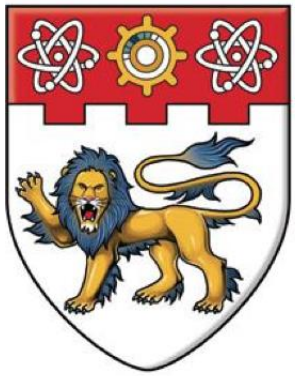

NANYANG TECHNOLOGICAL UNIVERSITY

ACTIVATION OF ALKYNES WITH $[Cp^*MCl_2]_2$ (M=Rh or Ir) TOWARDS HYDROAMINATION REACTIONS

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School of Physical and Mathematical Sciences
2014

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2014

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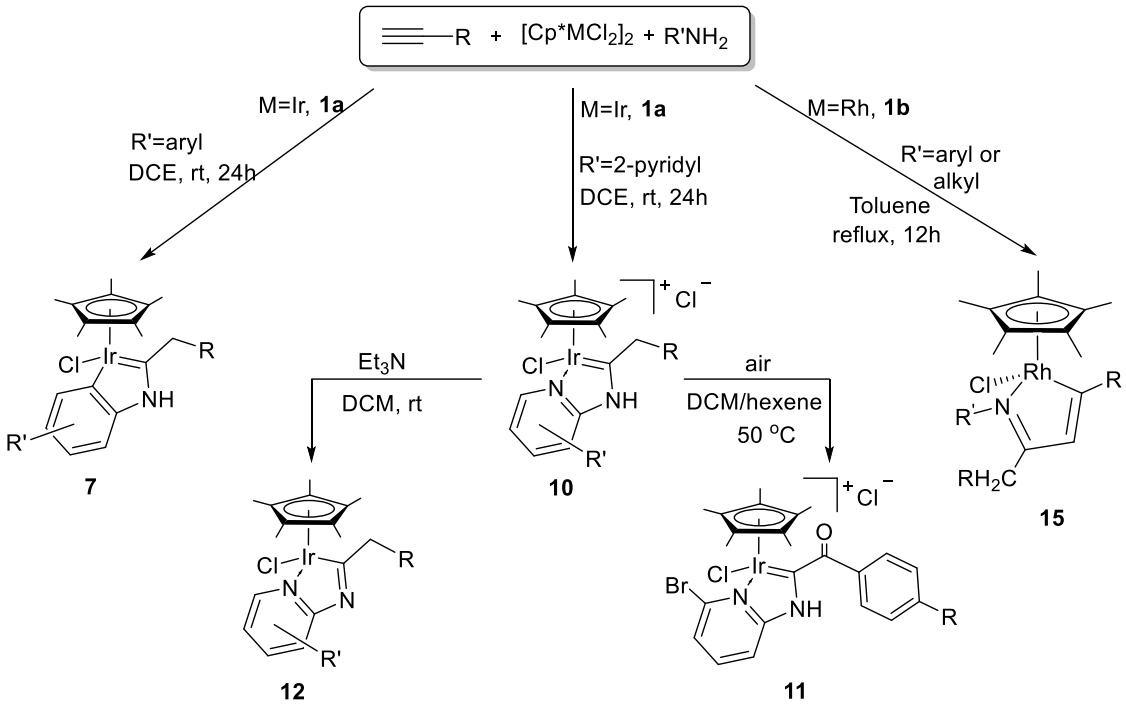
Table of Contents

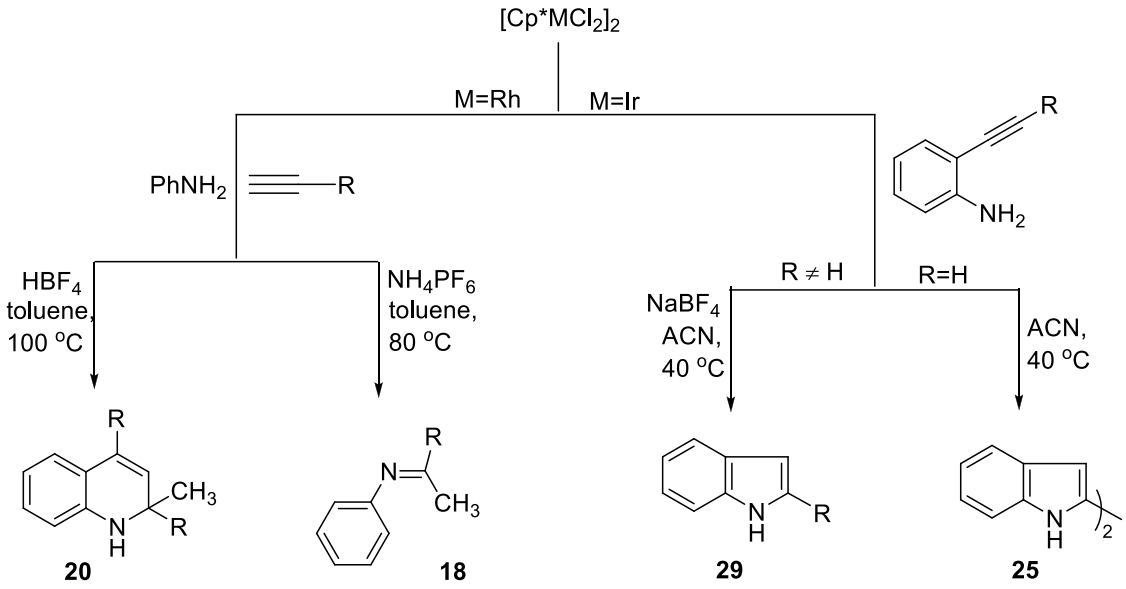
Summary

The activation of alkynes towards hydroamination reactions with $[Cp^*MCl_2]_2$ M=Ir (**1a**) or Rh (**1b**) has been investigated.

The first half of the thesis describes the stoichiometric hydroamination reactions of **1a** and **1b** with terminal alkynes and amines. In particular, a series of orthometallated amino-carbene complexes $Cp^*Ir(Cl)[=C(CH_2R)(NHC_6H_3R')]$, **7**, and pyridyl N-coordinated, cationic amino-carbenes $Cp^*Ir(Cl)[=C)(CH_2R)(NHNC_5H_3R')]$, **10**, have been synthesized from the reaction of **1a** with terminal alkynes and anilines or 2-aminopyridines, respectively. Aerial oxidation of the benzylic group α to the carbene carbon in **10** can occur to afford cationic keto-carbenes $Cp^*(Cl)[Ir=C(COPh)NHPy]Cl$, **11**. Similarly, **1b** reacts to give a range of rhodapyrrole derivatives $Cp^*Rh(Cl)[N(R')=C(CH_2R)CH=CR]$, **15**. The reaction pathways to **10**, **11** and **15** were investigated experimentally and computationally.



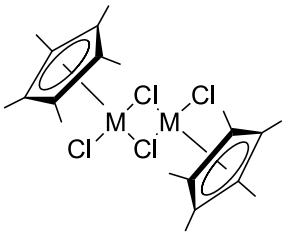
The second half of this thesis describes alkyne hydroamination reactions catalysed by **1a** and **1b**. In particular, **1b** catalyses the reaction of terminal alkynes and anilines in the presence of NH_4PF_6 or HBF_4 to afford ketimines **18** or 1,2-dihydroquinolines **20**, respectively. With **1a** as catalyst, the intramolecular hydroamination reaction of various 2-alkynylanilines with terminal and internal alkyne moieties afforded 2,2'-biindoles **25** or indoles **29**, respectively. The reaction pathways have also been studied experimentally and computationally.



Compound numbering scheme

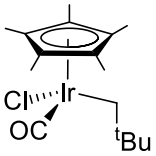
Formula **Structure**

$[Cp^*IrCl_2]_2$, **1a**
$[Cp^*RhCl_2]_2$, **1b**



M=Ir (**1a**), Rh (**1b**)

$[Cp^*Ir(Cl)(CO)(CH_2{}^tBu)]$ (**2**)

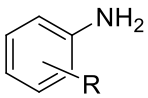


2

$HC{\equiv}C\text{-}C(CH_3)_3$ (**3a**)
$HC{\equiv}C\text{-}(CH_2)_2CH_3$ (**3b**)
$HC{\equiv}C\text{-}(CH_2)_3CH_3$ (**3c**)
$HC{\equiv}C\text{-}(CH_2)_4CH_3$ (**3d**)
$HC{\equiv}C\text{-}(CH_2)_5CH_3$ (**3e**)
$HC{\equiv}C\text{-}(CH_2)_7CH_3$ (**3f**)
$HC{\equiv}C\text{-}(CH_2)_2Ph$ (**3g**)
$HC{\equiv}C\text{-}C_{10}H_8$ (**3h**)
$HC{\equiv}C\text{-}C_6H_5$ (**3i**)
$HC{\equiv}C\text{-}C_6H_4\text{-}2\text{-}CH_3$ (**3j**)
$HC{\equiv}C\text{-}C_6H_3\text{-}2\text{-}CH_3\text{-}4\text{-}OCH_3$ (**3jt**)
$HC{\equiv}C\text{-}C_6H_4\text{-}3\text{-}CH_3$ (**3k**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}CH_3$ (**3l**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}(CH_2)_3CH_3$ (**3m**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}C(CH_3)_3$ (**3n**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}(CH_2)_4CH_3$ (**3o**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}CH_2OH$ (**3p**)
$HC{\equiv}C\text{-}C_6H_4\text{-}3\text{-}OH$ (**3q**)
$HC{\equiv}C\text{-}C_6H_4\text{-}2\text{-}OCH_3$ (**3r**)
$HC{\equiv}C\text{-}C_6H_4\text{-}3\text{-}OCH_3$ (**3s**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}OCH_3$ (**3t**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}OPh$ (**3u**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}Br$ (**3v**)
$HC{\equiv}C\text{-}C_6H_4\text{-}3\text{-}Cl$ (**3w**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}Cl$ (**3x**)
$HC{\equiv}C\text{-}C_6H_4\text{-}3\text{-}F$ (**3y**)
$HC{\equiv}C\text{-}C_6H_4\text{-}4\text{-}F$ (**3z)**

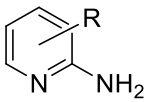
3

C_6H_5-NH_2 (**4a**)
CH_3-*3*-C_6H_4-NH_2 (**4b**)
$(CH_3)_2$-*3,5*-C_6H_3-NH_2 (**4c**)
CH_3-*4*-C_6H_4-NH_2 (**4d**)
Br-*3*-CH_3-*4*-C_6H_3-NH_2 (**4e**)
CH_3O-*2*-C_6H_4-NH_2 (**4f**)
CH_3O-*3*-C_6H_4-NH_2 (**4g**)
$(CH_3O)_2$-*3,5*-C_6H_4-NH_2 (**4h**)
CH_3O-*4*-C_6H_4-NH_2 (**4i**)
Br-*2*-C_6H_4-NH_2 (**4j**)
Br-*4*-C_6H_4-NH_2 (**4k**)
Cl-*2*-C_6H_4-NH_2 (**4l**)
Cl-*3*-C_6H_4-NH_2 (**4m**)
Cl-*4*-C_6H_4-NH_2 (**4n**)
NO_2-*3*-C_6H_4-NH_2 (**4o**)
NO_2-*4*-C_6H_4-NH_2 (**4p**)
$C_6H_5NHCH_3$ (**4q**)
$C_6H_5CH_2NH_2$ (**4r**)
$CH_3(CH_2)_3CH_2NH_2$ (**4s**)
$CH_3(CH_2)_6CH_2NH_2$ (**4t**)
C_2H_5O-*3*-C_6H_4-NH_2 (**4u**)
$(CH_3)_2CHO$-*3*-C_6H_4-NH_2 (**4v**)
$C_6H_{13}O$-*3*-C_6H_4-NH_2 (**4w**)
$PhCH_2O$-*3*-C_6H_4-NH_2 (**4x**)



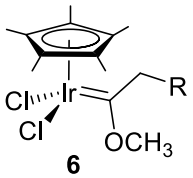
4

C_5H_4N-NH_2 (**5a**)
Br-*5*-C_5H_4N-NH_2 (**5b**)
Br-*6*-C_5H_4N-NH_2 (**5c**)
CH_3-*6*-C_5H_4N-NH_2 (**5d**)



5

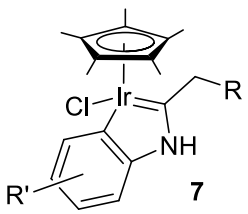
[Cp*Ir(=C(NHC_6H_4R')($CH_2{}^tBu$)Cl_2] (**6a**)
[Cp*Ir(=C(NHC_6H_4R')(CH_2Ph)Cl_2] (**6b**)



6

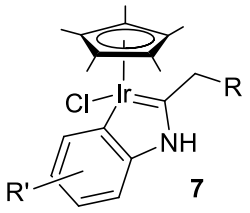
R=^{t}Bu (**6a**), Ph (**6b**)

R	**R'**
^{t}Butyl	H (**7a**)
^{t}Butyl	*3,5*-$(CH_3)_2$ (**7b**)
^{t}Butyl	*4*-CH_3 (**7c**)
^{t}Butyl	*3*-Br-*4*-CH_3 (**7d**)
^{t}Butyl	*2*-OCH_3 (**7e**)
^{t}Butyl	*4*-OCH_3 (**7f**)
^{t}Butyl	*2*-Br (**7g**)
^{t}Butyl	*2*-Cl (**7h**)
^{t}Butyl	*4*-Cl (**7i**)



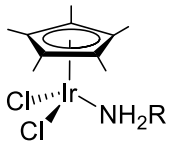
7

R	**R'**
^{t}Butyl	*4*-NO_2 (**7j**)
^{n}Butyl	H (**7k**)
^{n}Hexyl	H (**7l**)
^{n}Octyl	H (**7m**)
$PhCH_2CH_2$-	H (**7n**)
Ph	H (**7o**)
Ph	*4*-CH_3 (**7p**)
Ph	*4*-OCH_3 (**7q**)
Ph	*4*-Cl (**7r**)
Ph	*4*-NO_2 (**7s**)
4-$CH_3OC_6H_4$	H (**7t**)



7

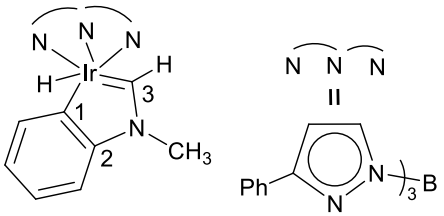
[$Cp^*IrCl_2(H_2NC_6H_5)$] (**8a**)
[$Cp^*IrCl_2(H_2NC_6H_4$-*4*-$CH_3)$] (**8c**)



8

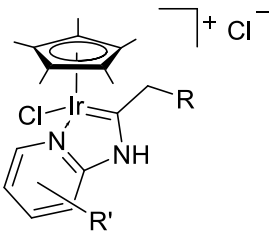
R=Ph (**8a**), *p*-tolyl (**8c**)

Tp^{Ph}-Ir(H)(=CHNMePh) (**9**)
Tp^{Ph}=hydridotris(3-phenypyrazole-1-yl)borate]



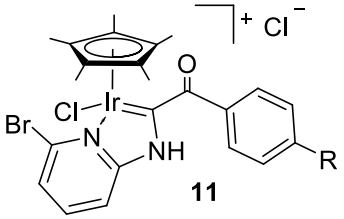
9

R	**R'**
tBu	H (**10a**)
tBu	*5*-Br (**10b**)
tBu	*6*-Br (**10c**)
tBu	*6*-CH_3 (**10d**)
Ph	*6*-Br (**10e**)
CH_3-*4*-C_6H_4	*6*-Br (**10f**)
Br-*4*-C_6H_4	*6*-Br (**10g**)



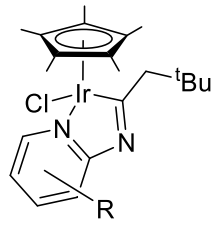
10

R
H (**11e**)
CH_3 (**11f**)
Br (**11g**)



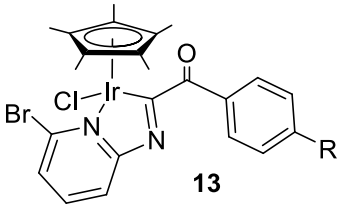
11

R
H (**12a**)
5-Br (**12b**)
6-Br (**12c**)



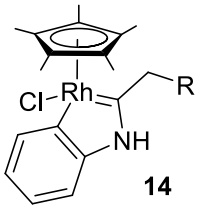
12

R
H (**13e**)
CH_3 (**13f**)
Br (**13g**)



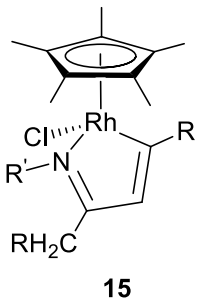
13

R
Ph (**14**)



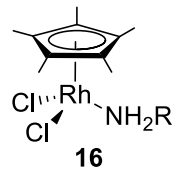
14

R	**R'**
Ph	Ph (**15a**)
Ph	*4*-$CH_3C_6H_4$ (**15b**)
Ph	*4*-$CH_3OC_6H_4$ (**15c**)
Ph	*4*-BrC_6H_4 (**15d**)
Ph	*4*-ClC_6H_4 (**15e**)
Ph	CH_2Ph (**15f**)
Ph	C_5H_{11} (**15g**)
3-$CH_3C_6H_4$	Ph (**15h**)
4-$CH_3C_6H_4$	Ph (**15i**)
4-$CH_3OC_6H_4$	Ph (**15j**)
4-BrC_6H_4	Ph (**15k**)
4-ClC_6H_4	Ph (**15l**)
3-$CH_3C_6H_4$	*4*-$CH_3OC_6H_4$ (**15m**)
4-$CH_3C_6H_4$	*4*-$CH_3OC_6H_4$ (**15n**)
4-$CH_3OC_6H_4$	*4*-$CH_3OC_6H_4$ (**15o**)



15

$[Cp^*RhCl_2(H_2NC_6H_5)]$ (**16**)



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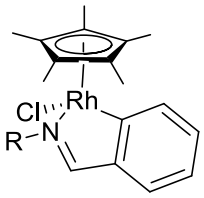
[Cp*RhCl{C_6H_4-*2*-C(H)=N$(CH_2)_2OCH_3$-κC,N}] (**17a**)
[Cp*RhCl{C_6H_4-*2*-C(H)=NPh-κC,N}] (**17b**)



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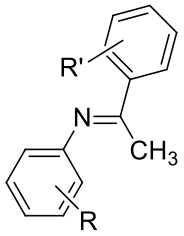
R	**R'**
H	H (**18a**)
H	*4*-CH_3 (**18b**)
H	*4*-OCH_3 (**18c**)
H	*4*-Cl (**18d**)
4-CH_3	H (**18e**)
4-OCH_3	H (**18f**)
4-OCH_3	*3*-CH_3 (**18g**)
4-OCH_3	*4*-CH_3 (**18h**)
4-OCH_3	*4*-OCH_3 (**18i**)
4-OCH_3	*4*-Cl (**18j**)
3-OCH_3	Ph (**18k**)



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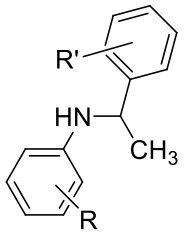
R	**R'**
H	$C_{10}H_7$ (**19a**)
H	*2*-CH_3 (**19b**)
H	*2*-CH_3,*4*-OCH_3 (**19c**)
H	*3*-CH_3 (**19d**)
H	*4*-^{t}Bu (**19e**)
H	*4*-CH_2OH (**19f**)
H	*2*-OCH_3 (**19g**)
H	*3*-OCH_3 (**19h**)
H	*4*-Br (**19i**)
H	*3*-Cl (**19j**)
H	*3*-F (**19k**)
H	*4*-F (**19l**)
3-OCH_3	H (**19m**)
3,5-$(OCH_3)_2$	H (**19n**)
4-OCH_3	H (**19o**)
4-Br	H (**19p**)
4-Cl	H (**19q**)
4-OCH_3	*2*-OCH_3 (**19r**)
4-OCH_3	*3*-OCH_3 (**19s**)



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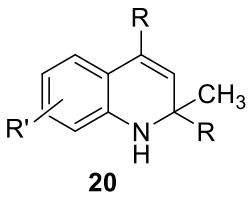
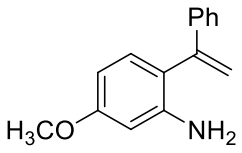
R	**R'**
C_6H_5	*3*-OCH_3 (**20a**)
H_3C-*3*-C_6H_4	*3*-OCH_3 (**20b**)
H_3C-*4*-C_6H_4	*3*-OCH_3 (**20c**)
$CH_3(CH_2)_3$-*4*-C_6H_4	*3*-OCH_3 (**20d**)
$(CH_3)_3C$-*4*-C_6H_4	*3*-OCH_3 (**20e**)
$CH_3(CH_2)_4$-*4*-C_6H_4	*3*-OCH_3 (**20f**)
$HOCH_2$-*4*-C_6H_4	*3*-OCH_3 (**20g**)
HO-*3*-C_6H_4	*3*-OCH_3 (**20h**)
H_3CO-*4*-C_6H_4	*3*-OCH_3 (**20i**)
PhO-*4*-C_6H_4	*3*-OCH_3 (**20j**)
Br-*4*-C_6H_4	*3*-OCH_3 (**20k**)
Cl-*3*-C_6H_4	*3*-OCH_3 (**20l**)
Cl-*4*-C_6H_4	*3*-OCH_3 (**20m**)
F-*4*-C_6H_4	*3*-OCH_3 (**20n**)
-$(CH_2)_2CH_3$	*3*-OCH_3 (**20o**)
-$(CH_2)_4CH_3$	*3*-OCH_3 (**20p**)
-$(CH_2)_5CH_3$	*3*-OCH_3 (**20q**)
-$(CH_2)_7CH_3$	*3*-OCH_3 (**20r**)
-$(CH_2)_2$Ph	*3*-OCH_3 (**20s**)
C_6H_5	*3*-OCH_2CH_3 (**20t**)
C_6H_5	*3*-$OCH(CH_3)_2$ (**20u**)
C_6H_5	*3*-$O(CH_2)_5CH_3$ (**20v**)
C_6H_5	*3*-$OCH_2C_6H_5$ (**20w**)
C_6H_5	*3,5*-$(OCH_3)_2$ (**20x**)
-$(CH_2)_3CH_3$	H (**20y**)
-$(CH_2)_3CH_3$	*3*-CH_3 (**20z**)



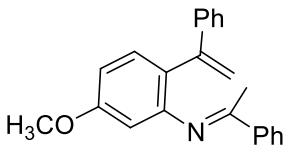
20

$C_{15}H_{15}NO$ (**21**)



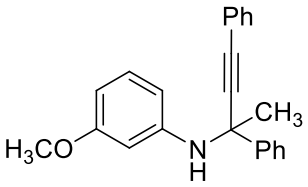
21

$C_{23}H_{21}NO$ (**22**)



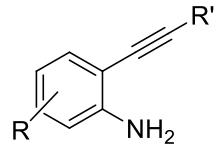
22

$C_{23}H_{21}NO$ (**23**)



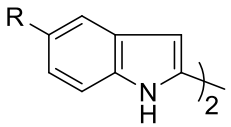
23

R	**R'**
4-H	H (**24a**)
4-CH_3	H (**24b**)
4-$C(CH_3)_3$	H (**24c**)
4-Br	H (**24d**)
4-Cl	H (**24e**)
4-NO_2	H (**24f**)
4-CN	H (**24g**)
4-$COOCH_3$	H (**24h**)
4-$COOC_2H_5$	H (**24i**)
4-H	Ph (**24j**)
4-CH_3	Ph (**24k**)
4-$C(CH_3)_3$	Ph (**24l**)
4-Cl	Ph (**24m**)
4-NO_2	Ph (**24n**)
4-$COOC_2H_5$	Ph (**24o**)
4-$COOC_2H_5$-*6*-C_2Ph	Ph (**24p**)
4-H	^{n}Bu-*4*-Ph (**24q**)
4-H	Cl-*4*-Ph (**24r**)
4-H	^{n}Bu (**24s**)



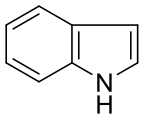
24

R
H (**25a**)
CH_3 (**25b**)
$C(CH_3)_3$ (**25c**)
Br (**25d**)
Cl (**25e**)
NO_2 (**25f**)
CN (**25g**)
$COOCH_3$ (**25h**)
$COOC_2H_5$ (**25i**)



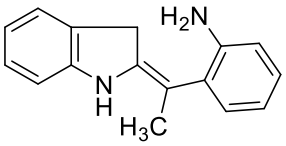
25

C_8H_7N (**26**)



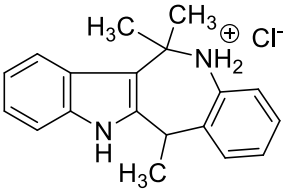
26

$C_{16}H_{16}N_2$ (**27**)



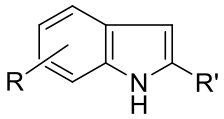
27

$C_{19}H_{21}N_2Cl$ (**28**)



28

R	**R'**
4-H	Ph (**29a**)
4-CH_3	Ph (**29b**)
4-$C(CH_3)_3$	Ph (**29c**)
4-Cl	Ph (**29d**)
4-NO_2	Ph (**29e**)
4-$COOC_2H_5$	Ph (**29f**)
4-$COOC_2H_5$-*6*-C_2Ph	Ph (**29g**)
4-H	^{n}Bu-*4*-Ph (**29h**)
4-H	Cl-*4*-Ph (**29i**)
4-H	^{n}Bu (**29j**)



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List of Abbreviations

Standard abbreviations and IUPAC nomenclature are used throughout this thesis. Less common usages are as follows:

Cp	cyclopentadiene
Cp*	pentamethylcyclopentadiene
acac	acetylacetonate
DCM	dichloromethane
DCE	1,2-dichloroethane
Hex	hexane
ACN	acetonitrile
TLC	thin layer chromatography
HCl	hydrochloric acid
DFT	density functional theory
h	hour
i.e	this is (latin id est)

Infrared (IR) spectroscopy

ν_{CO}	stretching frequency in the carbonyl region
vw	very weak
w	weak
m	medium
s	strong
vs	very strong
sh	shoulder
br	broad

Nuclear Magnetic Resonance (NMR) Spectroscopy

δ	chemical shift
J	coupling constant
s	singlet
d	doublet
t	triplet
q	quartet
m	multiplet
br	broad
bs	broad singlet
ppm	parts per million
DEPT	distortionless enhancement by polarization transfer

Mass Spectrometry

GC	gas chromatography
ESI	electrospray ionization
FAB	fast atom bombardment
m/z	mass to charge ratio
HRMS	high resolution mass spectroscopy

Publications

1. Kumaran, E.; Sridevi, V. S.; Leong, W. K. Orthometallated Amino-carbene Derivatives of Iridium via Anilines and Terminal alkynes, *Organometallics*, **2010**, *29*, 6417-6421.
2. Kumaran, E.; Leong, W. K. Rhodium (III)-catalysed Hydroamination of Aromatic Terminal Alkynes with Anilines, *Organometallics*, **2012**, *31*, 1068-1072.
3. Kumaran, E.; Leong, W. K. The reaction of $[Cp^*RhCl_2]_2$, Aniline, and a Terminal Alkyne: Formation of Cyclometallated Rhodium(III) Complexes, *Organometallics*, **2012**, *31*, 4849-4853.
4. Kumaran, E.; Sonia How, K. T.; Ganguly, R.; Li, Y.; Leong, W. K. Synthesis and Reactivity of Cationic Iridium Amino-Carbenes Derived from Terminal Alkynes and 2-Aminopyridines, *Organometallics*, **2013**, *32*, 4149-4152.
5. Kumaran, E.; Fan, W, Y.; Leong, W. K. $[Cp^*IrCl_2]_2$ catalysed Formation of 2,2'-Biindoles From 2-Ethynylanilines, *Org. Lett*. **2014**, *16*, 1342-1345.

