)	6.28(14)
C(2)-C(7)-P(7)-C(29) 123.72(12) C(8)-C(7)-P(7)-C(35) 67.25(12) C(2)-C(7)-P(7)-C(35) -112.26(12) C(2)-C(7)-C(8)-O(8) 170.51(13) P(7)-C(7)-C(8)-O(8) -8.99(17) C(2)-C(7)-C(8)-C(9) -15.0(2) P(7)-C(7)-C(8)-C(9) 165.49(11) O(8)-C(8)-C(9)-C(10) -39.88(19) C(7)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(10) 145.41(14) O(8)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(14) 133.58(15) C(7)-C(8)-C(9)-C(11) 0.7(2) C(14)-C(9)-C(10)-C(11) 0.7(2) C(8)-C(9)-C(10)-C(11) 174.32(14) C(9)-C(10)-C(11)-C(12) -1.9(2) C(10)-C(11)-C(12)-C(13) 1.3(2) C(10)-C(11)-C(12)-C(13) 1.3(2) C(10)-C(11)-C(12)-C(13) 1.1(2) C(10)-C(11)-C(13) -172.38(14) O(1)-S(1)-C(16)-C(17) 29.66(14) N(1)-S(1)-C(16)-C(17) -21.88(14) O(1)-S(1)-C(16)-C(21) -21.88(14)	C(8)-C(7)-P(7)-C(29)	-56.77(12)
C(8)-C(7)-P(7)-C(35) $67.25(12)$ C(2)-C(7)-P(7)-C(35) $-112.26(12)$ C(2)-C(7)-C(8)-O(8) $170.51(13)$ P(7)-C(7)-C(8)-O(8) $-8.99(17)$ C(2)-C(7)-C(8)-C(9) $-15.0(2)$ P(7)-C(7)-C(8)-C(9) $165.49(11)$ O(8)-C(8)-C(9)-C(10) $-39.88(19)$ C(7)-C(8)-C(9)-C(10) $145.41(14)$ O(8)-C(8)-C(9)-C(10) $145.41(14)$ O(8)-C(8)-C(9)-C(14) $133.58(15)$ C(7)-C(8)-C(9)-C(14) $-41.1(2)$ C(14)-C(9)-C(10)-C(11) $0.7(2)$ C(8)-C(9)-C(10)-C(11) $174.32(14)$ C(9)-C(10)-C(11) $1.3(2)$ C(10)-C(11)-C(12)-C(13) $1.3(2)$ C(10)-C(11)-C(12)-C(13) $1.3(2)$ C(11)-C(12)-C(13)-C(14) $0.4(2)$ C(12)-C(13)-C(14)-C(9) $-1.6(2)$ C(10)-C(9)-C(14)-C(13) $1.1(2)$ C(8)-C(9)-C(14)-C(13) $-1.72.38(14)$ O(1)-S(1)-C(16)-C(17) $29.66(14)$ N(1)-S(1)-C(16)-C(17) $-84.42(13)$ O(1)-S(1)-C(16)-C(21) $-21.88(14)$ O(2)-S(1)-C(16)-C(21) $-153.05(12)$	C(2)-C(7)-P(7)-C(29)	123.72(12)
C(2)-C(7)-P(7)-C(35) $-112.26(12)$ $C(2)-C(7)-C(8)-O(8)$ $170.51(13)$ $P(7)-C(7)-C(8)-O(8)$ $-8.99(17)$ $C(2)-C(7)-C(8)-C(9)$ $15.0(2)$ $P(7)-C(7)-C(8)-C(9)$ $165.49(11)$ $O(8)-C(8)-C(9)-C(10)$ $-39.88(19)$ $C(7)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(14)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(8)-C(7)-P(7)-C(35)	67.25(12)
C(2)-C(7)-C(8)-O(8) $170.51(13)$ $P(7)-C(7)-C(8)-O(8)$ $-8.99(17)$ $C(2)-C(7)-C(8)-C(9)$ $165.49(11)$ $O(8)-C(8)-C(9)-C(10)$ $-39.88(19)$ $C(7)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(2)-C(7)-P(7)-C(35)	-112.26(12)
P(7)-C(7)-C(8)-O(8) $-8.99(17)$ $C(2)-C(7)-C(8)-C(9)$ $-15.0(2)$ $P(7)-C(7)-C(8)-C(9)$ $165.49(11)$ $O(8)-C(8)-C(9)-C(10)$ $-39.88(19)$ $C(7)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.1(2)$ $C(10)-C(14)-C(13)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $-1.72.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(2)-C(7)-C(8)-O(8)	170.51(13)
C(2)-C(7)-C(8)-C(9) $-15.0(2)$ $P(7)-C(7)-C(8)-C(9)$ $165.49(11)$ $O(8)-C(8)-C(9)-C(10)$ $-39.88(19)$ $C(7)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(14)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	P(7)-C(7)-C(8)-O(8)	-8.99(17)
