

**Consecutive Gold[II]-Catalysed Cyclisation Reactions
Leading to Polyfused Heterocycles
of Agrochemical Relevance**

A thesis submitted for the degree of Doctor of Philosophy

of The Australian National University

by

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Declaration

Unless otherwise indicated, the material presented in this thesis represents the results of original work carried out by myself during the period 2008-2011 and has not been presented for examination for any other degree. This thesis is less than 100 000 words in length.



Phillip Patrick Sharp

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First, I would like to thank my PhD supervisor, Professor Martin Banwell, for the inspiration, encouragement, chemical expertise and personal wisdom that has been extended to me.

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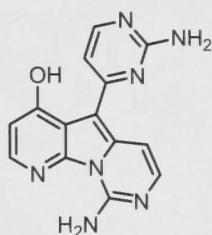
In addition to the past and present members of the Banwell group, I would like to thank the friends that I have made during my time at the RSC. Thank you for the excellent advice and comradery.

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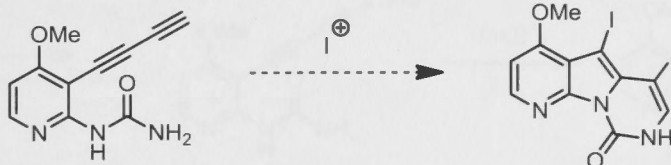
Abstract

Variolin B (**1.8**), a marine natural product isolated from the Antarctic sponge *Kirkpatrickia variolosa*, possesses a rare heterocyclic framework and is a potent CDK inhibitor. Such properties have prompted the industry partner associated with this project, namely the German chemical commodities company BASF, to select this compound as a lead for the development of new agrochemicals. This thesis details the development of new synthetic methods specifically designed to produce complex heterocyclic frameworks related to variolin B.



1.8 variolin B

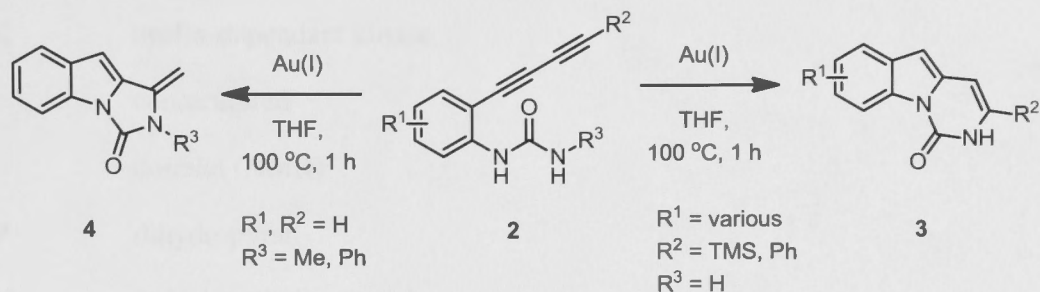
The synthetic plan, which involved consecutive electrophile-promoted nucleophilic ring-closure reactions of 1-[2-(buta-1,3-diynyl)pyridyl]ureas (such as compound **4.3**) potentially leading to pyrido[3',2':4,5]pyrrolo[1,2-*c*]pyrimidin-9(8*H*)-ones, is outlined in *Chapter One*.



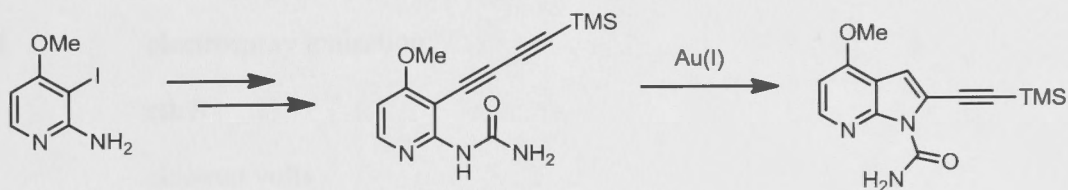
4.3

The first part of *Chapter Two* describes the synthesis of alkynylphenylureas as model cascade cyclisation precursors and the second part details the outcomes of reactions of these model compounds with various sources of iodine. The reactions delivered mono-cyclised compounds in some cases although intermolecular side-reactions prevented cascading cyclisation reactions from occurring.

Details of the successful development of consecutive gold-catalysed nucleophilic ring-closure reaction of 2-(buta-1,3-diynyl)phenylureas (**2**) that deliver pyrimido[1,6-*a*]indol-1(2*H*)-ones (**3**) are provided in *Chapter Three*. The effect that substituents have on the outcome of these gold-promoted reactions were also assessed and it was found that *N,N'*-disubstituted cyclisation precursors give 1-methylene-1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones (**4**) as the major products.



Chapter Four outlines the preparation of pyridine-based cyclisation precursors and attempts to synthesise variolin B by applying the gold-catalysed cyclisation methodology to them. These reactions led to mono-cyclised products in some cases but side reactions were also observed.



Many of the heterocycles produced during the course of this work are unprecedented and, accordingly, they are being tested for their agrochemical properties by BASF Crop-Protection Division. This aspect of the work is discussed in *Appendix 1*.

Glossary

The following scientific abbreviations have been used throughout this thesis:

Ac	acetyl
Bn	benzyl
n-Bu	butyl
Bz	benzoyl
CDK	cyclin-dependant kinase
conc.	concentrated
d	doublet (NMR)
DHP	dihydropyran
DMA	<i>N,N</i> -dimethylacetamide
DME	1,2-dimethoxyethane
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
DtBA	di- <i>tert</i> -butylacetal
EI	electron impact
ESI	electrospray ionisation
Et	ethyl
eV	electron volts
h	hours
HSV	herpes simplex virus
HRMS	high resolution mass spectrometry
IC ₅₀	concentration giving half-maximum inhibition
IR	infrared spectroscopy
ⁱ Pr	isopropyl
<i>J</i>	coupling constant (Hz)

lit.	literature value
LiHMDS	lithium hexamethyldisilazide
m	multiplet (NMR)
M ^{•+}	molecular ion (as encountered in EIMS)
<i>m</i> -CPBA	<i>m</i> -chloroperbenzoic acid
Me	methyl
mins.	minutes
Ms	methanesulfonyl (mesyl)
m.p.	melting point
n-AChR	nicotinic acetylcholine receptor
NBS	<i>N</i> -bromosuccinimide
NCB	noncompetitive blocker
NIS	<i>N</i> -iodosuccinimide
NMR	nuclear magnetic resonance
ORTEP	Oak Ridge Thermal Ellipsoid Program
<i>p</i>	<i>para</i>
Ph	phenyl
PMB	<i>p</i> -methoxybenzyl
ppm	parts per million
q	quartet
quant.	quantitative
<i>R</i> _f	retardation factor
s	singlet (NMR)
SAR	structure activity relationship
SEM	[2-(trimethylsilyl)ethoxy]methyl
TLC	thin layer chromatography
TMS	trimethylsilyl

Tf	trifluoromethanesulfonyl (triflyl)
Ts	<i>p</i> -toluenesulfonyl (tosyl)
TTMSS	tris-trimethylsilylsilane
UV	ultraviolet
v/v	volume-to-volume (ratio)
1°	primary
2°	secondary
3°	tertiary
δ	chemical shift
ν_{max}	Infrared absorption maxima (cm^{-1})

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Chapter One

Introduction

1.1 Agrochemicals

It is the use of crop protection chemicals (agrochemicals) that has, in large measure, led to the spectacular increase in agricultural productivity observed over the last century. However, pests such as weeds, insects and pathogenic fungi remain responsible for the destruction of about 32% of all food crops globally. This is equivalent to the total annual agricultural output of the US.¹ Furthermore, without systematically controlling such pests it is estimated that, on average, 70% of global crop yields would be lost in the field (preharvest), during storage and/or during transport (postharvest).^{2,3} Additionally, exponential population growth, climate change and a shrinking land area available for cultivation are challenging mankind's ability to meet future food demands using the current suite of crop protection chemicals.⁴

Currently, about \$40 billion USD is spent worldwide on crop protection products annually, of which 39% is spent on herbicides, 28% on insecticides, 23% on fungicides and 9% on other pesticides. The majority of these products are formulations of synthetically-derived, low molecular weight chemical pesticides.¹

Between 1930-1960 synthetic chemical pesticides such as organochlorines, organophosphates, and carbamates (**Figure 1.1**) were introduced into agriculture and rapidly became the primary means of pest control. Typically, these types of compounds are very potent. Organochlorines (DDT, for example) act by opening the sodium channels in the neurons of the target organism resulting in spasms and eventual death, while organophosphates and carbamates act as powerful, but non-selective, cholinesterase

inhibitors that destroy normal neuron function.^{5,6} Despite their successful deployment, environmental concerns about the acute toxicity, and bioaccumulation of these compounds need to be addressed, especially since a number of traditional compounds have either been banned or heavily restricted in many countries.^{7,8}

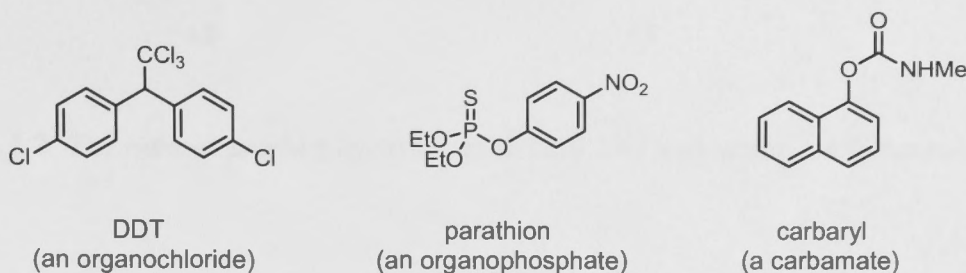


Figure 1.1. Examples of widely used, traditional synthetic pesticides.

1.2 Agrochemicals Derived from Natural Products

In seeking more selective and environmentally benign agents for crop protection, the agrochemical industry is capitalizing on the value of metabolites derived from living organisms (natural products). The advantages of natural products over synthetic pesticides are: a) natural products often have interesting biological properties; and b) natural products usually have much shorter environmental half-lives than synthetically-derived chemical pesticides.

The interesting biological properties of a natural product can often be improved by modifying its structure so as to optimize it for maximum activity and minimum negative (side) effects. For example, leptospermone (**1.0**) (**Figure 1.2**) is a naturally occurring constituent of *Leptospermum scoparium* that exerts unique bleaching effects on several weed species, albeit at relatively high application rates (5 kg.ha⁻¹).⁹ By synthesising an analogue devoid of superfluous functionality and containing a more acidic α -triketo proton, sulcotrione (**1.1**) was developed. This compound showed enhanced herbicidal activity against a wide range of broad-leaved weeds at application rates of about 300–450 g.ha⁻¹ and with good corn tolerance when applied both pre- and post-emergence. It is now sold by BAYER under the trade name Mikado.¹⁰

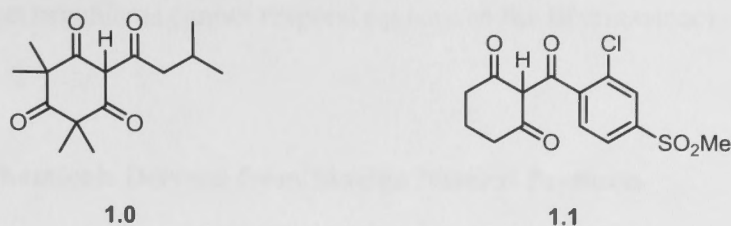


Figure 1.2. The natural product leptospermone (1.0) and a synthetic analogue sulcotrione (1.1).

The pyrethroids represent examples of a highly effective class of insecticides based on a natural product template. Since the first structural assignment of the acidic fragment of pyrethrin I (1.2), (**Figure 1.3**) in 1916, there has been almost 100 years of detailed scientific research into the pyrethroids. This has resulted in the discovery of numerous compounds with superior insecticidal properties, including deltamethrin (1.3) which is about 1700 times more active than pyrethrin I but still retains low mammalian toxicity.¹¹

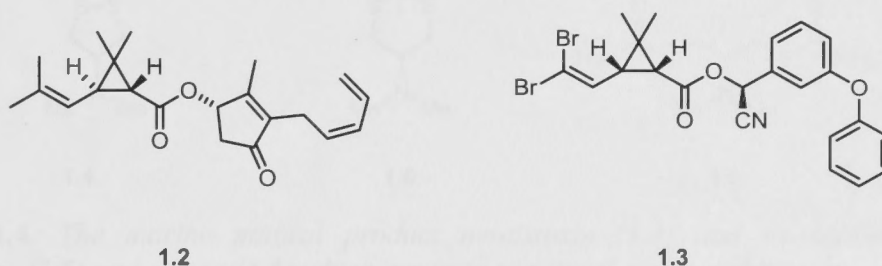


Figure 1.3. The natural product pyrethrin I (1.2) and a synthetic analogue deltamethrin (1.3).

Despite their many impressive features these types of pesticides still have major drawbacks, particularly because of the development of resistance to them. In fact, between 1984 and 1990 insect and mite resistance to pesticides increased by 13% and now more than 500 species of pesticide resistant arthropods are known.^{12,13} Furthermore, the number of herbicide resistant biotypes has increased from 0 to more than 250 since 1957.¹⁴ This is undoubtedly due to excessive application of compounds that have similar modes of action and/or are structurally similar. Applying multiple agents with diverse molecular architectures provides a

higher barrier to resistance because such compounds often exhibit distinct modes of action to which the target organisms cannot respond (at least in the first instance).

1.2.1 Agrochemicals Derived from Marine Natural Products

The marine environment offers particular potential for finding new lead compounds with unique structures and novel modes of action. Marine natural products (MNPs) often arise through evolutionary paths quite different from those of their terrestrial counterparts. This results in their often distinct molecular architectures and biological activity profiles.¹⁵ Therefore, the marine environment represents a source of potential lead compounds for the development of agrochemicals. However, while more than 40 marine natural products with pesticidal activity are known, nereistoxin (**1.4**), isolated from the sea worm *Lumbriconereis heteropoda*, is currently the only type of marine-derived metabolite that has been deployed as a commercial agrochemical (**Figure 1.4**).¹⁶

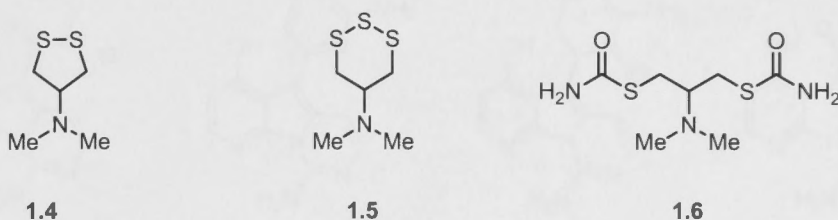


Figure 1.4. The marine natural product nereistoxin (**1.4**) and its synthetic analogs thiocyclam (**1.5**) and cartap (**1.6**) which are used to control moths and beetles.

Gathering enough material from rare and difficult to access marine organisms is a significant barrier to progress in this area. Fortunately, synthesis provides a solution to this problem. For example, nereistoxin **1.4** as well as certain synthetic analogs, namely, thiocyclam (**1.5**) and cartap (**1.6**) are produced synthetically on an industrial (ton) scale (**Figure 1.4**).^{17,18} These compounds are used to control chewing and sucking insects, such as moths and beetles, by acting on the binding site for non-competitive blockers (NCBs) of the target insect's nicotinic acetylcholine receptor (nAChR). This is a different mode of action to that of most other insecticides and in this manner target-site cross-resistance is prevented.^{19,20}

1.3 Variolins

The variolins are a particularly interesting class of four MNPs that were discovered in 1991 by Blunt, Munro and coworkers *via* P388 murine leukaemia-based bioassay-guided isolation from extracts of the Antarctic sponge *Kirkpatrickia variolosa*.²¹ These compounds, **1.7**, **1.8**, **1.9**, **1.10**, all incorporate an unprecedented pyrido[3',2':4,5]pyrrolo[1,2-*c*]pyrimidine core and differ only in the nature of the substituent at C-5 (**Figure 1.5**). NMR spectroscopic analysis alone was insufficient to definitively assign the structures of these compounds due to the large number of ring nitrogens and relatively few hydrogen atoms. Eventually, small crystals of the TFA salt of variolin B were obtained which allowed the structure to be unambiguously assigned as **1.8** using single-crystal X-ray analytical techniques. The structures of the other members of the class could then be assigned based on a combination of chemical derivitisation and comparison of the derived NMR spectral data with those of variolin B.

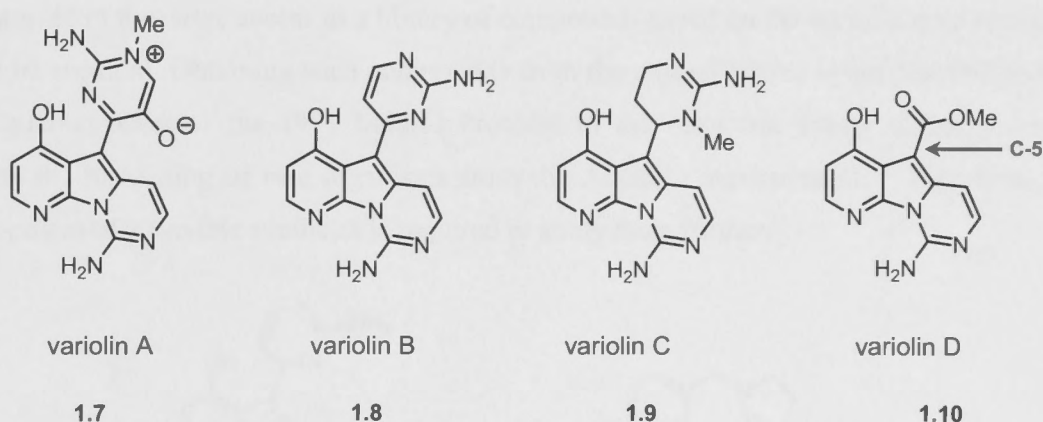


Figure. 1.5. The four known variolin natural products.

1.3.1. Variolin B

Variolin B (**1.8**) is a particularly interesting compound. It displays an IC_{50} of 210 ng/mL against P388 murine leukemia cells and also shows activity against *Herpes simplex* type-1 virus (HSV-1).¹⁰ Cyclin-dependant kinase (CDK) inhibition was subsequently established as the mode of action for the antitumor properties of variolin B.²² Since inhibition of CDKs causes the disruption of cell cycle processes, including cell-division in animals, plants and

other higher organisms, it follows that variolin B also has potential as a marine natural product-based pesticide.²³ Currently, the Spanish pharmaceutical company PharmaMar is evaluating variolin B in clinical trials focused on developing it as an anti-tumor agent. Interestingly, no programs have been initiated to uncover the potential of variolins as agrochemical agents.

Variolin B (**1.8**) shares some intriguing structural similarities to important agrochemicals such as imidacloprid (**1.11**), a widely used neonicotinoid, ametoctradin (**1.12**), a state-of-the-art fungicide, and ethirimol (**1.13**) which is also a fungicide. All of these compounds contain an amino group attached to a densely nitrogenated heterocyclic ring system (**Figure 1.6**). Therefore, in all likelihood, analogs of variolins that share some of these structural features will also possess some, or even improved pesticidal activity. A structure activity relationship (SAR) analysis of these types of heterocycles designed to uncover such properties would therefore appear to be a worthwhile endeavour. Ultimately, in order to develop a thorough SAR profile in this area, access to a library of compounds based on the variolin core structure would be required. Obtaining such compounds from the natural source is not possible due to the implementation of the 1991 Madrid Protocol to the Antarctic Treaty which severely restricts the harvesting of rare organisms from the Antarctic environment.²⁴ Therefore, the development of a flexible synthesis is required to study them further.

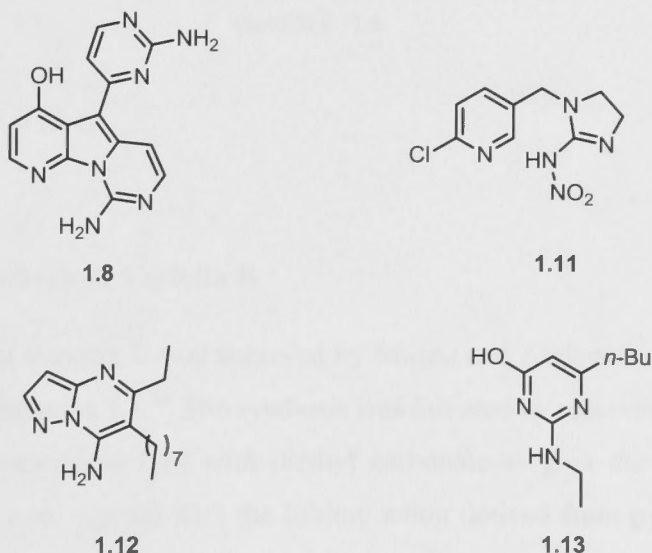
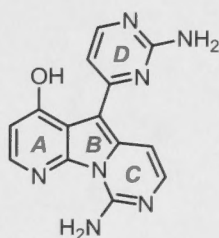


Figure 1.6. Structural resemblances between variolin B (**1.8**), imidacloprid (**1.11**), ametoctradin (**1.12**) and ethirimol (**1.13**).

1.4 Synthesis of Variolins

Developing synthetic approaches to the variolins and related compounds presents some significant synthetic challenges. The novel modes of fusion between the A, B and C rings (**Figure 1.7**) was essentially unprecedented at the time of the isolation of the variolins and while the reactivity of pyridines, pyrroles, and pyrimidines is well documented, the reactivity of a tricyclic system containing all three of these types of heterocycles would be expected to be somewhat more complex. There are also some practical challenges. For example, the highly polar and aromatic nature of these compounds means that they are not very soluble in most organic solvents and, therefore, particularly difficult to work with in the laboratory. Also, the similarity between the environments surrounding the few protons in the target compounds means that spectroscopic analysis of such systems is non-trivial. That having been said, four distinct total syntheses of variolin B have been described.²⁵ Details of these are provided in the following section.



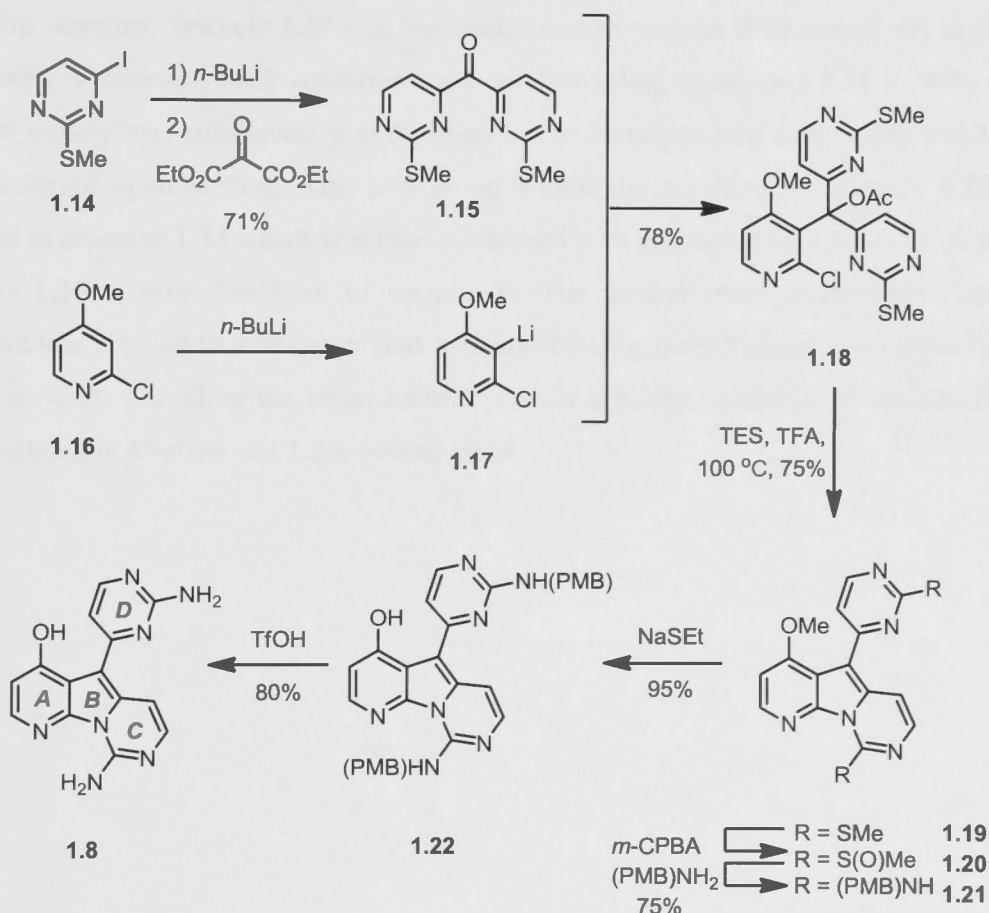
variolin B 1.8

Figure 1.7. *Variolin B (1.8).*

1.4.1 Morris' Synthesis of Variolin B

The first synthesis of variolin B was achieved by Morris and Anderson using the convergent strategy outlined in **Scheme 1.1**.²⁶ The synthesis was initiated by reaction of the lithium anion derived from iodopyrimidine **1.14** with diethyl carbonate to give the symmetrical ketone **1.15**, which was, in turn, reacted with the lithium anion derived from pyridine **1.16** (namely **1.17**). The ensuing oxyanion was quenched with acetyl chloride to afford the C-2 symmetrical acetate **1.18** in 78% yield. Under conditions the group had previously optimised on a model system, compound **1.18** underwent cyclisation, to forge the central B-ring, upon

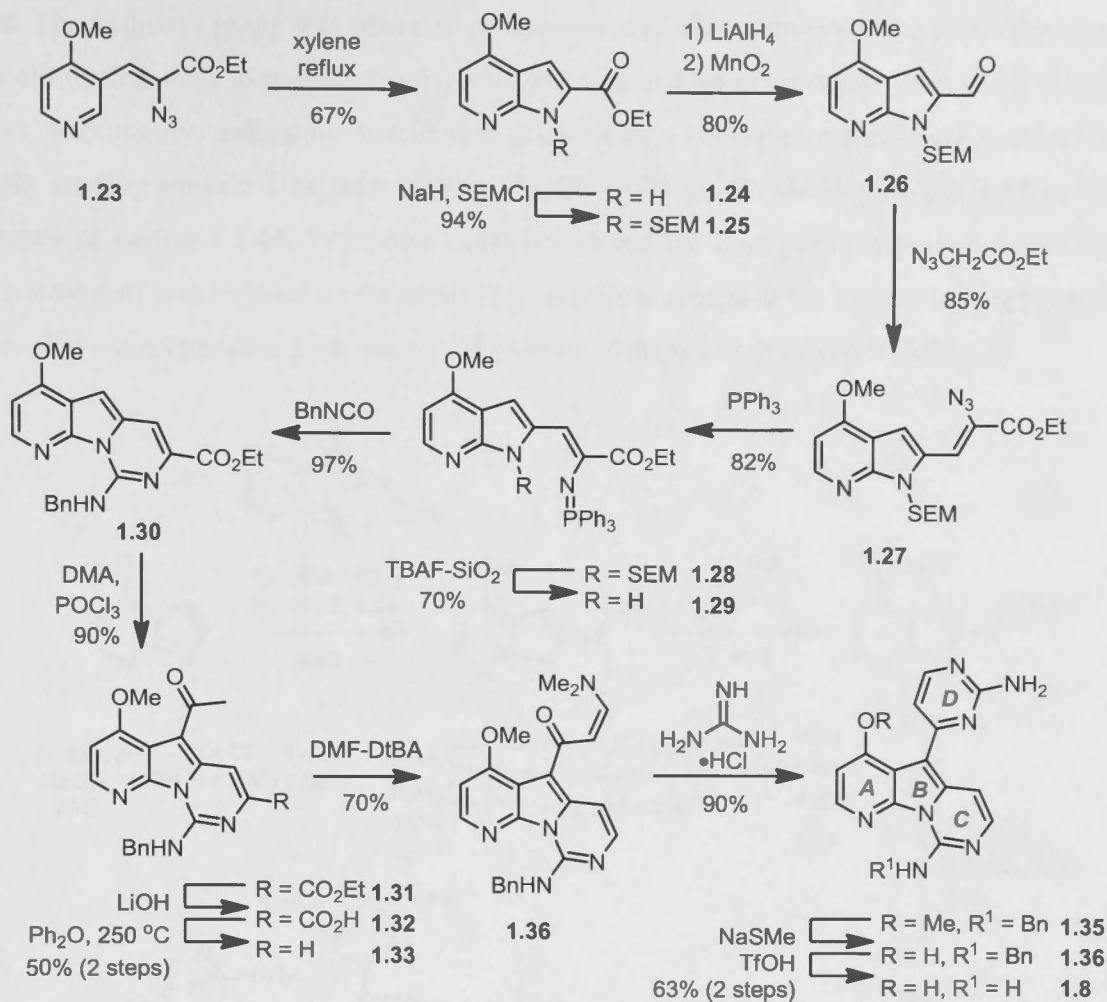
treatment with trifluoroacetic acid and triethylsilane, and so affording tetracycle **1.19** in 75% yield. The cyclisation is believed to occur *via* an acid-promoted nucleophilic aromatic substitution at the chlorinated carbon of the pyridine by the neighbouring pyrimidine ring, followed by reduction of the acetate group. A series of functional group interconversions beginning with oxidation of the thiomethyl moieties, which gave bis-sulfoxide **1.20**, followed by substitution of both sulfoxide groups with *p*-methoxybenzylamine producing 2° amine **1.21** and demethylation of this with sodium ethanthioate then gave compound **1.22**. The two polar amino groups within variolin B (**1.8**) were then finally revealed by treatment of substrate **1.22** with triflic acid. By such means, the natural product was obtained in 17% yield over 8 steps.



Scheme 1.1: Total synthesis of variolin B by Morris et al.²⁵

1.4.2 Molina's Synthesis of Variolin B

Molina and Fresneda synthesised variolin B using an iterative linear strategy that closed the B- and C-rings sequentially using azide chemistry (**Scheme 1.2**).²⁷ Thus, vinyl azide **1.23** (available in two steps from 4-methoxypyridine) underwent, on heating in refluxing xylene, cyclisation *via* a nitrene insertion to produce the azaindole **1.24**. This last compound was converted, *via* intermediates **1.25** and **1.26**, into a second vinyl azide (**1.27**) (64% over 3 steps). Compound **1.27** was then treated with PPh₃, and thus inducing a Staudinger reaction that afforded the iminophosphorane **1.28** (82%). After removal of the unwanted SEM group, treatment of the ensuing azaylide **1.29** with benzyl isocyanate resulted in ring closure *via* an intermediate carbodiimide to produce the desired product **1.30** which embodies the tricyclic core of the variolins. Tricycle **1.30** was then elaborated to variolin B by selectively acylating at C-5 using Vilsmeier-Haack conditions and thus providing compound **1.31** in 90% yield. The ester moiety was subsequently hydrolysed to the corresponding acid (**1.32**) which was then eliminated upon heating. The acyl group within the resulting heterocycle **1.33** was converted to enamine **1.34** which was then condensed with guanidine hydrochloride to afford tetracycle **1.35**, a protected form of variolin B. The methyl ether group within the last compound was cleaved to give compound **1.36** and then the benzyl group was cleaved under acidic conditions providing the target natural product **1.8**. The synthesis of variolin B was thus completed in 16 steps and 1.2% overall yield.

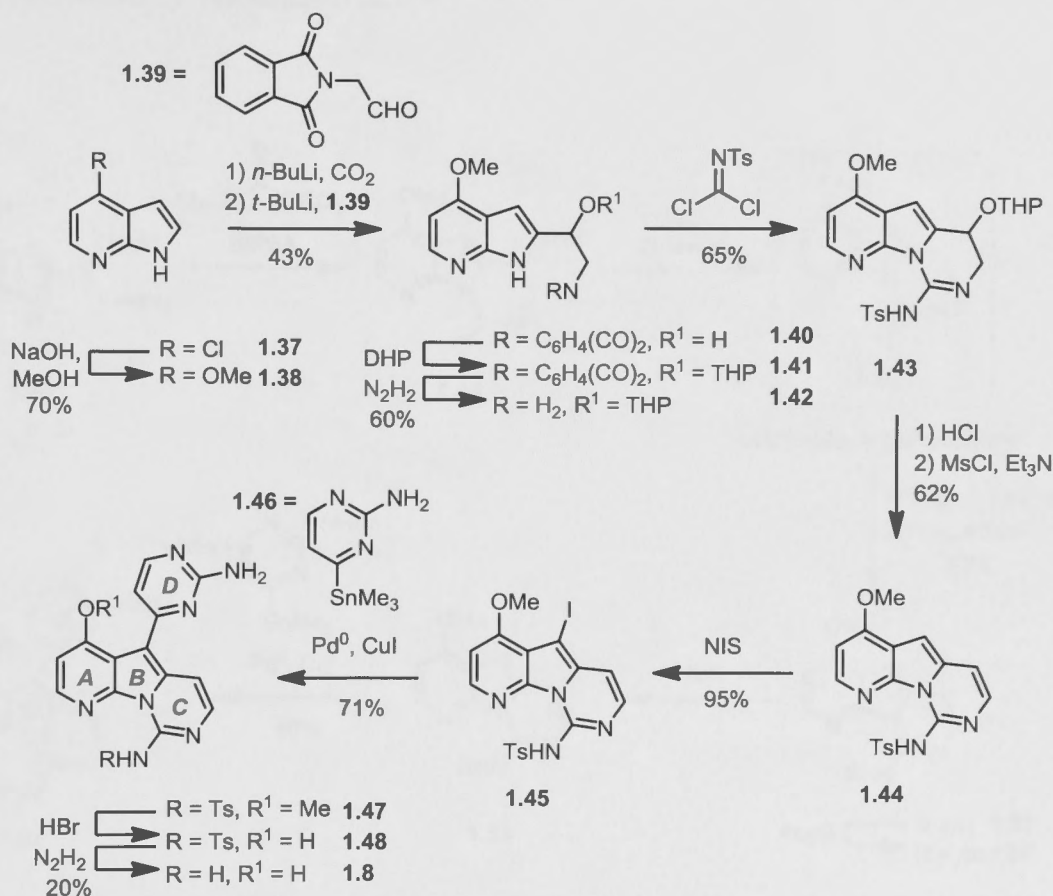


Scheme 1.2: Molina's synthesis of variolin B.²⁷

1.4.3 Álvarez's Synthesis of Variolin B.

Álvarez and Joule also developed a linear total synthesis of variolin B that exploited results of an extensive series of model studies concerned with effecting closure of the C-ring (**Scheme 1.3**).²⁸ The reaction sequence began with commercially available chloroazaindole **1.37** which was converted into the corresponding methoxy azaindole **1.38**. Selective lithiation at C-2 of the latter compound using Katritzky's method²⁹ gave the azaindole-2-lithium species which was quenched with *N*-phthalimidoaminoacetaldehyde **1.39** to afford compound **1.40** in 43% yield. The ensuing hydroxyl group was protected as the corresponding tetrahydropyran ether **1.41** and then the amino group was revealed by cleavage of the phthalimide moiety and so affording 1° amine **1.42**. Cyclisation to form the C-ring was affected with *N*-tosyldichloromethanimine to give the *N*-tosyaminopyrimidine **1.43** in 65%

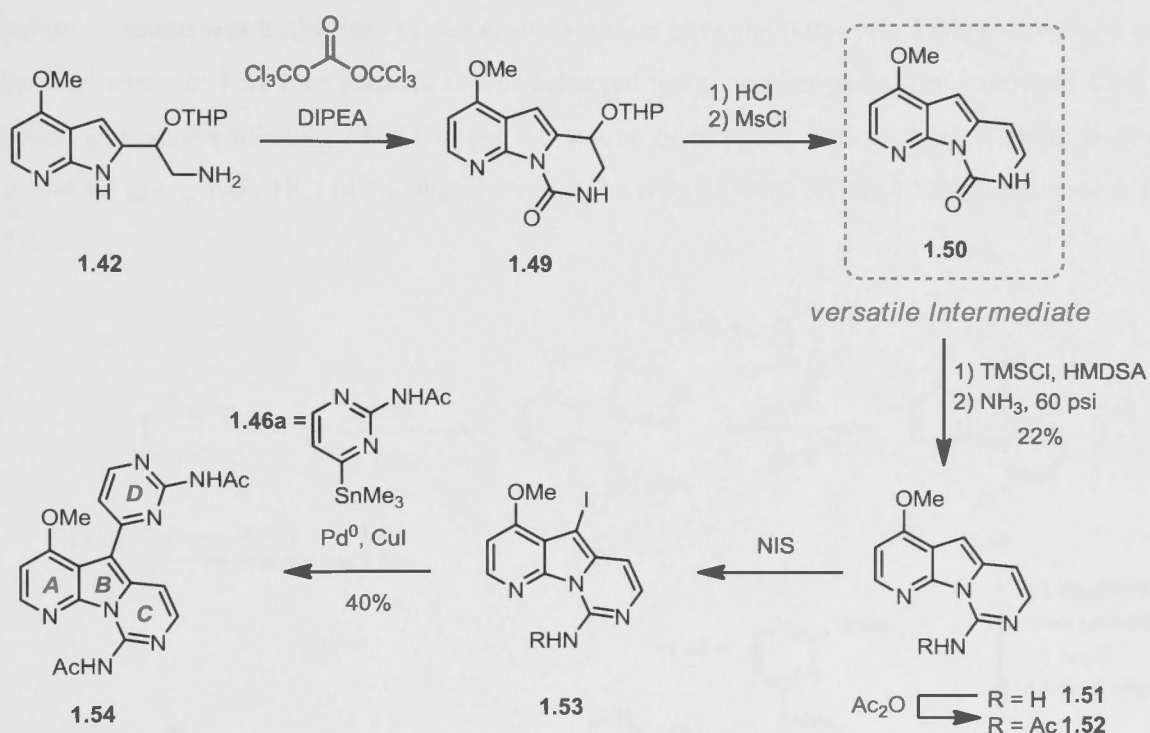
yield. The hydroxyl group was liberated in aqueous acid, then converted into a mesylate and then eliminated so as to provide the tricyclic pyrimidine **1.44** in moderate yield (62% over 2 steps). Importantly, iodination at C-5 was effected in a selective and efficient manner by simply treating tricycle **1.44** with NIS in CH_2Cl_2 (95% yield). Heating iodide **1.45** in the presence of stannane **1.46**, $\text{Pd}[0]$ and $\text{Cu}(\text{I})$ introduced the final pyrimidine ring, providing compound **1.47** and removal of the remaining protecting groups of the cross-coupling product gave, *via* hydroxypyridine **1.48**, variolin B (**1.8**) in 10 steps and 2% overall yield.



Scheme 1.3: Total synthesis of variolin B by Álvarez et al.²⁸

Álvarez and coworkers also devised a second route to the variolins *via* the pyridinone **1.50** (as shown in **Scheme 1.4**).²⁸ This was achieved by reacting the previously described azaindole **1.42** with a phosgene synthon in place of the *N*-tosylmethylimine to give the cyclised product **1.49**. Elimination of the hydroxyl group as a mesylate afforded the pyrimidine-containing tricycle **1.50**. Amination of pyridone **1.50** gave a polar amine **1.51**, which was immediately acylated, to afford amide **1.52**. Selective iodination of the last

compound with NIS provided iodide **1.53** that was subjected to a Stille cross-coupling reaction with stannane **1.46a** to provide a protected form, **1.54**, of variolin B. Although this synthetic pathway represents a less efficient means of producing variolin B compared with that involving direct introduction of the nitrogen as the imine (**Scheme 1.3** above), tricycle **1.50** provides a versatile intermediate for more diverse functionalization of the tricyclic core of this type of natural product. For example, the pyrimidone **1.50** could potentially also be converted into a triflate and used in cross-coupling reactions. The triflation of pyrimidones has been reported by Traquandi *et al.*³⁰

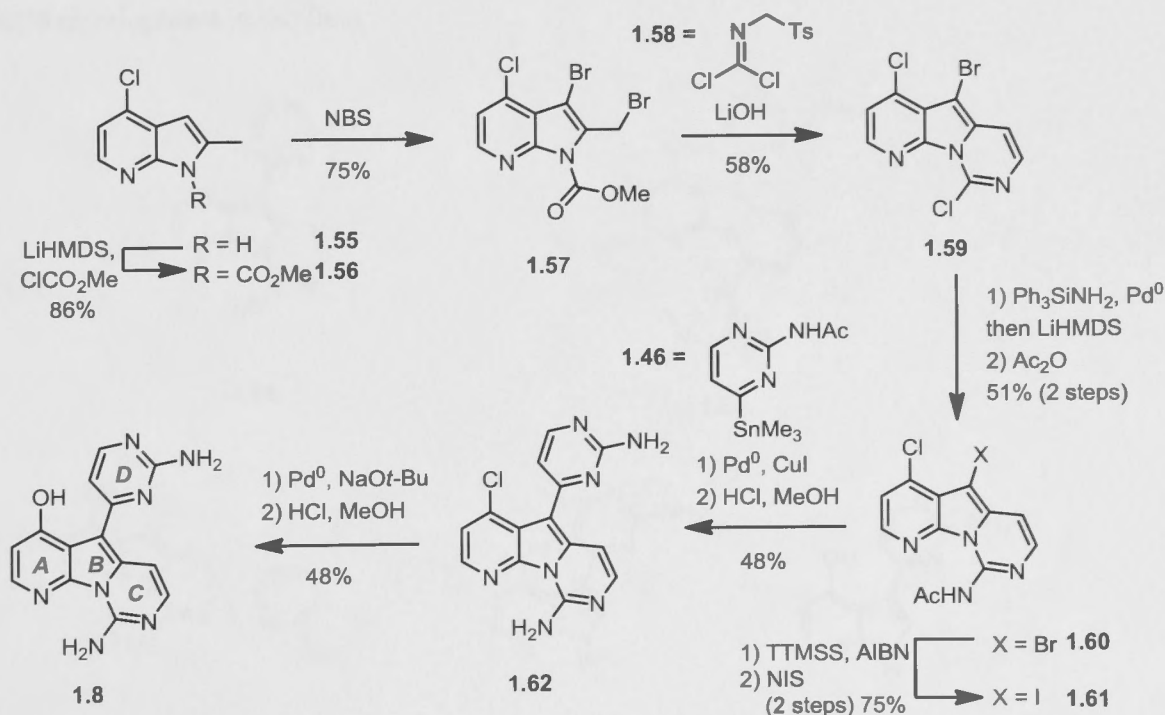


Scheme 1.4: Alternative route to variolins via the pyridinone **1.48**.²⁸

1.4.4 Vaquero's Synthesis of Variolin B

Vaquero and coworkers also used an approach to the variolins that was linear and started with a commercially available 7-azaindole (**Scheme 1.5**).³¹ Initially, 2-methylazaindole **1.55** was protected as the corresponding methyl carbamate **1.56**, then dibromination with NBS gave cyclisation precursor **1.57** in 91% yield. Closure of the C-ring was affected by treatment of

compound **1.57** with tosylmethyldichloroformimide (**1.58**) and proceeded with 58% yield. This cyclisation reaction involves the alkylation of reagent **1.58** with the bromomethylazaindole (**1.57**) and deprotection of the pyrrolic nitrogen, followed by cyclisation of this nitrogen onto the pendant dichloroimine moiety and then 1,2-elimination of the toluenesulfinic acid to deliver tricycle **1.59**. Selective palladium-catalysed amination of the chloropyrimidine unit within product **1.59** gave a polar amine that was immediately acylated to provide compound **1.60** in 51% yield over two steps. In order to effect the required cross-coupling reaction in an efficient manner, bromide **1.60** was converted into the iodide **1.61** using a two-step radical mediated procedure (75%). Palladium-catalysed cross coupling of this iodide with stannane **1.46** introduced the final pyrimidine ring (D-ring) before a subsequent hydrolysis of the ensuing amide gave the tetracycle **1.62**. Conversion of the aryl chloride **1.62** into variolin B was achieved using another palladium-catalysed cross-coupling reaction utilising *t*-BuONa (as the source of oxygen), followed by removal of the *tert*-butyl group with HCl (48% over 2 steps). The overall yield for the 11 step sequence was 3.3%.



Scheme 1.5: Total synthesis of variolin B by Vaquero et al.³¹

1.4.5 Synthetically-Derived Variolin Analogues

Several variolin analogs (**Figure 1.8**) have been produced by modifications of the routes defined above. For example, deoxyvariolin B (**1.63**) has been prepared by Morris and coworkers using strategies similar to those employed in their syntheses of the natural product.²⁵ Alvarez and coworkers prepared the same compound (**1.63**) by replacing the aromatic starting materials associated with their synthesis of variolin B with the corresponding demethoxy aromatic compound.²⁵ The functionalization of variolin B itself represents another method for preparing variolin analogs, including the alkylated derivative **1.64**. Similarly, Molina was able to synthesise compound **1.65** by a slight divergence from their synthetic approach to variolin B. This methodology was also used to prepare the simpler meriolin compounds (such as **1.66**), which are a synthetic hybrid between the variolins and the meridianins (compound **1.67** is meridian A, an example of another class of biologically active marine natural product).²⁵ Some of these methods are ingenious and very efficient, but a general synthetic strategy that could be used to access all of these analogues, as well as generating a large compound library containing many more new congeners, would represent a useful development in the field.

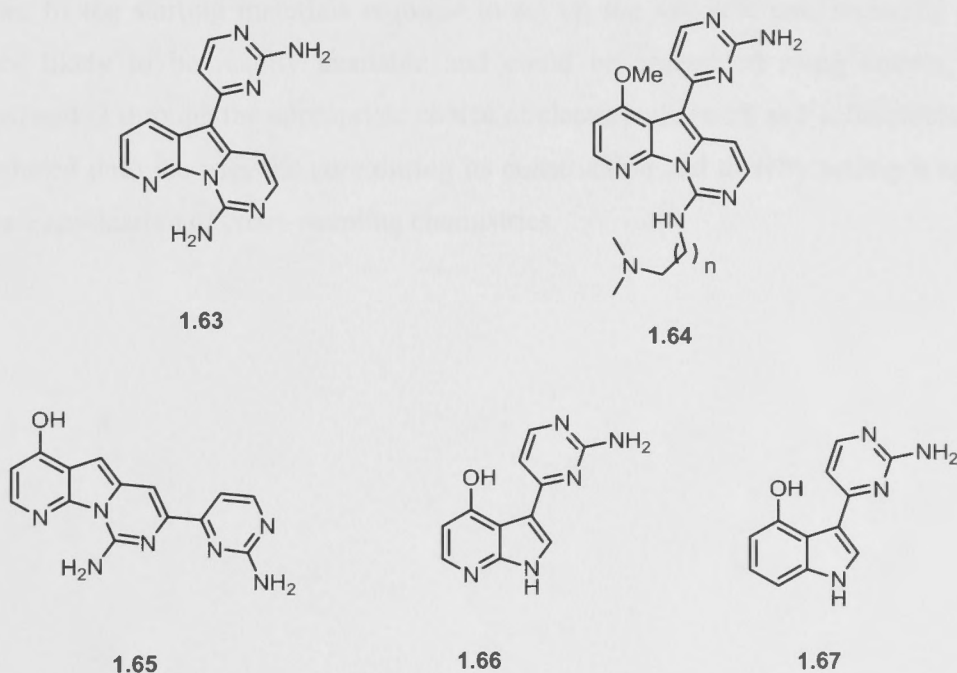
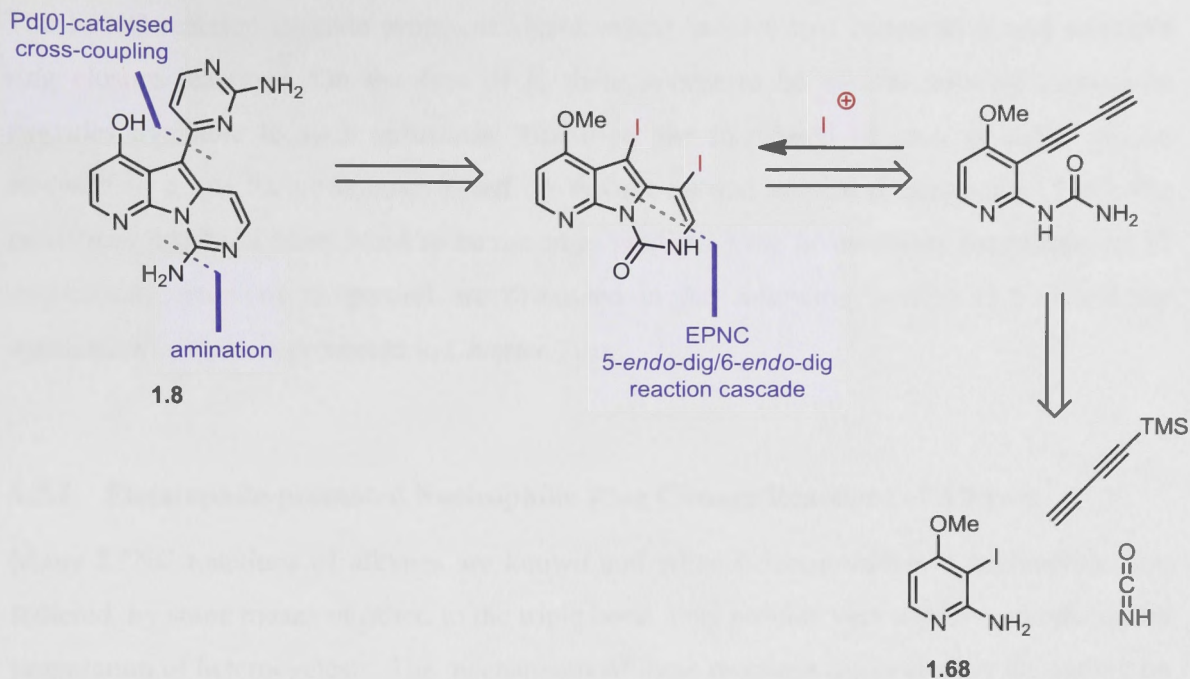


Figure 1.8. Some synthetic variolin analogues (**1.63-1.66**) and meridianin A (**1.67**) which is naturally occurring.

The culmination of investigations into the synthesis of the variolins has provided some robust methods for elaboration of appropriately functionalized tricyclic core structures. However, with the exception of Morris' synthesis, the methods that have been reported for the assembly of the tricyclic core are linear, relatively lengthy and not particularly compatible with the inclusion of a diverse array of functional groups. Morris' synthesis, although very efficient, exploits the unique hidden symmetry associated with variolin B, a feature that only exists in this particular natural product.

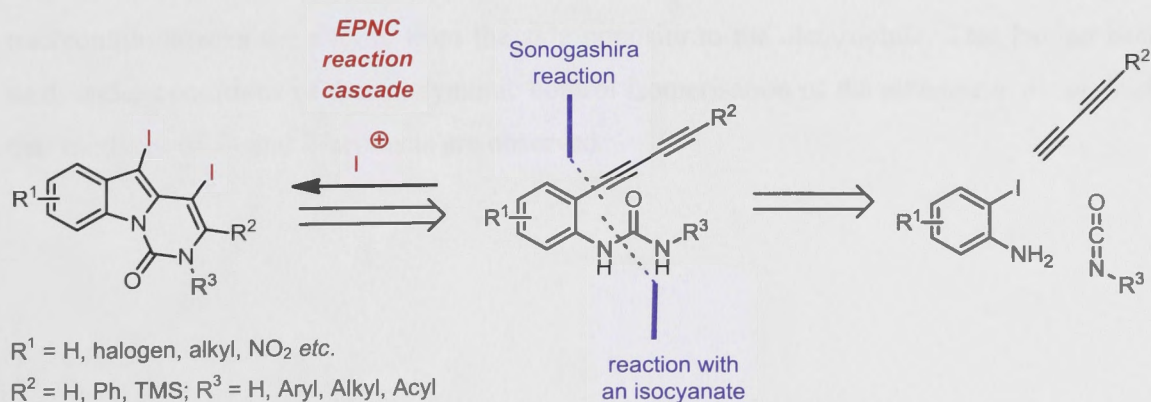
1.5 Design of a General Strategy for Synthesising Variolin-Based Compounds

As noted above, the development of a general strategy for the preparation of pyrido[3',2':4,5]pyrrolo[1,2-*c*]pyrimidin-9(8*H*)-ones would be of considerable value. We envisaged that a *cascading* electrophile-promoted nucleophilic closure (EPNC) reaction sequence, involving 1-(3-(buta-1,3-diyn-1-yl)-4-methoxypyridin-2-yl)ureas, may provide an efficient method for this purpose (**Scheme 1.6**). There are a number advantages to this approach: a) two of the rings, namely the B and C rings, could be constructed in a single operation; b) the starting materials required to set up the key reaction (including pyridine **1.68**) are likely to be readily available and could be assembled using known, reliable reactions; and c) through the appropriate choice of electrophile (such as Γ^+), functionality may be introduced onto the tricyclic core during its construction and thereby setting it up for the immediate application of cross-coupling chemistries.



Scheme 1.6: Retrosynthetic analysis of variolin B(1.8) involving a 5-endo-dig/6-endo-dig EPNC reaction cascade as the key step.

In principle, this strategy could also be used to produce other analogs such as those shown in **Scheme 1.7**, wherein the pyridine ring has been replaced with a simple benzene unit. The simplicity of this approach also makes it an attractive vehicle for conducting model studies, wherein the effects of different functional groups could also be assessed by simply replacing various fragments, i.e. the R^1 , R^2 and/or R^3 groups, during the preparation of the substrates to be used in the proposed cyclisation reactions.

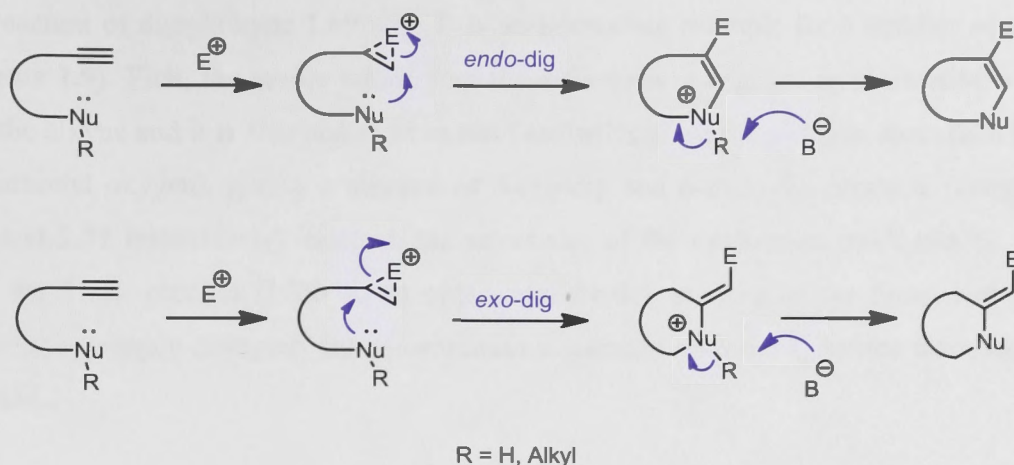


Scheme 1.7: Retrosynthetic analysis of pyrimido[1,6-a]indol-1(2H)-ones involving a 5-endo-dig/6-endo-dig EPNC reaction cascade as the key step.

The EPNC reaction cascade proposed above would involve two consecutive and selective ring closure reactions. On the face of it, there appear to be several possible cyclisation cascades available to such substrates. However, the likelihood of each of these can be assessed in a qualitative manner based on theoretical and empirical arguments. The basic guidelines that have been found to be useful in predicting the favourability (or otherwise) of ring-closing reactions in general are discussed in the following Section (1.5.1) and the application of them is presented in *Chapter Two*.

1.5.1 Electrophile-promoted Nucleophilic Ring Closure Reactions of Alkynes

Many EPNC reactions of alkynes are known and when heteroatom-based nucleophiles are tethered, by some means or other, to the triple bond, they provide very useful methods for the preparation of heterocycles.³² The mechanisms of these reactions differ slightly depending on the nature of the nucleophilic species, the electrophile and the substituents on the alkyne but, generally speaking, they are believed to follow the same basic pathway (**Scheme 1.8**).³³ Thus, it is proposed that initially the electrophile coordinates to the π -system of the alkyne, activating it towards intramolecular attack by the pendant nucleophile. Both *endo*-dig and *exo*-dig cyclisation modes are favoured for rings with more than 4 atoms and both modes of ring closure have been observed experimentally. However, it should be noted that the frontier molecular orbitals of the alkyne involved in the reaction are significantly distorted by the coordinated electrophile and Baldwin's rules can break down in such settings. Additionally, when strong thermodynamic driving forces are available, Baldwin's rules cannot always account for the selectivity observed.³⁴ The stereochemistry of the olefin resulting from the *exo* mode of cyclisation is usually *trans* due to the stereoelectronic requirement that the nucleophile attacks the alkyne from the side opposite to the electrophile. That having been said, under conditions of thermodynamic control isomerisation of the alkene can occur, such that mixtures of *E*- and *Z*-products are observed.



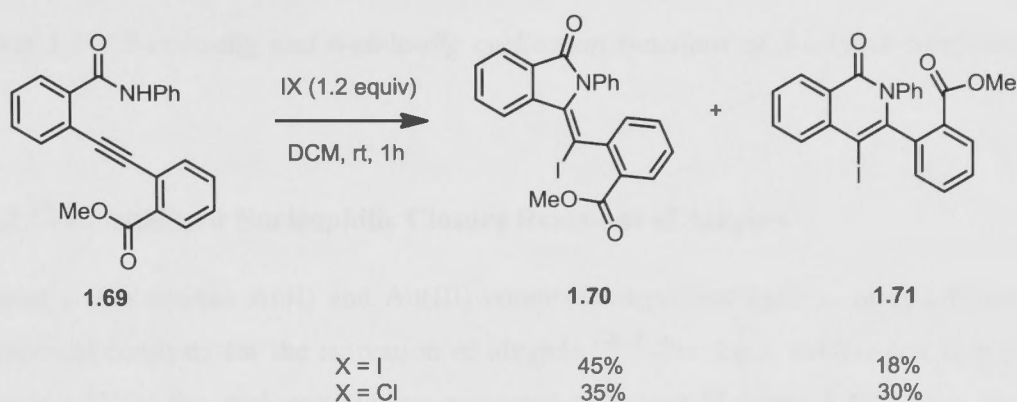
Scheme 1.8: General pathways associated with intramolecular EPNC reactions of alkynes.

The specific regio- and stereo-chemical outcomes observed in each case depends on the particular internal geometry of the substrate and the nature of the nucleophilic and electrophilic entities employed, in the latter case these can include H^+ , Br^+ , I^+ , RSe^+ and M^+ (where M is a metal). In most cases, only one of the two possible products is obtained, or when a mixture of isomers is obtained, one isomer is obtained preferentially. This suggests that a hierarchy of functional group reactivity exists and, therefore, that a judicious choice of substrates and conditions can lead to the desired outcome being achieved.²⁸

1.5.1.1 Iodine-promoted Nucleophilic Closure Reactions of Alkynes

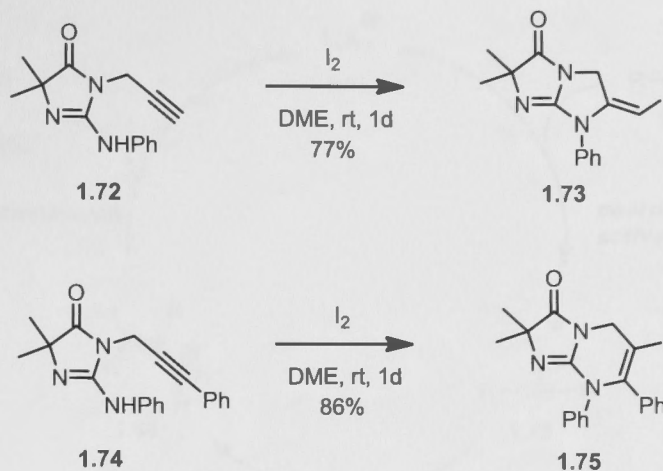
Molecular iodine (I_2) is the most common electrophile used in the title reactions but ICl , NIS and bis-collidine hexafluorophosphate iodine can also be effective.³⁵ Alkyl amines are the most common heteroatomic nucleophilic partners employed although imines, alcohols, ethers, acids, esters, carbamates and thiols are also known to participate in these reactions. The various reactivities of these functional groups toward EPNC reactions have been assessed in competition studies conducted by Larock's group.³⁶ These studies indicated that the nucleophilicity of the functional group, polarisation of the alkyne triple bond and the cationic nature of the intermediate are the most important factors in determining the outcomes of such reactions.³⁶

The reaction of diarylalkyne **1.69** with I^+ is an interesting example for a number of reasons (**Scheme 1.9**). First, the amide rather than the ester moiety engages in a selective reaction with the alkyne and it is also observed to react exclusively *via* the nitrogen atom (and not *via* the carbonyl oxygen), giving a mixture of 5-*exo*-dig and 6-*endo*-dig products (compounds **1.70** and **1.71** respectively). Second, the selectivity of the cyclisation mode can be shifted from the 5-*exo* product (**1.70**) to an approximately 1:1 mixture of the 5-*exo* and 6-*endo* products by simply changing the counteranion associated with the I^+ source from iodide to chloride.



Scheme 1.9: *Exo*- vs *endo*- modes of cyclisation involved in EPNC reaction of a tethered amido-alkyne.

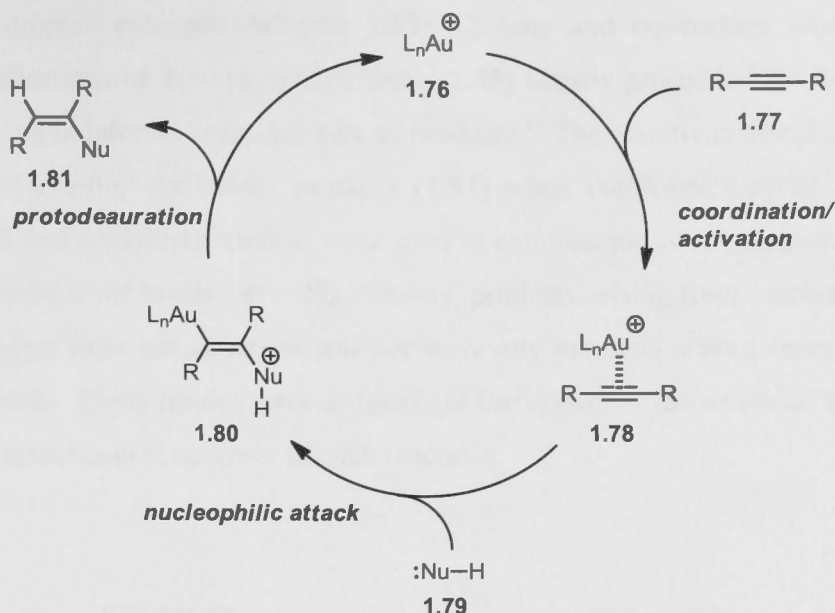
The selectivity in EPNC reactions, *viz.* either giving 5-*exo* or 6-*endo* products, can also be strongly influenced by the substituent on the alkyne as demonstrated in the reaction of 3-alkynyl-4-imidazolin-1-ones with iodine (**Scheme 1.10**).³⁷ Terminal alkyne **1.72** gave mainly the 5-*exo*-dig product (**1.73**), while the phenyl-substituted analogue **1.74** gave predominately the 6-*endo*-dig cyclisation product (**1.75**). In the latter case the phenyl ring activates the benzylic position of the alkyne toward nucleophilic attack and the 6-*endo*-dig cyclisation product is obtained in high yield (86%) despite the steric crowding between the 1,2-related phenyl rings in the product. Thus, the selectivity of EPNC reactions can be modulated by varying a number of reaction parameters and this is essential in order to develop a multiply selective reaction. These examples serve as something of a guide to conditions that need to be deployed in achieving the desired mode of cyclisation.



Scheme 1.10: 5-endo-dig and 6-endo-dig cyclisation reactions of 3-alkynyl-1-imidazolin-4-ones.

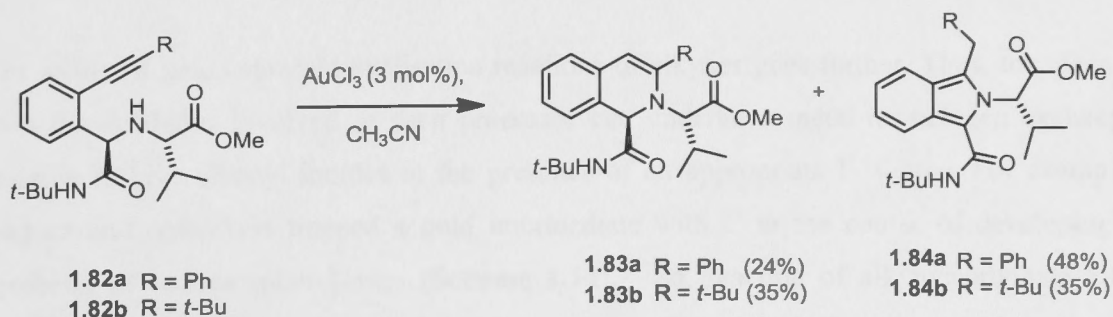
1.5.1.2 Gold-catalysed Nucleophilic Closure Reactions of Alkynes

In recent years, various Au(I) and Au(III) complexes have emerged as especially selective and efficient catalysts for the activation of alkynes.^{33b,38} The basic mechanism is similar to that proposed for the analogous iodine-promoted processes (**Scheme 1.11**). Thus, the gold catalyst (**1.76**) initially forms a complex with the alkyne (**1.77**) giving the pivotal intermediate **1.78** and this electron-deficient species is attacked by the added (or tethered) nucleophile **1.79** to afford an alkenyl gold species **1.80** that, under certain conditions, is stable enough to be isolated.³⁹ However, such alkenyl gold species normally undergo protodeauration to give alkenes of the general form **1.81** while simultaneously regenerating the catalytically active gold complex **1.76**.



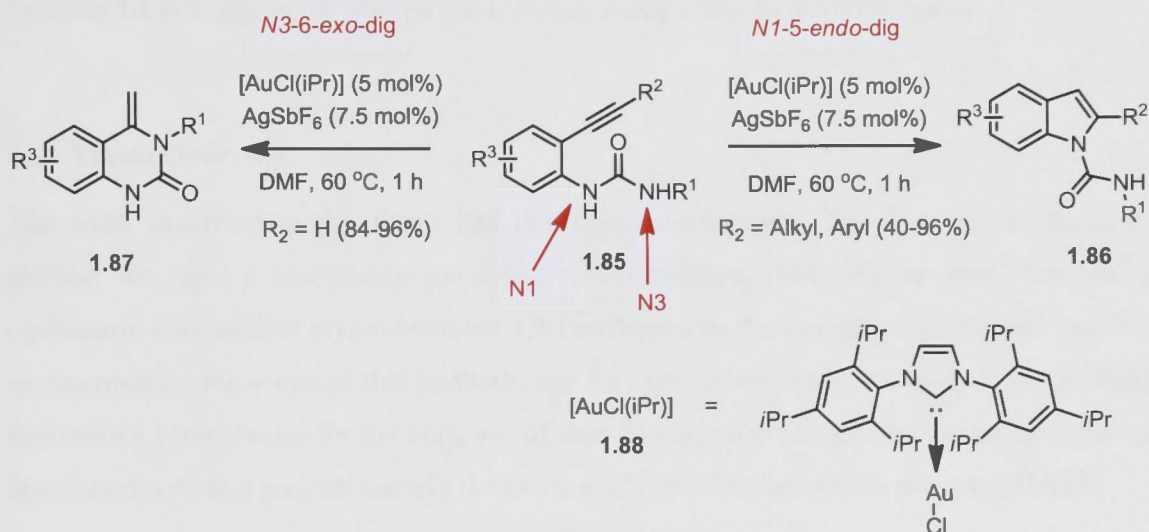
Scheme 1.11: Proposed catalytic cycle for gold-promoted nucleophilic additions to alkynes.