Chapter 1: Activation of Alkynes by Transition Metals

1.1 Activation of Alkynes

Activation of the carbon-carbon triple bond (C≡C) of alkynes is one of the most attractive and fascinating subjects for chemists because the coordination of the alkyne to a metal centre renders it susceptible for further transformations, such as C-C,[1] C-N,[2] C-O,[3] and other bond formation.[4] Inactivated carbon-carbon multiple bonds are generally unreactive towards nucleophiles because of the high electrostatic repulsion between the highly electron-rich π-orbital and heteroatom of nucleophiles. The use of transition metal catalysts enables the addition of nucleophiles to these carbon-carbon multiple bonds,[5] and the activation of the C≡C triple bond towards nucleophilic attack can be performed by metals with high Lewis acidity (alkyne activation). The electronic properties of the alkyne, i.e., the presence of electron-donating or electron-withdrawing substituents, the steric bulk of the substituents on the alkyne, and of course, the nature of the metal complex, are also expected to play an important role in the alkyne activation.

Alkynes can react with transition metals in several ways (Figure 1.1) for further transformation: (i) both internal and terminal alkynes can coordinate to yield π-alkyne complexes **I**; (ii) terminal alkynes frequently undergo C-H activation to yield alkynyl complexes **II**; and (iii) the hydrido-alkynyl complexes **II**, can undergo rapid hydride transfer to afford metal vinylidene complexes **III**, which can also be obtained directly from the rearrangement of π-coordinated terminal alkynes.

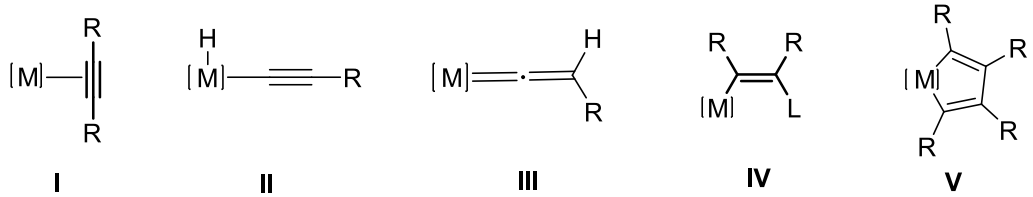
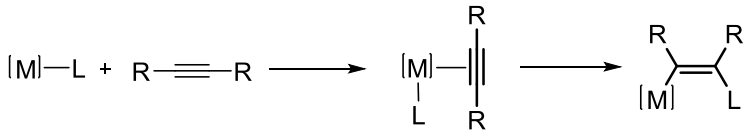


Figure 1.1. Five common structures from the reaction of alkynes with a metal.

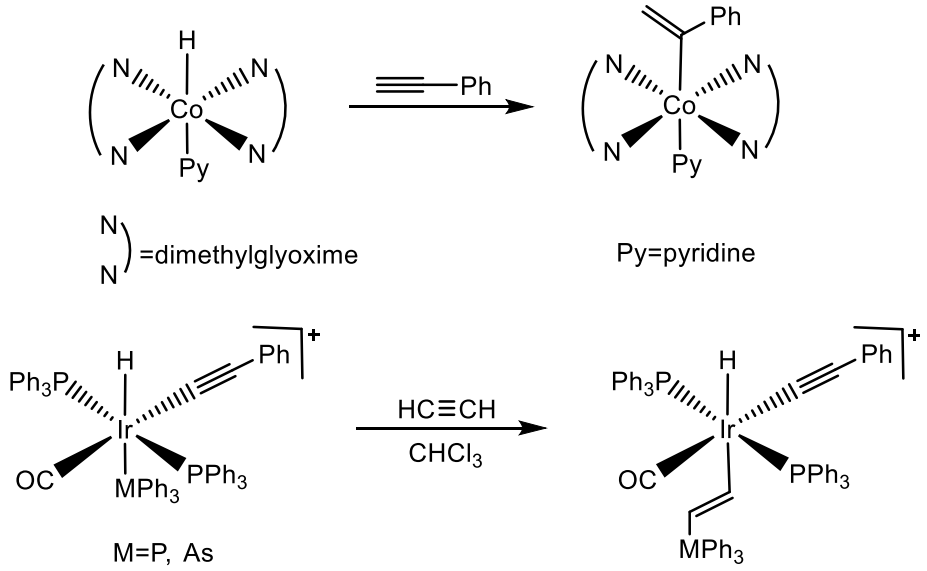
1.2 π-alkyne complexes

In the π-alkyne adducts, donation of the π electrons of the alkyne to the metal center assists further rearrangement or reaction. These complexes can undergo an intramolecular insertion reaction to afford metal-alkenyl complexes **IV** or metallacyclopentadienes **V**. The metal-alkenyl complexes are typically formed via *1,2*-insertion of M-L bond into the π-coordinated alkyne ligand (Scheme 1.1).



Scheme 1.1

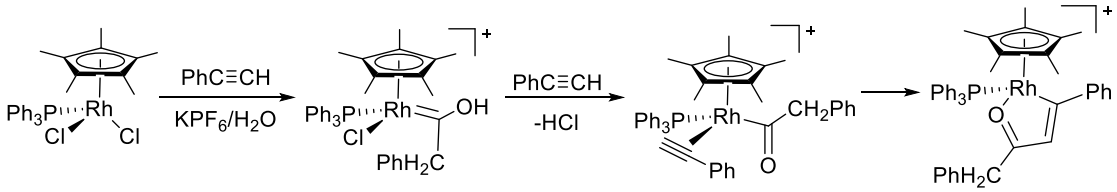
A vast number of M-L bonds are found to undergo this insertion reaction; the ligand **L** includes C=C=CR'$_2$,[6] C≡C-R',[7] H,[8] Cl,[9] SiR'$_3$,[10] NR'$_3$,[11] PR'$_3$,[12] and AsR'$_3$.[12b,c] The formation of the transition metal-alkenyl complexes that have been isolated are shown in Scheme 1.2.



Scheme 1.2

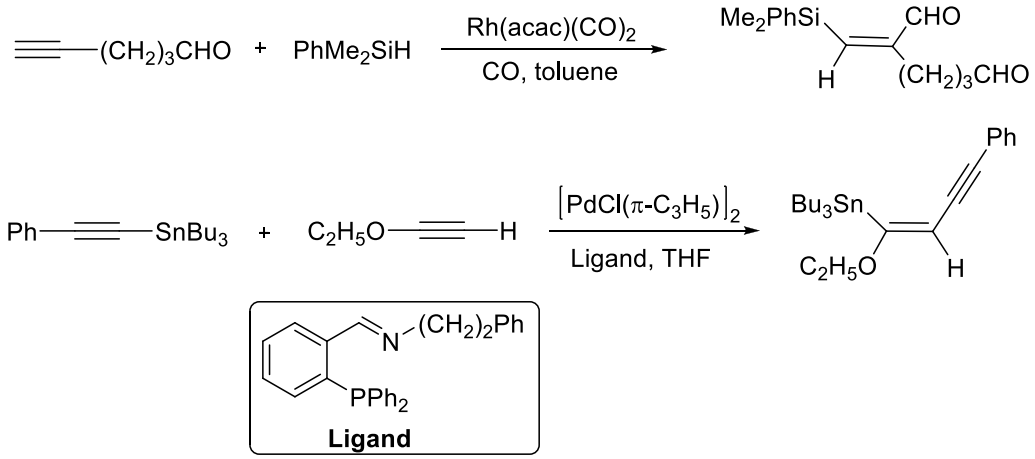
Interestingly, it has also been found that the M-COR bond can undergo migratory insertion reaction under certain conditions.[13] Using this procedure, some

alkenyl ketone complexes have been prepared and the proposed reaction pathway involved acyl migration (Scheme 1.3).[13]



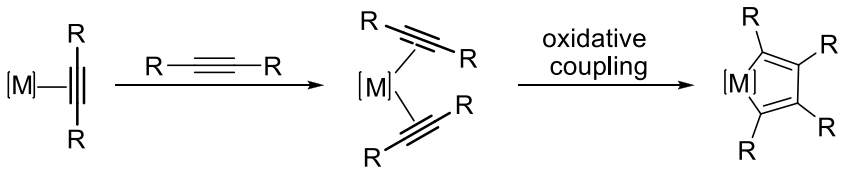
Scheme 1.3

Alkenyl complexes can undergo further reactions such as reductive elimination or protolytic demetallation leading to many useful catalytic organic reactions, such as hydrothiolation,[14] hydrosilylation,[15] hydroamination,[2] hydrostannylation,[16] hydrocarboxylation[17] and silylformylation.[10b,c] Two examples are depicted in Scheme 1.4.



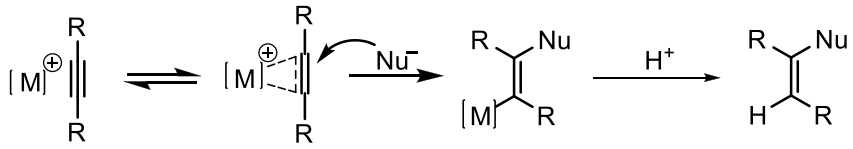
Scheme 1.4

Metallacyclopentadiene complexes are commonly involved as intermediates in alkyne cyclotrimerization and [2+2+2] cycloaddition reactions involving alkynes. Two π-coordinated alkyne ligands undergo oxidative coupling to give this cyclic complex (Scheme 1.5). Both terminal and internal alkynes can be involved and it is mainly dependent on the nature of the metal and substituents on the alkynes. Examples are known for titanium, tantalum, molybdenum, ruthenium, cobalt, rhodium, iridium and platinum.[18]



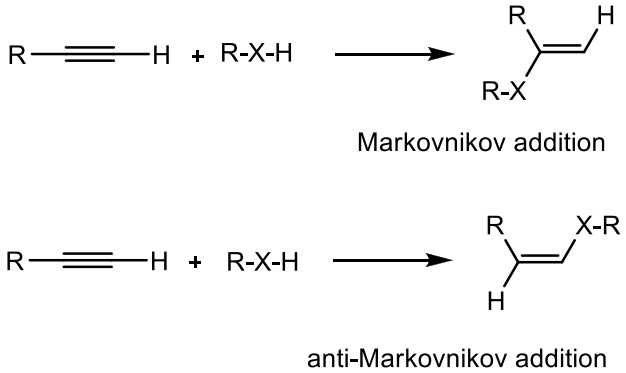
Scheme 1.5

Another class of reaction of π-alkyne complexes is nucleophilic attack onto the coordinated alkyne by external nucleophiles. Anti-addition of the external nucleophile to the activated alkyne generally affords the product with *trans*-stereochemistry (Scheme 1.6).



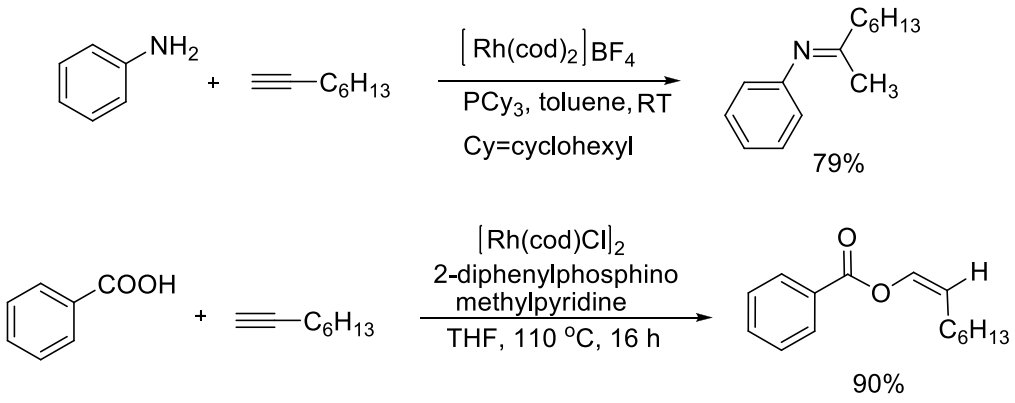
Scheme 1.6

In principle, the nucleophilic addition of a heteroatom-hydrogen bond across C≡C of an unsymmetrical alkyne should lead to two regioisomers: the Markovnikov and anti-Markovnikov addition products (Scheme 1.7).



Scheme 1.7

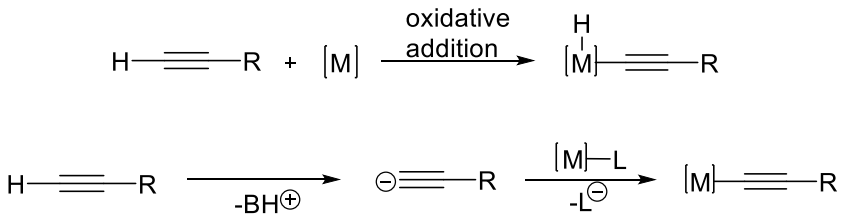
Nucleophiles that have been employed include water,[19] alcohol,[20] amine,[2] carboxylic acid[17] and phosphine.[21] For example, rhodium catalysed alkyne hydroamination and hydrocarboxylation are depicted in Scheme 1.8.



Scheme 1.8

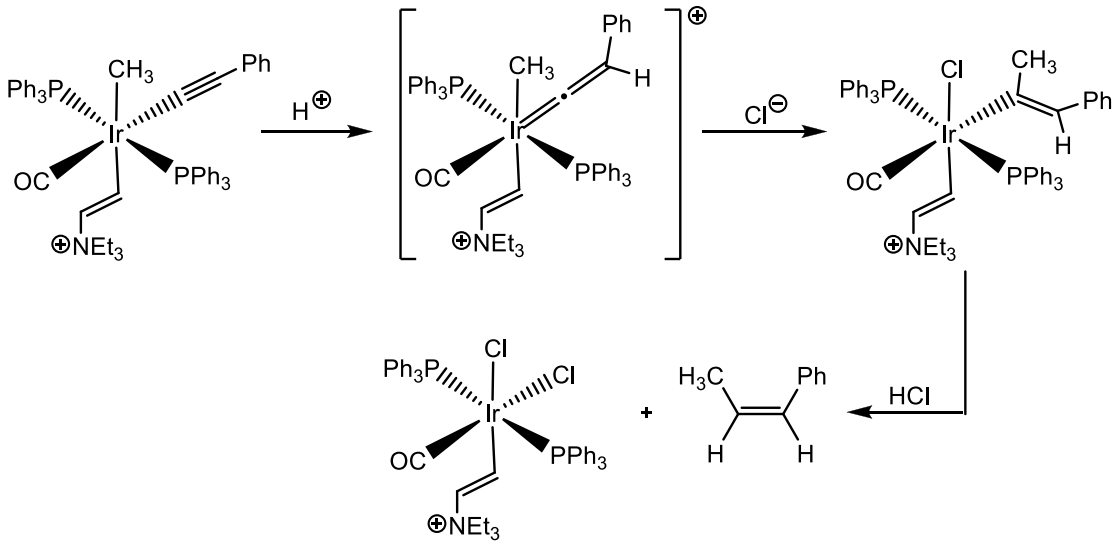
1.3 Alkynyl complexes

Hydrido alkynyl complexes can, in general, be obtained via oxidative addition of the H-C≡ bond of a terminal alkyne onto a metal centre, whereas metal alkynyls can be obtained via a base-assisted ligand substitution reaction (Scheme 1.9). Alkynyl complexes can also be obtained from haloalkynes and alkynylboronates through oxidative addition reactions.



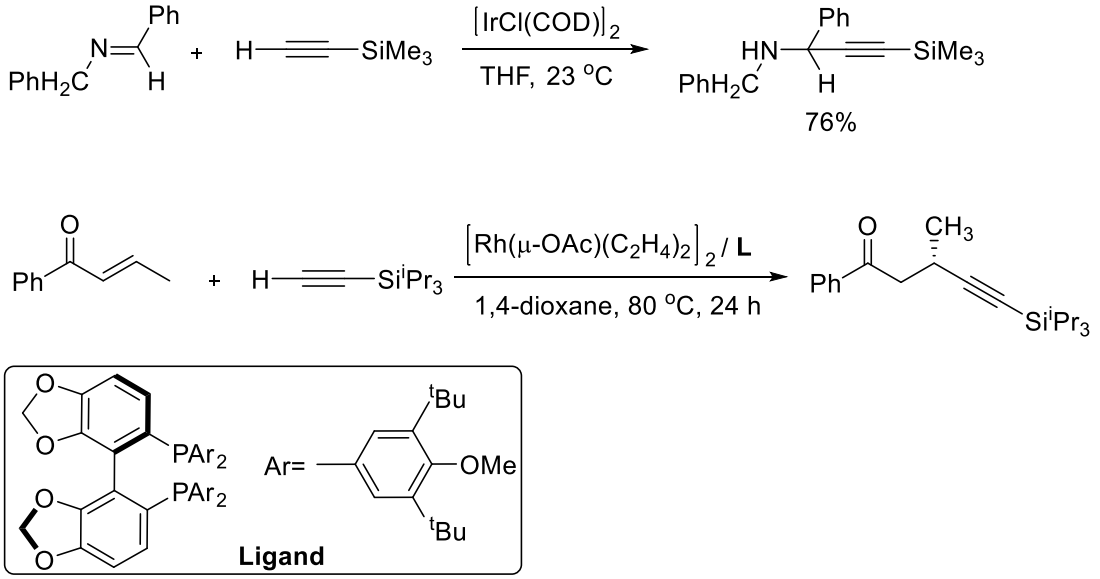
Scheme 1.9

These alkynyl ligands can undergo further coupling reactions with adjacent hydrocarbyl ligands in the presence of proton. The process involves protonation at the alkynyl ligand to afford a cationic vinylidene intermediate, followed by hydrocarbyl ligand migration onto the α-carbon of the vinylidene intermediate, and protonolysis, to afford the organic alkene and a metal complex (Scheme 1.10).[22]



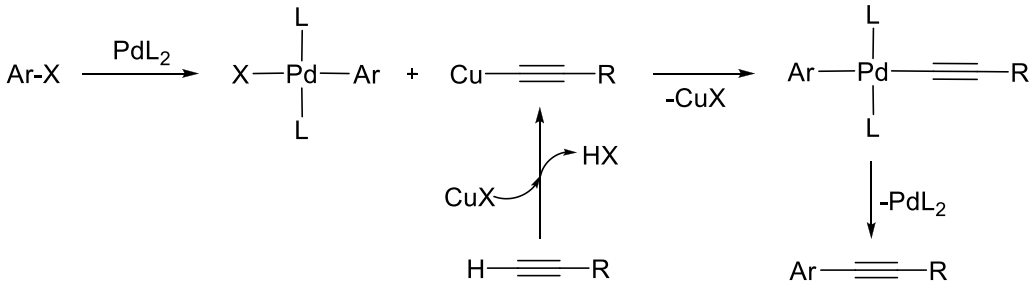
Scheme 1.10

Alkynyl ligands have been shown to act as nucleophiles, reacting with electrophiles such as carbonyl compounds,[23] conjugated alkenes,[24] and imines,[25] to afford the corresponding alkyne derivatives. This alkynylation reaction has been explored with a number of metals, including, copper, zinc, indium, ruthenium, nickel, palladium, cobalt, rhodium and iridium.[23-25] Some examples are given in Scheme 1.11.



Scheme 1.11

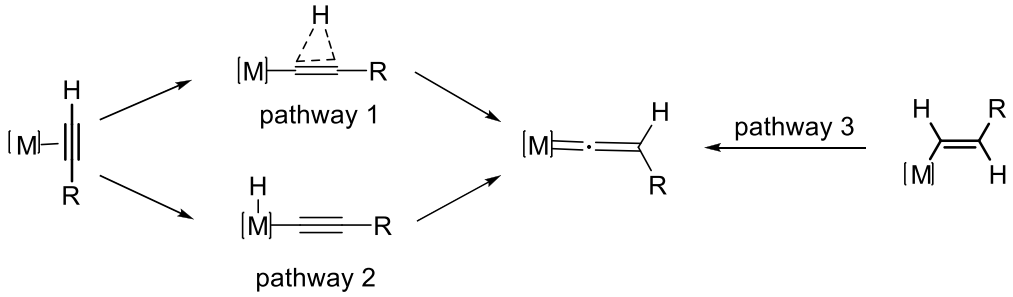
Another common reaction that makes use of alkynyl complexes is the Sonogashira coupling reaction. In this reaction, the alkynyl ligand undergoes reductive elimination with an adjacent aryl or vinyl ligand to afford an internal alkyne. The general scheme of this reaction is shown in Scheme 1.12.



Scheme 1.12

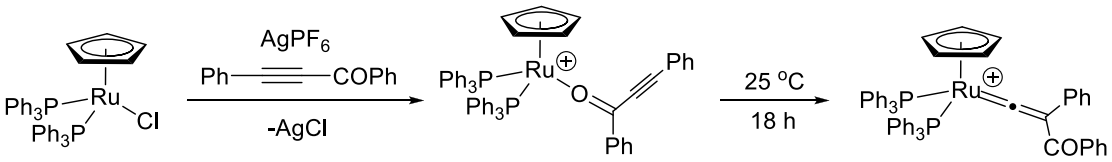
1.4 Vinylidene complexes

Metal vinylidene complexes can be formed by one of three pathways: i) 1,2-hydride shift from a π–alkyne complex, ii) 1,3-hydride shift from a hydridoalkynyl complex, or iii) α-H abstraction from an alkenyl complex (Scheme 1.13).[26] The pathway adopted depends on the nature of the metal, nature of the other ligands presents in the metal complex, and the electronic property of the alkyne.



Scheme 1.13

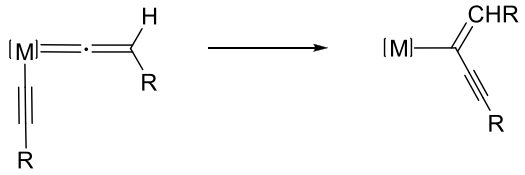
Interestingly, internal alkynes can also undergo vinylidene rearrangement under certain conditions.[27] For example, a ruthenium complex was found to react with internal alkynones to form vinylidene complexes via a C-C bond migration (Scheme 1.14).[27a]



Scheme 1.14

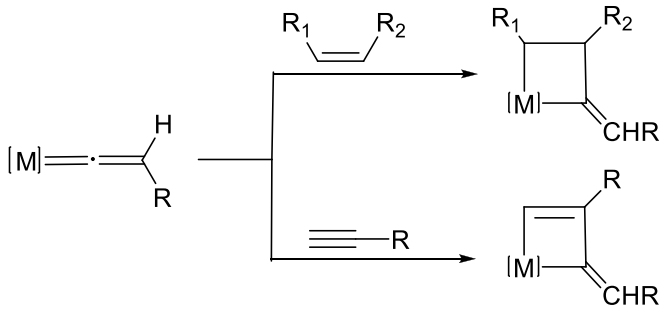
There are three general types of reactions which vinylidene complexes can undergo:

i) Intramolecular 1,2-migratory insertion of an adjacent ligand onto the α-carbon (Scheme 1.15). This is the basis for alkyne dimerization.[28]



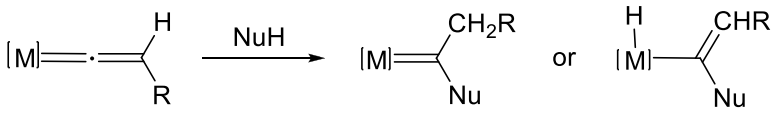
Scheme 1.15

ii) Formal [2+2] cycloaddition reaction between an M=C and a C-C multiple bond (Scheme 1.16). The [2+2] cycloaddition reaction of a vinylidene complex with an alkyne initiates alkyne polymerization via metathesis.[29] For example, $W(CO)_6$ was shown to be an active catalyst for phenylacetylene polymerization via the $[W(CO)_5(=C=CHPh)]$ intermediate.[30] Some ruthenium complexes were also found to be active catalysts for reactions such as polymerization,[31] the dimerization of alkynes,[28] and the formation of unsaturated ketones,[32] all of which were believed to proceed via ruthenium vinylidene intermediates.



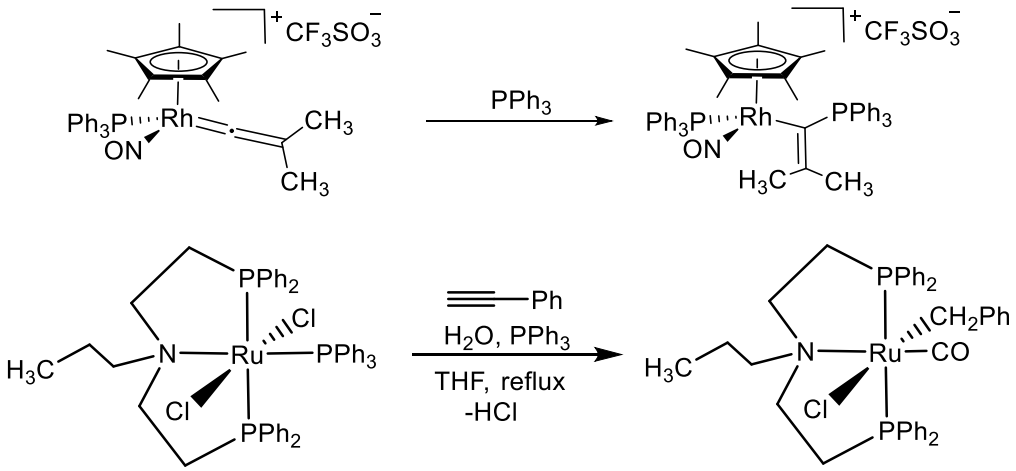
Scheme 1.16

As vinylidene complexes may be regarded as unsaturated carbenes, they can be either nucleophilic or electrophilic, depending on the nature of metal. Generally, early transition metal vinylidenes are nucleophilic, whereas late transition metal vinylidenes tend to be electrophilic. Since late transition metal vinylidenes are electrophilic, they tend to react with nucleophiles. The nucleophiles attack at the α-carbon to afford either a carbene or an alkenyl hydride complex (Scheme 1.17).