P(7)-C(7)-C(8)-C(9) $165.49(11)$ $O(8)-C(8)-C(9)-C(10)$ $-39.88(19)$ $C(7)-C(8)-C(9)-C(10)$ $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(2)-C(7)-C(8)-C(9)	-15.0(2)
O(8) - C(8) - C(9) - C(10) $-39.88(19)$ $C(7) - C(8) - C(9) - C(10)$ $145.41(14)$ $O(8) - C(8) - C(9) - C(14)$ $133.58(15)$ $C(7) - C(8) - C(9) - C(14)$ $-41.1(2)$ $C(14) - C(9) - C(10) - C(11)$ $0.7(2)$ $C(8) - C(9) - C(10) - C(11)$ $174.32(14)$ $C(9) - C(10) - C(11) - C(12)$ $-1.9(2)$ $C(10) - C(11) - C(12) - C(13)$ $1.3(2)$ $C(11) - C(12) - C(13) - C(14)$ $0.4(2)$ $C(12) - C(13) - C(14) - C(9)$ $-1.6(2)$ $C(10) - C(9) - C(14) - C(13)$ $1.1(2)$ $C(8) - C(9) - C(14) - C(13)$ $-172.38(14)$ $O(1) - S(1) - C(16) - C(17)$ $29.66(14)$ $N(1) - S(1) - C(16) - C(17)$ $-84.42(13)$ $O(1) - S(1) - C(16) - C(21)$ $-21.88(14)$ $O(2) - S(1) - C(16) - C(21)$ $-153.05(12)$	P(7)-C(7)-C(8)-C(9)	165.49(11)
C(7)-C(8)-C(9)-C(10) $145.41(14)$ $O(8)-C(8)-C(9)-C(14)$ $133.58(15)$ $C(7)-C(8)-C(9)-C(14)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	O(8)-C(8)-C(9)-C(10)	-39.88(19)
O(8)-C(8)-C(9)-C(14)133.58(15) $C(7)-C(8)-C(9)-C(10)$ $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(7)-C(8)-C(9)-C(10)	145.41(14)
C(7)-C(8)-C(9)-C(14) $-41.1(2)$ $C(14)-C(9)-C(10)-C(11)$ $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	O(8)-C(8)-C(9)-C(14)	133.58(15)
C(14)-C(9)-C(10)-C(11) $0.7(2)$ $C(8)-C(9)-C(10)-C(11)$ $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(7)-C(8)-C(9)-C(14)	-41.1(2)
C(8)-C(9)-C(10)-C(11) $174.32(14)$ $C(9)-C(10)-C(11)-C(12)$ $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(14)-C(9)-C(10)-C(11)	0.7(2)
C(9)-C(10)-C(11)-C(12) $-1.9(2)$ $C(10)-C(11)-C(12)-C(13)$ $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(17)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(8)-C(9)-C(10)-C(11)	174.32(14)
C(10)-C(11)-C(12)-C(13) $1.3(2)$ $C(11)-C(12)-C(13)-C(14)$ $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(9)-C(10)-C(11)-C(12)	-1.9(2)
C(11)-C(12)-C(13)-C(14) $0.4(2)$ $C(12)-C(13)-C(14)-C(9)$ $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(10)-C(11)-C(12)-C(13)	1.3(2)
C(12)-C(13)-C(14)-C(9) $-1.6(2)$ $C(10)-C(9)-C(14)-C(13)$ $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(11)-C(12)-C(13)-C(14)	0.4(2)
C(10)-C(9)-C(14)-C(13) $1.1(2)$ $C(8)-C(9)-C(14)-C(13)$ $-172.38(14)$ $O(1)-S(1)-C(16)-C(17)$ $160.83(12)$ $O(2)-S(1)-C(16)-C(17)$ $29.66(14)$ $N(1)-S(1)-C(16)-C(17)$ $-84.42(13)$ $O(1)-S(1)-C(16)-C(21)$ $-21.88(14)$ $O(2)-S(1)-C(16)-C(21)$ $-153.05(12)$	C(12)-C(13)-C(14)-C(9)	-1.6(2)