In cases where the alkyne is tethered to the nucleophile both *exo* and *endo* modes of cyclisation are observed. The specific outcome in each case depends on the internal geometry of the system, the nature of the nucleophile, the substituents on the alkyne and the nature of the ligands on the gold. For example, as illustrated in **Scheme 1.12**, Dyker showed that 2-(2-phenylethynyl)benzylamine (**1.82a**) cyclises in the presence of 3 mol% $AuCl_3$ to give a 1:2 mixture of 6-*endo*-dig and 5-*exo*-dig products (**1.83a** and **1.84a**, respectively).⁴⁰ In contrast, reaction of 2-(2-*tert*-butylethynyl)benzylamine (**1.82b**) under the same conditions gave a 1:1 mixture of 6-*endo*-dig and 5-*exo*-dig products (**1.83b** and **1.84b**, respectively).



Scheme 1.12: 6-*endo*-dig and 5-*exo*-dig products arising from reactions of 2-ethynylbenzylamines with $AuCl_3$.

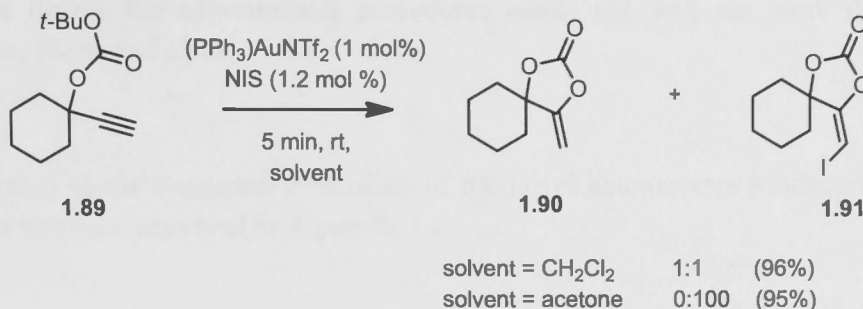
In a more complex example (**Scheme 1.13**), Gimeno and co-workers found that gold-catalysed cyclisations of 2-ethynylphenylureas (**1.85**) usually proceeded *via* the *N1-5-endo-dig* mode giving indolecarboxamides **1.86** as products.⁴¹ The selectivity could be switched to give the *N3-6-exo-dig* cyclisation products (**1.87**) when the *N*-heterocyclic carbene gold complex **1.88** and a silver co-catalyst were used in combination with substrates that contain mono-substituted triple bonds ($R^2 = H$). Notably, products arising from reaction through the carbonyl oxygen were not observed and nor were any products arising from a *7-endo-dig* cyclisation mode. These results serve to highlight the impact of the nature of the ligands on gold on the regiochemical outcome of such reactions.



Scheme 1.13: *N1-5-endo-dig* vs. *N3-6-exo-dig* cyclisation modes of 2-ethynylphenylureas.

The utility of gold-catalysed cyclisation reactions of alkynes goes further. Thus, the alkenyl gold intermediates involved in such processes can undergo a metal-for-halogen exchange reaction to give alkenyl iodides in the presence of an appropriate I^+ source. For example, Gagosz and coworkers trapped a gold intermediate with I^+ in the course of developing a synthesis of iododioxolan-2-ones (**Scheme 1.14**).⁴² So, reaction of alkynylcarbonate **1.89** with $(Ph_3P)AuNTf_2$ gave the alkene **1.90**. However, addition of NIS to the reaction mixture afforded iodoalkene **1.91**. The facility of the iodination reaction depends on the longevity of the ionic alkenyl gold species, which they found to be far greater in polar solvents such as acetone. The iodinated product **1.91** is the same as that expected from the reaction of

carbonate **1.89** with molecular iodine. Thus, an Au(I)/I⁺ system offers alternate conditions for effecting EPNC reactions of alkynes whereby a halogen is incorporated into the product.



Scheme 1.14: *Trapping of alkenyl gold intermediates with electrophilic iodine.*

1.6 Thesis Overview

The work described in this thesis had two distinct objectives. The first was to develop a method for rapidly assembling pyridopyrrolopyrimidines, focussing on new, “cascading” cyclisation reactions of aryl-substituted 1,3-butadiynes as the key step. The second goal was to demonstrate the scope of this methodology for synthesising compounds such as variolin B and related heterocycles for the purposes of their biological evaluation by the industry partner associated with this project, namely the German chemical commodities company BASF.

Chapter Two describes the modular assembly of cyclisation precursors ethynylphenyl- and butadiynylphenyl-ureas through sequential Sonagashira cross-coupling reactions of iodoanilines with alkynes and treatment of the ensuing products with isocyanates. The iodine-promoted nucleophilic ring-closure reactions of these compounds are then discussed.

Chapter Three details the development of gold-catalysed nucleophilic ring-closure reactions of butadiynylphenylureas that deliver pyrimido[1,6-*a*]indol-1(2*H*)-ones related to the variolins. The effect of substituents placed at different positions on the cyclisation substrates on the selectivity and yield of such reactions are also discussed.

Chapter Four outlines the preparation of pyridine-based cyclisation precursors and attempts to synthesise variolin B by applying the gold-catalysed cyclisation methodology to them.

Chapter Five details the experimental procedures associated with the work described in *Chapters Two, Three and Four*.

Remarks relating to the biological evaluation of the novel heterocycles produced during the course of this work are provided in *Appendix 1*.

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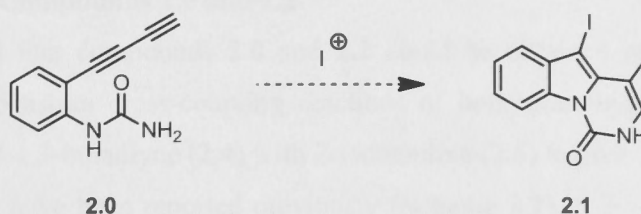
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Chapter Two

Syntheses and I^+ -Promoted Cyclisation Reactions of *o*-Alkynylphenylureas

2.1 Overview

As stated in *Chapter One*, a key objective of the work described herein was to develop an electrophile-promoted nucleophilic closure (EPNC) reaction cascade involving 1-(2-(buta-1,3-diyn-1-yl)aryl)ureas (such as **2.0**) and leading to pyrimido[1,6-*a*]indol-1(2*H*)-ones (such as **2.1**) (**Scheme 2.1**). Electrophilic iodine and gold have both been reported to promote smooth and controllable EPNC reactions of alkynes and so appeared to be ideal reagents for the present purpose. Iodine was chosen as the electrophile for the initial studies as it offers, potentially, the cheapest and more direct route to the desired, iodinated heterocycles.



Scheme 2.1: *Proposed electrophile-promoted nucleophilic ring closure reaction.*

The substrate sought for the initial investigation was 1-(2-(buta-1,3-diyn-1-yl)phenyl)urea (**2.0**). This compound contains the minimum structural features required to test the proposed cascade cyclisation and offers a basic platform from which to build

and assess the effects of substituents on the outcome of such reactions. It should also be noted that it was necessary to test the impact of features such as the presence of a terminal diyne unit and a mono-substituted urea moiety, since additional substituents at these positions would lead to cyclisation products incorporating groups not observed amongst the natural variolins. Of course, the option of substitution at these positions would increase the scope of the methodology. The outcomes of such studies are discussed in *Chapter Three*.

Before exploring the potentially complex reactivity of these systems it was important to gain a better understanding of the selectivity of the first proposed cyclisation event in isolation. Accordingly, the simpler ethynyl-containing substrate, **2.2**, which contains the urea moiety but only one alkyne unit was also sought. In an overall sense, then, two model compounds, **2.0** and **2.2**, were required for the initial studies (**Figure 2.1**).

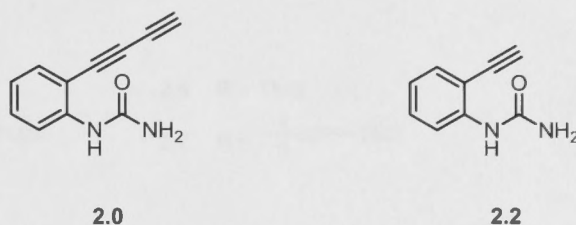
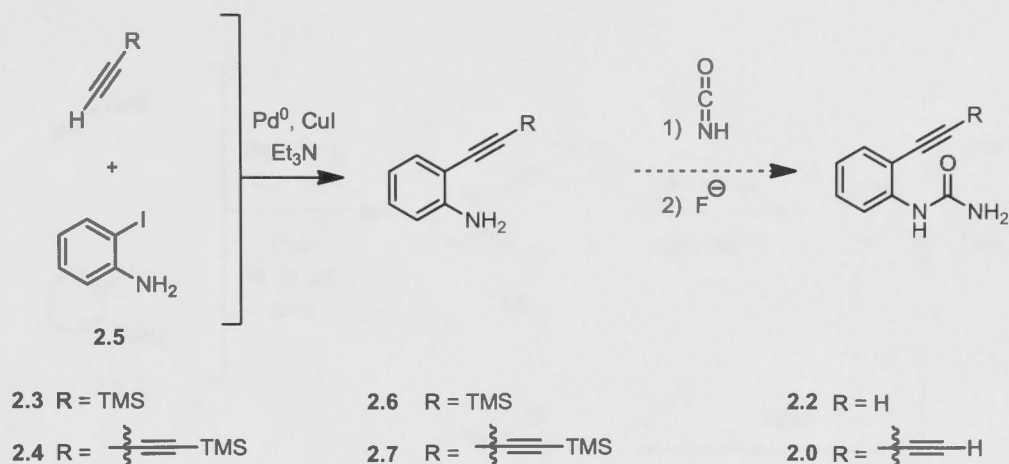


Figure 2.1. Model compounds sought for initial investigations into the EPNC reaction.

2.2 Synthesis of Compounds **2.0** and **2.2**

It was envisaged that compounds **2.0** and **2.2** could be obtained by related synthetic routes. The Sonogashira cross-coupling reactions of both trimethylsilylacetylene (**2.3**) and trimethylsilyl-1,3-butadiyne (**2.4**) with 2-iodoaniline (**2.5**) to give compounds **2.6** and **2.7**, respectively, have been reported previously (**Scheme 2.2**).^{1,2} It was anticipated that ureation of these anilines could be achieved by treating them with an isocyanate using well established procedures.^{3,4} Various “sources” of isocyanate are available. For example, silicon tetrakisocyanate, chlorosulfonylisocyanate and trichloroacetylisocyanate have all been reported to efficiently ureate amines, although, when the second and third of these reagents are used a second hydrolytic step is required to remove the

chlorosulfonyl and trichloroacetyl groups, respectively. The trimethylsilyl group could also be easily cleaved from the alkyne using either a fluoride ion source or base. Therefore, the sequence of Sonogashira cross-coupling reaction, followed by ureation with an isocyanate, then deprotection, appeared to offer an efficient but flexible route to the desired model compounds (**Scheme 2.2**). The simplicity of this scheme should allow it to be readily adapted to the synthesis of more complex cyclisation precursors, as would be required for developing approaches to more complex targets such as variolin B.

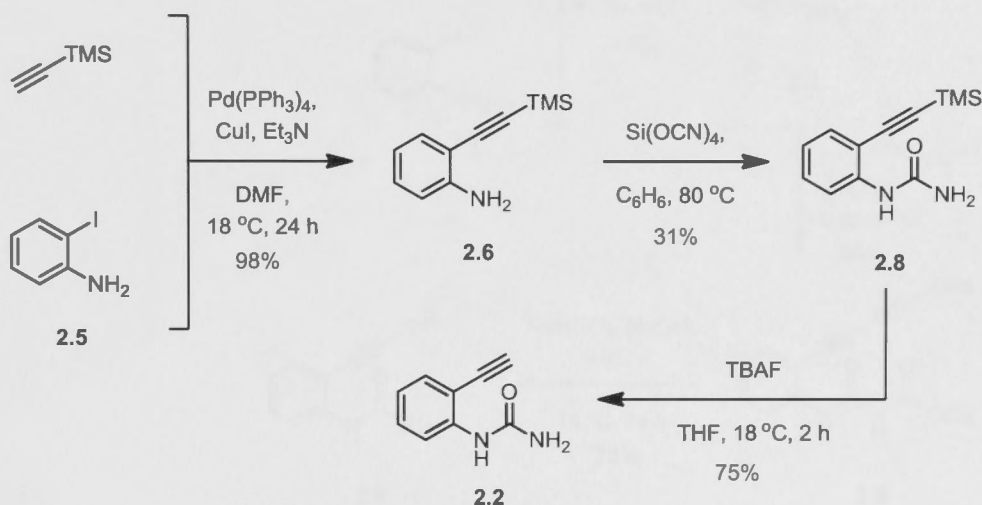


Scheme 2.2: Synthetic route to the cyclisation precursors **2.0** and **2.2**.

2.2.1 Synthesis of 1-(2-Ethynylphenyl)urea (**2.2**)

Initial studies involved pursuing a Sonogashira reaction between iodoaniline and TMS-acetylene following a procedure reported by Mikami *et al.*¹ In the event, the reported cross-coupling reaction which is catalysed by $\text{Pd(PPh}_3)_4$ (5 mol%) and Cu(I) (10 mol%) in the presence of triethylamine as base, worked efficiently and provided alkyne **2.6** in 98% yield (**Scheme 2.3**). The urea moiety was installed in a single, subsequent step by treating compound **2.6** with silicon tetrakisocyanate in refluxing benzene and so affording alkyne **2.8** in 31% yield. Although the yield for the ureation reaction was low, it allowed the preparation of enough material for further investigation. Thus, removal of the trimethylsilyl group from the alkyne was readily achieved using tetra-*n*-butylammonium fluoride (TBAF) and thereby providing the desired terminal alkyne **2.2** in 83% yield.

Evidence for the successful preparation of urea **2.2** derives from the signals observed in the derived ^1H NMR spectrum, which showed two broadened signals at δ 7.89 and 6.45 and integrating for 1 and 2 protons respectively, and thus assigned to the N-H protons of the arylurea group. The appearance of a one-proton singlet in the same spectrum at δ 4.56, supported the presence of the terminal alkyne moiety. The ^{13}C NMR spectrum displayed signals at δ 87.4 and 80.0, typical chemical shifts of aryl-substituted alkynyl carbons. Furthermore, the IR spectrum displayed a C=O stretching band at 1666 cm^{-1} that is assigned to the urea moiety.

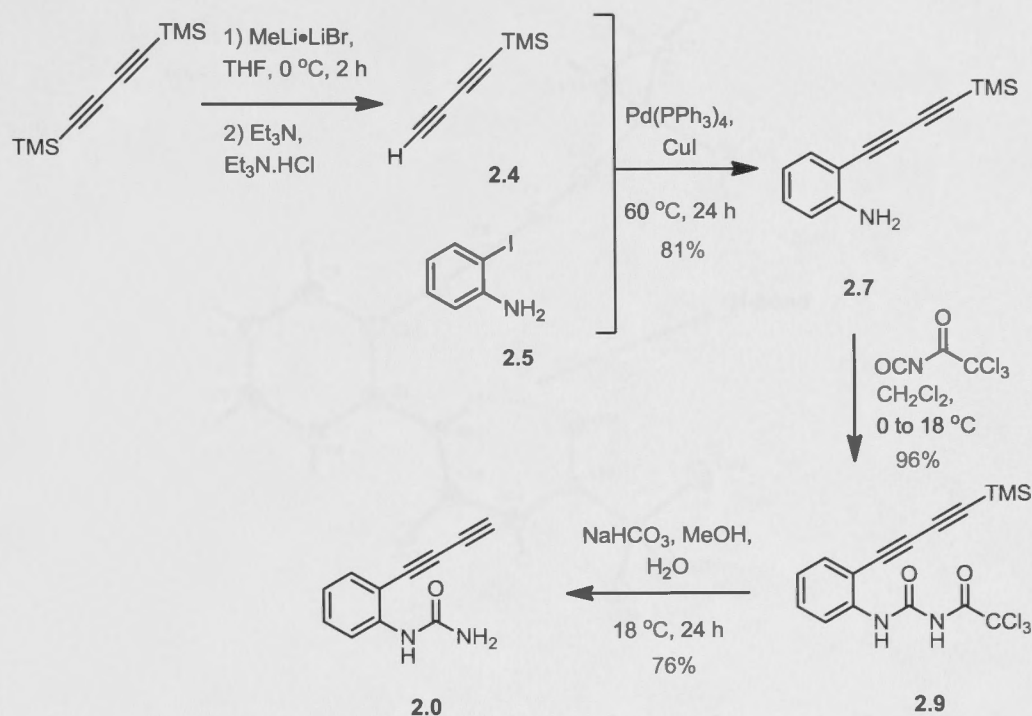


Scheme 2.3 Synthesis of 1-(2-Ethynylphenyl)urea (**2.2**)

2.2.2 Synthesis of 1-[2-(Buta-1,3-diynyl)phenyl]urea (**2.0**)

The same strategy that had been used to synthesise the compound **2.2** was employed in preparing the *o*-butadiynylurea **2.0**. Effecting a palladium- and copper-catalyzed Sonogashira cross-coupling reaction between a 1,3-butadiyne and iodoaniline appeared to provide some challenges, particularly with regard to selectively generating a mono-substituted butadiynyl product. Fortunately, these problems had largely been addressed by Cheng *et al* who reported a one-pot procedure for generating a mono-lithiated-1,3-butadiynyl anion from bis-trimethylsilyl-buta-1,3-diyne then successfully subjecting this to a Sonogashira cross-coupling reaction with iodoaniline.² Accordingly, a synthesis of *o*-butadiynylaniline (**2.7**) was achieved in 81% yield by treating a solution of commercially

available 1,4-bis-trimethylsilyl-1,3-butadiyne in tetrahydrofuran with methyl lithium bromide complex. The solution of acetylide **2.4** thus obtained was quenched with $\text{Et}_3\text{N}\cdot\text{HCl}$ and subjected directly to reaction with iodoaniline in the presence of $\text{Pd}(\text{PPh}_3)_4$ (5 mol%) and CuI (10 mol%) (Scheme 2.4).



Scheme 2.4: Synthesis of 1-(2-(buta-1,3-diynyl)phenyl)urea.

The ureation of the resulting aniline **2.7** (81%) with isocyanate was then effected. In an effort to avoid using the toxic, inefficient and not readily available reagent silicon tetrakisocyanate for this purpose, the utility of the commercially available trichloroacetyl isocyanate was investigated. While such an approach would require an extra step, namely cleavage of the trichloroacetyl group from the initially formed product, it was anticipated this would proceed smoothly. In the event, simply adding trichloroacetyl isocyanate to an anhydrous solution of amine **2.7** in CH_2Cl_2 resulted in the quantitative formation of urea **2.9**. The structure of compound **2.9** was confirmed by single crystal X-ray analysis which clearly showed the presence of the *ortho*-related 1,3-butadiynyl and urea moieties (Figure 2.2) and revealed an interesting conformation of the trichloroacetylurea group

which adopts a planar conformation through hydrogen bonding interactions between the oxygen of the trichloroacetyl group and a urea hydrogen. This places the lone pair on the internal nitrogen in an orthogonal arrangement with the plane of the flanking aromatic ring.

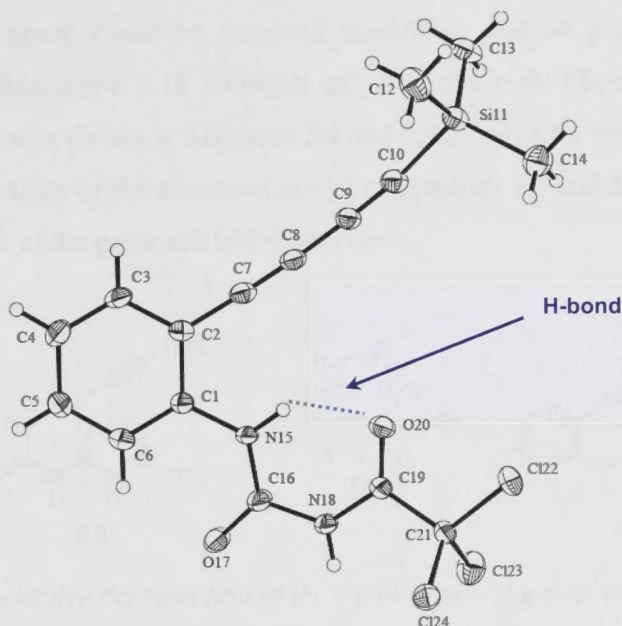
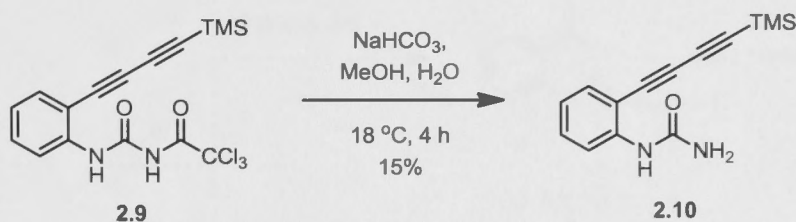


Figure 2.2. ORTEP plot derived from the single-crystal X-ray analysis of diynylphenylurea **2.9**.

Cleavage of the trichloroacetyl group within compound **2.9** was achieved by treating it with methanol and aqueous sodium bicarbonate. Fortuitously, this also effected cleavage of the trimethylsilyl moiety in an efficient manner and thus provided the desired urea **2.0** in 76% yield. The neat form of this material was rather unstable and it was, therefore, used immediately after isolation or stored as a dilute solution in $\text{CH}_2\text{Cl}_2/\text{MeOH}$, EtOAc or THF. The presence of the mono-substituted urea moiety within compound **2.0** was confirmed by its ^1H NMR spectrum which displayed slightly broadened one- and two-proton signals at δ 8.10 and 6.45, respectively, that are assigned to the three N-H protons. A one-proton singlet appearing at δ 4.17 is assigned to the terminal diynyl functionality within the product. The IR spectrum displayed a C=O stretching band at 1661 cm^{-1} . The

^{13}C NMR spectrum showed signals at δ 79.1, 77.5, 71.5 and 68.2 which are attributed to the four sp-hybridised carbons within compound **2.0**. Finally, high resolution mass spectral analysis established the molecular formula as $\text{C}_{11}\text{H}_8\text{N}_2\text{O}$.

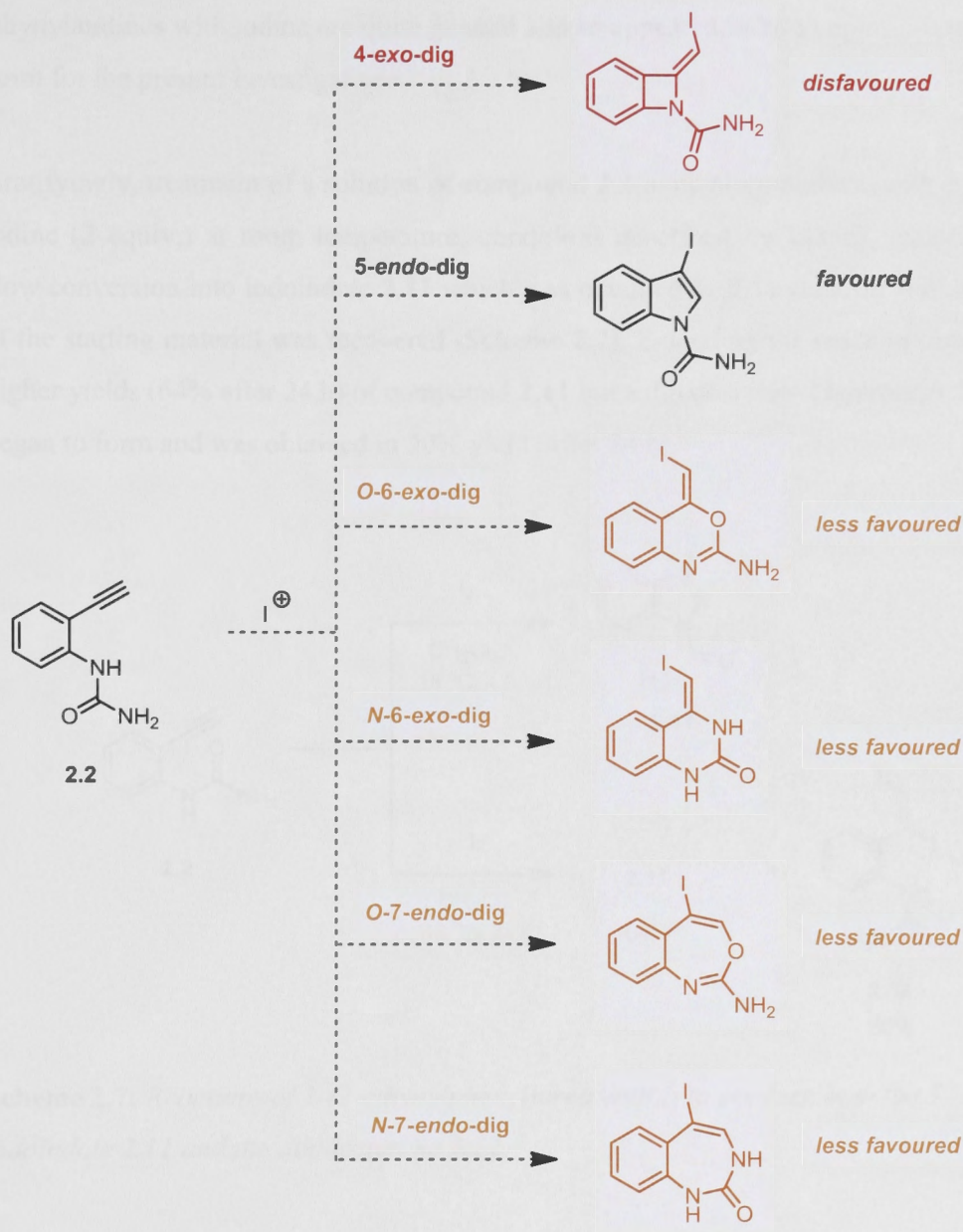
Interestingly, by treating compound **2.9** with low concentrations of bicarbonate, the trichloroacetyl group could be removed selectively and so giving the trimethylsilyl-capped and stable diyne **2.10** although only in 15% yield (**Scheme 2.5**). Overall, the synthetic sequences shown in **Schemes 2.4** and **2.5** allowed for the rapid accumulation of multigram quantities of the advanced model compounds **2.0** and **2.10** and so allowing for an investigation of the proposed EPNC reactions.



Scheme 2.5: Selective deprotection of the trichloroacetyl group within urea **2.9**.

2.3 Reactions of Compounds **2.0** and **2.2** with Various Sources of I^+

With ready access to compounds **2.0** and **2.2** now available, an assessment of their reactions with various sources of iodine could be considered. A recent review of Baldwin's rules for ring closure reactions of alkynes provides an analysis of the different reaction pathways available.⁵ Applying these to compound **2.2** suggests the *N*-5-*endo*-dig mode of cyclisation is likely to be favoured (**Scheme 2.6**). In contrast, the related *N*-4-*exo*-dig cyclisation mode is not mainly because of the significant ring strain that would result. The *N*- or *O*-6-*exo*-dig and the *N*- or *O*-7-*endo*-dig cyclisation modes, despite being favoured in general by Baldwin's Rules, were expected to be less likely due to the increased distance between the two reacting termini compared to the competing 5-*endo* cyclisation mode.

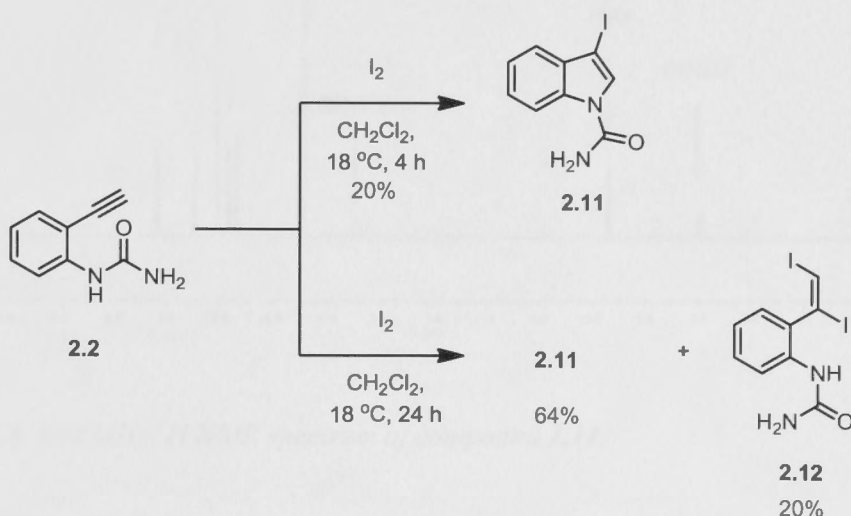


Scheme 2.6: Possible products arising from the EPNC reaction of substrate **2.2**.

2.3.1 Reaction of 1-(2-Ethynylphenyl)urea with Molecular Iodine

The conditions used by Larock and other groups to induce 5-*endo*-dig cyclisations of ethynylanilines with iodine are quite general and so appeared to be an appropriate starting point for the present investigations.⁶

Gratifyingly, treatment of a solution of compound **2.2** in dichloromethane with molecular iodine (2 equiv.) at room temperature, conditions described by Larock, resulted in its slow conversion into iodoindole **2.11** which was obtained in 20% yield. In addition, 80% of the starting material was recovered (**Scheme 2.7**). Extending the reaction times led to higher yields (64% after 24 h) of compound **2.11** but a diiodostyrenyl byproduct **2.12** also began to form and was obtained in 20% yield (after 24 h).



Scheme 2.7: Reactions of 1-(2-ethynylphenyl)urea with I_2 to produce both the 3-iodoindole **2.11** and the diiodostyrene **2.12**.

Evidence for the formation of the *NI*-5-*endo*-dig product, namely the indole **2.11**, derived from the 1H NMR spectrum of this material (**Figure 2.3**) which displayed a single, broad two-proton singlet at δ 7.06 that is attributed to the N-H protons of the carboxamide. A sharp, one-proton singlet at δ 6.24 was observed which was assigned to the proton attached to C-2. The ^{13}C NMR spectrum showed a signal at δ 50.1 arising from the

iodinated sp^2 -hybridized carbon atom. The IR spectrum showed a strong band at 1678 cm^{-1} corresponding to the $\text{C}=\text{O}$ stretching vibration of the carboxamide group. High resolution mass measurements established the molecular formula as $\text{C}_9\text{H}_7\text{IN}_2\text{O}$.

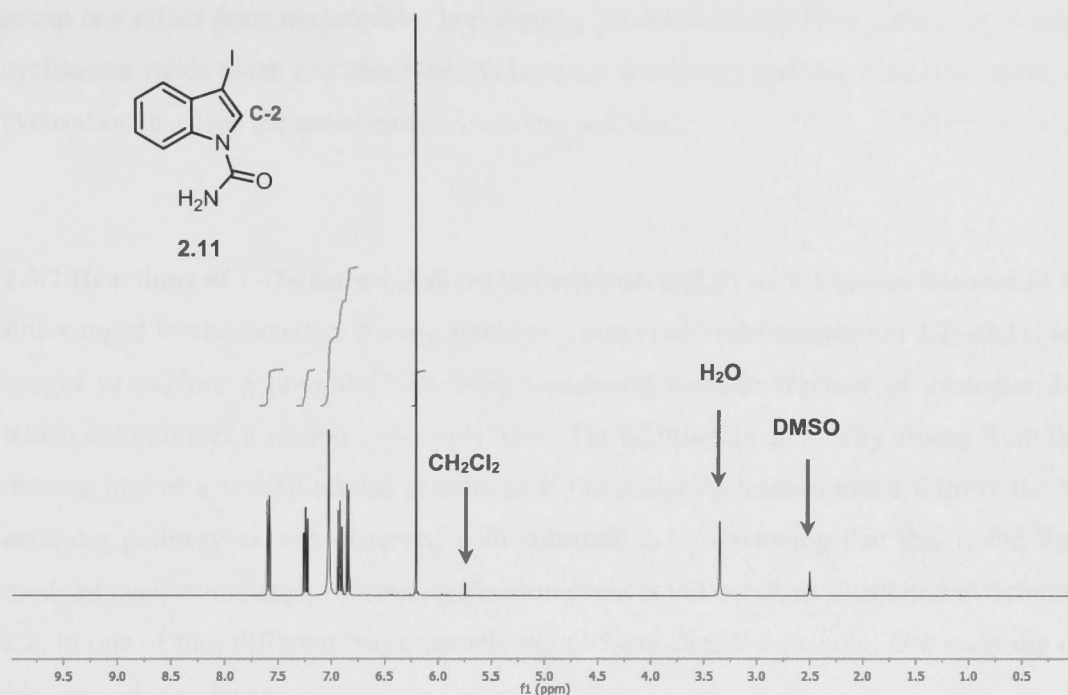


Figure 2.3. 400 MHz ^1H NMR spectrum of compound **2.11**.

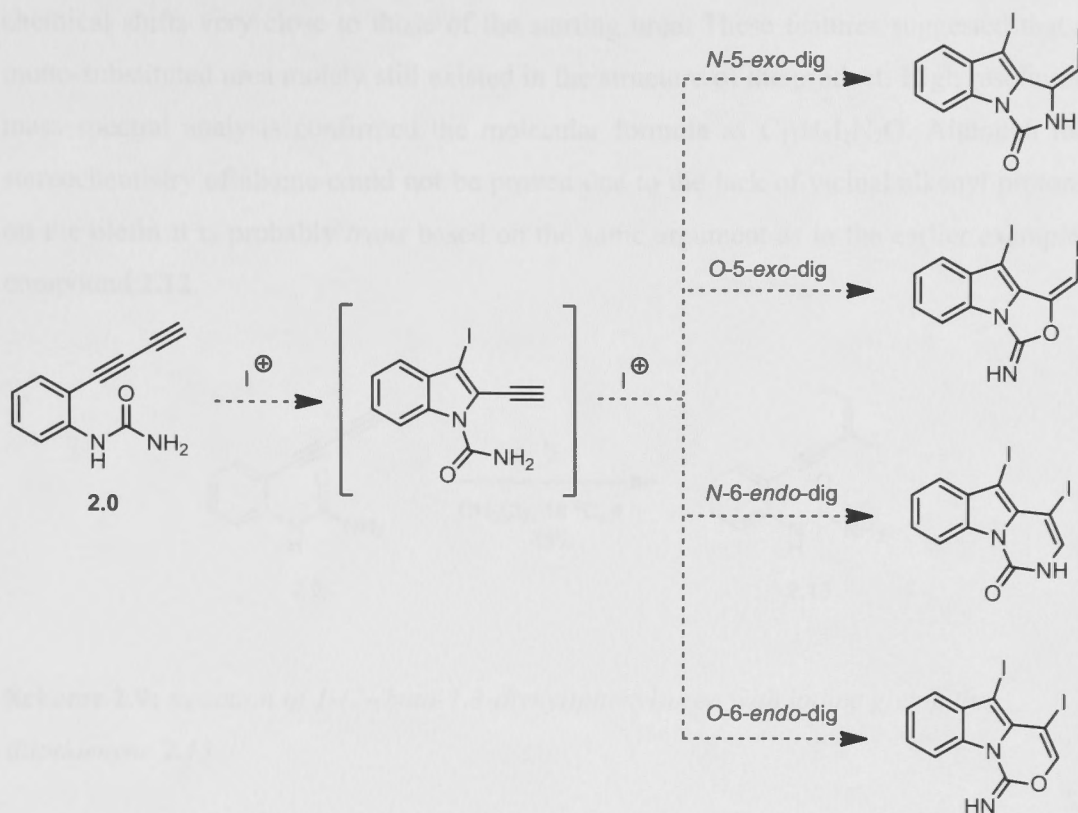
The structure of the diiodostyrene byproduct **2.12** was assigned on the basis of the derived spectroscopic data. In particular, the ^1H NMR spectrum displayed broad one and two-proton singlets at δ 6.25 and 7.75, respectively, corresponding to the three N-H protons of the urea moiety and a one-proton singlet at δ 7.47 corresponding to the alkenyl proton. The ^{13}C NMR spectrum showed signals at δ 95.1 and 90.2 corresponding to the iodinated sp^2 -carbons while the IR spectrum displayed a band at 1666 cm^{-1} and was assigned to urea $\text{C}=\text{O}$ stretching. This absorption appears at a frequency $\sim 10\text{ cm}^{-1}$ lower than that due to the same moiety within the carboxamide within **2.11**. High resolution mass measurements established the molecular formula as $\text{C}_9\text{H}_8\text{I}_2\text{N}_2\text{O}$. However, the

stereochemistry of the alkene within diiodostyrene **2.12** could not be established spectroscopically and the illustrated structure is based on literature precedence.⁷

Although the diiodination of alkynes is a known process, it is somewhat surprising that it proceeds rapidly enough to compete with the cyclisation process and suggests the urea group is a rather poor nucleophile. Importantly, products arising from a 6-*exo* or 7-*endo* cyclisation mode were not observed. This result confirmed that the preferred mode of cyclisation involves the anticipated 5-*endo*-dig pathway.

2.3.2 Reactions of 1-[2-(Buta-1,3-diynyl)phenyl]urea (**2.0**) with Various Sources of I⁺

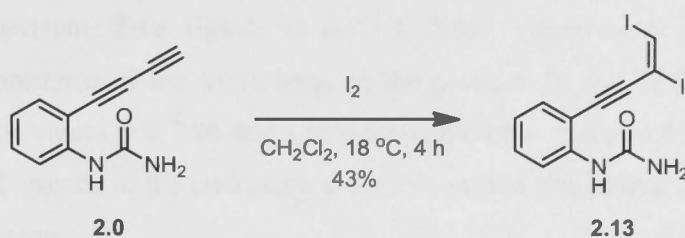
Encouraged by the excellent 5-*endo* selectivity observed in the conversion **2.2**→**2.11**, we sought to explore a possible 5-*endo*-dig/6-*endo*-dig cascade reaction of analogue **2.0** which incorporates a second C≡C triple bond. The additional complexity arising from the introduction of a second alkyne is reduced if the initial cyclisation mode follows the 5-*endo*-dig pathway as was observed with substrate **2.2**. Assuming that this is the first mode of cyclisation, then a second cyclisation event could occur, as illustrated in **Scheme 2.8**, in one of four different ways, namely via *O*-5-*exo*-dig, *N*-5-*exo*-dig, *O*-6-*endo*-dig or *N*-6-*endo*-dig pathways.



Scheme 2.8: Possible cascade products arising from the reaction of substrate **2.0** with molecular iodine.

In the event, treating the diyne-containing substrate **2.0** with molecular iodine in CH_2Cl_2 resulted in the exclusive formation of the diiodoenyne **2.13** in 43% yield (**Scheme 2.9**). The structure of this compound was assigned on the basis of 1H NMR, ^{13}C NMR, IR and MS spectral analyses. For example, the IR spectrum displayed a $C=O$ carbonyl stretching band at 1659 cm^{-1} (essentially unchanged compared with the starting material) and a $C\equiv C$ stretching band at 2189 cm^{-1} suggesting the presence of an alkyne. The presence of an alkyne moiety was confirmed by ^{13}C NMR spectroscopy which showed two equally intense signals due to sp -hybridised carbons appearing at δ 91.9 and 72.8. The 1H NMR spectrum showed a one-proton singlet at δ 7.85 corresponding to the alkenyl proton and, additionally, two broad N-H signals that integrated to a total of three protons and had

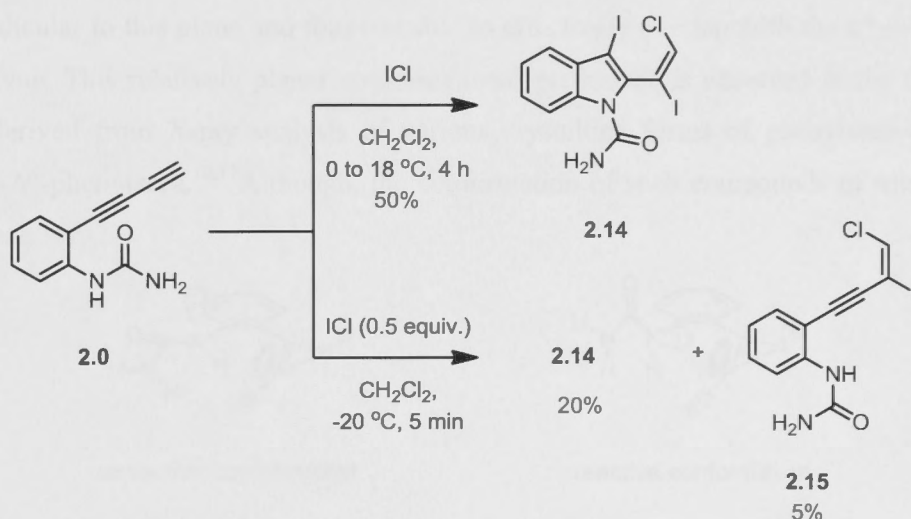
chemical shifts very close to those of the starting urea. These features suggested that a mono-substituted urea moiety still existed in the structure of the product. High resolution mass spectral analysis confirmed the molecular formula as $C_{11}H_8I_2N_2O$. Although the stereochemistry of alkene could not be proven due to the lack of vicinal alkenyl protons on the olefin it is probably *trans* based on the same argument as in the earlier example, compound **2.12**.



Scheme 2.9: Reaction of 1-(2-(buta-1,3-diynyl)phenyl)urea with iodine giving the diiodoenyne **2.13**.

It was clear that under these conditions iodination of the terminal triple bond proceeded faster than the hoped-for cyclisation process. On the basis that the rate of formation of addition product **2.13** could be reduced if the source of I^+ involved a less nucleophilic counterion, diyne **2.0** was treated with ICl at $18\text{ }^\circ\text{C}$ for 24 h (**Scheme 2.10**). Interestingly, this resulted in the exclusive formation of iodoindole **2.14** which was obtained in 50% yield. The ^1H NMR spectrum of the product showed a broad, two-proton singlet at δ 6.18 which is attributed to the remaining NH_2 protons of the urea residue. The presence of the chlorine atom in the product was confirmed through the observation of the relevant molecular ion cluster in the EI mass spectrum. An accurate mass measurement on these ions served to confirm the molecular formula as $C_{11}H_7ClI_2N_2O$. In the IR spectrum a $\text{C}=\text{O}$ carbonyl absorption band was observed at 1702 cm^{-1} and this is assigned to the urea. The regiochemistry associated with the addition of ICl across the terminal alkyne and stereochemistry of the resulting alkene was assigned based on literature precedent.⁸

In order to establish the sequence of events associated with the conversion **2.0**→**2.14**, the reaction was performed at $-20\text{ }^{\circ}\text{C}$ for 5 min and employing only 0.5 equiv of ICl. As a result, a new compound, assigned as enyne **2.15**, could be isolated albeit in low (5%) yield. The IR spectrum of this product showed a weak band at 2201 cm^{-1} which was assigned to the alkyne while the strong band observed at 1669 cm^{-1} was assigned to a carbonyl C=O stretching absorption arising from the urea. The presence of chlorine in the compound was confirmed through the observation of the relevant molecular ion cluster in the EI mass spectrum. Two signals in the ^{13}C NMR spectrum, at δ 86.4 and 76.4, confirmed the presence of the triple bond in the product. In the ^1H NMR spectrum a broad, one-proton signal at δ 7.98 and a broad two-proton signal at δ 6.39 were assigned to the three N-H protons of the urea and a sharp one-proton singlet at δ 7.63 was assigned to the alkenyl proton.



Scheme 2.10: Reactions of 1-(2-(buta-1,3-diynyl)phenyl)urea with ICl giving both the iodoindole **2.14** and the dihaloenyne **2.15**.

Other sources of iodine were then investigated including *N*-iodosuccinimide (NIS). Disappointingly, treatment of compound **2.0** with NIS failed to trigger a reaction under the standard conditions while over extended reaction periods (days) and/or higher temperatures only complex reaction mixtures were observed. Treatment of substrate **2.0** with bis(2,4,6-trimethylpyridyl)iodine hexafluorophosphate, a reagent reported to

promote nucleophilic ring closure reactions of alkynes by Barluenga,⁹ gave similar results.

2.3 Summary

It has been established that 5-*endo*-dig cyclisations are the preferred initial mode of cyclisation of *o*-ethynylphenylureas. However, it appears that nucleophiles present in the reaction mixture can compete intermolecularly with the desired cyclisation process. This unexpected result indicates that the urea moiety is a rather poor internal nucleophile. The reason for this is probably the result, to some extent at least, of conformational restrictions imposed upon the phenyl urea group which may adopt an arrangement whereby the atoms within the aromatic ring and urea moieties essentially occupy the same plane (**Figure 2.4**). This would place the relevant nitrogen lone electron pairs perpendicular to this plane and thus not able to effectively overlap with the π^* -orbital of the alkyne. This relatively planar conformational preference is observed in the ORTEP plots derived from X-ray analysis of various crystalline forms of phenylurea and *N*-methyl-*N'*-phenylurea.^{10,11} Although, the conformation of such compounds in solution is less clear.



Figure 2.4. Conformational effects during the iodine-promoted reactions of **2.0**.

Promoting the desired intramolecular reaction *via* a nucleophilic attack of the urea onto the alkyne may be possible in the absence of competing nucleophiles. Thus, electrophilic reagents that do not introduce potential nucleophiles would appear to be better reagents for the present purposes. The outcomes of reactions employing electrophiles of this type are discussed in *Chapter Three*.

2.5 References

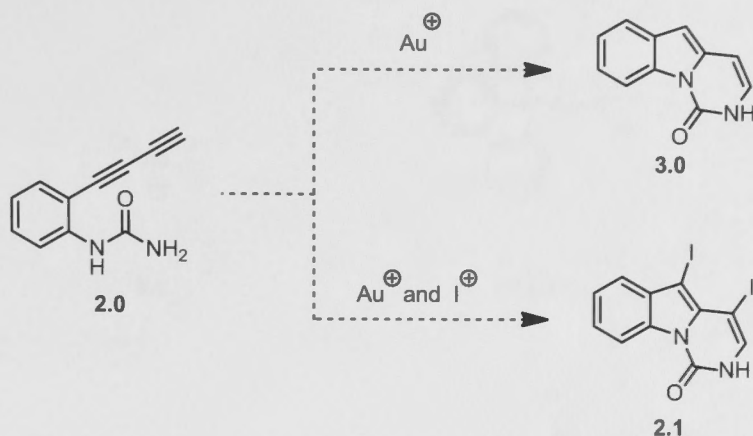
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Chapter Three

Gold-Catalysed Cyclisation Reactions of *o*-Diynylarylureas

3.1 Overview

The results presented in *Chapter Two* demonstrated that intermolecular addition processes interfere with the desired, and relatively slow, iodine-promoted nucleophilic cyclisation reactions of *o*-alkynylarylureas. Gold-promoted nucleophilic cyclisation reactions offer a possible solution to this problem. This is because, nucleophilic ring closure reactions of alkynes promoted by gold Au(I) and Au(III) complexes often proceed with very low catalyst loadings (0.5-10 mol%) and so limiting the amount of external nucleophile (as in the counterion of the gold complex) present in the reaction mixture. Also, the literature on gold-catalysed cyclisation reactions of alkynes suggests that the correct choice of gold complex and reaction conditions can lead to the desired product being obtained in good yield.¹ On this basis initial investigations focussed on the capacity of gold complexes to promote the desired cascade cyclisation (*viz.* the conversion **2.0**→**3.0**). Gold catalysis also provides the possibility of incorporating iodine into the tricyclic product through the addition of a source of I^+ such as NIS which, if successful, could give diiodinated tricycle **2.1** (**Scheme 3.1**).



Scheme 3.1: Proposed gold-catalysed EPNC reaction cascade.

3.1.1 Gold Complexes

Various gold complexes have been shown to catalyse the nucleophilic cyclisation reactions of alkynes with remarkable selectivity.¹ Compounds **3.1** – **3.4** (**Figure 3.1**) have all been reported to catalyse highly efficient and very selective cyclisation reactions of alkynes that lead to heterocycles. The latter three complexes contain bulky and strongly σ -donating ligands and are therefore stable in the +1 oxidation state throughout the catalytic cycle.² Reactions that involve Au(I) chloride complexes often also employ a silver co-catalyst, that assists in abstraction of a chloride ligand from the gold complex and, thereby, creating a vacant coordination site on the gold atom that can accommodate the π -system of the alkyne and thereby activating it toward attack from a neighbouring nucleophile.² Thus, most gold complexes used in homogenous catalysis contain a labile ligand of some description. For example, $\text{PPh}_3\text{AuNTf}_2$ (**3.2**) has a strongly coordinating phosphine ligand and a weakly coordinating triflamide ligand that dissociates easily in solution without the aid of a co-catalyst. Au(I) salt **3.3** has a weakly coordinating acetonitrile ligand that dissociates in solution and while this feature makes the complex quite reactive, the bulky phosphine ligand protects the gold centre and so increases the air and moisture stability of the complex.³

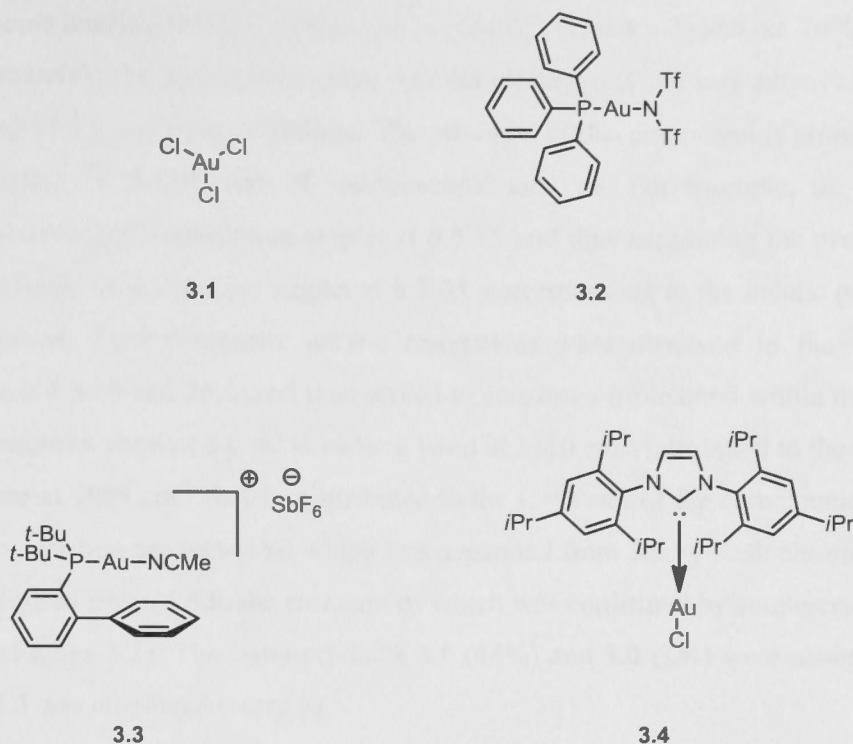


Figure 3.1. Some catalytically active gold complexes.

3.2 Gold-catalysed Reactions of Compound 2.0

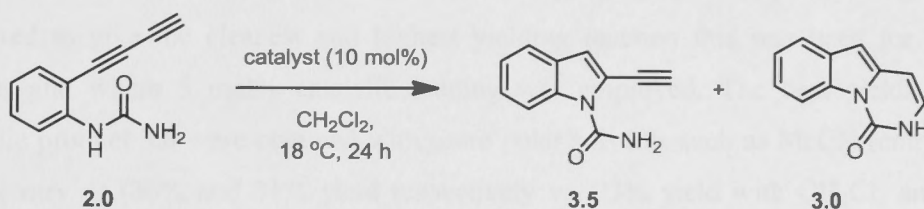
3.2.1 Catalyst Screening

The initial screening focused on gold complexes known to promote nucleophilic cyclisation reactions of alkynes without the need to employ a co-catalyst. Accordingly, complexes **3.2** and **3.3** were screened for their capacity to effect the desired cyclisation of substrate **2.0**. AuCl_3 (**3.1**) was also included in the screening regime for purposes of comparison.

The results of the initial screening are shown in **Table 3.1**. The reactions were conducted by treating compound **2.0** with 10 mol% of the gold complex in CH_2Cl_2 at room temperature. Under these conditions, AuCl_3 was ineffective, causing only decomposition of the substrate (entry 1). On the other hand, treatment of compound **2.0** with the Au(I) complex **3.2** gave a mixture of two products in a 94:6 ratio (as judged by ^1H NMR

spectroscopic analysis) and in a combined yield of 22% (entry 2) and *ca.* 70% unreacted starting material. The major component was the product mixture was ethynyl indole **3.5**, the product of a 5-*endo*-dig cyclisation. The structure of this compound is proposed based on ^1H NMR, ^{13}C NMR, and IR spectroscopic analysis. For example, the ^1H NMR spectrum displayed a one-proton singlet at δ 3.75 and thus suggesting the presence of a terminal alkyne. A one-proton singlet at δ 7.05, corresponding to the indolic proton, was also observed. Two diagnostic alkyne resonances were observed in the ^{13}C NMR spectrum, at δ 86.4 and 76.4, and thus served to confirm a triple bond within the product. The IR spectrum showed a $\text{C}\equiv\text{C}$ stretching band at 2110 cm^{-1} (attributed to the alkyne) as well as one at 1688 cm^{-1} that was attributed to the $\text{C}=\text{O}$ unit of the carboxamide moiety. The minor reaction product (1%) which was separated from **3.5** by flash chromatography was the desired tricycle **3.0**, the structure of which was confirmed by single-crystal X-ray analysis (**Figure 3.2**). The same products **3.5** (44%) and **3.0** (1%) were observed when catalyst **3.3** was employed (entry 3).

Table 3.1: Screening of gold complexes for their ability to induce cyclisation of **2.0**.



entry	catalyst	ratio 3.5 : 3.0	yield (%)
1	AuCl_3	-	decomposition
2	$\text{Ph}_3\text{PAuNTf}_2$	94 : 6	22
3	3.3	>99 : 1	45

a) Reactions were carried out in anhydrous CH_2Cl_2 (0.2 M concentration of substrate), employing 10 mol% gold complex, at $18\text{ }^\circ\text{C}$ for 24 h.

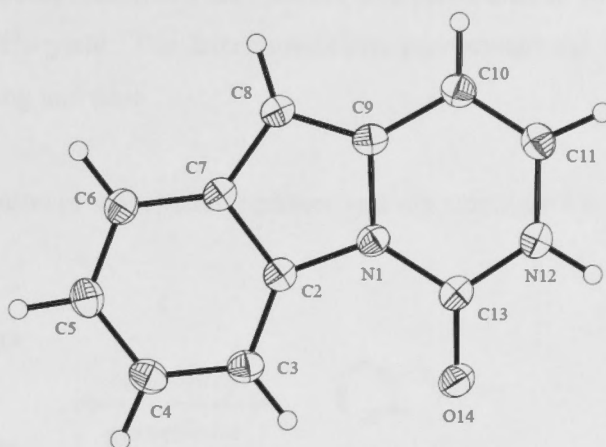


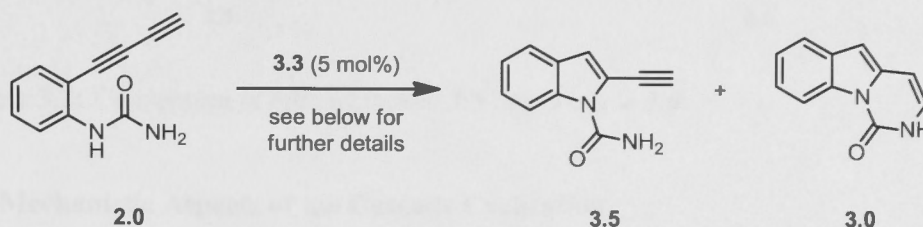
Figure 3.2. ORTEP plot derived from the single-crystal X-ray analysis of compound **3.0**.

3.2.2 Optimisation of Tandem-Cyclisation Process Leading to Target Compound **3.0**

Encouraged by the excellent selectivity observed in the gold-catalysed cascade reaction an investigation of reaction parameters such as solvent, time and temperature was carried out in order to optimise the yield of the desired tricyclic product **3.0** and, hopefully, perform the reaction with lower catalyst loadings (Table 3.2). Since complex **3.3** appeared to give the cleanest and highest yielding reaction this was used for further studies and where 5 mol% catalytic loading was employed. The best yields of the tricyclic product **3.0** were obtained with more polar solvents such as MeCN (entry 2) or THF (entry 4) (36% and 31% yield respectively vs. 23% yield with CH₂Cl₂ and only trace amounts of product with toluene). This is probably because of the increased solubility of the urea **2.0** in these solvents. However, when MeCN was used, the formation of a number of unidentified by-products was also observed. Addition of K₂CO₃ (entry 5) appeared to severely slow the reaction and completely inhibited the formation of the tricyclic product. Overall, the best solvent appeared to be THF. Using this and employing extended reaction times and a catalyst loading of 10 mol% resulted in a 1:9 mixture of compounds **3.5** and **3.0** which was obtained in 92% yield after 168 h (entry 6). Increasing the reaction temperature using microwave irradiation significantly increased the rate of the reaction such that after 8 h at 60 °C a 51% yield of a *ca* 1:4 mixture of compounds **3.5** and **3.0** was obtained (entry 7). Complete conversion of substrate **2.0** into

the tricycle **3.0** was observed when the reaction was performed at 100 °C (entry 8) and it was obtained in 76% yield. The latter conditions represented the best compromise of yield, catalyst loading and time.

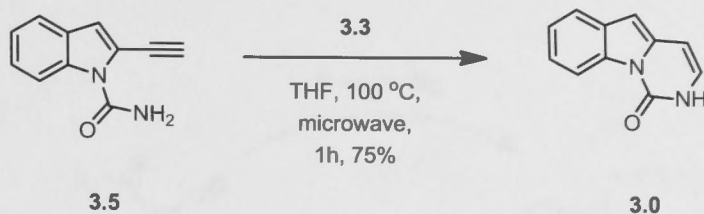
Table 3.2 Optimisation of solvent, temperature and reaction time for the formation of tricycle **3.0**.



entry	catalyst	solvent	temp (°C)	time (h)	ratio 3.5:3.0	yield (%) ^a
1	3.3	CH ₂ Cl ₂	r.t.	24	>99:1	23
2	3.3	MeCN	r.t.	24	76:24	36 ^b
3	3.3	Toluene	r.t.	24	-	Trace
4	3.3	THF	r.t.	24	93:07	31
5	3.3 ^c	THF	r.t.	24	>99:1	9
6	3.3^d	THF	r.t.	168	10:90	92
7	3.3	THF	60	8	21:79	51
8	3.3	THF	100	1	<1:99	76

a) Average of two isolated yields. b) Multiple by-products also observed. c) K₂CO₃ (1 equiv.) was added. d) 10 mol% loading of **3.3** used.

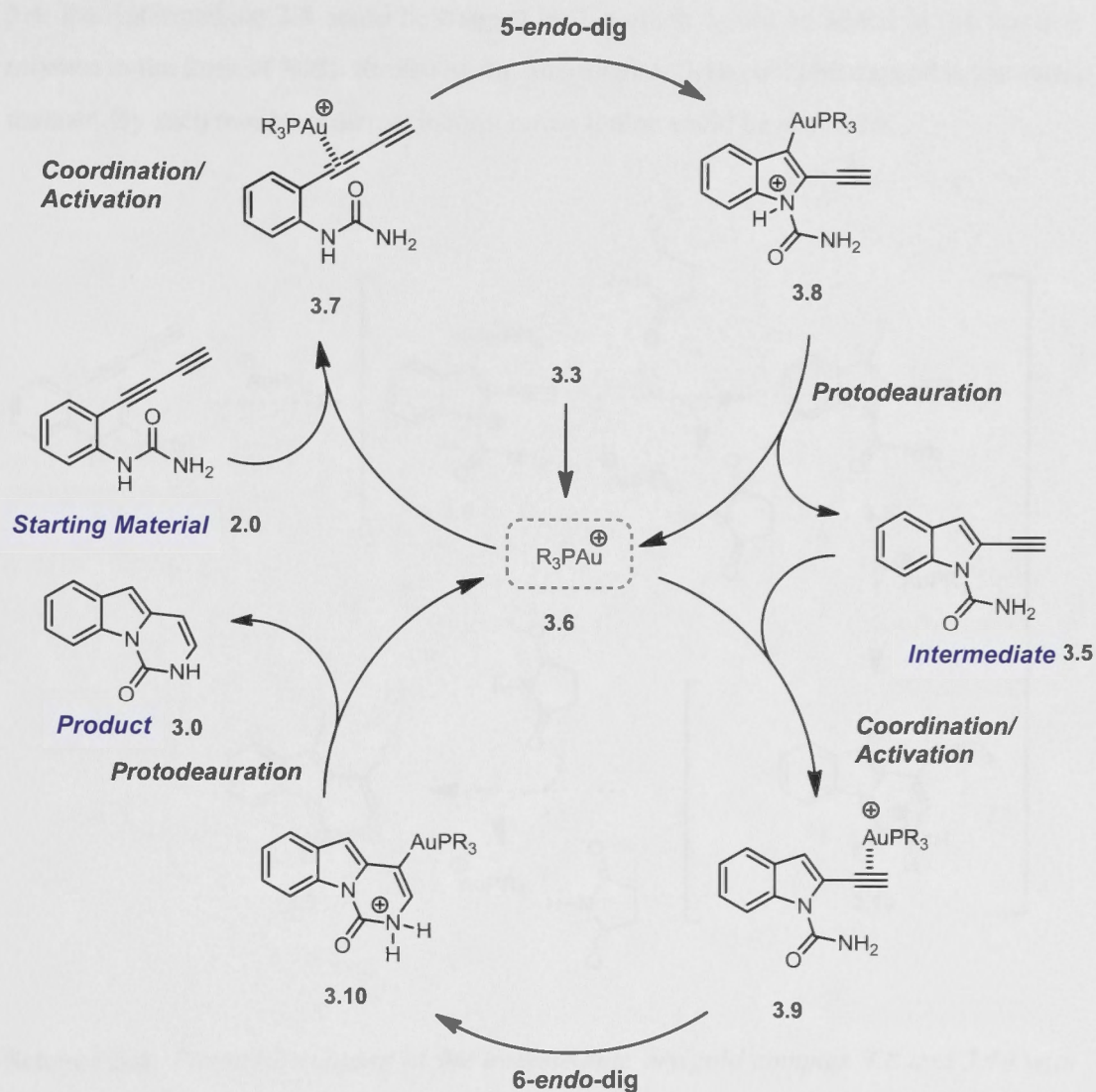
Subjection of the indole **3.5** to the optimised reaction conditions led to its complete conversion into tricycle **3.0** which was obtained in 75% yield (**Scheme 3.2**).



Scheme 3.2: Conversion of ethynyl indole **3.5** into tricycle **3.0**.

3.2.3 Mechanistic Aspects of the Cascade Cyclisation

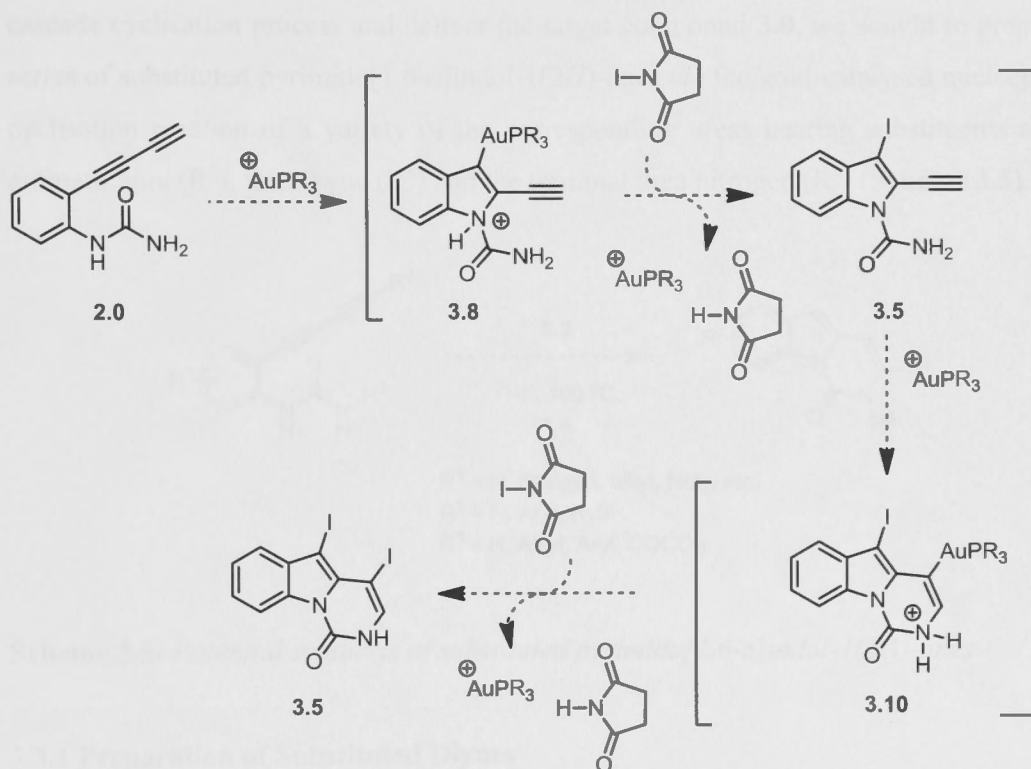
The basic reaction pathway involved in gold-induced alkyne cyclisations have been detailed in many recent reviews.⁴ Applying these principles to the observed conversion of **2.0**→**3.5**→**3.0** suggests the involvement of a catalytic cycle of the type shown in **Scheme 3.3**. Thus, the dissociation of an acetonitrile ligand from complex **3.3** generates the catalytically active Au(I) species **3.6** which can coordinate to the π -system of the internal or terminal alkyne and thereby activating it (the alkyne) toward nucleophilic attack. However, it is only the activated internal alkyne (**3.7**) that can undergo ready reaction due to the reasonable proximity of the pendant urea group. A 5-*endo*-dig cyclisation of this complex, **3.7**, gives the auric indolinium cation **3.8** protodeauration of which then gives 2-ethynylindole **3.5** and simultaneously liberates the catalytically active gold complex **3.6**. Indole **3.5** itself can now coordinate through the terminal C≡C triple bond to the Au(I) catalyst **3.6** giving complex **3.9** which can undergo a second 6-*endo*-dig cyclisation to form the second C-N bond and thus generate the aurated intermediate **3.10**. Protodeauration of this last compound then furnishes the observed tricycle (**3.0**) and regenerates the catalyst (**3.6**).



Scheme 3.3: Proposed mechanism for the conversion 2.0→3.5→3.0.

3.2.4 Attempts to Introduce Iodine onto the Tricyclic Framework During the Gold-Catalysed Cyclisation Reaction

It has been shown that alkenylgold species are often quite stable and in some cases they can be isolated and fully characterized.⁵ Thus, the possibility arises, as shown in **Scheme 3.4**, that intermediate **3.8** could be trapped by I^+ (which would be added to the reaction mixture in the form of NIS). Similarly, the intermediate **3.10** could be trapped in the same manner. By such means, products incorporating iodine could be produced.