Scheme 1.17

Reactions with a wide range of nucleophiles have been reported, including amines,[33] water,[34] alcohols,[35] thiols,[36] phosphines,[37] and even fluoride.[38] Some examples are shown in Scheme 1.18.

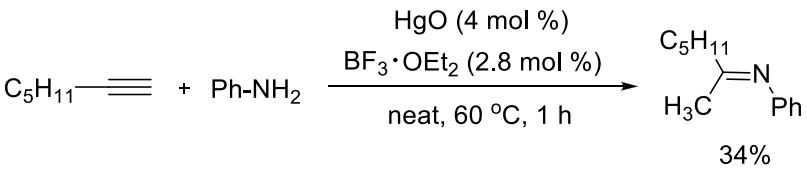


Scheme 1.18

1.5 Alkyne hydroamination

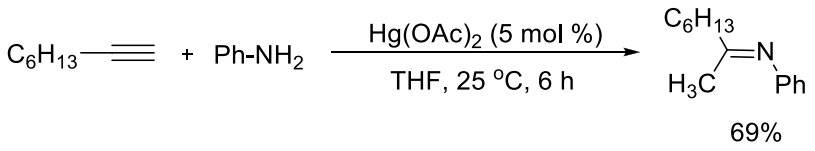
The addition of an amine N-H bond across C-C multiple bonds, the hydroamination reaction, offers an effective synthetic route to all sorts of amines (primary, secondary, and tertiary amines), imines, and enamines, by converting readily available alkynes and alkenes into desired, highly-substituted, N-containing products in a single step. Furthermore, catalytic hydroamination proceeds with 100% atom economy compared to classical organic synthesis and hence offers environmental benefits. This catalytic reaction has been shown to proceed well in the presence of metals,[2] acids,[39] and even bases.[40]

The first metal-catalysed hydroamination of alkynes with selective formation of products was reported in 1939 by Loritsch *et al*; the hydroamination 1-heptyne with aniline in the presence of mercuric oxide with $BF_3 \cdot OEt_2$ resulted in the formation of (*E*)-*N*-(heptan-2-ylidene)aniline (Scheme 1.19).[41] With secondary amines, enamines were the resulting products. Even though this catalyst was applicable to internal alkynes, such as 3-octyne, it had the drawback that it was limited to aryl amines only.



Scheme 1.19

About forty years later, in 1975, Barluenga employed mercury(II) salts to prepare ketimines.[42] In that work, they were able to demonstrate selective and superior (better yield) formation of enamine and imine products from the reaction of various amines with alkynes. For example, aniline reacted with 1-octyne in the presence of 5 mol% of mercuric acetate to produce (*E*)-*N*-(heptan-2-ylidene)aniline in 69% yield (Scheme 1.20).



Scheme 1.20

Alkyne activation by transition metals has the advantages of milder reaction conditions and good or excellent regio- and stereoselectivity. Nucleophilic addition to alkynes activated by late transition metals have been known for several decades, and these metal complexes have an advantage over the early transition metal and rare earth metal complexes of reduced oxophilicity, which means that they are less sensitive to moisture and air, and hence ease of handling, and they have greater functional group tolerance. They are also superior to the condensation of amines with ketones,[43] which involves elimination of water as a by-product, or the aminomercuration/demercuration of alkynes,[39,40] that involves toxic mercury reagents.

The typical reaction pathway for late transition metal catalysed hydroamination is shown in Figure 1.2. Coordination of the alkyne activates it towards nucleophilic attack by the amine moiety.[2a] Even though coordination of the amine into the metal centre has been shown to represent the resting state of the catalytic cycle, nucleophilic attack by the amine becomes possible upon metal coordination to the π–system.[44] Activation of the C≡C bond followed by nucleophilic attack of the amine leads to formation of an alkenyl-metal intermediate. This intermediate then undergoes a proton loss and protonolysis process to yield the enamine product directly. With primary amines, more stable imine products result after tautomerization from the enamine.

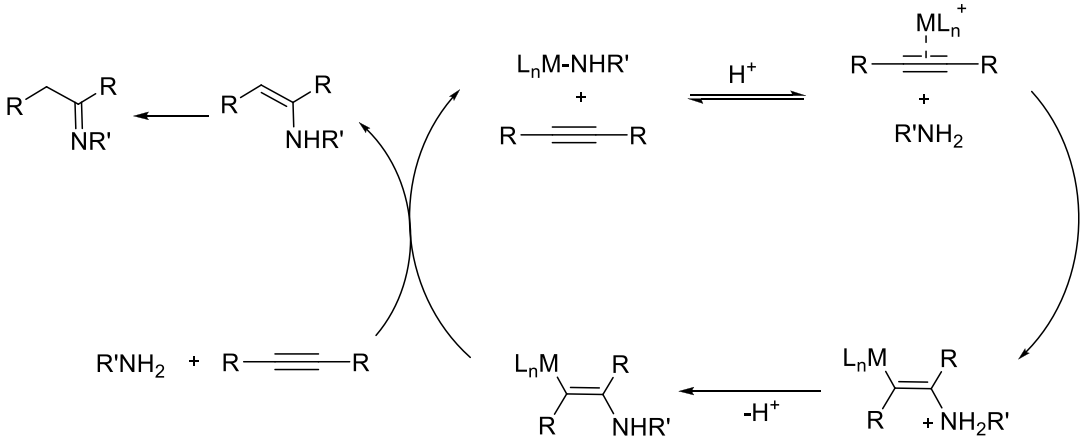
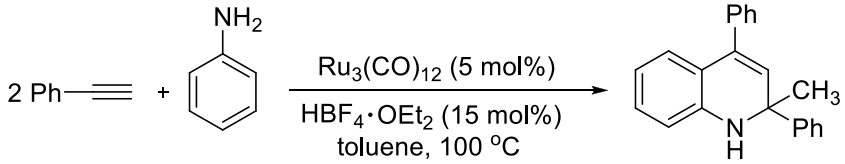


Figure 1.2: Mechanism of the late transition metal-catalysed hydroamination**.**

In 1999 Wakatsuki *et al*. reported the Markovnikov addition of aniline across the C≡C bond of both aliphatic and aromatic terminal alkynes, mediated by the $[Ru_3(CO)_{12}]/NH_4PF_6$ catalytic system.[45] After this report, various groups have investigated this reaction with various transition metals, including Pd,[46] Pt,[47] Au,[48] and Zn.[49] Though a few other transition metal complexes have also been used for this transformation, they are limited to either aromatic alkynes,[50] or aliphatic alkynes.[51] Transition metal-catalysed hydroamination of terminal alkynes with primary aliphatic amines,[52] and secondary amines,[53] have also been reported and the transition metal-induced cycloisomerization of terminal aminoalkynes have been carried out to afford either Markovnikov,[54] or anti-Markovnikov,[55] addition products.

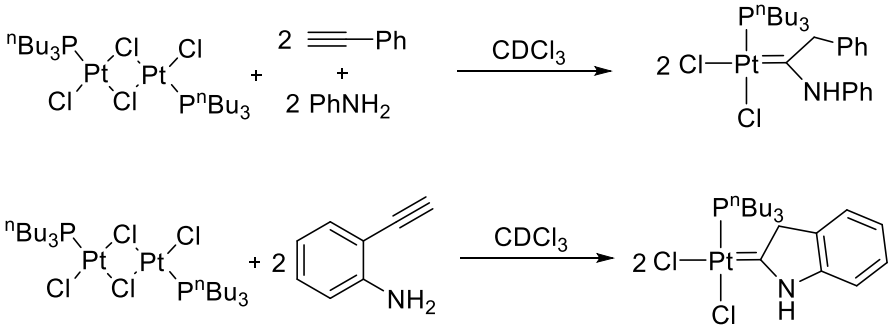
There is another class of hydroamination reaction which affords 1,2-dihydroquinoline via alkyne hydroamination followed by annulation with another molecule of alkyne. For example, Yi *et. al*. reported the $Ru_3(CO)_{12}$ catalysed sequential hydroamination and annulation reaction with arylamines of terminal alkynes to afford 1,2-dihydroquinolines (Scheme 1.21).[56] Similar reactions have been performed with various amines and alkynes, facilitated by various transition metals such as gold, silver, zirconium and zinc.[57]



Scheme 1.21

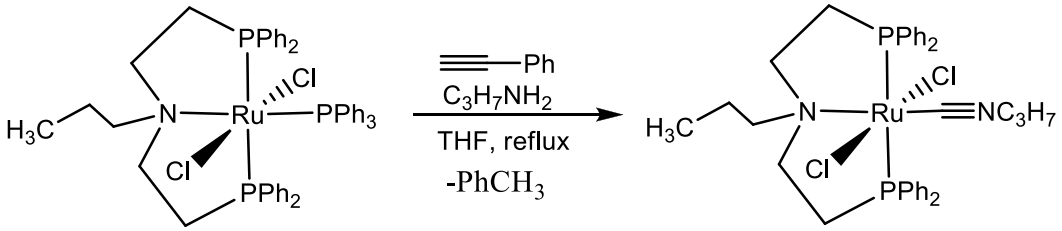
1.6 Organometallic complexes by alkyne hydroamination

Alkyne hydroamination has also been used to prepare organometallic complexes via the stoichiometric reaction of metal complexes with alkynes and amines.[33, 58-59] For example, in 1988, a number of platinum carbene complexes was prepared by Cross et al (Scheme 1.22).[58]



Scheme 1.22

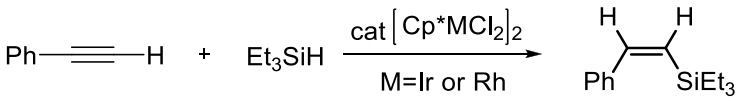
The reaction pathway was proposed to involve the formation of a vinylidene intermediate, followed by amine nucleophilic attack at the vinylidene α-carbon. Since then, the use of this reaction for the preparation of a large number of transition metal carbene complexes has appeared.[59] A range of ruthenium isonitrile complexes have also been prepared by the hydroamination of terminal alkynes with both aliphatic and aromatic amines (Scheme 1.23).[33b]



Scheme 1.23

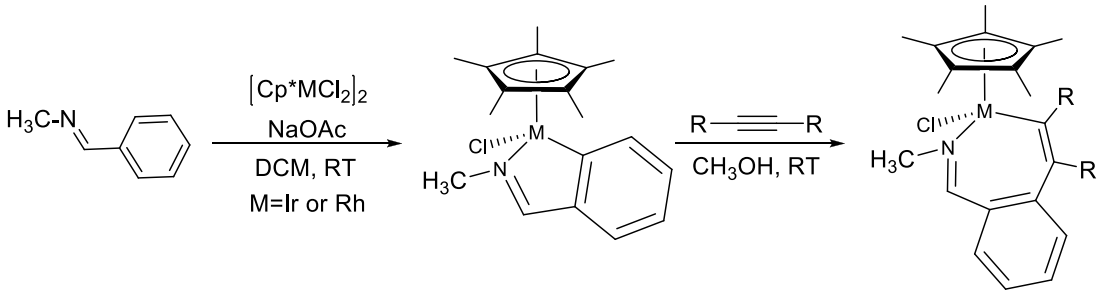
1.7 Alkyne activation by $[Cp^*MCl_2]_2$; M=Ir and Rh

The dimeric iridium complex $[Cp^*IrCl_2]_2$, **1a**, is known to activate terminal alkyne towards further reactions such as hydrosilylation (Scheme 1.24).[60] The rhodium analogue $[Cp^*RhCl_2]_2$, **1b**, was also found to be efficient for this transformation.[61]

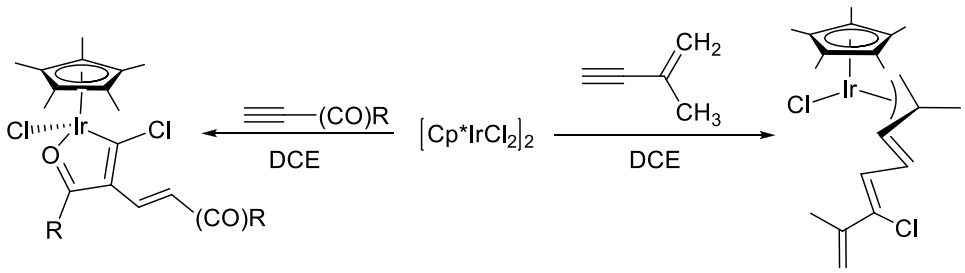


Scheme 1.24

The complexes **1a** and **1b** are also known to react with various unsaturated substrates to afford organometallic complexes. Thus they undergo ortho C-H activation and insertion reaction with imines to afford the metallacyclic complexes (Scheme 1.25),[62] and we have previously found that **1a** reacted with alkynones and enynes to afford iridafurans,[63] and tetraenyl-iridium complexes,[64] respectively, via alkyne dimerization (Scheme 1.26).

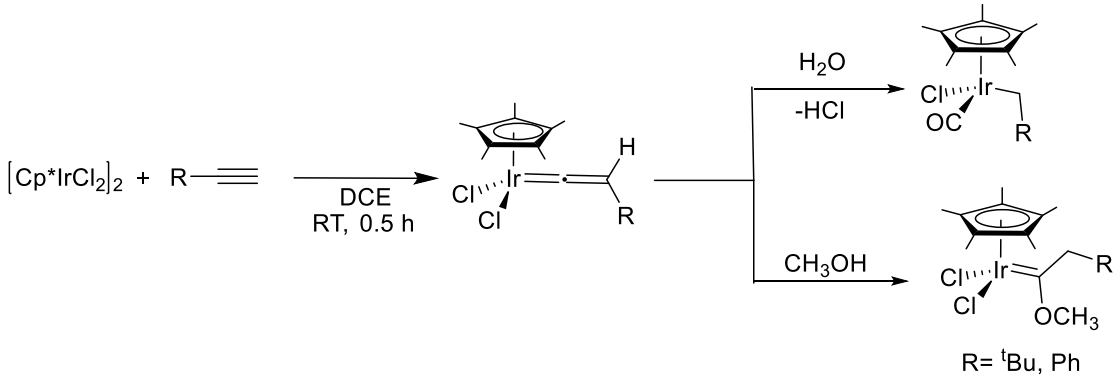


Scheme 1.25



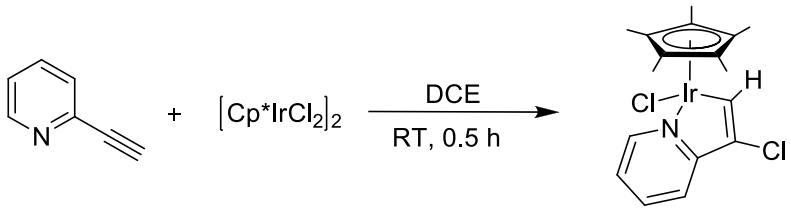
Scheme 1.26

Most notably, **1a** reacted with terminal alkynes resulting in the cleavage of the C≡C bond in the presence of water; while in the presence of methanol, methoxy-carbene derivatives were formed instead.[65] These reactions were believed to proceed via a vinylidene intermediate (Scheme 1.27).



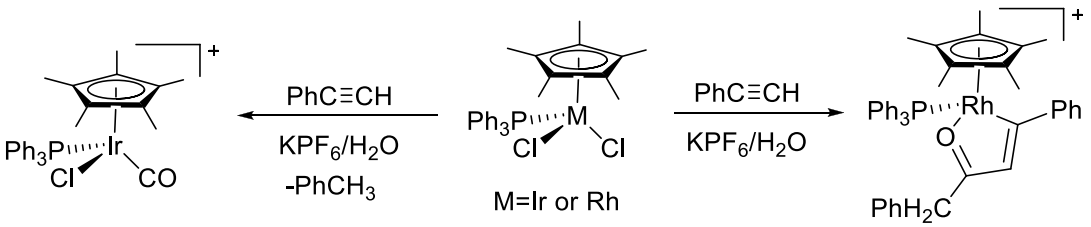
Scheme 1.27

From the proposed mechanism,[65] we realised that using nitrogen based nucleophiles such as amines under identical condition may lead to amino-carbene derivatives. An investigation into the reaction of **1a** with alkynes and amines would therefore be worthwhile. Interestingly, its reaction with the heteroalkyne, 2-ethynylpyridine has been found to afford a cyclometallated complex (Scheme 1.28).[66]



Scheme 1.28

The rhodium analogue **1b** could also undergo a variety of reactions with alkynes, including, alkyne insertion,[67] oxidative coupling,[68] and hydrosilylation.[61] In some cases, the reactivity of **1b** differed from that of the iridium analogue **1a** (Scheme 1.29).[69]



Scheme 1.29

1.8 Aim and objectives

Given the above, the aim of this project was to study the reactivity of **1a** and **1b** with alkynes in the presence of N-donors. Specifically, we set out to examine the following:

(1) The possible catalytic activity of $[Cp^*IrCl_2]_2$, **1a**, for the reaction of alkynes with amines,

(2) The stoichiometric reactivity of **1a** with an alkyne and an amine,

(3) The analogous reactivity with aminoalkynes, and

(4) The analogous chemistry with $[Cp^*RhCl_2]_2$, **1b**.

1.9 References

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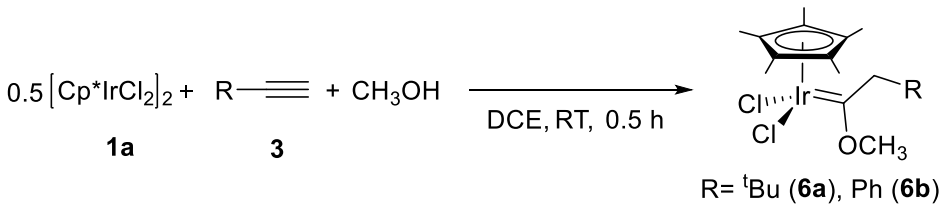
Chapter 2: The Reactivity of $[Cp^*IrCl_2]_2$ with Terminal Alkynes and Arylamines: Synthesis and Reactivity of Iridium Amino-carbene Derivatives

Earlier studies from our laboratory have shown that the dimeric iridium species $[Cp^*IrCl_2]_2$, **1a**, can activate alkynes towards further transformations.[1] For example, **1a** reacts with terminal alkynes **3** and methanol to give iridium methoxy-carbene complexes **6** (Scheme 2.1).[1b] The reaction is believed to proceed via alkyne coordination with iridium, followed by rearrangement to a vinylidene and subsequent nucleophilic attack at the α-carbon of the vinylidene intermediate. It was expected that a similar reaction with an amine ($R'NH_2$) in place of methanol can afford an iridium amino-carbene complex of the type $[Cp^*Ir(=C(NHR')(CH_2R))Cl_2]$. So, the objective here is to study the reactivity of **1a** with alkyne and amine.



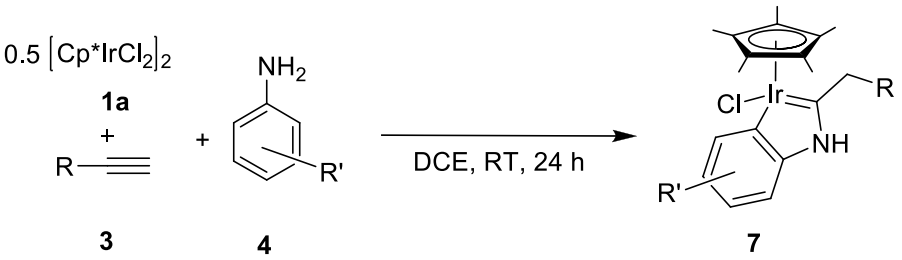
Scheme 2.1

2.1 Reaction of 1a with Terminal Alkynes and Anilines

A test reaction of **1a** with a 3,3-dimethyl-1-butyne in the presence of aniline afforded the orthometallated iridium amino-carbene complex **7a** in 81% yield. Using a similar procedure, a variety of orthometallated iridium amino-carbene complexes of type **7** were synthesized in yields from 30-81% for a wide variety of anilines ($R'C_6H_4NH_2$), **4** and terminal alkynes (RCCH), **3** (Table 2.1). Transition metal amino-carbene complexes of these type have been synthesized by various methods, including, aminolysis of alkoxy-carbene,[2] C-H activation of *N*-alkylamines[3] or aldimines,[4]

condensation of amides,[5] and nucleophilic attack of an amine onto coordinated alkyne moiety.[6] A detailed literature search on amino-carbene complexes shown that those of iridium are relatively rare and less extensively studied,[7] and most reports on their syntheses involved double α-hydride elimination of *N*-alkylamines.[7d-i]

Table 2.1. Substrate scope study for orthometallated iridium amino-carbenes.



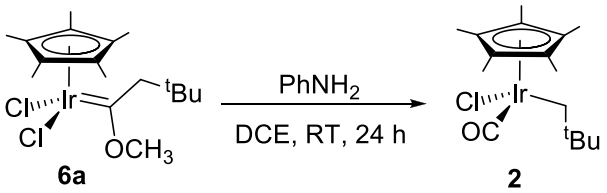
	R	R'	Yield (%)		R	R'	Yield (%)
1	^{t}Bu	H	**7a**, 81	11	$CH_3(CH_2)_3$-	H	**7k**, 51
2	^{t}Bu	*3,5*-CH_3	**7b**, 30	12	$CH_3(CH_2)_5$-	H	**7l**, 59
3	^{t}Bu	*4*-CH_3	**7c**, 79	13	$CH_3(CH_2)_7$-	H	**7m**, 48
4	^{t}Bu	*3*-Br-*4*-CH_3	**7d**, 71	14	$PhCH_2CH_2$-	H	**7n**, 60
5	^{t}Bu	*2*-OCH_3	**7e**, 68	15	Ph	H	**7o**, 64
6	^{t}Bu	*4*-OCH_3	**7f**, 81	16	Ph	*4*-CH_3	**7p**, 71
7	^{t}Bu	*2*-Br	**7g**, 73	17	Ph	*4*-OCH_3	**7q**, 73
8	^{t}Bu	*2*-Cl	**7h**, 69	18	Ph	*4*-Cl	**7r**, 69
9	^{t}Bu	*4*-Cl	**7i**, 72	19	Ph	*4*-NO_2	**7s**, 65
10	^{t}Bu	*4*-NO_2	**7j**, 76	20	*4*-$CH_3OC_6H_4$	H	**7t**, 62

[a]Coditions: **1a** (0.05 mmol), arylamine (0.1 mmol) and alkyne (1.0 mmol) in DCE (4 mL) at RT for 24 h. [b]Isolated yields.

Essentially, a large excess (20-equivalent) of the terminal alkyne is required for complete conversion of **1a** into **7**; use of stoichiometric amounts gave incomplete reaction along with the aniline coordinated product [Cp*$IrCl_2NH_2C_6H_4$R'], **8**;[8] the adducts with aniline, **8a**, and 4-methylaniline, **8c**, were isolated and characterized. On the other hand, in the absence of aniline, the reaction afforded the C≡C triple bond cleavage product **2**, which has previously been reported to be due to the reaction of **1a** with a terminal alkyne in the presence of moisture.[1b] Changing the solvent (to DCM, THF or toluene) or temperature (to reflux) did not lead to any improvement in yield. Attempts at isolating the non-orthometallated amino-carbene complexes, by

employing *2,6*-disubstituted anilines (e.g., *2,6*-dichloroaniline and *2,6*-difluoroaniline) or aliphatic amines (e.g., benzylamine and *1*-aminopentane), with *3,3*-dimethyl-*1*-butyne failed. The reaction is fairly robust as it appears unaffected by the presence of water. ^{1}H NMR and GC-MS analyses of the crude reaction mixture also did not show the presence of alkyne polymerization products; excess alkyne was recoverable.

Although aminolysis of methoxy-carbene complexes of type **6** is a well-known synthetic route to amino-carbene complexes,[2] the reaction of **6** with aniline was unsuccessful and gave **2** instead (Scheme 2.2). In the absence of aniline, the conversion of **6a** to **2** occurs only very slowly (~15% after 24 h). The failure of this reaction can therefore be rationalised on the basis of general base catalysis by aniline in the presence of adventitious water leading to hydroxide attack on **6**. In support of this, the reaction in the presence of aq. KOH led to the formation of **2**.



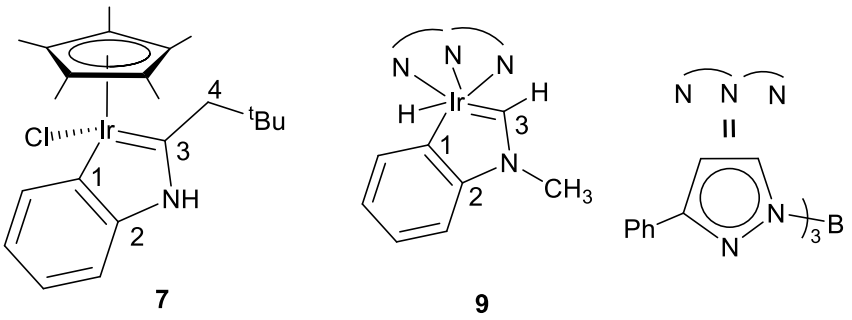
6a **2**

Scheme 2.2

The products **7** and **8** have all been characterised by spectroscopic and analytical methods. The ^{1}H NMR spectra of the amino-carbene complexes **7** exhibit two doublet resonances between ~2.7-4.7 ppm and a broad singlet resonance at ~10 ppm that are assigned to diastereotopic CH_2 protons and NH protons, respectively. The $^{13}C\{^{1}H\}$ NMR spectrum exhibits a resonance in the range 220-233 ppm assigned to Ir=C which is typical for transition metal amino-carbene complexes.[7d,7g] The complexes **7a**, **7c** and **8c** have also been confirmed by single crystal X-ray diffraction study. The ORTEP plot for **7c** and **8c** are shown in Figure 2.1 and Figure 2.2, respectively. A common atomic numbering scheme and selected bond parameters for **7a** and **7c** are given in Table 2.2, together with a similar iridium amino-carbene

complex which has been structurally characterized and reported earlier, *viz.*, Tp^{Ph}-Ir(H)(=CHNMePh), **9**.[7g] The Ir-C(3) bond length is significantly shorter than Ir-C(1) bond length which indicates the carbene nature of C(3) carbon. Surprisingly, both the Ir-C(3) and Ir-C(1) bond lengths in **7a** and **7c**, (1.992(9) and 2.047(9)Å, (1.989(6) and 2.036(6)Å, respectively) are longer than the corresponding bonds (1.930(3) and 2.015(3) Å, respectively) in **9**.[7g] The differences may be due to the different bonding nature of Cp* vs Tp^{Ph}.[9] The chelate bite angle of C(1)-Ir-C(3) is ~78 for **7** which is similar to the corresponding angle in **9** (79.2(1). There is significant double bond character in the C(3)-N bonds (1.291(11), 1.314(8) and 1.320(4) Å for **7a**, **7c** and **9**, respectively) due to resonance form, generally preferred by Fischer carbenes. This is also consistent with the C(2)-N-C(3) bond angle of ~117º, which is indicative of sp^2 hybridisation at the N atom.