C(8)- $C(9)$ - $C(14)$ - $C(13)$ $-172.38(14)$ $O(1)$ - $S(1)$ - $C(16)$ - $C(17)$ $160.83(12)$ $O(2)$ - $S(1)$ - $C(16)$ - $C(17)$ $29.66(14)$ $N(1)$ - $S(1)$ - $C(16)$ - $C(17)$ $-84.42(13)$ $O(1)$ - $S(1)$ - $C(16)$ - $C(21)$ $-21.88(14)$ $O(2)$ - $S(1)$ - $C(16)$ - $C(21)$ $-153.05(12)$	C(10)-C(9)-C(14)-C(13)	1.1(2)
O(1)-S(1)-C(16)-C(17)160.83(12)O(2)-S(1)-C(16)-C(17)29.66(14)N(1)-S(1)-C(16)-C(17)-84.42(13)O(1)-S(1)-C(16)-C(21)-21.88(14)O(2)-S(1)-C(16)-C(21)-153.05(12)	C(8)-C(9)-C(14)-C(13)	-172.38(14)
O(2)-S(1)-C(16)-C(17)29.66(14)N(1)-S(1)-C(16)-C(17)-84.42(13)O(1)-S(1)-C(16)-C(21)-21.88(14)O(2)-S(1)-C(16)-C(21)-153.05(12)	O(1)-S(1)-C(16)-C(17)	160.83(12)
N(1)-S(1)-C(16)-C(17)-84.42(13)O(1)-S(1)-C(16)-C(21)-21.88(14)O(2)-S(1)-C(16)-C(21)-153.05(12)	O(2)-S(1)-C(16)-C(17)	29.66(14)
O(1)-S(1)-C(16)-C(21)-21.88(14)O(2)-S(1)-C(16)-C(21)-153.05(12)	N(1)-S(1)-C(16)-C(17)	-84.42(13)
O(2)-S(1)-C(16)-C(21) -153.05(12)	O(1)-S(1)-C(16)-C(21)	-21.88(14)
	O(2)-S(1)-C(16)-C(21)	-153.05(12)

N(1)-S(1)-C(16)-C(21)	92.87(13)
C(21)-C(16)-C(17)-C(18)	0.5(2)
S(1)-C(16)-C(17)-C(18)	177.72(11)
C(16)-C(17)-C(18)-C(19)	-0.3(2)
C(17)-C(18)-C(19)-C(20)	0.0(2)
C(17)-C(18)-C(19)-C(22)	-178.64(14)
C(18)-C(19)-C(20)-C(21)	0.0(2)
C(22)-C(19)-C(20)-C(21)	178.70(15)
C(19)-C(20)-C(21)-C(16)	0.2(2)
C(17)-C(16)-C(21)-C(20)	-0.4(2)
S(1)-C(16)-C(21)-C(20)	-177.73(12)
C(7)-P(7)-C(23)-C(24)	-68.45(13)
C(29)-P(7)-C(23)-C(24)	172.10(11)
C(35)-P(7)-C(23)-C(24)	58.55(13)
C(7)-P(7)-C(23)-C(28)	108.83(13)
C(29)-P(7)-C(23)-C(28)	-10.62(14)
C(35)-P(7)-C(23)-C(28)	-124.18(12)
C(28)-C(23)-C(24)-C(25)	-0.8(2)
P(7)-C(23)-C(24)-C(25)	176.57(11)
C(23)-C(24)-C(25)-C(26)	-0.6(2)
C(24)-C(25)-C(26)-C(27)	1.6(2)
C(25)-C(26)-C(27)-C(28)	-1.1(2)
C(26)-C(27)-C(28)-C(23)	-0.3(2)
C(24)-C(23)-C(28)-C(27)	1.2(2)
P(7)-C(23)-C(28)-C(27)	-176.00(11)
C(7)-P(7)-C(29)-C(34)	159.43(12)
C(23)-P(7)-C(29)-C(34)	-81.59(13)
C(35)-P(7)-C(29)-C(34)	29.51(14)
C(7)-P(7)-C(29)-C(30)	-20.94(14)
C(23)-P(7)-C(29)-C(30)	98.04(13)
C(35)-P(7)-C(29)-C(30)	-150.86(12)
C(34)-C(29)-C(30)-C(31)	-1.5(2)
P(7)-C(29)-C(30)-C(31)	178.83(12)
C(29)-C(30)-C(31)-C(32)	1.0(2)

C(30)-C(31)-C(32)-C(33)	0.5(2)
C(31)-C(32)-C(33)-C(34)	-1.4(2)
C(32)-C(33)-C(34)-C(29)	0.9(2)
C(30)-C(29)-C(34)-C(33)	0.6(2)
P(7)-C(29)-C(34)-C(33)	-179.75(11)
C(7)-P(7)-C(35)-C(40)	-19.49(15)
C(23)-P(7)-C(35)-C(40)	-140.93(12)
C(29)-P(7)-C(35)-C(40)	105.88(13)
C(7)-P(7)-C(35)-C(36)	161.52(11)
C(23)-P(7)-C(35)-C(36)	40.08(13)
C(29)-P(7)-C(35)-C(36)	-73.11(13)
C(40)-C(35)-C(36)-C(37)	-3.4(2)
P(7)-C(35)-C(36)-C(37)	175.59(11)
C(35)-C(36)-C(37)-C(38)	2.6(2)
C(36)-C(37)-C(38)-C(39)	0.1(2)
C(37)-C(38)-C(39)-C(40)	-2.0(2)
C(38)-C(39)-C(40)-C(35)	1.1(2)
C(36)-C(35)-C(40)-C(39)	1.6(2)
P(7)-C(35)-C(40)-C(39)	-177.40(12)

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