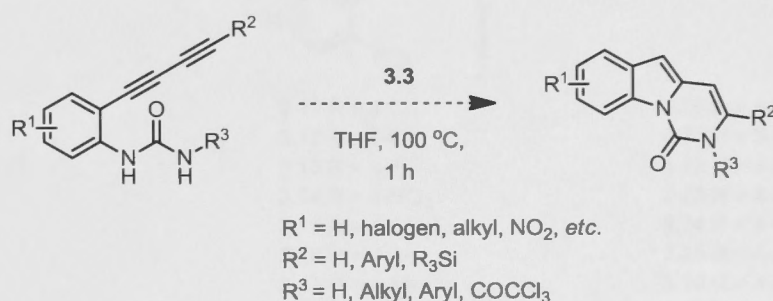
Scheme 3.4: Potential trapping of the intermediate arylgold complex **3.8** and **3.10** with iodine.

Having optimised conditions for the conversion of substrate **2.0** into the tricyclic product **3.5**, the introduction of iodine into the framework of the latter *via* reaction of the proposed intermediates **3.8** and **3.10** with a relevant source of halogen was investigated. NIS and bis-(2,4,6-trimethylpyridine)iodine(I) hexafluorophosphate appeared to be good

candidates for this purpose, especially given that they showed little reactivity toward **2.2** under standard conditions. However, when 2 equivalents of NIS were introduced into the relevant reaction mixture a multitude of products was observed. Similar results were obtained when bis-(2,4,6-trimethylpyridine)iodine(I) hexafluorophosphate was used in place of NIS.

3.3 Substrate Scope

Based on the capacity of the gold salt **3.3** to effect the desired 5-*endo*-dig/6-*endo*-dig cascade cyclisation process and deliver the target compound **3.0**, we sought to prepare a series of substituted pyrimido[1,6-*a*]indol-1(2*H*)-ones *via* the gold-catalysed nucleophilic cyclisation reaction of a variety of the corresponding ureas bearing substituents at the aromatic ring (R^1), the alkyne (R^2) and the terminal urea nitrogen (R^3) (**Scheme 3.5**).

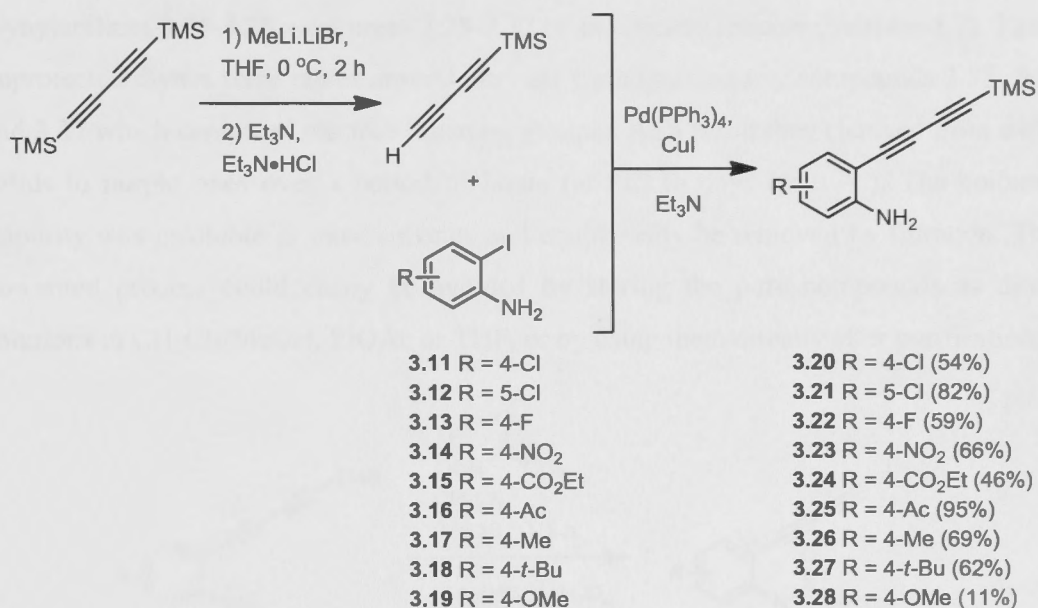


Scheme 3.5: Potential synthesis of substituted pyrimido[1,6-*a*]indol-1(2*H*)-ones.

3.3.1 Preparation of Substituted Diynes

In pursuing the objectives defined directly above, we sought to prepare the required substrates by the same means as used to generate compound **2.0**, namely replacing the relevant fragments in each reaction and/or adding substituents *via* further modification of the urea products as shown in **Scheme 3.6**.

To such ends the iodoaniline in the original Sonagashira cross-coupling reaction was replaced by its substituted analogues **3.11-3.19**.^{*} Most of the cross-coupling reactions proceeded smoothly with the exception of that involving electron-rich 3-iodoaniline, which gave the desired product in just 11% yield (**Scheme 3.6**). This disappointing outcome was probably due to a slow oxidative addition of the palladium complex to the electron-rich aryl iodide at the start of the catalytic cycle. Nevertheless, the reaction proved suitable for the preparation of a diverse range of arylated diynes **3.20-3.28**.



Scheme 3.6: Synthesis of *o*-diynylanilines **3.20-3.28** via Sonagashira reaction.

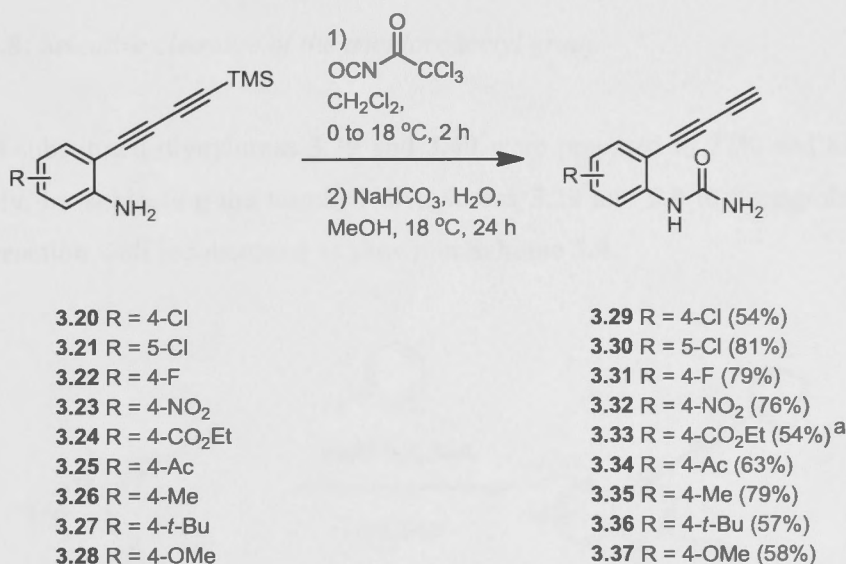
The ¹³C NMR spectra derived from compounds **3.20-3.28** all displayed four signals between δ 70-95 corresponding to the four sp-hybridized carbons of the buta-1,3-diynyl moiety within each of the products. The ¹H NMR spectra of these compounds displayed a nine-proton singlet at *ca.* δ 0.25 corresponding to the trimethylsilyl group and a broad two-proton singlet[†] in the range δ 4.1-4.8 corresponding to the NH₂ group. The IR spectra

^{*} These compounds were either commercially available or prepared using reported procedures as described in *Chapter Five*.

[†] Except for the ¹H NMR spectra derived from the NO₂-substituted compound **3.23** in which no NH₂ signal was observed.

derived from these compounds all showed a band at *ca* 2200 cm^{-1} and another at *ca* 2100 cm^{-1} which derive from the two distinct $\text{C}\equiv\text{C}$ triple bonds in each of the products.

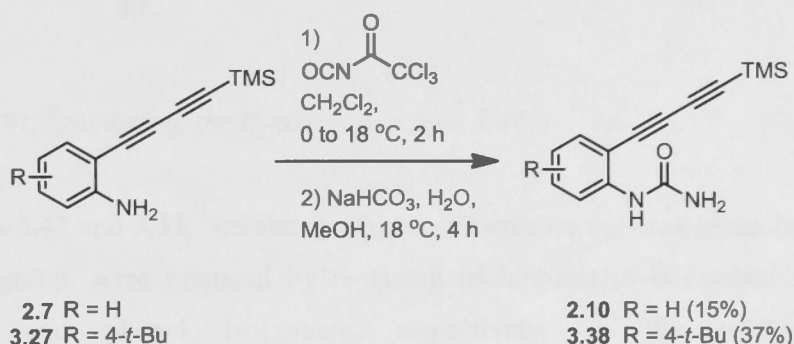
In an effort to streamline the ureation/deprotection protocol, a one-pot procedure was developed whereby once the initial ureation had occurred (to give the corresponding trichloroacetylurea) the solvent was removed from the reaction mixture under reduced pressure then methanol and aqueous sodium bicarbonate were added and the ensuing mixture stirred at ambient temperature overnight. Applying this protocol to *o*-diynylanilines **3.20**–**3.28** gave ureas **3.29**–**3.37** in an efficient manner (Scheme 3.7). These unprotected diynes were rather unstable in neat form (particularly compounds **3.35**, **3.36** and **3.37** which contained electron donating groups). As a result they changed from white solids to purple ones over a period of hours (at r.t.) to days (at 0 °C). The coloured impurity was insoluble in most solvents and could easily be removed by filtration. This unwanted process could easily be avoided by storing the pure compounds as dilute solutions in $\text{CH}_2\text{Cl}_2/\text{MeOH}$, EtOAc or THF, or by using them directly after purification.



Scheme 3.7: *Synthesis of ureas 3.29–3.37.*

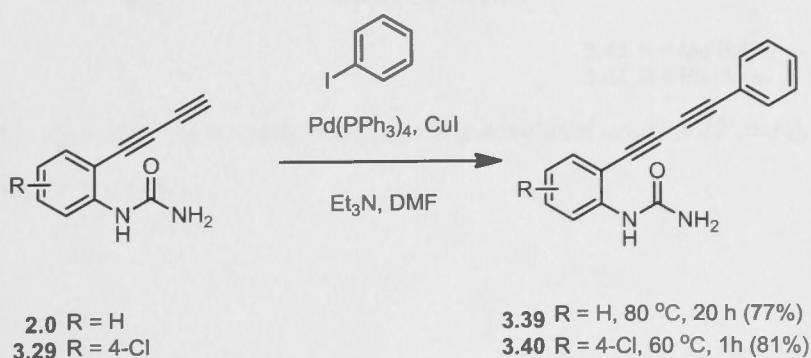
a) EtOH used as solvent in place of MeOH.

Trimethylsilyl-substituted diynes **2.10** and **3.38** were prepared in 15% and 37% yield, respectively, by a mild hydrolysis of the trichloroacetyl group following the ureation of compounds **2.0** and **3.27** respectively (**Scheme 3.8**). This selective deprotection process was rather difficult to control and often significant amounts of the fully deprotected compounds (*viz.* **2.0** and **3.36**) were obtained along with starting material. The trimethylsilyl-substituted diynes **2.10** and **3.38** were completely stable under standard conditions.



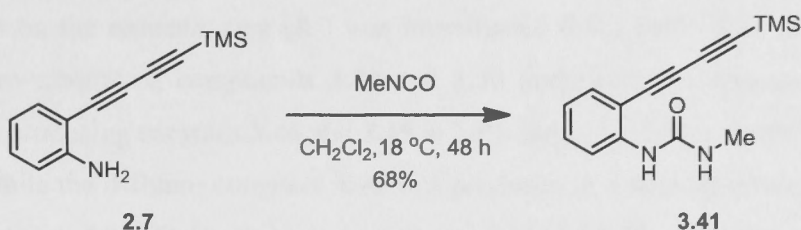
Scheme 3.8: Selective cleavage of the trichloroacetyl group.

The diaryl-substituted diynylureas **3.39** and **3.40** were prepared in 77% and 81% yield, respectively, by subjecting the terminal diynylureas **3.29** and **2.0** to Sonagashira cross-coupling reaction with iodobenzene as shown in **Scheme 3.9**.



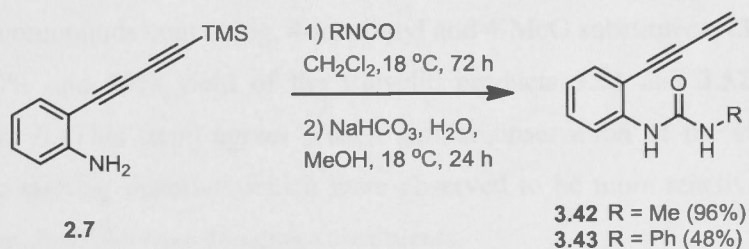
Scheme 3.9: Synthesis of diaryl-substituted diynes **3.39** and **3.40**.

N-Methyl-substituted urea **3.41** could be obtained in (68%) by simply treating a solution of diyne **2.7** in CH_2Cl_2 with methyl isocyanate as shown in **Scheme 3.10**.



Scheme 3.10: Synthesis of the *N*-methylated urea **3.41**.

Compounds **3.42** and **3.43**, containing two substituents on the urea group but no alkyne “capping” group, were prepared by replacing trichloroacetyl isocyanate with methyl isocyanate and phenyl isocyanate, respectively, in the relevant one-pot ureation/deprotection protocol (**Scheme 3.11**). These isocyanates proved far less reactive than trichloroacetyl isocyanate so extended reaction times were required in order to achieve moderate yields of the desired *N,N'*-disubstituted ureas **3.42** and **3.43**.

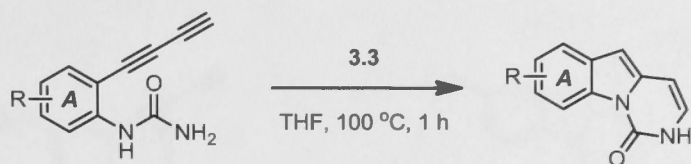


Scheme 3.11: Synthesis of *N*-methylated and *N*-phenylated ureas **3.42** and **3.43** from the corresponding isocyanates.

3.3.2 Effects of Substituents on the Gold(I)-catalysed Cyclisation Reaction

3.3.2.1 Substitution on the Aromatic Ring (R¹)

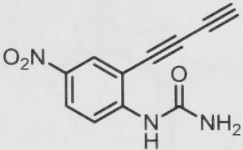
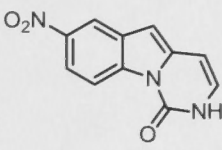
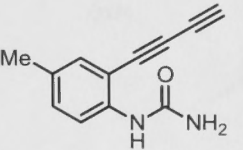
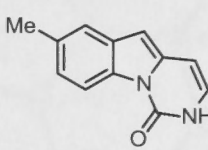
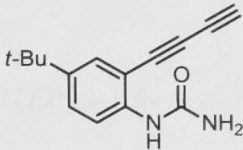
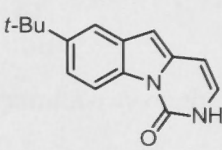
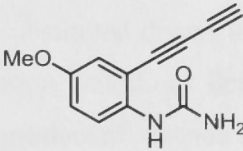
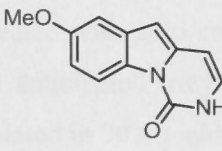
Substitution on the aromatic ring (R¹) was investigated first (Table 3.3). The 4-chloro- and 5-chloro-substituted compounds **3.29** and **3.30** underwent the anticipated cascade cyclisation, producing tricycles **3.44** and **3.45** in 70% and 67% yield, respectively (entries 1 and 2), while the 4-fluoro congener **3.46** was produced in a slightly lower yield (62%, entry 3). 4-Ac- and 4-EtO₂C-substituted substrates **3.34** and **3.33** were tolerated under the reaction conditions (entries 4 and 5), affording the corresponding tricyclic products **3.47** and **3.48** in yields of 59% and 65%, respectively. The 4-NO₂-substituted compound **3.32** reacted less efficiently and only produced the desired tricyclic product **3.49** in 49% yield and the formation of this compound was accompanied by various unidentified by-products (entry 6). The lower yields may be understood by considering the delocalisation of electron density from the nitrogen lone pair toward the *para*-related and electron withdrawing groups, thereby reducing its nucleophilicity. Substrates containing electron-donating substituents such as Me, *t*-Bu, and MeO appeared to participate poorly in the desired cyclisation cascade. For example, methyl-substituted system **3.35** was converted into the tricyclic compound **3.50** in only a modest yield (56%, entry 7) and the more electron-rich compounds containing, 4-*tert*-butyl and 4-MeO substituents (**3.36** and **3.37**), gave only 40% and 39% yield of the tricyclic products **3.51** and **3.52**, respectively (entries 8 and 9). This trend agrees with a similar observation of the stability of the corresponding starting materials which were observed to be more reactive (less stable) when they contained electron-donating substituents.

Table 3.3: Reactions of A-ring Substituted *o*-Diynylphenylureas.

entry	substrate	product	yield (%)
1	3.29	3.44	70
2	3.30	3.45	67
3	3.31	3.46	62
4	3.34	3.47	59
5	3.33	3.48	61

Continued on the next page.

Table 3.3 continued from previous page.

6	 3.32	 3.49	49
7	 3.35	 3.50	56
8	 3.36	 3.51	40
9	 3.37	 3.52	39

The aryl-substituted compounds **3.44-3.52** had a number of spectroscopic features in common. For example, their IR spectra which all displayed a C=O stretching band in the range 1691-1713 cm^{-1} while the corresponding ^1H NMR spectra all displayed a sharp singlet between δ 6.49 and 6.94 (assigned to the indolic proton) and a broad singlet[§] between δ 10.76 and 11.16 corresponding to the N-H proton. Single-crystal X-ray analytical techniques served to confirm the structure of tricycle **3.48** and thereby supporting the structural assignments of the other tricycles. The derived ORTEP plot is shown in **Figure 3.3**.

[§] In some cases a small coupling ($J \sim 4$ Hz) was observed.

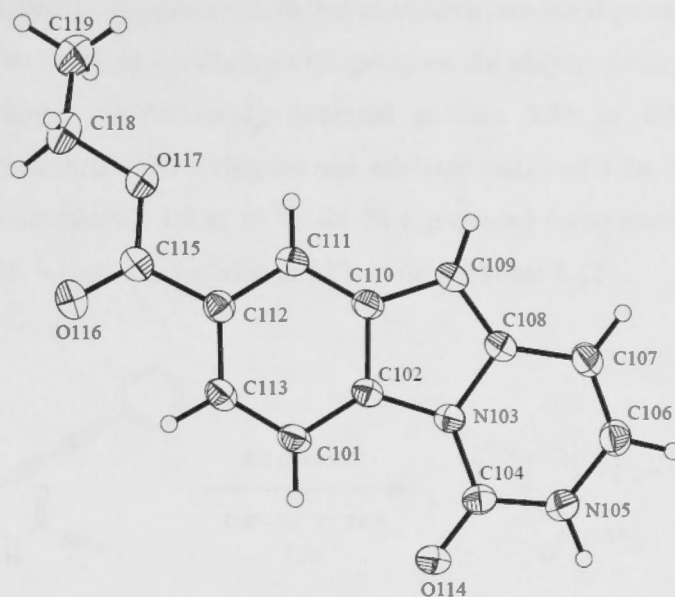
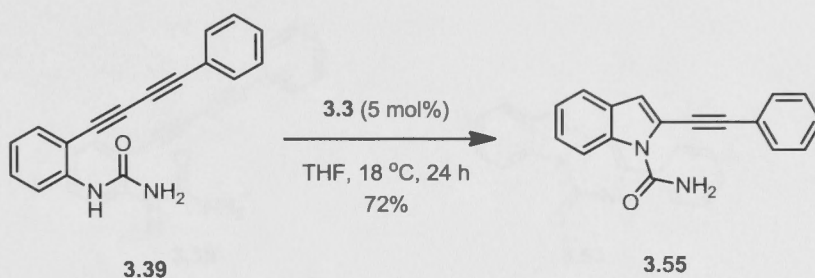


Figure 3.3. ORTEP plot derived from the single crystal X-ray analysis of tricycle **3.48**.

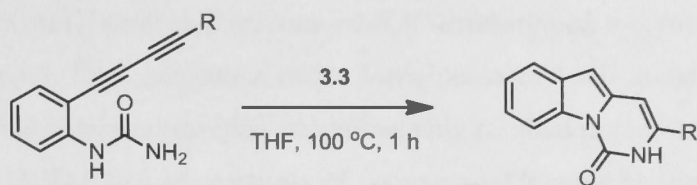
3.3.2.2 Substitution on the Alkyne (R^2)

When phenyl-substituted diynyl urea **3.39** was treated with gold complex **3.3** under the optimized reaction conditions defined above the anticipated tricyclic heterocycle **3.53** was the major product of reaction and could be isolated in 70% yield (entry 1, **Table 3.4**). Similarly, under the same reaction conditions compound **3.40**, which also contains a second phenyl substituent on the alkyne, gave the corresponding tricyclic compound **3.54** in 68% yield (entry 2). The IR stretching frequency of the urea carbonyl group in the latter two products were 1691 cm^{-1} and 1696 cm^{-1} , respectively, indicating the inclusion of the carbonyl group in a 6-membered ring. Substrates containing a trimethylsilyl group on the alkyne could potentially affect the regio-selectivity of the second cyclisation event in the cascade due to the β -effect often displayed by such groups. In the event, substrate **2.10**, which contains such a substituent, underwent the usual 5-*endo*-dig/6-*endo*-dig cyclisation reaction affording the previously obtained compound **3.0**, in which the trimethylsilyl group had been cleaved during the reaction (entry 3). This was a useful result as it offered an opportunity to subject protected cyclisation precursors to the reaction and thereby providing the same products as would be expected from reactions of the less stable congeners that do not contain a silyl-substituent on the alkyne. For

example, the electron rich compound **3.38** that contains a *tert*-butyl group on the aromatic ring and which also contains a trimethylsilyl group on the alkyne underwent the cascade cyclisation, providing the previously obtained product **3.51** in 49% yield, a 9% improvement on the reaction involving the non-silylated congener **3.36**. Also treatment of compound **3.39** with catalyst **3.3** at 18 °C for 24 h provided the mono-cyclised product, namely indole **3.55**, which was isolated in 72% yield (**Scheme 3.12**).



Scheme 3.12: Mono-cyclisation product **3.55**.

Table 3.4: Reactions of phenyl- or trimethylsilyl-capped *o*-diynylarylureas.

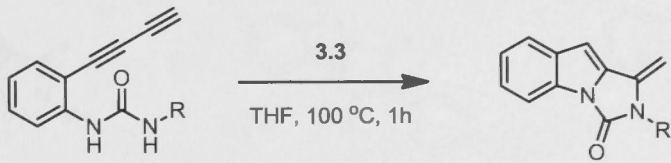
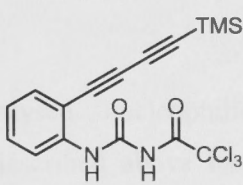
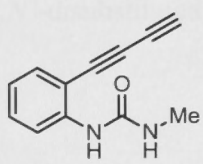
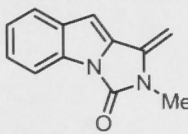
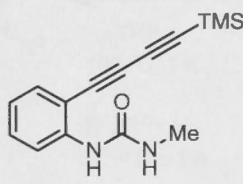
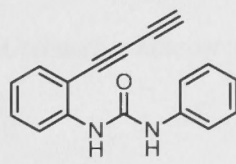
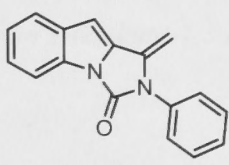
entry	substrate	product	yield (%) ^a
1	3.39	3.53	70
2	3.40	3.54	68
3	2.10	3.0	75
4	3.38	3.51	49

3.3.2.3 Substitution on the Urea (R^3)

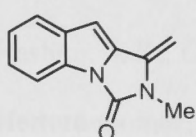
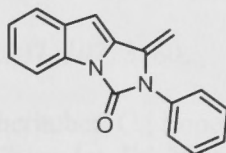
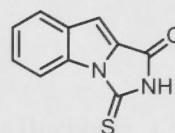
The outcomes of Au(I)-catalysed reaction of *N,N'*-disubstituted *o*-diynylphenylureas are shown in **Table 3.5**. Thus, subjection of the *N*-trichloroacetyl-substituted substrate **2.9** to the optimised gold-catalysed reaction conditions only resulted in recovery of the starting material (entry 1). The lack of reactivity of compound **2.9** could be the result of one or other of several effects. First, the trichloroacetyl group inductively withdraws a significant amount of electron density from the urea nitrogens rendering them even less nucleophilic. Second, based on the X-ray crystal structure of the starting material, a hydrogen bond exists between the oxygen on the trichloroacetyl group and one of the hydrogen atoms attached to the urea and therefore the entire functional group is locked into a planar conformation, parallel to the aromatic ring and thereby preventing the required orbital overlap between the lone pairs of electrons on either nitrogen and the π^* -orbital of the internal alkyne.⁶ In contrast, the *N*-methyl-substituted compound **3.42** underwent rapid reaction under the usual conditions giving a mixture of products (entry 2). The major one was the 1-methylene-1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one **3.56**, which was obtained in 29% yield. The presence of an exocyclic double bond in this product was evident from the ¹H NMR spectrum which displayed two doublets at δ 5.01 and 4.65 with coupling constants of 2.4 and 2.4 Hz, constituting an olefinic AB system. The IR spectrum displayed a stretching band at 1730 cm⁻¹, ~30 cm⁻¹ higher than in the 6-membered ring analogs and suggesting the incorporation of this moiety within a 5-membered ring. This change in selectivity contrasts with the work of Gimeno *et al*, who found that *N*-substitution had no effect on the selectivity of gold-catalysed cyclisation reaction of ethynylphenylureas.⁷ When substrate **3.41**, which contains both an *N*-methyl and a “capping” trimethylsilyl group on the alkyne, was subjected to reaction with complex **3.3** an intractable mixture of products was obtained (entry 3). The reasons for this are unclear although analysis of the crude reaction mixture by ¹H NMR spectroscopy suggested that the trimethylsilyl group was incompletely cleaved during the reaction and this probably contributed to the large number of products observed. Reaction of *N*-phenyl-substituted substrate **3.43**, produced 1-methylene-1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one **3.57** in 56% yield (entry 4). The spectral characteristics associated with compound **3.57** closely resembled those of congener **3.56**, particularly the C=O carbonyl stretching

frequency in the IR spectrum, which appeared at 1744 cm^{-1} . The products **3.56** and **3.57** arise from 5-*endo*-dig/5-*exo*-dig reaction cascade process. The conformational effect imposed on the urea group by the methyl or phenyl substituents appears to favour the formation of a smaller ring during the second cyclisation event. However, the electronic impact of such groups cannot be ruled out.

Table 3.5: Reactions of *N,N'*-disubstituted *o*-diynylarylureas **2.9**, **3.41**, **3.42** and **3.43**

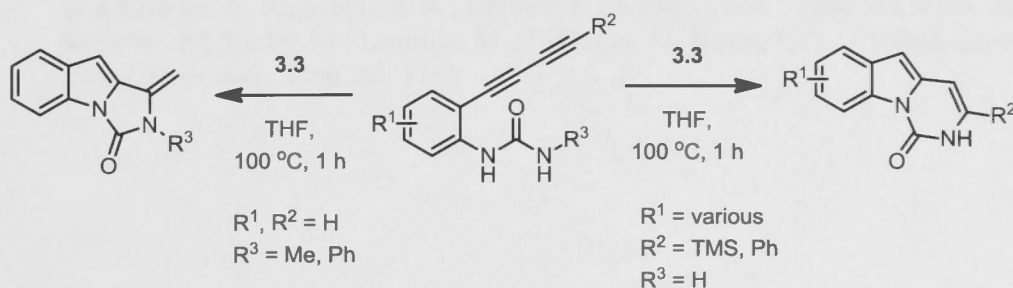
entry	substrate	product	yield (%) ^a
			
1	 2.9		Starting material recovered
2	 3.42	 3.56	29
3	 3.41		Complex mixture
4	 3.43	 3.57	56

Interestingly, the 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one framework associated with compounds **3.56** and **3.57** bears a strong resemblance to the heterocyclic framework of known fungicide **3.58**.⁸ Thus, gold-catalysed reactions of *N,N'*-disubstituted diyndiarylureas would also seem to provide an opportunity to thoroughly investigate the agrochemical properties of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones.

**3.56****3.57****3.58**

3.4 Summary

The gold-catalysed nucleophilic cyclisation reactions of 1-[2-(buta-1,3-diyn-1-yl)aryl]ureas described above has allowed access to pyrimido[1,6-*a*]indol-1(2*H*)-ones substituted at both the aromatic ring and the remote end of the aryldiynes unit, while reactions of *N,N'*-disubstituted substrates led to 1-methylene-1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones.



Scheme 3.10: Alternative heterocycles derived from 1-(2-(buta-1,3-diyn-1-yl)phenyl)ureas.

The collection of compounds generated during these investigations constitutes a small library of novel heterocycles with unknown but potentially interesting biological

activities. Most of them are now being evaluated for their potential agrochemical properties (see *Appendix 1*).

3.5 References

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Chapter Four

Gold-catalysed Cyclisation Reactions of *o*-Diynylpyridylureas: Towards the Total Synthesis of Variolin B

4.1 Overview

The primary synthetic target associated with this work, variolin B (**1.8**), contains a pyridine ring, as do many important agrochemicals such as nicotine (**4.0**) (a naturally occurring insecticide), imidocloprid (**1.11**) (a neoniconatoid insecticide) and trichlopyr (**4.2**) (a herbicide) (**Figure 4.1**). Accordingly, methods that allow for the synthesis of novel compounds incorporating a pyridine ring, such as variolin B, are of great value to the agrochemical industry.

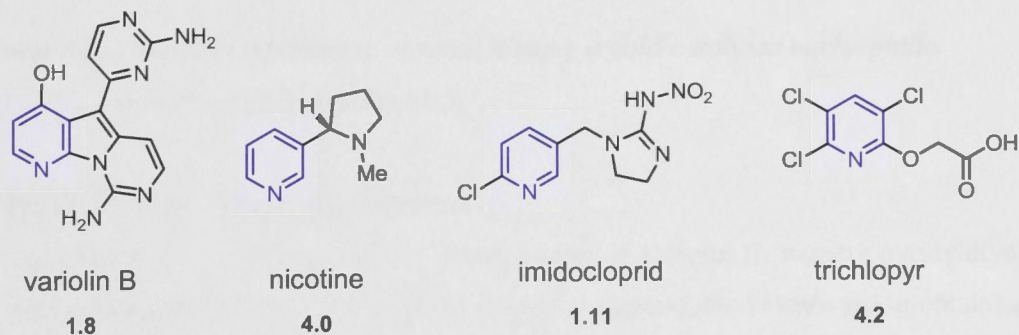


Figure 4.1. Variolin B and some agrochemicals that contain a pyridine ring (pyridine ring highlighted in blue).

analysis, iodopyridine (**1.68**) is required for the synthesis of variolin B. However, there is no reported synthesis of this compound. Accordingly, we sought to develop one.

4.2.1 Preparation of the Pyridine 1.68.

The reactivity and physical properties of the pyridine ring are significantly different from those of simple benzenoid systems. For example, the 2- and 4-positions of the pyridine ring are electrophilic, and the 3-position is nucleophilic, in contrast to the essentially entirely nucleophilic nature of the phenyl ring (**Figure 4.2**).² Furthermore, the lone pair of electrons on the nitrogen give pyridine a pK_aH of 5.20 making compounds embodying this ring rather basic.³

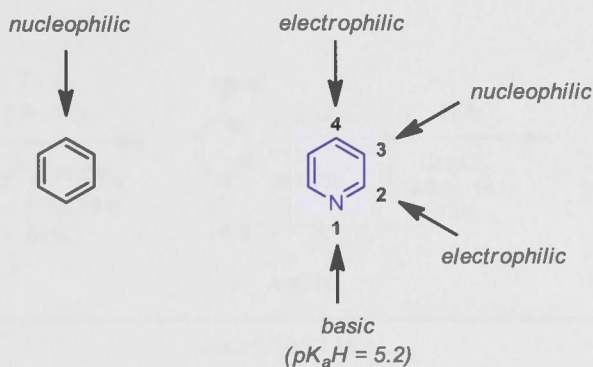
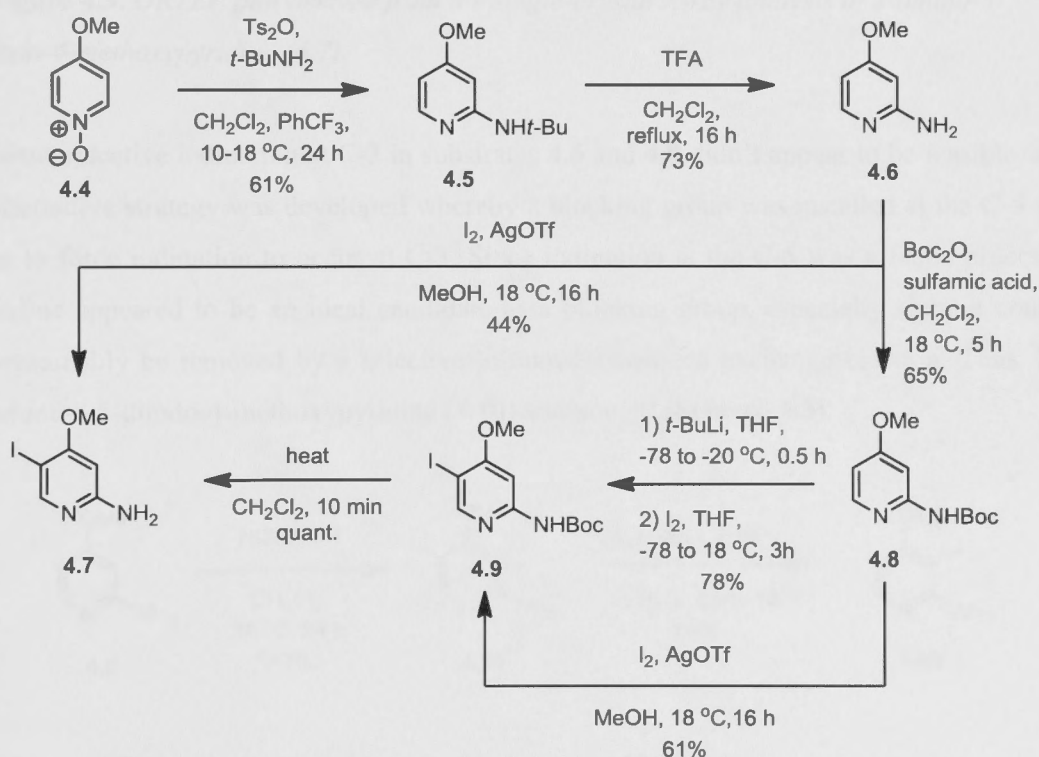


Figure 4.2. Comparison of the reactivities of the benzene and pyridine ring systems.

Thus, it was expected the amino and/or methoxy groups required on the pyridine ring in sub-target **1.68** could be introduced at the electrophilic positions of the pyridine ring and the iodine at the nucleophilic positions. Initially, amination of 4-methoxypyridine-*N*-oxide (**4.4**) (**Scheme 4.2**) with *tert*-BuNH₂ in the presence of tosic anhydride was performed following protocols reported by Yin *et al.*⁴ This afforded 2-(*tert*-butylamino)-4-methoxypyridine (**4.5**) in 61% yield. Treatment of compound **4.5** in refluxing trifluoroacetic acid effected removal of the *tertiary*-butyl group and thus providing 2-amino-4-methoxypyridine **4.6** in 73% yield. It was envisaged that the iodine atom required at the 3-position in sub-target **1.71** could be introduced by direct iodination given that this position on the pyridine ring is nucleophilic and *ortho*-related to two

electron-donating substituents. However, attempts to do so using $I_2/AgOTf$ led exclusively to the undesired 5-iodo regioisomer **4.7**, the structure of which was established by single-crystal X-ray analysis (**Figure 4.3**). Highly selective *o*-iodinations are commonly reported for pyridines using the *Directed-ortho-Metallation* (DoM) method.⁵ Accordingly, compound **4.6** was converted into the carbamate **4.8** in 65% yield by treating it with di-*tert*-butyl dicarbonate in the presence of sulfamic acid (5 mol%) as a catalyst.⁶ Unfortunately, the lithium anion derived from compound **4.8** reacted to give the 5-iodopyridylcarbamate **4.9** (78%) exclusively as established through acid-catalysed conversion of this into the previously observed iodide **4.7**. Similarly, treatment of compound **4.8**, with $I_2/AgOTf$ gave compound **4.9** in 61% yield and as the only identifiable product of reaction.



Scheme 4.2: Outcomes of the iodination of pyridines **4.6** and **4.8**.

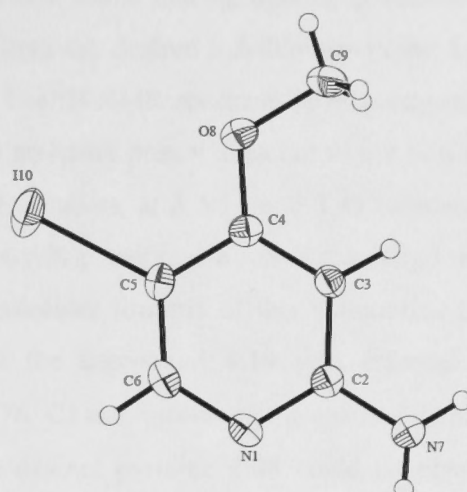
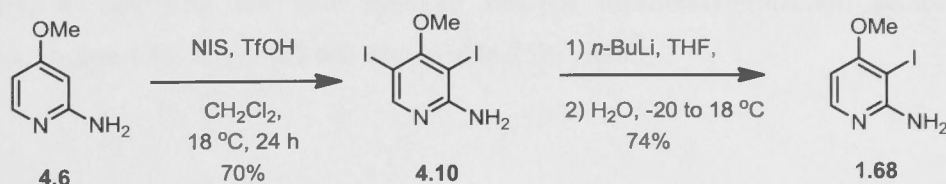


Figure 4.3. ORTEP plot derived from the single-crystal X-ray analysis of 2-amino-5-iodo-4-methoxypyridine (**4.7**).

Since selective iodination at C-3 in substrates **4.6** and **4.8** didn't appear to be feasible, an alternative strategy was developed whereby a blocking group was installed at the C-5 so as to force iodination to occur at C-3. Since iodination at the C-5 was a facile process, iodine appeared to be an ideal candidate as a blocking group, especially since it could presumably be removed by a selective lithium-for-halogen exchange reaction. Thus, 2-amino-3,5-diiodo-4-methoxypyridine (**4.10**) was sought (**Scheme 4.3**).



Scheme 4.3: Preparation of the desired iodopyridine **1.68**.

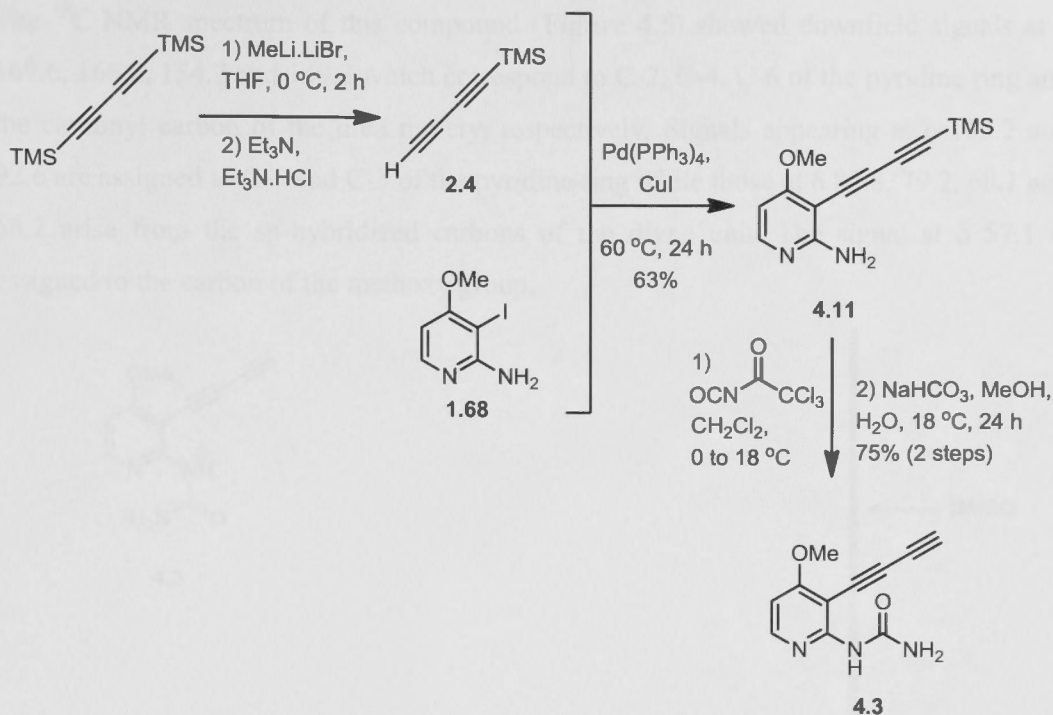
Attempts to directly diiodinate compound **4.6** using an excess of either $I_2/AgOTf$, I_2/Ag_2CO_3 or NIS/Ag_2SO_4 proved ineffective, giving mainly the undesired 5-iodo regioisomer although, encouragingly, this was accompanied by traces of the desired 3,5-

diiodo-product. Finally, it was found that by treating pyridine **4.6** with a mixture of an excess of NIS in TfOH, then the desired 3,5-diiodopyridine **4.10** could be obtained in 70% yield (**Scheme 4.3**). The ^1H NMR spectrum of this compound showed a singlet at δ 8.14 corresponding to the aromatic proton adjacent to the nitrogen atom in the pyridine ring. Two other diagnostic singlets, at δ 5.17 and 3.85 (corresponding to the N-H₂ and methoxy protons, respectively), were also observed. High resolution mass spectral analysis confirmed the molecular formula of this material as C₆H₆I₂N₂O. Gratifyingly, selective deiodination of the compound **4.10** was effected by treating it with *n*-butyllithium (2 equiv. at -78 °C) and quenching the ensuing dianion with water at -20 °C. Using this procedure the desired pyridine **1.68** could be obtained in 74% yield. The regioselectivity of the deiodination process was confirmed by ^1H NMR spectral analysis. In particular, the relevant spectrum displayed two mutually coupled doublets ($J = 6.0$ Hz) at δ 7.88 and 6.17 that correspond to the vicinally related hydrogens at C-6 and C-5, respectively, in **1.68**.

4.2.1 Completion of the synthesis of compound 1.68

4.2.2 Preparation of *o*-Diynylpyridylureas Cyclisation Precursor **4.3** and **4.12**

With access to multi-gram quantities of the required pyridine (**1.71**) achieved, its elaboration into the required cyclisation substrate **4.3** could be pursued. Thus, 3-iodopyridine **1.71** was converted, *via* a Sonagashira cross-coupling reaction with freshly prepared diyne **2.4**, into compound **4.11** which was obtained in 63% yield (**Scheme 4.4**). Finally, by applying the now standard one-pot ureation/deprotection protocol to aminopyridine **4.11**, target **4.3** was obtained in 75% yield.



Scheme 4.4: Completion of the synthesis of cyclisation precursor **4.3**.

With some exceptions, this compound displayed the anticipated spectroscopic characteristics shared by the other diynylaryleureas prepared during the course of this work. For example the C=O stretching band observed in the IR spectrum appeared at 1730 cm⁻¹. The high frequency of this absorption is likely to be the result of hydrogen bonding between the urea and the pyridyl nitrogen moieties (**Figure 4.4**).

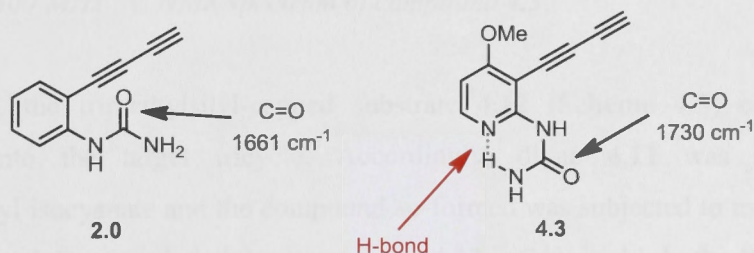


Figure 4.4: Effect of hydrogen bonding on the C=O stretching frequency of the urea moiety within compound **4.3**.

The ^{13}C NMR spectrum of this compound (**Figure 4.5**) showed downfield signals at δ 169.6, 166.2, 154.7 and 149.3 which correspond to C-2, C-4, C-6 of the pyridine ring and the carbonyl carbon of the urea moiety, respectively. Signals appearing at δ 102.2 and 92.6 are assigned to C-5 and C-3 of the pyridine ring while those at δ 84.8, 79.2, 68.1 and 66.2 arise from the sp-hybridized carbons of the diyne unit. The signal at δ 57.1 is assigned to the carbon of the methoxy group.

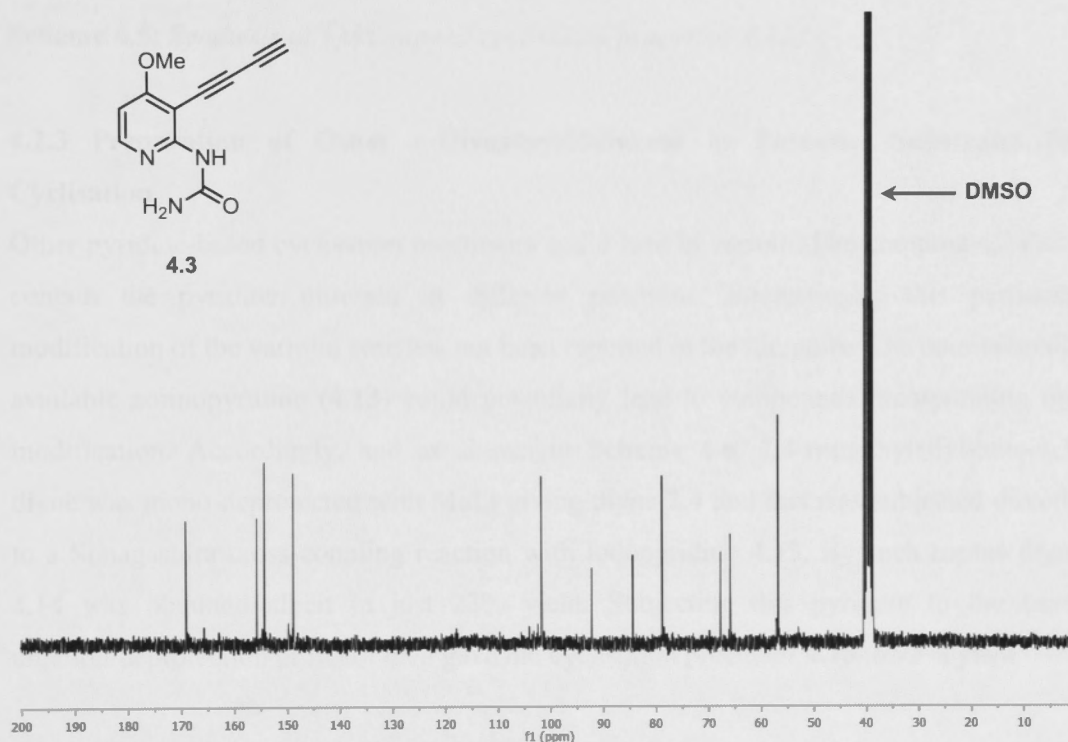
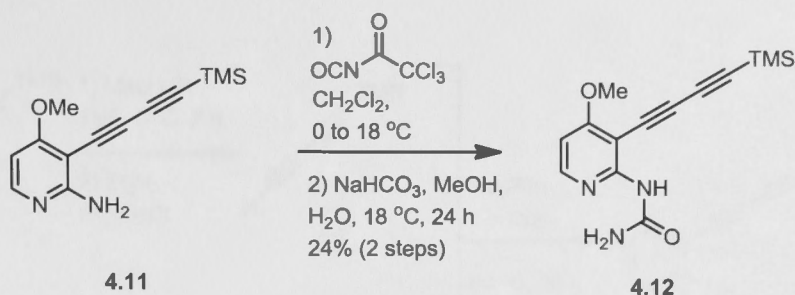


Figure 4.5. 300 MHz ^{13}C NMR spectrum of compound **4.3**.

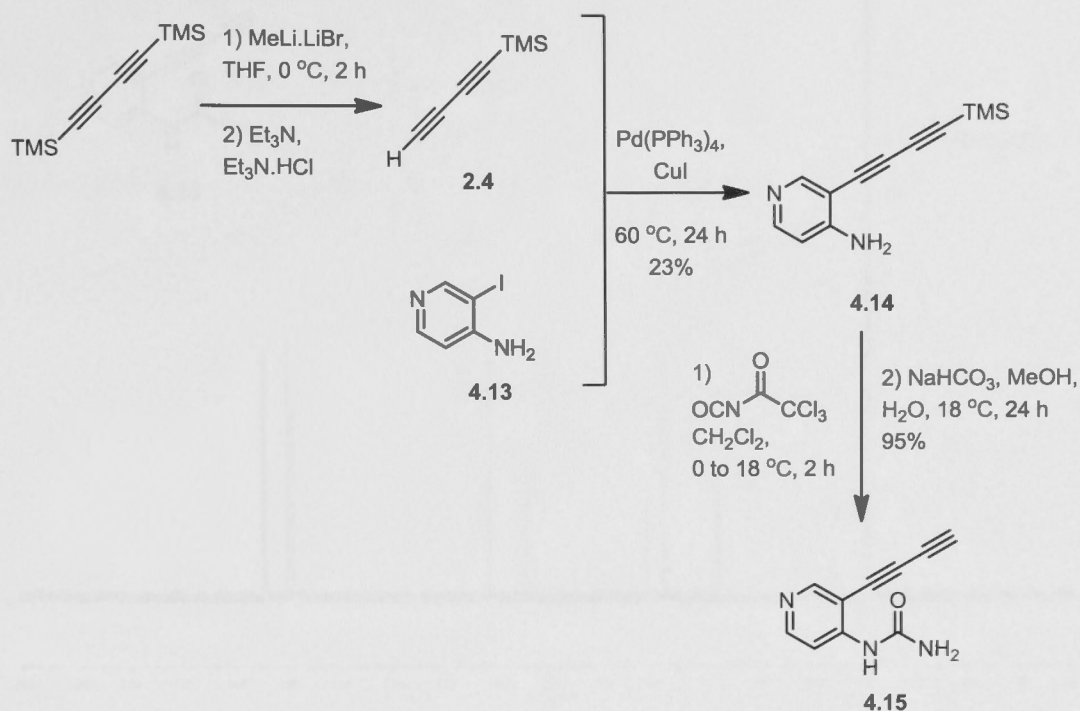
In principle, the trimethylsilyl-capped substrate **4.12** (**Scheme 4.5**) could also be converted into the target tricycle. Accordingly, diyne **4.11** was ureated with trichloroacetyl isocyanate and the compound so-formed was subjected to mild hydrolysis which produced the trimethylsilyl-capped diyne **4.12** in 24% yield. In the IR spectrum of this compound the C=O stretching band was observed at 1712 cm^{-1} .



Scheme 4.5: *Synthesis of TMS-capped cyclisation precursor 4.12.*

4.2.3 Preparation of Other *o*-Diynylpyridylureas as Potential Substrates for Cyclisation

Other pyridine-based cyclisation precursors could lead to variolin-like compounds which contain the pyridine nitrogen in different positions. Interestingly, this particular modification of the variolin core has not been reported in the literature. The commercially available aminopyridine (**4.13**) could potentially lead to compounds incorporating this modification. Accordingly, and as shown in **Scheme 4.6**, 1,4-trimethylsilyl-buta-1,3-diyne was mono-deprotected with MeLi giving diyne **2.4** and this was subjected directly to a Sonagashira cross-coupling reaction with iodopyridine **4.13**. By such means diyne **4.14** was obtained albeit in just 23% yield. Subjecting this pyridine to the usual ureation/deprotection protocol then gave the cyclisation precursor **4.15** in 95% yield.



Scheme 4.6: Preparation of cyclisation precursor **4.15**

The ^{13}C NMR spectrum of compound **4.15** displayed signals at δ 81.9, 78.7, 69.1 and 68.3 arising from the four sp-hybridised carbons in of the diynyl unit. The IR spectrum showed a C=O stretching band at 1680 cm^{-1} suggesting that no intramolecular hydrogen bonding existed with this compound (*c.f.* **Figure 4.4**).

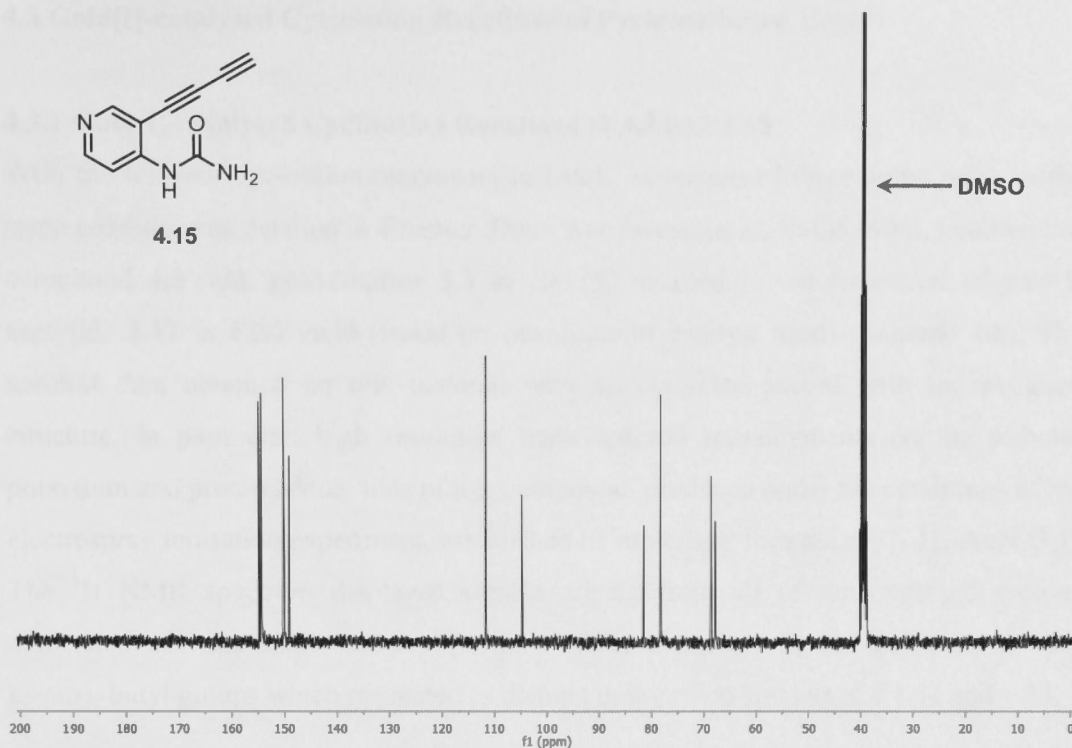
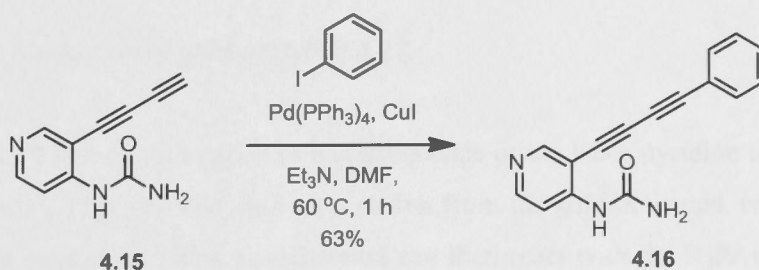


Figure 4.6. 400 MHz ^{13}C NMR spectrum of compound **4.15** (recorded in D_6 -DMSO).

Pyridyldiyne **4.15** could also be capped with a phenyl group. This was affected by employing a second Sonagashira cross-coupling reaction, this time between **4.15** and iodobenzene and so providing the “capped” system **4.16** in 63% yield (Scheme 4.7).

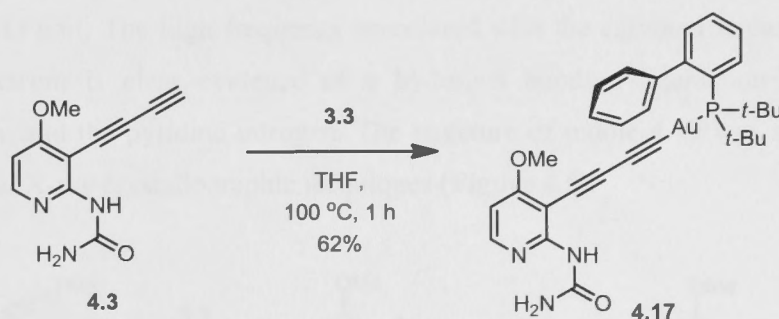


Scheme 4.7: Sonagashira cross-coupling reaction of terminal diyne **4.15** to produce the phenyl-capped system **4.16**.

4.3 Gold[I]-catalysed Cyclisation Reactions of Pyridine-based Diynes

4.3.1 Gold[I]-catalysed Cyclisation Reactions of 4.3 and 4.18

With the relevant cyclisation precursors in hand, subjection of these compounds to the same conditions as detailed in *Chapter Three* was investigated. In the event, treatment of compound **4.3** with gold-catalyst **3.3** at 100 °C resulted in the formation of gold(I) acetylide **4.17** in 62% yield (based on quantities of catalyst used) (**Scheme 4.8**). The spectral data obtained on this material were in complete accord with the assigned structure. In particular, high resolution mass spectral measurements on the sodium, potassium and proton adduct ions of this compound, produced under the conditions of the electrospray ionisation experiment, established its molecular formula as $C_{31}H_{35}AuN_3O_2P$. The 1H NMR spectrum displayed signals arising from all of the expected protons associated with the alkyl- and aryl-portions of the phosphine ligand including the two *tertiary*-butyl groups which resonated as distinct nine-proton singlets at δ 1.43 and 1.38.

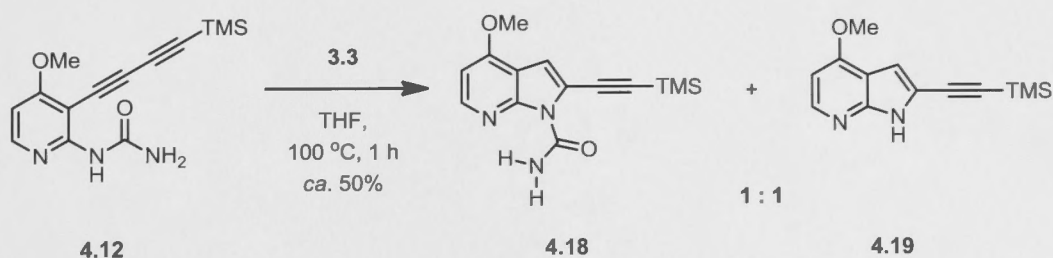


Scheme 4.8: Formation of gold-acetylide **4.17**.

Compound **4.17** is thought to arise as a consequence of the basic pyridine unit within the starting material. This unit can abstract a proton from the gold-activated, terminal diyne group and the acetylenic anion so-generated can then react with the R_3PAu^+ form of the catalyst, resulting in the observed neutral and stable gold acetylide complex **4.17**.

In an effort to prevent the formation of acetylide **4.17**, the TMS-substituted compound **4.12** was investigated. Under the optimal reaction conditions defined earlier compound

4.12 was converted into a 1:1 mixture of the 7-aza-indoles **4.18** and **4.19**. These products could not be completely separated using flash chromatographic techniques and, as a result, were isolated as a mixture in 46% combined yield (**Scheme 4.9**). However, small quantities of both compound **4.18** and **4.19** could be obtained in essentially pure form by selective crystallisation of compound **4.19** from a solution of the mixture in CH_2Cl_2 . Compound **4.19** was thereby obtained as colourless plates, and the solution retained was enriched in 7-aza-indolecarboxamide **4.18**. The structure of the compound **4.18** was established using a combination of MS, ^1H NMR, ^{13}C NMR and IR spectroscopic techniques. In particular, high resolution mass measurements on compound **4.18** confirmed the molecular formula as $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_2\text{Si}$. The ^1H NMR spectrum displayed an “indolic proton” resonance at δ 6.95 and two distinct, broad N-H signals, one at δ 9.95 (corresponding to a hydrogen-bonded N-H proton of the urea) and a second at δ 5.53 (corresponding to the ‘free’ N-H proton of the urea). The ^{13}C NMR spectrum revealed signals due to sp-hybridized carbons at δ 96.4 and 84.1, while the IR spectrum showed a $\text{C}\equiv\text{C}$ stretching band at 1958 cm^{-1} due to the alkyne and another band at 1727 cm^{-1} due to the urea $\text{C}=\text{O}$ unit. The high frequency associated with the carbonyl stretching band in the IR spectrum is clear evidence of a hydrogen bonding interaction between the carboxamide and the pyridine nitrogen. The structure of indole **4.19** was secured using single crystal X-ray crystallographic techniques (**Figure 4.5**).



Scheme 4.9: Formation of aza-indoles **4.18** and **4.19** via the Au(I)-catalysed cyclisation of diyne **4.12**.

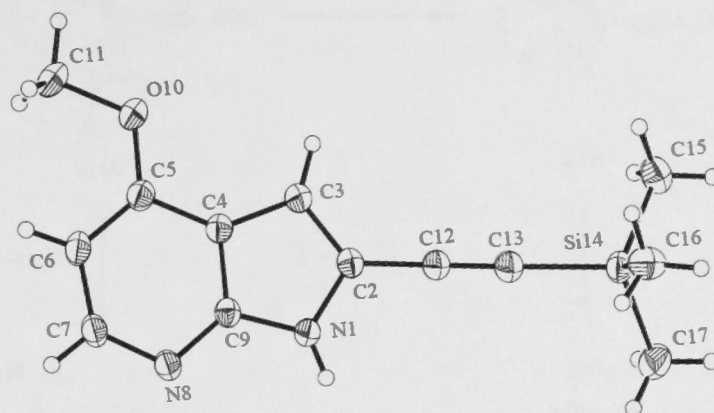
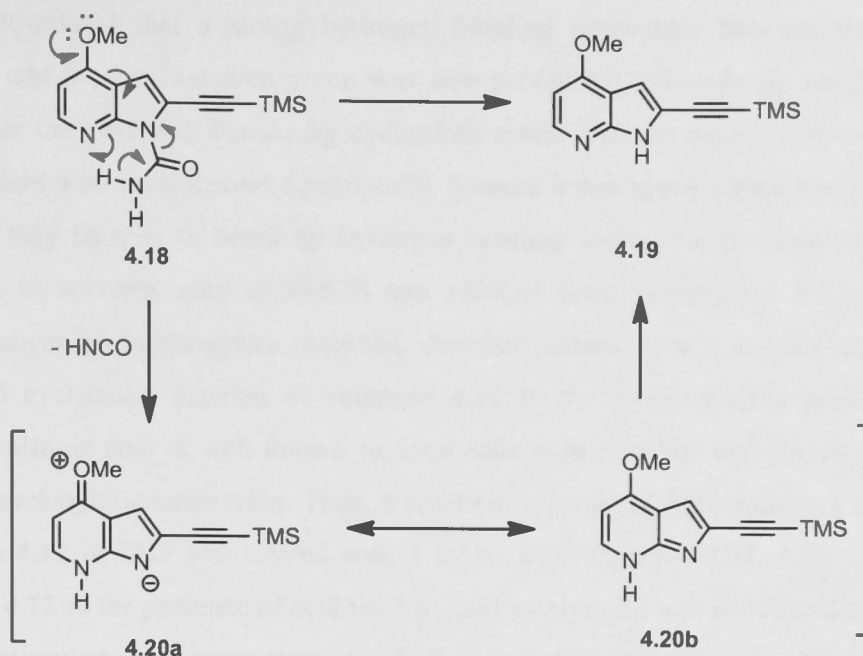


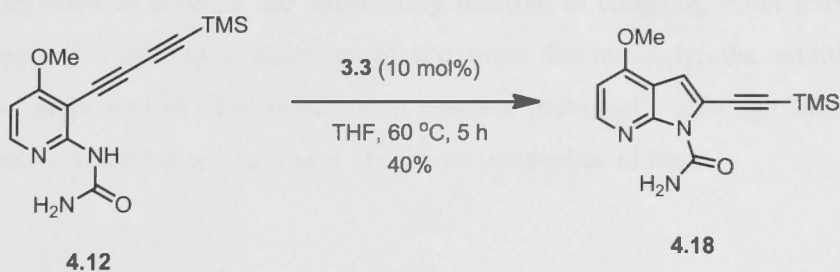
Figure 4.5. ORTEP plot derived from the single-crystal X-ray analysis of indole **4.19**.

Cleavage of the carboxamide moiety within compound **4.18** to give indole **4.19** may well occur *via* the fragmentation process shown in **Scheme 4.10** and thus giving, in the first instance, the resonance stabilised species **4.20** and isocyanate. Tautomerisation of compound **4.20** would give the (presumably thermodynamically more stable) 7-azaindole **4.19**.



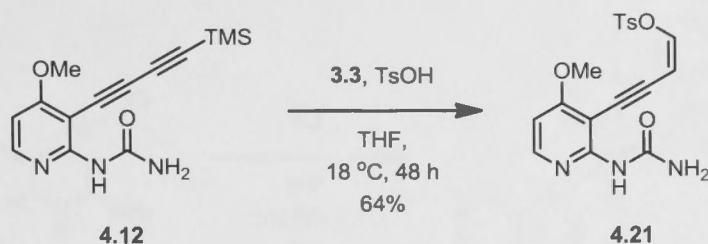
Scheme 4.10: Possible mechanism for the formation of **4.19**.

Reaction of compound **4.12** under milder conditions (microwave irradiation at 60 °C for 5 h and employing 10 mol% of **3.3**) gave product **4.18** in 40% yield with no indication of the formation of fragmentation product **4.19** (Scheme 4.11).



Scheme 4.11: Formation of indoles **4.18** via the Au(I)-catalysed cyclisation of diyne **4.12** at 60 °C.

It was postulated that a strong hydrogen bonding interaction between the pyridine nitrogen and the pendant urea group was also preventing a 6-*endo*-dig reaction taking place after the observed 5-*endo*-dig cyclisation event. Various methods for overcoming this problem were investigated. Specifically, because it was hypothesised that polar protic solvents may be able to break up hydrogen bonding within the pyridylurea substrate, reactions in solvents such as MeOH and *t*-BuOH were investigated but under such circumstances no reaction was observed. Another possibility was to conduct the gold-catalysed cyclisation reaction of substrate **4.12** in the presence of a protic acid. *p*-Toluenesulfonic acid is well known to form salts with pyridine derivatives, and has a weakly nucleophilic counterion. Thus, a reaction was carried out whereby a solution of substrate **4.12** in THF was treated with 1 molar equivalent *p*-TsOH. After stirring the pyridine **4.12** in the presence of acid for 1 h, gold-catalyst **3.3** was added and the reaction mixture stirred at room temperature for 48 h. However, under these conditions, the tosyl enolate **4.21** was obtained in 64% and as the sole isolable product of reaction (**Scheme 4.12**). The structure of the compound **4.21** was assigned based on the ^1H NMR spectrum, which displayed two mutually coupled doublets ($J = 5.7$ Hz) δ 6.83 and 5.66 corresponding to the *cis*-related vicinal enol protons. High resolution mass spectral analysis established the molecular formula as $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_5\text{S}$. The *Z*-configured nature of the alkene residue within product **4.21** is likely the result of the stereospecific addition of the tosylate nucleophile to the opposite side of the alkyne to gold. Thus, even weak nucleophiles such as tosylate are sufficiently reactive to compete, in an intermolecular fashion, with the desired cyclisation of the urea. Interestingly, the addition of the elements of tosic acid to alkynes has been reported previously, although such processes normally occur at higher temperatures and under unusual conditions.⁷



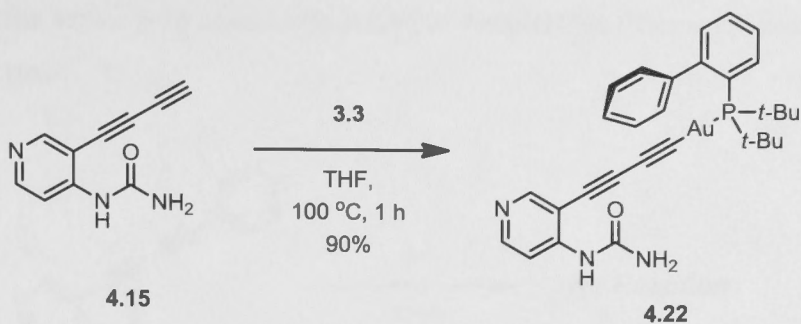
Scheme 4.12: Reaction of **4.12** with gold in the presence of tosic acid, producing **4.21**.