Table 2.2. Common atomic numbering scheme and selected bond parameters for **7a**, **7c** and **9**.



Bond length (Å)	**7a**	**7c**	**9**
Ir-Cl	2.385(2)	2.4087(14)	
Ir-C(1)	2.047(9)	2.036(6)	2.015(3)
Ir-C(3)	1.992(9)	1.989(6)	1.930(3)
N-C(2)	1.428(12)	1.397(8)	
N-C(3)	1.291(11)	1.314(8)	1.320(4)
C(1)-C(2)	1.381(12)	1.382(8)	
C(3)-C(4)	1.496(12)	1.506(9)	
Bond angle (^{o})			
C(1)-Ir-C(3)	78.1(4)	78.4(2)	79.20(1)
C(2)-N-C(3)	117.2(7)	117.0(5)	
C(1)-C(2)-N	112.3(8)	113.3(5)	
N-C(3)-Ir	117.7(7)	116.8(4)	

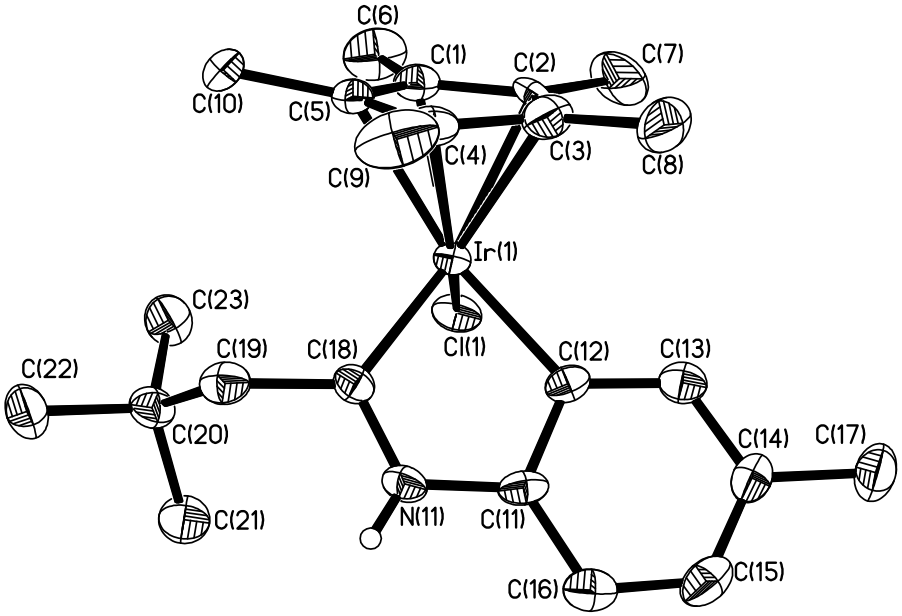


Figure 2.1. ORTEP plot (50% probability thermal ellipsoids) of **7c**. All but one H atoms omitted.

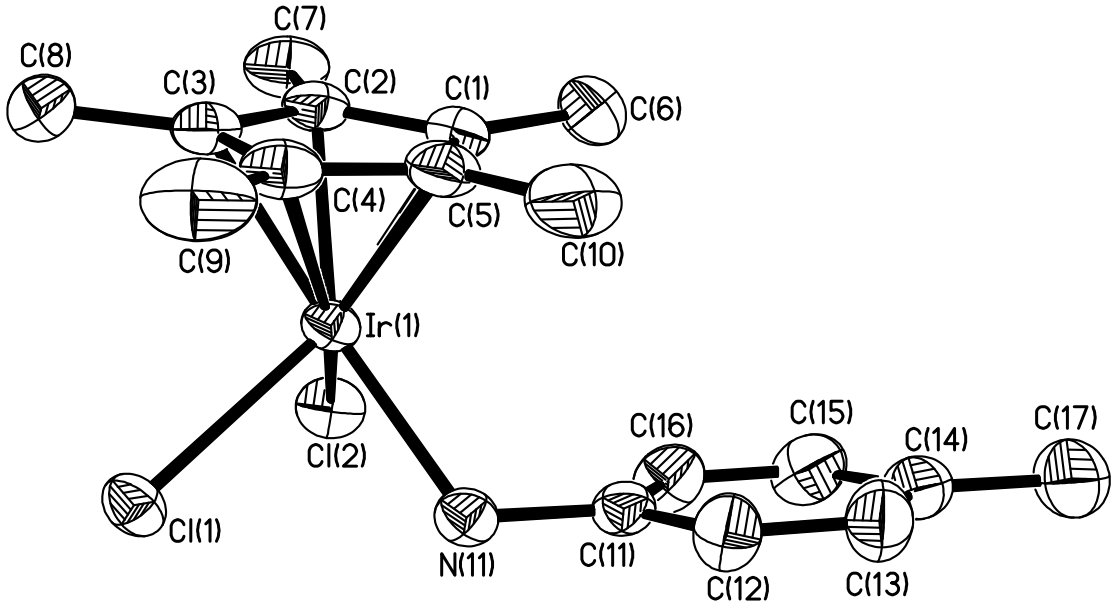
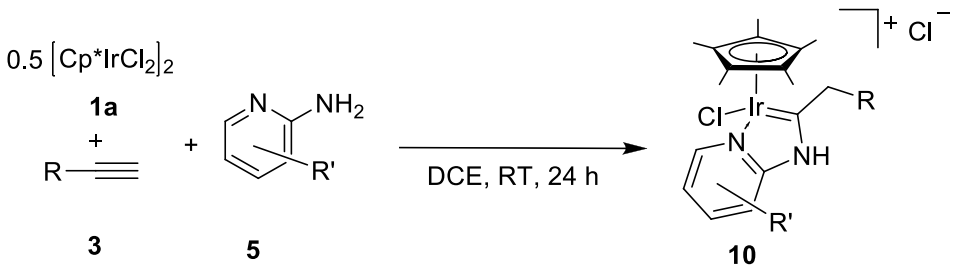


Figure 2.2. ORTEP plot (50% probability thermal ellipsoids) of **8c**. H atoms omitted. Selected bond lengths (Å) and angles (^{o}): Ir(1)-N(11) = 2.169(3); Ir(1)-Cl(2) = 2.4033(7); Ir(1)-Cl(1) = 2.4315(7); N(11)-C(11) = 1.453(4); N(11)-Ir(1)-Cl(2) = 83.31(8); N(11)-Ir(1)-Cl(1) = 80.67(7);Cl(2)-Ir(1)-Cl(1) = 87.50(3).

2.2 Reaction of 1a with Terminal Alkynes and 2-aminopyridines

Extension of the above methodology to 2-aminopyridines ($R^{'}C_5H_3NNH_2$), **5**, in place of the aniline afforded the iridium amino-carbene complexes [Cp*Ir(=C(NHNC$_5$H$_3$R$^{'}$)(CH$_2$R))Cl], **10**, in 59-82% yields (Table 2.3). Similar transition metal amino-carbene complexes have been prepared by nucleophilic addition of amines onto coordinated alkyne[10] and aminolysis of the corresponding alkoxy-carbene derivatives.[11] However, the analogue of iridium complexes are rare[12] and all have been prepared by double C-H bond activation of corresponding *N*-alkyl 2-aminopyridines.

Table 2.3. Substrate scope study for cationic iridium amino-carbenes.



	R	**R'**	**Yield(%)**
1	^{t}Bu	H	**10a**, 80
2	^{t}Bu	*5*-Br	**10b**, 76
3	^{t}Bu	*6*-Br	**10c**, 82
4	^{t}Bu	*6*-CH_3	**10d**, 59
5	Ph	*6*-Br	**10e**, 79
6	*4*-CH_3-C_6H_4	*6*-Br	**10f**, 64
7	*4*-Br-C_6H_4	*6*-Br	**10g**, 69

[a]Coditions: **1a** (0.05 mmol), 2-aminopyridines (0.1 mmol) and alkyne (1.0 mmol) in DCE (4 mL) at RT for 24 h. [b]Isolated yields.

The reaction proceeded smoothly with both aliphatic and aromatic terminal alkynes but failed to proceed with internal alkynes (diphenyl acetylene and prop-1-ynylbenzene). Both electron-withdrawing and electron-donating, on alkyne and aminopyridine are tolerated. The products have all been characterised completely by spectroscopic and analytical methods. As for the complexes **7**, ^{1}H NMR and ^{13}C{^{1}H} NMR spectra of these complexes also exhibit two doublet resonances between ~3.5-5.2 ppm for the diastereotopic CH_2 protons and a singlet resonance in the range ~237-242 ppm for carbene carbon, respectively. The carbene complex **10c** have been confirmed by a single-crystal X-ray structural study as well; an ORTEP plot of **10c** is shown in Figure 2.3, and selected bond parameters are given in Table 2.4. The Ir-C(16) bond length in **10c** is essentially the same as the corresponding bond in the orthometallated amino-carbenes **7** and shorter than in the most similar complexes reported earlier,[12] and is indicative of an Ir=C double bond. The N(2)-C(16)-Ir(1) and

C(15)-N(2)-C(16) bond angles, and N(2)-C(16) and C(15)-N(2) bond lengths are 114.6° and 120.9°, and 1.332(2) and 1.332(2), respectively; that are within the range of sp^2-hybridised carbon and nitrogen atoms which indicates the possible resonances within the metallacycle.

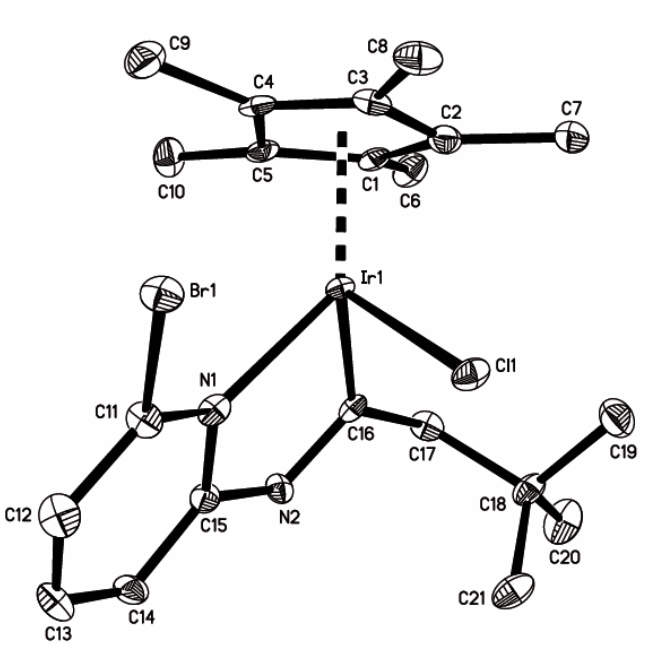
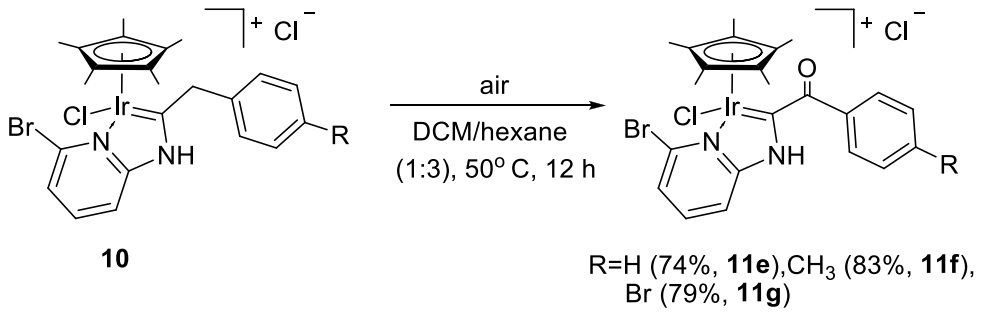


Figure 2.3. ORTEP plot (50% probability thermal ellipsoids) showing the molecular structure of **10c**. H atoms are omitted for clarity.

2.3 Reactivity of the cationic iridium amino-carbenes 10

Cationic amino-carbenes **10e-g**, which have a benzyl group α to the carbenic carbon, undergo aerial oxidation to yield a ketone (Scheme 2.3); the non benzylic CH_2 protons in **10a-d** are resistant to oxidation under similar conditions. The driving force for this may be extension of conjugation between the phenyl ring and the metal carbene. However, an attempt at the synthesis of this ketone complex in a single-step, for example, by reacting **1a** with *2*-amino-*6*-bromopyridine and phenylacetylene in DCM/hexane at 50 ^oC failed to give **11e**. The products **11e-g** have been characterised completely spectroscopically and analytically, and also by single-crystal X-ray structural studies for **11e** and **11f**.

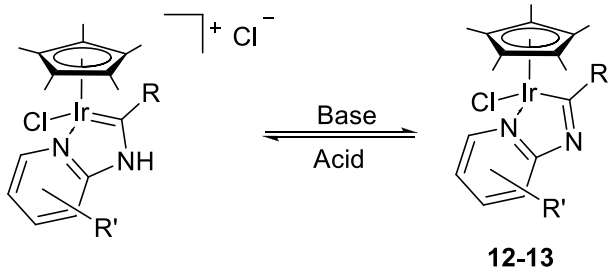


10

R=H (74%, **11e**),CH_3 (83%, **11f**),
Br (79%, **11g**)

Scheme 2.3

Treatment of **10** and **11** with a base (triethylamine) afforded the neutral species **12** and **13**, respectively (Scheme 2.4). Complex **12c** can be reprotonated with HBF_4 or con.HCl to afford $[Cp^*(Cl)Ir=C(CH_2{}^tBu)NHPy]^+$, **10c**, as the BF_4^- or Cl^- salt. The molecular structures of **10**, **12** and **13** have been determined via single-crystal X-ray structural studies. Common atomic numbering schemes, together with selected bond parameters, for the complexes which have been crystallographically characterised are given in Table 2.4.

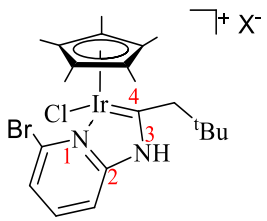
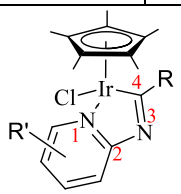
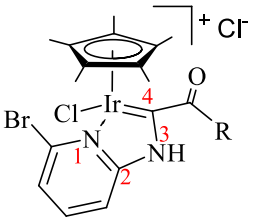


12-13

R= $CH_2{}^tBu$ (**12**) : R'= H (91%, **a**), *5*-Br (93%, **b**), *6*-Br (94%, **c**).
R'= 6-Br (**13**) : R= COPh (90%, **e**), COC_6H_4-*4*-CH_3 (92%, **f**).

Scheme 2.4

Table 2.4: Selected bond parameters for **10c·Cl**, **10c·BF$_4$**, **11e**, **11f**, **12b** and **13e**. The two sets of values given for **11e** and **11f** are for the two crystallographically independent molecules found in the crystals.

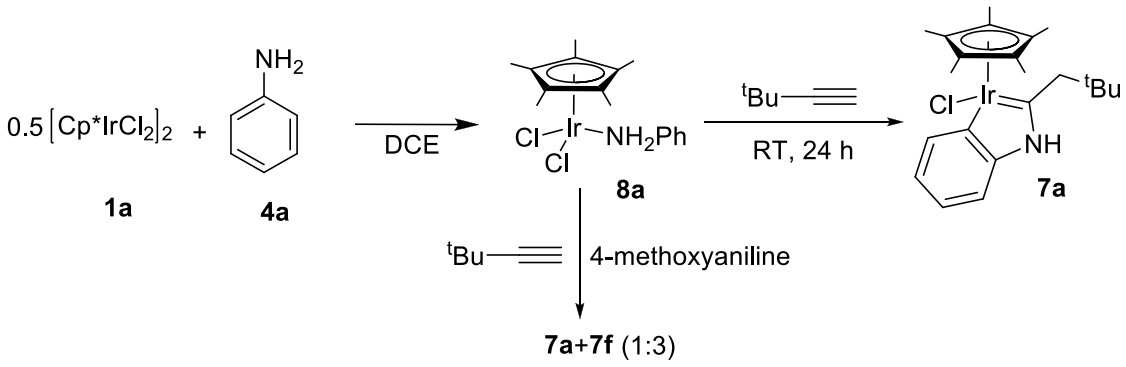
Bond parameters	**10c·Cl**	**10c·BF$_4$**	**12b**	**13e**	**11e**	**11f**
	 X = Cl orBF$_4$		 R=CH$_2$^{t}Bu: R'=*5*-Br (**b**) R=COPh: R'=*6*-Br (**e**)		 R = Ph (**e**), *p*-tolyl (**f**)	
Bond lengths / Å						
Ir-Cl	2.379(2)	2.385(2)	2.388(2)	2.399(13)	2.392(2) 2.403(2)	2.392(18) 2.395(19)
Ir-N(1)	2.118(8)	2.120(7)	2.060(6)	2.113(5)	2.121(7) 2.130(7)	2.142(6) 2.124(6)
Ir-C(4)	1.990(10)	1.967(9)	2.002(8)	2.015(6)	1.971(8) 1.969(9)	1.978(8) 1.981(8)
N(1)-C(2)	1.359(12)	1.340(10)	1.361(10)	1.369(7)	1.353(11) 1.345(11)	1.347(9) 1.370(9)
N(3)-C(2)	1.382(13)	1.391(12)	1.382(11)	1.388(7)	1.397(11) 1.384(11)	1.380(9) 1.383(9)
N(3)-C(4)	1.332(12)	1.338(11)	1.320(10)	1.284(7)	1.324(11) 1.309(11)	1.323(9) 1.315(9)
Bond angles / degree						
N(1)-Ir-C(4)	77.9(3)	78.3(3)	76.2(3)	75.0(2)	76.7(3) 76.3(3)	77.0(3) 76.8(3)
C(2)-N(3)-C(4)	120.9(8)	118.9(7)	112.7(7)	112.6(5)	118.6(7) 117.3(8)	119.5(6) 118.5(7)
N(1)-C(2)-N(3)	112.2(8)	114.0(7)	116.9(7)	117.4(5)	112.1(7) 114.0(7)	113.3(7) 113.2(6)
N(3)-C(4)-Ir	114.6(7)	114.8(6)	120.1(6)	122.2(4)	117.4(6) 118.5(6)	116.3(6) 117.7(6)

The Ir-C(4) bond lengths of **10c·Cl**, **10c·BF$_4$**, **11e**, **11f** and the neutral species (**12b** and **13e**) are comparable or shorter than the corresponding bond length in similar amino-carbene complexes,[12] and hence suggest carbenic nature for the C(4) carbon. Indeed, the C-N bond lengths for all six crystals show double bond character, suggesting delocalisation of electrons around the metallacycles. The $^{13}C\{^1H\}$ NMR

spectra also corroborate this; the C(4) resonance is distinctly downfield at ~ 225 –245 ppm for all the complexes in this study, both cationic and neutral. The structures of **11e**, **11f** and **13e** suggest that the ketone functional group in these complexes is not involved in conjugation with the metallacycle; the dihedral angle between the Ir-C(4)-N(3) and C(4)-C=O planes range from about 68^{o} to 79^{o}. However, the infrared spectroscopic data in DCM ($\nu_{C=O}$ are 1659, 1654, 1653 and 1651 cm^{-1} for **11e**, **11f**, **13e** and **13f**, respectively, compared to 1686 cm^{-1} in acetophenone) suggests conjugation in solution.

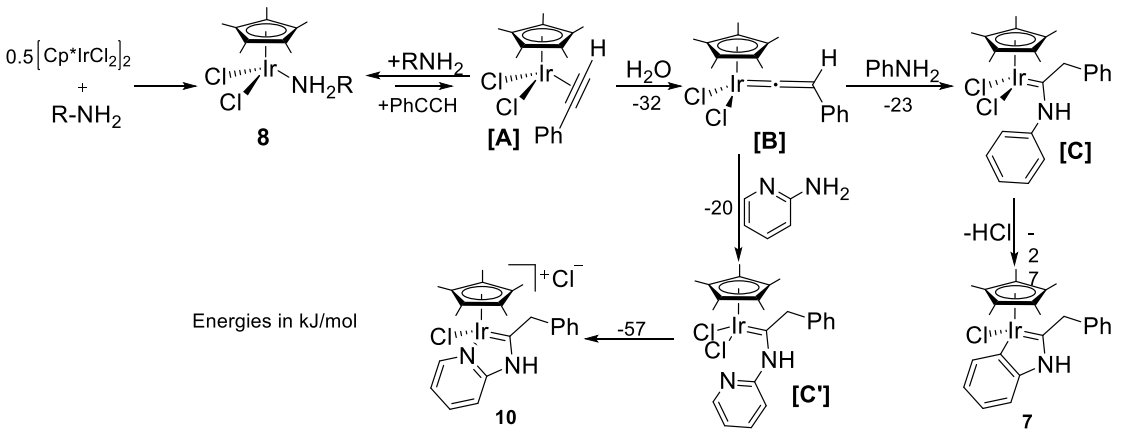
2.4 Mechanistic investigations into the formation of the amino-carbenes

The reaction towards **7** afforded **8** in the absence of a large excess of the alkyne suggested that the latter may be an intermediate in the reaction pathway. This was shown to be the case; the reaction of aniline with **1a** afforded **8a** almost immediately in quantitative yields, and subsequent reaction with excess of t-butylacetylene afforded **7a** in yields similar to that for the one-pot reaction. Similarly, addition of ^{t}BuCCH and an equivalent of 4-methoxyaniline to a sample of **8a** afforded **7a** and **7f** in a 1:3 ratio (Scheme 2.5), indicating that dissociation of the aniline ligand from **8a** is facile.



Scheme 2.5

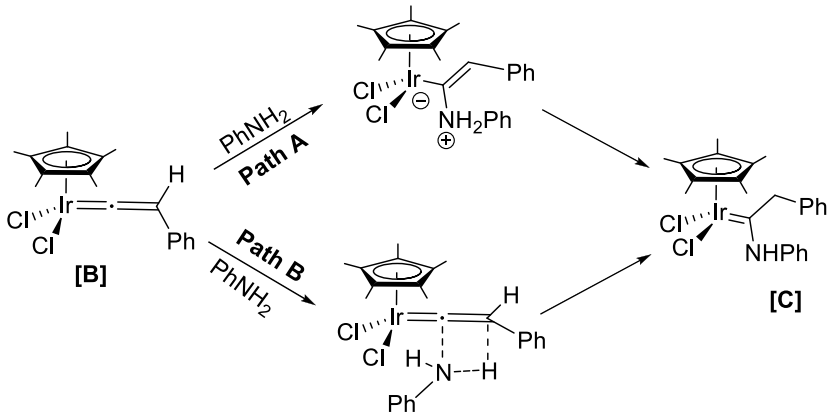
Proposed reaction pathways to both **7** and **10** are shown in Scheme 2.6. The energetics for this pathway have been studied computationally using DFT theory at the 6-311+G(2d,p)/LANL2DZ+p level of theory, and the computed energies ($\Delta G^{\ominus}$, in kJ mol^{-1}) from **A** onwards are also given. With the exception of the steps for the formation of **8** and the final orthometallation, the reaction pathway is similar to what was proposed earlier for the C≡C triple bond cleavage reaction with water.[1b] Presumably, the coordinated aniline in **8** is replaced in the presence of large excess of the alkyne to give **A**, which rapidly rearranges to the vinylidene complex **B**. This step is believed to proceed via an intermolecular deprotonation-protonation sequence for the *1,2*-H shift with adventitious water, and is consistent with what has been observed earlier,[1b] and is also supported by the observation that reaction of **1a** with phenylacetylene-d and aniline showed no deuterium incorporation in the product **7o**.



Scheme 2.6

The step from **B** to the proposed amino-carbene intermediate **C** is a hydroamination reaction and the $\Delta G^{\ominus}$ associated with this step is -23 and -20 kJ mol^{-1} for aniline and 2-aminopyridine, respectively. There are two alternative pathways for this step: A nucleophilic attack of aniline at the α-carbon of the vinylidene intermediate **B** to form a zwitterion followed by proton transfer (may be intramolecular or intermolecular) (Scheme 2.7 path A),[6f] or a concerted process

involving a 4-membered transition state (Scheme 2.7 path B).[6b] Although the reaction solvent is rather nonpolar, which should disfavour the first alternative, it cannot be ruled out at this point. The structures of **C** and **C'** are typical of Fischer carbenes (that for **C** is shown in Figure 2.4) and show considerable double bond character in the N-C bond (1.36 Å).



Scheme 2.7

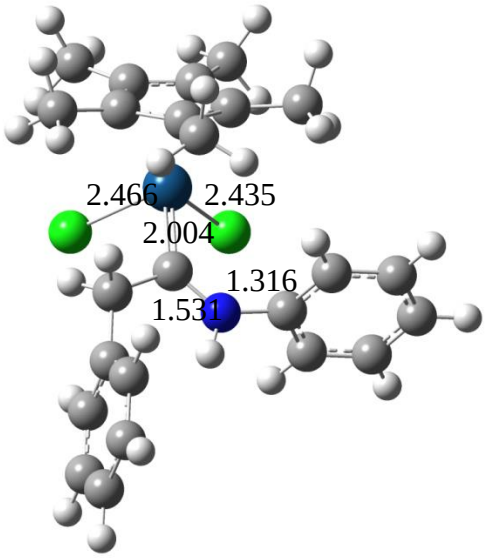
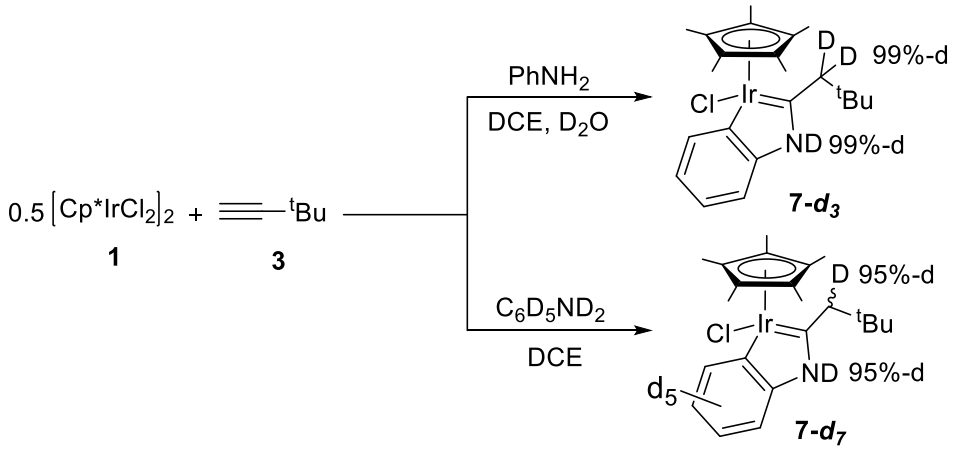


Figure 2.4. Computationally optimized geometry of intermediate **C**. Bond lengths given in Å.

Isotopic labelling experiments employing (a) d_5-aniline and ^{t}BuCCH, (b) d_7-aniline and ^{t}BuCCH, and (c) aniline and ^{t}BuCCH in the presence of D_2O, afforded **7a** with none, one and both of the diastereotopic CH_2 protons being deuterated, respectively (Scheme 2.8). These results suggested that the source of the diastereotopic CH_2 protons being water and aniline; an intermolecular proton transfer for step **B** to **C** is therefore unlikely, as that would be expected to involve water or free aniline.

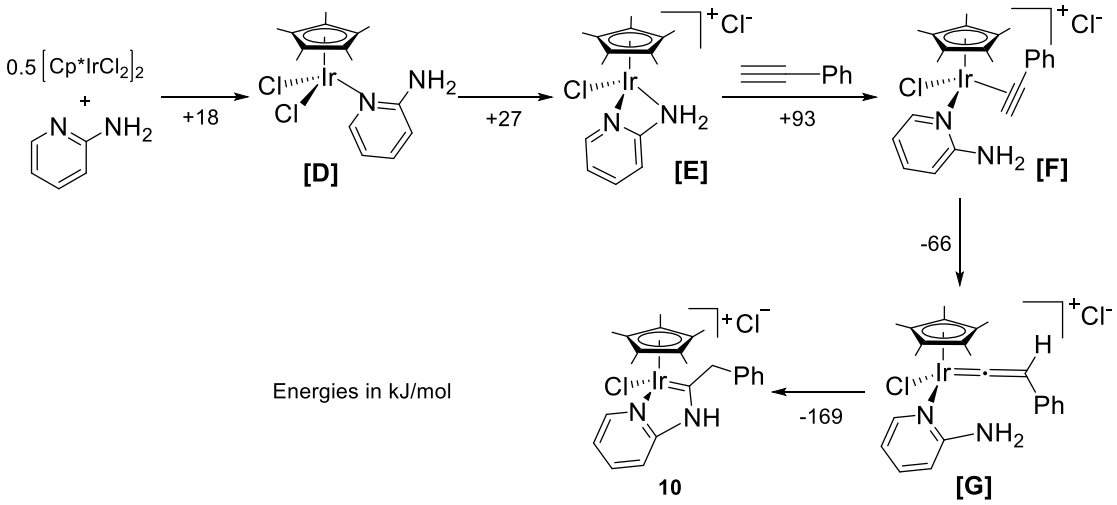


Scheme 2.8

The final step is an orthometallation,[6a] and the computed $\Delta G^{\ominus}$ value for this step is -27 kJ mol^{-1}; this can certainly become considerably more downhill in the presence of moisture (ΔG_{298} for formation of HCl acid is about -96 kJ mol^{-1}),[13] and is probably the main driving force for this step. In the case of 2-aminopyridine, the final step is ligand substitution and the free energy change associated with this step is -57 kJ mol^{-1}. Even though the calculated $\Delta G^{\ominus}$ value is negative (-31 kJ mol^{-1}) for the orthometallation step, this is less favoured than ligand substitution.

Although no kinetic barriers were computed, the negative free energy changes involved in each of the steps suggest that the proposed reaction pathway above is reasonable.

An alternative reaction pathway which we have also considered involves ionic intermediates (Scheme 2.9), and is similar to one proposed for the formation of ruthenium amino-carbene complexes.[10] The initial coordination of the 2-aminopyridine is probably via the pyridyl-N as has generally been observed,[3a,14] although the computed $\Delta G^{\ominus}$ values for pyridine vs amine coordination is only 8 kJ mol^{-1}. The subsequent two steps involving chloride displacement and alkyne coordination are endergonic, although last two steps (a vinylidene rearrangement and a nucleophilic attack at the vinylidene carbon with a proton transfer) are exergonic. The computed free energies are thus rather unconvincing; steps which are quite endergonic followed by quite exergonic ones. That, together with the fact that the suitable reaction solvent can be rather non-polar, such as DCE, and hence disfavouring ionic intermediates, suggests that this route is unlikely.

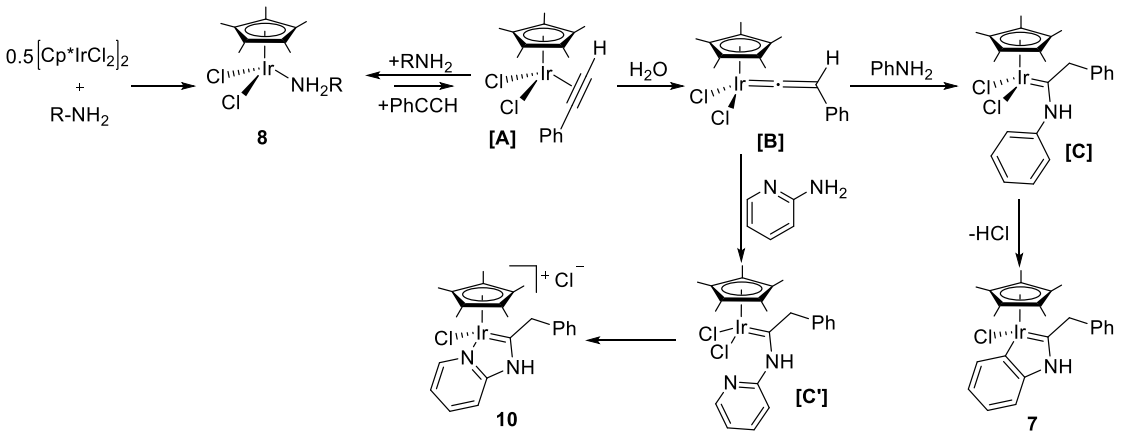


Scheme 2.9

2.5 Conclusion

The reaction of $[Cp^*IrCl_2]_2$, **1a** with terminal alkynes in the presence of anilines or 2-aminopyridines was found to give orthometallated amino-carbenes $[Cp^*Ir(=C(NHC_6H_4R')(CH_2R))Cl]$, **7**, or cationic iridium amino-carbenes $[Cp^*(Cl)Ir=C(CH_2R)NHPy]Cl$, **10**, respectively. It was also found that cationic iridium amino-carbenes which contain a benzylic group α to the carbene moiety were susceptible to aerial oxidation to form the complexes $[Cp^*(Cl)Ir=C(COPh)NHPy]Cl$, **11**. In both **10** and **11**, the NH proton is acidic.

The reaction pathways to the formation of **7** and **10** have also been studied using labelling and computational studies. The proposed pathways to both involve a similar route to a vinylidene intermediate **B** as well as subsequent nucleophilic attack at the vinylidene α-carbon to form **C** or **C'** (Scheme 2.10), In the case of aniline, orthometallation occurs while in the case of 2-aminopyridine, displacement of chloride by the pyridine is energetically more favourable. Although the free energy for displacement of a chloride by a second aniline molecule in **C** has not been computed, it is likely to be less favourable entropically. Furthermore, the coordinated aniline will still be susceptible to decoordination.



Scheme 2.10

2.6 Experimental Section

2.6.1 General Procedure. All reactions and manipulations, except for TLC separations, were performed under argon by using standard Schlenk techniques. The starting material **1a** was prepared according to the published method.[15] The aniline-d_7 (98%) and phenylacetylene-*d* (99%) were purchased from Aldrich and used as received. All other chemicals were from commercial sources and used as supplied without further purification. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded in $CDCl_3$ on a JEOL ECA400 or ECA400SL spectrometer and were referenced to residual solvent resonances. High resolution mass spectra (HRMS) were recorded in ESI mode on a Waters UPLC-Q-TOF mass spectrometer. Elemental analyses were performed by the microanalytical laboratory in NTU. The crystal structure determinations were carried out by Dr Rakesh Ganguly or Yongxin Li.

Crystallographic studies. Diffraction quality crystals were grown by slow diffusion from hexane into a dichloromethane solution and then mounted onto quartz fibres. X-ray data were collected at 223 K on a Bruker X8 APEX system, using Mo Kα radiation, with the SMART suite of programs.[16] Data were processed and corrected for Lorentz and polarisation effects with SAINT,[17] and for absorption effects with SADABS.[18] Structural solution and refinement were carried out with the SHELXTL suite of programs.[19]

The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light, non-hydrogen atoms. Hydrogen atoms were placed in calculated positions and refined with a riding model. There were two formula units per asymmetric unit for **11e** and **11f**. Dichloromethane solvates were found in the crystals of **10c**, **11e** and **11f**. For the latter two crystals, four sites were found for the solvates, which were modelled with various occupancies, and with **11e**,

one of the solvate was modelled as disordered with two alternative positions for one of the Cl atoms. The crystal of **10c·BF_4** showed disorder of the anion which was modelled with two alternative sites for each of the F atoms, with occupancies of 0.7 and 0.3, respectively. The crystal of **12b** exhibited disorder of the $CH_2{}^tBu$ group, which was modelled with two alternative sites with their occupancies summed to unity. Appropriate restraints on the bond and thermal parameters were placed on all the disordered parts. All non-hydrogen atoms were given anisotropic displacement parameters in the final model.

Computational studies. The reaction energetics were studied using DFT theory utilising the Becke's three parameter hybrid function[20] and Lee-Yang-Parr's gradient-corrected correlation function[21] (B3LYP). The LANL2DZ (Los Alamos Effective Core Potential Double-ζ) basis set together with polarisation functions are employed for the Ir atom, and the 6-311+G(2d,p) basis set for all the other atoms. Spin-restricted calculations were used for geometry optimization, and harmonic frequencies were then calculated to characterize the stationary points as equilibrium structures with all real frequencies, and to evaluate zero-point energy (ZPE) corrections. All calculations were performed using the Gaussian 09 suite program.[22]

2.6.2 Formation of orthometallated iridium amino-carbenes 7

In a typical reaction, to a solution of **1a** (40 mg, 50 µmol) and *3,3*-dimethyl-*1*-butyne (125 µL, 20-fold excess) in *1,2*-dichloroethane (4 mL) was added aniline (9 µL, 100 µmol). There was an immediate colour change from bright orange to yellow, and upon stirring for 24 h at RT, it turned orange. The solvent was then removed under reduced pressure and the residue obtained was dissolved in the minimum amount of dichloromethane for chromatographic separation on silica gel TLC plates. Elution with hexane/ethylacetate (3:2, v/v) yielded **7a** as a yellow solid. Similar procedures were

used with the other alkynes and anilines for **7b**-**7t**. The amount of reagents used, product formed (with yield) and, HRMS and elemental analysis for the products are given in the Table 2.6.

2.6.3 Preparation of 8a and 8c

To a solution of **1a** (40 mg, 50 µmol) in *1,2*-dichloroethane (4 mL) was added aniline (9 µL, 100 µmol), and the reaction mixture was stirred at RT for 15 min. The reaction solvent was then removed under reduced pressure to obtain **8a** (48 mg, 96%). HRMS $[M\text{-}Cl+H]^+$: Found (Calc); 457.1146 (457.1148). ^{1}H NMR ($CDCl_3$): 1.38 (s, 15H, Cp*), 5.55 (bs, 2H, NH), 7.13-7.15 (m, 1H, aromatic), 7.26-7.33 (m, 4H, aromatic).

Similarly, *4*-methylaniline (10.7mg, 100 µmol) was reacted with **1a** (40 mg, 50 µmol) in *1,2*-dichloroethane (4 mL) to afford **8c** (49 mg, 98%). HRMS $[M\text{-}Cl+H]^+$: Found (Calc); 471.1300 (471.1305). ^{1}H NMR ($CDCl_3$): 1.38 (s, 15H, Cp*), 2.32 (s, 3H, CH_3), 5.52 (bs, 2H, NH), 7.11 (d, $^3J_{HH}$= 8.7 1H, aromatic), 7.20 (d, $^3J_{HH}$= 8.3 1H, aromatic).

2.6.4 Reaction of 8a with 3a

To a solution of **8a** (25 mg, 25 µmol) in *1,2*-dichloroethane (4 mL) was added *3,3*-dimethyl-*1*-butyne (62 µL, 20-fold excess) and the reaction mixture was stirred at RT for 24 h. The solvent was then removed under reduced pressure and the residue obtained was dissolved in the minimum amount of dichloromethane for chromatographic separation on silica gel TLC plates. Elution with hexane/ethylacetate (3:2, v/v) yielded **7a** (21.5mg, 80%).

2.6.5 Reaction of 8a with 3a and 4i

To a solution of **8a** (25 mg, 50 µmol) in *1,2*-dichloroethane (4 mL) was added *4*-methoxyaniline (6.2mg, 50 µmol) and *3,3*-dimethyl-*1*-butyne (62 µL, 20-fold excess) and the reaction mixture was stirred at RT for 24 h. The solvent was then removed under reduced pressure and the residue obtained was dissolved in the minimum amount of dichloromethane for chromatographic separation on silica gel TLC plates. Elution with hexane/ethylacetate (3:2, v/v) yielded **7a** (5.5 mg, 21%) and **7f** (20 mg, 60%).

2.6.6 Formation of cationic iridium amino-carbenes 10

In a 50 mL carius tube, *1,2*-dichloroethane solution (5 mL) of $[Cp^*IrCl_2]_2$ (40 mg, 50 µmol), *3,3*-dimethyl-*1*-butyne (125 µL, 1 mmol) and *2*-aminopyridine (10 mg, 100 µmol) was stirred at ambient temperature for 24 h. The reaction solvent was then removed under reduced pressure, followed by recrystallization from dichloromethane/diethyl ether gave pure **10a** (45 mg, 80%). Similar procedures were used with the other alkynes and *2*-aminopyridines for **10b**-**10g**. The amount of reagents used, product formed (with yield) and, HRMS, ESI-Ms and elemental analysis for the products aregiven in the Table 2.7.

2.6.7 Aerial oxidation of 10e-g

In a 50 mL round-bottomed flask, **10e** (20 mg, 29.7µmol) was dissolved in dicholoromethane (5 mL) and hexane (15 mL) and the reaction was left to reflux in the open air at 50 ^oC overnight. The solvent was then removed under reduced pressure, followed by recrystallization from dichloromethane/diethyl ether gave pure **11e** (15 mg, 74%). Similar procedures were used with **10f**-**10g** for **11f**-**11g**. The amount of reagents used, product formed (with yield) and, HRMS and ESI-Ms for the products are given in the Table 2.8.

2.6.8 Reversible deprotonation of 10 and 11

To asolution of **10a** (20 mg, 34.8 µmol) in dichlororomethane (5 mL) was added triethylamine (6 µL, 42 µmol) and stirred at RT for 15 min, filtered through silica gel and the solvent was evaporated under reduced pressure to afford pure **12a** (17 mg, 91%). The reversible protonation of **12c** (20 mg, 32.5 µmol) in dichloromethane (5 ml) with $HBF_4.OEt_2$ (5 µL, 39 µmol) afforded **10c·BF_4** (22 mg, 96%). Similar procedures were used with the other **10** and **11** for **12b**, **12c**, **13e** and **13f**. The amount of reagents used, product formed (with yield) and, HRMS, ESI-Ms and elemental analysis for the products are given in the Table 2.8.

2.6.9 Deuterium labelling experiments for 7

To a solution of **1a** (20 mg, 25 µmol) and *3,3*-dimethyl-*1*-butyne or phenylacetylene (125 or 110 µL, 20-fold excess) in *1,2*-dichloroethane (3 mL) was added the aniline (4.5 µL, 50 µmol). The reaction mixture was stirred for 24h at ambient temperature. The reaction solvent was then removed under reduced pressure and the solid obtained was analyzed by ^{1}H NMR spectroscopy.

Table 2.5. The reagents used, product formed, and ^{1}H NMR data for products**7**.

Aniline	**Alkyne**	**Product**	**δ_H, ppm**
Aniline	PhCCD	$C_{24}H_{27}ClIrN$, **7o**	1.87 (s, 15H, Cp*), 4.57 (d, $^2J_{HH}$=19.2 Hz, 1H, CH_2), 4.75 (d, 1H, CH_2), 6.84 (t, $^3J_{HH}$= 7.6 Hz, 1H, aromatic), 6.95-6.99 (m, 2H, aromatic), 7.25 (d, $^3J_{HH}$=5.5 Hz, 2H, aromatic), 7.39-7.46 (m, 3H, aromatic), 7.67 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 9.50 (s, 1H, NH).
d_7-aniline	^{t}BuCCH	$C_{22}H_{25}D_6ClIrN$ **7a-*d*$_6$**	1.13 (s, 9H, 3×CH_3), 1.75 (s, 15H, Cp*),2.74 & 3.56 (s, 1H, CH_2).
d_5-aniline	^{t}BuCCH	$C_{22}H_{27}D_4ClIrN$ **7a-*d*$_4$**	1.16 (s, 9H, 3×CH_3), 1.77 (s, 15H, Cp*), 2.79 (d, $^2J_{HH}$=12.6 Hz, 1H, CH_2), 3.63 (d, 1H, CH_2), 10.04 (s, 1H, NH).
aniline & D_2O (20µL)	^{t}BuCCH	$C_{22}H_{28}D_3ClIrN$ **7a-*d*$_3$**	1.16 (s, 9H, 3×CH_3), 1.76 (s, 15H, Cp*), 6.89 (t, $^3J_{HH}$=7.6 Hz, 1H, aromatic), 6.97 (t, $^3J_{HH}$=7.1 Hz, 1H, aromatic), 7.19 (d, $^3J_{HH}$=6.4 Hz, 1H, aromatic), 7.55 (d, $^3J_{HH}$=7.80 Hz, 1H, aromatic).

Table 2.6. Amount of reagents used, product formed, and elemental analyses and HRMS data for products **7**. In all experiments, amount of reagents used are: **1a** (40 mg, 0.05mmol), anilines, **4** (0.10mmol) andalkynes, **3** (1 mmol).

	Aniline	**Alkyne**	**Product (mg, %)**	**HRMS $[M\text{-}Cl+H]^+$:**	**Elemental analysis Found (calculated)**
1	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	^{t}BuCCH, **3a** (125 µL, 1 mmol)	$C_{22}H_{31}ClIrN$, **7a** (43.7 mg, 81%)	Found: 503.2177 Calc: 503.2164	Found: C, 48.95; H, 6.08; N, 2.98 Calc: C, 49.19; H, 5.82; N, 2.61
2	*3,5*-CH_3-C_6H_3, **4c** (13 µL, 0.1mmol)	tBuCCH, **3a** (125 µL, 1mmol	$C_{24}H_{35}ClIrN$, **7b** (17.0 mg, 30%)	Found: 531.2460 Calc: 531.2477	Found: C, 50.94; H, 6.31; N, 2.58 Calc: C, 51.00; H, 6.24; N, 2.48
3	*4*-$MeC_6H_4NH_2$, **4d** (10.7 mg, 0.1µmol)	tBuCCH, **3a** (125 µL, 1mmol)	$C_{23}H_{33}ClIrN$, **7c** (43.7 mg, 79%)	Found: 517.2318 Calc: 517.2321	Found: C, 50.23; H, 6.35; N, 2.75 Calc: C, 50.12; H, 6.03; N, 2.54
4	*3*-Br-*4*-CH_3-$C_6H_3NH_2$, **4e**(18.6 mg, 0.1mmol)	tBuCCH, **3a** (125 µL, 1mmol	$C_{23}H_{32}BrClIrN$, **7d** (44.8 mg, 71%)	Found: 595.1397 Calc: 595.1426	Found: C, 44.22; H, 5.00; N, 2.64 Calc: C, 43.84; H, 5.12; N, 2.22
5	*2*-OCH_3-$C_6H_4NH_2$, **4f** (11 µL, 0.1mmol)	tBuCCH, **3a** (125 µL, 1mmol	$C_{23}H_{33}ClIrNO$, **7e** (38.7 mg, 68%)	Found: 533.2264 Calc: 533.2270	Calc: C, 48.70; H, 5.86; N, 2.47
6	*4*-$MeOC_6H_4NH_2$, **4i** (12.4 mg, 0.1µmol)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{23}H_{33}ClIrNO$, **7f** (56.9 mg, 81%)	Found: 531.2245 Calc: 531.2246	Found: C, 48.96; H, 6.05; N, 2.61 Calc: C, 48.70; H, 5.86; N, 2.47
7	*2*-Br-$C_6H_4NH_2$, **4j** (17.2 mg, 0.1mmol	tBuCCH, **3a** (125 µL, 1mmol	$C_{22}H_{30}BrClIrN$, **7g** (45.0 mg, 73%)	Found: 581.1249 Calc: 581.1269	Found: C, 43.05; H, 5.01; N, 2.67 Calc: C, 42.89; H, 4.91; N, 2.27
8	*2*-Cl-$C_6H_4NH_2$, **4l** (11 µL, 0.1mmol)	tBuCCH, **3a** (125 µL, 1mmol)	$C_{22}H_{30}Cl_2IrN$, **7h** (39.5 mg, 69%)	Found: 537.1763 Calc: 537.1774	Found: C, 46.23; H, 5.16; N, 2.16 Calc: C, 46.23; H, 5.29; N, 2.45
9	*4*-$ClC_6H_4NH_2$, **4n** (12.8 mg, 0.1mmol)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{22}H_{30}Cl_2IrN$, **7i** (57.3 mg, 72)	Found: 535.1766 Calc: 535.1751	Found: C, 45.97; H, 5.03; N, 2.12 Calc: C, 46.23; H, 5.29; N, 2.45
10	*4*-$O_2NC_6H_4NH_2$, **4p** (13.8 mg, 0.1 mmol)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{22}H_{30}ClIrN_2O_2$, **7j** (44.4 mg, 76%)	Found: 548.2006 Calc: 548.2015	Found: C, 45.09; H, 5.04; N, 4.61 Calc: C, 45.39; H, 5.19; N, 4.81
11	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	$CH_3(CH_2)_3CCH$, **3c** (115 µL, 1mmol)	$C_{22}H_{31}ClIrN$, **7k** (27.5 mg, 51%)	Found: 503.2152 Calc: 503.2164	Found: C, 48.95; H, 6.25; N, 2.35 Calc: C, 49.19; H, 5.82; N, 2.61
12	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	$CH_3(CH_2)_5CCH$, **3e** (148 µL, 1mmol)	$C_{24}H_{35}ClIrN$, **7l** (33.4 mg, 59%)	Found: 531.2470 Calc: 531.2477	Found: C, 50.89; H, 6.34; N, 2.16 Calc: C, 51.00; H, 6.24; N, 2.48

Table 2.6 continued……

13	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	$CH_3(CH_2)_7CCH$, **3f** (181 µL, 1mmol)	$C_{26}H_{39}ClIrN$, **7m** (28.5 mg, 48%)	Found: 559.2789 Calc: 559.2790	Found: C, 52.95; H, 6.60; N, 2.72 Calc: C, 52.64; H, 6.63; N, 2.36
14	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	$Ph(CH_2)_2CCH$, **3h** (141 µL, 1mmol)	$C_{26}H_{31}ClIrN$, **7n** (35.2 mg, 60%)	Found: 585.1771 Calc: 585.1774	Found: C, 53.46; H, 5.24; N, 2.46 Calc: C, 53.36; H, 5.34; N, 2.39
15	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol)	PhCCH, **3i** (110 µL, 1 mmol)	$C_{24}H_{27}ClIrN$, **7o** (35.8 mg, 64)	Found: 523.1826 Calc: 523.1851	Found: C, 52.05; H, 4.91; N, 2.64 Calc: C, 51.74; H, 4.88; N, 2.51
16	*4*-$MeC_6H_4NH_2$, **4d** (10.7 mg, 0.1µmol)	PhCCH, **3i** (110 µL, 1 mmol)	$C_{25}H_{29}ClIrN$, **7p** (40.7 mg, 71%)	Found: 537.2003 Calc: 537.2008	Found: C, 52.16; H, 5.41; N, 2.53 Calc: C, 52.57; H, 5.12; N, 2.45
17	*4*-$MeOC_6H_4NH_2$, **4i** (12.4 mg, 0.1µmol)	PhCCH, **3i** (110 µL, 1 mmol)	$C_{25}H_{29}ClIrNO$, **7q** (43.0 mg, 73%)	Found: 553.1960 Calc: 553.1957	Found: C, 51.16; H, 4.98; N, 2.51 Calc: C, 51.14; H, 5.05; N, 2.39
18	*4*-$ClC_6H_4NH_2$, **4n** (12.8 mg, 0.1mmol)	PhCCH, **3i** (110 µL, 1 mmol))	$C_{24}H_{26}Cl_2IrN$, **7r** (40.9 mg, 69%)	Found: 557.1445 Calc: 557.1461	Found: C, 48.91; H, 4.56; N, 2.35 Calc: C, 48.73; H, 4.43; N, 2.37
19	*4*-$O_2NC_6H_4NH_2$, **4p** (13.8 mg, 0.1µmol)	PhCCH, **3i** (110 µL, 1 mmol)	$C_{24}H_{26}ClIrN_2O_2$, **7s** (39.3 mg, 65%)	Found: 568.1725 Calc: 568.1702	Found: C, 48.05; H, 64.25; N,4.76 Calc: C, 47.87; H, 4.35; N, 4.65
20	$C_6H_5NH_2$, **4a** (9 µL, 0.1mmol	*4*-$CH_3OC_6H_4CCH$, **2k**(132 µL, 1mmol)	$C_{25}H_{29}ClIrNO$, **7t** (36.5 mg, 62%)	Found: 551.1934 Calc: 551.1933	Found: C, 51.26; H, 5.06; N, 2.58 Calc: C, 51.14; H, 4.98; N, 2.39
21	$C_6H_5NHCH_3$, **4q** (10 µL, 0.1mmol)	tBuCCH, **3a** (125 µL, 1 mmol)	C23H33ClIrN, **7u** (44.0 mg, 80%)	Found: 517.2331 Calc: 517.2321	Calc: C, 50.12; H, 6.03; N, 2.54

Table 2.7. Amount of reagents used, product formed, and elemental analyses and HRMS data for products **10**. All experiments carried out using **1a** (40 mg, 0.05mmol) with aminopyridines, **5** (0.10 mmol) andalkynes, **3** (1 mmol).