In order to avoid introducing nucleophiles into the reaction mixture while still providing a proton source, non-nucleophilic protic acid HBF₄ was added to a reaction containing substrate **4.12** and catalyst **3.3**. However, this led to the formation of complex mixtures. Attempts to protect the substrate **4.12** as the corresponding *N*-oxide also failed, as did attempts to ‘tie-up’ the pyridyl nitrogen as the corresponding borane, or triethylborane adducts.⁸

The vastly different reactivity that was observed for the pyridine-based cyclisation precursors as compared with the benzene based counterparts was unexpected. Therefore, other pyridine-containing cyclisation precursors were investigated in order to better understand the factors contributing to these disappointing results.

4.3.2 Gold[I]-catalysed Cyclisation Reactions of **4.15** and **4.16**

Under the optimised reaction conditions defined earlier, the pyridyldiyne **4.15** was converted, quantitatively, into the gold acetylide **4.22** (Scheme 4.13) as determined by single-crystal X-ray analysis. The derived ORTEP plot is shown in Figure 4.6. The formation of compound **4.22** presumably involves deprotonation of the terminal acetylene by the basic nitrogen atom within the pyridine ring. The anion thus formed then adds to the vacant coordination site on the gold cation giving the neutral product observed. This process may well be facilitated by coordination of the gold complex to the π -system of the alkyne in the first instance.



Scheme 4.13: Reaction of 4-pyridyl-based substrate **4.15** with Au(I) catalyst **3.3** to form gold acetylide **4.22**.

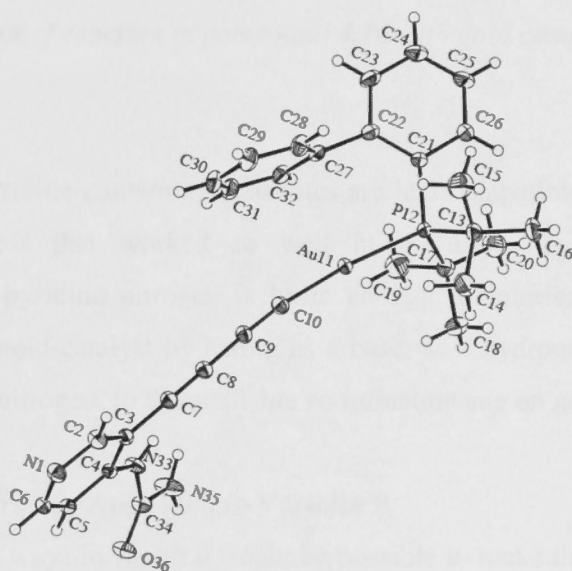
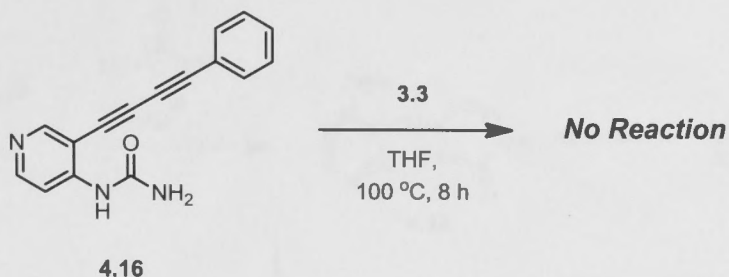


Figure 4.6. ORTEP plot derived from the single crystal X-ray analysis of gold acetylide **4.22**.

In an effort to better understand the factors contributing to the formation of compound **4.22**, the reaction of the phenyl-capped substrate, which cannot form a gold acetylide complex, was investigated. In the event, treatment of compound **4.16** with catalyst **3.3** both under the optimised conditions and ones involving extended reaction times gave no reaction (**Scheme 4.14**). In this case, strong ligation of the substrate, through the pyridyl-

nitrogen, to the active gold complex is probably stopping the desired cyclisation reaction from taking place.



Scheme 4.14: Lack of reaction of compound **4.16** with gold complex **3.3**.

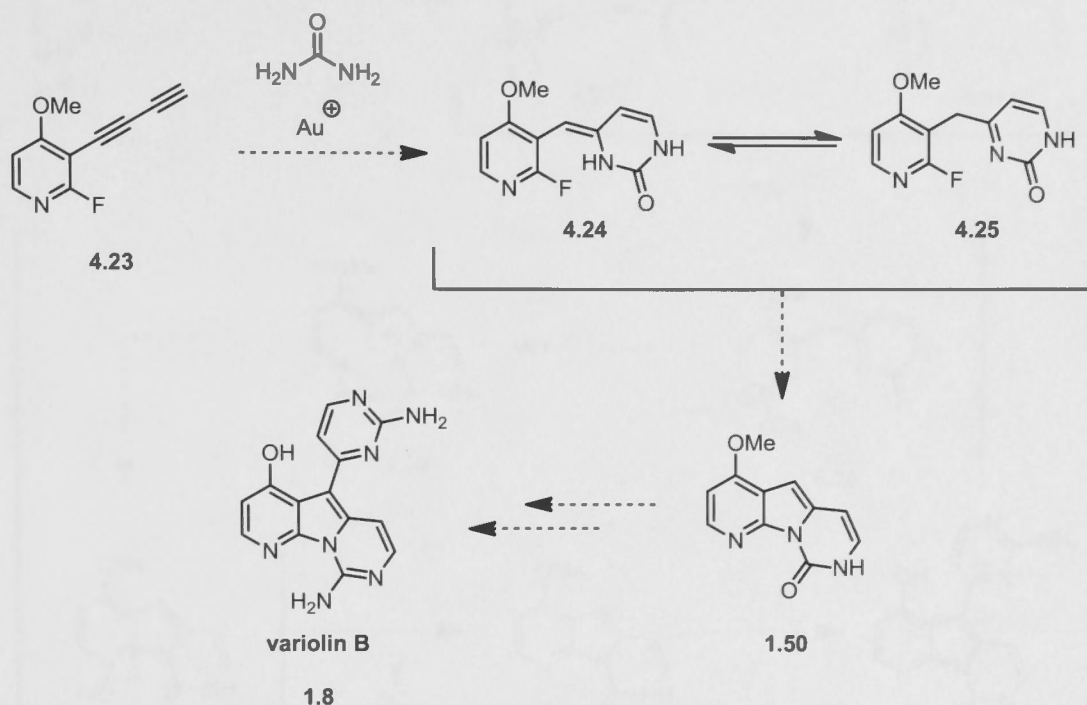
4.4 Summary

It appears that pyridine-containing substrates are less compatible with the gold-catalysed cyclisation process that worked so well in the case of benzene-based systems. Presumably, the pyridine nitrogen is basic enough to interfere significantly with the operation of the gold-catalyst by acting as a base, as a hydrogen bond acceptor and by ligation, through nitrogen, to the available coordination site on gold.

4.5 Second Generation Approach to Variolin B

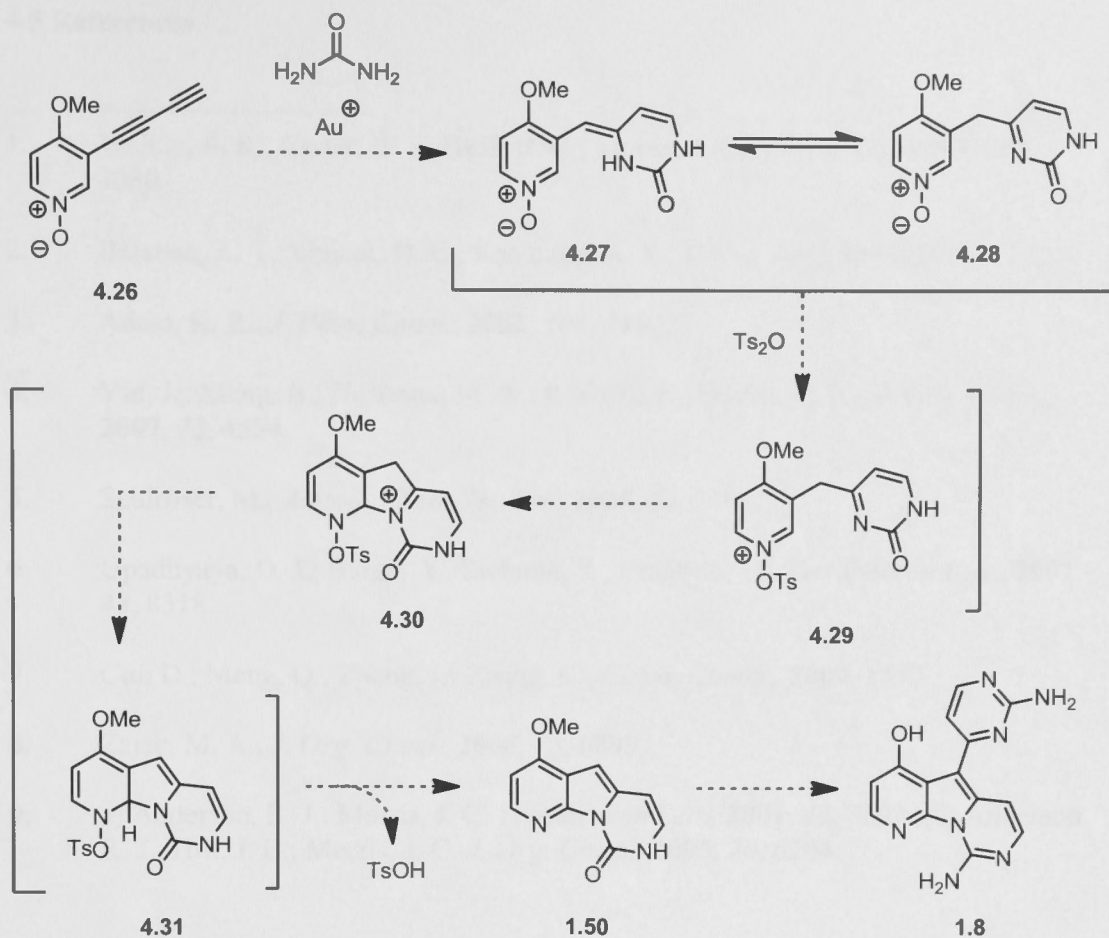
There are various ways in which it might be possible to make the gold-catalysed cascade reaction of a diyne compatible with pyridine-based substrates. For example, an intermolecular/intramolecular cascade reaction of compound **4.23** may be possible, given the demonstrated propensity for these aryldiynes to undergo intermolecular reactions (**Scheme 4.15**). Thus, introducing urea as a reagent in the presence of a gold-catalyst may result in an intermolecular addition to the more accessible terminal alkyne and this could be followed by a 6-*exo*-dig cyclisation to give compounds such as **4.24** or **4.25**. These types of products could then undergo the illustrated intramolecular nucleophilic substitution at the 2-pyridyl position in the presence of base (similar to that demonstrated by Morris).⁹ The fluoride anion not only provides a leaving group for this nucleophilic substitution reaction but, by virtue of being an strongly electron-withdrawing group, it would also be expected to reduce the basicity of the pyridine ring. This reaction sequence

would provide the desired heterocycle **1.50**. Another benefit of this approach is that the starting material **4.23** may be even simpler to prepare than the corresponding urea.



Scheme 4.15: A second generation approach to variolin B.

Similarly, the pyridine *N*-oxide **4.25** (Scheme 4.16) could also undergo an analogous reaction sequence to diene **4.23** shown above. Thus, urea could undergo an addition reaction to the terminal alkyne in the presence of a gold catalyst, followed by a 6-*exo*-dig cyclisation to give products such as **4.27** or **4.28**. Treatment of these products with tosic anhydride would lead to the pyridyltosylate **4.29** which could then undergo a cyclisation reaction and so affording tricycle **4.30**. Deprotonation of compound **4.30** to give conjugate base **4.31**, followed by elimination of *p*-toluenesulfonic acid from the latter compound would then give the desired tricycle **1.50**.



Scheme 4.16: An alternative second generation approach to tricyclic core of variolin B.

Assessing the feasibility or otherwise of the reactions proposed above is now underway.

4.5 References

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Chapter Five

Experimental Section

5.1 General Considerations

Unless otherwise specified, proton (^1H) and carbon (^{13}C) spectra were recorded at 20 °C in CDCl_3 unless specified otherwise (*viz.* either $\text{D}_6\text{-DMSO}$, CD_2Cl_2 or CD_3CN) on a Bruker 800 spectrometer operating at 800 MHz for proton and 200 MHz for carbon nuclei or Varian Mercury 400 spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei or Mercury 300 spectrometer operating at 300 MHz for proton or 75 MHz for carbon nuclei. Signals arising from the residual protio-forms of the solvent were used as the internal standard. ^1H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant J (Hz), relative integral] and multiplicity is defined as: s=singlet; d=doublet; t=triplet; q=quartet; m=multiplet or combinations of the above. The residual CHCl_3 (δ 7.26), DMSO (δ 2.49), CH_2Cl_2 (δ 5.32) or CH_3CN (δ 1.94) were used to reference the ^1H NMR spectra. The central peak (δ 77.0) of the CDCl_3 “triplet” or the central peak (δ 39.5) of the $\text{D}_6\text{-DMSO}$ “septet” were used as the reference signal in proton-decoupled ^{13}C NMR spectra.

Infrared spectra (ν_{max}) were recorded as KBr plates (for solids) or as thin films on KBr discs (for liquids) on a Perkin-Elmer 1800 Series FTIR Spectrometer.

A VG Fisons AutoSpec three sector (ESA/Magnet/ESA) double focussing mass spectrometer was used to obtain low and high resolution electron impact (EI) mass spectra. Low and high resolution electrospray (ESI) mass spectra were obtained on a VG Quattro II triple quadrupole MS instrument operating in either positive and/or negative ionisation modes.

Melting points were measured on an Optimelt automated melting point system and are uncorrected.

The Australian National University's Microanalytical Services Unit based at the Research School of Chemistry, Canberra, Australia, performed the reported elemental analyses.

Analytical thin layer chromatography (TLC) was performed on aluminium backed 0.2 mm thick silica gel 60 F254 plates as supplied by Merck. Eluted plates were visualised using a 254 nm UV lamp and/or by treatment with vanillin/EtOH/water/sulfuric acid (conc.) (12 g:190 mL:10 mL:2 mL) followed by heating. Flash chromatography¹ was performed using the analytical grade solvents indicated and silica gel 60 (0.040-0.0063 mm) as the stationary phase.

Starting materials, reagents and catalyst **3.3** were generally available from the Sigma-Aldrich, Merck, TCI, Strem or Lancaster Chemical Companies and were used as supplied. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. All other solvents were dried using a solvent purification system that is based upon a technology originally described by Grubbs *et al.*²

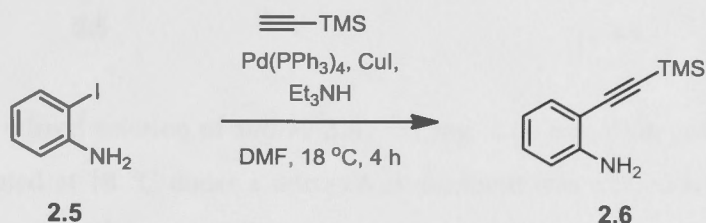
Organic solutions obtained from the work-up of reaction mixtures were dried with anhydrous sodium sulfate (Na_2SO_4) before being filtered and concentrated under reduced pressure on a rotary evaporator.

Room temperature is assumed to be *ca.* 18 °C.

5.2 Experimental Procedures

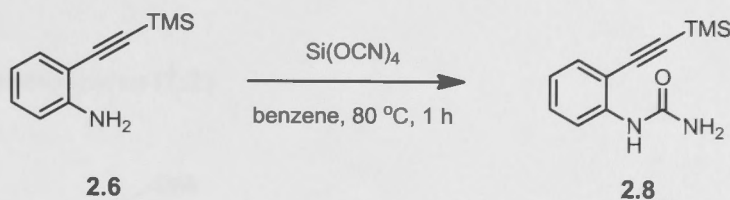
5.2.1 Procedures Associated with Work Described in Chapter Two

2-[(Trimethylsilyl)ethynyl]aniline (2.6)



Following protocols reported by Mikami *et al.*,³ a magnetically stirred solution of 2-iodoaniline (5.00 g, 22.8 mmol) in diethylamine (26 mL) and DMF (5 mL) maintained at 18 °C under a nitrogen atmosphere was treated with ethynyltrimethylsilane (5.05 mL, 36.5 mmol), Pd(PPh₃)₄ (266 mg, 0.23 mmol) and CuI (130 mg, 0.68 mmol). After 4 h a solution of HCl (25 mL of a 1.0 M aqueous solution) was added and the separated aqueous phase was extracted with Et₂O (2 × 25 mL). The combined organic fractions were washed with brine (1 × 25 mL), before being dried (MgSO₄) then filtered and concentrated under reduced pressure. The ensuing crude yellow oil was subjected to flash chromatography (5:95 *v/v* ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (*R_f* = 0.4 in 1:9 *v/v* ethyl acetate/hexane), the title alkyne **2.6**² (4.21 g, 98%) as a yellow oil.

¹H NMR (300 MHz) δ 7.28 (dd, *J*=7.8 and 1.2 Hz, 1H), 7.11 (dd, *J*=7.8 and 1.2 Hz, 1H), 6.68 (td, *J*=7.8 and 1.2 Hz, 1H), 6.65 (td, *J*=7.8 and 1.2 Hz, 1H), 4.21 (broad s, 2H), 0.26 (s, 9H).

1-{2-[2-(Trimethylsilyl)ethynyl]phenyl}urea (**2.8**)

A magnetically stirred solution of aniline **2.6** (757 mg, 4.00 mmol) in anhydrous benzene (1 mL) maintained at 18 °C under a nitrogen atmosphere was treated with a solution of silicon tetraisocyanate (0.14 mL, 200 mg, 1.02 mmol) in anhydrous benzene (6 mL). The ensuing mixture was heated at reflux for 1 h then cooled and the solvent removed under reduced pressure. The crude material thus obtained was dissolved in a solution of water/isopropanol (2 mL of a 1:9 *v/v* mixture) and refluxed for 0.5 h. The gelatinous slurry thus obtained was filtered through a hot sintered glass funnel and the solids thus retained washed with warm acetone (3 × 10 mL). The combined filtrates were concentrated under reduced pressure to a dark-brown oil that was subjected to flash chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂ elution). Concentration of the relevant fractions (*R_f* = 0.2 in 1:19 *v/v* MeOH/CH₂Cl₂) gave the *title urea* **2.8** (286 mg, 31%) as a white powder, m.p. = 175-177 °C.

¹H NMR (300 MHz) D₆-DMSO δ 8.04 (d, *J* = 8.7 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 8.7 Hz, 1H), 7.09 (broad s, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 4.70 (broad s, 2H), 0.28 (s, 9H).

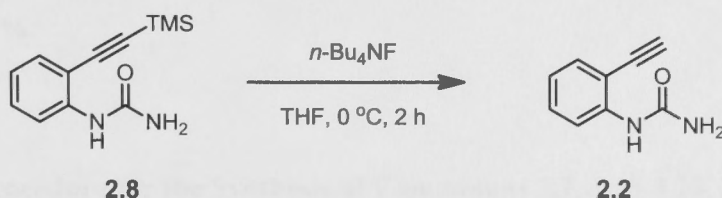
¹³C NMR (100 MHz) D₆-DMSO δ 156.4, 142.1, 133.1, 130.5, 122.4, 120.5, 111.9, 102.0, 101.5, 0.90.

IR ν_{max} /cm⁻¹ 3484, 3342, 3311, 2155, 1666, 1602, 1576, 1540, 1446, 1340, 1249, 867, 845, 755, 645.

Mass Spectrum (ESI) *m/z* 255 [(M+Na)⁺, 73%], 233 [(M+H)⁺, 100], 217 (16), 73 (24).

HRESIMS found: $(M+H)^+$, 233.1101. $C_{12}H_{16}N_2O$ requires $(M+H)^+$, 233.1110.

1-(2-Ethynylphenyl)urea (**2.2**)



A magnetically stirred solution of urea **2.8** (106 mg, 0.46 mmol) in THF (23 mL) maintained at 0 °C (ice-bath) under a nitrogen atmosphere was treated, dropwise, with tetra-*n*-butylammonium fluoride in THF (0.9 mL of a 1.0 M solution in THF). After addition was complete the ice-bath was removed and the reaction mixture was stirred for a further 0.25 h then quenched with NH_4Cl (5 mL of a saturated aqueous solution) and extracted with diethyl ether (4×5 mL). The combined organic fractions were washed with brine (1×25 mL) before being dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing yellow oil was subjected to flash chromatography (silica, 2:98 v/v ethyl acetate/*n*-hexane elution) and concentration of the relevant fractions ($R_f = 0.6$ in 1:9 v/v ethyl acetate/*n*-hexane) afforded the *title urea* **2.2** (55 mg, 75%) as a white powder, m.p. = 164-166 °C.

1H NMR (300 MHz) D_6 -DMSO δ 8.08 (d, $J=8.1$ Hz, 1H), 7.89 (broad s, 1H), 7.35 (d, $J=7.5$ Hz, 1H), 7.26 (t, $J=8.1$ Hz, 1H), 6.90 (t, $J=7.5$ Hz, 1H), 6.45 (broad s, 2H), 4.56 (s, 1H).

^{13}C NMR (75 MHz) D_6 -DMSO δ 155.9, 142.0, 132.6, 129.7, 121.5, 119.2, 110.2, 87.4, 80.0.

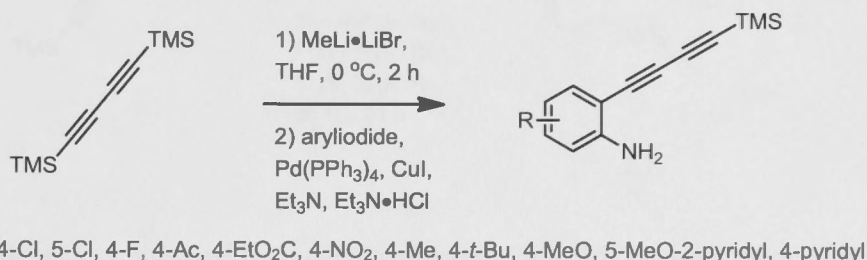
IR ν_{max}/cm^{-1} 3427, 3303, 3209, 1666, 1608, 1578, 1550, 1447, 1360, 753.

Mass Spectrum (EI) m/z 160 ($M^{+\bullet}$, 59%), 117 (100), 90 (62).

HREIMS found: $M^{+\bullet}$, 160.0639. $C_9H_8N_2O$ requires $M^{+\bullet}$, 160.0637.

Elemental Analysis found: C, 67.56; H, 5.27; N, 17.40. $C_9H_8N_2O$ requires C, 67.49; H, 5.03; N, 17.40 %.

A) General Procedure for the Synthesis of Compounds 2.7, 3.20-3.28, 4.11 and 4.14.



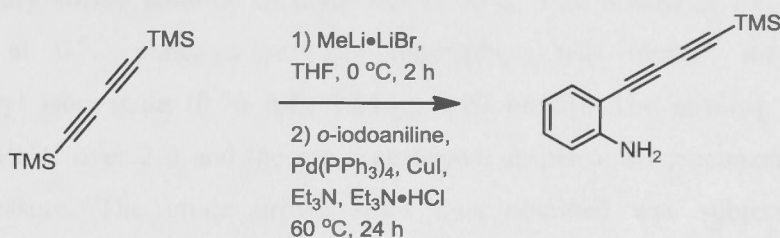
The *title reactions* were performed using a variation of the two-step method reported by Cheng *et al.*⁴

Step 1: A magnetically stirred solution of bis-(trimethylsilyl)-1,3-butadiyne (2 equiv.) in THF (0.75 mL/mmol) maintained at 0 °C under a nitrogen atmosphere was treated with an ethereal solution of methyllithium/lithium bromide complex (2.2 equiv. of a 1.5 M solution in Et_2O). The resultant solution was stirred at 0 °C for 30 min then warmed to 18 °C and stirred at this temperature for a further 60 min. The solution of 1-lithium-4-trimethylsilylbuta-1,3-diyne thus obtained was used immediately in *Step 2* as described below.

Step 2: Et_3N (2 mL/mmol), $\text{Et}_3\text{N}\cdot\text{HCl}$ (2 equiv.), aryl iodide (1 equiv.), $\text{Pd(PPh}_3)_4$ (0.05 equiv.), CuI (0.15 equiv.), were added sequentially to the reaction mixture obtained from *Step 1*. The ensuing dark mixture was stirred vigorously at the specified temperature for

the specified time then SiO₂ (*ca.* 50 equiv.) was added to the cooled reaction mixture and the ensuing slurry was concentrated under reduced pressure then filtered through a short plug of chromatography grade silica that was then washed with ethyl acetate/*n*-hexane or MeOH/CH₂Cl₂. The combined filtrates were concentrated under reduced pressure and the resulting crude material purified as defined below.

2-[(Trimethylsilyl)buta-1,3-diynyl]aniline (**2.7**)

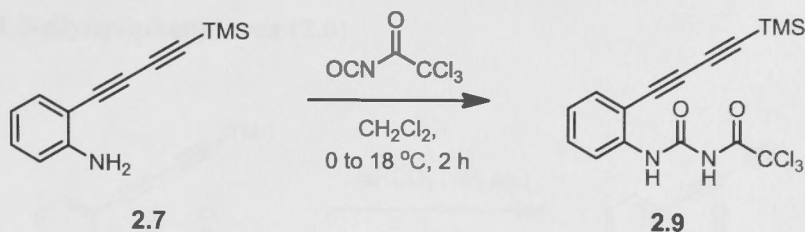


2.7

The *title diyne* was synthesised from *o*-iodoaniline (3.29 g, 15.0 mmol), using the general procedure 5.2.1-A defined above, heating at 60 °C for 24 h. The crude material was subjected to flash chromatography (silica, 2:98 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions (*R*_f = 0.5 in 1:9 *v/v* EtOAc/*n*-hexane) the title diyne **2.7**⁴ (2.60 g, 81% yield) as a brown oil.

¹H NMR (400 MHz) δ 7.30 (d, *J*=6.8 Hz, 1H), 7.14 (dd, *J*=8.0 Hz and 2.0 Hz, 1H), 6.67-6.63 (complex m, 2H), 4.28 (broad s, 2H), 0.24 (s, 9H).

1-(2,2,2-Trichloroacetyl)-3-{2-[4-(trimethylsilyl)buta-1,3-diynyl]phenyl}urea (2.9)



A magnetically stirred solution of diyne **2.7** (1.55 g, 7.26 mmol) in CH_2Cl_2 (15 mL) maintained at 0°C under a nitrogen atmosphere was treated, dropwise, with trichloroacetyl isocyanate (0.96 mL, 1.51 g, 8.00 mmol). The ensuing mixture was warmed to 18°C over 2 h and the resulting brown suspension was concentrated under reduced pressure. The crude brown solid thus obtained was subjected to flash chromatography (silica, CH_2Cl_2) and so affording, after concentration of the appropriate fractions ($R_f = 0.9$ in 5:95 v/v MeOH/ CH_2Cl_2), the *title urea* **2.9** (2.78g, 96%) as a pale yellow solid. Recrystallisation of this material (CH_2Cl_2) afforded colourless needles, m.p. = $174\text{--}179^\circ\text{C}$ (decomp.)

^1H NMR (400 MHz) δ 10.63 (broad s, 1H), 9.23 (broad s, 1H), 8.28 (d, $J=7.6$ Hz, 1H), 7.50 (d, $J=7.6$ Hz, 1H), 7.40 (t, $J=7.6$ Hz, 1H), 7.11 (t, $J=7.6$ Hz, 1H), 0.25 (s, 9H).

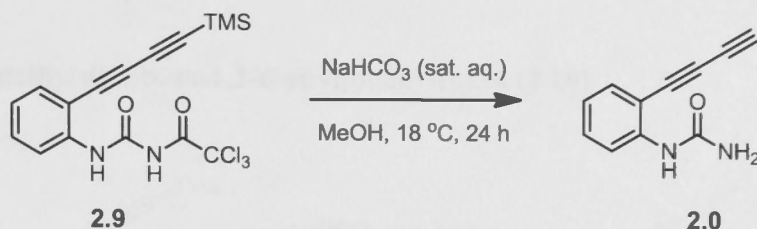
^{13}C NMR (100 MHz) δ 162.5, 149.8, 140.8, 133.4, 131.4, 121.1, 120.8, 112.7, 94.3, 92.3, 87.8, 82.5, 72.1, 0.3.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3236, 3118, 2962, 2201, 2101, 1726, 1711, 1601, 1577, 1538, 1502, 1451, 1250, 841.

Mass Spectrum (EI) m/z 406, 404, 402, 400 ($\text{M}^{+\bullet}$, 2, 13, 30 and 30% respectively), 239 (84), 224 (100).

HREIMS found: M^{+} , 399.9954. $C_{16}H_{15}^{35}Cl_3N_2O_2Si$ requires M^{+} , 399.9968.

1-(2-Buta-1,3-diynyl)phenylurea (**2.0**)



A magnetically stirred solution of urea **2.9** (0.850 g, 2.12 mmol) in MeOH (10 mL) maintained at 18 °C was treated with NaHCO_3 (5 mL of a saturated aqueous solution), after 24 h the ensuing mixture was diluted with water (5 mL) then concentrated under reduced pressure. The resulting mixture was extracted with ethyl acetate (4×50 mL) and the combined organic fractions were then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The white solid thus obtained was subjected to flash chromatography (silica, 1:49 v/v MeOH/ CH_2Cl_2). Concentration of the appropriate fractions ($R_f = 0.4$ in 1:19 v/v MeOH/ CH_2Cl_2) afforded the *title urea* **2.0** (304 mg, 76%) as an unstable white powder, m.p. = 145 °C (decomp.).

$^1\text{H NMR}$ (300 MHz) $\text{D}_6\text{-DMSO}$ δ 8.10 (s, 1H), 8.06 (d, $J=8.7$ Hz, 1H), 7.46 (d, $J=7.8$ Hz, 1H), 7.32 (t, $J=8.7$ Hz, 1H), 6.92 (t, $J=7.8$ Hz, 1H), 6.45 (broad s, 2H), 4.17 (s, 1H).

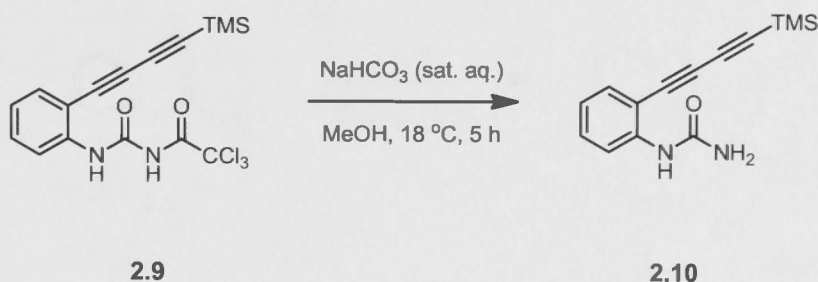
$^{13}\text{C NMR}$ (75 MHz) $\text{D}_6\text{-DMSO}$ δ 155.6, 143.1, 133.7, 130.7, 121.6, 199.6, 108.5, 79.1, 77.5, 71.5, 68.2.

$\text{IR } \nu_{\text{max}}/\text{cm}^{-1}$ 3498, 3332, 3273, 2213, 2198, 1966, 1931, 1897, 1661, 1570, 1542, 1449, 1347.

Mass Spectrum (EI) m/z 184 (M^{+} , 34 %), 167 (9), 141 (100), 140 (30), 114 (26), 113 (26), 63 (15), 40 (22)

HREIMS found: M^{+} , 184.0645. $C_{11}H_8N_2O$ requires M^{+} , 184.0637.

1-{2-[4-(Trimethylsilyl)buta-1,3-diynyl]phenyl}urea (2.10)



A magnetically stirred solution of urea (**2.9**) (168 mg, 0.42 mmol) in MeOH (15 mL) maintained at 18 °C was treated NaHCO₃ (0.1 mL of a saturated aqueous solution), after 5 h the ensuing mixture was diluted with water (5 mL) and concentrated under reduced pressure. The white solid thus obtained was extracted with EtOAc (4 × 50 mL) and the combined organic fractions were dried (Na₂SO₄) and concentrated under reduced pressure. The white solid thus obtained was subjected to flash chromatography (silica, 1:49 v/v MeOH/CH₂Cl₂). Concentration of the appropriate fractions (R_f = 0.4 in 1:19 v/v MeOH/CH₂Cl₂) afforded the *title urea* **2.10** as a white solid (26 mg, 15%).

¹H NMR (400 MHz) δ 8.10 (d, J =7.6 Hz, 1H), 7.42 (t, J =7.6 Hz, 1H), 7.34 (t, J =7.2 Hz, 1H), 7.07 (s, 1H), 6.97 (t, J =7.2 Hz, 1H), 4.86 (s, 2H), 0.24 (s, 9H).

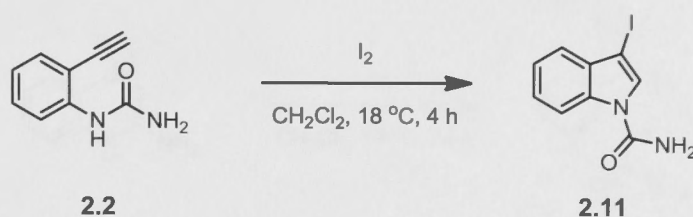
¹³C NMR (100 MHz) δ 155.1, 141.5, 133.3, 130.7, 122.7, 119.5, 110.2, 93.1, 87.3, 80.4, 72.3, -0.4.

IR ν_{max} /cm⁻¹ 3484, 3318, 2204, 2101, 1663, 1533, 1349, 845, 751.

Mass Spectrum (EI) m/z 256 ($M^{+\bullet}$, 33 %), 224 (23), 213 (69), 198 (100), 99 (14).

HREIMS found: $M^{+\bullet}$, 256.1027. $C_{14}H_{16}N_2OSi$ requires $M^{+\bullet}$, 256.1032.

3-Iodo-1*H*-indole-1-carboxamide (**2.11**)



A magnetically stirred suspension of urea (**2.2**) (50 mg, 0.31 mmol) in CH_2Cl_2 (3.6 mL) maintained at 18 °C under a nitrogen atmosphere was treated with iodine (158 mg, 0.62 mmol). After stirring for 4 h in the absence of light $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL of a saturated aqueous solution) was added and the ensuing mixture was stirred vigorously for 5 min. The organic phase was separated then the aqueous phase was extracted with Et_2O (4×3 mL) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The orange solid thus obtained was subjected to flash chromatography (silica, 2:98 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 5:95 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$) the *title indole* **2.11** (18 mg, 20%) as a white solid, m.p. = 130-132 °C (decomp.).

^1H NMR (400 MHz) D_6 -DMSO δ 7.63 (d, $J=8.0$ Hz, 1H), 7.28 (t, $J=8.0$ Hz, 1H), 7.06 (broad s, 2H) 6.96 (t, $J=8.4$ Hz, 1H), 6.82 (d $J=8.4$ Hz, 1H), 6.24 (s, 1H).

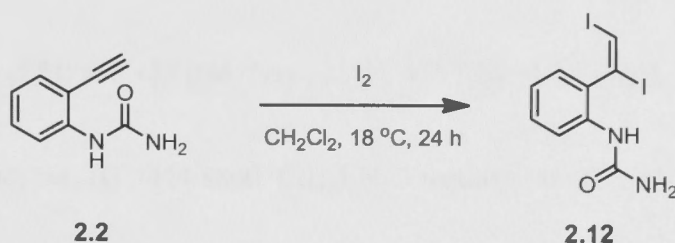
^{13}C NMR (100 MHz) D_6 -DMSO δ 153.4, 152.5, 142.8, 131.9, 124.1, 123.7, 123.4, 118.1, 50.1.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3441, 3093, 2570, 1678, 1612, 1518, 1477, 1464, 1302, 759.

Mass Spectrum (EI) m/z 286 ($M^{+\bullet}$ 100%), 159 (30), 131 (81), 89 (44).

HREIMS found: $M^{+\bullet}$, 285.9604 $C_9H_8IN_2O$ requires $M^{+\bullet}$, 285.9603.

(*E*)-1-[2-(1,2-Diodovinyl)phenyl]urea (2.12)



A magnetically stirred suspension of compound (**2.2**) (350 mg, 2.18 mmol) in CH_2Cl_2 (20 mL) maintained at 18°C under an atmosphere of nitrogen was treated with iodine (1.11 g, 4.37 mmol). After stirring for 24 h in the absence of light $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL of a saturated aqueous solution) was added and the ensuing mixture was stirred vigorously for 5 min. The layers were separated then aqueous layer was extracted with Et_2O (3×10 mL) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (2:98 v/v MeOH/ CH_2Cl_2) and two fractions, A and B were thereby obtained.

Concentration of fraction A ($R_f = 0.5$ in 5:95 v/v MeOH/ CH_2Cl_2) gave indole **2.11** (403 mg, 64%) as a white solid that was identical, as judged by ^1H NMR spectroscopic analysis, with authentic material.

Concentration of fraction B ($R_f = 0.4$ in 5:95 v/v MeOH/ CH_2Cl_2) gave the *title urea* **2.12** (182 mg, 20%) as a pale yellow solid, m.p. $120\text{--}131^\circ\text{C}$ (decomp.).

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.08 (d, $J=8.0$ Hz, 1H), 7.75 (s, 1H), 7.47 (s, 1H) 7.20 (t, $J=6.8$ Hz, 1H), 6.98-6.90 (m, 2H), 6.25 (broad s, 2H).

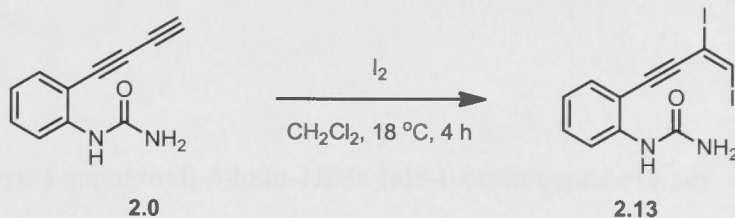
^{13}C NMR (75 MHz) $\text{D}_6\text{-DMSO}$ δ 156.6, 136.8, 133.2, 129.9, 128.9, 122.4, 121.3, 95.1, 90.2.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3488, 3408, 3383, 3350, 3314, 3057, 1954, 1921, 1666, 1574, 1528, 1444, 1341, 1100.

Mass Spectrum (ESI) m/z 437 $[(\text{M}+\text{Na})^+]$, 23%, 415 $[(\text{M}+\text{H})^+]$, 100%, 161 (75).

HRESIMS found: $(\text{M}+\text{H})^+$, 414.8800. $\text{C}_9\text{H}_8\text{I}_2\text{N}_2\text{O}$ requires $(\text{M}+\text{H})^+$, 414.8804.

(*E*)-1-[2-(3,4-Diiodobut-3-en-1-ynyl)phenyl]urea (2.13)



A magnetically stirred solution of urea **2.0** (150 mg, 0.82 mmol) in CH_2Cl_2 (15 mL) maintained at 18°C under a nitrogen atmosphere was treated with iodine (1.25 g, 4.93 mmol). After 4 h stirring in the absence of light $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL of a saturated aqueous solution) was added and the ensuing mixture was stirred vigorously for 5 min. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (4×10 mL) and combined organic portions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The orange solid was subjected to flash chromatography (silica, 1:99 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$) to afford, after concentration of the appropriate fractions ($R_f =$

0.6 in 5:95 v/v MeOH/CH₂Cl₂), the *title enyne* **2.13** (198 mg, 43%) as a white solid, m.p. = 134-140 °C (decomp.).

¹H NMR (300 MHz) D₆-DMSO δ 7.99 (d, *J*=8.0 Hz, 1H), 7.86 (s, 1H), 7.85 (s, 1H), 7.36 (d, *J*=7.6 Hz, 1H), 7.32 (t, *J*=8.0 Hz 1H), 6.95 (t, *J*=7.6 Hz, 1H), 6.35 (s, 2H).

¹³C NMR (75 MHz) D₆-DMSO δ 155.4, 141.2, 132.1, 130.4, 121.7, 119.9, 109.8, 96.9, 94.1, 91.9, 72.8.

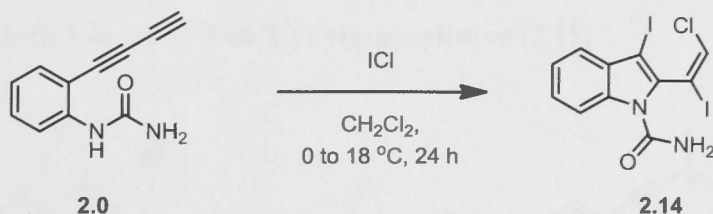
IR ν_{max}/cm⁻¹ 3410, 3372, 3345, 2189, 1659, 1530, 1445, 756.

Mass Spectrum (ESI) *m/z* 461 [(M + Na)⁺, 100%], 414 (12).

HRESIMS found: (M+Na)⁺, 460.8625. C₁₁H₈N₂OI₂ requires (M+Na)⁺, 460.8624.

Elemental Analysis Found: C, 30.25; H, 1.55; N, 6.15. C₁₁H₈N₂OI₂ requires C, 30.16; H, 1.84; N, 6.40 %.

2-[(*E*)-2-Chloro-1-iodovinyl]-3-iodo-1*H*-indole-1-carboxamide (**2.14**)



A magnetically stirred solution of urea **2.0** (101 mg, 0.54 mmol) in CH₂Cl₂ (30 mL) maintained at 0 °C under a nitrogen atmosphere was treated, dropwise, with iodine monochloride (0.165 mL, 534 mg, 3.28 mmol). The mixture was warmed to 18 °C over 24 h in the absence of light then Na₂S₂O₃ (10 mL of a saturated aqueous solution) was added and the ensuing mixture was stirred vigorously for 5 min. The organic phase was

separated and the aqueous phase was extracted with ethyl acetate (3×10 mL). The combined organic portions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The orange solid thus obtained was subjected to flash chromatography (silica, 0.5:99.5 v/v MeOH/ CH_2Cl_2) to afford, after concentration of the appropriate fractions ($R_f = 0.6$ in 5:95 v/v MeOH/ CH_2Cl_2), the *title indole* **2.14** (157 mg, 50%) as a yellow powder, m.p. = 120-130 °C (decomp.).

^1H NMR (300 MHz) δ 7.40 (d, $J=7.8$ Hz, 1H), 7.04 (d, $J=7.2$ Hz 1H), 6.75-6.67 (m, 2H), 6.54 (s, 1H), 6.18 (broad s, 2H).

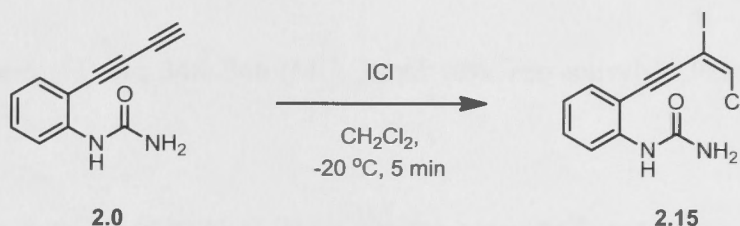
^{13}C NMR (75 MHz) $\text{D}_6\text{-DMSO}/\text{CDCl}_3$ δ 152.8, 149.7, 143.6, 135.5, 132.1, 125.4, 123.5, 123.1, 115.8, 82.2, 70.0.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3448, 3057, 1702, 1673, 1617, 1583, 1564, 1460, 1380, 1294, 750.

Mass Spectrum (EI) m/z 474 and 472 ($\text{M}^{+\bullet}$, 13 and 38%, respectively), 345 (75), 310 (100) 218 (81), 155 (44).

HREIMS found: $\text{M}^{+\bullet}$, 471.8322. $\text{C}_{11}\text{H}_7^{35}\text{ClI}_2 \text{N}_2\text{O}$ requires $\text{M}^{+\bullet}$, 471.8336.

(E)-1-[2-(4-Chloro-3-iodobut-3-en-1-ynyl)phenyl]urea (2.15)



A magnetically stirred solution of diene **2.0** (245 mg, 1.33 mmol) in CH_2Cl_2 (40 mL) maintained at -20°C under a nitrogen atmosphere was treated, dropwise, with iodine

monochloride (0.35 mL of a 1.0 M solution in CH_2Cl_2). After 5 min $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL of a saturated aqueous solution) and the ensuing mixture was stirred vigorously for 5 min. The organic layer was then separated and the aqueous layer was extracted with ethyl acetate (4×20 mL) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated. The orange solid thus obtained was subjected to flash chromatography ($0.5:0.5:99 \rightarrow 0.5:2:97.5$ v/v/v $\text{Et}_3\text{N}/\text{MeOH}/\text{CH}_2\text{Cl}_2$ gradient elution) and two fractions, A and B, were thereby obtained.

Concentration of fraction A ($R_f = 0.5$ in 5:95 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$) gave the previously described vinyl indole **2.14** (98 mg, 20%) as a white solid that was identical, as judged by ^1H NMR spectroscopic analysis, to authentic material.

Concentration of fraction B ($R_f = 0.5$ in 5:95 v/v MeOH/DCM) afforded the title enyne **2.15** (23 mg, 5%) as a pale yellow solid, m.p. 154-157 °C (decomp.).

^1H NMR (300 MHz) D_6 -DMSO δ 8.05 (d, $J=7.5$ Hz, 1H), 7.98 (s, 1H), 7.63 (s, 1H), 7.46 (d, $J=7.5$ Hz 1H), 7.38 (t, $J=7.5$ Hz, 1H), 7.00 (t, $J=7.5$ Hz 1H), 6.39 (s, 2H).

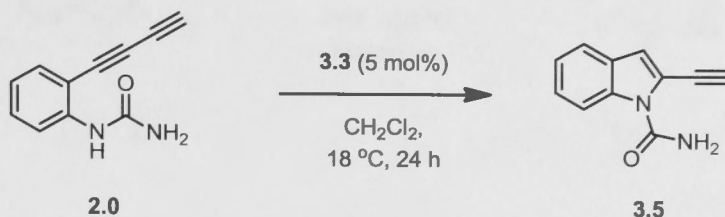
^{13}C NMR (75 MHz) D_6 -DMSO δ 155.4, 141.6, 132.5, 130.8, 121.7, 119.9, 115.3, 109.1, 91.5, 91.2, 90.0.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3374, 3212, 3071, 2922, 2852, 2201, 1669, 1574, 1527, 1452, 1341, 1004, 753.

Mass Spectrum (EI) m/z 348, 346 ($\text{M}^{+\bullet}$, 3 and 10%, respectively), 303 (19), 219 (21), 141 (75), 69 (100).

HREIMS found: $\text{M}^{+\bullet}$, 345.9370. $\text{C}_{11}\text{H}_8^{35}\text{ClIN}_2\text{O}$ requires $\text{M}^{+\bullet}$, 345.9370.

5.2.2 Procedures Associated with Work Described in Chapter Three

2-Ethynyl-1*H*-indole-1-carboxamide (3.5)

A magnetically stirred solution of diyne **2.0** (115 mg, 0.62 mmol) in anhydrous CH₂Cl₂ (7 mL) maintained at 18 °C, under a nitrogen atmosphere was treated with gold complex **3.3** (21 mg 0.03 mmol). After stirring for 24 h at 18 °C chromatography grade silica (*ca.* 200 mg) was added to the reaction mixture and the ensuing slurry was concentrated under reduced pressure. The free flowing powder thus obtained was subjected to flash chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the relevant fractions (*R_f* = 0.7 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title indole* **3.5** (25 mg, 22%) as a white solid, m.p. = 149-151 °C.

¹H NMR (400 MHz) δ 8.41 (d, *J*=8.8 Hz, 1H), 7.52 (d, *J*=7.2 Hz 1H), 7.38 (t, *J*=8.8 Hz 1H), 7.24 (t, *J*=7.2 Hz, 1H), 7.05 (s, 1H), 3.75 (s, 1H), (NH₂ signal not observed).

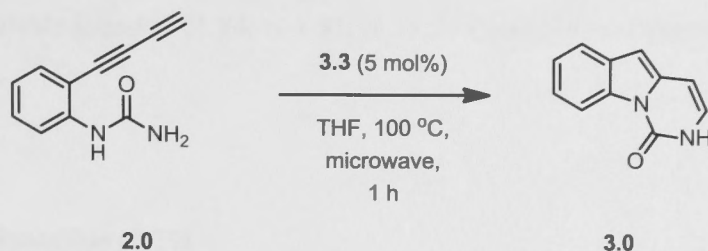
¹³C NMR (100 MHz) δ 152.6, 137.1, 127.6, 126.4, 123.3, 120.7, 118.2, 116.6, 116.4, 86.4, 76.4.

IR ν_{max} /cm⁻¹ 3445, 3293, 2925, 2110, 1688, 1614, 1448, 1407, 1318, 800.

Mass Spectrum *m/z* (EI) 184 (M⁺, 37%), 149 (6), 141 (100), 114 (20).

HREIMS found: M⁺, 184.0639. C₁₁H₈N₂O requires M⁺, 184.0637.

Pyrimido[1,6-a]indol-1(2*H*)-one (3.0)



A 10 mL microwave vessel was charged with diyne **2.0** (35 mg, 0.19 mmol), gold complex **3.3** (8 mg, 0.06 mmol) and capped with a rubber seal. The reaction vessel was evacuated and backfilled with nitrogen several times then anhydrous THF (2 mL) was added and the solution was subjected to microwave irradiation (100 °C for 1 h, ramp time 1 min, power not exceeding 200 W). Chromatography grade silica (~ca. 100 mg) was added then the ensuing slurry was concentrated under reduced pressure. The free flowing powder thus obtained was subjected to flash chromatography (silica, 1:99 v/v MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.6 in v/v 1:19 MeOH/CH₂Cl₂), the *title tricycle* **3.0** (25 mg, 72%) as an off-white solid. Recrystallisation of this material from MeOH/CH₂Cl₂ gave colourless needles. Sublimation 157-162 °C @ atmospheric pressure.

¹H NMR (300 MHz) D₆-DMSO δ 10.84 (broad s, 1H), 8.50 (d, *J*=7.8 Hz, 1H), 7.64 (d, *J*=7.5 Hz 1H), 7.33-7.23 (m, 2H), 6.92 (d, *J*=7.5 Hz, 1H), 6.59 (s, 1H), 6.55 (d, *J*=7.8 Hz 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.7, 136.7, 132.8, 130.7, 126.7, 124.1, 122.4, 120.3, 116.1, 98.7, 97.5.

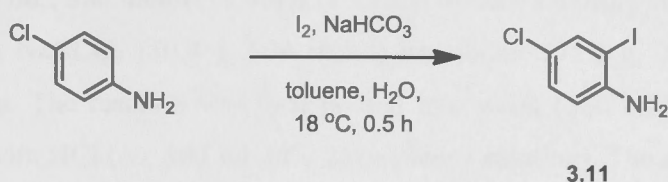
IR ν_{max}/cm⁻¹ 3443, 3205, 3084, 2949, 1842, 1697, 1638, 1449, 1403, 1197, 783.

Mass Spectrum *m/z* (EI) 184 (M⁺, 100%), 155 (31), 129 (16), 102 (20), 92 (19).

HREIMS found: $M^{+\bullet}$, 184.0635. $C_{11}H_8N_2O$ requires $M^{+\bullet}$, 184.0637.

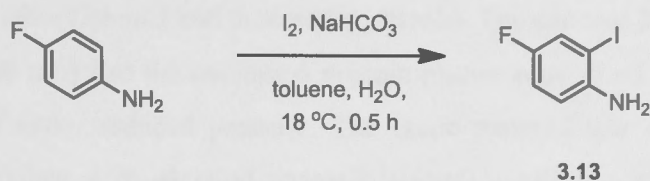
Elemental Analysis found C 71.84, H 4.51, N 15.27 $C_{11}H_8N_2O$ requires C 71.73, H 4.38, N 15.21.

4-Chloro-2-iodoaniline (**3.11**)



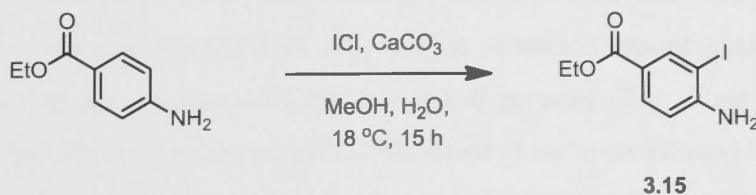
Following protocols reported by Sturino *et al.*,⁵ a magnetically stirred emulsion of 4-chloroaniline (4.84 g, 37.9 mmol) in water (100 mL and toluene (3 mL) maintained at 18 °C was treated with $NaHCO_3$ (5.4 g, 60 mmol) and iodine (7.50 g, 29.8 mmol) over a period of 30 min. The reaction was then poured into water (500 mL) and the pH was adjusted to 6-7 with HCl (*ca.* 30 mL of a 2M aqueous solution). The aqueous layer was extracted with Et_2O (2×30 mL), washed with $Na_2S_2O_3$ (2×5 mL of a 5% aqueous solution) then brine (5 mL). The resulting solution was dried (Na_2SO_4), filtered through a plug of silica then concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 2:98 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the title aniline **3.11**⁶ (9.76 g, 99%) as a low melting, brown solid.

1H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, $J=2.4$ Hz, 1H), 7.10 (dd, $J=8.7$ and 2.4 Hz, 1H), 6.65 (d, $J=8.7$ Hz, 1H), 4.09 (broad s, 2H).

4-Fluoro-2-iodoaniline (3.13)

Following protocols reported by Sturino *et al.*,⁵ a magnetically stirred emulsion of 4-fluoroaniline (36 mL, 380 mmol) in water (1 L) and toluene (30 mL) maintained at 18 °C was treated with NaHCO₃ (50.4 g, 599 mmol) and iodine (75.4 g, 298 mmol) over a period of 30 min. The reaction was then poured into water (500 mL) and the pH was adjusted to 6-7 with HCl (*ca.* 300 mL of a 2M aqueous solution). The aqueous layer was extracted with Et₂O (2 × 300 mL), washed with Na₂S₂O₃ (2 × 50 mL of a 5% aqueous solution) then brine (50 mL). The resulting solution was dried (Na₂SO₄), filtered through a plug of silica then concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of appropriate fractions (*R_f* = 0.7 in 1:9 *v/v* ethyl acetate/*n*-hexane) the title aniline **3.13**⁵ (22.6 g, 25%) as a low melting, brown solid.

¹H NMR (CDCl₃, 300 MHz) δ 7.35 (dd, *J*=7.9 and 2.6 Hz, 1H), 6.90-6.85 (m, 1H), 6.68-6.65 (m, 1H), 3.92 (broad s, 2H).

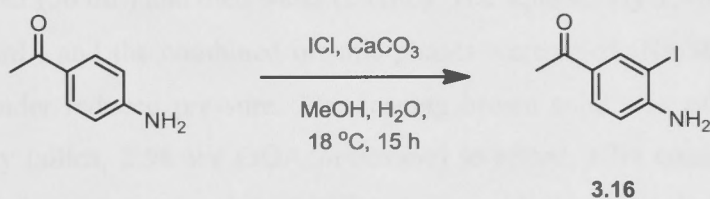
Ethyl 4-amino-3-iodobenzoate (3.15)

Following a modified version of the protocol reported by Gabriele *et al.*,⁷ a magnetically stirred solution of ethyl 4-aminobenzoate (7.0 g, 40 mmol) in ethanol (62 mL) maintained

at 18 °C was treated with a solution of CaCO_3 (6.9 g, 69 mmol) in water (20 mL) followed by ICl (7.3 g, 45 mmol). The mixture was stirred at room temperature for 15 h then diluted with ether (30 mL) and then water (20 mL). The aqueous layer was extracted with ether (3×20 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 4:96 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.3$ in 1:9 v/v ethyl acetate/*n*-hexane), the title aniline **3.15**⁸ (9.89 g, 85%) as an orange solid.

¹H NMR (CDCl_3 , 400 MHz) δ 8.28 (s, 1H), 7.77 (d, $J=8.4$ Hz, 1H), 6.65 (d, $J=8.4$ Hz, 1H), 4.51 (broad s, 2H), 4.27 (q, $J=7.1$ Hz, 2H), 1.32 (t, $J=7.1$ Hz, 3H).

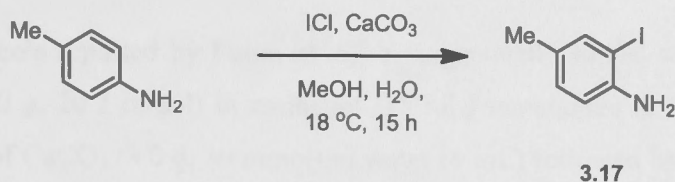
1-(4-Amino-3-iodophenyl)ethanone (**3.16**)



Following protocols reported by Fujita *et al.*,⁹ a magnetically stirred solution of 1-(4-aminophenyl)ethanone (4.05 g, 30.0 mmol) in methanol (20 mL) maintained at 18 °C was treated with a solution of CaCO_3 (4.7 g, 47 mmol) in water (12 mL) followed by a solution of ICl (5.16 g, 31.8 mmol) in methanol (20 mL). The mixture was stirred at 18 °C for 15 h then diluted with ether (30 mL) and then water (20 mL). The aqueous layer was extracted with ether (3×20 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 4:96 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.2$ in 1:9 v/v ethyl acetate/*n*-hexane), the title aniline **3.16**¹⁰ (6.47 g, 83%) as an orange solid.

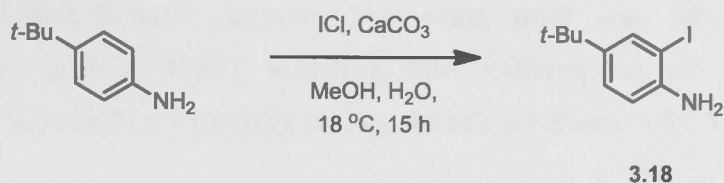
^1H NMR (CDCl_3 , 400 MHz) δ 8.27 (d, $J=1.9$ Hz, 1H), 7.76 (dd, $J=8.2$ and 1.9 Hz, 1H), 6.71 (d, $J=8.2$ Hz, 1H), 2.49 (s, 3H).

2-Iodo-4-methylaniline (3.17)



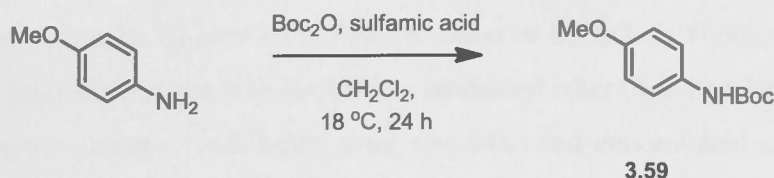
Following protocols reported by Fujita *et al.*,⁹ a magnetically stirred solution of *p*-toluidine (3.33 g, 31.0 mmol) in methanol (25 mL) maintained at 18 °C was treated with a solution of CaCO_3 (4.6 g, 46 mmol) in water (12 mL) followed by a solution of ICl (5.10 g, 31.5 mmol) in methanol (25 mL). The mixture was stirred at 18 °C for 15 h then diluted with ether (30 mL) and then water (20 mL). The aqueous layer was extracted with ether (3×20 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The ensuing brown solid was subjected to flash chromatography (silica, 2:98 v/v EtOAc/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.6$ in 1:9 v/v EtOAc/*n*-hexane), the title aniline **3.17**¹¹ (1.30g, 18%) as a low melting, brown solid.

^1H NMR (CDCl_3 , 400 MHz) δ 7.45 (d, $J=2.4$ Hz, 1H), 6.95 (dd, $J=8.5$ and 2.4 Hz, 1H), 6.66 (d, $J=8.5$ Hz, 1H), 3.85 (broad s, 2H), 2.20 (s, 3H).

4-(*tert*-Butyl)-2-iodoaniline (3.18)

Following protocols reported by Fujita *et al.*,⁹ a magnetically stirred solution of 4-(*tert*-butyl)aniline (3.0 g, 20.2 mmol) in methanol (15 mL) maintained at 18 °C was treated with a solution of CaCO₃ (3.0 g, 30 mmol) in water (8 mL) followed by a solution of ICl (3.30 g, 20.5 mmol) in methanol (16 mL). The mixture was stirred at 18 °C for 15 h then diluted with ether (30 mL) and then water (20 mL). The aqueous layer was extracted with ether (3 × 20 mL) and the combined organic phases were dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 2:98 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions (*R*_f = 0.6 in 1:9 *v/v* ethyl acetate/*n*-hexane), the title aniline **3.18**¹² (1.56 g, 28%) as a dark-brown viscous oil.

¹H NMR (CDCl₃, 400 MHz) δ 7.64 (d, *J*=1.8 Hz, 1H), 7.18 (dd, *J*=8.4 and 1.8 Hz, 1H), 6.71 (d, *J*=8.4 Hz, 1H), 3.97 (broad s, 2H), 1.27 (s, 9H).

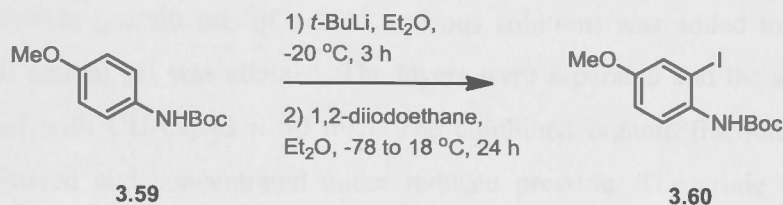
***tert*-Butyl (4-methoxyphenyl)carbamate (3.59)**

Following protocols reported by Upadhyaya *et al.*,¹³ a magnetically stirred suspension of sulfamic acid (93 mg, 0.96 mmol) in *tert*-butyloxycarbonyl (3.90 g, 17.9 mmol) maintained at 18 °C under an atmosphere of nitrogen was treated with *p*-anisidine (2.00 g,

16.2 mmol). After 2 h CH_2Cl_2 (5 mL) was added and the reaction left to stir at 18 °C for a further 22 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), filtered and concentrated under reduced pressure. The white solid was subjected to flash chromatography (silica, CH_2Cl_2) affording, after concentration of the appropriate fractions ($R_f = 0.8$ in 5:95 v/v MeOH/ CH_2Cl_2), the title compound **3.59**¹³ (3.62 g, 99%) as a white solid.

¹H NMR (CDCl_3 , 400 MHz) δ 7.28-7.26 (m, 2H), 6.85-6.83 (m, 2H), 6.38 (broad s, 1H), 3.78 (s, 3H), 1.52 (s, 9H).

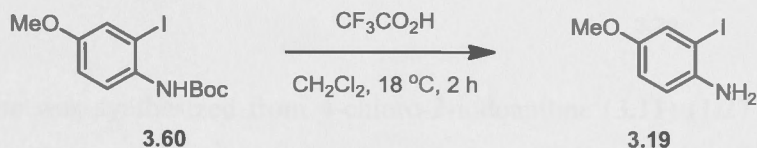
tert-Butyl (2-iodo-4-methoxyphenyl)carbamate (**3.60**)



Following protocols reported by Murphy *et al.*,¹⁴ a magnetically stirred solution of *tert*-butyl (4-methoxyphenyl)carbamate (**3.59**) (2.94 g, 13.1 mmol) in anhydrous diethyl ether (20 mL) maintained at -20 °C under an atmosphere of nitrogen was treated with *tert*-butyllithium (19.7 mL of a 1.4 M solution in pentane, CAUTION!). After stirring at this temperature for 3 h the reaction mixture was cooled to -78 °C and 1,2-diiodoethane (5.54 g, 19.7 mmol) in dry diethyl ether (44 mL) was added and the reaction was gradually warmed to 18 °C over 16 h. After addition of Na_2SO_3 (100 mL of a saturated aqueous solution) the mixture was extracted with diethyl ether (3 $\times$ 20 mL). The organic extracts were then washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 1:9 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.5$ in 1:9 v/v ethyl acetate/*n*-hexane), the title compound **3.60**¹³ (3.519 g, 77%) as a white solid.

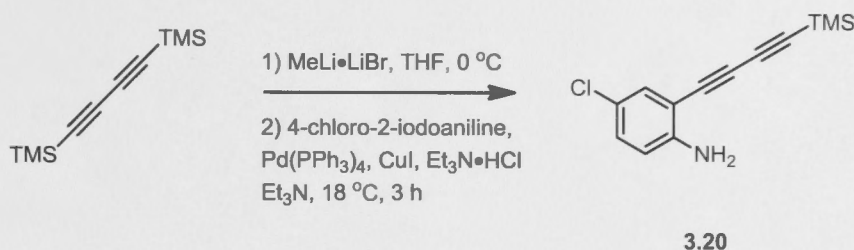
^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (d, $J=9.0$ Hz, 1H), 7.28 (d, $J=2.8$ Hz, 1H), 6.85 (dd, $J=9.0$ and 2.8 Hz, 1H), 6.55 (broad s, 1H), 3.72 (s, 3H), 1.51 (s, 9H).

2-Iodo-4-methoxyaniline (3.19)



Following protocols reported by Murphy *et al.*,¹⁴ a magnetically stirred solution of carbamate **3.60** (3.53 g, 10.1 mmol) in anhydrous CH_2Cl_2 (50 mL) maintained at $18\text{ }^\circ\text{C}$ under a nitrogen atmosphere was treated with TFA (9.33 mL, 121 mmol). After 2 h sodium hydroxide (*ca.* 60 mL of a 2 M aqueous solution) was added to the reaction mixture until neutral pH was attained. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to chromatography (silica, 1:9 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.5$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the title aniline **3.19**¹³ (1.85 g, 74%) as an orange oil.

^1H NMR (CDCl_3 , 400 MHz) δ 7.21 (d, $J=2.4$ Hz, 1H), 6.77 (dd, $J=8.7$ and 2.4 Hz, 1H), 6.68 (d, $J=8.7$ Hz, 1H), 3.76 (broad s, 2H), 3.71 (s, 3H).

4-Chloro-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (**3.20**)

The *title diyne* was synthesized from 4-chloro-2-iodoaniline (**3.11**) (1.27 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 3 h. The crude material was subjected to flash chromatography (silica, 1:49 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.7$ in 1:9 v/v ethyl acetate/*n*-hexane), the *title aniline* **3.20** (675 mg, 54% yield) as a brown low melting solid.