	Aminopyridine	**Alkyne**	**Product (mg, %)**	**ESI-MS $[M\text{-}Cl]^+$**	**HRMS $[M\text{-}Cl+H]^+$:**	**Elemental analysis Found (calculated)**
1	*2*-NH_2-pyridine, **5a**(10.0 mg)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{21}H_{31}Cl_2IrN_2$, **10a** (45.0 mg, 80%)	539	Found: 540.1882 Calc: 540.1883	C:43.79; H:5.35; N:4.53 (C:43.90; H: 5.44; N:4.88)
2	*5*-Br-*2*-NH_2-pyridine, **5b**(17.5 mg)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{21}H_{30}BrCl_2IrN_2$, **10b** (47.1 mg, 76%)	617	Found: 618.0958 Calc: 618.0988	C:38.32; H:4.49; N:4.02 (C:38.60; H:4.63; N:4.29)
3	*6*-Br-*2*-NH_2-pyridine, **5c** (17.5 mg)	tBuCCH,**3a** (125 µL, 1 mmol)	$C_{21}H_{30}BrCl_2IrN_2$, **10c**. **Cl** (50.7 mg, 82%)	617	Found: 618.0980 Calc: 618.0988	C:38.41; H:4.52; N:4.12 (C:38.60; H:4.63; N:4.29)
4	*6*-Me-*2*-NH_2-pyridine,**5d**(11.5 mg)	tBuCCH, **3a** (125 µL, 1 mmol)	$C_{22}H_{33}Cl_2IrN_2$, **10d** (34.0 mg, 59%)	553	Found: 554.2029 Calc: 554.2040	NA
5	*6*-Br-*2*-NH_2-pyridine,**5c**(17.5 mg)	PhCCH, **3i** (110 µL, 1 mmol)	$C_{23}H_{26}BrCl_2IrN_2$, **10e** (50.8 mg, 79%)	637	Found: 638.0676 Calc: 638.0676	NA
6	*6*-Br-*2*-NH_2-pyridine,**5c**(17.5 mg)	*4*-$CH_3C_6H_4CCH$, **3l** (125 µL, 1 mmol)	$C_{24}H_{28}BrCl_2IrN_2$, **10f** (42.0 mg, 64%)	651	Found: 652.0811 Calc: 652.0832	NA
7	*6*-Br-*2*-NH_2-pyridine, **5c**(17.5 mg)	*4*-BrC_6H_4CCH, **3v** (180 mg, 1 mmol)	$C_{23}H_{25}Br_2Cl_2IrN_2$, **10g** (49.6 mg, 69%)	717	Found: 719.9765 Calc: 719.9740	NA

Table 2.8. Amount of reagents used, product formed, and elemental analyses and HRMS data for products **10**-**13**.

	Compound	**Reagents**	**product (mg, %)**	**ESI-MS**	**HRMS $[M-Cl+H]^+$:**
1	$C_{23}H_{26}BrCl_2IrN_2$, **10e** (20 mg, 29.7 µmol)	-	$C_{23}H_{24}BrCl_2IrN_2O$, **11e** (15.1 mg, 74%)	651 $[M-Cl]^+$	Found: 652.0441 Calc: 652.0468
2	$C_{24}H_{28}BrCl_2IrN_2$, **10f** (20 mg, 29.7 µmol)	-	$C_{24}H_{26}BrCl_2IrN_2O$, **11f** (16.9 mg, 83%)	665 $[M-Cl]^+$	Found: 666.0662 Calc: 666.0625
3	$C_{23}H_{25}Br_2Cl_2IrN_2$, **10g** (23 mg, 29.7 µmol)	-	$C_{23}H_{23}Br_2Cl_2IrN_2O$, **11g** (18.1 mg, 79%)	730 $[M-Cl]^+$	
4	$C_{21}H_{31}Cl_2IrN_2$, **10a** (20 mg, 34.8 µmol)	Triethylamine (6 µL, 41.8 µmol)	$C_{21}H_{30}ClIrN_2$, **12a** (17.0 mg, 91%)	539 $[M+H]^+$	Found: 504.2111 Calc: 504.2117
5	$C_{21}H_{30}BrCl_2IrN_2$, **10b** (22.7 mg, 34.8 µmol)	Triethylamine (6 µL, 41.8 µmol)	$C_{21}H_{29}BrClIrN_2$, **12b** (19.9 mg, 93%)	617 $[M+H]^+$	Found: 582.1206 Calc: 582.1222
6	$C_{21}H_{30}BrCl_2IrN_2$, **10c** (22.7 mg, 34.8 µmol)	Triethylamine (6 µL, 41.8 µmol)	$C_{21}H_{29}BrClIrN_2$, **12c** (20.0 mg, 94%)	617 $[M+H]^+$	Found: 582.1208 Calc: 582.1222
7	$C_{23}H_{24}BrCl_2IrN_2O$, **11e** (23.9 mg, 34.8 µmol)	Triethylamine (6 µL, 41.8 µmol)	$C_{23}H_{23}BrClIrN_2O$, **13e** (20.3 mg, 90%)	651 $[M+H]^+$	Found: 616.0673 Calc: 616.0701
8	$C_{24}H_{26}BrCl_2IrN_2O$, **11f** (24.4 mg, 34.8 µmol)	Triethylamine (6 µL, 41.8 µmol)	$C_{24}H_{25}BrClIrN_2O$, **13f** (21.2 mg, 92%)	665 $[M+H]^+$	Found: 630.0828 Calc: 630.0858
9	$C_{21}H_{30}BrCl_2IrN_2$, **12c** (20 mg, 32.5 µmol)	$HBF_4.OEt_2$ (5 µL, 39 µmol)	$C_{21}H_{30}BrClIrN_2BF_4$, **10c.BF$_4$** (22 mg, 96%)	539 $[M]^+$	Found: 618.0972 Calc: 618.0988
10	$C_{21}H_{30}BrCl_2IrN_2$, **12c** (20 mg, 32.5 µmol)	HCl (5 µL, 39 µmol)	$C_{21}H_{30}BrCl_2IrN_2$, **10c.Cl** (22 mg, 96%)	539 $[M]^+$	Found: 618.0972 Calc: 618.0988

Table 2.9.^{1}H and ^{13}C{^{1}H} NMR data for **7**, **8**, **10**, **11**, **12** and **13**.

	δ_H, ppm	**^{13}C{^{1}H},ppm**
7a	1.16 (s, 9H, ^{t}Bu), 1.77 (s, 15H, Cp*), 2.77 (d, $^{2}J_{HH}$= 12.6 Hz, 1H, CH_2), 3.64 (d, 1H, CH_2), 6.91 (t, $^{3}J_{HH}$= 7.5 Hz, 1H, aromatic), 6.99 (t, $^{3}J_{HH}$= 7.6 Hz, 1H, aromatic), 7.18 (d, $^{3}J_{HH}$= 8.2 Hz, 1H, aromatic), 7.56 (d, $^{3}J_{HH}$= 7.3 Hz, 1H, aromatic), 9.93 (s, 1H, NH).	9.68 (CH_3, Cp*), 30.99 (CH_3, ^{t}Bu), 35.36 (C, ^{t}Bu), 60.00 (CH_2), 95.04 (C, Cp*), 112.38, 122.58, 125.35 and 135.53, (aromatic CH), 144.89 and 151.00 (aromatic C), 227.44 (Ir=C).
7b	1.09 (s, 9H, 3×CH_3), 1.72 (s, 15H, Cp*), 2.32(s, CH_3), 2.54 (s, CH_3), 2.73 (d, $^{2}J_{HH}$=12.8 Hz, 1H, CH_2), 3.76 (d, 1H, CH_2), 6.77 (s, 1H, aromatic), 6.82 (s, 1H, aromatic), 9.93 (s, 1H, NH)	10.10 (CH_3, Cp*), 20.86 and 24.92 (Ar-CH_3), 30.9 2 (CH_3, ^{t}Bu), 35.52 (C, ^{t}Bu), 59.67 (CH_2), 95.44 (C, Cp*), 110.68 and 126.99 (CH, aromatic), 132.27, 140.29, 144.47 and 150.18 (C, aromatic), 226.29 (Ir=C).
7c	1.15 (s, 9H, ^{t}Bu), 1.77 (s, 15H, Cp*), 2.34 (s, Me), 2.75 (d, $^{2}J_{HH}$=12.6 Hz, 1H, CH_2), 3.61 (d, 1H, CH_2), 6.72 (d, $^{3}J_{HH}$= 7.8 Hz, 1H, aromatic), 7.07 (d, $^{3}J_{HH}$= 7.8 Hz, 1H, aromatic), 7.36 (s, 1H, aromatic), 9.90 (s, 1H, NH).	9.68 (CH_3, Cp*), 21.68 (CH_3, Ar), 30.98 (CH_3, ^{t}Bu), 35.30 (C, ^{t}Bu), 59.81 (CH_2), 94.78 (C, Cp*), 112.09, 123.16 and 136.16 (CH, aromatic), 134.57, 144.92 and 148.76 (C, aromatic), 225.77 (Ir=C).
7d	1.13 (s, 9H, 3×CH_3), 1.78 (s, 15H, Cp*), 2.37(s, CH_3), 2.74 (d, $^{2}J_{HH}$= 12.6 Hz, 1H, CH_2), 3.61 (d, 1H, CH_2), 7.34 (s, 1H, aromatic), 7.38 (s, 1H, aromatic), 9.90 (s, 1H, NH).	9.67 (CH_3, Cp*), 22.95 (Ar-CH_3), 30.97 (CH_3, ^{t}Bu), 35.46 (C, ^{t}Bu), 59.99 (CH_2), 95.17 (C, Cp*), 115.96 and 137.30 (CH, aromatic), 117.94, 133.89, 143.88 and 150.35 (C, aromatic), 228.15 (Ir=C).
7e	1.16 (s, 9H, 3×CH_3), 1.77 (s, 15H, Cp*), 2.83 (d, $^{2}J_{HH}$=12.8 Hz, 1H, CH_2), 3.62 (d, 1H, CH_2), 3.84 (s, OCH_3), 6.46 (d, $^{3}J_{HH}$=7.8 Hz, 1H aromatic), 7.01 (t, $^{3}J_{HH}$=7.8 Hz, 1H, aromatic), 7.16 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 10.31 (s, 1H, NH).	9.66 (CH_3, Cp*), 30.97 (CH_3, ^{t}Bu), 35.09 (C, ^{t}Bu), 55.39 (Ar-OCH_3), 59.75 (CH_2), 94.77 (C, Cp*), 104.32, 126.45 and 127.57 (CH, aromatic), 139.40, 146.33 and 146.62 (C, aromatic), 225.23 (Ir=C).
7f	1.15 (s, 9H, ^{t}Bu), 1.77 (s, 15H, Cp*), 2.75 (d, $^{2}J_{HH}$ = 12.6 Hz, 1H, CH_2), 3.58 (d, 1H, CH_2), 3.82 (s, OMe), 6.48 (m, 1H, aromatic), 7.11 (m, 1H, aromatic), 7.14 (m, 1H, aromatic), 9.89 (s, 1H, NH)	9.65 (CH_3, Cp*), 30.97 (CH_3, ^{t}Bu), 35.19 (C, ^{t}Bu), 55.56 (OMe), 59.70 (CH_2), 94.66 (C, Cp*), 107.29, 112.91 and 120.90 (CH, aromatic), 145.10, 146.92 and 156.88 (C, aromatic), 223.91 (Ir=C)

Table 2.9. continued. ……

7g	1.18 (s, 9H, 3×CH_3), 1.77 (s, 15H, Cp*), 2.88 (d, $^2J_{HH}$=13.3 Hz, 1H, CH_2), 3.63 (d, 1H, CH_2), 6.88 (t, $^3J_{HH}$=7.6 Hz, 1H aromatic), 7.03 (d, $^3J_{HH}$=7.8, 1H, aromatic), 7.45 (d, $^3J_{HH}$=6.9 Hz, 1H, aromatic), 10.21 (s, 1H, NH).	9.63 (CH_3, Cp*), 30.96 (CH_3, ^{t}Bu), 35.08 (C, ^{t}Bu), 60.13 (CH_2), 95.45 (C, Cp*), 105.70, 146.22 and 149.14 (C, aromatic), 125.08, 127.30 and 134.31 (CH, aromatic), 228.96 (Ir=C).
7h	1.17 (s, 9H, 3×CH_3), 1.77 (s, 15H, Cp*), 2.87 (d, $^2J_{HH}$=13.0 Hz, 1H, CH_2), 3.64 (d, 1H, CH_2), 6.88 (d, $^3J_{HH}$=8.2 Hz, 1H aromatic), 6.96 (t, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 7.41 (d, $^3J_{HH}$= 7.3 Hz, 1H, aromatic), 10.23 (s, 1H, NH).	9.64 (CH_3, Cp*), 30.97 (CH_3, ^{t}Bu), 35.17 (C, ^{t}Bu), 60.17(CH_2), 95.46 (C, Cp*), 117.02, 145.99 and 147.75 (C, aromatic), 122.16, 126.91 and 133.68 (CH, aromatic), 229.16 (Ir=C).
7i	1.15 (s, 9H, ^{t}Bu), 1.77 (s, 15H, Cp*), 2.77 (d, $^2J_{HH}$ = 12.8 Hz, 1H, CH_2), 3.63 (d, 1H, CH_2), 6.90 (m, 1H, aromatic), 7.11 (m, 1H, aromatic), 7.47 (m, 1H, aromatic), 9.91 (s, 1H, NH)	9.66 (CH_3, Cp*), 31.00 (CH_3, ^{t}Bu), 35.44 (C, ^{t}Bu), 60.05 (CH_2), 95.30 (C, Cp*), 113.20, 122.43 and 134.81 (CH, aromatic), 129.77, 146.97 and 149.70 (C, aromatic), 227.73 (Ir=C)
7j	1.17 (s, 9H, ^{t}Bu), 1.80 (s, 15H, Cp*), 2.80 (d, $^2J_{HH}$ = 12.8 Hz, 1H, CH_2), 3.70 (d, 1H, CH_2), 7.26 (d, $^3J_{HH}$= 7.8 Hz, 1H, aromatic), 7.85 (d, $^3J_{HH}$= 8.7 Hz, 1H, aromatic), 8.41 (s, 1H, aromatic), 10.04 (s, 1H, NH).	9.73 (CH_3, Cp*), 31.06 (CH_3, ^{t}Bu), 35.96 (C, ^{t}Bu), 60.56 (CH_2), 96.48 (C, Cp*), 111.53, 120.02 and 130.26 (CH, aromatic), 144.32, 145.49 and 156.62 (C, aromatic), 233.64 (Ir=C).
7k	0.92 (t, $^3J_{HH}$=7.1 Hz, 3H, CH_3), 1.35-1.44 (m, 4H, 2×CH_2), 1.63-1.70 (m, 1H, CH_2), 1.80 (s, 15H, Cp*), 1.82-1.96 (m, 1H, CH_2), 3.11-3.19 (m, 1H, CH_2), 3.35-3.42 (m, 1H, CH_2), 6.90 (t, $^3J_{HH}$=7.6 Hz, 1H, aromatic), 6.99 (t, $^3J_{HH}$=7.3 Hz, 1H, aromatic), 7.18 (d, $^3J_{HH}$=7.6 Hz, 1H, aromatic), 7.63 (d, $^3J_{HH}$ = 7.6 Hz, 1H, aromatic), 10.05 (s, 1H, NH).	9.55 (CH_3, Cp*), 14.27 (CH_3), 22.66, 26.08, 32.04 and 47.20 (CH_2), 94.18 (C, Cp*), 113.13, 122.38, 125.37 and 135.26 (CH, aromatic), 144.63 and 151.41 (C, aromatic), 227.70 (Ir=C).
7l	0.89 (t, J_{HH}=7.1 Hz, 3H, CH_3), 1.25-1.42 (m, 8H, 4×CH_2), 1.54-1.66 (m, 2H, CH_2), 1.77-1.87 (m, 16H, Cp*+CH_2), 3.11-3.19 (m, 1H, CH_2), 3.28-3.36 (m, 1H, CH_2), 6.88 (t, $^3J_{HH}$ = 7.6 Hz, 1H, aromatic), 6.97 (t, $^3J_{HH}$= 7.6 Hz, 1H, aromatic), 7.17 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 7.62 (d, $^3J_{HH}$=7.3 Hz, 1H, aromatic), 10.16 (s, 1H, NH).	9.55 (CH_3, Cp*), 14.30 (CH_3), 22.83, 26.35, 29.23, 29.82, 31.95 and 47.21(CH_2), 94.14 (C, Cp*), 113.19, 122.35, 125.34 and 135.24 (CH, aromatic), 144.62 and 151.49 (C, aromatic), 227.64 (Ir=C).

Table 2.9. continued. ……

7m	0.88 (t, *J*=6.86, 3H, CH_3), 1.25-1.58 (m, 12H, 6×CH_2), 1.61-1.79 (m, 1H, CH_2), 1.82 (s, 15H, Cp*), 1.83-1.95 (m, 1H, CH_2), 3.12-3.20 (m, 1H, CH_2), 3.32-3.40 (m, 1H, CH_2), 6.89 (t, $^3J_{HH}$=7.5 Hz, 1H, aromatic), 6.98 (t, $^3J_{HH}$=7.4 Hz, 1H, aromatic), 7.18 (d, $^3J_{HH}$=7.6 Hz, 1H, aromatic), 7.63 (d, $^3J_{HH}$=7.1 Hz, 1H, aromatic), 10.10 (s, 1H, NH).	9.55 (CH_3, Cp*), 14.34 (CH_3), 22.89, 26.35, 29.50, 29.59, 29.73, 29.87, 32.09 and 47.26 (CH_2), 94.19 (C, Cp*), 113.08, 122.40, 125.40 and 135.28 (CH, aromatic), 144.62 and 151.37 (CH, aromatic), 227.72 (Ir=C).
7n	1.73 (s, 15H, Cp*), 1.95-2.04 (m, 1H, CH_2), 2.12-2.21 (m, 1H, CH_2), 2.71 (t, $^3J_{HH}$=7.3 Hz, 2H, CH_2Ph), 3.04-3.12 (m, 1H, CH_2), 3.31-3.39 (m, 1H, CH_2), 6.89 (t, $^3J_{HH}$= 7.6 Hz, 1H, aromatic), 6.98 (t, $^3J_{HH}$=7.4 Hz, 1H, aromatic), 7.13-7.23 (m, 4H, aromatic), 7.29-7.32 (m, 2H, aromatic), 7.62 (d, $^3J_{HH}$= 7.6 Hz, 1H, aromatic), 10.08 (s, 1H, NH).	9.48 (CH_3, Cp*), 28.02, 35.64 and 46.43 (CH_2), 94.30 (C, Cp*), 113.14, 122.42, 125.44, 126.32, 128.69, 128.97 and 135.29 (CH, aromatic), 141.75, 144.75 and 151.05 (C, aromatic), 226.88 (Ir=C).
7o	1.87 (s, 15H, Cp*), 4.58 (d, $^2J_{HH}$ = 18.8 Hz, 1H, CH_2), 4.76 (d, 1H, CH_2), 6.85 (t, $^3J_{HH}$= 7.5 Hz, 1H, aromatic), 6.97 (t, $^3J_{HH}$= 7.4 Hz, 2H, aromatic), 7.27 (d, $^3J_{HH}$= 5.5 Hz, 2H, aromatic), 7.39-7.46 (m, 3H, aromatic), 7.68 (d, $^3J_{HH}$= 7.4 Hz, 1H, aromatic), 9.50 (s, 1H, NH).	9.65 (CH_3, Cp*), 52.80 (CH_2), 94.07 (C, Cp*), 113.40, 122.41, 125.60, 128.12, 129.75, 130.39 and 135.28 (CH, aromatic), 134.48, 144.50 and 151.10 (C, aromatic), 224.22 (Ir=C).
7p	1.87 (s, 15H, Cp*), 2.34 (s, Me), 4.55 (d, $^2J_{HH}$ = 19.0 Hz, 1H, CH_2), 4.73 (d, 1H, CH_2), 6.65 (d, $^3J_{HH}$= 7.8 Hz, 1H, aromatic), 6.87 (d, $^3J_{HH}$= 7.8 Hz, 1H, aromatic), 7.26 (d, $^3J_{HH}$= 5.7 Hz, 2H, aromatic), 7.38-7.48 (m, 4H, aromatic), 9.47 (s, 1H, NH).	9.65 (CH_3, Cp*), 21.66 (CH_3, Ar), 52.75 (CH_2), 93.83 (C, Cp*), 113.04, 123.01, 128.13, 129.71, 130.38, 134.72, 134.86, 135.93, 144.58 and 148.92 (aromatic), 222.76 (Ir=C).
7q	1.87 (s, 15H, Cp*), 3.82 (s, OMe), 4.54 (d, $^2J_{HH}$ = 19.0 Hz, 1H, CH_2), 4.70 (d, 1H, CH_2), 6.41 (d, $^3J_{HH}$= 8.5 Hz, 1H, aromatic), 6.91 (d, $^3J_{HH}$= 8.2 Hz, 1H, aromatic), 7.24-7.27 (m, 3H, aromatic), 7.38-7.45 (m, 3H, aromatic), 9.46 (s, 1H, NH).	9.61 (CH_3, Cp*), 52.53 (CH_2), 55.48 (OMe), 93.75 (C, Cp*), 107.09, 113.91, 120.63, 128.12, 129.69 and 130.39 (CH, aromatic), 134.67, 145.21, 146.57 and 157.00 (C, aromatic), 220.88 (Ir=C).

Table 2.9. continued. ……

7r	1.86 (s, 15H, Cp*), 4.55 (d, $^{2}J_{HH}$ = 19.2 Hz, 1H, CH_2), 4.72 (d, 1H, CH_2), 6.82 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 6.91 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.25 (d, $^{3}J_{HH}$ = 6.4 Hz, 2H, aromatic), 7.39-7.46 (m, 3H, aromatic), 7.58 (s, 1H aromatic), 9.53 (s, 1H, NH).	9.61 (CH_3, Cp*), 52.88 (CH_2), 94.30 (C, Cp*), 114.26, 122.19, 128.29, 129.79, 130.20, 130.35, 134.32, 134.56, 146.79 and 149.76 (aromatic), 225.14 (Ir=C).
7s	1.89 (s, 15H, Cp*), 4.58 (d, $^{2}J_{HH}$ = 19.0 Hz, 1H, CH_2), 4.78 (d, 1H, CH_2), 7.08 (d, $^{3}J_{HH}$= 8.2 Hz, 1H, aromatic), 7.25-7.27 (m, 2H, aromatic), 7.40-7.48 (m, 3H, aromatic), 7.76 (d, $^{3}J_{HH}$= 8.7 Hz, 1H, aromatic), 8.51 (s, 1H, aromatic), 9.78 (s, 1H, NH).	9.65 (CH_3, Cp*), 53.58 (CH_2), 95.35 (C, Cp*), 113.01, 113.51, 119.48, 126.51, 128.52, 129.92, 130.31, 133.94, 144.47, 145.53 and 156.73 (aromatic), 231.29 (Ir=C).
7t	1.86 (s, 15H, Cp*), 3.85 (s, OCH3), 4.52 (d, $^{2}J_{HH}$=19.20 Hz, 1H, CH_2), 4.69 (d, 1H, CH_2), 6.84 (t, $^{3}J_{HH}$ = 7.6 Hz, 1H, aromatic), 6.95-7.00 (m, 4H, aromatic), 7.17 (d, $^{3}J_{HH}$=8.2 Hz, 1H, aromatic), 7.25 (s, 1H, aromatic), 7.67 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 9.55 (s, 1H, NH).	9.64 (CH_3, Cp*), 52.08 (CH_2), 55.56 (Ar-OCH_3), 93.98 (C, Cp*), 113.38, 115.06, 122.38, 125.54, 126.43, 131.50, 135.27, 144.69, 151.10 and 159.43 (C & CH, aromatic), 225.07 (Ir=C).
7u	1.20 (s, 9H, 3×CH_3), 1.73 (s, 15H, Cp*), 3.43 (d, $^{2}J_{HH}$= 12.4 Hz, 1H, CH_2), 3.58(s, CH_3, N-CH_3), 3.76 (d, 1H, CH_2), 6.98(t, $^{3}J_{HH}$=7.6 Hz, 1H, aromatic), 7.05-7.09 (m, 2H, aromatic), 7.56 (d, $^{3}J_{HH}$=7.8 Hz, 1H, aromatic).	9.96 (CH_3, Cp*), 31.44 (CH_3, ^{t}Bu), 36.46 (C, ^{t}Bu), 37.19 (N-CH_3), 56.19 (CH_2), 95.23 (C, Cp*), 113.71, 122.06, 126.32 and 135.62 (CH, aromatic), 146.69 and 154.93 (C, aromatic), 227.53 (Ir=C).
10a	1.17 (s, 9H, ^{t}Bu), 1.70 (s, 15H, Cp*), 3.51 (d, $^{2}J_{HH}$= 10.6 Hz, 1H, CH_2), 3.65 (d, 1H, CH_2), 7.35 (t, $^{3}J_{HH}$=6.4 Hz, 1H, aromatic), 7.85 (t, $^{3}J_{HH}$=7.6 Hz, 1H, aromatic), 8.25 (d, $^{3}J_{HH}$=5.5 Hz, 1H, aromatic), 8.55 (d, $^{3}J_{HH}$=8.2 Hz, 1H, aromatic).	9.47 (CH_3, Cp*), 31.08 (CH_3, ^{t}Bu), 37.22 (C, ^{t}Bu), 58.14 (CH_2), 95.49 (C, Cp*), 116.52, 123.13, 141.29, 148.99 and 158.72 (C, aromatic), 241.51 (Ir=C).
10b	1.19 (s, 9H, ^{t}Bu), 1.73 (s, 15H, Cp*), 3.52 (d, $^{2}J_{HH}$=10.5 Hz, 1H, CH_2), 3.65 (d, 1H, CH_2), 7.96 (d, $^{3}J_{HH}$=7.8 Hz, 1H, aromatic), 8.27 (s, 1H, aromatic), 8.56 (d, $^{3}J_{HH}$=8.7 Hz, 1H, aromatic).	9.52 (CH_3, Cp*), 31.16 (CH_3, ^{t}Bu), 37.53 (C, ^{t}Bu), 58.49 (CH_2), 95.82 (C, Cp*), 117.27, 117.51, 143.97, 149.15 and 157.73 (C, aromatic), 242.39 (Ir=C).

Table 2.9. continued. ……

10c. Cl	1.17 (s, 9H, ^{t}Bu), 1.72 (s, 15H, Cp*), 3.57 (d, $^{2}J_{HH}$=10.5 Hz, 1H, CH_2), 3.79 (d, 1H, CH_2), 7.66-7.69 (m, 2H, aromatic), 8.62 (d, $^{3}J_{HH}$=5.0 Hz, 1H, aromatic).	10.76 (CH_3, Cp*), 31.18 (CH_3, ^{t}Bu), 37.71 (C, ^{t}Bu), 57.61 (CH_2), 96.83 (C, Cp*), 114.81, 127.41, 142.24, 144.04 and 159.21 (C, aromatic), 242.31 (Ir=C).
10c. BF_4	1.13 (s, 9H, ^{t}Bu), 1.75 (s, 15H, Cp*), 3.33 (d, $^{2}J_{HH}$=11.5 Hz, 1H, CH_2), 3.72 (d, 1H, CH_2), 7.70 (d, $^{3}J_{HH}$= 8.0 Hz, 1H, aromatic), 7.77 (t, $^{3}J_{HH}$= 8.0 Hz, 1H, aromatic), 8.06 (d, $^{3}J_{HH}$=8.0 Hz, 1H, aromatic).	10.58 (CH_3, Cp*), 31.08 (CH_3, ^{t}Bu), 37.79 (C, ^{t}Bu), 58.96 (CH_2), 97.54 (C, Cp*), 113.69, 127.68, 142.97, 144.54 and 158.01 (C, aromatic), 244.37 (Ir=C).
10d	1.18 (s, 9H, ^{t}Bu), 1.70 (s, 15H, Cp*), 2.96 (s, 3H, CH_3), 3.58 (d, $^{2}J_{HH}$=10.5 Hz, 1H, CH_2), 3.84 (d, 1H, CH_2), 7.28 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 7.7 (t, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 8.43 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic).	10.32 (CH_3, Cp*), 26.61 (CH_3), 31.21 (CH_3, ^{t}Bu), 37.46 (C, ^{t}Bu), 57.66 (CH_2), 95.65 (C, Cp*), 113.80, 122.23, 141.00, 145.57 and 160.44 (C, aromatic), 239.78 (Ir=C).
10e	1.74 (s, 15H, Cp*), 4.81 (d, $^{2}J_{HH}$=13.3 Hz, 1H, CH_2), 5.20 (d, 1H, CH_2), 7.18 (t, $^{3}J_{HH}$= 7.3 Hz, 1H, aromatic), 7.24-7.28 (m, 2H, aromatic), 7.53 (d, $^{3}J_{HH}$= 7.8 Hz, 2H, aromatic), 7.60-7.64 (m, 2H, aromatic), 8.58 (d, $^{3}J_{HH}$= 7.8 Hz, 1H, aromatic).	10.66 (CH_3, Cp*), 51.90 (CH_2), 96.94 (C, Cp*), 115.18, 127.11, 127.69, 128.69, 130.92, 132.75, 142.04, 144.18 and 159.87 (C, aromatic), 237.91 (Ir=C).
10f	1.75 (s, 15H, Cp*), 2.23 (s, 3H, CH_3), 4.81 (d, $^{2}J_{HH}$=13.3 Hz, 1H, CH_2), 5.13 (d, 1H, CH_2), 7.06 (d, $^{3}J_{HH}$=7.8 Hz, 2H, aromatic), 7.43 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic), 7.59-7.64 (m, 2H, aromatic), 8.56 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic).	10.67 (CH_3, Cp*), 21.30 (CH_3), 51.62 (CH_2), 96.89 (C, Cp*), 115.09, 127.01, 129.37, 129.58, 130.77, 137.23, 142.01, 144.14 and 159.88 (C, aromatic), 238.17 (Ir=C).
10g	1.76 (s, 15H, Cp*), 4.77 (d, $^{2}J_{HH}$=12.8 Hz, 1H, CH_2), 5.16 (d, 1H, CH_2), 7.38 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic), 7.47 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic), 7.62-7.66 (m, 2H, aromatic), 8.53 (d, $^{3}J_{HH}$=7.4 Hz, 1H, aromatic).	10.73 (CH_3, Cp*), 51.11 (CH_2), 97.06 (C, Cp*), 115.13, 121.97, 127.25, 131.68, 131.77, 132.70, 142.17, 144.28 and 159.81 (C, aromatic), 237.08 (Ir=C).
11e	1.67 (s, 15H, Cp*), 7.48 (t, $^{3}J_{HH}$= 7.6 Hz, 2H, aromatic), 7.61 (t, $^{3}J_{HH}$= 7.3 Hz,1H, aromatic), 7.76-7.79 (m, 2H, aromatic), 8.17 (d, $^{3}J_{HH}$=7.8 Hz, 2H, aromatic), 8.77(d, $^{3}J_{HH}$= 6.9 Hz, 1H, aromatic).	10.16 (CH_3, Cp*), 98.00 (C, Cp*), 116.93, 128.46, 129.28, 130.67, 133.57, 135.51, 142.53 and 144.62, 159.66 (C, aromatic), 193.95 (C=O), 231.26 (Ir=C).

Table 2.9. continued. ……

11f	1.66 (s, 15H, Cp*), 2.39 (s, 3H, CH_3), 7.27 (d, $^3J_{HH}$= 6.4 Hz, 2H, aromatic), 7.75-7.83 (m, 2H, aromatic), 8.05 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 8.76 (d, $^3J_{HH}$= 5.0 Hz 1H, aromatic).	10.20 (CH_3, Cp*), 22.27 (CH_3), 97.94 (C, Cp*), 116.84, 128.43, 130.01, 130.74, 131.21, 142.49, 144.63 and 146.80, 159.68 (C, aromatic), 193.46 (C=O), 231.54 (Ir=C).
11g	1.67 (s, 15H, Cp*), 7.62 (d, $^3J_{HH}$= 8.2 Hz, 2H, aromatic), 7.74-7.82 (m, 2H, aromatic), 8.05 (d, $^3J_{HH}$= 8.7 Hz, 2H, aromatic), 8.65-8.68 (m, 1H, aromatic).	10.21 (CH_3, Cp*), 97.76 (C, Cp*), 116.37, 117.02 128.37, 131.16, 131.93, 132.39, 132.70, 142.46 and 144.64 (C, aromatic), 193.40 (C=O), 230.18 (Ir=C).
12a	1.17 (s, 9H, ^{t}Bu), 1.69 (s, 15H, Cp*), 3.16 (d, $^2J_{HH}$= 16.0 Hz, 1H, CH_2), 3.32 (d, 1H, CH_2), 6.91 (t, $^3J_{HH}$=6.4 Hz, 1H, aromatic), 7.59 (t, $^3J_{HH}$=8.0 Hz, 1H, aromatic), 7.68 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 8.29 (d, $^3J_{HH}$=5.9 Hz, 1H, aromatic).	9.32 (CH_3, Cp*), 30.81 (CH_3, ^{t}Bu), 33.84 (C, ^{t}Bu), 61.92 (CH_2), 91.08 (C, Cp*), 118.34, 118.89, 138.98, 148.08 and 173.94 (C, aromatic), 231.16 (Ir=C).
12b	1.16 (s, 9H, ^{t}Bu), 1.69 (s, 15H, Cp*), 3.14 (d, $^2J_{HH}$=16.0 Hz, 1H, CH_2), 3.29 (d, 1H, CH_2), 7.55 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 7.68 (d, $^3J_{HH}$= 9.2 Hz, 1H, aromatic), 8.34 (s, 1H, aromatic).	9.31 (CH_3, Cp*), 30.77 (CH_3, ^{t}Bu), 33.79 (C, ^{t}Bu), 62.10 (CH_2), 91.39 (C, Cp*), 112.33, 119.10, 141.54, 148.31 and 172.99 (C, aromatic), 232.92 (Ir=C).
12c	1.13 (s, 9H, ^{t}Bu), 1.66 (s, 15H, Cp*), 3.19 (d, $^2J_{HH}$=16.9 Hz, 1H, CH_2), 3.34 (d, 1H, CH_2), 7.22 (d, $^3J_{HH}$= 7.3 Hz, 1H, aromatic), 7.37 (t, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 7.53 (d, $^3J_{HH}$= 8.2 Hz, 1H, aromatic).	10.36 (CH_3, Cp*), 30.67 (CH_3, ^{t}Bu), 33.54 (C, ^{t}Bu), 61.97 (CH_2), 92.03 (C, Cp*), 116.25, 122.14, 139.49, 142.08 and 173.99 (C, aromatic), 233.53 (Ir=C).
13e	1.63 (s, 15H, Cp*), 7.40-7.54 (m, 5H, aromatic), 7.77 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 8.24 (d, $^3J_{HH}$=8.24 Hz, 2H, aromatic).	10.05 (CH_3, Cp*), 93.59 (C, Cp*), 118.38, 124.70, 128.54, 130.80, 133.73, 134.43, 140.58, 142.84, 173.51 (C, aromatic), 198.95 (C=O), 226.19 (Ir=C).
13f	1.63 (s, 15H, Cp*), 2.37 (s, 3H, CH_3), 7.22 (d, $^3J_{HH}$= 7.8 Hz, 2H, aromatic), 7.43-7.51 (m, 2H, aromatic), 7.76 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 8.12 (d, $^3J_{HH}$= 8.2 Hz 1H, aromatic).	10.03 (CH_3, Cp*), 22.07 (CH_3), 93.54 (C, Cp*), 118.33, 124.62, 129.29, 130.90, 132.00, 140.54, 142.82, 144.57 and 173.58 (C, aromatic), 198.69 (C=O), 226.53 (Ir=C).

Table 2.10. Crystal and refinement data for **7a**, **7c** and **8c**.

Identification code	**7a**	**7c**	**8c**
Empirical formula	C_{22} H_{31} Cl Ir N	C_{23} H_{18} Cl Ir N.¼CH_2Cl_2	C_{17} H_{24} Cl_2 Ir N
Formula weight	537.13	557.17	505.47
Crystal system	Monoclinic	Tetragonal	Triclinic
Space group	$P2_1/c$	$I\bar{4}$	$P\bar{1}$
a, Å	a = 11.2917(8) Å	a = 22.7532(4) Å	a = 7.6373(3) Å
b, Å	b = 9.0419(6) Å	b = 22.7532(4) Å	b = 10.1289(4) Å
c, Å	c = 21.5490(16) Å	c = 9.0625(4) Å	c = 12.9160(5) Å
α, deg	90	90	111.5660(10)
β, deg	104.6680(10)	90	91.2870(10)
γ, deg	90	90	98.6600(10)
Volume, $Å^3$	2128.4(3)	4691.7(2)	915.31(6)
Z	4	8	2
Density(calc) Mg/m^3	1.676	1.578	1.834
Abs coefficient, mm^{-1}	6.403	5.868	7.579
F(000)	1056	2140	488
Crystal size, mm^3	0.27 x 0.16 x 0.12	0.33 x 0.06 x 0.05	0.30 x 0.28 x 0.28
Reflections collected	20603	19841	14003
Independent reflections	4352 [R(int) = 0.0371]	4803 [R(int) = 0.0361]	3752 [R(int) = 0.0238]
Completeness (to θ, deg)	26.37 (100.0)	26.36 (99.8)	26.37 (100.0)
Max. and min. transmission	0.5138 and 0.2768	0.7579 and 0.2476	0.2254 and 0.2095
Data / restraints / parameters	4352 / 0 / 238	4803 / 19 / 270	3752 / 0 / 204
Goodness-of-fit on F^2	1.231	1.128	1.053
Final R indices [I>2sigma(I)]	R1 = 0.0511, wR2 = 0.1101	R1 = 0.0284, wR2 = 0.0701	R1 = 0.0175, wR2 = 0.0439
R indices (all data)	R1 = 0.0573, wR2 = 0.1125	R1 = 0.0295, wR2 = 0.0744	R1 = 0.0183, wR2 = 0.0442
Absolute structure parameter	-	-0.013(11)	-
Largest diff. peak and hole, $e.Å^{-3}$	3.948 and -2.576	1.226 and -0.479	1.102 and -0.600

Table 2.11. Crystal and refinement data for **10c**, **10c·BF_4** and **11e**.

Identification code	**10c·Cl**	**10c·BF4**	**11e**
Empirical formula	$C_{23}H_{34}BrCl_6Ir\ N_2$	$C_{21}H_{29}BBrClF_4Ir\ N_2$	$C_{25}H_{27}BrCl_5Ir\ N_2O$
Formula weight	823.33	703.83	814.84
Temperature, K	103(2)	296(2)	103(2)
Crystal system	Monoclinic	orthorhombic	Monoclinic
Space group	P2(1)/c	Pbca	P2(1)/c
a, Å	17.1605(7)	13.5702(11)	9.6911(4)
b, Å	10.9386(3)	13.1705(10)	22.7375(7)
c, Å	15.6735(6)	27.7649(18)	27.3923(8)
β, deg	96.499(10)	90.0	95.046(10)
Volume, $Å^3$	2923.19(18)	4964.0(6)	6012.4(4)
Z	4	8	8
Density(calc) Mg/m^3	1.871	1.884	1.800
Abs coefficient, mm^{-1}	6.499	7.138	6.235
F(000)	1600	2712	3144
Crystal size, mm^3	0.30 x 0.20 x 0.12	0.30 x 0.30 x 0.20	0.40 x 0.14 x 0.02
Reflections collected	35751	47498	91092
Independent reflections	5966 [R(int) = 0.0374]	5072 [R(int) = 0.0624]	12236 [R(int) =0.0636]
Completeness (to θ, deg)	99.7 % (26.37°)	99.9 % (26.37°)	99.7 % (26.37°)
Max.and min. transmission	0.5093 and 0.2459	0.3294 and0.2233	0.8854 and0.1894
Data / restraints / parameters	5966/6/306	5072/316/300	12236/54/662
Goodness-of-fit on F^2	1.191	1.125	1.108
Final R indices [I>2sigma(I)]	R1 = 0.0518, wR2 = 0.1252	R1 = 0.0404, wR2 = 0.1067	R1 = 0.0497, wR2 = 0.1081
R indices (all data)	R1 = 0.0600, wR2 = 0.1287	R1 = 0.0711, wR2 = 0.1362	R1 = 0.0790, wR2 = 0.1287
Largest diff. peak and hole, $e.Å^{-3}$	4.146 and -3.269	1.775 and -1.817	3.294 and -2.815

Table 2.12. Crystal and refinement data for **11f**, **12b** and **13e**.

Identification code	**11f**	**12b**	**13e**
Empirical formula	$C_{26}H_{30}BrCl_6Ir\ N_2O$	$C_{21}H_{29}BrClIr\ N_2$	$C_{23}H_{23}BrClIr\ N_2O$
Formula weight	850.10	617.02	650.99
Temperature, K	103(2)	296(2)	103(2)
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	P2(1)/c	P-1	P2(1)/n
a, Å	9.4513(2)	8.0767(5)	15.1691(7)
b, Å	22.3781(5)	11.9633(9)	9.8575(3)
c, Å	29.0848(6)	12.6252(9)	16.1962(6)
β, deg	92.5970(10)	96.291(4)	117.412(10)
Volume, $Å^3$	6145.2(2)	1129.83(14)	2149.88(9)
Z	8	2	4
Density(calc) Mg/m^3	1.838	1.814	2.011
Abs coefficient, mm^{-1}	6.147	7.802	8.210
F(000)	3292	596	1248
Crystal size, mm^3	0.20 x 0.20 x 0.10	0.40 x 0.22 x 0.20	0.12 x 0.08 x 0.06
Reflections collected	64543	22240	31091
Independent reflections	15631R(int) = 0.0937]	6855[R(int) = 0.0565]	4389[R(int) = 0.0457]
Completeness (to θ, deg)	98.7 % (28.66°)	99.0 % (30.56°)	99.9 % (26.37°)
Max.and min. transmission	0.5785 and 0.3728	0.3044 and 0.1464	0.6386 and 0.4391
Data / restraints / parameters	15631/0/679	6855/669/373	4389/0/268
Goodness-of-fit on F^2	1.019	1.046	1.131
Final R indices [I>2sigma(I)]	R1 = 0.0479, wR2 =0.1019	R1 = 0.0420, wR2 = 0.1003	R1 = 0.0278, wR2 = 0.0769
R indices (all data)	R1 = 0.1105, wR2 = 0.1296	R1 = 0.0820, wR2 = 0.1360	R1 = 0.0387, wR2 = 0.0847
Largest diff. peak and hole, $e.Å^{-3}$	1.850 and -2.025	1.113 and -1.983	2.485 and -1.568

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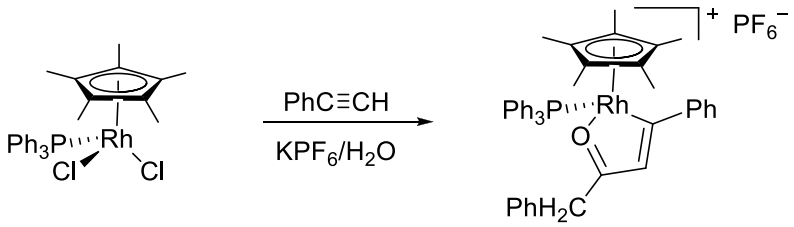
Chapter 3: The Reactivity of $[Cp^*RhCl_2]_2$ with Terminal Alkynes and Amines: Formation of Rhodapyrrole Derivatives

In chapter 2, we have described the reactivity of $[Cp^*IrCl_2]_2$, **1a** with a number of arylamines and terminal alkynes to afford a series of iridium amino-carbene derivatives. A similar rhodium complex has also been shown to activate terminal alkynes in the presence of water to afford a variety of rhodium alkenyl ketone complexes (Scheme 3.1).[1]



Scheme 3.1

The proposed reaction pathways for both reactions involve the formation of a vinylidene intermediate followed by nucleophilic attack at the α-carbon of the vinylidene and further rearrangements to furnish the final product. It therefore became of interest to extend our study to the analogous rhodium complex $[Cp^*RhCl_2]_2$, **1b**. From the reaction of $[Cp^*RhCl_2]_2$, **1b** with terminal alkyne and aniline, we can expect two possible products: i) an orthometallated rhodium amino-carbene complex of type **14**, or ii) a cyclometallated rhodium complex of type **15** (Figure 3.1).

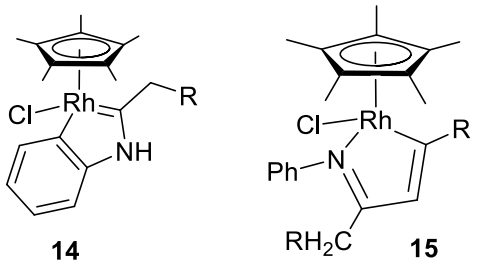
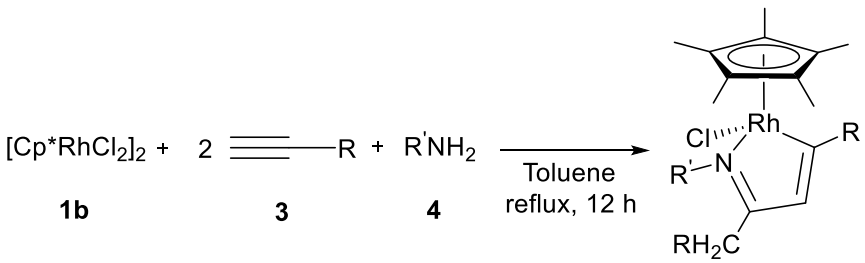


Figure 3.1. Possible products from the reaction of **1b** with aniline and terminal alkyne.

3.1 Reaction of 1b with phenylacetylenes and amines

The reaction of **1b** with a primary aliphatic or aromatic amine ($R'NH_2$), **4**, and a terminal alkyne (RCCH), **3**, afforded the cyclometallated rhodium complexes **15** in good isolated yields; no aminocarbenes were observed (Table 3.1). Similar metallacyclic complexes for various transition metals have been synthesized by various methods such as transmetallation,[2] condensation of ketone complexes with amines,[3] and ortho C-H activation of the corresponding aromatic imine,[4] or amine.[5] In particular, the syntheses of N-containing cyclometallated complexes of Cp*Rh (Cp*= pentamethylcyclopentadienyl) have involved base-assisted cyclometallation of 2-acetylpyridine,[6] or orthometallation of an imine, pyridine or related species.[7]

Table 3.1. Substrate scope study for rhoda-pyrrole derivatives.



1b **3** **4** **15**

	R	R'	Yield (%)		R	R'	Yield (%)
1	Ph	Ph	**15a**, 68	8	*3*-$CH_3C_6H_4$	Ph	**15h**, 64
2	Ph	*4*-$CH_3C_6H_4$	**15b**, 70	9	*4*-$CH_3C_6H_4$	Ph	**15i**, 63
3	Ph	*4*-$CH_3OC_6H_4$	**15c**, 72	10	*4*-$CH_3OC_6H_4$	Ph	**15j**, 69
4	Ph	*4*-BrC_6H_4	**15d**, 67	11	*4*-BrC_6H_4	Ph	**15k**, 63
5	Ph	*4*-ClC_6H_4	**15e**, 60	12	*4*-ClC_6H_4	Ph	**15l**, 71
6	Ph	CH_2Ph	**15f**, 62	13	*3*-$CH_3C_6H_4$	*4*-$CH_3OC_6H_4$	**15m**, 69
7	Ph	C_5H_{11}	**15g**, 55	14	*4*-$CH_3C_6H_4$	*4*-$CH_3OC_6H_4$	**15n**, 64
				15	*4*-$CH_3OC_6H_4$	*4*-$CH_3OC_6H_4$	**15o**, 66

[a]Coditions: **1b** (0.065 mmol), amine (0.13 mmol) and arylalkyne (1.30 mmol) in toluene (4 mL), reflux for 12 h. [b]Isolated yields.

The overall reaction involves an alkyne hydroamination as well as coupling of a second alkyne molecule. Typically, ten equivalents of the alkyne is required. The use of four equivalents gave incomplete reaction, including the aniline adduct [Cp*$RhCl_2NH_2R$'], **16**; the adduct with aniline, **16a**, was isolated and characterized completely. Changing the reaction solvent (to THF or DCE) did not improve the yield, and the reaction failed to proceed at room temperature. Both electron-donating and -withdrawing substituents on the alkyne and the aniline are tolerated well. The reaction proceeded smoothly with both aliphatic and aromatic amines but failed to proceed with aliphatic alkynes (1-hexyne and 1-octyne) or internal alkynes (diphenylacetylene and 1-phenyl-1-propyne). An attempt at a cross-coupling product between an internal and a terminal alkyne (phenylacetylene and diphenylacetylene) failed; only **15a** was formed, suggesting that coupling of an internal alkyne was not feasible.

The products **15** and **16a** have all been characterised by spectroscopic and analytical methods. In the ^{1}H NMR spectra of the metallacyclic rhodium complexes **15**, the characteristic diastereotopic -CH_2R and alkene =CH protons were observed as two doublet resonances and one singlet resonance at ~3.7, 3.8 ppm and ~6.4 ppm, respectively. In the $^{13}C\{^{1}H\}$ NMR spectra, a doublet resonance between 212-218 ppm for the Rh-C was observed. The structures of **15c**, **15k**, **15l** and **16a** have also been confirmed by single crystal X-ray diffraction studies. ORTEP plots for **15c** and **16a** are shown in Figures 3.2 and 3.3, respectively. A common atomic numbering scheme with selected bond parameters for **15c**, **15k** and **15l** are collected in Table 3.2, together with those for two similar cyclometallated rhodium complexes that have been structurally characterized and reported earlier, *viz.*, [Cp*RhCl{C_6H_4-*2*-C(H)=NPh-κC,N}], **17a** and [Cp*RhCl{C_6H_4-*2*-C(H)=N$(CH_2)_2$OMe-κC,N}], **17b**.[7f]

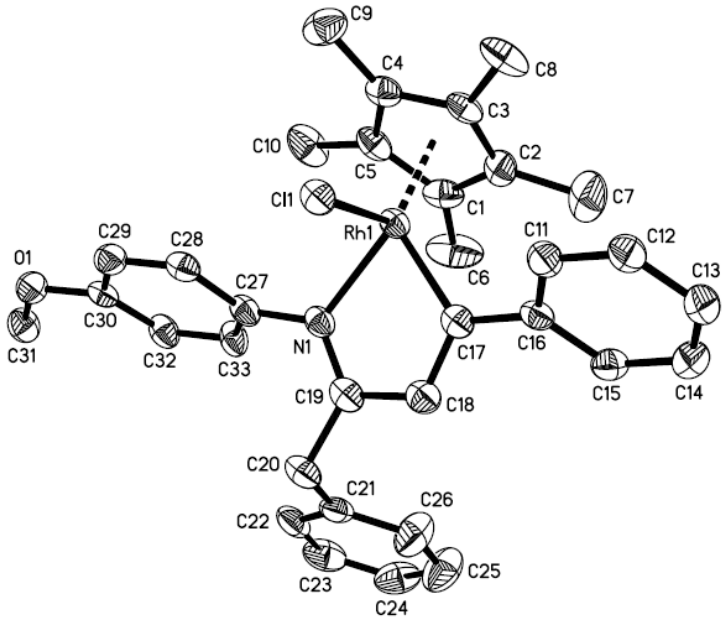


Figure 3.2. ORTEP plot of **15c**. H atoms (except amine H) have been omitted, and only one orientation of the disordered benzyl group is shown. Thermal ellipsoids are plotted at the 50% probability level.