¹H NMR (400 MHz) δ 7.24 (d, $J=2.4$ Hz, 1H), 7.08 (dd, $J=8.8$ and 2.4 Hz, 1H), 6.59 (d, $J=8.8$ Hz, 1H), 4.28 (broad s, 2H), 0.23 (s, 9H).

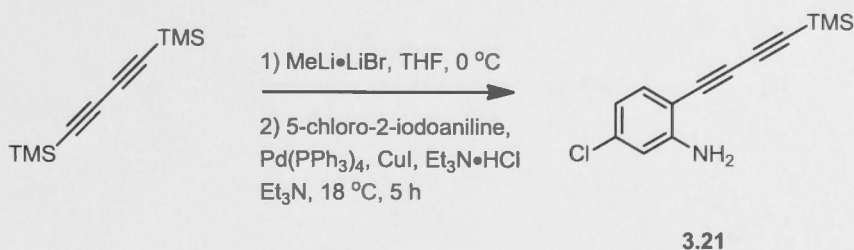
¹³C NMR (100 MHz) δ 148.4, 132.2, 130.8, 122.1, 115.5, 106.9, 92.6, 87.4, 80.1, 72.3, -0.4.

IR $\nu_{\max}/\text{cm}^{-1}$ 3480, 3389, 2959, 2198, 2098, 1615, 1485, 1249, 859, 842.

Mass Spectrum (EI) m/z 249, 247 ($M^{+\bullet}$, 39 and 76%, respectively), 234 (52), 232 (100).

HRMS found: $M^{+\bullet}$, 249.0558. C₁₃H₁₄³⁷ClNSi requires $M^{+\bullet}$, 249.0555.

5-Chloro-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (3.21)



The *title diyne* was synthesized from 5-chloro-2-iodoaniline (**3.12**) (1.27 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 5 h. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.7$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the *title aniline* **3.21** (1.020 g, 82%) as a brown low melting solid.

^1H NMR (400 MHz) δ 7.21 (d, $J=8.4$ Hz, 1H), 6.66 (d, $J=2.0$ Hz, 1H), 6.62 (dd, $J=8.4$ and 2.0 Hz, 1H), 4.35 (broad s, 2H), 0.23 (s, 9H).

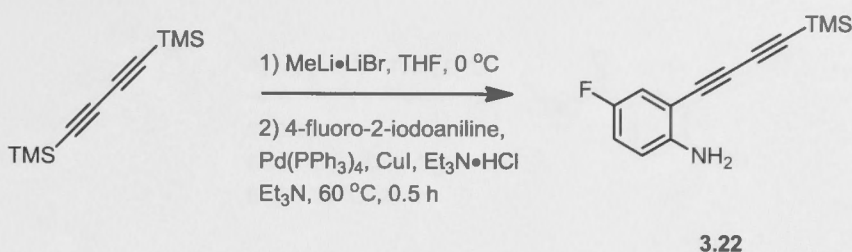
^{13}C NMR (100 MHz) δ 150.6, 136.5, 134.2, 118.2, 114.0, 104.1, 92.3, 87.5, 80.0, 72.8, -0.4.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3462, 3369, 2959, 2197, 2100, 1614, 1554, 1424, 1250, 843.

Mass Spectrum (EI) m/z 249, 247 ($M^{+\bullet}$, 33 and 75%, respectively), 234 (49), 232 (100).

HREIMS found: $M^{+\bullet}$, 249.0543. $\text{C}_{13}\text{H}_{14}^{37}\text{Cl}$ NSi requires $M^{+\bullet}$, 249.0555.

4-Fluoro-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (3.22)



The *title diyne* was synthesized from 4-fluoro-2-iodoaniline (**3.13**) (1.19 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was heated at 60 °C for 0.5 h. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.6$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the *title aniline* **3.22** (688 mg, 59% yield) as a low melting, brown solid.

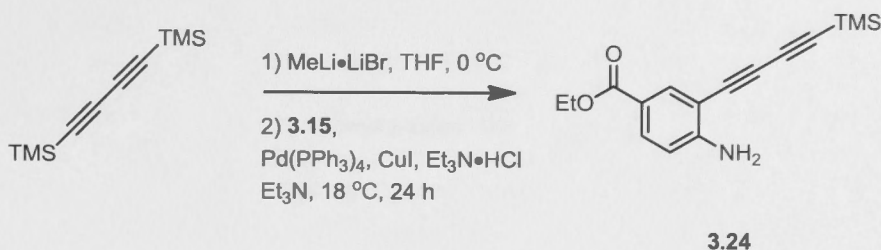
^1H NMR (400 MHz) δ 6.98 (dd, $J=8.8$ and 3.2 Hz, 1H), 6.88 (dt, $J=8.8$ and 3.2 Hz, 1H), 6.60 (m, 1H), 4.15 (broad s, 2H), 0.24 (s, 9H).

^{13}C NMR (100 MHz) δ 154.9 (d, $J^1_{\text{C-F}}=235$ Hz), 146.4, 118.6 (d, $J^2_{\text{C-F}}=24$ Hz), 118.3 (d, $J^2_{\text{C-F}}=23$ Hz), 115.5 (d, $J^3_{\text{C-F}}=7$ Hz), 106.2 (d, $J^3_{\text{C-F}}=9$ Hz), 92.5, 87.4, 79.8, 72.6, -0.5.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3480, 3387, 2960, 2195, 2099, 1605, 1496, 1275, 1251, 901, 845.

Mass Spectrum (EI) m/z 231 ($\text{M}^{+\bullet}$, 91%), 216 (100).

HREIMS found: $\text{M}^{+\bullet}$, 231.0880 $\text{C}_{13}\text{H}_{14}\text{FNSi}$ requires $\text{M}^{+\bullet}$, 231.0880.

Ethyl 4-amino-3-[4-(trimethylsilyl)buta-1,3-diynyl]benzoate (**3.24**)

The *title diyne* was synthesized from ethyl 4-amino-3-iodobenzoate (**3.15**) (1.46 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 24 h. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.8$ in ethyl acetate), the *title diyne* **3.24** (650 mg, 46 % yield) as a low melting, brown solid.

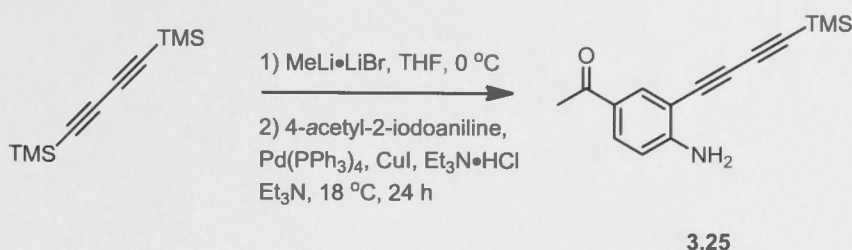
$^1\text{H NMR}$ (400 MHz) δ 8.03 (d, $J=2.0$ Hz, 1H), 7.82 (dd, $J=8.4$ and 2.0 Hz, 1H), 6.65 (dd, $J=8.4$ Hz, 1H), 4.68 (broad s, 2H), 4.31 (q, $J=7.2$ Hz, 2H), 1.35 (t, $J=7.2$ Hz, 3H), 0.24 (s, 9H).

$^{13}\text{C NMR}$ (100 MHz) δ 165.7, 153.1, 135.6, 132.3, 119.9, 104.9, 92.2, 87.5, 79.6, 72.6, 60.6, 14.3, -0.4.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3485, 3362, 2980, 2956, 2202, 2100, 1691, 1623, 1504, 1239, 842.

Mass Spectrum (EI) m/z 285 ($\text{M}^{+\bullet}$, 100%), 270 (95), 240 (20).

HREIMS found: $\text{M}^{+\bullet}$, 285.1185. $\text{C}_{16}\text{H}_{19}\text{NO}_2\text{Si}$ requires $\text{M}^{+\bullet}$, 285.1185.

4-Acetyl-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (**3.25**)

The *title diyne* was synthesized from 4-acetyl-2-iodoaniline (**3.16**) (1.31 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 24 h. The crude material was subjected to flash chromatography (silica, 1:49 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.8$ in ethyl acetate), the *title diyne* **3.25** (1.21 g, 95%) as a brown oil.

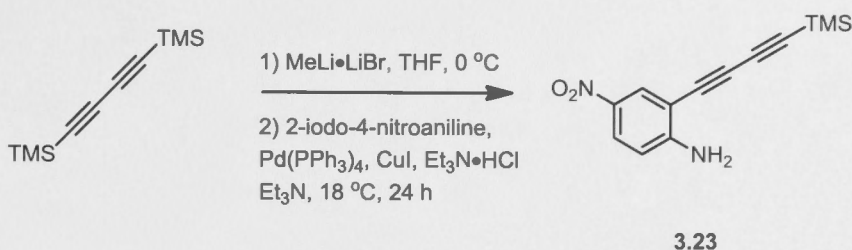
¹H NMR (400 MHz) δ 7.94 (d, $J=2.4$ Hz, 1H), 7.79 (dd, $J=8.8$ and 2.4 Hz, 1H), 6.66 (d, $J=8.8$ Hz, 1H), 4.77 (broad s, 2H), 2.48 (s, 3H), 0.24 (s, 9H).

¹³C NMR (100 MHz) δ 195.5, 153.4, 135.0, 131.2, 127.5, 113.6, 104.7, 92.4, 87.4, 79.7, 72.5, 26.0, -0.4.

IR $\nu_{\max}/\text{cm}^{-1}$ 3473, 3351, 2960, 2198, 2098, 1665, 1618, 1587, 1303, 1237, 869, 844.

Mass Spectrum (EI) m/z 255 ($M^{+\bullet}$, 81%), 240 (100).

HREIMS found: $M^{+\bullet}$, 255.1076. C₁₅H₁₇NOSi requires $M^{+\bullet}$, 255.1079.

4-Nitro-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (**3.23**)

The *title diyne* was synthesized from 2-iodo-4-nitroaniline (**3.14**) (660 mg, 2.5 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 24 h. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.6$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the *title diyne* **3.23** (427 mg, 66%) as a low melting, brown solid.

¹H NMR (400 MHz) δ 8.22 (d, $J=2.8$ Hz, 1H), 8.02 (dd, $J=9.2$ and 2.8 Hz, 1H), 6.66 (d, $J=9.2$ Hz, 1H), 0.25 (s, 9H).

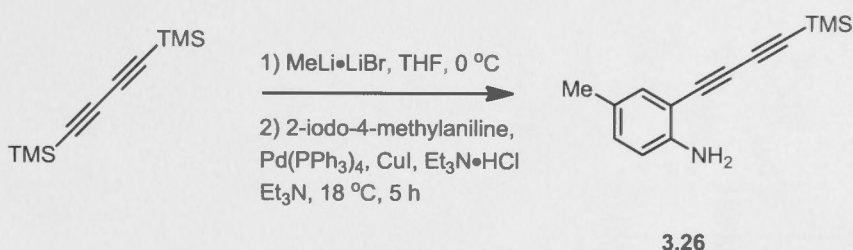
¹³C NMR (100 MHz) δ 154.4, 138.4, 129.9, 126.7, 113.1, 105.0, 93.5, 86.9, 80.7, 70.8, -0.5.

IR $\nu_{\max}/\text{cm}^{-1}$ 3480, 3369, 2960, 2202, 2101, 1621, 1492, 1318, 1251, 1103, 844.

Mass Spectrum (EI) m/z 258 ($M^{+\bullet}$, 80 %), 243 (100).

HREIMS found: $M^{+\bullet}$, 258.0827. C₁₃H₁₄N₂O₂Si requires $M^{+\bullet}$, 2258.0825.

4-Methyl-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (3.26)



The *title diyne* was synthesized from 2-iodo-4-methylaniline (**3.17**) (1.16 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 5 h. The crude material was subjected to flash chromatography (silica, 1:49 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.7$ in 1:9 v/v ethyl acetate/*n*-hexane), the *title aniline* **3.26** (781 mg, 69%) as a low melting, brown solid.

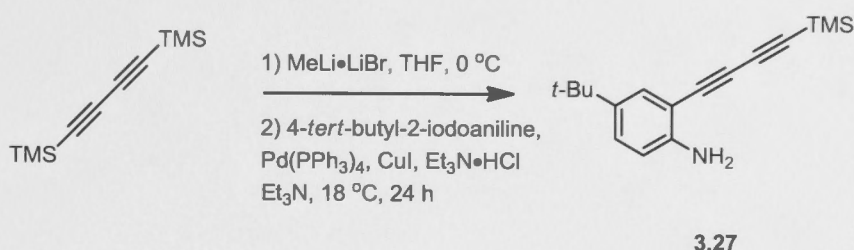
¹H NMR (400 MHz) δ 7.11 (s, 1H), 6.96 (d, $J=8.0$ Hz, 1H), 6.77 (d, $J=8.0$ Hz, 1H), 4.15 (broad s, 2H), 2.19 (s, 3H), 0.25 (s, 9H).

¹³C NMR (100 MHz) δ 147.7, 133.1, 131.7, 127.1, 114.5, 105.5, 91.5, 87.9, 79.0, 74.2, 20.2, -0.4.

IR $\nu_{\max}/\text{cm}^{-1}$ 3478, 3384, 2959, 2194, 2097, 1622, 1500, 1285, 1251, 889, 844.

Mass Spectrum (EI) m/z 227 ($M^{+\bullet}$, 90%), 212 (100).

HREIMS found: $M^{+\bullet}$, 227.1131. C₁₄H₁₇NSi requires $M^{+\bullet}$, 227.1130.

4-*tert*-Butyl-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (3.27)

The *title diyne* was synthesized from 4-*tert*-butyl-2-iodoaniline (**3.18**) (1.16 g, 4.2 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 24 h. The crude material was subjected to flash chromatography (silica, 1:49 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the appropriate fractions ($R_f = 0.8$ in 1:9 v/v ethyl acetate/*n*-hexane), the *title aniline* **3.27** (841 mg, 74%) as a brown oil.

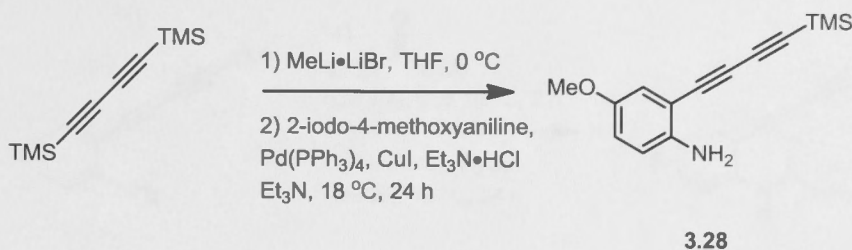
¹H NMR (400 MHz) δ 7.32 (d, $J=2.0$ Hz, 1H), 7.19 (dd, $J=8.4, 2.0$ Hz, 1H), 6.62 (d, $J=8.4$ Hz, 1H), 4.16 (broad s, 2H), 1.25 (s, 9H), 0.24 (s, 9H).

¹³C NMR (100 MHz) δ 147.5, 140.8, 129.7, 128.3, 114.3, 105.1, 91.4, 87.9, 78.8, 74.6, 33.9, 31.2, -0.4.

IR $\nu_{\max}/\text{cm}^{-1}$ 3481, 3386, 2961, 2196, 2098, 1619, 1499, 1250, 887, 845.

Mass Spectrum (EI) m/z 269 ($M^{+\bullet}$, 53%), 254 (100).

HREIMS found: $M^{+\bullet}$, 269.1599. C₁₇H₂₃NSi requires $M^{+\bullet}$, 269.1600.

4-Methoxy-2-[4-(trimethylsilyl)buta-1,3-diynyl]aniline (**3.28**)

The *title diyne* was synthesized from 2-iodo-4-methoxyaniline (**3.19**) (1.25 g, 5.0 mmol) using the general procedure 5.2.1-A. In *Step 2* the reaction mixture was stirred at 18 °C for 24 h. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.6$ in 1:9 *v/v* ethyl acetate/*n*-hexane), the *title diyne* **3.28** (134 mg, 11%) as a low melting, brown solid.

¹H NMR (400 MHz) δ 6.83 (d, $J=2.8$ Hz, 1H), 6.79 (dd, $J=8.4$ and 2.8 Hz, 1H), 6.62 (d, $J=8.4$ Hz, 1H), 4.01 (broad s, 2H), 3.71 (s, 3H), 0.24 (s, 9H).

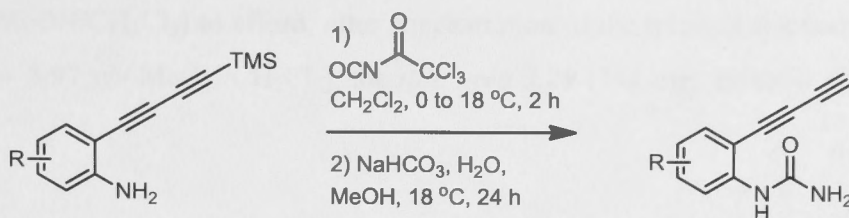
¹³C NMR (100 MHz) δ 151.7, 144.3, 118.9, 116.3, 116.1, 106.1, 91.9, 87.7, 79.2, 73.9, 55.8, -0.4.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3465, 3371, 2958, 2194, 2096, 1602, 1499, 1281, 1250, 1217, 890, 844.

Mass Spectrum (EI) m/z 243 ($M^{+\bullet}$, 100 %), 228 (59).

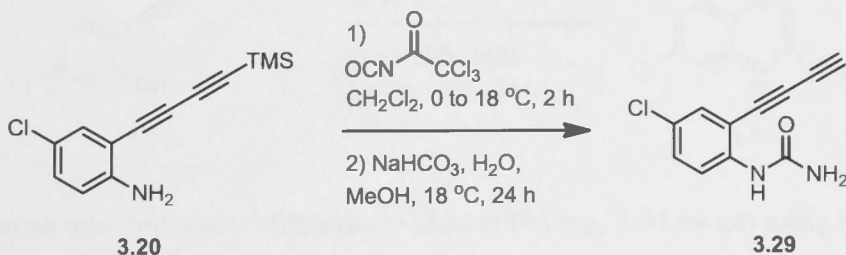
HREIMS found: $M^{+\bullet}$, 243.1076. C₁₄H₁₇NOSi requires $M^{+\bullet}$, 243.1079.

A) General Procedure for the Synthesis of Compounds 3.29-3.37, 4.3 and 4.15.



R = 4-Cl, 5-Cl, 4-F, 4-Ac, 4-EtO₂C, 4-NO₂, 4-Me, 4-*t*-Bu, 4-MeO, 5-MeO-2-pyridyl, 4-pyridyl

A magnetically stirred solution of the relevant diyne, *viz.* one of compounds **3.20-3.28** or **4.11** or **4.14**. *etc.*) (1 equiv) in CH_2Cl_2 (2 mL/mmol) maintained at 0 °C was treated with trichloroacetyl isocyanate (1.05 equiv) under a nitrogen atmosphere. The reaction mixture was warmed to 18 °C over 2 h and the ensuing brown suspension was concentrated under reduced pressure. The ensuing orange solid was dissolved in MeOH (5 mL/mmol) and treated with saturated aqueous solution of NaHCO_3 (2 mL/mmol) and the reaction mixture was stirred for 24 h. Water (2 mL/mmol) was added and the ensuing mixture was concentrated under reduced pressure. The mixture thus obtained was extracted with ethyl acetate (4×50 mL) and the combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The ensuing crude solid was purified as specified below for compounds **3.29-3.37** and in Section 5.2.3 for compounds **4.3** and **4.15**.

1-[2-(Buta-1,3-diynyl)-4-chlorophenyl]urea (**3.29**)

The *title urea* was synthesized from diyne (**3.20**) (496 mg, 2.00 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 v/v MeOH/CH₂Cl₂) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 1:19 → 3:97 v/v MeOH/CH₂Cl₂), the *title urea* **3.29** (344 mg, 79%) as a pale violet solid.

¹H NMR (400 MHz) D₆-DMSO δ 8.18 (s, 1H), 8.11 (d, $J=12.4$ Hz, 1H), 7.55 (d, $J=3.2$ Hz, 1H), 7.38 (dd, $J=12.4$ and 3.2 Hz, 1H), 6.50 (broad s, 2H), 4.24 (s, 0.6H).

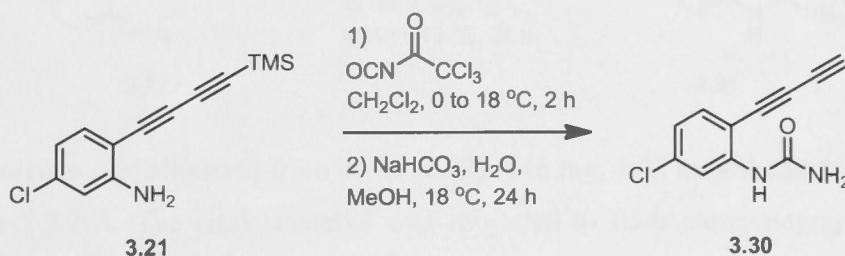
¹³C NMR (100 MHz) D₆-DMSO δ 155.8, 142.5, 132.9, 131.0, 125.2, 121.4, 110.5, 80.4, 78.6, 70.3, 68.3.

IR $\nu_{\max}/\text{cm}^{-1}$ 3488, 3334, 3272, 2224, 2207, 1662, 1570, 1533, 1582, 1350, 1092, 829, 658, 635.

Mass Spectrum (EI) m/z 218 ($M^{+\bullet}$, 22 %), 175 (100), 140 (40).

HREIMS found: $M^{+\bullet}$, 218.0250. C₁₁H₇³⁵ClN₂O requires $M^{+\bullet}$, 218.0247.

1-[2-(Buta-1,3-diyne)-5-chlorophenyl]urea (**3.30**)



The *title urea* was synthesized from diyne (**3.21**) (496 mg, 2.00 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica,

1:49 v/v MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (R_f = 0.5 in 1:19 v/v MeOH/CH₂Cl₂), the *title urea* **3.30** (356 mg, 81%) as a pale violet solid.

¹H NMR (400 MHz) D₆-DMSO δ 8.24 (d, J =2.4 Hz, 1H), 8.23 (s, 1H), 7.50 (d, J =8.0 Hz, 1H), 6.99 (dd, J =8.0 and 2.4 Hz, 1H), 6.60 (broad s, 2H), 4.23 (s, 0.6H).

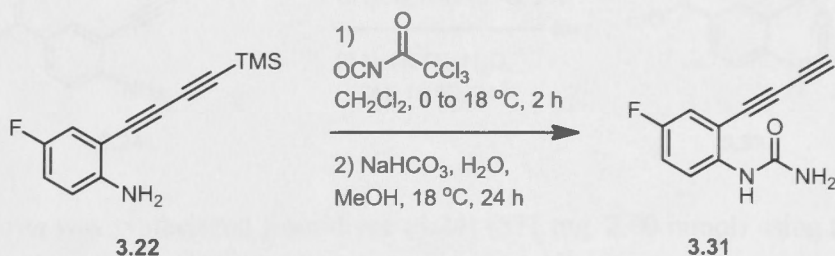
¹³C NMR (100 MHz) D₆-DMSO δ 155.7, 144.6, 135.6, 135.5, 121.8, 118.9, 107.4, 80.4, 78.4, 70.7, 68.4.

IR $\nu_{\max}/\text{cm}^{-1}$ 3469, 3340, 3295, 2212, 2210, 1667, 1599, 1562, 1529, 1338, 1259, 870, 810, 610.

Mass Spectrum (EI) m/z 220, 218 ($M^{+\bullet}$, 10 and 34%, respectively), 175 (100), 140 (34), 113 (26), 84 (32).

HREIMS found: $M^{+\bullet}$, 218.0246. C₁₁H₇³⁵ClN₂O requires $M^{+\bullet}$, 218.0247.

1-[2-(Buta-1,3-diynyl)-4-fluorophenyl]urea (**3.31**)



The *title urea* was synthesized from diyne (**3.22**) (446 mg, 1.93 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 v/v MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (R_f = 0.5 in 1:19 v/v MeOH/CH₂Cl₂), the *title urea* **3.31** (382 mg, 98%) as a pale violet solid.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.12 (s, 1H), 8.02 (dd, $J=9.3$ and 5.4 Hz, 1H), 7.37 (dd, $J=9.3$ and 3.0 Hz, 1H), 7.22 (m, 1H), 6.39 (broad s, 2H), 4.23 (s, 0.6H).

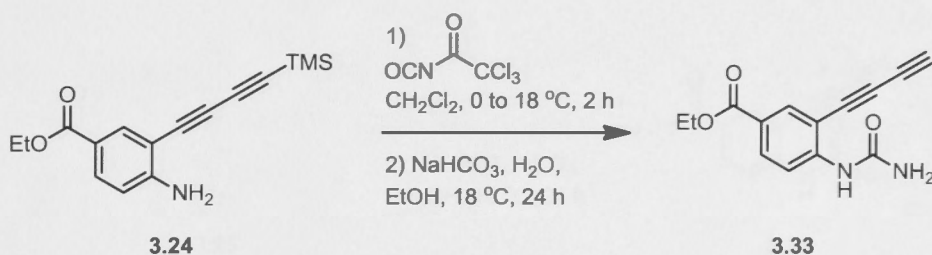
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 156.5 (d, $J_{\text{C-F}}^1=238$ Hz), 156.0, 140.1, 122.2 (d, $J_{\text{C-F}}^3=9$ Hz), 119.6 (d, $J_{\text{C-F}}^2=24$ Hz), 118.4 (d, $J_{\text{C-F}}^2=22$ Hz), 110.6 (d, $J_{\text{C-F}}^3=9$ Hz), 79.9, 78.4, 70.7, 68.3.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3499, 3346, 3288, 2214, 1661, 1582, 1548, 1582, 1548, 1353, 1169, 868, 662, 635.

Mass Spectrum (EI) m/z 202 ($\text{M}^{+\bullet}$, 42 %), 159 (100), 132 (32).

HREIMS found: $\text{M}^{+\bullet}$, 202.0546. $\text{C}_{11}\text{H}_7\text{FN}_2\text{O}$ requires $\text{M}^{+\bullet}$, 202.0542.

Ethyl 3-(buta-1,3-diynyl)-4-ureidobenzoate (**3.33**)



The *title urea* was synthesized from diyne (**3.24**) (571 mg, 2.00 mmol) using the general procedure 5.2.2-A except EtOH was used in place of MeOH. The crude material was subjected to flash chromatography (silica, 1:49 $\rightarrow$ 3:97 v/v MeOH/ CH_2Cl_2) to afford, after concentration of the appropriate fractions ($R_f = 0.3$ in ethyl acetate), the *title urea* **3.33** (275 mg, 54%) as a white solid.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.35 (s, 1H), 8.31 (d, $J=8.8$ Hz, 1H), 7.97 (s, 1H), 7.87 (dd, $J=8.8$ Hz, 1H), 6.69 (broad s, 2H), 4.28 (q, $J=6.8$ Hz, 2H), 4.20 (s, 0.8H), 1.29 (t, $J=6.8$ Hz, 3H).

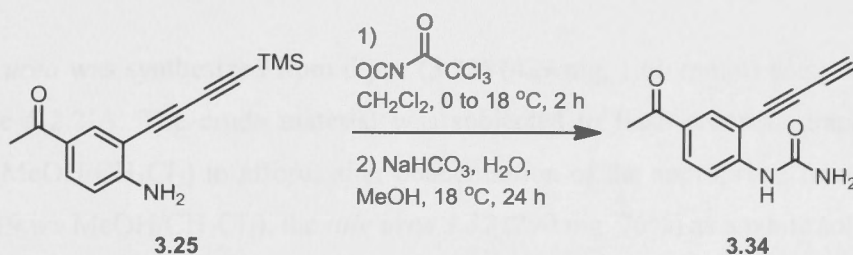
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 164.9, 155.5, 147.3, 135.3, 131.9, 122.9, 118.7, 108.3, 80.2, 78.3, 70.6, 68.3, 61.1, 14.6.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3448, 3345, 3261, 2212, 1701, 1666, 1571, 1529, 1360, 1304, 1249, 1022, 768, 748.

Mass Spectrum (EI) m/z 256 ($\text{M}^{+\bullet}$, 55 %), 213 (79), 168 (100), 140 (29).

HREIMS found: $\text{M}^{+\bullet}$, 256.0843. $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3$ requires $\text{M}^{+\bullet}$, 256.0848.

1-[4-Acetyl-2-(buta-1,3-diynyl)phenyl]urea (**3.34**)



The *title urea* was synthesized from diyne (**3.25**) (511 mg, 2.00 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 $\rightarrow$ 3:97 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$) to afford, after concentration of the relevant fractions ($R_f = 0.2$ in ethyl acetate), the *title urea* **3.34** (287 mg, 63%) as a pale violet solid.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.36 (s, 1H), 8.28 (d, $J=8.8$ Hz, 1H), 8.04 (d, $J=2.0$ Hz, 1H), 7.87 (dd, $J=8.8$ and 2.0 Hz, 1H), 6.67 (broad s, 2H), 4.19 (s, 0.7H), 2.48 (s, 3H).

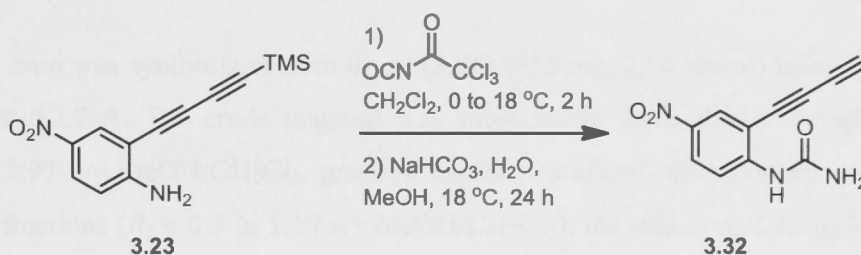
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 196.2, 155.6, 147.5, 135.2, 131.1, 130.5, 118.6, 108.3, 80.2, 78.4, 71.0, 68.5, 26.9.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3409, 3345, 3281, 3219, 1714, 1665, 1572, 1517, 1354, 1294, 826, 627.

Mass Spectrum (EI) m/z 226 ($\text{M}^{+\bullet}$, 7 %), 212 (100), 197 (78), 169 (48), 84 (52).

HREIMS found: $\text{M}^{+\bullet}$, 226.0741. $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_2$ requires $\text{M}^{+\bullet}$, 226.0742.

1-[4-Nitro-2-(buta-1,3-diynyl)phenyl]urea (**3.32**)



The *title urea* was synthesized from diyne (**3.23**) (429 mg, 1.66 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 v/v MeOH/ CH_2Cl_2) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 1:19 v/v MeOH/ CH_2Cl_2), the *title urea* **3.32** (290 mg, 76%) as a white solid.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.58 (s, 1H), 8.43 (d, J =9.6 Hz, 1H), 8.29 (d, J =2.8 Hz, 1H), 8.18 (dd, J =9.6 and 2.8 Hz, 1H), 6.84 (broad s, 2H), 4.26 (s, 0.5H).

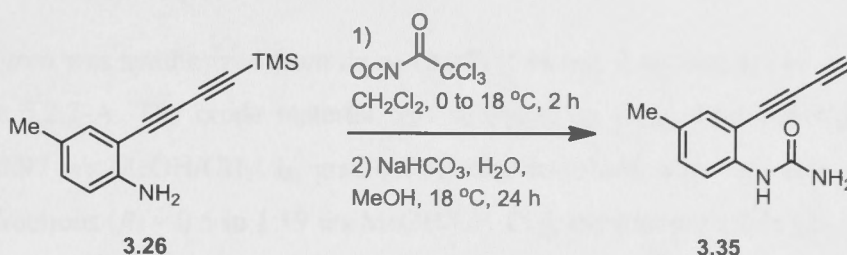
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 155.2, 149.0, 140.7, 129.8, 126.5, 118.6, 108.5, 81.0, 78.9, 69.3, 68.1.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3497, 3372, 3264, 2058, 1748, 1706, 1508, 1335, 1293, 1099, 834, 746.

Mass Spectrum (EI) m/z 229 ($M^{+\bullet}$, 38 %), 186 (100), 140 (34), 84 (38).

HRMS found: $M^{+\bullet}$, 229.0484. $C_{11}H_7N_3O_3$ requires $M^{+\bullet}$, 229.0487.

1-[2-(Buta-1,3-diynyl)-4-methylphenyl]urea (3.35)



The *title urea* was synthesized from diyne (**3.26**) (455 mg, 2.00 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 $\rightarrow$ 3:97 v/v $MeOH/CH_2Cl_2$, gradient elution) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 1:19 v/v $MeOH/CH_2Cl_2$), the *title urea* **3.35** (0.313 mg, 79 %) as a violet solid.

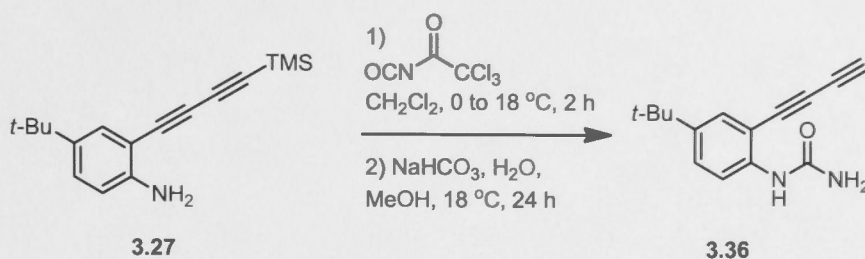
1H NMR (400 MHz) D_6 -DMSO δ 8.01 (s, 1H), 7.93 (d, $J=8.0$ Hz, 1H), 7.27 (s, 1H), 7.14 (d, $J=8.0$ Hz, 1H), 6.34 (br s, 2H), 4.13 (s, 0.7H), 2.19 (s, 3H).

^{13}C NMR (100 MHz) D_6 -DMSO δ 156.0, 141.1, 133.8, 131.8, 131.1, 120.2, 109.0, 79.1, 77.6, 72.2, 68.6, 20.3.

IR ν_{max}/cm^{-1} 3493, 3432, 3291, 2214, 1655, 1581, 1533, 1349, 1293, 812, 666, 636.

Mass Spectrum (EI) m/z 198 ($M^{+\bullet}$, 46 %), 155 (100), 127 (19).

HREIMS found: $M^{+\bullet}$, 198.0792. $C_{12}H_{10}N_2O$ requires $M^{+\bullet}$, 198.0793.

1-[2-(Buta-1,3-diynyl)-4-*tert*-butylphenyl]urea (**3.36**)

The *title urea* was synthesized from diyne (**3.27**) (538 mg, 2.00 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 $\rightarrow$ 3:97 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$, gradient elution) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 1:19 v/v $\text{MeOH}/\text{CH}_2\text{Cl}_2$), the *title urea* **3.36** (272 mg, 57%) as a violet solid.

^1H NMR (400 MHz) D_6 -DMSO δ 7.69 (d, $J=8.8$ Hz, 1H), 7.22 (d, $J=2.4$ Hz, 1H), 7.14 (dd, $J=8.8$ Hz, 1H), 7.03 (d, $J=2.4$ Hz, 1H), 4.90 (broad s, 2H), 4.40 (s, 0.4H), 1.97 (s, 9H).

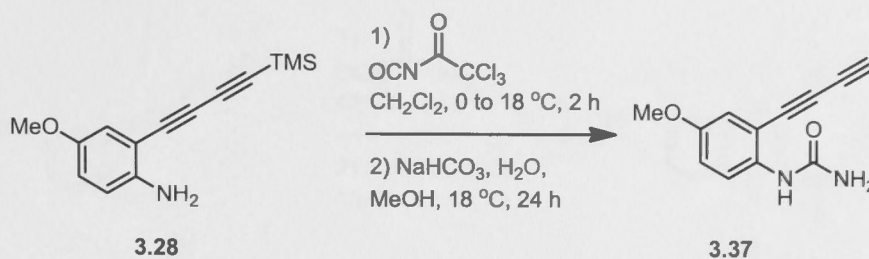
^{13}C NMR (100 MHz) D_6 -DMSO δ 155.9, 145.8, 139.1, 130.1, 128.3, 120.2, 110.1, 78.9, 73.1, 72.1, 67.9, 34.2, 31.1.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3487, 3292, 2962, 2205, 1671, 1580, 1524, 1343, 831, 627.

Mass Spectrum (EI) m/z 240 ($\text{M}^{+\bullet}$, 37 %), 255 (29) 182 (100), 84 (75).

HREIMS found: $\text{M}^{+\bullet}$, 240.1268. $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}$ requires $\text{M}^{+\bullet}$, 240.1263.

1-[4-Methoxy-2-(buta-1,3-diynyl)phenyl]urea (3.37)



The *title urea* was synthesized from diyne (**3.28**) (135 mg, 0.55 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 *v/v* MeOH/ CH_2Cl_2) to afford, after concentration of the relevant fractions (R_f 0.5 in 1:19 *v/v* MeOH/ CH_2Cl_2), the *title urea* **3.37** (69 mg, 58%) as a white solid.

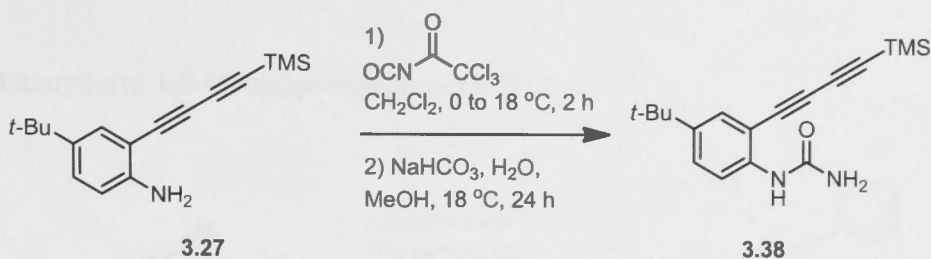
^1H NMR (400 MHz) D_6 -DMSO δ 7.96 (s, 1H), 7.85 (d, $J=9.2$ Hz, 1H), 7.02 (d, $J=2.8$ Hz, 1H), 6.96 (dd, $J=9.2$ and 2.8 Hz, 1H), 6.24 (broad s, 2H), 4.14 (s, 0.7H), 3.33 (s, 3H).

^{13}C NMR (100 MHz) D_6 -DMSO δ 156.2, 154.1, 137.0, 122.7, 118.2, 117.1, 110.7, 78.9, 77.7, 72.1, 68.5, 55.8.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3481, 3369, 3283, 2219, 2201, 1666, 1535, 1342, 1212, 1033, 856, 836, 644, 614.

Mass Spectrum (EI) m/z 214 ($\text{M}^{+\bullet}$, 94 %), 171 (100), 156 (95), 128 (40).

HREIMS found: $\text{M}^{+\bullet}$, 214.0744. $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2$ requires $\text{M}^{+\bullet}$, 214.0742.

1-{4-*tert*-Butyl-2-[4-(trimethylsilyl)buta-1,3-diynyl]phenyl}urea (**3.38**)

A magnetically stirred solution of diyne **3.27** (130 mg, 482 μmol) in CH_2Cl_2 (1 mL) maintained at 0°C under a nitrogen atmosphere was treated with trichloroacetyl isocyanate (61 μL , 96 mg, 0.510 μmol). The reaction mixture was warmed to 18°C over 2 h and the ensuing brown mixture was concentrated under reduced pressure. The crude material was dissolved in MeOH (10 mL) then treated with NaHCO_3 (0.1 mL of a saturated aqueous solution) and the reaction mixture was stirred for 3 h. Water (5 mL) was added and the ensuing mixture was concentrated under reduced pressure. The mixture thus obtained was extracted with ethyl acetate ($4 \times 30\text{ mL}$) and the combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 1:49, v/v , $\text{MeOH}/\text{CH}_2\text{Cl}_2$) to afford, after concentration of the relevant fractions ($R_f = 0.4$ in 1:9, v/v , $\text{MeOH}/\text{CH}_2\text{Cl}_2$), the *title urea* **3.38** (56 mg, 37%) as a white solid.

$^1\text{H NMR}$ (400 MHz) δ 7.70 (d, $J=9.2\text{ Hz}$, 1H), 7.44 (d, $J=2.4\text{ Hz}$, 1H), 7.37 (dd, $J=9.2$ and 2.4 Hz , 1H), 6.71 (broad s, 1H), 4.84 (broad s, 2H), 1.27 (s, 9H), 0.24 (s, 9H).

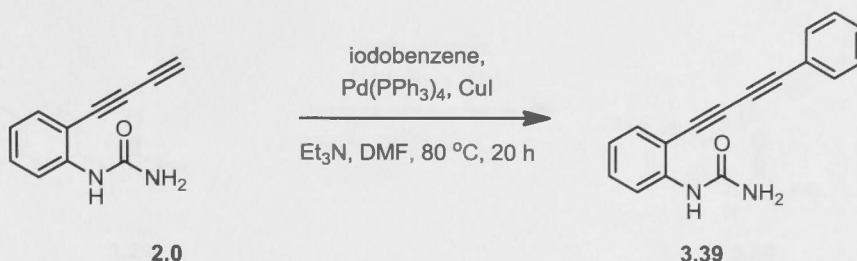
$^{13}\text{C NMR}$ (100 MHz) δ 155.4, 145.9, 138.8, 130.1, 128.2, 119.7, 110.3, 92.8, 87.4, 79.8, 73.0, 34.2, 31.1, -0.5.

$\text{IR } \nu_{\text{max}}/\text{cm}^{-1}$ 3474, 3313, 2957, 2202, 2097, 1959, 1664, 1514, 1345, 1249, 840.

Mass Spectrum (EI) m/z 312 (M^+ , 36 %), 297 (20), 280 (13), 269 (22), 254 (100).

HREIMS found: $M^{+\bullet}$, 312.1658. $C_{18}H_{24}N_2OSi$ requires $M^{+\bullet}$, 312.1658.

1-[2-(Phenylbuta-1,3-diynyl)phenyl]urea (3.39)



A magnetically stirred solution of diyne (**2.0**) (200 mg, 1.09 mmol) in a solution of DMF/ Et_3N (1.2 mL of a 1:5 v/v mixture) maintained at 18 $^\circ\text{C}$ under an atmosphere of nitrogen was treated with iodobenzene (670 mg, 3.28 mmol), $\text{Pd(PPh}_3)_4$ (62 mg, 0.05 mmol), CuI (21 mg, 0.11 mmol) and triethylamine (1.0 mL). The reaction mixture was heated to 80 $^\circ\text{C}$ and stirred at this temperature for 20 h. To the cooled reaction mixture was added SiO_2 (ca. 200 mg) and the ensuing brown slurry was concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 3:97 v/v $\text{MeOH/CH}_2\text{Cl}_2$) to afford, after concentration of the relevant fractions ($R_f = 0.6$ in 1:19 v/v $\text{MeOH/CH}_2\text{Cl}_2$), the *title diyne* **3.39** (221 mg, 77%) as a white solid, m.p. 176-178 $^\circ\text{C}$.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.13 (d, $J=8.0$ Hz, 1H), 7.54 (d, $J=8.0$ Hz, 2H), 7.47 (d, $J=7.6$ Hz, 1H), 7.41-7.36 (m, 4H), 7.08 (broad s, 1H), 7.00 (t, $J=7.6$ Hz), 4.79 (broad s, 2H).

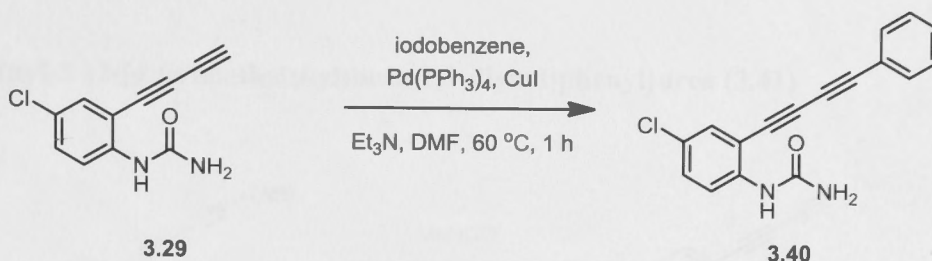
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 155.5, 142.8, 133.4, 132.3, 130.5, 130.0, 129.0, 121.6, 120.5, 119.5, 109.0, 83.0, 79.0, 78.4, 74.1.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3429, 3316, 3208, 2209, 2146, 1652, 1514, 1484, 754.

Mass Spectrum m/z (EI) 260 ($M^{+\bullet}$, 52%), 243 (10), 217 (100), 189 (41).

HREIMS found: M^{+} 260.0953. $C_{17}H_{12}N_2O$ requires M^{+} , 260.0950.

1-[4-Chloro-2-(phenylbuta-1,3-diyne-1-yl)phenyl]urea (3.40)



A magnetically stirred solution of diyne (**3.29**) (240 mg, 1.20 mmol) in a solution of DMF/ Et_3N (2.4 mL of a 1:5 v/v mixture) maintained at 18 $^\circ\text{C}$ under an atmosphere of nitrogen was treated with iodobenzene (670 mg, 3.28 mmol), $\text{Pd(PPh}_3)_4$ (62 mg, 0.05 mmol), CuI (21 mg, 0.11 mmol), triethylamine (1.0 mL). The reaction mixture was heated to 60 $^\circ\text{C}$ and stirred at this temperature for 1 h. To the cooled reaction mixture was added SiO_2 (ca. 200 mg, chromatography grade) and the ensuing brown slurry was concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 1:99 $\rightarrow$ 1:49 v/v $\text{MeOH/CH}_2\text{Cl}_2$, gradient elution) to afford, after concentration of the relevant fractions ($R_f = 0.5$ 1:19 v/v $\text{MeOH/CH}_2\text{Cl}_2$), the *title diyne* **3.40** (286 mg, 81%) as a white solid.

^1H NMR (400 MHz) $\text{D}_6\text{-DMSO}$ δ 8.23 (s, 1H), 8.16 (d, $J=9.2$ Hz, 1H), 7.63-7.61 (complex m, 2H), 7.56 (d, $J=2.4$ Hz, 1H), 7.50-7.45 (m, 3H), 7.39 (dd, $J=9.2$ and 2.4, 1H), 6.53 (broad s, 2H).

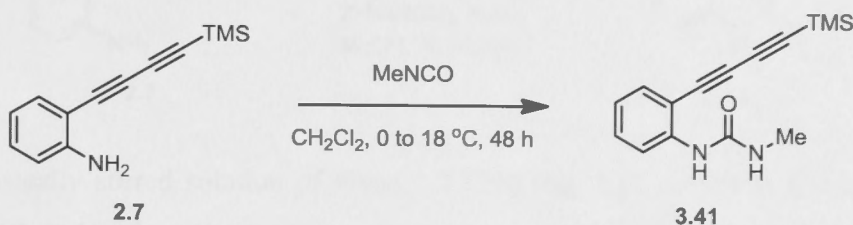
^{13}C NMR (100 MHz) $\text{D}_6\text{-DMSO}$ δ 155.4, 141.8, 132.4, 132.1, 130.5, 130.2, 129.0, 124.8, 120.9, 120.2, 110.6, 83.6, 80.0, 76.7, 73.8.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3507, 3357, 3303, 2219, 1898, 1656, 1569, 1531, 1343, 752.

Mass Spectrum m/z (EI) 296, 294 ($M^{+•}$, 14 and 38%, respectively), 277 (22), 253 (40), 251 (100), 214 (32).

HREIMS found: $M^{+•}$ 294.0561, $C_{17}H_{11}^{35}ClN_2O$ requires $M^{+•}$ 294.0560.

1-Methyl-3-{2-[4-(trimethylsilyl)buta-1,3-diynyl]phenyl}urea (3.41)



A magnetically stirred solution of diyne **2.7** (122 mg, 0.57 mmol) in CH_2Cl_2 (2 mL) maintained at 0°C under a nitrogen atmosphere was treated with methyl isocyanate (0.084 mL, 78 mg, 1.37 mmol). The reaction mixture was warmed to 18°C over 2 h, sealed with a glass stopper. After stirring for 48 h the reaction mixture was concentrated under reduced pressure. The ensuing orange gum was subjected to flash chromatography (silica, CH_2Cl_2) to afford, after concentration of the appropriate fractions ($R_f = 0.8$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title urea* **3.41** (105 mg, 68%) as a colourless crystalline solid.

^1H NMR (400 MHz) δ 8.03 (d, $J=8.0$ Hz, 1H), 7.34 (dd, $J=8.0$ and 1.2 Hz, 1H), 7.26–7.21 (complex m, 3H), 6.86 (dd, $J=7.2$ and 1.2 Hz 1H), 5.45 (s, 0.5H), 5.43 (s, 0.5H) 2.78 (s, 1.5H), 2.76 (s, 1.5H), 0.16 (s, 9H).

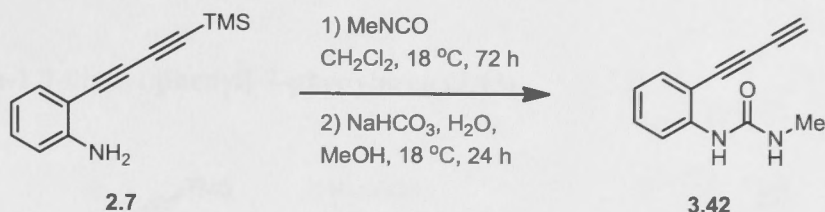
^{13}C NMR (100 MHz) δ 155.7, 142.0, 133.1, 130.5, 122.0, 119.5, 110.0, 92.4, 87.4, 80.2, 72.7, 26.9, -0.5.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3335, 2961, 2206, 2102, 1646, 1515, 1305, 1273, 1252, 1015, 844, 752.

Mass Spectrum (EI) m/z 270 ($M^{+•}$, 100 %), 213 (98), 199 (70), 99 (39).

HREIMS found: $M^{+\bullet}$, 270.1189. $C_{15}H_{18}N_2OSi$ requires $M^{+\bullet}$, 270.1188.

1-[2-(Buta-1,3-diynyl)phenyl]-3-methylurea (3.42)



A magnetically stirred solution of diyne **2.7** (250 mg, 1.17 mmol) in CH₂Cl₂ (5 mL) maintained at 18 °C under a nitrogen atmosphere was treated with methyl isocyanate (0.145 mL, 134 mg, 2.34 mmol). The reaction vessel was sealed with a glass stopper and stirring for 72 h then concentrated under reduced pressure. The crude solid dissolved in MeOH (20 mL) and treated with NaHCO₃ (10 mL of a saturated aqueous solution) and stirred magnetically for 24 h. The reaction mixture was diluted with water (5 mL) and most of the MeOH was removed under reduced pressure. The ensuing suspension was extracted with ethyl acetate (4 × 10 mL) and the combined organic fractions were dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 1:99 v/v MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 1:19 v/v MeOH/CH₂Cl₂), the *title urea* **3.42** (223 mg, 96%) as a white solid.

¹H NMR (400 MHz) δ 8.07 (d, J =8.4 Hz, 1H), 8.04 (s, 1H), 7.46 (dd, J =7.6 and 1.2 Hz, 1H), 7.33 (t, J =8.4 Hz, 1H), 6.99 (m, 1H), 6.92 (dt, J =7.6 and 1.2 Hz, 1H), 4.16 (s, 0.5H), 2.66 (s, 1.5H), 2.64 (s, 1.5H).

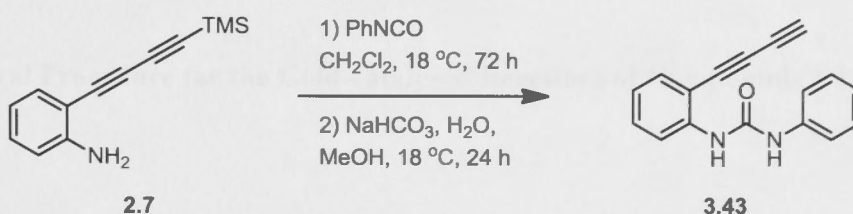
¹³C NMR (100 MHz) δ 155.2, 143.1, 133.6, 130.7, 121.4, 119.1, 108.2, 79.1, 77.4, 71.4, 68.1, 25.9.

IR $\nu_{\max}/\text{cm}^{-1}$ 3328, 3286, 2215, 1642, 1577, 1448, 1300, 1263, 755, 637.

Mass Spectrum (EI) m/z 198 ($M^{+\bullet}$, 31 %), 141 (100), 114 (20).

HRMS found: $M^{+\bullet}$, 198.0789. $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}$ requires $M^{+\bullet}$, 198.0793.

1-[2-(Buta-1,3-diyne)phenyl]-3-phenylurea (**3.43**)



A magnetically stirred solution of diyne **2.7** (752 mg, 3.51 mmol) in CH_2Cl_2 (70 mL) maintained at 18°C under a nitrogen atmosphere was treated with phenyl isocyanate (0.76 mL, 828 mg, 6.95 mmol). The reaction vessel was sealed with a glass stopper and stirring was continued for 72 h. The ensuing mixture was then concentrated under reduced pressure. The crude solid thus obtained was dissolved in MeOH (50 mL) and treated with NaHCO_3 (20 mL of a saturated aqueous solution) and stirred magnetically for 24 h. The ensuing mixture was diluted with water (15 mL) and concentrated under reduced pressure. The ensuing mixture was extracted with ethyl acetate (4×20 mL) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 1:19 v/v ethyl acetate/*n*-hexane) to afford, after concentration of the relevant fractions ($R_f = 0.2$ in 1:9 v/v ethyl acetate/*n*-hexane), the *title urea* **3.43** (439 mg, 48%) as a colourless crystalline solid.

^1H NMR (300 MHz) δ 9.38 (s, 1H), 8.37 (s, 1H), 8.11 (d, $J=8.1$, Hz, 1H), 7.55–7.38 (complex m, 4H), 7.30 (t, $J=7.8$ Hz 2H), 7.01 (m, 2H), 4.23 (s, 0.6H).

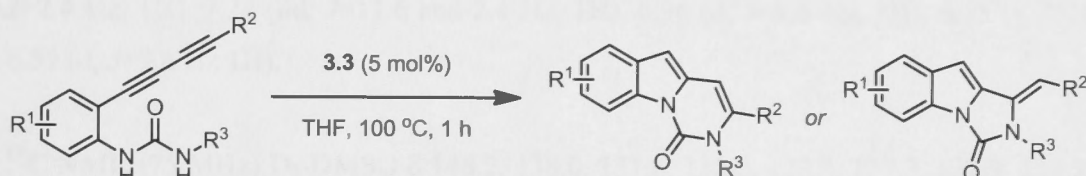
^{13}C NMR (100 MHz) δ 152.5, 142.3, 139.8, 134.3, 131.2, 129.3, 122.7, 122.7, 120.2, 118.8, 109.6, 79.7, 78.1, 71.7, 68.5.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3271, 2206, 1646, 1446, 1298, 1253, 1217, 758, 646, 619.

Mass Spectrum (EI) m/z 260 ($\text{M}^{+\bullet}$, 41%), 141 (100), 93 (59).

HREIMS found: $\text{M}^{+\bullet}$, 260.0949. $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}$ requires $\text{M}^{+\bullet}$, 260.0950.

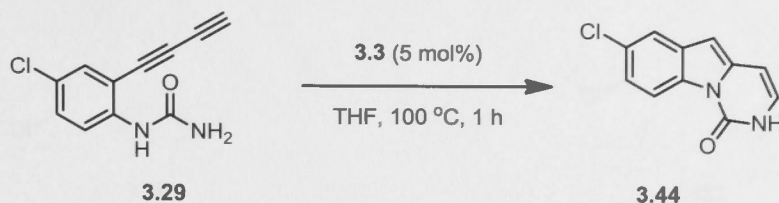
B) General Procedure for the Gold-catalysed Reactions of Compounds 3.29-3.37, 4.3 and 4.12.



$\text{R}^1 = \text{H}, 4\text{-Cl}, 5\text{-Cl}, 4\text{-F}, 4\text{-Ac}, 4\text{-EtO}_2\text{C}, 4\text{-NO}_2, 4\text{-Me}, 4\text{-t-Bu}, 4\text{-MeO}, 5\text{-MeO-2-pyridyl}, 4\text{-pyridyl}$

$\text{R}^2 = \text{H}, \text{Ph}, \text{TMS}; \text{R}^3 = \text{H}, \text{Ph}, \text{Me}, \text{CO}_2\text{CCl}_3$

A 10 mL microwave reaction vessel was charged with the relevant diyne *viz.* one of compounds **3.44-3.57** or **4.3** or **4.12** (1 equiv.) and gold complex **3.3** (0.05 equiv.) and capped with a rubber seal. The reaction vessel was evacuated and backfilled with nitrogen several times then anhydrous THF (10 mL/mmol) was added and the resulting solution was subjected to microwave irradiation (100 °C for 1 h, 1 min ramp time and power not exceeding 200 W). SiO_2 (*ca.* 50 equiv.) was added to the cooled reaction mixture which was then concentrated under reduced pressure. The crude material was subjected to flash chromatography under the conditions defined below for compounds **3.44-3.57** and in Section 5.2.3 for compounds **4.17** and **4.19**.

7-Chloropyrimido[1,6-*a*]indol-1(2*H*)-one (3.44)

The *title compound* was synthesised from diyne **3.29** (109 mg, 0.50 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R*_f = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.44** (76 mg, 70%) as an off-white solid.

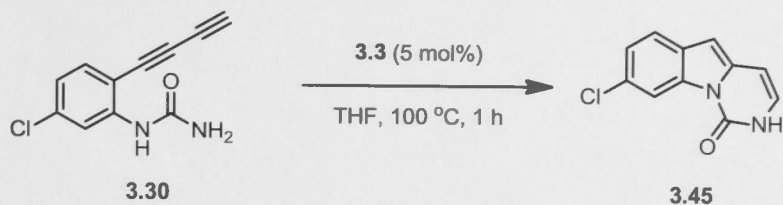
¹H NMR (300 MHz) D₆-DMSO δ 10.98 (broad s, 1H), 8.46 (d, *J*=11.6 Hz, 1H), 7.67 (d, *J*=2.4 Hz, 1H), 7.24 (dd, *J*=11.6 and 2.4 Hz, 1H), 6.96 (d, *J*=9.6 Hz, 1H), 6.55 (s, 1H), 6.51 (d, *J*=9.6 Hz 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.2, 138.0, 131.8, 131.0, 128.4, 127.3, 121.9, 119.2, 117.1, 98.4, 96.7.

IR ν_{max} /cm⁻¹ 3426, 3205, 3090, 2952, 1843, 1705, 1636, 1435, 1398, 1195, 1059, 800, 778.

Mass Spectrum *m/z* (EI) 220 and 218 (M⁺, 40 and 100%, respectively), 163 (32).

HREIMS found: M⁺, 218.0248. C₁₁H₇³⁵Cl N₂O requires M⁺, 218.0247.

8-Chloropyrimido[1,6-*a*]indol-1(2*H*)-one (3.45)

The *title compound* was synthesised from diene **3.30** (109 mg, 0.50 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.7 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.45** (73 mg, 67%) as an orange solid.

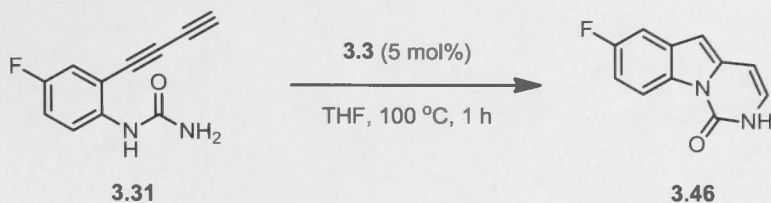
¹H NMR (300 MHz) D₆-DMSO δ 10.96 (broad d, *J*=3.6 Hz, 1H), 8.50 (d, *J*=2.0 Hz, 1H), 7.65 (d, *J*=8.4 Hz, 1H), 7.33 (dd, *J*=8.4 and 2.0, 1H), 6.94 (m, 1H), 6.60 (s, 1H), 6.50 (d, *J*=7.2 Hz 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.3, 137.4, 132.7, 129.2, 126.9, 126.3, 124.1, 121.3, 115.4, 98.5, 97.1.

IR ν_{max} /cm⁻¹ 3213, 3108, 2954, 1829, 1701, 1634, 1398, 1313, 1194, 1194, 814, 751.

Mass Spectrum *m/z* (EI) 220 and 218 (M⁺, 34 and 100%, respectively), 163 (25).

HREIMS found: M⁺, 218.0248. C₁₁H₇³⁵ClN₂O requires M⁺, 218.0247.

7-Fluoropyrimido[1,6-*a*]indol-1(2*H*)-one (3.46)

The *title compound* was synthesised from diene **3.31** (100 mg, 0.49 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.46** (62 mg, 62%) as an off-white solid.

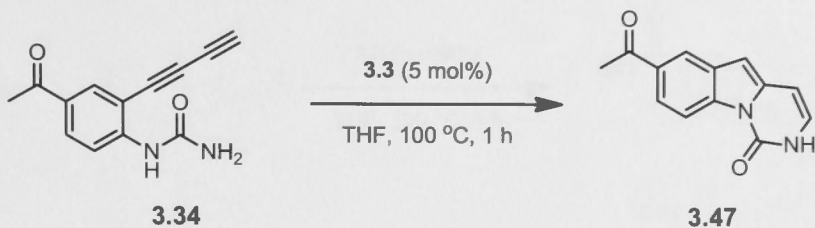
¹H NMR (300 MHz) D₆-DMSO δ 10.94 (s, 1H), 8.49 (dd, *J*=8.8 and 4.8 Hz, 1H), 7.42 (dd, *J*=9.6 and 2.8 Hz, 1H), 7.09 (dt, *J*=8.8 and 2.4 Hz, 1H), 6.97 (m, 1H), 6.59 (s, 1H), 6.52 (d, *J*=8.8 Hz, 1H), 6.67 (s, 1H).

¹³C NMR (75 MHz) D₆-DMSO δ, 159.5 (d, *J*_{C-F}=136 Hz), 148.2, 138.2, 131.5 (d, *J*_{C-F}=10.1 Hz), 129.2, 127.2, 117.0 (d, *J*_{C-F}=9.3 Hz), 109.9 (d, *J*_{C-F}=26 Hz), 105.0 (d, *J*_{C-F}=24 Hz), 98.3, 97.1 (d, *J*_{C-F}=5 Hz).

IR ν_{max} /cm⁻¹ 3213, 3106, 2954, 1701, 1642, 1441, 1399, 1171, 779, 595.

Mass Spectrum *m/z* (EI) 202 (*M*⁺, 100%), 173 (14), 147 (32).

HREIMS found: *M*⁺, 202.0540. C₁₁H₇FN₂O requires *M*⁺, 202.0542.

7-Acetylpyrimido[1,6-*a*]indol-1(2*H*)-one (3.47)

The *title compound* was synthesised from diene **3.34** (113 mg, 0.59 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fraction (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.47** (67 mg, 59%) as an off-white solid.

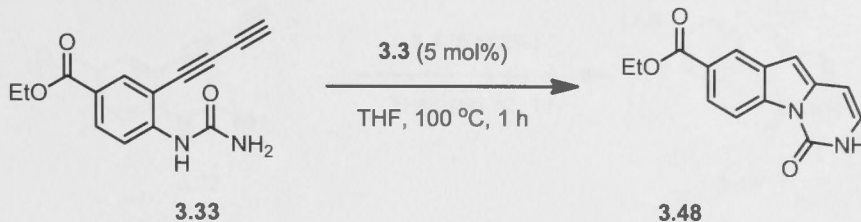
¹H NMR (400 MHz) D₆-DMSO δ 10.97 (broad s, 1H), 8.57 (d, *J*=8.8 Hz, 1H), 8.34 (d, *J*=1.2 Hz, 1H), 7.87 (dd, *J*=8.8, 1.2 Hz, 1H), 6.98-6.95 (m, 1H), 6.74 (s, 1H), 6.55 (d, *J*=7.2 Hz, 1H), 2.65 (s, 3H).

¹³C NMR (75 MHz) D₆-DMSO δ 197.5, 148.0, 137.6, 134.7, 132.6, 129.9, 121.5, 121.2, 115.3, 98.2, 97.8, 26.9.

IR ν_{max} /cm⁻¹ 3388, 3216, 3113, 2996, 1872, 1703, 1667, 1635, 1388, 1367, 1305, 1195, 839, 797, 585.

Mass Spectrum *m/z* (EI) 226 (M⁺•, 100%), 211 (92), 183 (69), 155 (20).

HREIMS found: M⁺•, 226.0742. C₁₃H₁₀N₂O₂ requires M⁺•, 226.0742.

Ethyl 1,2-dihydro-1-oxopyrimido[1,6-*a*]indole-7-carboxylate (**3.48**)

The *title compound* was synthesised from diyne **3.33** (128 mg, 0.50 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.5 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.48** (78 mg, 61%) as an off-white solid.

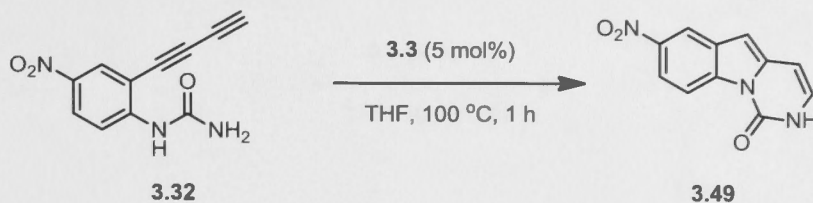
¹H NMR (300 MHz) D₆-DMSO δ 10.98 (broad s, 1H), 8.57 (d, *J*=8.8 Hz, 1H), 8.29 (s, 1H), 7.86 (d, *J*=8.8 Hz, 1H), 6.96 (d, *J*=7.6 Hz, 1H), 6.72 (s, 1H), 6.53 (d, *J*=7.6 Hz, 1H), 4.32 (q, *J*=7.2 Hz, 2H), 1.33 (t, *J*=7.2 Hz, 3H).

¹³C NMR (75 MHz) D₆-DMSO δ 166.6, 148.3, 137.9, 135.0, 130.2, 127.1, 125.4, 122.7, 121.9, 115.7, 98.5, 97.9, 61.0, 14.7.

IR ν_{max} /cm⁻¹ 3207, 3104, 2957, 1899, 1703, 1637, 1396, 1370, 1331, 1306, 1258, 1222, 1091, 805, 766.

Mass Spectrum *m/z* (EI) 256 (M⁺, 100%), 228 (54), 211 (59), 183 (39).

HREIMS found: M⁺, 256.0851. C₁₄H₁₂N₂O₃ requires M⁺, 256.0848.

7-Nitropyrimido[1,6-*a*]indol-1(2*H*)-one (3.49)

The *title compound* was synthesised from diene **3.32** (110 mg, 0.48 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.49** (54 mg, 49%) as a yellow solid.

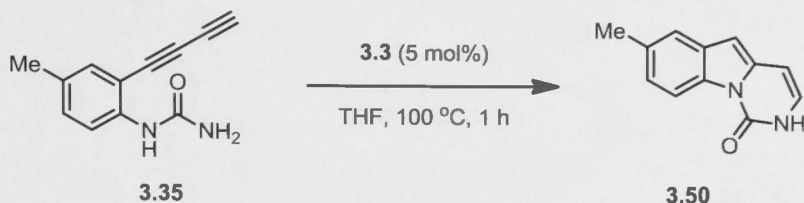
¹H NMR (400 MHz) D₆-DMSO δ 11.16 (broad s, 1H), 8.66 (d, *J*=9.2 Hz, 1H), 8.62 (d, *J*=2.4 Hz, 1H), 8.12 (dd, *J*=9.2 and 2.4 Hz, 1H), 7.04 (d, *J*=7.2 Hz, 1H), 6.84 (s, 1H), 6.60 (d, *J*=7.2 Hz, 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 147.7, 143.6, 139.1, 135.1, 129.9, 127.6, 116.4, 115.8, 98.0, 97.9 (one signal obscured or overlapping).

IR ν_{max} /cm⁻¹ 3375, 3214, 3106, 2926, 1713, 1636, 1516, 1343, 1195, 784, 754.

Mass Spectrum *m/z* (EI) 229 (*M*⁺, 100%), 183 (49).

HREIMS found: *M*⁺, 229.0487. C₁₁H₇N₃O₃ requires *M*⁺, 229.0487.

7-Methylpyrimido[1,6-*a*]indol-1(2*H*)-one (3.50)

The *title compound* was synthesised from diene **3.35** (108 mg, 0.54 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentrations of the relevant fractions (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.50** (60 mg, 56%) as an orange solid.

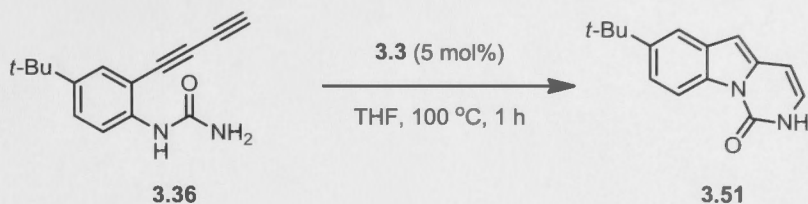
¹H NMR (400 MHz) D₆-DMSO δ 10.76 (broad s, 1H), 8.37 (d, *J*=8.0 Hz, 1H), 7.08 (s, 1H), 6.90-6.87 (complex m, 1H), 6.49 (s, 1H), 6.47 (d, *J*=7.2 Hz, 1H), 2.41 (s, 3H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.4, 136.5, 132.8, 130.9, 130.7, 126.2, 123.6, 119.7, 115.5, 98.5, 96.9, 21.7.

IR ν_{max} /cm⁻¹ 3205, 3205, 3091, 2951, 1819, 1703, 1638, 1400, 1198, 801, 774.

Mass Spectrum *m/z* (EI) 198 (M⁺, 100%), 169 (12), 143 (14).

HREIMS found: M⁺, 198.0798. C₁₂H₁₀N₂O requires M⁺, 198.0793.

7-*tert*-Butylpyrimido[1,6-*a*]indol-1(2*H*)-one (3.51)

The *title compound* was synthesised from diene **3.36** (105 mg, 0.44 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.49** (42 mg, 40%) as off-white solid.

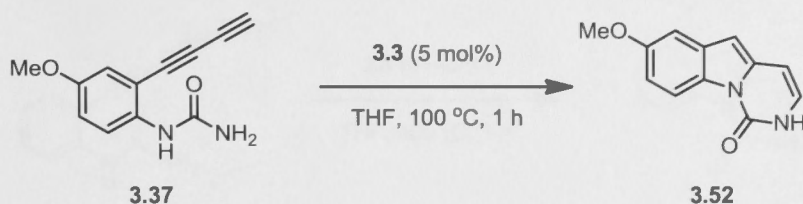
¹H NMR (300 MHz) D₆-DMSO δ 10.75 (broad d, *J*=4.4 Hz, 1H), 8.40 (d, *J*=8.8 Hz, 1H), 7.61 (d, *J*=1.6 Hz, 1H), 7.34 (dd, *J*=8.0 and 1.6 Hz, 1H), 6.88 (dd, *J*=8.8 and 4.4 Hz, 1H), 6.54 (s, 1H), 6.47 (d, *J*=8.0 Hz 1H), 1.34 (s, 9H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.4, 146.3, 136.4, 130.7, 130.4, 126.1, 120.2, 115.9, 115.3, 98.5, 97.4, 34.9, 32.0.

IR ν_{max} /cm⁻¹ 3206, 3205, 3096, 2946, 1822, 1696, 1640, 1396, 1196, 782.

Mass Spectrum *m/z* (EI) 240 (*M*⁺, 76%), 225 (100), 197 (13), 184 (19).

HREIMS found: *M*⁺, 240.1262. C₁₅H₁₆N₂O requires *M*⁺, 240.1263.

7-Methoxypyrimido[1,6-*a*]indol-1(2*H*)-one (3.52)

The *title compound* was synthesised from diene **3.37** (36 mg, 0.17 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the relevant fractions (*R_f* = 0.5 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.52** (14 mg, 39%) as dark solid.

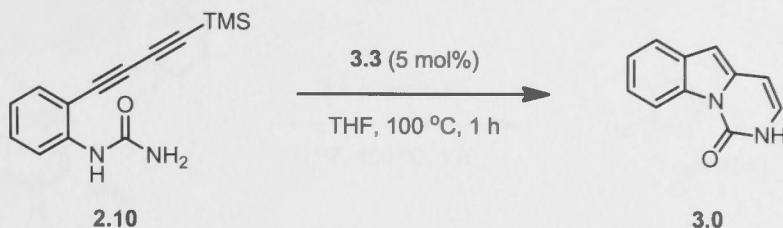
¹H NMR (400 MHz) D₆-DMSO δ 10.79 (broad d, *J*=4.4 Hz, 1H), 8.36 (d, *J*=8.8 Hz, 1H), 7.14 (d, *J*=2.4 Hz, 1H), 6.91–6.86 (complex m, 2H), 6.52 (s, 1H), 6.47 (dd, *J*=7.6 and 2.4 Hz, 1H), 3.80 (s, 3H).

¹³C NMR (100 MHz) D₆-DMSO δ 156.5, 148.2, 137.1, 131.5, 137.3, 126.3, 116.5, 111.5, 101.9, 98.3, 97.1, 55.7.

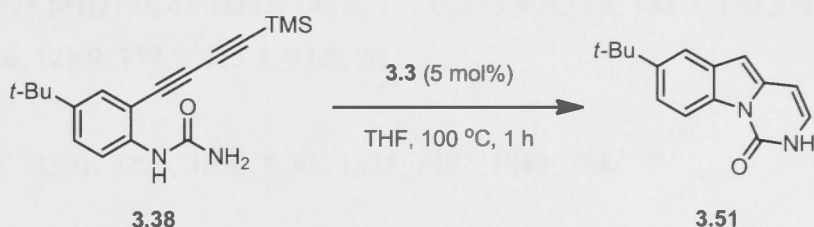
IR ν_{max} /cm⁻¹ 3426, 3205, 3093, 2953, 1843, 1703, 1639, 1607, 1481, 1403, 1204, 782.

Mass Spectrum *m/z* (EI) 214 (*M*⁺, 100%), 185 (14), 171 (59).

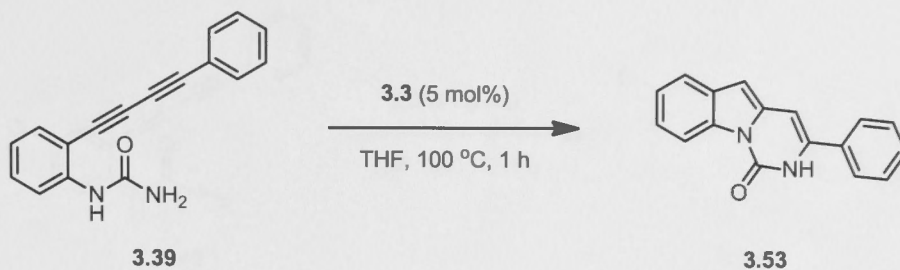
HREIMS found: *M*⁺, 214.0742 C₁₂H₁₀N₂O₂ requires *M*⁺, 214.0742.

Reaction of diyne **2.10** with gold complex **3.3**

The *title reaction* was conducted according to the general method 5.2.2-B using 1-(2-(4-(Trimethylsilyl)buta-1,3-diynyl)phenyl) urea **2.10** (26 mg, 0.10 mmol) as the starting material. The crude product was subjected to flash chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the previously described tricycle **3.0** (14 mg, 75 %) as white solid. The spectral data derived from this material was identical to that derived from an authentic example.

Reaction on diyne **3.38** with gold complex **3.3**

The *title reaction* was conducted according to the general procedure general procedure 5.2.2-B using diyne **3.38** (45 mg, 0.16 mmol) as the starting material. The crude product was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tricycle* **3.49** (24 mg, 56%) as an off-white solid. The spectral data derived from this material were identical to that derived from an authentic sample.

3-Phenylpyrimido[1,6-*a*]indol-1(2*H*)-one (3.39)

The *title compound* was synthesised from diyne **3.39** (163 mg, 0.63 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.8 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title tetracycle* **3.53** (92 mg, 60%) as a yellow powder, sublimation 233-238 °C @ atmospheric pressure.

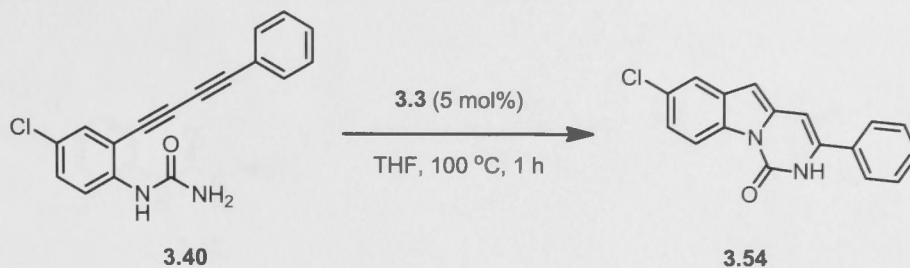
¹H NMR (300 MHz) D₆-DMSO δ 11.06 (broad s, 1H), 8.52 (d, *J*=7.5 Hz, 1H), 7.80 (d, *J*=8.1 Hz, 2H), 7.71 (d, *J*=8.1 Hz, 1H), 7.48 (m, 3H), 7.30 (m, 2H), 6.94 (s, 1H), 6.67 (s, 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 148.4, 137.0, 135.9, 132.8, 132.2, 130.5, 129.3, 128.8, 126.3, 123.6, 121.9, 119.7, 115.3, 97.8, 96.1.

IR ν_{max} /cm⁻¹ 3391, 3226, 3050, 1691, 1625, 1472, 1449, 754.

Mass Spectrum *m/z* (EI) 260 (*M*⁺, 100%), 217 (7), 189 (16).

HREIMS found: *M*⁺, 260.0950, C₁₇H₁₂N₂O requires *M*⁺, 260.0950.

7-Chloro-3-phenylpyrimido[1,6-*a*]indol-1(2*H*)-one (3.54)

The *title compound* was synthesised from diyne **3.40** (208 mg, 0.71 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 v/v MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (R_f = 0.7 in 1:19 v/v MeOH/CH₂Cl₂), the *title tetracycle* **3.54** (118 mg, 65%) as a yellow powder.

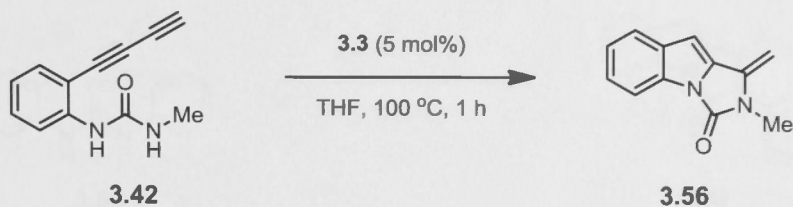
¹H NMR (800 MHz) D₆-DMSO δ 11.14 (broad s, 1H), 8.48 (d, J =8.4 Hz, 2H), 8.91 (s, 1H), 7.75 (d, J =6.8 Hz, 2H), 7.64 (s, 1H), 7.44 (m, 2H), 7.22 (d, J =8.4 Hz 1H), 6.85 (s, 1H), 6.59 (s, 1H).

¹³C NMR (200 MHz) D₆-DMSO δ 148.1, 137.9, 137.4, 132.6, 131.9, 130.6, 129.5, 128.8, 128.1, 126.4, 121.7, 118.8, 116.6, 97.1, 95.9.

IR ν_{max} /cm⁻¹ 3219, 1695, 1626, 1069, 804, 757.

Mass Spectrum m/z (EI) 296 and 294 (M^{+} , 41 and 100%, respectively), 258 (14), 163 (15).

HREIMS found: M^{+} , 294.0562. C₁₇H₁₁N₂O³⁵Cl requires M^{+} , 294.0560.

(Z)-3-Methyl-4-(prop-2-yn-1-ylidene)-3,4-dihydroquinazolin-2(1H)-one (3.56)

The *title compound* was synthesised from diyne **3.42** (100 mg, 0.37 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, CH₂Cl₂) to afford, after concentration of the relevant fractions (*R_f* = 0.7 in CH₂Cl₂), the *title tricycle* **3.56** (28 mg, 28%) as a white solid.

¹H NMR (400 MHz) δ 7.94 (d, *J*=8.4 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 2H), 7.33 (dt, *J*=8.4 and 1.2 Hz, 1H), 7.23 (dt, *J*=7.6 and 1.2, 1H), 6.66 (s, 1H), 5.01 (d, *J*=2.4 Hz, 1H), 4.65 (d, *J*=2.4 Hz, 1H), 3.18 (s, 3H).

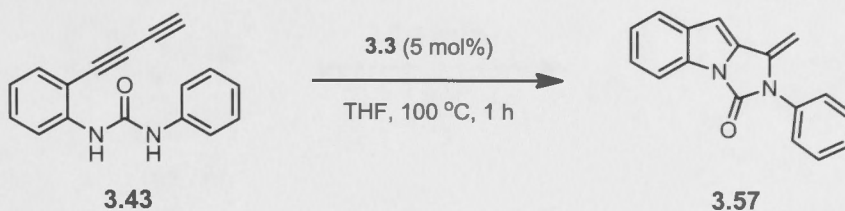
¹³C NMR (100 MHz) δ 149.8, 136.1, 133.3, 133.0, 131.0, 124.5, 122.9, 121.9, 112.6, 98.3, 87.4, 26.6.

IR ν_{max} /cm⁻¹ 3445, 3057, 2920, 1958, 1730, 1435, 1385, 747.

Mass Spectrum *m/z* (EI) 198 (M⁺, 100%), 170 (16), 141 (33), 114 (18).

HREIMS found: M⁺, 198.0790. C₁₂H₁₀N₂O requires M⁺, 198.0793.

1,2-Dihydro-1-methylene-2-phenylimidazo[1,5-a]indol-3-one (3.57)



The *title compound* was synthesised from diyne **3.43** (79 mg, 0.30 mmol) using the general procedure 5.2.2-B. The crude product was subjected to chromatography (silica, CH_2Cl_2) to afford, after concentration of the appropriate fractions ($R_f = 0.7$ in CH_2Cl_2), the *title tetracycle* **3.57** (44 mg, 56%) as a white solid.

$^1\text{H NMR}$ (400 MHz) δ 7.81 (dd, $J=8.4$ and 0.8 Hz, 1H), 7.45 (dd, $J=8.4$ and 0.8 Hz, 2H), 7.35 (m, 2H), 7.25 (m, 2H), 7.17 (td, $J=7.6$ and 1.2 Hz, 1H), 7.09 (td, $J=7.6$ and 1.2 Hz, 1H), 6.56 (s, 1H), 4.87 (d, $J=2.4$ Hz, 1H), 4.48 (d, $J=2.4$ Hz, 1H).

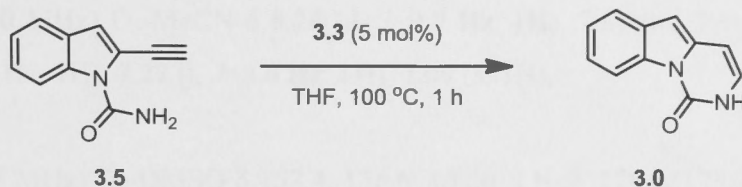
$^{13}\text{C NMR}$ (100 MHz) δ 163.4, 148.9, 136.3, 133.7, 133.2, 133.1, 130.9, 129.6, 127.9, 124.7, 123.3, 121.9, 112.9, 98.4, 89.2.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3057, 1897, 1744, 1644, 1448, 1380, 747, 707.

Mass Spectrum m/z (EI) 260 ($\text{M}^{+\bullet}$, 100%), 218 (15), 140 (28), 114 (18).

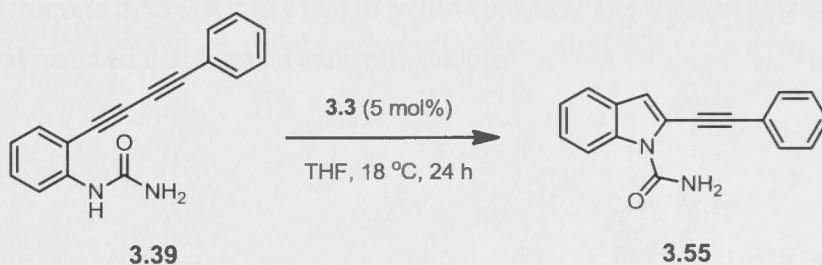
HREIMS found: $\text{M}^{+\bullet}$, 260.0945. $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}$ requires $\text{M}^{+\bullet}$, 260.0950.

Reaction of indole 3.5 with gold complex 3.3



The *title compound* was synthesised from indole **3.5** (20 mg, 0.11 mmol) using the general procedure 5.2.2-B. The crude material was subjected to chromatography (silica, 1:99 v/v MeOH/CH₂Cl₂) to afford, after concentration of the relevant fractions (R_f = 0.6 in 1:19 v/v MeOH/CH₂Cl₂), the *title tricycle* **3.0** (15 mg, 75%) as off-white solid. The spectral data derived from this material matched that of an authentic sample.

Reaction of diyne 3.39 with gold complex 3.3



A magnetically stirred solution of diyne **3.39** (94 mg, 0.36 mmol) in anhydrous CH₂Cl₂ (10 mL) maintained at 18 °C under an atmosphere of nitrogen was treated with gold complex **3.3** (14 mg, 0.02 mmol) and the reaction mixture was stirred for 24 h. Chromatography grade silica (*ca.* 100 mg) was then added to the reaction mixture and the ensuing slurry was concentrated under reduced pressure. The resultant free flowing yellow powder was subjected to chromatography (silica, 0:100→1:99 v/v MeOH/CH₂Cl₂, gradient elution) and two fractions A and B were thereby obtained.

Concentration of fraction A ($R_f = 0.8$ in 1:19 v/v MeOH/CH₂Cl₂) afforded the *title indole* **3.55** (68 mg, 72%) as a white powder.

¹H NMR (300 MHz) D₃-MeCN δ 8.24 (d, $J=9.7$ Hz, 1H), 7.61 (m, 3H), 7.49 (m, 3H), 7.38 (t, $J=9.7$ Hz, 1H), 7.27 (t, $J=8.6$ Hz, 1H), 7.09 (s, 1H).

¹³C NMR (75 MHz) D₆-DMSO δ 152.4, 136.6, 132.0, 130.0, 129.6, 128.2, 125.4, 122.8, 122.4, 121.6, 119.5, 114.8, 114.0, 96.2, 82.0.

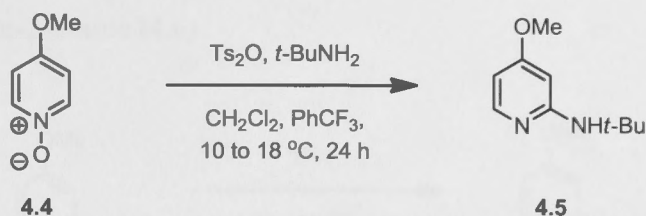
IR $\nu_{\max}/\text{cm}^{-1}$ 3391, 3185, 1945, 1676, 1617, 1448, 1412, 1331, 751, 741.

Mass Spectrum m/z (EI) 260 ($M^{+\bullet}$, 50%), 217 (100), 189 (13).

HREIMS found: $M^{+\bullet}$, 260.0950. C₁₇H₁₂N₂O requires $M^{+\bullet}$, 260.0950.

Concentration of fraction B ($R_f = 0.8$ in 1:19 v/v MeOH/CH₂Cl₂) afforded the previously obtained *tetracycle* **3.53** (19 mg, 21%) as yellow powder. The spectral data derived from this material matched that from an authentic sample.

5.2.3 Procedures Associated with Work Described in Chapter Four

N-*tert*-Butyl-4-methoxypyridin-2-amine (4.5)

Following protocols reported by Yin *et al.*,¹⁵ a solution of 4-methoxypyridine-*N*-oxide monohydrate (**4.4**) (8.10 g, 56.6 mmol) in CH₂Cl₂ (200 mL) and PhCF₃ (90 mL) at 5 °C was treated with *tert*-butylamine (30.0 mL, 285 mmol) followed by Ts₂O (37.0 g, 113 mmol) while controlling the temperature at 5–12 °C. After 0.5 h a second aliquot of *t*-BuNH₂ (30.0 mL, 285 mmol) was added followed by a second portion of Ts₂O (37.0 g, 113 mmol). The reaction mixture was then warmed to 18 °C and stirred for a further 24 h. The reaction mixture was filtered and washed with CH₂Cl₂ (200 mL) and then water (200 mL) was added to the filtrate and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (4 × 100 mL) and the combined organic fractions were dried (Na₂SO₄) and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 0:100→1:49 *v/v* MeOH/CH₂Cl₂, gradient elution) to afford, after concentration of the appropriate fractions (*R*_f = 0.6 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title compound* **4.5** (6.28 g, 61%) as a yellow oil.

¹H NMR (400 MHz) δ 7.86 (d, *J*=6.0 Hz, 1H), 6.14 (dd, *J*=6.0 and 2.0 Hz, 1H), 5.92 (d, *J*=2.0 Hz, 1H), 3.74 (s, 3H), 1.38 (s, 9H).

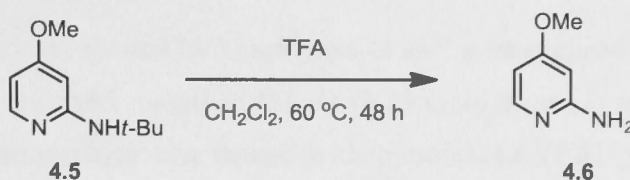
¹³C NMR (100 MHz) δ 166.7, 159.8, 148.9, 100.4, 92.6, 54.8, 50.6, 29.5.

IR ν_{max} /cm⁻¹ 3409, 2964, 1909, 1606, 1574, 1513, 1488, 1454, 1235, 1171, 1044, 820.

Mass Spectrum *m/z* (EI) 180 (M⁺, 38 %), 165 (100), 124 (77).

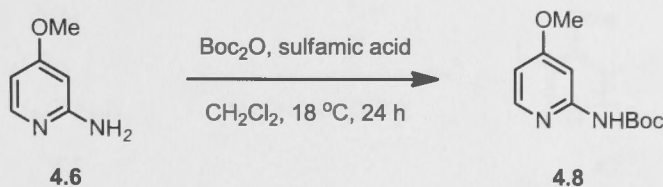
HREIMS found: $M^{+\bullet}$, 180.1262. $C_{10}H_{16}N_2O$ requires $M^{+\bullet}$, 180.1263

4-Methoxypyridin-2-amine (4.6)



A magnetically stirred solution of pyridine **4.5** (4.8 g, 26.6 mmol) in CH_2Cl_2 (30 mL) was treated with trifluoroacetic acid (20 mL, 270 mmol) and the reaction mixture was refluxed for 24 h. The cooled reaction mixture was diluted with CH_2Cl_2 (50 mL) and the pH was adjusted to 9-10 with a saturated aqueous solution of Na_2CO_3 . The aqueous layer was extracted with ethyl acetate ($5 \times 100\text{ mL}$) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The white solid thus obtained was subjected to flash chromatography (silica, 2:98→5:95 v/v MeOH/ CH_2Cl_2 , gradient elution) to afford, after concentration of the relevant fractions ($R_f = 0.2$ in 1:19 v/v MeOH/ CH_2Cl_2), the title pyridine **4.6**¹⁶ (2.45 g, 73%) as a white solid.

1H NMR (300 MHz) δ 7.86 (d, $J=6.0\text{ Hz}$, 1H), 6.28 (dd, $J=6.0$ and 2.2 Hz , 1H), 6.00 (d, $J=2.2\text{ Hz}$, 1H), 4.43 (broad s, 2H), 3.81 (s, 3H).

***tert*-Butyl 4-methoxypyridin-2-ylcarbamate (4.8)**

Following the protocol reported by Upadhyaya *et al.*,¹³ a magnetically stirred mixture of sulfamic acid (63 mg, 0.65 mmol) in Boc_2O (3.23 g, 14.8 mmol) maintained at 18 °C under a nitrogen atmosphere was treated with pyridine **4.6** (1.67 g, 13.5 mmol). The reaction mixture was stirred for a further 4 h before CH_2Cl_2 (2 mL) was added and stirring was continued for 18 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and filtered through a short plug of silica and washed with CH_2Cl_2 (50 mL). Concentration of the filtrate gave the *title pyridine* **4.8** (1.88 g, 65 %) as a white solid, (R_f = 0.8 in 1:19 *v/v* MeOH/ CH_2Cl_2).

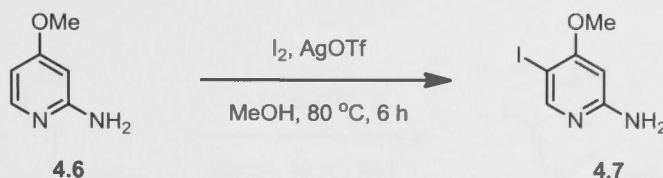
^1H NMR (300 MHz) δ 9.66 (broad s, 1H), 8.12 (d, J =6.0 Hz, 1H), 7.61 (d, J =2.5 Hz, 1H), 6.50 (dd, J =6.0 and 2.5 Hz, 1H), 3.88 (s, 3H), 1.54 (s, 9H).

^{13}C NMR (75 MHz) δ 167.6, 154.5, 152.9, 148.1, 106.4, 96.6, 80.7, 55.3, 28.4.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3176, 3121, 2978, 1726, 1608, 1586, 1237, 1156, 1049, 771 .

Mass Spectrum m/z (EI) 224 ($\text{M}^{+\bullet}$, 10%), 168 (15), 150 (18), 124 (65), 57 (100).

HREIMS found: $\text{M}^{+\bullet}$, 224.1159. $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_3$ requires $\text{M}^{+\bullet}$, 224.1161.

5-Iodo-4-methoxypyridin-2-amine (4.7)

A magnetically stirred solution of pyridine **4.6** (200 mg, 1.6 mmol) in MeOH (5 mL) maintained at 18 °C under a nitrogen atmosphere was treated with iodine (1.23 g, 4.8 mmol) and AgOTf (1.23 g, 4.8 mmol). The reaction mixture subjected to microwave irradiation (80 °C, 6 h), cooled then treated with a second aliquot of iodine (0.82 g, 3.2 mmol) and AgOTf (0.82 g, 3.2 mmol). The reaction mixture was subjected to microwave irradiation (80 °C, 4 h). The reaction mixture was quenched with NaHCO₃ (10 mL of a saturated aqueous solution), then Na₂S₂O₃ (5 mL of a saturated aqueous solution) and concentrated to *ca.* 1/5 of its volume. The aqueous layer was separated and extracted with CH₂Cl₂ (4 × 10 mL) and the combined organic fractions were dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 0:100 → 0.5:99.5, *v/v*, MeOH/CH₂Cl₂, gradient elution) to afford, after concentration of the relevant fractions (*R*_f = 0.8 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title pyridine* **4.7** (175 mg, 44%) as a white solid, m.p. = 140–145 °C.

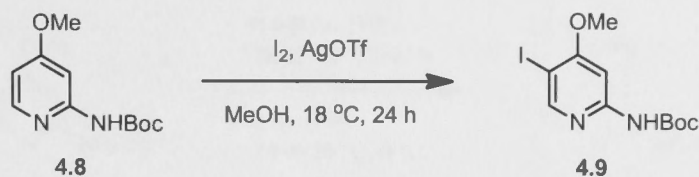
¹H NMR (400 MHz) δ 8.15 (s, 1H), 6.00 (s, 1H), 4.47 (broad s, 2H), 3.86 (s, 3H).

¹³C NMR (100 MHz) δ 164.9, 160.0, 155.4, 91.3, 71.4, 55.8.

IR ν_{max} /cm⁻¹ 3436, 3293, 3132, 1841, 1642, 1584, 1547, 1401, 1223, 1046, 829.

Mass Spectrum *m/z* (EI) 251 (18%), 250 (M⁺, 100%), 193 (32).

HREIMS found: M⁺, 249.9609. C₆H₇N₂OI requires M⁺, 249.9603.

tert*-Butyl (5-iodo-4-methoxypyridin-2-yl)carbamate (4.9)Method A*

A magnetically stirred solution of pyridine **4.8** (50 mg, 0.22 mmol) in MeOH (5 mL) maintained at 18 °C under nitrogen atmosphere was treated with iodine (57 mg, 0.22 mmol), and Ag(OTf) (57 mg, 0.22 mmol) and stirring was continued for 24 h in the absence of light. The reaction mixture was concentrated to *ca.* 1/5 of its volume and diluted with CH₂Cl₂ (5 mL) then quenched with a saturated aqueous solution of Na₂S₂O₃ (3 mL). The aqueous layer was separated and extracted with CH₂Cl₂ (4 × 5 mL) and the combined organic fractions were dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 0:100 → 0.5:99.5, *v/v*, MeOH/CH₂Cl₂) to afford, after concentration of the relevant fractions (*R_f* = 0.8 in 1:19 *v/v* MeOH/CH₂Cl₂), *title pyridine* **4.9** (48 mg, 61 %) as white solid.

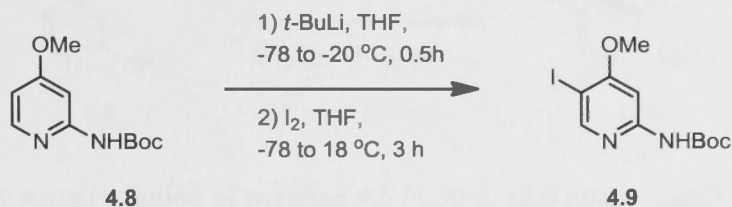
¹H NMR (400 MHz) δ 9.61 (broad s, 1H), 8.46 (s, 1H), 7.67 (s, 1H), 3.98 (s, 3H), 1.57 (s, 9H).

¹³C NMR (100 MHz) δ 165.5, 154.6, 152.7, 95.7, 81.3, 75.7, 56.3, 28.4.

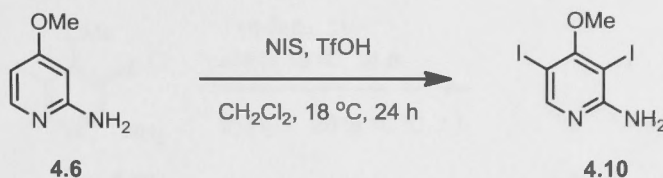
IR ν_{max} /cm⁻¹ 3149, 2974, 1859, 1718, 1570, 1155, 771.

Mass Spectrum *m/z* (EI) 350 (M⁺, 13%), 276 (53), 250 (100).

HREIMS found: M⁺, 350.0128. C₁₁H₁₅IN₂O₃ requires M⁺, 350.0127.

tert*-Butyl (5-iodo-4-methoxypyridin-2-yl)carbamate (4.9)Method B*

A magnetically stirred solution of pyridine **4.8** (1.17 g, 5.2 mmol) in THF (10 mL) maintained at -78 °C under a nitrogen atmosphere was treated, dropwise, with *tert*-butyllithium (9.4 mL of a 1.4 M solution in pentane, 13.0 mmol) and the solution was allowed to warm to -20 °C over 0.5 h. The reaction mixture was then cooled to -78 °C and iodine (3.96 g, 15.6 mmol) in THF (15 mL) was added, dropwise, over 0.5 h. The reaction was stirred at this temperature for 0.5 h before being warmed to 18 °C over 2 h. The reaction was quenched with Na₂S₂O₃ (10 mL of a sat. aq. solution), extracted with ethyl acetate (3 × 20 mL), dried (MgSO₄), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 0:100 → 0.5:99.5 v/v MeOH/CH₂Cl₂, gradient elution) to afford, after concentration of the appropriate fractions (*R*_f = 0.8 in 1:19 v/v MeOH/CH₂Cl₂), the pyridine **4.4** (1.42 g, 78%) as white solid. The spectral data derived from this material matched that of an authentic sample. A small portion of this material (*ca.* 50 mg) was dissolved in CH₂Cl₂ (*ca.* 10 mL) and heated for 10 mins which effected Boc-cleavage. Hexane (5 mL) was added and the white precipitate was filtered and shown to be identical by ¹H NMR spectroscopic analysis to pyridine **4.7**.

3,5-Diiodo-4-methoxypyridin-2-amine (4.10)

A magnetically stirred solution of pyridine **4.6** (1.50 g, 12.0 mmol) and NIS (6.75 g, 30.0 mmol) in CH_2Cl_2 (50 mL) maintained at 18 °C under a nitrogen atmosphere was treated, dropwise, with triflic acid (3.21 mL, 5.44 g, 36.0 mmol). The reaction mixture was stirred at 18 °C for 24 h in the absence of light. The reaction mixture was quenched with Na_2CO_3 (sat. aq. solution) until pH 9-10 was attained then the aqueous layer was separated and extracted with ethyl acetate (4×20 mL), and to the combined organic fractions was added a saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (25 mL of a sat. aq. solution). After stirring for 5 mins, the aqueous layer was separated and extracted with ethyl acetate (4×50 mL). The combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, CH_2Cl_2) to afford, after concentration of the relevant fractions ($R_f = 0.8$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title pyridine* **4.10** (3.14 g, 70%) as a white solid. Recrystallisation of this material (CH_2Cl_2) gave colourless needles, m.p. = 114-115 °C.

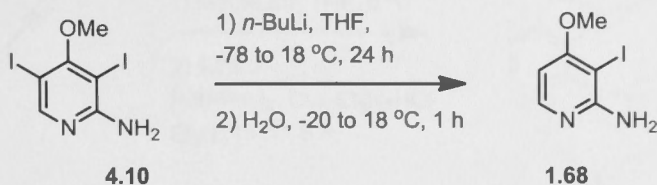
^1H NMR (400 MHz) CD_2Cl_2 δ 8.14 (s, 1H), 5.17 (broad s, 2H), 3.85 (s, 3H).

^{13}C NMR (100 MHz) D_6 -DMSO δ 162.3, 156.4, 151.9, 70.4, 69.4, 56.5.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3456, 3286, 3151, 2935, 1844, 1639, 1559, 1453, 1392, 1240, 1010, 652.

Mass Spectrum m/z (EI) 376 ($\text{M}^{+\bullet}$, 100%), 234 (33), 192 (33).

HREIMS found: $\text{M}^{+\bullet}$, 375.8570. $\text{C}_6\text{H}_6\text{I}_2\text{N}_2\text{O}$ requires $\text{M}^{+\bullet}$, 375.8570.

3-Iodo-4-methoxypyridin-2-amine (1.68)

A magnetically stirred solution of pyridine **4.10** (1.66 g, mmol) in THF (20 mL) at -78 °C under a nitrogen atmosphere was treated with *n*-BuLi (3.7 mL of a 1.8 M solution in pentane, 6.6 mmol). The reaction mixture was warmed to 18 °C over 1.5 h, then cooled to -20 °C and water (2 mL) was added. The reaction was warmed to 18 °C over 1 h then extracted with EtOAc (3 × 30 mL) and the organic fractions were dried (Na₂S₂O₄), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 0:100 → 1:99, v/v, MeOH/CH₂Cl₂, gradient elution) to afford, after concentration of the relevant fractions (*R*_f = 0.5 in 1:19 v/v MeOH/CH₂Cl₂), the *title pyridine* **1.68** (810 mg, 74%) as a white solid, m.p. = 161-162 °C.

¹H NMR (300 MHz) δ 7.88 (d, *J*=6.0 Hz, 1H), 6.17 (d, *J*=6.0 Hz, 1H), 4.97 (broad s, 2H), 3.90 (s, 3H).

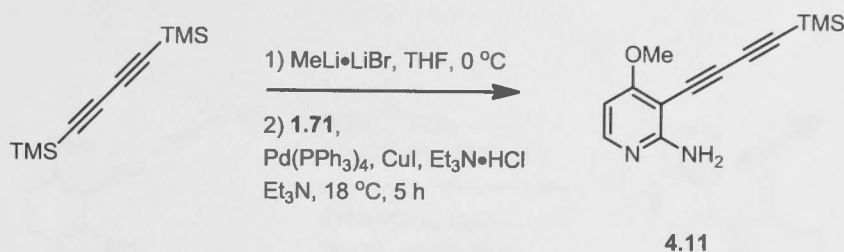
¹³C NMR (100 MHz) δ 165.3, 159.6, 149.3, 98.3, 67.3, 56.3.

IR $\nu_{\max}/\text{cm}^{-1}$ 3451, 3272, 3127, 2978, 1622, 1580, 1454, 1326, 1278, 1048, 795 .

Mass Spectrum *m/z* (EI) 250 (*M*⁺, 100%).

HREIMS found: *M*⁺, 249.9602. C₆H₇IN₂O requires *M*⁺, 249.9603.

4-Methoxy-3-[(trimethylsilyl)buta-1,3-diynyl]pyridin-2-amine (4.11)



A magnetically stirred solution of bis-trimethylsilyl-1,3-butadiyne (300 mg, 1.54 mmol) in THF (1 mL) under a nitrogen atmosphere was cooled to 0 °C then treated with MeLi·LiBr complex (1.3 mL of a 1.2 M solution in Et₂O, 1.60 mmol) *via* syringe. The reaction mixture was stirred at 0 °C for 0.5 h then warmed to 18 °C over 1 h. Et₃N (4 mL), Et₃NHCl (77 mg, 0.56 mmol), *o*-iodopyridine (350 mg, 1.40 mmol), Pd(PPh₃)₄ (80 mg, 0.07 mmol), CuI (27 mg, 0.14 mmol), were then added sequentially to the reaction mixture which was heated at 65 °C for 16 h. The reaction mixture was cooled then SiO₂ (*ca.* 0.5 g) was added and the ensuing slurry was concentrated under reduced pressure. Subjection of the ensuing white solid to flash chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) afforded, after concentration of the relevant fractions (*R*_f 0.5 in 1:19 *v/v* MeOH/CH₂Cl₂), to the *title diyne* **4.11** (248 mg, 63%) as a colourless solid.

¹H NMR (300 MHz) δ 7.90 (d, *J*=6.0 Hz, 1H), 6.22 (d, *J*=6.0 Hz, 1H), 5.22 (broad s, 2H), 3.86 (s, 3H), 0.21 (s, 9H).

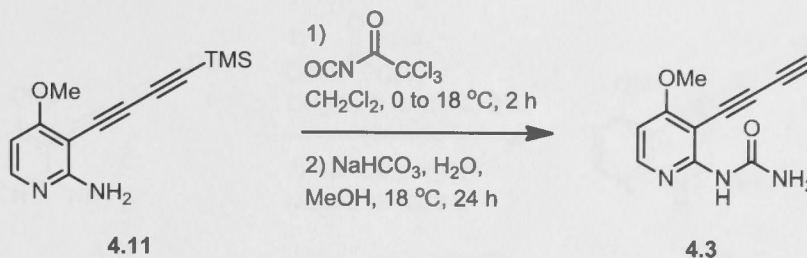
¹³C NMR (100 MHz) δ 168.8, 162.1, 149.8, 97.5, 92.9, 87.6, 83.6, 69.0, 55.9, -0.5.

IR ν_{max} /cm⁻¹ 3469, 3126, 2955, 2198, 2101, 1958, 1622, 1569, 1485, 1458, 1290, 1245, 841.

Mass Spectrum *m/z* (EI) 244 (M⁺, 100%), 229 (96), 69 (25).

HREIMS found: M⁺, 244.1033. C₁₃H₁₆N₂OSi requires M⁺, 244.1032.

1-[3-(Buta-1,3-diyn-1-yl)-4-methoxypyridin-2-yl]urea (4.3)



The *title urea* was synthesized from diyne (**4.11**) (240 mg, 0.14 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 1:49 v/v MeOH/ CH_2Cl_2) to afford, after concentration of the relevant fractions ($R_f = 0.4$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title urea* **4.3** (159 mg, 75%) as an off-white solid.

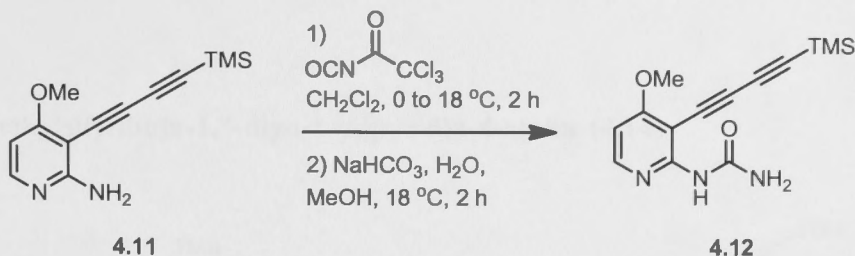
^1H NMR (300 MHz) δ 8.18 (d, $J=6.0$ Hz, 1H), 7.84 (s, 1H), 6.84 (d, $J=6.0$ Hz, 1H), 4.27 (s, 0.6H), 3.92 (s, 3H).

^{13}C NMR (75 MHz) δ 169.6, 166.2, 154.7, 149.3, 102.2, 92.6, 84.8, 79.2, 68.1, 66.2, 57.1.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3304, 3269, 2029, 1958, 1730, 1582, 1366, 1291, 1099, 817.

Mass Spectrum m/z (EI) 215 ($\text{M}^{+\bullet}$, 36%), 172 (100), 142 (59), 86 (21).

HREIMS found: $\text{M}^{+\bullet}$, 215.0693. $\text{C}_{11}\text{H}_9\text{N}_3\text{O}_2$ requires $\text{M}^{+\bullet}$, 215.0695.

1-{4-Methoxy-3-[(trimethylsilyl)buta-1,3-diyne-1-yl]pyridin-2-yl}urea (**4.12**)

A magnetically stirred solution of diyne **4.11** (62 mg, 0.25 mmol) in CH_2Cl_2 (3 mL) maintained at 0°C under a nitrogen atmosphere was treated with trichloroacetyl isocyanate (49 mg, 0.31 mL, 0.26 mmol) *via* syringe. The reaction mixture was warmed to 18°C over 2 h then concentrated under reduced pressure. The crude solid was taken up in MeOH (5 mL) and treated with NaHCO_3 (1 drop of a saturated aqueous solution) maintained at 18°C and left to stir at this temp for 2 h. The reaction mixture was diluted with water (1 mL) and the MeOH was removed under reduced pressure. The aqueous suspension was then extracted with ethyl acetate (4×5 mL) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 1:99→1:49 v/v MeOH/ CH_2Cl_2 , gradient elution) to afford, after concentration of the relevant fractions ($R_f = 0.5$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title compound* **4.12** (17 mg, 24 %) as a white solid.

$^1\text{H NMR}$ (300 MHz) δ 9.28 (broad s, 1H), 8.05 (d, $J=6.0$ Hz, 1H), 7.48 (broad s, 1H), 6.49 (d, $J=6.0$ Hz, 1H), 5.29 (broad s, 1H), 3.92 (s, 3H), 0.24 (s, 9H).

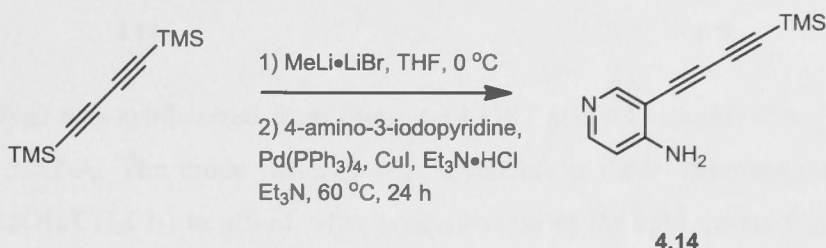
$^{13}\text{C NMR}$ (75 MHz) δ 168.9, 155.7, 155.2, 147.6, 100.8, 94.9, 93.4, 86.9, 86.2, 65.9, 56.3, -0.6.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3295, 2960, 2197, 2099, 1958, 1712, 1584, 1395, 1365, 1289, 1098, 842.

Mass Spectrum m/z (EI) 287 (M^{+} , 14%), 244 (100), 229 (77), 215 (32), 199 (16).

HREIMS found: $M^{+\bullet}$, 287.1093 $C_{14}H_{17}N_3O_2Si$ requires $M^{+\bullet}$, 287.1090.

3-[(Trimethylsilyl)buta-1,3-diyne-1-yl]pyridin-4-amine (**4.14**)



The *title diyne* was synthesized from 4-amino-3-iodopyridine (1.10 g, 5.00 mmol) using the general procedure 5.2.1-A, heated at 60 °C for 24 h. The crude material was subjected to flash chromatography (silica, 2:98 v/v MeOH/ CH_2Cl_2) to afford, after concentration of the appropriate fractions ($R_f = 0.5$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title diyne* **4.14** (247 mg, 23%) as a brown solid.

^1H NMR (300 MHz) δ 8.33 (s, 1H), 8.10 (d, $J=6.6$ Hz, 1H), 6.60 (d, $J=6.6$ Hz, 1H), 5.12 (broad s, 2H), 0.23 (s, 9H).

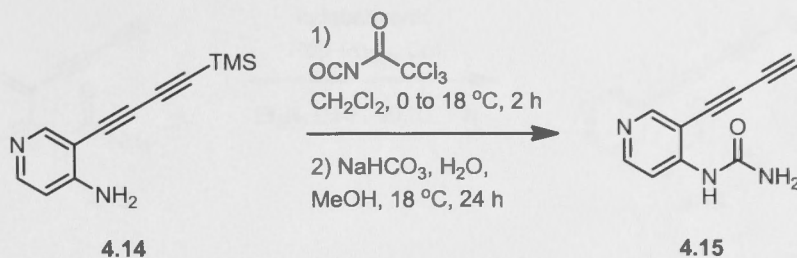
^{13}C NMR (75 MHz) δ 155.4, 154.5, 150.1, 108.8, 103.6, 93.5, 87.8, 82.4, 71.2, 0.2.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3128, 2960, 2199, 2101, 1636, 1620, 1591, 1265, 1250, 842.

Mass Spectrum m/z (EI) 214 ($M^{+\bullet}$, 77%), 199 (100).

HREIMS found: $M^{+\bullet}$, 214.0926. $C_{12}H_{14}N_2Si$ requires $M^{+\bullet}$, 214.0926.

1-[3-(Buta-1,3-diyne-1-yl)pyridin-4-yl]urea (4.15)



The *title diyne* was synthesized from diyne **4.14** (247 mg, 1.15 mmol) using the general procedure 5.2.2-A. The crude material was subjected to flash chromatography (silica, 2:98 *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R_f* = 0.1 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title diyne* **4.15** (203 mg, 95%) as a white solid.

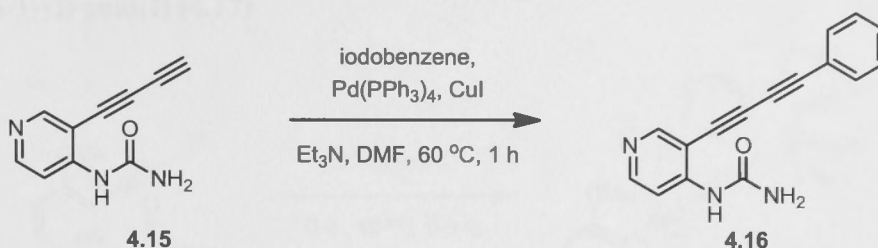
¹H NMR (300 MHz) δ 8.53 (s, 1H), 8.44 (s, 1H), 8.31 (d, *J*=6.0 Hz, 1H), 8.16 (d, *J*=6.0 Hz, 1H), 6.78 (broad s, 2H), 4.27 (s, 0.7 H).

¹³C NMR (75 MHz) δ 155.3, 154.8, 150.6, 149.5, 112.1, 105.2, 81.9, 78.7, 69.1, 68.3.

IR ν_{max} /cm⁻¹ 3399, 3268, 3117, 2210, 1926, 1680, 1567, 1520, 1320, 1015, 605.

Mass Spectrum *m/z* (EI) 185 (*M*⁺, 56%), 142 (100), 115 (23).

HREIMS found: *M*⁺, 185.0599. C₁₀H₇N₃O requires *M*⁺, 185.0598.

1-[3-(Phenylbuta-1,3-diyne-1-yl)pyridin-4-yl]urea (**4.16**)

A magnetically stirred solution of diyne **4.15** (70 mg, 0.38 mmol) in a solution of DMF (0.2 mL) and Et_3N (1 mL) maintained at 18 °C under an atmosphere of nitrogen was treated with iodobenzene (231 mg, 1.13 mmol), $\text{Pd(PPh}_3)_4$ (22 mg, 0.02 mmol), CuI (7 mg, 0.04 mmol). The reaction mixture was subjected to microwave irradiation at 60 °C for 1 h. SiO_2 (*ca.* 200 mg) was added to the cooled reaction mixture and the ensuing slurry was concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 3:97 *v/v* $\text{MeOH/CH}_2\text{Cl}_2$) to afford, after concentration of the relevant fractions ($R_f = 0.2$ in 1:19 *v/v* $\text{MeOH/CH}_2\text{Cl}_2$), the *title diyne* **4.16** (63 mg, 63%) as a white solid.

^1H NMR (300 MHz) δ 8.57 (s, 1H), 8.49 (s, 1H), 8.33 (d, $J=5.7$ Hz, 1H), 8.19 (d, $J=5.7$ Hz, 1H), 7.63 (d, $J=7.5$ Hz, 2H), 7.51-7.43 (complex m, 3H), 6.81 (broad s, 2H).

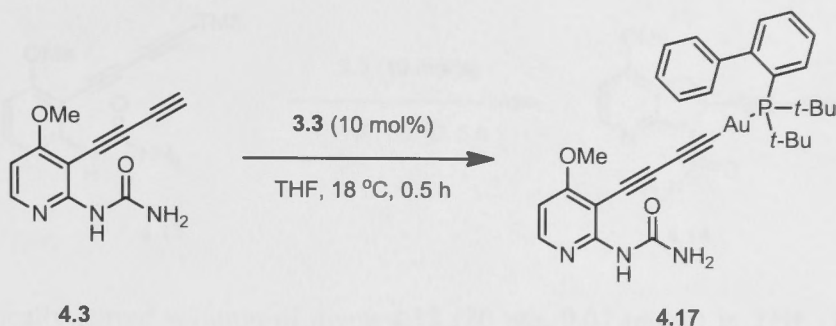
^{13}C NMR (75 MHz) δ 154.9, 154.1, 150.2, 148.8, 132.4, 130.3, 129.1, 120.2, 111.7, 105.3, 83.8, 81.5, 75.4, 73.8.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3371, 3299, 3128, 2213, 1950, 1680, 1566, 1521, 1316, 1014, 751, 612.

Mass Spectrum m/z (EI) 261 ($\text{M}^{+\bullet}$, 64%), 244 (52), 218 (100).

HREIMS found: $\text{M}^{+\bullet}$, 261.0902. $\text{C}_{16}\text{H}_{11}\text{N}_3\text{O}$ requires $\text{M}^{+\bullet}$, 261.0902.

([1,1'-Biphenyl]-2-yl-di-tert-butylphosphinyl)((4-methoxy-3-ureidopyridin-2-yl)buta-1,3-diyne-1-yl) gold(I) (4.17**)**



A magnetically stirred solution of diyne **4.3** (34 mg, 0.16 mmol) in THF (1 mL) maintained at 18 °C under positive pressure of nitrogen was treated with catalyst **3.3** (12 mg, 0.016 mmol). The reaction mixture was stirred at 18 °C for 24 h then SiO₂ (*ca.* 100 mg) was added and the ensuing slurry was concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, CH₂Cl₂) to afford, after concentration of the relevant fractions (*R_f* = 0.4 in CH₂Cl₂), the *title gold acetylide* **4.17** (7 mg, 62% based on **3.3**) as a white solid.

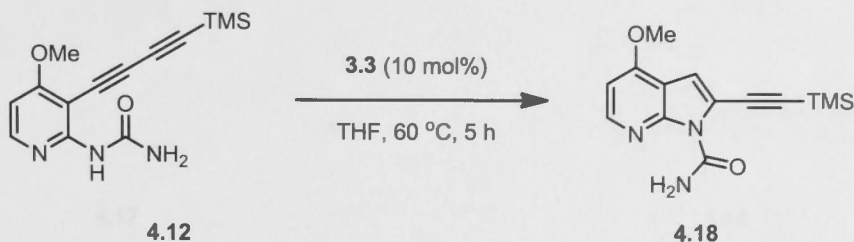
¹H NMR (300 MHz) CD₂Cl₂ δ 9.20 (broad s, 1H), 8.01 (d, *J*=6.0 Hz, 1H), 7.89 (m, 1H), 7.55-7.47 (complex m, 5H), 7.29-7.25 (complex m, 1H), 7.18 (dd, *J*=7.8 and 1.2 Hz, 2H), 6.52 (d, *J*=6.6 Hz, 1H), 5.08 (broad s, 1H), 3.94 (s, 3H), 1.43 (s, 9H), 1.38 (s, 9H).

¹³C NMR (75 MHz) CD₂Cl₂ δ 168.7, 155.8, 155.1, 156.2, 150.3, 146.3, 142.6, 141.5, 145.6, 139.7, 133.2, 139.0, 133.1, 135.3, 129.4, 128.1, 127.0, 126.9, 100.9, 101.1, 95.2, 58.1, 56.4, 37.8, 37.5, 31.0, 30.9, 29.9.

Mass Spectrum *m/z* (ESI) 748 [(M+K)⁺, 10%], 732 [(M+Na)⁺, 49], 710 [(M+H)⁺, 100], 667 (58), 495 (51), 216 (66), 199 (97), 173 (92).

HRESIMS found: M+H⁺, 710.2211. C₃₁H₃₆AuN₃O₂P requires M+H⁺, 710.2211.

4-Methoxy-2-[(trimethylsilyl)ethynyl]-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxamide
(4.18)



A magnetically stirred solution of diyne **4.12** (20 mg, 0.07 mmol) in THF (1 mL), was treated with gold complex **3.3** (5 mg, 0.01 μmol) maintained at 18 $^\circ\text{C}$ under an atmosphere of nitrogen. After 16 h the temperature was increased to 60 $^\circ\text{C}$ and stirring was continued for 5 h. The reaction mixture was cooled and SiO_2 (ca. 100 mg) was added and the ensuing slurry was concentrated under reduced pressure. The crude material was subjected to flash chromatography (silica, 1:99 $\rightarrow$ 1:49 v/v MeOH/ CH_2Cl_2 , gradient elution) to afford, after concentration of the appropriate fractions ($R_f = 0.5$ in 1:19 v/v MeOH/ CH_2Cl_2), the *title indole* **4.18** (8 mg, 40%) as a white solid.

$^1\text{H NMR}$ (300 MHz) δ 9.95 (broad s, 1H), 8.21 (d, $J=5.7$ Hz, 1H), 6.95 (s, 1H), 6.65 (d, $J=5.7$ Hz, 1H), 5.53 (broad s, 1H), 4.00 (s, 3H), 0.25 (s, 9H).

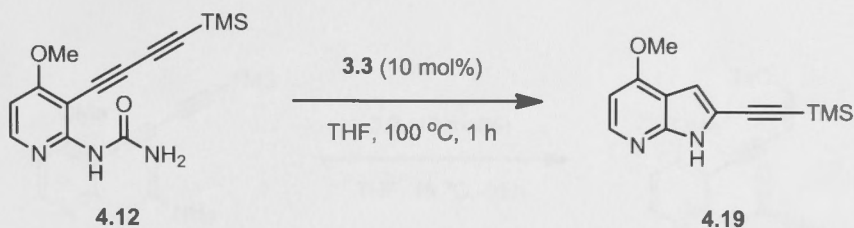
$^{13}\text{C NMR}$ (75 MHz) δ 159.8, 151.9, 148.2, 145.8, 111.9, 110.0, 102.2, 100.8, 96.3, 84.1, 55.8, -0.3.

$\text{IR } \nu_{\text{max}}/\text{cm}^{-1}$ 3306, 2957, 2153, 1958, 1727, 1574, 1340, 1288.

Mass Spectrum (EI) m/z 287 ($\text{M}^{+\bullet}$, 2%), 244 (82), 229 (100).

HREIMS found: $\text{M}^{+\bullet}$, 287.1086. $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_2\text{Si}$ requires $\text{M}^{+\bullet}$, 287.1090.

4-Methoxy-2-(2-(trimethylsilyl)ethynyl)-1*H*-pyrrolo[2,3-*b*]pyridine (**4.19**)



The *title compound* was synthesised according to the general method 5.2.2-B using diyne **4.12** (160 mg, 0.56 mmol) as the starting material and gold complex **3.3** (43 mg, 0.06 mmol). The crude material was subjected to flash chromatography (silica, 1:99 *v/v* MeOH/CH₂Cl₂) to afford an inseparable mixture of the indole **4.15** and the *title indole* **4.19** (68 mg, *ca.* 46%) in *ca.* 1:1 ratio as judged by ¹H NMR spectroscopic analysis. The mixture was recrystallised (CH₂Cl₂), to afford the *title indole* **4.19** (5 mg, 4% isolated) as colourless plates.

¹H NMR (300 MHz) δ 12.04 (broad s, 1H), 8.14 (d, *J*=5.6 Hz, 1H), 6.69 (s, 1H), 6.65 (d, *J*=5.6 Hz, 1H), 3.93 (s, 3H), 0.24 (s, 9H).

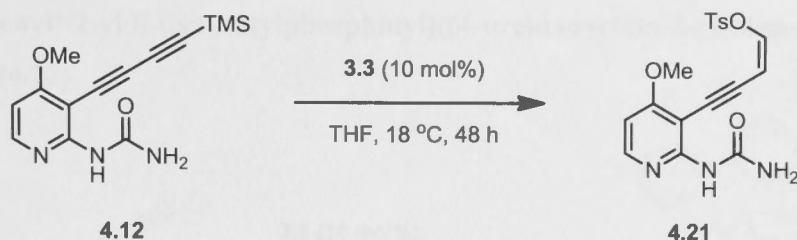
¹³C NMR (75 MHz) δ 160.0, 150.7, 147.9, 117.5, 110.5, 105.1, 99.4, 98.9, 98.7, 56.6, 0.8.

IR ν_{max} /cm⁻¹ 3105, 3064, 2769, 2690, 2158, 1876, 1701, 1608, 1587, 1520, 1458, 1328, 1294, 1286, 1155, 1110, 843.

Mass Spectrum *m/z* (EI) 244 (M⁺, 80%), 229 (100).

HREIMS found: M⁺, 244.1031 C₁₃H₁₆N₂OSi requires M⁺, 244.1032.

(E)-4-(4-Methoxy-2-ureidopyridin-3-yl)but-1-en-3-yn-1-yl 4-methylbenzenesulfonate (4.21)



A magnetically stirred solution of diyne **4.12** (61 mg, 0.21 mmol) in THF (2 mL) maintained at 18 °C under a nitrogen atmosphere was added *p*-toluenesulfonic acid monohydrate (40 mg, 21 mmol). After 15 min gold complex **3.3** (16 mg, 21 mmol) was added and stirring for 16 h at 18 °C. The reaction mixture was diluted with ethyl acetate (1 mL) and quenched with a saturated solution of Na₂CO₃. The aqueous layer was separated and extracted with ethyl acetate (4 × 2 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The crude solid was subjected to flash chromatography (silica, 2:98, *v/v* MeOH/CH₂Cl₂) to afford, after concentration of the appropriate fractions (*R*_f = 0.4 in 1:19 *v/v* MeOH/CH₂Cl₂), the *title enyne* **4.21** (52 mg, 64%) as white solid.

¹H NMR (300 MHz) δ 8.16 (d, *J*=6.3 Hz, 1H), 7.93 (d, *J*=8.7 Hz, 2H), 7.47 (d, *J*=8.7 Hz, 2H), 7.33 (s, 1H), 7.11 (d, *J*=6.3 Hz, 1H), 6.83 (d, *J*=5.7 Hz, 1H), 5.66 (d, *J*=5.7 Hz, 1H), 3.90 (s, 3H), 2.38 (s, 3H).

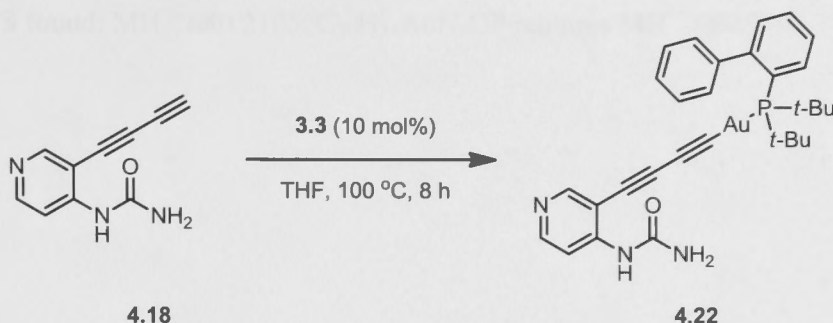
¹³C NMR (75 MHz) δ 166.9, 154.2, 153.8, 148.2, 144.1, 138.1, 131.5, 130.4, 128.0, 101.7, 97.7, 93.1, 85.5, 56.5, 21.2. (one signal obscured or overlapping).

IR ν_{max} /cm⁻¹ 3400, 2951, 2184, 1702, 1584, 1468, 1377, 1291, 1179, 1099, 681.

Mass Spectrum *m/z* (EI) 387 (M⁺, 11%), 370 (20), 344 (100), 297 (17), 244 (31), 232 (85), 215 (73).

HREIMS found: M^{+} , 387.0886. $C_{18}H_{17}N_3O_5S$ requires M^{+} , 387.0889.

[(1,1'-Biphenyl)-2-yl-di-tert-butylphosphinyl]((4-ureidopyridin-3-yl)buta-1,3-diyne-1-yl) gold(I) (4.22)



A magnetically stirred solution of diyne **4.18** (101 mg, 0.55 mmol) in THF (2 mL) in a 10 mL microwave reaction vessel was treated with gold complex **3.3** (42 mg, 0.06 mmol). The reaction vessel was evacuated and backfilled with nitrogen then subjected to microwave irradiation at 100 °C for 8 h (ramp time 1 min, power not exceeding 250 W). To the crude reaction mixture was added SiO_2 (*ca.* 200 mg) and the ensuing slurry was concentrated under reduced pressure, which gave a solid that was subjected to chromatography (silica, 1:99 *v/v* MeOH/ CH_2Cl_2) to afford, after concentration of the relevant fractions ($R_f = 0.4$ in 5:95 *v/v* MeOH/ CH_2Cl_2), the *title compound* **4.22** (33 mg, 90% based on **3.3**) as a white solid. Recrystallisation of this material (MeOH/ CH_2Cl_2) gave colourless needles.

^1H NMR (400 MHz) δ 8.39 (s, 1H), 8.24 (s, 1H), 8.20 (d, $J=6.0$ Hz, 1H), 8.10 (d, $J=6.0$ Hz, 1H), 7.94 (m, 1H), 7.57 (m, 2H), 7.45-7.37 (complex m, 3H), 7.21 (m, 1H), 7.12 (dd, $J=8.0$ and 1.6 Hz, 2H), 6.75 (broad s, 2H), 1.33 (s, 9H), 1.29 (s, 9H).

^{13}C NMR (100 MHz) δ 155.4, 153.6, 149.7, 149.6, 149.2, 148.5, 142.6, 142.5, 141.3, 140.0, 135.2, 133.0, 132.9, 131.2, 129.4, 129.3, 128.0, 127.8, 127.8, 126.5, 126.1, 111.9, 107.8, 85.9, 85.9, 85.1, 61.6, 55.5, 37.6, 37.3, 30.9, 30.8.

IR $\nu_{\text{max}}/\text{cm}^{-1}$ 3348, 2955, 2186, 2063, 1964, 1715, 1564, 1502, 1469, 1321, 1174, 1008, 699, 527.

Mass Spectrum m/z (ESI) 702 $[(\text{M}+\text{Na})^+]$, 26%], 680 $[(\text{M}+\text{H})^+]$, 100], 637 (6%).

HRESIMS found: MH^+ , 680.2105. $\text{C}_{30}\text{H}_{34}\text{AuN}_3\text{OP}$ requires MH^+ , 680.2105.

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Compound Library

The following compounds have been selected for synthesis to test the proposed mechanism of these tests have, so far, been encouraging.



2.10



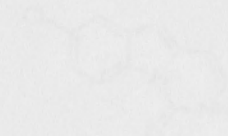
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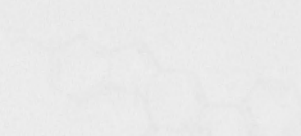
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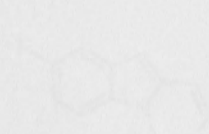
2.13



2.14



2.15



2.16



2.17



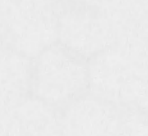
2.18



2.19



2.20

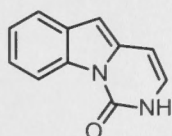


2.21

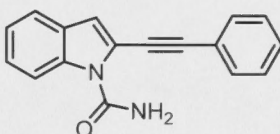
Appendix 1

Compound Library

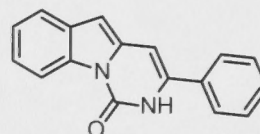
The following compounds have been submitted for biological testing. The preliminary results of these tests have, so-far, been encouraging.¹



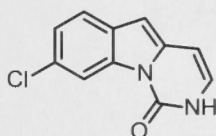
3.0



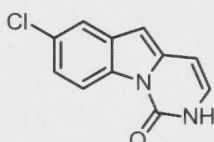
3.55



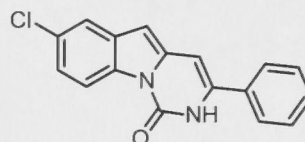
3.53



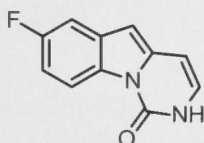
3.45



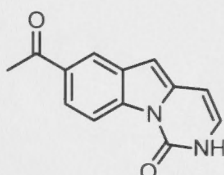
3.44



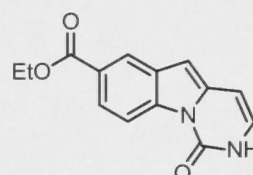
3.54



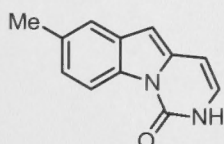
3.46



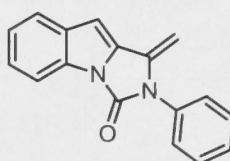
3.47



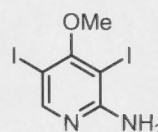
3.48



3.50



3.57



4.10

¹ Personal correspondence with Drs Jens Renner and Klaas Lohmann (BASF Crop-Protection Division).

Appendix 2

X-ray Crystallographic Data for Compounds 2.9, 3.0, 3.48, 4.7, 4.19 and 4.22

Crystal structure of $C_{16}H_{15}Cl_3N_2O_2Si$ — ban1106B

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Abstract

The crystal structure of $C_{16}H_{15}Cl_3N_2O_2Si$ is reported.

Comment

The crystallographic asymmetric unit consists of one molecule of $C_{16}H_{15}Cl_3N_2O_2Si$.

Experimental

The compound was prepared by PPS and recrystallised from a mixture of deuterated chloroform and dichloromethane. The sample ID is 011ps-606.

Computing details

Data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-II* (Johnson 1976) 'in *TEXSAN* (MSC, 1992-1997).; software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

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(ban1106B)

Crystal data

$C_{16}H_{15}Cl_3N_2O_2Si$	$F(000) = 824$
$M_r = 401.75$	$D_x = 1.371 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 6.1127 (2) \text{ \AA}$	Cell parameters from 76447 reflections
$b = 11.3456 (5) \text{ \AA}$	$\theta = 2.6\text{--}25^\circ$
$c = 28.0659 (11) \text{ \AA}$	$\mu = 0.54 \text{ mm}^{-1}$
$\beta = 91.5937 (18)^\circ$	$T = 200 \text{ K}$
$V = 1945.68 (13) \text{ \AA}^3$	Plate, Colourless
$Z = 4$	$0.42 \times 0.19 \times 0.05 \text{ mm}$

Data collection

Nonius KappaCCD diffractometer	2749 reflections with $I > 2.0\sigma(I)$
graphite	$R_{\text{int}} = 0.101$
φ and ω scans with CCD	$\theta_{\text{max}} = 25.0^\circ$, $\theta_{\text{min}} = 2.8^\circ$
Absorption correction: Integration via Gaussian method (Coppens, 1970) implemented in <i>h</i> = $-7 \rightarrow 7$	
<i>maXus</i> (2000)	
$T_{\text{min}} = 0.841$, $T_{\text{max}} = 0.973$	$k = -13 \rightarrow 13$
23034 measured reflections	$l = -33 \rightarrow 33$
3428 independent reflections	

Refinement

Refinement on F^2	Primary atom site location: Structure-invariant direct methods
Least-squares matrix: Full	Hydrogen site location: Inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.070$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.209$	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.11P)^2 + 5.36P]$, where $P = (\max(F_o^2, 0) + 2F_c^2)/3$
$S = 1.02$	$(\Delta/\sigma)_{\text{max}} = 0.012$
3425 reflections	$\Delta\rho_{\text{max}} = 0.50 \text{ e \AA}^{-3}$
224 parameters	$\Delta\rho_{\text{min}} = -0.44 \text{ e \AA}^{-3}$
6 restraints	

Special details

Refinement. The crystal is twinned. Many extra spots were observed on the CCD frames which fitted between those belonging to the major diffraction pattern. Examination of synthesised precession "photographs" suggested that the extra spots arose from a 180° rotational twinning about the (1 0 0) direct axis. Application of a twinning correction within CRYSTALS to allow for overlapping reflections, based on the above relationship, gave a substantial improvement in agreement factors [R-factor for unit weights, $F^2 > 3\sigma(F^2)$, decreased from 0.164 to 0.070]. Twin elements refined to 0.785 (2):0.215 (2).

H atoms attached to C were included at calculated positions; those attached to N were included where indicated in a difference electron density map. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularise their geometry (C—H in the range 0.93–0.98, N—H = 0.86 Å) and with $U_{\text{iso}}(\text{H})$ in the range 1.2–1.5 times U_{eq} of the parent atom, after which the positions were refined with riding constraints, except for the H's on nitrogen atoms where the coordinates were allowed to refine with loose restraints.

The largest peaks in the final difference electron density map are located randomly through the structure.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.4570 (9)	0.7863 (5)	0.48526 (19)	0.0358
C2	0.6579 (9)	0.8462 (5)	0.4931 (2)	0.0381
C3	0.7160 (10)	0.9321 (5)	0.4604 (2)	0.0471
C4	0.5845 (11)	0.9600 (6)	0.4216 (2)	0.0537
C5	0.3850 (11)	0.9023 (6)	0.4151 (2)	0.0494
C6	0.3215 (10)	0.8152 (5)	0.4466 (2)	0.0449
C7	0.7891 (9)	0.8247 (5)	0.5348 (2)	0.0412
C8	0.8975 (9)	0.8134 (5)	0.5705 (2)	0.0420
C9	1.0186 (9)	0.8139 (5)	0.6132 (2)	0.0398
C10	1.1222 (10)	0.8207 (6)	0.6506 (2)	0.0454
Si11	1.2795 (3)	0.85490 (15)	0.70588 (6)	0.0428
C12	1.2354 (13)	1.0137 (7)	0.7167 (3)	0.0683
C13	1.5690 (10)	0.8228 (7)	0.6951 (2)	0.0551
C14	1.1775 (12)	0.7656 (7)	0.7562 (2)	0.0634
N15	0.4010 (8)	0.7002 (4)	0.51927 (16)	0.0404
C16	0.2486 (11)	0.6168 (6)	0.5131 (2)	0.0512
O17	0.1453 (10)	0.5994 (5)	0.47597 (16)	0.0866
N18	0.2052 (9)	0.5448 (5)	0.55239 (16)	0.0480
C19	0.3045 (9)	0.5472 (5)	0.59619 (18)	0.0365
O20	0.4623 (6)	0.6071 (4)	0.60745 (14)	0.0460
C21	0.1966 (9)	0.4645 (5)	0.63286 (19)	0.0382
Cl22	0.3306 (3)	0.48121 (17)	0.68864 (6)	0.0628
Cl23	0.2260 (3)	0.31687 (14)	0.61379 (6)	0.0618
Cl24	−0.0814 (2)	0.49905 (16)	0.63752 (6)	0.0519
H31	0.8475	0.9718	0.4651	0.0562*
H41	0.6299	1.0169	0.4000	0.0641*
H51	0.2919	0.9223	0.3892	0.0587*
H61	0.1889	0.7750	0.4420	0.0536*
H121	1.3138	1.0364	0.7453	0.1021*
H122	1.0824	1.0292	0.7204	0.1023*
H123	1.2870	1.0592	0.6903	0.1020*
H131	1.6580	0.8320	0.7237	0.0834*
H132	1.6234	0.8747	0.6713	0.0830*
H133	1.5833	0.7437	0.6843	0.0832*

H141	1.2631	0.7837	0.7846	0.0949*
H142	1.0237	0.7840	0.7605	0.0952*
H143	1.1930	0.6831	0.7489	0.0951*
H151	0.476 (8)	0.699 (4)	0.5470 (13)	0.0493*
H181	0.116 (9)	0.486 (4)	0.5465 (12)	0.0580*

Atomic displacement parameters (Å²)

	<i>U</i> ¹¹	<i>U</i> ²²	<i>U</i> ³³	<i>U</i> ¹²	<i>U</i> ¹³	<i>U</i> ²³
C1	0.035 (3)	0.037 (3)	0.035 (3)	−0.007 (2)	−0.001 (2)	0.000 (2)
C2	0.034 (3)	0.038 (3)	0.042 (3)	−0.007 (2)	−0.002 (2)	−0.004 (2)
C3	0.044 (3)	0.046 (3)	0.052 (3)	−0.020 (3)	0.001 (3)	0.002 (3)
C4	0.063 (4)	0.049 (4)	0.050 (4)	−0.016 (3)	0.003 (3)	0.010 (3)
C5	0.053 (4)	0.048 (3)	0.047 (3)	−0.005 (3)	−0.012 (3)	0.005 (3)
C6	0.039 (3)	0.050 (3)	0.045 (3)	−0.011 (3)	−0.007 (3)	0.000 (3)
C7	0.035 (3)	0.047 (3)	0.042 (3)	−0.011 (3)	0.006 (3)	−0.003 (3)
C8	0.033 (3)	0.040 (3)	0.053 (4)	−0.009 (3)	0.003 (3)	0.003 (3)
C9	0.031 (3)	0.041 (3)	0.047 (3)	−0.003 (2)	−0.002 (3)	0.001 (3)
C10	0.036 (3)	0.051 (4)	0.049 (4)	−0.005 (3)	0.001 (3)	−0.002 (3)
Si11	0.0350 (8)	0.0529 (10)	0.0403 (8)	−0.0010 (8)	−0.0015 (7)	−0.0054 (7)
C12	0.079 (5)	0.068 (5)	0.058 (4)	0.007 (4)	−0.010 (4)	−0.012 (3)
C13	0.035 (3)	0.075 (5)	0.055 (4)	−0.003 (3)	−0.008 (3)	−0.010 (3)
C14	0.065 (5)	0.076 (5)	0.050 (4)	−0.005 (4)	0.011 (3)	0.002 (3)
N15	0.037 (3)	0.053 (3)	0.031 (2)	−0.022 (2)	−0.006 (2)	0.005 (2)
C16	0.060 (4)	0.060 (4)	0.033 (3)	−0.032 (3)	−0.005 (3)	0.004 (3)
O17	0.113 (5)	0.110 (4)	0.035 (2)	−0.080 (4)	−0.025 (3)	0.021 (3)
N18	0.052 (3)	0.058 (3)	0.033 (2)	−0.030 (3)	−0.008 (2)	0.007 (2)
C19	0.035 (3)	0.042 (3)	0.032 (3)	−0.005 (2)	−0.002 (2)	0.001 (2)
O20	0.035 (2)	0.060 (3)	0.042 (2)	−0.008 (2)	−0.0039 (17)	−0.001 (2)
C21	0.035 (3)	0.046 (3)	0.033 (3)	−0.001 (2)	−0.003 (2)	0.003 (2)
C122	0.0682 (11)	0.0817 (12)	0.0375 (8)	−0.0112 (9)	−0.0158 (7)	0.0102 (8)
C123	0.0802 (12)	0.0430 (9)	0.0623 (10)	0.0054 (8)	0.0046 (9)	0.0010 (7)
C124	0.0389 (8)	0.0644 (10)	0.0526 (9)	−0.0009 (7)	0.0057 (6)	0.0089 (7)

Geometric parameters (Å, °)

C1—C2	1.415 (7)	C12—H122	0.960
C1—C6	1.386 (8)	C12—H123	0.965
C1—N15	1.414 (7)	C13—H131	0.962
C2—C3	1.392 (8)	C13—H132	0.957
C2—C7	1.420 (8)	C13—H133	0.952
C3—C4	1.373 (9)	C14—H141	0.964
C3—H31	0.928	C14—H142	0.974
C4—C5	1.392 (9)	C14—H143	0.963
C4—H41	0.932	N15—C16	1.336 (7)
C5—C6	1.388 (8)	N15—H151	0.89 (3)
C5—H51	0.940	C16—O17	1.219 (7)
C6—H61	0.936	C16—N18	1.404 (7)
C7—C8	1.194 (8)	N18—C19	1.356 (7)
C8—C9	1.389 (8)	N18—H181	0.87 (3)
C9—C10	1.215 (8)	C19—O20	1.215 (6)

C10—Si11	1.844 (6)	C19—C21	1.553 (8)
Si11—C12	1.848 (8)	C21—Cl22	1.757 (5)
Si11—C13	1.840 (6)	C21—Cl23	1.769 (6)
Si11—C14	1.859 (7)	C21—Cl24	1.752 (6)
C12—H121	0.959		
Cl23...O17 ⁱ	3.476 (5)	O20...C10 ⁱⁱⁱ	3.435 (8)
Cl23...C4 ⁱⁱ	3.501 (7)	O20...C13 ⁱⁱⁱ	3.518 (8)
Cl23...C3 ⁱⁱ	3.533 (6)	O20...C9 ⁱⁱⁱ	3.593 (7)
Cl23...C5 ⁱⁱ	3.550 (7)	C2...C4 ^{iv}	3.600 (9)
Cl24...O20 ⁱⁱⁱ	3.141 (4)	C4...C7 ^{iv}	3.583 (9)
Cl24...O17 ⁱ	3.388 (5)	C5...C7 ^{iv}	3.576 (9)
O17...N18 ⁱ	2.794 (8)	C8...C16 ^v	3.517 (9)
O17...O17 ⁱ	3.19 (1)	C9...C19 ^v	3.533 (8)
O17...C16 ⁱ	3.457 (9)		
C2—C1—C6	120.4 (5)	H121—C12—H123	109.6
C2—C1—N15	116.8 (5)	H122—C12—H123	108.9
C6—C1—N15	122.8 (5)	Si11—C13—H131	111.4
C1—C2—C3	118.0 (5)	Si11—C13—H132	110.4
C1—C2—C7	120.9 (5)	H131—C13—H132	108.4
C3—C2—C7	121.0 (5)	Si11—C13—H133	109.7
C2—C3—C4	122.1 (5)	H131—C13—H133	108.3
C2—C3—H31	118.9	H132—C13—H133	108.6
C4—C3—H31	119.1	Si11—C14—H141	109.0
C3—C4—C5	119.1 (6)	Si11—C14—H142	108.8
C3—C4—H41	119.7	H141—C14—H142	110.8
C5—C4—H41	121.2	Si11—C14—H143	109.4
C4—C5—C6	120.8 (6)	H141—C14—H143	109.2
C4—C5—H51	119.8	H142—C14—H143	109.6
C6—C5—H51	119.4	C1—N15—C16	125.6 (5)
C5—C6—C1	119.7 (5)	C1—N15—H151	118.0 (19)
C5—C6—H61	121.0	C16—N15—H151	116.4 (19)
C1—C6—H61	119.3	N15—C16—O17	124.6 (5)
C2—C7—C8	176.1 (6)	N15—C16—N18	117.1 (5)
C7—C8—C9	173.4 (7)	O17—C16—N18	118.2 (5)
C8—C9—C10	176.5 (6)	C16—N18—C19	127.7 (5)
C9—C10—Si11	171.5 (6)	C16—N18—H181	115 (2)
C10—Si11—C12	105.6 (3)	C19—N18—H181	117 (2)
C10—Si11—C13	107.5 (3)	N18—C19—O20	125.4 (5)
C12—Si11—C13	111.4 (4)	N18—C19—C21	113.7 (5)
C10—Si11—C14	110.2 (3)	O20—C19—C21	121.0 (5)
C12—Si11—C14	110.6 (4)	C19—C21—Cl22	109.2 (4)
C13—Si11—C14	111.2 (3)	C19—C21—Cl23	108.8 (4)
Si11—C12—H121	109.1	Cl22—C21—Cl23	108.9 (3)
Si11—C12—H122	110.0	C19—C21—Cl24	110.2 (4)
H121—C12—H122	109.1	Cl22—C21—Cl24	109.8 (3)
Si11—C12—H123	110.0	Cl23—C21—Cl24	109.9 (3)
Cl22—C21—C19—O20	2.7 (7)	N18—C16—N15—C1	−175.3 (5)
Cl22—C21—C19—N18	−177.0 (4)	C1—C2—C3—C4	0.4 (9)
Cl23—C21—C19—O20	−116.0 (5)	C1—C6—C5—C4	0.8 (9)

Cl23—C21—C19—N18	64.3 (6)	C2—C1—N15—C16	−163.7 (6)
Cl24—C21—C19—O20	123.4 (5)	C2—C1—C6—C5	0.9 (9)
Cl24—C21—C19—N18	−56.3 (6)	C2—C3—C4—C5	1.2 (9)
O17—C16—N15—C1	4 (1)	C3—C2—C1—C6	−1.5 (8)
O17—C16—N18—C19	178.1 (6)	C3—C4—C5—C6	−2 (1)
O20—C19—N18—C16	−6 (1)	C4—C3—C2—C7	−175.5 (6)
N15—C1—C2—C3	−179.4 (5)	C6—C1—N15—C16	18.3 (9)
N15—C1—C2—C7	−3.5 (8)	C6—C1—C2—C7	174.4 (5)
N15—C1—C6—C5	178.7 (5)	C16—N18—C19—C21	173.3 (6)
N15—C16—N18—C19	−2 (1)		

Symmetry codes: (i) $-x, -y+1, -z+1$; (ii) $-x+1, -y+1, -z+1$; (iii) $x-1, y, z$; (iv) $-x+1, -y+2, -z+1$; (v) $x+1, y, z$.

Hydrogen-bond geometry (Å, °)

<i>D</i> —H $\cdots$ <i>A</i>	<i>D</i> —H	H $\cdots$ <i>A</i>	<i>D</i> $\cdots$ <i>A</i>	<i>D</i> —H $\cdots$ <i>A</i>
N15—H151 $\cdots$ O20	0.89 (3)	2.00 (3)	2.707 (9)	136 (3)
N18—H181 $\cdots$ O17 ⁱ	0.87 (3)	1.96 (3)	2.794 (9)	160 (5)

Symmetry code: (i) $-x, -y+1, -z+1$.

Crystal structure of $C_{11}H_8N_2O$ — ban0827a

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Abstract

The crystal structure of $C_{11}H_8N_2O$ is reported.

Comment

The crystallographic asymmetric unit consists of two $C_{11}H_8N_2O$ molecules, hydrogen-bonded into a dimer.

Experimental

The compound was prepared by PPS and recrystallized from ethylacetate/methanol/dichloromethane. The sample ID is 08 ps-146.

Refinement

The relatively large ratio of minimum to maximum corrections applied in the multiscan process (1:1.22) reflect changes in the illuminated volume of the crystal.

All hydrogen atoms were observed in a difference electron density map generated prior to their inclusion. They were included at geometrically determined positions and were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H in the range 0.93–0.98, N—H in the range 0.86–0.89) and $U_{iso}(H)$ (in the range 1.2–1.5 times U_{eq} of the parent atom). Finally all H atom positional and displacement parameters were refined without restraints.

The largest peaks in the final difference electron density map are located near carbon atoms.

Computing details

Data collection: *COLLECT* (Nonius, 1997-2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEPII* (Johnson 1976) in *TEXSAN* (MSC, 1992-1997); software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

(ban0827a)

Crystal data

$C_{22}H_{16}N_4O_2$	$V = 3481.52 (10) \text{ \AA}^3$
$M_r = 368.39$	$Z = 8$
Orthorhombic, $Pbca$	Mo $K\alpha$
$a = 14.7579 (2) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$b = 10.3799 (2) \text{ \AA}$	$T = 200 \text{ K}$
$c = 22.7275 (4) \text{ \AA}$	$0.46 \times 0.14 \times 0.04 \text{ mm}$

Data collection

Area diffractometer	3992 independent reflections
Absorption correction: multi-scan DENZO/SCALEPACK (Otwinowski & Minor, 1997)	2998 reflections with $I > 2.0\sigma(I)$
$T_{\min} = 0.815$, $T_{\max} = 0.996$	$R_{\text{int}} = 0.045$
39794 measured reflections	

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.036$	317 parameters
$wR(F^2) = 0.090$	All H-atom parameters refined
$S = 0.98$	$\Delta\rho_{\max} = 0.24 \text{ e \AA}^{-3}$
3992 reflections	$\Delta\rho_{\min} = -0.23 \text{ e \AA}^{-3}$

Table 1
Selected geometric parameters ($\text{\AA}$, $^\circ$)

O14—C13	1.2321 (14)	C5—C6	1.3755 (18)
O114—C113	1.2277 (14)	C6—C7	1.4045 (17)
N1—C2	1.4048 (15)	C7—C8	1.4274 (17)
N1—C9	1.4190 (14)	C8—C9	1.3653 (16)
N1—C13	1.3864 (14)	C9—C10	1.4263 (17)
N12—C11	1.3850 (16)	C10—C11	1.3354 (18)
N12—C13	1.3567 (16)	C102—C103	1.3891 (18)
N101—C102	1.4033 (15)	C102—C107	1.4094 (17)
N101—C109	1.4159 (15)	C103—C104	1.3875 (19)
N101—C113	1.3862 (15)	C104—C105	1.395 (2)
N112—C111	1.3826 (17)	C105—C106	1.376 (2)
N112—C113	1.3564 (16)	C106—C107	1.4018 (18)
C2—C3	1.3878 (17)	C107—C108	1.4281 (19)
C2—C7	1.4091 (16)	C108—C109	1.3640 (18)
C3—C4	1.3849 (19)	C109—C110	1.4245 (18)
C4—C5	1.3965 (19)	C110—C111	1.3330 (19)
C2—N1—C9	108.37 (9)	N12—C11—C10	121.25 (12)

C2—N1—C13	127.78 (10)	N1—C13—N12	114.48 (10)
C9—N1—C13	123.85 (10)	N1—C13—O14	122.42 (11)
C11—N12—C13	124.50 (11)	N12—C13—O14	123.10 (11)
C102—N101—C109	108.63 (10)	N101—C102—C103	130.88 (11)
C102—N101—C113	127.28 (10)	N101—C102—C107	106.71 (10)
C109—N101—C113	124.09 (10)	C103—C102—C107	122.40 (12)
C111—N112—C113	124.16 (11)	C102—C103—C104	117.03 (13)
N1—C2—C3	130.85 (11)	C103—C104—C105	121.53 (14)
N1—C2—C7	106.84 (10)	C104—C105—C106	121.22 (13)
C3—C2—C7	122.31 (11)	C105—C106—C107	118.82 (13)
C2—C3—C4	116.76 (12)	C102—C107—C106	119.00 (12)
C3—C4—C5	122.07 (12)	C102—C107—C108	108.06 (11)
C4—C5—C6	120.98 (12)	C106—C107—C108	132.93 (12)
C5—C6—C7	118.52 (12)	C107—C108—C109	108.12 (11)
C2—C7—C6	119.34 (11)	N101—C109—C108	108.47 (11)
C2—C7—C8	108.16 (10)	N101—C109—C110	116.77 (11)
C6—C7—C8	132.49 (11)	C108—C109—C110	134.76 (12)
C7—C8—C9	108.04 (10)	C109—C110—C111	119.07 (12)
N1—C9—C8	108.58 (10)	N112—C111—C110	121.32 (12)
N1—C9—C10	117.23 (11)	N101—C113—N112	114.57 (11)
C8—C9—C10	134.18 (11)	N101—C113—O114	122.19 (11)
C9—C10—C11	118.69 (12)	N112—C113—O114	123.24 (11)

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Crystal structure of C₁₁H₉N₂O — ban0827a

Phillip Patrick Sharp, Martin O. Jamveit and Anthony C. Wills

ban0827a

Crystal data

Chemical formula: C₁₁H₉N₂O
 M_r: 197.23
 Crystal system: monoclinic
 Space group: P2₁/c
 Unit cell dimensions: a = 10.458(4) Å, b = 12.158(4) Å, c = 12.158(4) Å
 Unit cell volume: V = 1554.8(10) Å³
 Z: 4

supplementary materials

CCDC 1000000
 0.100 0.100 0.100

Data collection

Wavelength: 0.71073 Å
 Source: Mo Kα
 Filter: graphite
 Detector: CCD
 Scanning method: ω-scan
 2θ range: 5.0–25.0°
 Data range: 2θ = 5.0–25.0°
 2θ range: 5.0–25.0°
 2θ range: 5.0–25.0°

Refinement

Refinement on F²
 R_{int} = 0.010
 R₁ = 0.010
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Crystal structure of C₁₁H₈N₂O — ban0827a

Phillip Patrick Sharp, Martin G. Banwell and Anthony C. Willis

(ban0827a)

Crystal data

C ₂₂ H ₁₆ N ₄ O ₂	$D_x = 1.406 \text{ Mg m}^{-3}$
$M_r = 368.39$	Mo $K\alpha$ radiation
	$\lambda = 0.71073 \text{ \AA}$
Orthorhombic, <i>Pbca</i>	Cell parameters from 30739 reflections
$a = 14.7579 (2) \text{ \AA}$	$\theta = 2.6\text{--}27.5^\circ$
$b = 10.3799 (2) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$c = 22.7275 (4) \text{ \AA}$	$T = 200 \text{ K}$
$V = 3481.52 (10) \text{ \AA}^3$	Plate, colourless
$Z = 8$	$0.46 \times 0.14 \times 0.04 \text{ mm}$
$F_{000} = 1536$	

Data collection

Area diffractometer	2998 reflections with $I > 2.0\sigma(I)$
Monochromator: graphite	$R_{\text{int}} = 0.045$
$T = 200 \text{ K}$	$\theta_{\text{max}} = 27.5^\circ$
φ and ω scans with CCD	$\theta_{\text{min}} = 2.6^\circ$
Absorption correction: multi-scan	$h = -19 \rightarrow 19$
DENZO/SCALEPACK (Otwinowski & Minor, 1997)	$k = -13 \rightarrow 13$
$T_{\text{min}} = 0.815$, $T_{\text{max}} = 0.996$	$l = -29 \rightarrow 28$
39794 measured reflections	
3992 independent reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	All H-atom parameters refined
	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.79P]$,
$R[F^2 > 2\sigma(F^2)] = 0.036$	where $P = (\max(F_o^2, 0) + 2F_c^2)/3$
$wR(F^2) = 0.090$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 0.98$	$\Delta\rho_{\text{max}} = 0.24 \text{ e \AA}^{-3}$
3992 reflections	$\Delta\rho_{\text{min}} = -0.23 \text{ e \AA}^{-3}$
317 parameters	Extinction correction: None
Primary atom site location: structure-invariant direct methods	

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (*Å*²)

	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
O14	0.73643 (6)	0.25172 (8)	0.25844 (4)	0.0440
O114	0.84299 (6)	0.49964 (8)	0.34784 (4)	0.0429
N1	0.84021 (6)	0.13501 (9)	0.20530 (4)	0.0350
N12	0.88675 (7)	0.29618 (10)	0.26831 (4)	0.0407
N101	0.74116 (7)	0.62843 (9)	0.39597 (4)	0.0368
N112	0.69218 (7)	0.46950 (10)	0.33250 (5)	0.0414
C2	0.78279 (8)	0.05045 (10)	0.17465 (5)	0.0347
C3	0.68911 (8)	0.03891 (12)	0.17475 (6)	0.0407
C4	0.65248 (9)	−0.05749 (13)	0.13997 (6)	0.0440
C5	0.70654 (9)	−0.13924 (12)	0.10607 (6)	0.0434
C6	0.79929 (9)	−0.12614 (12)	0.10538 (5)	0.0406
C7	0.83880 (8)	−0.02928 (11)	0.14008 (5)	0.0358
C8	0.93066 (8)	0.00846 (11)	0.14955 (5)	0.0383
C9	0.93104 (8)	0.10725 (11)	0.18921 (5)	0.0364
C10	1.00057 (9)	0.18162 (12)	0.21653 (5)	0.0410
C11	0.97686 (9)	0.27260 (12)	0.25511 (6)	0.0429
C13	0.81591 (8)	0.23024 (11)	0.24506 (5)	0.0372
C102	0.80055 (8)	0.70664 (11)	0.42837 (5)	0.0377
C103	0.89449 (9)	0.70639 (13)	0.43213 (6)	0.0442
C104	0.93405 (10)	0.79951 (14)	0.46760 (6)	0.0506
C105	0.88185 (11)	0.88921 (14)	0.49826 (6)	0.0518
C106	0.78876 (10)	0.88830 (13)	0.49482 (6)	0.0490
C107	0.74646 (9)	0.79578 (12)	0.45926 (5)	0.0418
C108	0.65378 (9)	0.76965 (13)	0.44569 (6)	0.0457
C109	0.65115 (8)	0.66823 (12)	0.40757 (5)	0.0403
C110	0.58079 (9)	0.59884 (13)	0.37864 (6)	0.0458
C111	0.60274 (9)	0.50212 (13)	0.34278 (6)	0.0453
C113	0.76395 (8)	0.52942 (11)	0.35781 (5)	0.0367
H31	0.6520 (9)	0.0954 (13)	0.1980 (6)	0.049 (4)*
H41	0.5863 (10)	−0.0696 (13)	0.1387 (6)	0.051 (4)*
H51	0.6766 (9)	−0.2060 (13)	0.0822 (6)	0.047 (4)*
H61	0.8379 (9)	−0.1829 (13)	0.0814 (6)	0.048 (4)*
H81	0.9861 (9)	−0.0273 (12)	0.1308 (6)	0.049 (4)*
H101	1.0630 (9)	0.1647 (12)	0.2075 (5)	0.045 (3)*
H111	1.0210 (9)	0.3253 (13)	0.2771 (6)	0.046 (4)*
H121	0.8714 (10)	0.3607 (15)	0.2953 (7)	0.066 (4)*
H1031	0.9301 (9)	0.6441 (13)	0.4106 (6)	0.050 (4)*
H1041	1.0022 (10)	0.8019 (14)	0.4703 (6)	0.060 (4)*
H1051	0.9129 (10)	0.9538 (15)	0.5230 (7)	0.064 (4)*
H1061	0.7518 (9)	0.9490 (15)	0.5168 (6)	0.057 (4)*
H1081	0.5993 (10)	0.8161 (14)	0.4598 (6)	0.058 (4)*
H1101	0.5184 (10)	0.6216 (13)	0.3853 (6)	0.052 (4)*
H1111	0.5596 (9)	0.4520 (13)	0.3220 (6)	0.052 (4)*
H1121	0.7081 (10)	0.4012 (15)	0.3079 (7)	0.063 (4)*

Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O14	0.0439 (5)	0.0411 (5)	0.0471 (5)	0.0027 (4)	0.0092 (4)	−0.0036 (4)
O114	0.0411 (5)	0.0412 (5)	0.0465 (5)	0.0013 (4)	0.0036 (4)	−0.0044 (4)
N1	0.0369 (5)	0.0335 (5)	0.0346 (5)	0.0016 (4)	0.0038 (4)	0.0015 (4)
N12	0.0464 (6)	0.0377 (5)	0.0379 (6)	0.0008 (5)	0.0013 (5)	−0.0027 (4)
N101	0.0394 (5)	0.0363 (5)	0.0346 (5)	−0.0003 (4)	0.0028 (4)	0.0008 (4)
N112	0.0439 (6)	0.0394 (6)	0.0410 (6)	−0.0034 (5)	0.0024 (5)	−0.0024 (5)
C2	0.0392 (6)	0.0306 (6)	0.0341 (6)	0.0011 (5)	0.0017 (5)	0.0054 (5)
C3	0.0386 (7)	0.0409 (7)	0.0428 (7)	0.0019 (5)	0.0049 (5)	0.0041 (5)
C4	0.0387 (7)	0.0465 (7)	0.0468 (7)	−0.0039 (6)	0.0009 (6)	0.0078 (6)
C5	0.0495 (8)	0.0392 (7)	0.0417 (7)	−0.0055 (6)	−0.0032 (6)	0.0025 (5)
C6	0.0464 (7)	0.0359 (6)	0.0394 (7)	0.0021 (5)	0.0017 (5)	0.0002 (5)
C7	0.0396 (6)	0.0328 (6)	0.0350 (6)	0.0022 (5)	0.0023 (5)	0.0040 (5)
C8	0.0372 (6)	0.0375 (6)	0.0401 (7)	0.0041 (5)	0.0040 (5)	−0.0002 (5)
C9	0.0352 (6)	0.0364 (6)	0.0375 (6)	0.0034 (5)	0.0027 (5)	0.0057 (5)
C10	0.0382 (7)	0.0435 (7)	0.0413 (7)	−0.0011 (5)	0.0013 (5)	0.0018 (5)
C11	0.0434 (7)	0.0440 (7)	0.0413 (7)	−0.0045 (6)	−0.0013 (6)	0.0011 (6)
C13	0.0443 (7)	0.0336 (6)	0.0335 (6)	0.0024 (5)	0.0050 (5)	0.0035 (5)
C102	0.0468 (7)	0.0345 (6)	0.0317 (6)	−0.0028 (5)	0.0018 (5)	0.0029 (5)
C103	0.0481 (8)	0.0451 (7)	0.0395 (7)	−0.0020 (6)	0.0014 (6)	0.0011 (6)
C104	0.0522 (8)	0.0535 (8)	0.0462 (7)	−0.0095 (6)	−0.0043 (6)	0.0028 (6)
C105	0.0704 (10)	0.0455 (8)	0.0396 (7)	−0.0119 (7)	−0.0013 (7)	−0.0016 (6)
C106	0.0681 (9)	0.0404 (7)	0.0384 (7)	−0.0020 (7)	0.0062 (6)	−0.0024 (6)
C107	0.0536 (7)	0.0373 (6)	0.0345 (6)	−0.0001 (5)	0.0061 (5)	0.0036 (5)
C108	0.0510 (8)	0.0424 (7)	0.0436 (7)	0.0052 (6)	0.0085 (6)	0.0017 (6)
C109	0.0411 (7)	0.0411 (6)	0.0389 (6)	0.0026 (5)	0.0061 (5)	0.0064 (5)
C110	0.0395 (7)	0.0503 (8)	0.0476 (7)	0.0001 (6)	0.0034 (6)	0.0047 (6)
C111	0.0422 (7)	0.0482 (8)	0.0455 (7)	−0.0072 (6)	−0.0007 (6)	0.0022 (6)
C113	0.0420 (7)	0.0344 (6)	0.0338 (6)	−0.0009 (5)	0.0023 (5)	0.0032 (5)

Geometric parameters ($\text{\AA}$, $^\circ$)

O14—C13	1.2321 (14)	C7—C8	1.4274 (17)
O114—C113	1.2277 (14)	C8—C9	1.3653 (16)
N1—C2	1.4048 (15)	C8—H81	0.995 (14)
N1—C9	1.4190 (14)	C9—C10	1.4263 (17)
N1—C13	1.3864 (14)	C10—C11	1.3354 (18)
N12—C11	1.3850 (16)	C10—H101	0.960 (13)
N12—C13	1.3567 (16)	C11—H111	0.986 (14)
N12—H121	0.937 (16)	C102—C103	1.3891 (18)
N101—C102	1.4033 (15)	C102—C107	1.4094 (17)
N101—C109	1.4159 (15)	C103—C104	1.3875 (19)
N101—C113	1.3862 (15)	C103—H1031	0.967 (14)
N112—C111	1.3826 (17)	C104—C105	1.395 (2)
N112—C113	1.3564 (16)	C104—H1041	1.008 (14)
N112—H1121	0.933 (16)	C105—C106	1.376 (2)

supplementary materials

C2—C3	1.3878 (17)	C105—H1051	0.988 (15)
C2—C7	1.4091 (16)	C106—C107	1.4018 (18)
C3—C4	1.3849 (19)	C106—H1061	0.972 (15)
C3—H31	0.960 (14)	C107—C108	1.4281 (19)
C4—C5	1.3965 (19)	C108—C109	1.3640 (18)
C4—H41	0.985 (14)	C108—H1081	0.991 (15)
C5—C6	1.3755 (18)	C109—C110	1.4245 (18)
C5—H51	0.984 (14)	C110—C111	1.3330 (19)
C6—C7	1.4045 (17)	C110—H1101	0.962 (14)
C6—H61	0.984 (14)	C111—H1111	0.948 (14)
O14…N112	2.893 (1)	N101…C106 ⁱ	3.385 (2)
O14…C113 ⁱ	3.229 (1)	N112…C13 ⁱⁱⁱ	3.360 (2)
O14…N101 ⁱ	3.394 (1)	N112…C102 ⁱ	3.493 (2)
O14…O114 ⁱ	3.514 (1)	N112…C107 ⁱ	3.517 (2)
O14…N112 ⁱ	3.539 (1)	C2…C5 ⁱⁱⁱ	3.582 (2)
O114…N12	2.854 (1)	C3…C13 ⁱ	3.581 (2)
O114…C108 ⁱ	3.263 (2)	C4…C13 ⁱ	3.283 (2)
O114…C10 ⁱⁱ	3.322 (2)	C5…C13 ⁱ	3.453 (2)
O114…C8 ⁱⁱ	3.342 (2)	C8…C11 ^{iv}	3.543 (2)
O114…C107 ⁱ	3.554 (2)	C11…C110 ⁱ	3.444 (2)
N1…C5 ⁱⁱⁱ	3.325 (2)	C13…C111 ⁱ	3.461 (2)
N1…N112 ⁱ	3.397 (1)	C13…C113 ⁱ	3.507 (2)
N1…C111 ⁱ	3.518 (2)	C104…C111 ⁱⁱⁱ	3.573 (2)
N1…C4 ⁱⁱⁱ	3.522 (2)	C105…C110 ⁱⁱⁱ	3.526 (2)
N12…C110 ⁱ	3.273 (2)	C105…C109 ⁱⁱⁱ	3.588 (2)
N12…C4 ⁱⁱⁱ	3.339 (2)	C106…C113 ⁱⁱⁱ	3.528 (2)
N12…C109 ⁱ	3.478 (2)	C107…C113 ⁱⁱⁱ	3.350 (2)
N12…C3 ⁱⁱⁱ	3.482 (2)	C108…C113 ⁱⁱⁱ	3.568 (2)
N12…C111 ⁱ	3.494 (2)		
C2—N1—C9	108.37 (9)	N12—C11—C10	121.25 (12)
C2—N1—C13	127.78 (10)	N12—C11—H111	115.2 (8)
C9—N1—C13	123.85 (10)	C10—C11—H111	123.5 (8)
C11—N12—C13	124.50 (11)	N1—C13—N12	114.48 (10)
C11—N12—H121	120.0 (9)	N1—C13—O14	122.42 (11)
C13—N12—H121	115.5 (9)	N12—C13—O14	123.10 (11)
C102—N101—C109	108.63 (10)	N101—C102—C103	130.88 (11)
C102—N101—C113	127.28 (10)	N101—C102—C107	106.71 (10)
C109—N101—C113	124.09 (10)	C103—C102—C107	122.40 (12)
C111—N112—C113	124.16 (11)	C102—C103—C104	117.03 (13)
C111—N112—H1121	121.8 (9)	C102—C103—H1031	120.9 (8)
C113—N112—H1121	114.0 (9)	C104—C103—H1031	122.1 (8)
N1—C2—C3	130.85 (11)	C103—C104—C105	121.53 (14)
N1—C2—C7	106.84 (10)	C103—C104—H1041	118.2 (8)
C3—C2—C7	122.31 (11)	C105—C104—H1041	120.3 (8)
C2—C3—C4	116.76 (12)	C104—C105—C106	121.22 (13)

C2—C3—H31	121.0 (8)	C104—C105—H1051	118.8 (9)
C4—C3—H31	122.2 (8)	C106—C105—H1051	120.0 (9)
C3—C4—C5	122.07 (12)	C105—C106—C107	118.82 (13)
C3—C4—H41	119.7 (8)	C105—C106—H1061	121.8 (8)
C5—C4—H41	118.2 (8)	C107—C106—H1061	119.4 (8)
C4—C5—C6	120.98 (12)	C102—C107—C106	119.00 (12)
C4—C5—H51	118.4 (8)	C102—C107—C108	108.06 (11)
C6—C5—H51	120.7 (8)	C106—C107—C108	132.93 (12)
C5—C6—C7	118.52 (12)	C107—C108—C109	108.12 (11)
C5—C6—H61	121.6 (8)	C107—C108—H1081	127.9 (8)
C7—C6—H61	119.9 (8)	C109—C108—H1081	123.9 (8)
C2—C7—C6	119.34 (11)	N101—C109—C108	108.47 (11)
C2—C7—C8	108.16 (10)	N101—C109—C110	116.77 (11)
C6—C7—C8	132.49 (11)	C108—C109—C110	134.76 (12)
C7—C8—C9	108.04 (10)	C109—C110—C111	119.07 (12)
C7—C8—H81	127.9 (8)	C109—C110—H1101	120.1 (8)
C9—C8—H81	124.0 (8)	C111—C110—H1101	120.9 (8)
N1—C9—C8	108.58 (10)	N112—C111—C110	121.32 (12)
N1—C9—C10	117.23 (11)	N112—C111—H1111	115.0 (8)
C8—C9—C10	134.18 (11)	C110—C111—H1111	123.7 (8)
C9—C10—C11	118.69 (12)	N101—C113—N112	114.57 (11)
C9—C10—H101	119.9 (8)	N101—C113—O114	122.19 (11)
C11—C10—H101	121.4 (8)	N112—C113—O114	123.24 (11)
O14—C13—N1—C2	0.0 (2)	C3—C4—C5—C6	−0.7 (2)
O14—C13—N1—C9	−179.6 (1)	C4—C3—C2—C7	1.4 (2)
O14—C13—N12—C11	178.6 (1)	C4—C5—C6—C7	0.6 (2)
O114—C113—N101—C102	−0.6 (2)	C5—C6—C7—C8	179.4 (1)
O114—C113—N101—C109	178.3 (1)	C6—C7—C8—C9	−178.3 (1)
O114—C113—N112—C111	−179.5 (1)	C7—C2—N1—C9	0.3 (1)
N1—C2—C3—C4	−178.7 (1)	C7—C2—N1—C13	−179.4 (1)
N1—C2—C7—C6	178.6 (1)	C7—C8—C9—C10	178.3 (1)
N1—C2—C7—C8	−0.6 (1)	C8—C9—N1—C13	179.8 (1)
N1—C9—C8—C7	−0.5 (1)	C8—C9—C10—C11	−179.0 (1)
N1—C9—C10—C11	−0.3 (2)	C10—C9—N1—C13	0.8 (2)
N1—C13—N12—C11	−0.6 (2)	C10—C11—N12—C13	1.2 (2)
N12—C11—C10—C9	−0.6 (2)	C102—N101—C109—C108	0.7 (1)
N12—C13—N1—C2	179.3 (1)	C102—N101—C109—C110	−179.6 (1)
N12—C13—N1—C9	−0.3 (2)	C102—C103—C104—C105	0.2 (2)
N101—C102—C103—C104	178.5 (1)	C102—C107—C106—C105	0.2 (2)
N101—C102—C107—C106	−178.9 (1)	C102—C107—C108—C109	−0.2 (1)
N101—C102—C107—C108	0.6 (1)	C103—C102—N101—C109	180.0 (1)
N101—C109—C108—C107	−0.3 (1)	C103—C102—N101—C113	−1.1 (2)
N101—C109—C110—C111	−0.1 (2)	C103—C102—C107—C106	0.4 (2)
N101—C113—N112—C111	0.1 (2)	C103—C102—C107—C108	180.0 (1)
N112—C111—C110—C109	−1.0 (2)	C103—C104—C105—C106	0.4 (2)
N112—C113—N101—C102	179.8 (1)	C104—C103—C102—C107	−0.6 (2)
N112—C113—N101—C109	−1.4 (2)	C104—C105—C106—C107	−0.6 (2)
C2—N1—C9—C8	0.1 (1)	C105—C106—C107—C108	−179.2 (1)
C2—N1—C9—C10	−178.9 (1)	C106—C107—C108—C109	179.2 (1)

C2—C3—C4—C5	−0.3 (2)	C107—C102—N101—C109	−0.8 (1)
C2—C7—C6—C5	0.4 (2)	C107—C102—N101—C113	178.2 (1)
C2—C7—C8—C9	0.7 (1)	C107—C108—C109—C110	−179.9 (1)
C3—C2—N1—C9	−179.6 (1)	C108—C109—N101—C113	−178.4 (1)
C3—C2—N1—C13	0.7 (2)	C108—C109—C110—C111	179.5 (1)
C3—C2—C7—C6	−1.5 (2)	C110—C109—N101—C113	1.4 (2)
C3—C2—C7—C8	179.3 (1)	C110—C111—N112—C113	1.1 (2)

Symmetry codes: (i) $-x+3/2, y-1/2, z$; (ii) $-x+2, y+1/2, -z+1/2$; (iii) $-x+3/2, y+1/2, z$; (iv) $-x+2, y-1/2, -z+1/2$.

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N12—H121...O114	0.94 (2)	1.92 (2)	2.854 (2)	177 (1)
N112—H1121...O14	0.93 (2)	1.96 (2)	2.893 (2)	177 (1)

The structure was determined by single-crystal X-ray diffraction. The structure was refined by full-matrix least-squares on F^2 . The structure is shown as a 50% probability displacement ellipsoid plot. The H atoms were placed at calculated positions and refined as riding on their parent atoms. The structure is shown as a 50% probability displacement ellipsoid plot.

Experimental

The compound was prepared by PPS and reported in the literature. The compound was purified by recrystallization from the mother liquor. The sample was dried in a vacuum oven at 100 °C for 24 h.

Computing details

The structure was solved by direct methods and refined by full-matrix least-squares on F^2 . The structure is shown as a 50% probability displacement ellipsoid plot. The H atoms were placed at calculated positions and refined as riding on their parent atoms. The structure is shown as a 50% probability displacement ellipsoid plot.

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Crystal structure of $C_{14}H_{12}N_2O_3$ — ban1113

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Abstract

The crystal structure of $C_{14}H_{12}N_2O_3$ is reported.

Comment

The crystallographic asymmetric unit consists of two $C_{14}H_{12}N_2O_3$ molecules. These molecules are hydrogen-bonded to each other to form dimers, with the H of N5 donating towards O114 of the other molecule and the H of N105 of that molecule donating back to O14 of the original molecule.

Experimental

The compound was prepared by PPS and recrystallised from a mixture of methanol, dichloromethane and dimethylsulphoxide. The sample ID is 011ps-590.

Computing details

Data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-II* (Johnson 1976) in *TEXSAN* (MSC, 1992-1997), *PLATON* (Spek 2001); software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

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(ban1113)

Crystal data

$C_{14}H_{12}N_2O_3$	$F(000) = 1072$
$M_r = 256.26$	$D_x = 1.394 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/a$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 16.2144 (2) \text{ \AA}$	Cell parameters from 28769 reflections
$b = 7.7047 (1) \text{ \AA}$	$\theta = 2.6\text{--}27.5^\circ$
$c = 19.5669 (3) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$\beta = 92.7801 (8)^\circ$	$T = 295 \text{ K}$
$V = 2441.56 (6) \text{ \AA}^3$	Block, Colourless
$Z = 8$	$0.30 \times 0.21 \times 0.20 \text{ mm}$

Data collection

Nonius KappaCCD diffractometer	4202 reflections with $I > 2.0\sigma(I)$
graphite	$R_{\text{int}} = 0.034$
φ and ω scans with CCD	$\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 2.7^\circ$
Absorption correction: Integration via Gaussian method (Coppens, 1970) implemented in <i>h</i> = $-20 \rightarrow 20$ <i>maXius</i> (2000)	
$T_{\text{min}} = 0.974$, $T_{\text{max}} = 0.985$	$k = -9 \rightarrow 10$
48630 measured reflections	$l = -25 \rightarrow 25$
5568 independent reflections	

Refinement

Refinement on F^2	Hydrogen site location: Inferred from neighbouring sites
Least-squares matrix: Full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.040$	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.54P]$, where $P = (\max(F_o^2, 0) + 2F_c^2)/3$

$wR(F^2) = 0.110$	$(\Delta/\sigma)_{\max} = 0.001$
$S = 0.96$	$\Delta\rho_{\max} = 0.23 \text{ e } \text{\AA}^{-3}$
5568 reflections	$\Delta\rho_{\min} = -0.21 \text{ e } \text{\AA}^{-3}$
350 parameters	Extinction correction: Larson (1970), Equation 22
0 restraints	Extinction coefficient: 220 (30)
Primary atom site location: Structure-invariant direct methods	

Special details

Refinement. The H atoms were all located in a difference map, but were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularise their geometry (C—H in the range 0.93–0.98, N—H = 0.86 Å) and with $U_{\text{iso}}(\text{H})$ in the range 1.2–1.5 times U_{eq} of the parent atom, after which the positions were refined with riding constraints. The exceptions were the H's on nitrogen atoms where the coordinates were allowed to refine freely.

The largest peaks in the final difference electron density map are located midway along bonds.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.43143 (9)	0.94034 (19)	0.60829 (7)	0.0521
C2	0.51708 (8)	0.93086 (17)	0.61681 (7)	0.0453
N3	0.57542 (7)	0.85402 (14)	0.57608 (5)	0.0470
C4	0.55975 (9)	0.75415 (18)	0.51799 (7)	0.0501
N5	0.62787 (8)	0.68974 (18)	0.48991 (6)	0.0577
C6	0.70800 (10)	0.7208 (2)	0.51506 (8)	0.0607
C7	0.72345 (9)	0.8149 (2)	0.57130 (8)	0.0587
C8	0.65557 (8)	0.88534 (19)	0.60617 (7)	0.0511
C9	0.64736 (9)	0.9789 (2)	0.66448 (8)	0.0557
C10	0.56114 (8)	1.00675 (17)	0.67277 (7)	0.0470
C11	0.51699 (8)	1.08964 (18)	0.72314 (7)	0.0495
C12	0.43197 (8)	1.09952 (17)	0.71552 (7)	0.0480
C13	0.39009 (9)	1.02668 (19)	0.65768 (7)	0.0534
O14	0.48910 (6)	0.72800 (15)	0.49501 (5)	0.0612
C15	0.38177 (9)	1.18364 (19)	0.76761 (8)	0.0523
O16	0.30896 (7)	1.21552 (16)	0.75957 (6)	0.0736
O17	0.42581 (6)	1.21949 (14)	0.82540 (5)	0.0569
C18	0.38038 (10)	1.2920 (2)	0.88065 (8)	0.0592
C19	0.43760 (11)	1.3028 (3)	0.94237 (8)	0.0757
C101	0.64747 (8)	0.32486 (19)	0.23982 (7)	0.0470
C102	0.56300 (7)	0.35501 (16)	0.23096 (6)	0.0410
N103	0.50724 (6)	0.42823 (14)	0.27488 (5)	0.0425
C104	0.52406 (8)	0.49380 (17)	0.34018 (6)	0.0448
N105	0.45715 (7)	0.55519 (16)	0.37101 (6)	0.0510
C106	0.37864 (9)	0.5658 (2)	0.34017 (8)	0.0550
C107	0.36271 (8)	0.5080 (2)	0.27676 (8)	0.0548
C108	0.42817 (8)	0.43381 (18)	0.24044 (7)	0.0468
C109	0.43411 (8)	0.3651 (2)	0.17705 (7)	0.0514
C110	0.51797 (7)	0.31429 (18)	0.16967 (6)	0.0445
C111	0.55938 (8)	0.24081 (18)	0.11582 (7)	0.0471
C112	0.64353 (8)	0.21095 (17)	0.12391 (7)	0.0451
C113	0.68662 (8)	0.25263 (18)	0.18577 (7)	0.0486

O114	0.59400 (6)	0.49452 (13)	0.36716 (5)	0.0546
C115	0.69122 (8)	0.13756 (19)	0.06785 (7)	0.0519
O116	0.76279 (7)	0.09893 (19)	0.07316 (6)	0.0833
O117	0.64607 (6)	0.11973 (17)	0.00976 (5)	0.0682
C118	0.68726 (12)	0.0510 (3)	−0.04872 (9)	0.0881
C119	0.64670 (14)	0.1123 (4)	−0.11094 (10)	0.1174
H11	0.4045	0.8902	0.5700	0.0619*
H51	0.6206 (10)	0.627 (2)	0.4509 (9)	0.0703*
H61	0.7511	0.6723	0.4896	0.0718*
H71	0.7794	0.8334	0.5885	0.0717*
H91	0.6919	1.0172	0.6946	0.0672*
H111	0.5445	1.1406	0.7621	0.0589*
H131	0.3307	1.0376	0.6540	0.0637*
H181	0.3607	1.4088	0.8660	0.0706*
H182	0.3332	1.2161	0.8865	0.0709*
H191	0.4092	1.3544	0.9811	0.1112*
H192	0.4876	1.3749	0.9334	0.1113*
H193	0.4556	1.1861	0.9552	0.1117*
H1011	0.6775	0.3544	0.2819	0.0561*
H1051	0.4671 (9)	0.608 (2)	0.4138 (8)	0.0624*
H1061	0.3373	0.6162	0.3675	0.0656*
H1071	0.3099	0.5176	0.2548	0.0675*
H1091	0.3912	0.3552	0.1447	0.0620*
H1111	0.5300	0.2143	0.0740	0.0574*
H1131	0.7454	0.2336	0.1890	0.0577*
H1181	0.6820	−0.0747	−0.0457	0.1098*
H1182	0.7465	0.0799	−0.0437	0.1078*
H1191	0.6740	0.0671	−0.1504	0.1737*
H1192	0.5901	0.0732	−0.1110	0.1754*
H1193	0.6499	0.2375	−0.1096	0.1762*

Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0509 (8)	0.0565 (8)	0.0481 (7)	−0.0085 (7)	−0.0058 (6)	−0.0019 (6)
C2	0.0496 (7)	0.0417 (7)	0.0441 (7)	−0.0021 (6)	−0.0024 (6)	0.0013 (5)
N3	0.0496 (6)	0.0466 (6)	0.0443 (6)	−0.0017 (5)	−0.0040 (5)	−0.0025 (5)
C4	0.0563 (8)	0.0512 (8)	0.0423 (7)	−0.0030 (6)	−0.0034 (6)	−0.0007 (6)
N5	0.0611 (7)	0.0637 (8)	0.0479 (6)	0.0033 (6)	−0.0018 (6)	−0.0110 (6)
C6	0.0570 (9)	0.0659 (10)	0.0590 (9)	0.0074 (7)	−0.0003 (7)	−0.0069 (7)
C7	0.0503 (8)	0.0632 (9)	0.0619 (9)	0.0049 (7)	−0.0044 (7)	−0.0084 (7)
C8	0.0489 (7)	0.0521 (8)	0.0515 (8)	0.0007 (6)	−0.0076 (6)	−0.0027 (6)
C9	0.0485 (8)	0.0603 (9)	0.0569 (8)	0.0030 (7)	−0.0107 (6)	−0.0115 (7)
C10	0.0496 (7)	0.0440 (7)	0.0465 (7)	−0.0011 (6)	−0.0062 (6)	−0.0015 (6)
C11	0.0524 (8)	0.0477 (8)	0.0480 (7)	−0.0029 (6)	−0.0035 (6)	−0.0040 (6)
C12	0.0508 (8)	0.0425 (7)	0.0506 (7)	−0.0041 (6)	0.0012 (6)	0.0013 (6)
C13	0.0449 (7)	0.0591 (9)	0.0559 (8)	−0.0064 (6)	−0.0012 (6)	0.0014 (7)
O14	0.0573 (6)	0.0761 (7)	0.0494 (5)	−0.0065 (5)	−0.0048 (5)	−0.0132 (5)
C15	0.0503 (8)	0.0470 (8)	0.0598 (8)	−0.0075 (6)	0.0051 (6)	−0.0001 (6)
O16	0.0487 (6)	0.0876 (8)	0.0847 (8)	−0.0016 (6)	0.0049 (5)	−0.0164 (7)
O17	0.0544 (6)	0.0635 (6)	0.0531 (6)	0.0020 (5)	0.0060 (4)	−0.0067 (5)

C18	0.0638 (9)	0.0576 (9)	0.0575 (8)	0.0012 (7)	0.0159 (7)	−0.0009 (7)
C19	0.0838 (12)	0.0897 (13)	0.0540 (9)	0.0094 (10)	0.0074 (8)	−0.0069 (9)
C101	0.0422 (7)	0.0550 (8)	0.0427 (7)	0.0007 (6)	−0.0083 (5)	0.0038 (6)
C102	0.0407 (6)	0.0422 (7)	0.0396 (6)	−0.0012 (5)	−0.0028 (5)	0.0031 (5)
N103	0.0398 (5)	0.0478 (6)	0.0396 (5)	−0.0008 (5)	−0.0031 (4)	−0.0006 (5)
C104	0.0510 (7)	0.0427 (7)	0.0404 (6)	−0.0034 (6)	−0.0014 (6)	0.0016 (5)
N105	0.0517 (7)	0.0560 (7)	0.0451 (6)	−0.0022 (5)	0.0017 (5)	−0.0059 (5)
C106	0.0462 (7)	0.0565 (8)	0.0629 (9)	−0.0030 (7)	0.0080 (6)	−0.0086 (7)
C107	0.0385 (7)	0.0621 (9)	0.0635 (9)	−0.0005 (6)	−0.0004 (6)	−0.0100 (7)
C108	0.0379 (6)	0.0525 (8)	0.0493 (7)	−0.0028 (6)	−0.0042 (5)	−0.0020 (6)
C109	0.0373 (6)	0.0667 (9)	0.0492 (7)	−0.0007 (6)	−0.0077 (5)	−0.0072 (7)
C110	0.0392 (6)	0.0503 (7)	0.0433 (7)	−0.0024 (6)	−0.0045 (5)	0.0000 (6)
C111	0.0438 (7)	0.0544 (8)	0.0425 (7)	−0.0020 (6)	−0.0050 (5)	−0.0027 (6)
C112	0.0435 (7)	0.0453 (7)	0.0463 (7)	0.0005 (6)	0.0013 (5)	0.0025 (6)
C113	0.0386 (6)	0.0545 (8)	0.0519 (7)	0.0036 (6)	−0.0042 (6)	0.0049 (6)
O114	0.0517 (6)	0.0658 (6)	0.0451 (5)	0.0030 (5)	−0.0097 (4)	−0.0053 (5)
C115	0.0453 (7)	0.0547 (8)	0.0554 (8)	0.0002 (6)	0.0010 (6)	0.0004 (6)
O116	0.0485 (6)	0.1222 (11)	0.0790 (8)	0.0179 (7)	0.0005 (5)	−0.0226 (8)
O117	0.0548 (6)	0.1011 (9)	0.0489 (6)	0.0119 (6)	0.0043 (5)	−0.0124 (6)
C118	0.0772 (12)	0.1272 (18)	0.0614 (10)	0.0182 (12)	0.0181 (9)	−0.0184 (11)
C119	0.0903 (15)	0.204 (3)	0.0579 (11)	0.0375 (17)	0.0058 (10)	−0.0206 (15)

Geometric parameters (Å, °)

C1—C2	1.3927 (19)	C101—C102	1.3917 (17)
C1—C13	1.374 (2)	C101—C113	1.3770 (19)
C1—H11	0.932	C101—H1011	0.963
C2—N3	1.3976 (17)	C102—N103	1.3962 (16)
C2—C10	1.4055 (18)	C102—C110	1.4089 (16)
N3—C4	1.3858 (17)	N103—C104	1.3887 (16)
N3—C8	1.4212 (16)	N103—C108	1.4198 (15)
C4—N5	1.3517 (19)	C104—N105	1.3520 (18)
C4—O14	1.2268 (16)	C104—O114	1.2275 (15)
N5—C6	1.3877 (19)	N105—C106	1.3845 (18)
N5—H51	0.909 (17)	N105—H1051	0.939 (16)
C6—C7	1.331 (2)	C106—C107	1.332 (2)
C6—H61	0.955	C106—H1061	0.959
C7—C8	1.430 (2)	C107—C108	1.4251 (19)
C7—H71	0.962	C107—H1071	0.943
C8—C9	1.361 (2)	C108—C109	1.3563 (19)
C9—C10	1.431 (2)	C109—C110	1.4290 (18)
C9—H91	0.956	C109—H1091	0.921
C10—C11	1.4001 (19)	C110—C111	1.3965 (18)
C11—C12	1.3815 (19)	C111—C112	1.3851 (18)
C11—H111	0.949	C111—H1111	0.949
C12—C13	1.4080 (19)	C112—C113	1.4051 (18)
C12—C15	1.484 (2)	C112—C115	1.4844 (19)
C13—H131	0.966	C113—H1131	0.963
C15—O16	1.2087 (17)	C115—O116	1.1976 (17)
C15—O17	1.3366 (17)	C115—O117	1.3290 (17)
O17—C18	1.4496 (17)	O117—C118	1.4528 (18)

C18—C19	1.489 (2)	C118—C119	1.435 (3)
C18—H181	0.992	C118—H1181	0.974
C18—H182	0.974	C118—H1182	0.986
C19—H191	0.988	C119—H1191	0.972
C19—H192	1.004	C119—H1192	0.966
C19—H193	0.975	C119—H1193	0.967
O14...N105	2.794 (2)	N3...C104 ⁱⁱ	3.567 (2)
O14...C2 ⁱ	3.418 (2)	N5...C1 ⁱ	3.544 (2)
O14...N105 ⁱⁱ	3.489 (2)	N103...C2 ⁱⁱ	3.519 (2)
O14...O114 ⁱⁱ	3.519 (1)	N105...C4 ⁱⁱ	3.245 (2)
O14...O14 ⁱⁱ	3.536 (2)	N105...C11 ⁱ	3.337 (2)
O14...C1 ⁱ	3.539 (2)	N105...C10 ⁱ	3.491 (2)
O14...O114	3.578 (1)	N105...C4	3.595 (2)
O14...C104	3.595 (2)	C1...C4 ⁱ	3.421 (2)
O16...C107 ⁱⁱⁱ	3.259 (2)	C1...C104 ⁱⁱ	3.557 (2)
O17...C102 ⁱ	3.466 (2)	C2...C104 ⁱⁱ	3.451 (2)
O17...N103 ⁱ	3.550 (2)	C9...C106 ⁱ	3.534 (2)
O114...N5	2.864 (2)	C10...C106 ⁱ	3.448 (2)
O114...C1 ⁱⁱ	3.413 (2)	C11...C106 ⁱ	3.413 (2)
O114...C7 ^{iv}	3.432 (2)	C11...C104 ⁱ	3.493 (2)
O114...C12 ⁱ	3.537 (2)	C12...C104 ⁱ	3.404 (2)
O116...C109 ^v	3.373 (2)	C13...C101 ⁱⁱ	3.442 (2)
N3...N105 ⁱⁱ	3.368 (2)		
C2—C1—C13	117.30 (13)	C102—C101—C113	117.35 (12)
C2—C1—H11	120.0	C102—C101—H1011	121.4
C13—C1—H11	122.7	C113—C101—H1011	121.3
C1—C2—N3	130.73 (12)	C101—C102—N103	130.81 (11)
C1—C2—C10	122.53 (13)	C101—C102—C110	122.35 (12)
N3—C2—C10	106.73 (11)	N103—C102—C110	106.83 (10)
C2—N3—C4	126.91 (11)	C102—N103—C104	127.53 (11)
C2—N3—C8	108.81 (11)	C102—N103—C108	108.48 (10)
C4—N3—C8	124.17 (12)	C104—N103—C108	123.93 (11)
N3—C4—N5	114.61 (12)	N103—C104—N105	114.32 (11)
N3—C4—O14	121.51 (13)	N103—C104—O114	122.23 (12)
N5—C4—O14	123.89 (13)	N105—C104—O114	123.45 (12)
C4—N5—C6	124.19 (13)	C104—N105—C106	124.53 (12)
C4—N5—H51	117.6 (11)	C104—N105—H1051	116.3 (10)
C6—N5—H51	118.1 (11)	C106—N105—H1051	118.6 (10)
N5—C6—C7	121.50 (15)	N105—C106—C107	121.27 (13)
N5—C6—H61	116.4	N105—C106—H1061	115.7
C7—C6—H61	122.1	C107—C106—H1061	123.1
C6—C7—C8	118.86 (14)	C106—C107—C108	118.89 (13)
C6—C7—H71	120.4	C106—C107—H1071	121.9
C8—C7—H71	120.7	C108—C107—H1071	119.2
C7—C8—N3	116.58 (12)	C107—C108—N103	116.92 (12)
C7—C8—C9	135.21 (13)	C107—C108—C109	134.43 (12)
N3—C8—C9	108.20 (12)	N103—C108—C109	108.64 (11)
C8—C9—C10	108.08 (12)	C108—C109—C110	108.03 (11)
C8—C9—H91	125.4	C108—C109—H1091	125.1
C10—C9—H91	126.6	C110—C109—H1091	126.8

C9—C10—C2	108.16 (12)	C109—C110—C102	108.02 (11)
C9—C10—C11	133.14 (12)	C109—C110—C111	133.00 (12)
C2—C10—C11	118.70 (12)	C102—C110—C111	118.96 (11)
C10—C11—C12	119.39 (12)	C110—C111—C112	119.22 (12)
C10—C11—H111	121.2	C110—C111—H1111	119.8
C12—C11—H111	119.4	C112—C111—H1111	120.9
C11—C12—C13	120.31 (13)	C111—C112—C113	120.42 (12)
C11—C12—C15	121.85 (12)	C111—C112—C115	121.63 (12)
C13—C12—C15	117.83 (12)	C113—C112—C115	117.94 (12)
C12—C13—C1	121.70 (13)	C112—C113—C101	121.70 (12)
C12—C13—H131	117.7	C112—C113—H1131	118.1
C1—C13—H131	120.5	C101—C113—H1131	120.2
C12—C15—O16	124.35 (14)	C112—C115—O116	124.61 (14)
C12—C15—O17	112.52 (12)	C112—C115—O117	112.72 (11)
O16—C15—O17	123.13 (14)	O116—C115—O117	122.67 (14)
C15—O17—C18	116.14 (11)	C115—O117—C118	117.14 (12)
O17—C18—C19	107.89 (13)	O117—C118—C119	109.80 (16)
O17—C18—H181	107.6	O117—C118—H1181	105.7
C19—C18—H181	111.2	C119—C118—H1181	109.9
O17—C18—H182	106.6	O117—C118—H1182	108.7
C19—C18—H182	113.6	C119—C118—H1182	114.5
H181—C18—H182	109.6	H1181—C118—H1182	107.8
C18—C19—H191	110.4	C118—C119—H1191	110.3
C18—C19—H192	111.4	C118—C119—H1192	107.1
H191—C19—H192	108.7	H1191—C119—H1192	110.9
C18—C19—H193	109.0	C118—C119—H1193	106.5
H191—C19—H193	108.5	H1191—C119—H1193	110.7
H192—C19—H193	108.7	H1192—C119—H1193	111.1
O14—C4—N3—C2	2.4 (2)	C2—C1—C13—C12	−1.4 (2)
O14—C4—N3—C8	178.3 (1)	C2—C10—C9—C8	−1.4 (2)
O14—C4—N5—C6	179.0 (1)	C2—C10—C11—C12	−2.0 (2)
O16—C15—O17—C18	3.1 (2)	C4—N3—C2—C10	175.3 (1)
O16—C15—C12—C11	170.1 (1)	C4—N3—C8—C7	3.2 (2)
O16—C15—C12—C13	−10.8 (2)	C4—N3—C8—C9	−176.3 (1)
O17—C15—C12—C11	−10.6 (2)	C4—N5—C6—C7	2.0 (2)
O17—C15—C12—C13	168.6 (1)	C6—C7—C8—C9	177.0 (2)
O114—C104—N103—C102	0.4 (2)	C7—C8—C9—C10	−178.6 (2)
O114—C104—N103—C108	−176.3 (1)	C8—N3—C2—C10	−1.1 (1)
O114—C104—N105—C106	175.8 (1)	C8—C9—C10—C11	178.4 (1)
O116—C115—O117—C118	−0.3 (2)	C9—C10—C11—C12	178.1 (1)
O116—C115—C112—C111	−175.1 (2)	C10—C2—C1—C13	−0.6 (2)
O116—C115—C112—C113	5.9 (2)	C10—C11—C12—C13	0.1 (2)
O117—C115—C112—C111	5.4 (2)	C10—C11—C12—C15	179.2 (1)
O117—C115—C112—C113	−173.5 (1)	C12—C15—O17—C18	−176.3 (1)
N3—C2—C1—C13	−179.7 (1)	C15—O17—C18—C19	173.4 (1)
N3—C2—C10—C9	1.5 (2)	C101—C102—N103—C104	1.3 (2)
N3—C2—C10—C11	−178.3 (1)	C101—C102—N103—C108	178.4 (1)
N3—C4—N5—C6	−1.1 (2)	C101—C102—C110—C109	−178.6 (1)
N3—C8—C7—C6	−2.2 (2)	C101—C102—C110—C111	0.1 (2)
N3—C8—C9—C10	0.7 (2)	C101—C113—C112—C111	−0.4 (2)
N5—C4—N3—C2	−177.4 (1)	C101—C113—C112—C115	178.5 (1)

N5—C4—N3—C8	−1.6 (2)	C102—N103—C108—C107	−178.8 (1)
N5—C6—C7—C8	−0.1 (2)	C102—N103—C108—C109	0.4 (2)
N103—C102—C101—C113	−178.7 (1)	C102—C101—C113—C112	0.1 (2)
N103—C102—C110—C109	0.4 (1)	C102—C110—C109—C108	−0.1 (2)
N103—C102—C110—C111	179.1 (1)	C102—C110—C111—C112	−0.4 (2)
N103—C104—N105—C106	−4.5 (2)	C104—N103—C102—C110	−177.6 (1)
N103—C108—C107—C106	−0.6 (2)	C104—N103—C108—C107	−1.6 (2)
N103—C108—C109—C110	−0.2 (2)	C104—N103—C108—C109	177.7 (1)
N105—C104—N103—C102	−179.3 (1)	C104—N105—C106—C107	2.7 (2)
N105—C104—N103—C108	3.9 (2)	C106—C107—C108—C109	−179.5 (2)
N105—C106—C107—C108	0.1 (2)	C107—C108—C109—C110	178.9 (2)
C1—C2—N3—C4	−5.5 (2)	C108—N103—C102—C110	−0.5 (1)
C1—C2—N3—C8	178.1 (1)	C108—C109—C110—C111	−178.6 (2)
C1—C2—C10—C9	−177.8 (1)	C109—C110—C111—C112	177.9 (1)
C1—C2—C10—C11	2.4 (2)	C110—C102—C101—C113	0.0 (2)
C1—C13—C12—C11	1.7 (2)	C110—C111—C112—C113	0.6 (2)
C1—C13—C12—C15	−177.4 (1)	C110—C111—C112—C115	−178.3 (1)
C2—N3—C8—C7	179.7 (1)	C112—C115—O117—C118	179.2 (1)
C2—N3—C8—C9	0.3 (2)	C115—O117—C118—C119	−153.2 (2)

Symmetry codes: (i) $-x+1, -y+2, -z+1$; (ii) $-x+1, -y+1, -z+1$; (iii) $-x+1/2, y+1/2, -z+1$; (iv) $-x+3/2, y-1/2, -z+1$; (v) $x+1/2, -y+1/2, z$.

Hydrogen-bond geometry (Å, °)

<i>D</i> —H $\cdots$ <i>A</i>	<i>D</i> —H	H $\cdots$ <i>A</i>	<i>D</i> $\cdots$ <i>A</i>	<i>D</i> —H $\cdots$ <i>A</i>
N5—H51 $\cdots$ O114	0.909 (17)	1.958 (17)	2.864 (2)	174.7 (15)
N105—H1051 $\cdots$ O14	0.939 (16)	1.857 (17)	2.794 (2)	175.8 (14)

Crystal structure of C₆H₇IN₂O — ban0917

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Abstract

The crystal structure of C₆H₇IN₂O is reported.

Comment

The crystallographic asymmetric unit consists of three C₆H₇IN₂O molecules.

Experimental

The compound was prepared by PPS and recrystallized from ethylacetate/methanol/dichloromethane. The sample ID is 09 ps-262.

Refinement

All hydrogen atoms were observed in a difference electron density map generated prior to their inclusion. They were included at geometrically determined positions and were initially refined with soft restraints on the bond lengths and angles, to regularize their geometry (C—H in the range 0.93–0.98 Å, N—H in the range 0.86–0.89 Å), and on $U_{\text{iso}}(\text{H})$ (in the range 1.2–1.5 times U_{eq} of the parent atom). Finally the H atom positional parameters were refined without restraints.

The largest peaks in the final difference electron density map are located near iodine atoms.

Computing details

Data collection: *COLLECT* (Nonius, 1997-2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEPII* (Johnson 1976) in *TEXSAN* (MSC, 1992-1997); software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

(ban0917)

Crystal data

$C_6H_7IN_2O$	$V = 2391.66 (6) \text{ \AA}^3$
$M_r = 250.04$	$Z = 12$
Monoclinic, $P2_1/a$	Mo $K\alpha$
$a = 8.2495 (1) \text{ \AA}$	$\mu = 3.95 \text{ mm}^{-1}$
$b = 22.3491 (3) \text{ \AA}$	$T = 200 \text{ K}$
$c = 13.1812 (2) \text{ \AA}$	$0.40 \times 0.23 \times 0.16 \text{ mm}$
$\beta = 100.2178 (7)^\circ$	

Data collection

Area diffractometer	5398 independent reflections
Absorption correction: integration via Gaussian method (Coppens, 1970) implemented in maXus (2000)	4510 reflections with $I > 2.0\sigma(I)$
$T_{\min} = 0.310$, $T_{\max} = 0.577$	$R_{\text{int}} = 0.034$
36962 measured reflections	

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.025$	334 parameters
$wR(F^2) = 0.062$	Only H-atom coordinates refined
$S = 0.98$	$\Delta\rho_{\max} = 1.32 \text{ e \AA}^{-3}$
5398 reflections	$\Delta\rho_{\min} = -1.21 \text{ e \AA}^{-3}$

Table 1
Selected geometric parameters ($\text{\AA}$, $^\circ$)

I10—C5	2.079 (2)	N21—C22	1.347 (3)
I20—C15	2.090 (2)	N21—C26	1.337 (3)
I30—C25	2.087 (2)	N27—C22	1.359 (3)
O8—C4	1.347 (3)	C2—C3	1.401 (4)
O8—C9	1.435 (4)	C3—C4	1.376 (4)
O18—C14	1.345 (3)	C4—C5	1.404 (3)
O18—C19	1.439 (3)	C5—C6	1.369 (4)
O28—C24	1.355 (3)	C12—C13	1.403 (3)
O28—C29	1.431 (3)	C13—C14	1.380 (3)
N1—C2	1.339 (3)	C14—C15	1.409 (3)
N1—C6	1.346 (3)	C15—C16	1.366 (4)
N7—C2	1.352 (4)	C22—C23	1.402 (3)
N11—C12	1.345 (3)	C23—C24	1.382 (3)
N11—C16	1.347 (3)	C24—C25	1.409 (3)
N17—C12	1.354 (3)	C25—C26	1.369 (3)
C4—O8—C9	117.1 (2)	C12—C13—C14	119.4 (2)
C14—O18—C19	117.2 (2)	C13—C14—O18	125.1 (2)

C24—O28—C29	117.1 (2)	C13—C14—C15	117.8 (2)
C2—N1—C6	116.7 (2)	O18—C14—C15	117.2 (2)
C12—N11—C16	116.7 (2)	C14—C15—I20	121.43 (18)
C22—N21—C26	116.8 (2)	C14—C15—C16	118.8 (2)
N7—C2—N1	116.7 (2)	I20—C15—C16	119.77 (18)
N7—C2—C3	120.4 (2)	C15—C16—N11	124.5 (2)
N1—C2—C3	122.9 (2)	N27—C22—N21	116.5 (2)
C2—C3—C4	119.3 (2)	N27—C22—C23	120.7 (2)
C3—C4—O8	124.7 (2)	N21—C22—C23	122.7 (2)
C3—C4—C5	118.2 (2)	C22—C23—C24	119.0 (2)
O8—C4—C5	117.1 (2)	C23—C24—O28	124.6 (2)
C4—C5—I10	121.64 (19)	C23—C24—C25	118.5 (2)
C4—C5—C6	118.3 (2)	O28—C24—C25	116.9 (2)
I10—C5—C6	120.02 (19)	C24—C25—I30	122.26 (17)
C5—C6—N1	124.6 (2)	C24—C25—C26	117.8 (2)
N17—C12—N11	117.2 (2)	I30—C25—C26	119.91 (18)
N17—C12—C13	120.1 (2)	C25—C26—N21	125.2 (2)
N11—C12—C13	122.8 (2)		

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Crystal structure of C₆H₇IN₂O — ban0917

Phillip Patrick Sharp, Martin G. Banwell and Anthony C. Willis

(ban0917)

Crystal data

C ₆ H ₇ IN ₂ O	$F_{000} = 1416$
$M_r = 250.04$	$D_x = 2.083 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/a$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 8.2495 (1) \text{ \AA}$	Cell parameters from 31434 reflections
$b = 22.3491 (3) \text{ \AA}$	$\theta = 3\text{--}27.5^\circ$
$c = 13.1812 (2) \text{ \AA}$	$\mu = 3.95 \text{ mm}^{-1}$
$\beta = 100.2178 (7)^\circ$	$T = 200 \text{ K}$
$V = 2391.66 (6) \text{ \AA}^3$	Plate, colourless
$Z = 12$	$0.40 \times 0.23 \times 0.16 \text{ mm}$

Data collection

Area diffractometer	4510 reflections with $I > 2.0\sigma(I)$
Monochromator: graphite	$R_{\text{int}} = 0.034$
$T = 200 \text{ K}$	$\theta_{\text{max}} = 27.5^\circ$
φ and ω scans with CCD	$\theta_{\text{min}} = 2.7^\circ$
Absorption correction: integration via Gaussian method (Coppens, 1970) implemented in maXus (2000)	$h = -10 \rightarrow 10$
$T_{\text{min}} = 0.310$, $T_{\text{max}} = 0.577$	$k = -27 \rightarrow 28$
36962 measured reflections	$l = -17 \rightarrow 17$
5398 independent reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	Only H-atom coordinates refined
$R[F^2 > 2\sigma(F^2)] = 0.025$	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.01P)^2 + 0.72P]$, where $P = (\max(F_o^2, 0) + 2F_c^2)/3$
$wR(F^2) = 0.062$	$(\Delta/\sigma)_{\text{max}} = 0.002$
$S = 0.98$	$\Delta\rho_{\text{max}} = 1.32 \text{ e \AA}^{-3}$
5398 reflections	$\Delta\rho_{\text{min}} = -1.21 \text{ e \AA}^{-3}$
334 parameters	Extinction correction: None
Primary atom site location: structure-invariant direct methods	

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
I10	0.19055 (3)	0.526653 (10)	0.92490 (2)	0.0710
I20	1.06746 (3)	0.700504 (11)	0.044076 (15)	0.0611
I30	0.72209 (2)	0.449477 (8)	0.725299 (15)	0.0474
O8	0.5142 (2)	0.59454 (9)	0.89407 (15)	0.0482
O18	0.7747 (2)	0.64567 (9)	0.14062 (14)	0.0429
O28	0.36053 (19)	0.49817 (8)	0.64046 (14)	0.0394
N1	0.1067 (2)	0.68690 (10)	0.74194 (17)	0.0385
N7	0.2697 (3)	0.75878 (12)	0.6874 (2)	0.0530
N11	1.1477 (3)	0.70088 (9)	0.37622 (17)	0.0367
N17	1.0096 (3)	0.66346 (11)	0.49978 (18)	0.0410
N21	0.7057 (2)	0.61663 (9)	0.56152 (17)	0.0370
N27	0.5038 (3)	0.68223 (11)	0.4878 (2)	0.0489
C2	0.2584 (3)	0.70825 (11)	0.74212 (19)	0.0353
C3	0.4009 (3)	0.67966 (12)	0.79323 (19)	0.0355
C4	0.3865 (3)	0.62694 (11)	0.84487 (18)	0.0346
C5	0.2278 (3)	0.60461 (11)	0.84612 (19)	0.0375
C6	0.0957 (3)	0.63594 (12)	0.7947 (2)	0.0405
C9	0.6766 (4)	0.61599 (18)	0.8892 (3)	0.0546
C12	1.0134 (3)	0.67343 (10)	0.39889 (19)	0.0328
C13	0.8829 (3)	0.65394 (10)	0.32298 (19)	0.0322
C14	0.8923 (3)	0.66160 (10)	0.22027 (19)	0.0327
C15	1.0357 (3)	0.68841 (11)	0.19657 (19)	0.0348
C16	1.1553 (3)	0.70704 (11)	0.2755 (2)	0.0374
C19	0.6222 (4)	0.62353 (17)	0.1647 (3)	0.0503
C22	0.5438 (3)	0.62897 (11)	0.53541 (19)	0.0350
C23	0.4211 (3)	0.59106 (10)	0.56017 (19)	0.0337
C24	0.4672 (3)	0.53883 (10)	0.61363 (18)	0.0307
C25	0.6364 (3)	0.52603 (11)	0.64210 (19)	0.0328
C26	0.7461 (3)	0.56601 (12)	0.6140 (2)	0.0364
C29	0.1886 (3)	0.51100 (14)	0.6117 (3)	0.0434
H31	0.508 (4)	0.6968 (12)	0.792 (2)	0.0432*
H61	−0.011 (4)	0.6227 (13)	0.793 (2)	0.0489*
H71	0.369 (5)	0.7751 (16)	0.693 (3)	0.0625*
H72	0.185 (5)	0.7740 (16)	0.659 (3)	0.0628*
H91	0.739 (5)	0.5896 (19)	0.923 (3)	0.0803*
H92	0.686 (5)	0.654 (2)	0.920 (3)	0.0796*
H93	0.695 (5)	0.6144 (18)	0.820 (3)	0.0795*
H131	0.797 (3)	0.6342 (12)	0.340 (2)	0.0386*
H161	1.249 (4)	0.7283 (13)	0.259 (2)	0.0451*
H171	1.077 (4)	0.6798 (15)	0.542 (2)	0.0501*
H172	0.919 (4)	0.6512 (14)	0.518 (2)	0.0492*
H191	0.561 (5)	0.6123 (17)	0.099 (3)	0.0748*
H192	0.567 (5)	0.6562 (17)	0.203 (3)	0.0744*
H193	0.646 (5)	0.5877 (18)	0.199 (3)	0.0746*
H231	0.310 (3)	0.6027 (12)	0.540 (2)	0.0390*

H261	0.862 (4)	0.5580 (12)	0.633 (2)	0.0432*
H271	0.579 (5)	0.7005 (15)	0.461 (3)	0.0580*
H272	0.409 (5)	0.6886 (15)	0.465 (3)	0.0578*
H291	0.126 (4)	0.4793 (16)	0.635 (3)	0.0641*
H292	0.155 (4)	0.5477 (16)	0.641 (3)	0.0644*
H293	0.162 (4)	0.5164 (15)	0.533 (3)	0.0640*

Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
I10	0.08290 (17)	0.05201 (13)	0.08271 (18)	−0.01092 (11)	0.02717 (13)	0.02333 (11)
I20	0.06671 (14)	0.08090 (16)	0.04127 (11)	−0.02674 (11)	0.02456 (10)	−0.00633 (10)
I30	0.03750 (10)	0.04694 (11)	0.05681 (12)	0.00715 (7)	0.00556 (8)	0.01146 (8)
O8	0.0437 (10)	0.0505 (11)	0.0488 (11)	0.0070 (9)	0.0039 (9)	0.0154 (9)
O18	0.0368 (9)	0.0545 (11)	0.0375 (10)	−0.0099 (8)	0.0064 (7)	0.0006 (8)
O28	0.0267 (8)	0.0393 (9)	0.0526 (11)	−0.0006 (7)	0.0079 (7)	0.0050 (8)
N1	0.0317 (10)	0.0434 (12)	0.0399 (12)	−0.0012 (9)	0.0049 (9)	−0.0024 (10)
N7	0.0393 (13)	0.0523 (15)	0.0653 (17)	0.0011 (11)	0.0037 (12)	0.0242 (13)
N11	0.0369 (11)	0.0343 (11)	0.0394 (12)	−0.0055 (9)	0.0082 (9)	−0.0026 (9)
N17	0.0414 (12)	0.0465 (13)	0.0355 (12)	−0.0049 (10)	0.0083 (9)	0.0004 (10)
N21	0.0314 (10)	0.0363 (11)	0.0432 (12)	−0.0044 (8)	0.0065 (9)	−0.0048 (9)
N27	0.0364 (12)	0.0384 (12)	0.0697 (17)	−0.0041 (10)	0.0033 (12)	0.0109 (12)
C2	0.0382 (13)	0.0374 (13)	0.0303 (12)	0.0006 (10)	0.0061 (10)	−0.0004 (10)
C3	0.0310 (12)	0.0407 (13)	0.0354 (13)	−0.0024 (10)	0.0072 (10)	0.0016 (10)
C4	0.0379 (12)	0.0385 (13)	0.0269 (12)	0.0022 (10)	0.0044 (9)	−0.0001 (10)
C5	0.0444 (14)	0.0351 (12)	0.0346 (13)	−0.0059 (10)	0.0113 (11)	0.0017 (10)
C6	0.0350 (13)	0.0454 (15)	0.0427 (15)	−0.0065 (11)	0.0115 (11)	−0.0051 (12)
C9	0.0372 (15)	0.067 (2)	0.056 (2)	0.0084 (14)	0.0002 (14)	0.0154 (17)
C12	0.0351 (12)	0.0256 (11)	0.0386 (13)	0.0021 (9)	0.0089 (10)	−0.0008 (10)
C13	0.0302 (11)	0.0287 (11)	0.0394 (13)	0.0000 (9)	0.0109 (10)	0.0014 (10)
C14	0.0306 (11)	0.0295 (11)	0.0385 (13)	0.0012 (9)	0.0077 (9)	−0.0012 (10)
C15	0.0398 (13)	0.0326 (12)	0.0348 (13)	−0.0023 (10)	0.0144 (10)	−0.0012 (10)
C16	0.0384 (13)	0.0318 (12)	0.0447 (14)	−0.0055 (10)	0.0145 (11)	−0.0013 (11)
C19	0.0366 (14)	0.065 (2)	0.0481 (17)	−0.0125 (14)	0.0046 (12)	0.0008 (15)
C22	0.0336 (12)	0.0305 (12)	0.0399 (14)	−0.0022 (9)	0.0044 (10)	−0.0061 (10)
C23	0.0286 (11)	0.0297 (11)	0.0419 (14)	−0.0006 (9)	0.0037 (10)	−0.0051 (10)
C24	0.0276 (11)	0.0317 (11)	0.0329 (12)	−0.0019 (9)	0.0057 (9)	−0.0053 (9)
C25	0.0315 (11)	0.0326 (12)	0.0342 (12)	0.0036 (9)	0.0058 (9)	−0.0018 (10)
C26	0.0269 (12)	0.0413 (13)	0.0407 (14)	0.0002 (10)	0.0051 (10)	−0.0063 (11)
C29	0.0255 (12)	0.0443 (15)	0.0610 (19)	−0.0012 (11)	0.0094 (12)	0.0007 (14)

Geometric parameters ($\text{\AA}$, $^\circ$)

I10—C5	2.079 (2)	C3—H31	0.96 (3)
I20—C15	2.090 (2)	C4—C5	1.404 (3)
I30—C25	2.087 (2)	C5—C6	1.369 (4)
O8—C4	1.347 (3)	C6—H61	0.93 (3)
O8—C9	1.435 (4)	C9—H91	0.85 (4)
O18—C14	1.345 (3)	C9—H92	0.95 (4)

supplementary materials

O18—C19	1.439 (3)	C9—H93	0.95 (4)
O28—C24	1.355 (3)	C12—C13	1.403 (3)
O28—C29	1.431 (3)	C13—C14	1.380 (3)
N1—C2	1.339 (3)	C13—H131	0.89 (3)
N1—C6	1.346 (3)	C14—C15	1.409 (3)
N7—C2	1.352 (4)	C15—C16	1.366 (4)
N7—H71	0.89 (4)	C16—H161	0.97 (3)
N7—H72	0.80 (4)	C19—H191	0.96 (4)
N11—C12	1.345 (3)	C19—H192	1.04 (4)
N11—C16	1.347 (3)	C19—H193	0.92 (4)
N17—C12	1.354 (3)	C22—C23	1.402 (3)
N17—H171	0.80 (3)	C23—C24	1.382 (3)
N17—H172	0.86 (3)	C23—H231	0.94 (3)
N21—C22	1.347 (3)	C24—C25	1.409 (3)
N21—C26	1.337 (3)	C25—C26	1.369 (3)
N27—C22	1.359 (3)	C26—H261	0.96 (3)
N27—H271	0.86 (4)	C29—H291	0.96 (4)
N27—H272	0.80 (4)	C29—H292	0.97 (4)
C2—C3	1.401 (4)	C29—H293	1.02 (4)
C3—C4	1.376 (4)		
O8…C19 ⁱ	3.579 (4)	N11…N27 ^v	3.071 (3)
O18…C9 ⁱⁱ	3.336 (4)	N11…N27 ^{vi}	3.319 (3)
N1…N7 ⁱⁱⁱ	3.002 (3)	N17…N21	2.961 (3)
N1…N17 ^{iv}	3.193 (3)	N17…N27 ^{vi}	3.452 (4)
N1…C3 ⁱⁱⁱ	3.555 (3)	N17…C26	3.591 (4)
N7…N21 ⁱⁱⁱ	3.236 (3)	N27…C12 ⁱⁱⁱ	3.438 (3)
N7…N27 ⁱⁱⁱ	3.380 (3)	C24…C24 ^{vii}	3.585 (5)
N7…C22 ⁱⁱⁱ	3.529 (3)	C26…C29 ^{vii}	3.560 (5)
C4—O8—C9	117.1 (2)	C12—C13—C14	119.4 (2)
C14—O18—C19	117.2 (2)	C12—C13—H131	121.3 (18)
C24—O28—C29	117.1 (2)	C14—C13—H131	119.2 (18)
C2—N1—C6	116.7 (2)	C13—C14—O18	125.1 (2)
C2—N7—H71	117 (2)	C13—C14—C15	117.8 (2)
C2—N7—H72	118 (3)	O18—C14—C15	117.2 (2)
H71—N7—H72	125 (3)	C14—C15—I20	121.43 (18)
C12—N11—C16	116.7 (2)	C14—C15—C16	118.8 (2)
C12—N17—H171	118 (2)	I20—C15—C16	119.77 (18)
C12—N17—H172	119 (2)	C15—C16—N11	124.5 (2)
H171—N17—H172	119 (3)	C15—C16—H161	118.3 (17)
C22—N21—C26	116.8 (2)	N11—C16—H161	117.1 (17)
C22—N27—H271	118 (2)	O18—C19—H191	103 (2)
C22—N27—H272	118 (3)	O18—C19—H192	110 (2)
H271—N27—H272	119 (3)	H191—C19—H192	115 (3)
N7—C2—N1	116.7 (2)	O18—C19—H193	107 (2)
N7—C2—C3	120.4 (2)	H191—C19—H193	105 (3)
N1—C2—C3	122.9 (2)	H192—C19—H193	116 (3)
C2—C3—C4	119.3 (2)	N27—C22—N21	116.5 (2)

C2—C3—H31	120.3 (17)	N27—C22—C23	120.7 (2)
C4—C3—H31	120.4 (17)	N21—C22—C23	122.7 (2)
C3—C4—O8	124.7 (2)	C22—C23—C24	119.0 (2)
C3—C4—C5	118.2 (2)	C22—C23—H231	118.3 (17)
O8—C4—C5	117.1 (2)	C24—C23—H231	122.7 (17)
C4—C5—I10	121.64 (19)	C23—C24—O28	124.6 (2)
C4—C5—C6	118.3 (2)	C23—C24—C25	118.5 (2)
I10—C5—C6	120.02 (19)	O28—C24—C25	116.9 (2)
C5—C6—N1	124.6 (2)	C24—C25—I30	122.26 (17)
C5—C6—H61	121.4 (19)	C24—C25—C26	117.8 (2)
N1—C6—H61	114.0 (19)	I30—C25—C26	119.91 (18)
O8—C9—H91	103 (3)	C25—C26—N21	125.2 (2)
O8—C9—H92	107 (2)	C25—C26—H261	118.9 (17)
H91—C9—H92	114 (4)	N21—C26—H261	115.9 (17)
O8—C9—H93	110 (2)	O28—C29—H291	109 (2)
H91—C9—H93	106 (3)	O28—C29—H292	114 (2)
H92—C9—H93	116 (3)	H291—C29—H292	107 (3)
N17—C12—N11	117.2 (2)	O28—C29—H293	108.4 (19)
N17—C12—C13	120.1 (2)	H291—C29—H293	112 (3)
N11—C12—C13	122.8 (2)	H292—C29—H293	106 (3)
I10—C5—C4—O8	2.2 (3)	N21—C22—C23—C24	0.1 (4)
I10—C5—C4—C3	−178.3 (2)	N21—C26—C25—C24	0.1 (4)
I10—C5—C6—N1	179.7 (2)	N27—C22—N21—C26	176.0 (2)
I20—C15—C14—O18	−1.8 (3)	N27—C22—C23—C24	−176.5 (2)
I20—C15—C14—C13	178.4 (2)	C2—N1—C6—C5	−1.2 (4)
I20—C15—C16—N11	−179.4 (2)	C2—C3—C4—C5	−1.5 (4)
I30—C25—C24—O28	−1.7 (3)	C3—C2—N1—C6	0.5 (4)
I30—C25—C24—C23	178.8 (2)	C3—C4—O8—C9	−2.0 (4)
I30—C25—C26—N21	−179.4 (2)	C3—C4—C5—C6	0.9 (4)
O8—C4—C3—C2	177.9 (2)	C5—C4—O8—C9	177.5 (3)
O8—C4—C5—C6	−178.5 (2)	C12—N11—C16—C15	1.2 (4)
O18—C14—C13—C12	−179.0 (2)	C12—C13—C14—C15	0.7 (3)
O18—C14—C15—C16	177.8 (2)	C13—C12—N11—C16	−2.5 (3)
O28—C24—C23—C22	−178.8 (2)	C13—C14—O18—C19	5.4 (4)
O28—C24—C25—C26	178.8 (2)	C13—C14—C15—C16	−2.0 (3)
N1—C2—C3—C4	0.8 (4)	C15—C14—O18—C19	−174.3 (2)
N1—C6—C5—C4	0.4 (4)	C22—N21—C26—C25	0.6 (4)
N7—C2—N1—C6	178.7 (2)	C22—C23—C24—C25	0.6 (4)
N7—C2—C3—C4	−177.3 (2)	C23—C22—N21—C26	−0.6 (4)
N11—C12—C13—C14	1.6 (4)	C23—C24—O28—C29	−0.5 (4)
N11—C16—C15—C14	1.0 (4)	C23—C24—C25—C26	−0.7 (4)
N17—C12—N11—C16	175.7 (2)	C25—C24—O28—C29	180.0 (2)
N17—C12—C13—C14	−176.6 (2)		

Symmetry codes: (i) $x, y, z+1$; (ii) $x, y, z-1$; (iii) $x-1/2, -y+3/2, z$; (iv) $x-1, y, z$; (v) $x+1, y, z$; (vi) $x+1/2, -y+3/2, z$; (vii) $-x+1, -y+1, -z+1$.

Hydrogen-bond geometry ($\text{\AA}, ^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
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supplementary materials

N7—H71...N1 ^{vi}	0.89 (4)	2.13 (4)	3.001 (4)	167 (4)
N17—H172...N21	0.86 (3)	2.10 (3)	2.961 (4)	177 (3)
N27—H271...N11 ⁱⁱⁱ	0.86 (4)	2.58 (4)	3.319 (4)	144 (4)
N27—H272...N11 ^{iv}	0.80 (4)	2.28 (4)	3.072 (4)	171 (4)

Symmetry codes: (vi) $x+1/2, -y+3/2, z$; (iii) $x-1/2, -y+3/2, z$; (iv) $x-1, y, z$.

Crystal structure of $C_{13}H_{16}N_2OSi$ — ban1007

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The crystal structure of $C_{13}H_{16}N_2OSi$ is reported.

Comment

The crystallographic asymmetric unit consists of one $C_{13}H_{16}N_2OSi$ molecule.

Molecules of $C_{13}H_{16}N_2OSi$ are hydrogen-bonded into pairs, with the H of N1 donating towards N8 of an adjacent molecule and the H of N1 of that molecule donating back to N8 of the original molecule.

Experimental

The compound was prepared by PPS. The sample ID is 010ps-395-a.

Crystal data

$C_{13}H_{16}N_2OSi$	$V = 2737.29 (10) \text{ \AA}^3$
$M_r = 244.37$	$Z = 8$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 12.3949 (2) \text{ \AA}$	$\mu = 0.16 \text{ mm}^{-1}$
$b = 12.5045 (3) \text{ \AA}$	$T = 200 \text{ K}$
$c = 17.7115 (4) \text{ \AA}$	$0.43 \times 0.30 \times 0.17 \text{ mm}$
$\beta = 94.3358 (13)^\circ$	

Data collection

Area diffractometer	3123 independent reflections
Absorption correction: Integration via Gaussian method (Coppens, 1970) implemented in <i>maXus</i> (2000)	2692 reflections with $I > 2.0\sigma(I)$
$T_{\min} = 0.948$, $T_{\max} = 0.977$	$R_{\text{int}} = 0.040$
26370 measured reflections	

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.042$	0 restraints
$wR(F^2) = 0.119$	H atoms treated by a mixture of independent and constrained refinement
$S = 1.00$	$\Delta\rho_{\max} = 0.30 \text{ e \AA}^{-3}$
3123 reflections	$\Delta\rho_{\min} = -0.36 \text{ e \AA}^{-3}$
157 parameters	

Table 1

Selected geometric parameters ($\text{\AA}$, $^\circ$)

N1—C2	1.3864 (18)	C6—C7	1.394 (2)
N1—C9	1.3632 (18)	C7—N8	1.336 (2)
C2—C3	1.3760 (19)	N8—C9	1.3457 (18)
C2—C12	1.4233 (19)	O10—C11	1.4381 (19)
C3—C4	1.424 (2)	C12—C13	1.206 (2)
C4—C5	1.406 (2)	C13—Si14	1.8458 (16)
C4—C9	1.4064 (19)	Si14—C15	1.862 (2)

C5—C6	1.384 (2)	Si14—C16	1.8520 (19)
C5—O10	1.3558 (18)	Si14—C17	1.857 (2)
C2—N1—C9	108.42 (12)	C7—N8—C9	113.55 (13)
N1—C2—C3	109.51 (12)	C4—C9—N1	108.38 (12)
N1—C2—C12	120.11 (12)	C4—C9—N8	126.94 (13)
C3—C2—C12	130.30 (13)	N1—C9—N8	124.67 (13)
C2—C3—C4	106.56 (12)	C5—O10—C11	117.32 (13)
C3—C4—C5	136.05 (13)	C2—C12—C13	177.08 (16)
C3—C4—C9	107.11 (12)	C12—C13—Si14	179.53 (14)
C5—C4—C9	116.78 (13)	C13—Si14—C15	107.54 (8)
C4—C5—C6	117.64 (13)	C13—Si14—C16	109.71 (8)
C4—C5—O10	116.18 (13)	C15—Si14—C16	110.11 (10)
C6—C5—O10	126.17 (13)	C13—Si14—C17	106.56 (8)
C5—C6—C7	119.66 (14)	C15—Si14—C17	111.79 (11)
C6—C7—N8	125.36 (14)	C16—Si14—C17	110.99 (10)

The H atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularise their geometry (C—H in the range 0.93–0.98, N—H = 0.86 Å) and with $U_{\text{iso}}(\text{H})$ in the range 1.2–1.5 times U_{eq} of the parent atom, after which the positions were refined with riding constraints. The exception was the H on N1 where the coordinates were allowed to refine freely.

The largest peaks in the final difference electron density map are located midway along C—C bonds.

Data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-II* (Johnson 1976) in *TEXSAN* (MSC, 1992–1997); software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

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supplementary materials

Crystal structure of $C_{12}H_{14}N_4O_8$ (201807)

Phillip Patrick Sharp, David C. Sawyer¹ and Anthony C. Willis²

(201807)

Crystal data

$C_{12}H_{14}N_4O_8$	$M_r = 342.30$
$M_n = 344.32$	$F(000) = 328$
Monoclinic, $P2_1$	$a = 12.345(15)$ Å
$b = 12.345(15)$ Å	$c = 12.345(15)$ Å
$\beta = 90.0^\circ$	

supplementary materials

1. $a = 12.345(15)$ Å	$b = 12.345(15)$ Å
2. $c = 12.345(15)$ Å	$\beta = 90.0^\circ$

Data collection

Area	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²
Area (mm ²)	1000 mm ²

Refinement

Refinement on F^2	Primary structure: $C_{12}H_{14}N_4O_8$
Least-squares method	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2
Refinement on F^2	Refinement on F^2

Fractional coordinates (x, y, z) of non-hydrogen atoms (Occupancy of 1.00000)

Atom	x	y	z	Occupancy
N1	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
N2	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
N3	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
N4	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O1	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O2	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O3	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O4	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O5	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O6	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O7	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O8	0.1234(5)	0.1234(5)	0.1234(5)	1.00000
O9	0.1234(5)	0.1234(5)	0.1234(5)	1.00000

Crystal structure of C₁₃H₁₆N₂OSi — ban1007

Phillip Patrick Sharp, Martin G. Banwell and Anthony C. Willis*

(ban1007)

Crystal data

C ₁₃ H ₁₆ N ₂ OSi	$F(000) = 1040$
$M_r = 244.37$	$D_x = 1.186 \text{ Mg m}^{-3}$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 12.3949 (2) \text{ \AA}$	Cell parameters from 23806 reflections
$b = 12.5045 (3) \text{ \AA}$	$\theta = 2.6\text{--}27.5^\circ$
$c = 17.7115 (4) \text{ \AA}$	$\mu = 0.16 \text{ mm}^{-1}$
$\beta = 94.3358 (13)^\circ$	$T = 200 \text{ K}$
$V = 2737.29 (10) \text{ \AA}^3$	Block, Yellow
$Z = 8$	$0.43 \times 0.30 \times 0.17 \text{ mm}$

Data collection

Area diffractometer	2692 reflections with $I > 2.0\sigma(I)$
graphite	$R_{\text{int}} = 0.040$
φ and ω scans with CCD	$\theta_{\text{max}} = 27.5^\circ$, $\theta_{\text{min}} = 2.6^\circ$
Absorption correction: Integration via Gaussian method (Coppens, 1970) implemented in <i>maXus</i> (2000)	$h = -16 \rightarrow 16$
$T_{\text{min}} = 0.948$, $T_{\text{max}} = 0.977$	$k = -16 \rightarrow 16$
26370 measured reflections	$l = -22 \rightarrow 22$
3123 independent reflections	

Refinement

Refinement on F^2	Primary atom site location: Structure-invariant direct methods
Least-squares matrix: Full	Hydrogen site location: Inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.042$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.119$	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.07P)^2 + 2.09P]$, where $P = (\max(F_o^2, 0) + 2F_c^2)/3$
$S = 1.00$	$(\Delta/\sigma)_{\text{max}} = 0.011$
3123 reflections	$\Delta\rho_{\text{max}} = 0.30 \text{ e \AA}^{-3}$
157 parameters	$\Delta\rho_{\text{min}} = -0.36 \text{ e \AA}^{-3}$
0 restraints	

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.35416 (10)	0.29251 (10)	0.57029 (7)	0.0332
C2	0.42245 (11)	0.33577 (11)	0.62797 (8)	0.0322
C3	0.52457 (11)	0.29360 (11)	0.62496 (8)	0.0338
C4	0.51992 (11)	0.22317 (11)	0.56159 (8)	0.0319
C5	0.59427 (12)	0.16040 (12)	0.52497 (8)	0.0356
C6	0.55699 (13)	0.10778 (13)	0.45934 (9)	0.0409
C7	0.44810 (14)	0.11516 (13)	0.43378 (9)	0.0423
N8	0.37327 (10)	0.17131 (10)	0.46714 (7)	0.0378
C9	0.41282 (11)	0.22475 (11)	0.52913 (8)	0.0318

O10	0.69683 (8)	0.15822 (10)	0.55752 (7)	0.0448
C11	0.77517 (14)	0.09678 (14)	0.52016 (11)	0.0505
C12	0.38342 (11)	0.41524 (12)	0.67658 (8)	0.0342
C13	0.34983 (12)	0.48561 (13)	0.71504 (9)	0.0398
Si14	0.29907 (4)	0.59285 (4)	0.77459 (3)	0.0420
C15	0.3706 (2)	0.58047 (17)	0.87048 (11)	0.0649
C16	0.32764 (16)	0.72487 (14)	0.73310 (12)	0.0547
C17	0.15118 (16)	0.57102 (19)	0.77682 (14)	0.0677
H11	0.2884 (15)	0.3067 (15)	0.5628 (10)	0.0410*
H31	0.5835	0.3104	0.6596	0.0397*
H61	0.6020	0.0677	0.4326	0.0492*
H71	0.4247	0.0796	0.3892	0.0515*
H111	0.8438	0.1029	0.5503	0.0751*
H112	0.7543	0.0221	0.5177	0.0743*
H113	0.7837	0.1242	0.4693	0.0744*
H151	0.3349	0.6206	0.9058	0.0965*
H152	0.4457	0.6027	0.8679	0.0986*
H153	0.3713	0.5085	0.8885	0.0977*
H161	0.3091	0.7769	0.7667	0.0829*
H162	0.4023	0.7321	0.7286	0.0825*
H163	0.2913	0.7340	0.6846	0.0830*
H173	0.1225	0.6213	0.8109	0.1016*
H172	0.1361	0.4983	0.7918	0.1012*
H171	0.1166	0.5828	0.7236	0.1011*

Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0306 (6)	0.0337 (6)	0.0348 (6)	0.0030 (5)	−0.0004 (5)	−0.0030 (5)
C2	0.0338 (7)	0.0317 (7)	0.0312 (6)	−0.0007 (5)	0.0021 (5)	−0.0009 (5)
C3	0.0320 (7)	0.0347 (7)	0.0343 (7)	0.0005 (5)	0.0003 (5)	−0.0026 (6)
C4	0.0329 (7)	0.0300 (7)	0.0330 (7)	−0.0001 (5)	0.0033 (5)	0.0012 (5)
C5	0.0359 (7)	0.0325 (7)	0.0388 (7)	0.0026 (6)	0.0057 (6)	0.0019 (6)
C6	0.0459 (8)	0.0366 (8)	0.0412 (8)	0.0068 (6)	0.0099 (6)	−0.0045 (6)
C7	0.0506 (9)	0.0386 (8)	0.0372 (8)	0.0043 (7)	0.0002 (7)	−0.0085 (6)
N8	0.0405 (7)	0.0352 (6)	0.0367 (6)	0.0029 (5)	−0.0028 (5)	−0.0057 (5)
C9	0.0352 (7)	0.0285 (6)	0.0318 (6)	0.0010 (5)	0.0027 (5)	0.0003 (5)
O10	0.0321 (5)	0.0503 (7)	0.0524 (6)	0.0083 (5)	0.0046 (5)	−0.0058 (5)
C11	0.0395 (8)	0.0492 (10)	0.0644 (11)	0.0099 (7)	0.0157 (8)	−0.0009 (8)
C12	0.0325 (7)	0.0364 (7)	0.0333 (7)	0.0008 (5)	0.0001 (5)	−0.0006 (6)
C13	0.0388 (8)	0.0413 (8)	0.0391 (8)	0.0032 (6)	0.0024 (6)	−0.0052 (6)
Si14	0.0452 (3)	0.0370 (2)	0.0444 (3)	0.00502 (17)	0.00672 (19)	−0.00831 (18)
C15	0.0930 (16)	0.0532 (11)	0.0475 (10)	0.0169 (10)	−0.0009 (10)	−0.0107 (8)
C16	0.0575 (10)	0.0409 (9)	0.0650 (11)	0.0028 (8)	−0.0001 (9)	−0.0011 (8)
C17	0.0539 (11)	0.0610 (12)	0.0913 (15)	0.0008 (9)	0.0260 (11)	−0.0205 (11)

Geometric parameters ($\text{\AA}$, $^\circ$)

N1—C2	1.3864 (18)	C11—H111	0.973
N1—C9	1.3632 (18)	C11—H112	0.969
N1—H11	0.835 (19)	C11—H113	0.978
C2—C3	1.3760 (19)	C12—C13	1.206 (2)
C2—C12	1.4233 (19)	C13—Si14	1.8458 (16)
C3—C4	1.424 (2)	Si14—C15	1.862 (2)
C3—H31	0.941	Si14—C16	1.8520 (19)
C4—C5	1.406 (2)	Si14—C17	1.857 (2)

C4—C9	1.4064 (19)	C15—H151	0.939
C5—C6	1.384 (2)	C15—H152	0.976
C5—O10	1.3558 (18)	C15—H153	0.955
C6—C7	1.394 (2)	C16—H161	0.922
C6—H61	0.908	C16—H162	0.939
C7—N8	1.336 (2)	C16—H163	0.947
C7—H71	0.933	C17—H173	0.959
N8—C9	1.3457 (18)	C17—H172	0.969
O10—C11	1.4381 (19)	C17—H171	1.016
O10...C11 ⁱ	3.387 (2)	C5...C11 ⁱ	3.560 (2)
O10...O10 ⁱ	3.401 (2)	C5...C7 ^v	3.569 (2)
O10...C16 ⁱⁱ	3.497 (2)	C6...C7 ^v	3.373 (2)
N1...N8 ⁱⁱⁱ	2.882 (2)	C6...C6 ^v	3.412 (3)
N8...C15 ^{iv}	3.544 (2)		
C2—N1—C9	108.42 (12)	O10—C11—H113	111.1
C2—N1—H11	124.7 (13)	H111—C11—H113	109.1
C9—N1—H11	126.9 (13)	H112—C11—H113	110.1
N1—C2—C3	109.51 (12)	C2—C12—C13	177.08 (16)
N1—C2—C12	120.11 (12)	C12—C13—Si14	179.53 (14)
C3—C2—C12	130.30 (13)	C13—Si14—C15	107.54 (8)
C2—C3—C4	106.56 (12)	C13—Si14—C16	109.71 (8)
C2—C3—H31	124.1	C15—Si14—C16	110.11 (10)
C4—C3—H31	129.4	C13—Si14—C17	106.56 (8)
C3—C4—C5	136.05 (13)	C15—Si14—C17	111.79 (11)
C3—C4—C9	107.11 (12)	C16—Si14—C17	110.99 (10)
C5—C4—C9	116.78 (13)	Si14—C15—H151	110.3
C4—C5—C6	117.64 (13)	Si14—C15—H152	108.9
C4—C5—O10	116.18 (13)	H151—C15—H152	112.2
C6—C5—O10	126.17 (13)	Si14—C15—H153	112.0
C5—C6—C7	119.66 (14)	H151—C15—H153	105.9
C5—C6—H61	121.3	H152—C15—H153	107.5
C7—C6—H61	119.0	Si14—C16—H161	108.0
C6—C7—N8	125.36 (14)	Si14—C16—H162	109.8
C6—C7—H71	118.3	H161—C16—H162	106.4
N8—C7—H71	116.3	Si14—C16—H163	112.1
C7—N8—C9	113.55 (13)	H161—C16—H163	112.0
C4—C9—N1	108.38 (12)	H162—C16—H163	108.4
C4—C9—N8	126.94 (13)	Si14—C17—H173	109.3
N1—C9—N8	124.67 (13)	Si14—C17—H172	110.8
C5—O10—C11	117.32 (13)	H173—C17—H172	110.7
O10—C11—H111	107.4	Si14—C17—H171	107.9
O10—C11—H112	110.4	H173—C17—H171	109.8
H111—C11—H112	108.6	H172—C17—H171	108.3
O10—C5—C4—C3	4.4 (3)	C2—C3—C4—C5	176.0 (2)
O10—C5—C4—C9	−179.0 (1)	C2—C3—C4—C9	−0.8 (2)
O10—C5—C6—C7	178.2 (1)	C3—C2—N1—C9	−1.5 (2)
N1—C2—C3—C4	1.4 (2)	C3—C4—C5—C6	−175.0 (2)
N1—C9—N8—C7	175.9 (1)	C4—C3—C2—C12	−175.4 (1)
N1—C9—C4—C3	−0.1 (2)	C4—C5—O10—C11	−178.5 (1)
N1—C9—C4—C5	−177.6 (1)	C4—C5—C6—C7	−2.5 (2)
N8—C7—C6—C5	0.9 (3)	C4—C9—N8—C7	−2.5 (2)
N8—C9—N1—C2	−177.7 (1)	C6—C5—O10—C11	0.9 (2)
N8—C9—C4—C3	178.5 (1)	C6—C5—C4—C9	1.6 (2)
N8—C9—C4—C5	1.0 (2)	C6—C7—N8—C9	1.5 (2)

Crystal structure of $C_{30}H_{33}AuN_3OP$ — ban1121

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Abstract

The crystal structure of $C_{30}H_{33}AuN_3OP$ is reported.

Comment

The crystallographic asymmetric unit consists of one $C_{30}H_{33}AuN_3OP$ molecule.

Experimental

The compound was prepared by PPS and recrystallised from dichloromethane/methanol. The sample ID is 011ps-625.

Computing details

Data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-II* (Johnson 1976) in *TEXSAN* (MSC, 1992-1997).; software used to prepare material for publication: *CRYSTALS* (Betteridge *et al.*, 2003).

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(ban1121)

Crystal data

$C_{30}H_{33}AuN_3OP$

$M_r = 679.55$

Monoclinic, $P2_1/n$

$a = 13.3557(1) \text{ \AA}$

$b = 15.3193(2) \text{ \AA}$

$c = 14.7851(2) \text{ \AA}$

$\beta = 107.1923(8)^\circ$

$V = 2889.87(6) \text{ \AA}^3$

$Z = 4$

$F(000) = 1344$

$D_x = 1.562 \text{ Mg m}^{-3}$

Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$

Cell parameters from 46010 reflections

$\theta = 2.6\text{--}30^\circ$

$\mu = 5.17 \text{ mm}^{-1}$

$T = 200 \text{ K}$

Needle, Colourless

$0.39 \times 0.09 \times 0.08 \text{ mm}$

Data collection

Nonius KappaCCD
diffractometer

graphite

φ and ω scans with CCD

Absorption correction: Multi-scan

DENZO/SCALEPACK (Otwinowski & Minor, 1997)

$T_{\min} = 0.55$, $T_{\max} = 0.66$

82634 measured reflections

8437 independent reflections

6955 reflections with $I > 2.0\sigma(I)$

$R_{\text{int}} = 0.042$

$\theta_{\max} = 30.0^\circ$, $\theta_{\min} = 2.7^\circ$

$h = -18 \rightarrow 18$

$k = -21 \rightarrow 21$

$l = -20 \rightarrow 19$

Refinement

Refinement on F^2

Least-squares matrix: Full

$R[F^2 > 2\sigma(F^2)] = 0.025$

$wR(F^2) = 0.055$

$S = 0.99$

8436 reflections

334 parameters

0 restraints

Primary atom site location: Structure-invariant direct methods

Hydrogen site location: Inferred from neighbouring sites

H atoms treated by a mixture of independent and constrained refinement

Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.02P)^2 + 2.98P]$,

where $P = (\max(F_o^2, 0) + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.024$

$\Delta\rho_{\max} = 0.98 \text{ e \AA}^{-3}$

$\Delta\rho_{\min} = -1.10 \text{ e \AA}^{-3}$

Special details

Refinement. H atoms attached to C were added at calculated positions. H atoms attached to N were added at positions indicated in a difference electron density map. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularise their geometry (C—H in the range 0.93–0.98, N—H = 0.86 Å) and with $U_{\text{iso}}(\text{H})$ in the range 1.2–1.5 times U_{eq} of the parent atom, after which the positions were refined with riding constraints. The exceptions were the H's on nitrogen atoms where the coordinates were allowed to refine freely.

The largest peaks in the final difference electron density map are located randomly through the structure.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
Au11	0.744417 (7)	0.373000 (6)	0.373423 (7)	0.0314
P12	0.77030 (5)	0.25340 (5)	0.28992 (5)	0.0346
O36	0.95341 (16)	0.61429 (12)	0.96039 (14)	0.0425
N33	0.83253 (18)	0.61094 (14)	0.81408 (16)	0.0349
N35	0.8960 (2)	0.48437 (17)	0.8904 (2)	0.0548
N1	0.77362 (19)	0.87621 (13)	0.74786 (16)	0.0375
C2	0.7641 (2)	0.81494 (18)	0.68161 (19)	0.0377
C3	0.78549 (18)	0.72667 (16)	0.70043 (17)	0.0290
C4	0.81832 (17)	0.69950 (15)	0.79585 (16)	0.0263
C5	0.83072 (18)	0.76335 (16)	0.86518 (17)	0.0291
C6	0.80753 (19)	0.84856 (17)	0.83791 (18)	0.0323
C7	0.77293 (19)	0.66419 (17)	0.62617 (17)	0.0321
C8	0.76191 (19)	0.60579 (16)	0.56991 (17)	0.0304
C9	0.74683 (19)	0.53783 (16)	0.50666 (17)	0.0300
C10	0.73852 (19)	0.47613 (17)	0.45356 (17)	0.0320
C13	0.8357 (2)	0.2895 (2)	0.1989 (2)	0.0490
C14	0.9132 (3)	0.3634 (3)	0.2426 (3)	0.0683
C15	0.7483 (3)	0.3273 (3)	0.1166 (3)	0.0699
C16	0.8950 (3)	0.2189 (3)	0.1617 (3)	0.0710
C17	0.8484 (2)	0.1714 (2)	0.3775 (2)	0.0493
C18	0.9566 (3)	0.2106 (3)	0.4276 (3)	0.0696
C19	0.7881 (3)	0.1596 (3)	0.4508 (3)	0.0650
C20	0.8623 (3)	0.0813 (3)	0.3372 (3)	0.0752
C21	0.64919 (18)	0.19736 (18)	0.22545 (18)	0.0345
C22	0.55028 (18)	0.22359 (17)	0.23174 (18)	0.0331
C23	0.4630 (2)	0.1747 (2)	0.1820 (2)	0.0487
C24	0.4703 (2)	0.1035 (2)	0.1278 (2)	0.0536
C25	0.5661 (2)	0.0793 (2)	0.1200 (2)	0.0484
C26	0.6543 (2)	0.1255 (2)	0.1683 (2)	0.0455
C27	0.52788 (17)	0.29993 (17)	0.28495 (18)	0.0320
C28	0.5024 (2)	0.38011 (19)	0.2403 (2)	0.0412
C29	0.4697 (2)	0.4493 (2)	0.2858 (2)	0.0473
C30	0.4634 (2)	0.4384 (2)	0.3769 (2)	0.0479
C31	0.4875 (2)	0.3590 (2)	0.4214 (2)	0.0449
C32	0.51880 (19)	0.28952 (19)	0.37627 (19)	0.0373
C34	0.8981 (2)	0.57162 (17)	0.89398 (18)	0.0334
H21	0.7408	0.8364	0.6192	0.0452*
H51	0.8541	0.7487	0.9288	0.0348*
H61	0.8156	0.8899	0.8854	0.0387*
H141	0.9469	0.3834	0.1972	0.1026*
H142	0.9651	0.3417	0.2978	0.1026*
H143	0.8768	0.4124	0.2603	0.1025*
H151	0.7781	0.3582	0.0746	0.1045*
H152	0.7061	0.3685	0.1380	0.1045*
H153	0.7033	0.2818	0.0815	0.1050*
H161	0.9220	0.2445	0.1145	0.1066*
H162	0.9530	0.1971	0.2135	0.1067*
H163	0.8494	0.1715	0.1339	0.1063*
H181	0.9940	0.1728	0.4792	0.1037*

H182	0.9965	0.2157	0.3834	0.1038*
H183	0.9496	0.2680	0.4521	0.1036*
H191	0.8236	0.1173	0.4972	0.0967*
H192	0.7830	0.2147	0.4817	0.0972*
H193	0.7186	0.1375	0.4199	0.0963*
H201	0.9071	0.0458	0.3870	0.1125*
H202	0.8950	0.0879	0.2879	0.1126*
H203	0.7945	0.0529	0.3117	0.1128*
H231	0.3977	0.1924	0.1860	0.0581*
H241	0.4093	0.0717	0.0964	0.0638*
H251	0.5716	0.0324	0.0824	0.0577*
H261	0.7195	0.1076	0.1640	0.0551*
H281	0.5067	0.3883	0.1788	0.0482*
H291	0.4527	0.5022	0.2545	0.0573*
H301	0.4427	0.4853	0.4081	0.0567*
H311	0.4822	0.3508	0.4818	0.0539*
H321	0.5344	0.2354	0.4069	0.0448*
H331	0.812 (2)	0.580 (2)	0.772 (2)	0.0416*
H351	0.939 (3)	0.455 (3)	0.934 (3)	0.0659*
H352	0.853 (3)	0.458 (3)	0.845 (3)	0.0661*

Atomic displacement parameters ($\text{\AA}^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Au11	0.02910 (5)	0.03235 (5)	0.03344 (5)	−0.00122 (4)	0.01042 (4)	−0.01143 (4)
P12	0.0234 (3)	0.0394 (4)	0.0411 (4)	−0.0024 (2)	0.0099 (3)	−0.0189 (3)
O36	0.0521 (11)	0.0292 (10)	0.0341 (10)	−0.0010 (8)	−0.0062 (8)	−0.0014 (8)
N33	0.0441 (12)	0.0248 (11)	0.0284 (11)	−0.0014 (9)	−0.0004 (9)	−0.0044 (8)
N35	0.0705 (18)	0.0262 (12)	0.0468 (16)	−0.0065 (12)	−0.0150 (13)	0.0046 (11)
N1	0.0478 (12)	0.0253 (11)	0.0372 (12)	0.0035 (10)	0.0091 (9)	−0.0021 (9)
C2	0.0467 (15)	0.0307 (13)	0.0321 (13)	0.0065 (11)	0.0062 (11)	0.0019 (11)
C3	0.0296 (11)	0.0293 (12)	0.0269 (11)	0.0033 (9)	0.0066 (9)	−0.0027 (9)
C4	0.0246 (10)	0.0250 (11)	0.0286 (11)	−0.0006 (8)	0.0067 (8)	−0.0019 (9)
C5	0.0280 (11)	0.0324 (12)	0.0253 (11)	−0.0022 (9)	0.0053 (9)	−0.0037 (9)
C6	0.0316 (12)	0.0312 (12)	0.0336 (13)	−0.0005 (9)	0.0090 (10)	−0.0104 (10)
C7	0.0359 (12)	0.0302 (13)	0.0282 (12)	0.0046 (10)	0.0063 (10)	0.0000 (10)
C8	0.0349 (12)	0.0300 (12)	0.0248 (11)	0.0044 (9)	0.0064 (9)	0.0035 (9)
C9	0.0350 (12)	0.0280 (12)	0.0265 (11)	0.0043 (9)	0.0085 (9)	0.0000 (9)
C10	0.0361 (12)	0.0318 (13)	0.0275 (12)	0.0008 (10)	0.0084 (9)	0.0012 (10)
C13	0.0365 (14)	0.065 (2)	0.0538 (18)	−0.0152 (13)	0.0255 (13)	−0.0298 (15)
C14	0.059 (2)	0.080 (3)	0.080 (3)	−0.0353 (19)	0.0434 (19)	−0.037 (2)
C15	0.065 (2)	0.092 (3)	0.060 (2)	−0.010 (2)	0.0298 (19)	0.006 (2)
C16	0.056 (2)	0.090 (3)	0.081 (3)	−0.0149 (19)	0.0417 (19)	−0.048 (2)
C17	0.0352 (14)	0.0490 (18)	0.0564 (19)	0.0100 (12)	0.0024 (13)	−0.0190 (15)
C18	0.0398 (17)	0.086 (3)	0.069 (2)	0.0106 (17)	−0.0060 (15)	−0.023 (2)
C19	0.068 (2)	0.062 (2)	0.062 (2)	0.0155 (18)	0.0129 (18)	0.0080 (18)
C20	0.071 (2)	0.056 (2)	0.086 (3)	0.0243 (19)	0.003 (2)	−0.021 (2)
C21	0.0258 (11)	0.0379 (14)	0.0378 (14)	−0.0035 (10)	0.0063 (10)	−0.0125 (11)
C22	0.0261 (11)	0.0379 (14)	0.0337 (13)	−0.0018 (10)	0.0065 (9)	0.0009 (11)
C23	0.0253 (12)	0.0519 (18)	0.065 (2)	−0.0047 (12)	0.0067 (12)	−0.0102 (15)
C24	0.0394 (15)	0.0545 (19)	0.059 (2)	−0.0154 (13)	0.0023 (14)	−0.0166 (16)

C25	0.0443 (16)	0.0435 (17)	0.0507 (18)	−0.0093 (13)	0.0038 (13)	−0.0193 (14)
C26	0.0346 (13)	0.0480 (17)	0.0528 (17)	−0.0015 (12)	0.0113 (12)	−0.0225 (14)
C27	0.0210 (10)	0.0391 (14)	0.0354 (13)	0.0014 (9)	0.0073 (9)	−0.0001 (11)
C28	0.0402 (14)	0.0433 (16)	0.0438 (15)	0.0059 (12)	0.0181 (12)	0.0086 (12)
C29	0.0458 (16)	0.0391 (16)	0.0598 (19)	0.0115 (12)	0.0198 (14)	0.0077 (14)
C30	0.0393 (15)	0.0488 (18)	0.0595 (19)	0.0126 (13)	0.0205 (13)	−0.0066 (15)
C31	0.0365 (14)	0.061 (2)	0.0409 (15)	0.0080 (13)	0.0170 (12)	0.0004 (13)
C32	0.0289 (12)	0.0442 (16)	0.0384 (14)	0.0061 (10)	0.0092 (10)	0.0050 (11)
C34	0.0379 (13)	0.0278 (12)	0.0305 (12)	−0.0013 (10)	0.0038 (10)	0.0027 (10)

Geometric parameters (Å, °)

Au1—P12	2.2920 (6)	C16—H163	0.960
Au1—C10	1.990 (3)	C17—C18	1.537 (4)
P12—C13	1.891 (3)	C17—C19	1.540 (5)
P12—C17	1.883 (3)	C17—C20	1.536 (5)
P12—C21	1.830 (2)	C18—H181	0.970
O36—C34	1.228 (3)	C18—H182	0.960
N33—C4	1.385 (3)	C18—H183	0.966
N33—C34	1.383 (3)	C19—H191	0.961
N33—H331	0.76 (3)	C19—H192	0.971
N35—C34	1.338 (4)	C19—H193	0.967
N35—H351	0.86 (4)	C20—H201	0.967
N35—H352	0.85 (4)	C20—H202	0.961
N1—C2	1.335 (3)	C20—H203	0.973
N1—C6	1.342 (3)	C21—C22	1.410 (3)
C2—C3	1.393 (4)	C21—C26	1.402 (4)
C2—H21	0.942	C22—C23	1.397 (4)
C3—C4	1.411 (3)	C22—C27	1.488 (4)
C3—C7	1.429 (3)	C23—C24	1.375 (5)
C4—C5	1.391 (3)	C23—H231	0.931
C5—C6	1.374 (4)	C24—C25	1.369 (4)
C5—H51	0.927	C24—H241	0.944
C6—H61	0.928	C25—C26	1.378 (4)
C7—C8	1.201 (4)	C25—H251	0.924
C8—C9	1.374 (3)	C26—H261	0.933
C9—C10	1.213 (3)	C27—C28	1.388 (4)
C13—C14	1.541 (4)	C27—C32	1.400 (4)
C13—C15	1.529 (5)	C28—C29	1.393 (4)
C13—C16	1.535 (4)	C28—H281	0.937
C14—H141	0.962	C29—C30	1.385 (4)
C14—H142	0.961	C29—H291	0.926
C14—H143	0.972	C30—C31	1.375 (4)
C15—H151	0.956	C30—H301	0.938
C15—H152	0.961	C31—C32	1.384 (4)
C15—H153	0.965	C31—H311	0.925
C16—H161	0.958	C32—H321	0.938
C16—H162	0.973		
O36...N35 ⁱ	2.928 (3)	C8...C30 ^{iv}	3.396 (4)
O36...C32 ⁱⁱ	3.556 (4)	C8...C31 ^{iv}	3.414 (4)

N1...N35 ⁱⁱ	3.053 (3)	C9...C26 ^v	3.501 (4)
N35...C2 ⁱⁱⁱ	3.331 (4)	C9...C25 ^v	3.594 (4)
C6...C23 ^{iv}	3.555 (4)	C10...C26 ^v	3.472 (4)
C7...C31 ^{iv}	3.358 (4)	C10...C25 ^v	3.488 (4)
C7...C30 ^{iv}	3.514 (4)		
P12—Au11—C10	173.75 (7)	P12—C17—C20	116.0 (2)
Au11—P12—C13	108.93 (10)	C18—C17—C20	109.5 (3)
Au11—P12—C17	107.70 (10)	C19—C17—C20	108.4 (3)
C13—P12—C17	113.98 (15)	C17—C18—H181	109.7
Au11—P12—C21	113.87 (8)	C17—C18—H182	109.7
C13—P12—C21	106.83 (13)	H181—C18—H182	108.9
C17—P12—C21	105.66 (14)	C17—C18—H183	110.8
C4—N33—C34	127.5 (2)	H181—C18—H183	109.3
C4—N33—H331	116 (2)	H182—C18—H183	108.4
C34—N33—H331	115 (2)	C17—C19—H191	109.3
C34—N35—H351	120 (3)	C17—C19—H192	110.7
C34—N35—H352	121 (3)	H191—C19—H192	109.8
H351—N35—H352	119 (4)	C17—C19—H193	109.6
C2—N1—C6	115.9 (2)	H191—C19—H193	107.6
N1—C2—C3	124.5 (2)	H192—C19—H193	109.7
N1—C2—H21	113.9	C17—C20—H201	109.2
C3—C2—H21	121.6	C17—C20—H202	109.5
C2—C3—C4	118.1 (2)	H201—C20—H202	108.5
C2—C3—C7	121.8 (2)	C17—C20—H203	110.3
C4—C3—C7	120.1 (2)	H201—C20—H203	109.8
C3—C4—N33	117.9 (2)	H202—C20—H203	109.4
C3—C4—C5	117.6 (2)	P12—C21—C22	122.21 (19)
N33—C4—C5	124.5 (2)	P12—C21—C26	119.31 (19)
C4—C5—C6	119.0 (2)	C22—C21—C26	118.5 (2)
C4—C5—H51	120.6	C21—C22—C23	117.7 (2)
C6—C5—H51	120.4	C21—C22—C27	126.7 (2)
C5—C6—N1	124.9 (2)	C23—C22—C27	115.6 (2)
C5—C6—H61	117.5	C22—C23—C24	122.7 (3)
N1—C6—H61	117.7	C22—C23—H231	117.6
C3—C7—C8	173.8 (3)	C24—C23—H231	119.7
C7—C8—C9	178.1 (3)	C23—C24—C25	119.5 (3)
C8—C9—C10	176.6 (3)	C23—C24—H241	119.8
C9—C10—Au11	172.7 (2)	C25—C24—H241	120.7
P12—C13—C14	108.1 (2)	C24—C25—C26	119.6 (3)
P12—C13—C15	105.82 (19)	C24—C25—H251	120.2
C14—C13—C15	108.4 (3)	C26—C25—H251	120.2
P12—C13—C16	116.4 (3)	C21—C26—C25	122.0 (3)
C14—C13—C16	108.3 (3)	C21—C26—H261	119.0
C15—C13—C16	109.5 (3)	C25—C26—H261	119.1
C13—C14—H141	109.7	C22—C27—C28	120.2 (2)
C13—C14—H142	109.2	C22—C27—C32	120.6 (2)
H141—C14—H142	109.5	C28—C27—C32	118.7 (2)
C13—C14—H143	110.7	C27—C28—C29	120.8 (3)
H141—C14—H143	108.5	C27—C28—H281	120.2
H142—C14—H143	109.3	C29—C28—H281	119.0
C13—C15—H151	109.8	C28—C29—C30	119.7 (3)

C13—C15—H152	111.8	C28—C29—H291	119.3
H151—C15—H152	106.6	C30—C29—H291	121.0
C13—C15—H153	111.2	C29—C30—C31	119.9 (3)
H151—C15—H153	108.7	C29—C30—H301	119.8
H152—C15—H153	108.6	C31—C30—H301	120.3
C13—C16—H161	108.5	C30—C31—C32	120.8 (3)
C13—C16—H162	109.6	C30—C31—H311	120.4
H161—C16—H162	109.3	C32—C31—H311	118.8
C13—C16—H163	110.9	C27—C32—C31	120.1 (3)
H161—C16—H163	109.1	C27—C32—H321	119.8
H162—C16—H163	109.4	C31—C32—H321	120.1
P12—C17—C18	108.7 (3)	N33—C34—N35	113.6 (2)
P12—C17—C19	105.3 (2)	N33—C34—O36	122.0 (2)
C18—C17—C19	108.6 (3)	N35—C34—O36	124.4 (2)
Au11—P12—C13—C14	36.3 (2)	C14—C13—P12—C17	−84.0 (2)
Au11—P12—C13—C15	−79.6 (2)	C14—C13—P12—C21	159.7 (2)
Au11—P12—C13—C16	158.4 (2)	C15—C13—P12—C17	160.1 (2)
Au11—P12—C17—C18	−63.7 (3)	C15—C13—P12—C21	43.8 (3)
Au11—P12—C17—C19	52.5 (2)	C16—C13—P12—C17	38.1 (2)
Au11—P12—C17—C20	172.4 (2)	C16—C13—P12—C21	−78.2 (2)
Au11—P12—C21—C22	−3.3 (3)	C17—P12—C21—C22	114.7 (2)
Au11—P12—C21—C26	177.2 (2)	C17—P12—C21—C26	−64.8 (3)
P12—C21—C22—C23	−178.0 (2)	C18—C17—P12—C21	174.2 (2)
P12—C21—C22—C27	3.2 (4)	C19—C17—P12—C21	−69.5 (2)
P12—C21—C26—C25	178.3 (2)	C20—C17—P12—C21	50.3 (3)
O36—C34—N33—C4	−0.1 (5)	C21—C22—C23—C24	−0.3 (4)
N1—C2—C3—C4	0.8 (4)	C21—C22—C27—C28	91.9 (3)
N1—C2—C3—C7	179.5 (3)	C21—C22—C27—C32	−96.4 (3)
N1—C6—C5—C4	−0.4 (4)	C21—C26—C25—C24	−0.2 (5)
N33—C4—C3—C2	175.6 (2)	C22—C21—C26—C25	−1.2 (4)
N33—C4—C3—C7	−3.1 (4)	C22—C23—C24—C25	−1.2 (5)
N33—C4—C5—C6	−175.7 (2)	C22—C27—C28—C29	172.6 (2)
N35—C34—N33—C4	−179.1 (3)	C22—C27—C32—C31	−173.4 (2)
C2—N1—C6—C5	−1.1 (4)	C23—C22—C21—C26	1.5 (4)
C2—C3—C4—C5	−2.2 (4)	C23—C22—C27—C28	−86.9 (3)
C3—C2—N1—C6	0.8 (4)	C23—C22—C27—C32	84.8 (3)
C3—C4—N33—C34	153.7 (3)	C23—C24—C25—C26	1.4 (4)
C3—C4—C5—C6	2.0 (4)	C24—C23—C22—C27	178.5 (3)
C5—C4—N33—C34	−28.6 (4)	C26—C21—C22—C27	−177.2 (3)
C5—C4—C3—C7	179.1 (2)	C27—C28—C29—C30	0.6 (4)
C13—P12—C17—C18	57.3 (3)	C27—C32—C31—C30	1.0 (4)
C13—P12—C17—C19	173.5 (2)	C28—C27—C32—C31	−1.6 (3)
C13—P12—C17—C20	−66.6 (3)	C28—C29—C30—C31	−1.2 (4)
C13—P12—C21—C22	−123.6 (2)	C29—C28—C27—C32	0.8 (4)
C13—P12—C21—C26	56.9 (3)	C29—C30—C31—C32	0.4 (4)

Symmetry codes: (i) $-x+2, -y+1, -z+2$; (ii) $-x+3/2, y+1/2, -z+3/2$; (iii) $-x+3/2, y-1/2, -z+3/2$; (iv) $-x+1, -y+1, -z+1$; (v) $-x+3/2, y+1/2, -z+1/2$.

Hydrogen-bond geometry (Å, °)

<i>D</i> —H··· <i>A</i>	<i>D</i> —H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> —H··· <i>A</i>
N35—H351···O36 ⁱ	0.86 (4)	2.07 (4)	2.928 (4)	178 (4)
N35—H352···N1 ⁱⁱⁱ	0.85 (4)	2.22 (4)	3.052 (4)	167 (4)

Symmetry codes: (i) $-x+2, -y+1, -z+2$; (iii) $-x+3/2, y-1/2, -z+3/2$.