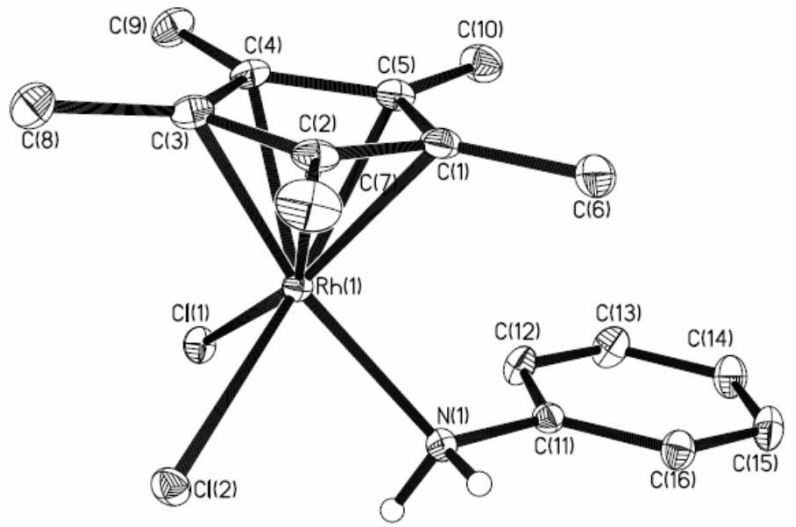
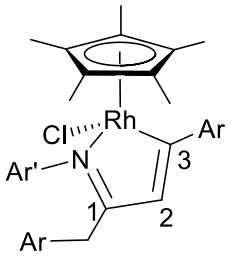
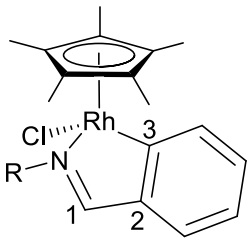


Figure 3.3. ORTEP plot of **16a**. All H atoms (except amine H) have been omitted, and thermal ellipsoids are plotted at the 50% probability level. Selected bond lengths (Å) and angles (deg): Rh-Cl(1), 2.4117(5); Rh-Cl(2), 2.4406(5); Rh-N(1), 2.1826(18); N(1)-C(11), 1.449(3); N(1)-Rh-Cl(1), 84.99(5); N(1)-Rh-Cl(2), 82.06(5); Cl(1)-Rh-Cl(2), 89.101(18); C(11)-N(1)-Rh, 122.70(13).

Table 3.2. Common atomic numbering scheme and selected bond lengths (Å) and angles (^{o}) for **15c**, **15k**, **15l**, and the structures of known complexes **17a** and **17b**.



15



R= Ph (**17a**), -$(CH_2)_2$OMe (**17b**)

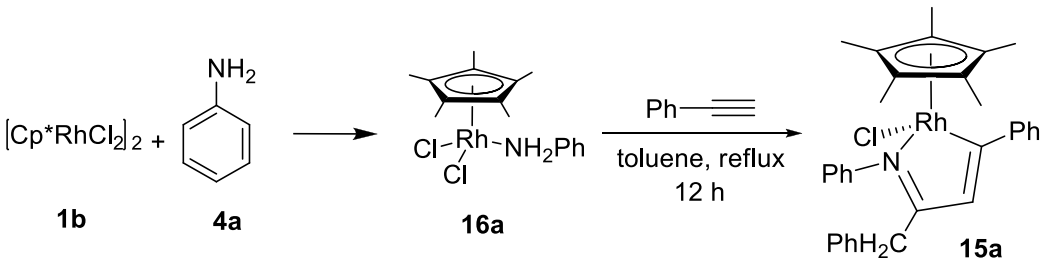
Bond parameter	**15c**	**15k**	**15l**
Rh-Cl	2.4036(10)	2.399(2)	2.3910(8)
Rh-N	2.093(4)	2.096(7)	2.093(3)
Rh-C3	2.012(4)	2.036(8)	2.021(3)
N-C1	1.303(5)	1.301(10)	1.301(4)
N-C(Ar')	1.430(5)	1.432(11)	1.434(3)
C1-C2	1.433(6)	1.452(12)	1.439(5)
C2-C3	1.357(6)	1.347(12)	1.354(5)
N-Rh-C3	78.14(15)	78.7(3)	78.48(12)
C1-N-C(Ar')	121.4(5)	122.6(7)	122.5(3)
C1-C2-C3	117.1(4)	117.0(7)	116.3(3)

The Rh-N bond lengths in **15** (~2.093 Å) are similar to those reported for **17a** and **17b** (2.115(3) Å and 2.089(2) Å, respectively), as are the chelate bite angles (~78^{o} vs 78.33(12)^{o} and 78.73(7)^{o}, respectively). The C(1)-N bond lengths in **15** (~1.30 Å) suggest significant double bond character, and the C1-N-C(Ar') bond angles (~122^{o}) are consistent with the presence of an sp^2 hybridized N atom. In fact, the C(2)-C(3) bond lengths in **15** (~1.35 Å) are significantly shorter than the corresponding bond lengths in **17a** and **17b** (1.399(5) and 1.407(3) Å, respectively) even though this is part of an aromatic ring in the latter compounds. The $^{13}C\{^{1}H\}$ NMR spectra of the complexes **15** exhibit a resonance at ~216 ppm for the C(3) carbon, a value typical of a carbene carbon, in contrast to the ~184 ppm reported for **17**. Although the Rh-C(3) bond lengths are not appreciably shorter than in **17**, the $^{13}C\{^{1}H\}$ NMR spectra and shorter C(2)-C(3) bond lengths suggest delocalisation of the π-electrons within the

metallacycle. Thus these complexes may be regarded as rhodapyrroles. Presumably, the difference between **15** and **17** lies in the fused aromatic ring system which tends to localise the π-electron density within the aromatic ring in the later.

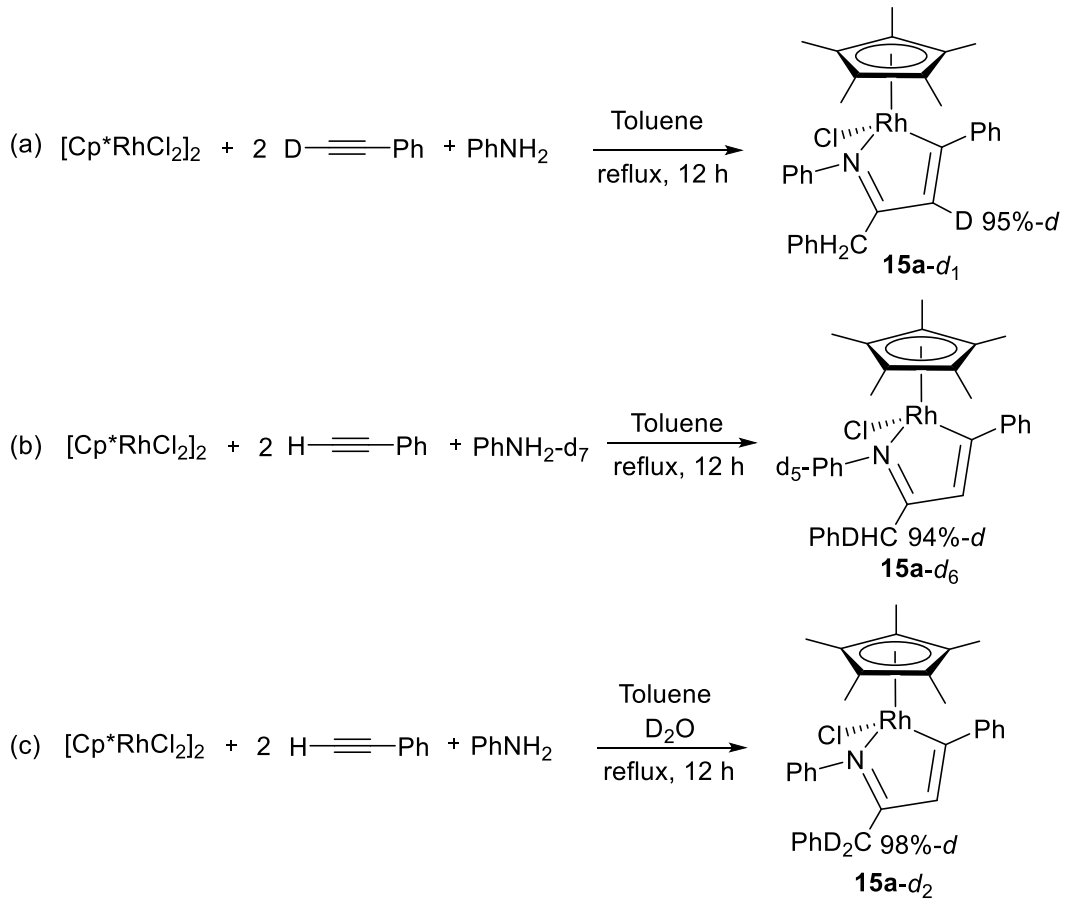
3.2 Mechanistic investigations into the formation of the rhodapyrroles

In the absence of a large excess of the alkyne, the adduct **16** was obtained; in the reaction of aniline with **1b**, the corresponding adduct **16a** was formed in quantitative yield within 15 minutes. In the presence of excess phenylacetylene, **16a** was converted to **15a** in a similar yield to that for the one-pot reaction (Scheme 3.2). These results suggested that **16** was the initial product of the reaction.



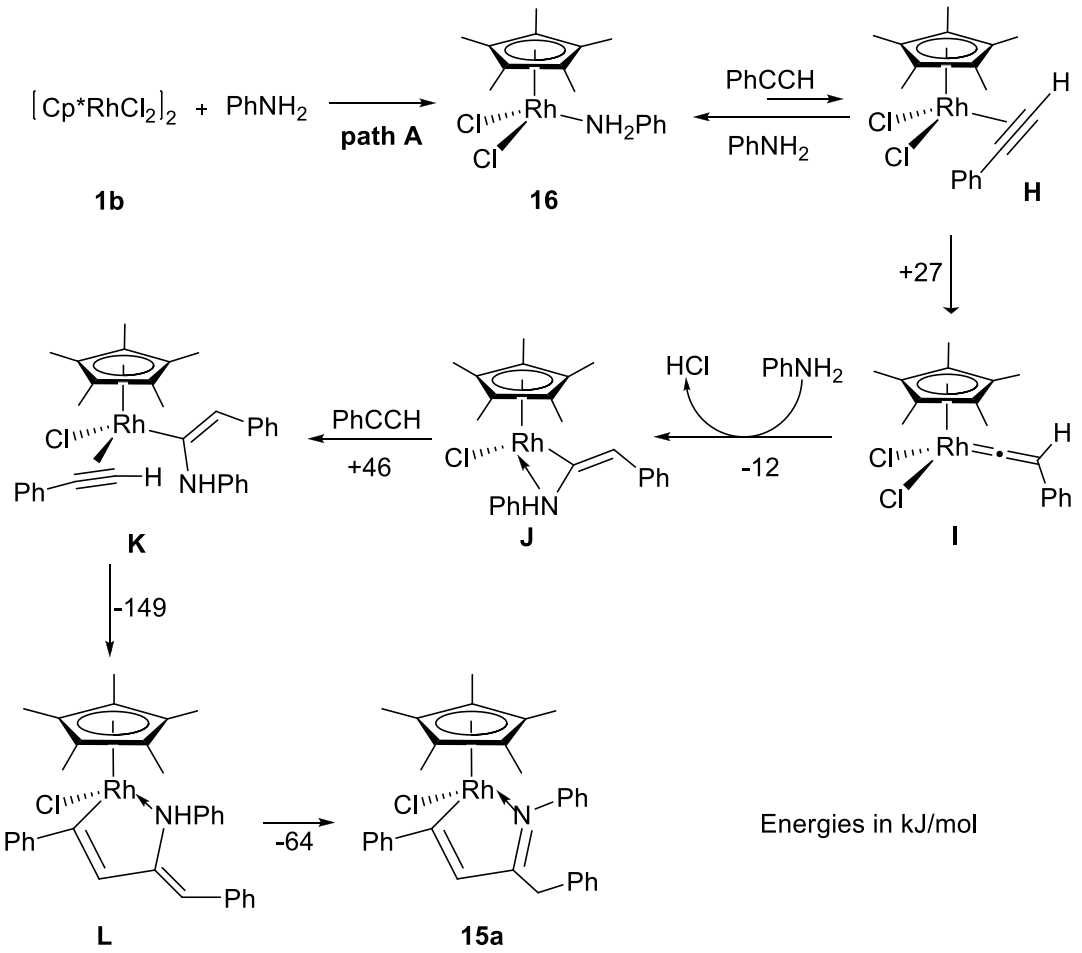
Scheme 3.2

Isotopic labelling experiments employing (a) aniline and PhCCD, (b) d_7-aniline and PhCCH, and (c) aniline and phenylacetylene in the presence of D_2O, yielded **15a** with none, one and both, respectively, of the diastereotopic CH_2 protons being deuterated (Scheme 3.3). These results suggested that the source for each of diastereotopic protons were water and aniline. In case (a), the alkenic CH proton of the rhodapyrrole was also deuterated, pointing to retention of the ≡C-H bond during the coupling of the second alkyne (Scheme 3.3).



Scheme 3.3

A proposed reaction pathway that can account for the above observations is shown in Scheme 3.4; the free energies for the various steps (for $PhNH_2$ and PhCCH) have also been computed with DFT, and the computed free energy changes ($\Delta G^{\ominus}$, in kJ mol^{-1}) from **H** onwards are given. Although no kinetic barriers were computed, the negative or small computed free energy changes involved in the steps suggest that the proposed reaction pathway is reasonable. Presumably, the coordinated aniline in the initial reaction product **16** is replaced in the presence of large excess of the appropriate alkyne. The vinylidene species **I** is formed via rapid intermolecular 1,3-H shift from the alkyne complex **H**, as has been proposed for the Ir analogue (chapter 2). The vinylidene complex **I** undergoes nucleophilic attack of aniline at the α-vinylidene carbon, followed by HCl elimination to afford the enamine intermediate **J**; this is similar to what has been proposed for a hydrido ruthenium(II) enamine complex.[8]



Scheme 3.4

The steps from **J** through to the final product **15a** involve a 1,2-insertion of an alkyne, coordination of the N atom to Rh, and an enamine-imine tautomerisation to form the metallacycle **15a**. A 1,2-insertion of an alkyne has previously been described for a ruthenium complex,[8] and coordination of the enamine N atom leads to the formation metallacycle **L**, with a $\Delta G^{\ominus}$ of -103 kJ mol^{-1}. This process from **J** to **L** should presumably proceeds via the alkyne-coordinated intermediate **K**, which lies +46 kJ mol^{-1} above **J**. The deuterium labelling experiment (a) above shows that the ≡C-H bond is retained in the insertion step.

The computationally optimized structures of **J** and **K**, together with selected bond parameters, are shown in Figures 3.4 and 3.5, respectively. The structure of **J** contains a metallaaziridine moiety; the alternative structure **J'** in which the N atom is

not coordinated to the Rh atom lies 2 kJ mol^{-1} higher in energy. The Rh-N bond length (2.283 Å) is similar to the corresponding crystallographically derived Rh-N bond lengths in **16a** (2.1826(18) Å) and **15** (~2.093 Å). The alkyne in **K** is asymmetrically coordinate; the non-substituted end is closer to the metal than the substituted end (Rh-C bond lengths of 2.193 and 2.399 Å, respectively) but may be attributed to the asymmetrical nature of the alkyne, where the bulkier substituent on the alkyne is oriented further away from the metal center. This can be contrasted with the alkyne coordination in the cationic rhodium intermediate $[Cp^*RhCl(NH_2Ph)]^+$, **P**, later in chapter 4.

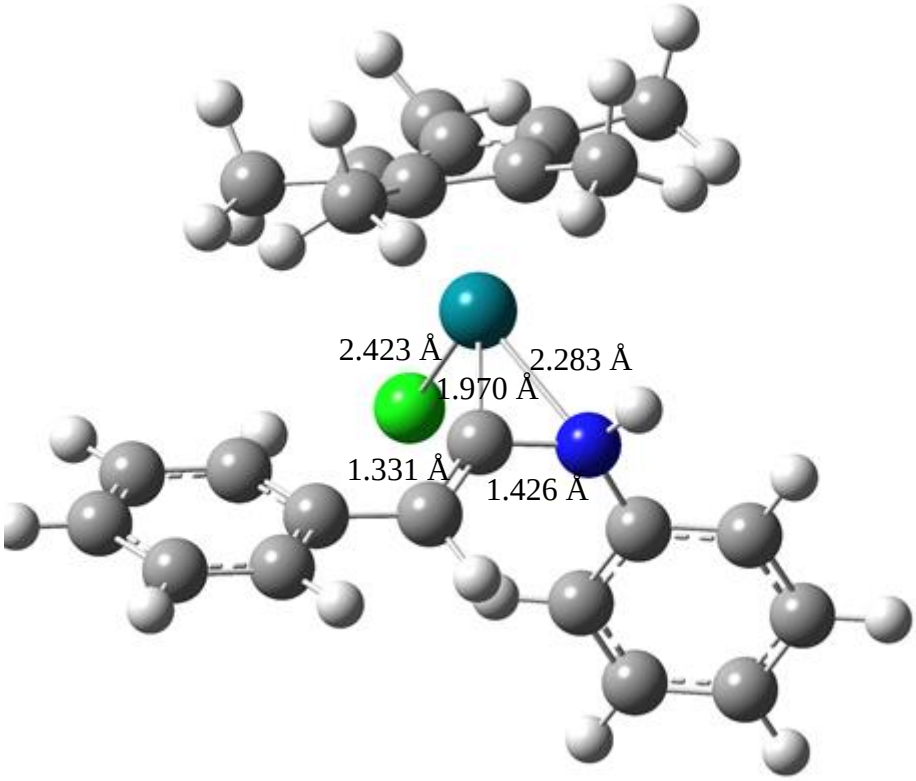


Figure 3.4. Computationally optimized geometry of intermediate **J**. Bond lengths given in Å.

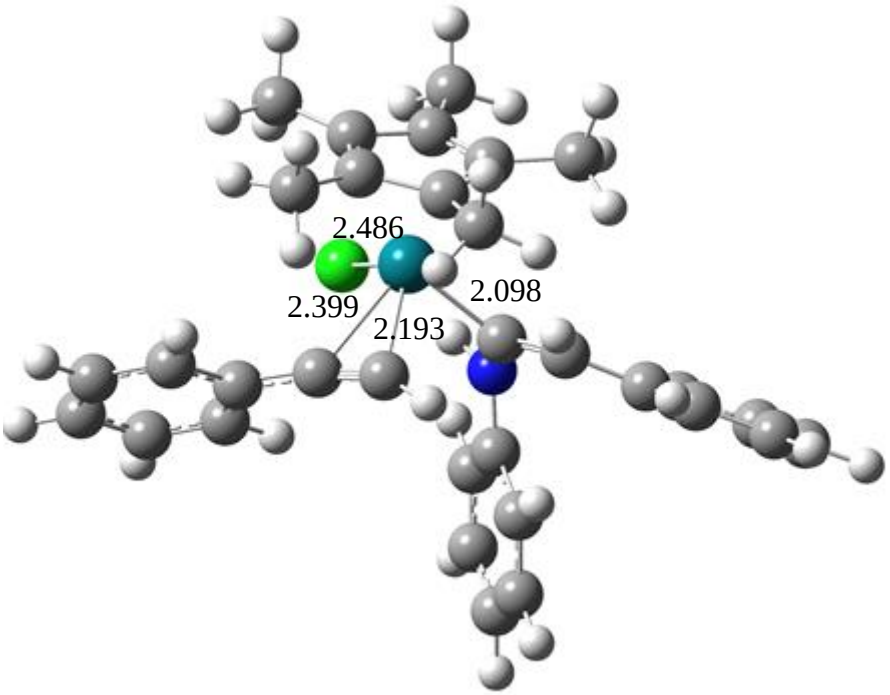


Figure 3.5. Computationally optimized geometry of intermediate **K**. Bond lengths given in Å.

The final step is an enamine to imine tautomerisation, which has been shown to proceed via an intramolecular 1,3-H shift,[9] and is also consistent with the labelling experiment (b). The associated isomerization stabilization energy for this step is -64 kJ mol^{-1}, and is tantamount to the aromatic stabilisation energy of the metallacycle in **15a**. Similar isomerization stabilization energy studies have also been carried out for various iridium complexes, and these suggest that such metallacycles (**VII**, Figure 3.6) are more stabilised than those in which one of the double bonds is exocyclic (**VI**, Figure 3.6).[10] However, from the proposed reaction pathway and optimized intermediate structures we could not able to explain for the failure of this reaction with aliphatic alkynes.

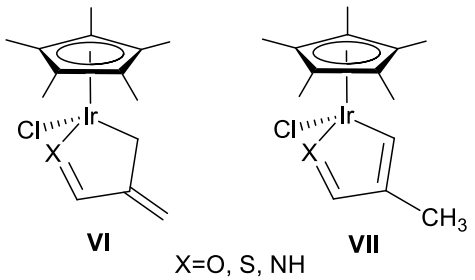
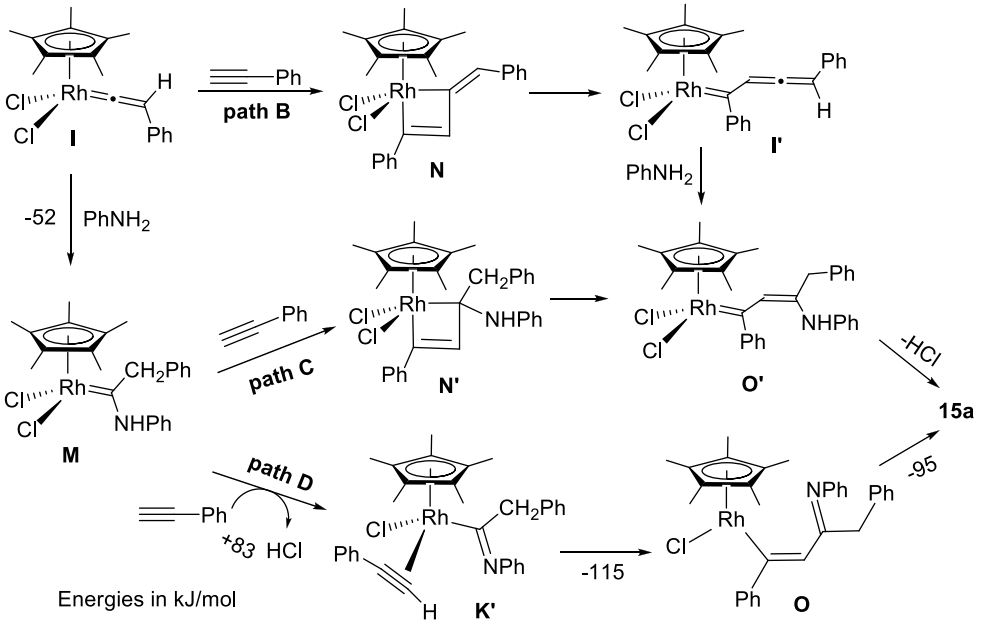


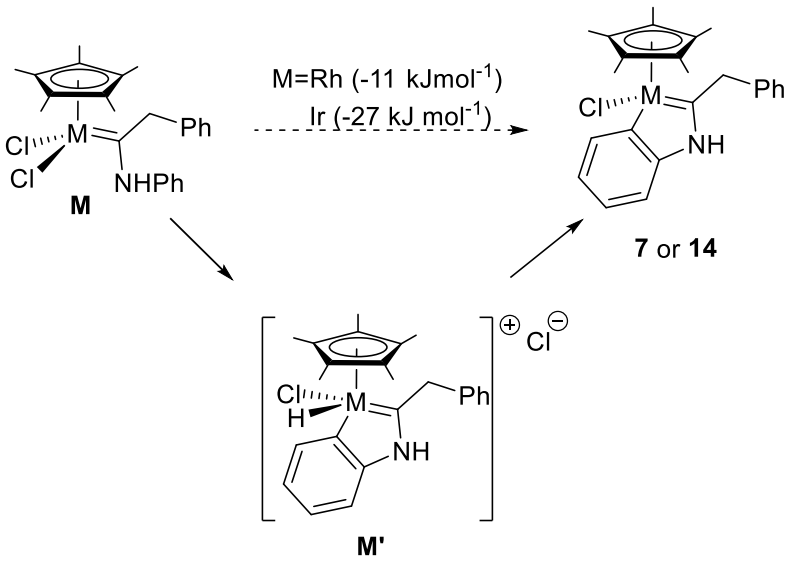
Figure 3.6. The structures used for isomerization stabilization energy (ISE) study.

A number of alternative reaction pathways have also been examined computationally. One involves the formation of a 4-membered metallacycle via a [2+2] cycloaddition reaction of **I** with an alkyne (paths B and C in Scheme 3.5),[11] but attempts at optimization of the structures **N** and **N'**, which formally contain a Rh(V), failed. Another reaction pathway considered involving an amino-carbene intermediate **M** (path D in Scheme 3.5) following that proposed earlier for the reaction of the Ir analogue **1a** with water.[12] This differs from that for pathway **A** in the sequence of addition of the aniline and alkyne, and the elimination of HCl; the computed free energy changes do not allow a definitive choice between them. We could not isolate nor detect the amino-carbene intermediate, **M** from the reaction mixture but its intermediary between **I** and **J** cannot be ruled out.



Scheme 3.5

One intriguing aspect of this reaction was the absence of any amino-carbene derivatives **14**, as may have been expected in analogy to the reaction with the iridium analogue **1a**, which afford **7**. It can be envisaged that a rhodium amino-carbene **14** may be obtained from ortho C-H bond activation in the intermediate **M**. Indeed, the $\Delta G^{\ominus}$ values for this hypothetical reaction, as well as that for the formation of the iridium analogue **7**, have been computed to be -11 and -27 kJ mol^{-1}, respectively (Scheme 3.6). The difference in the reaction pathways taken for rhodium and iridium is thus not clear from the energetic alone. We believe, however, that the orthometallation should proceed via an oxidative addition through an intermediate **M'**, which is formally an M(V) species. Our attempts at optimisation of the structure **M'** for M = Rh invariably failed. In contrast, for M=Ir, the computed $\Delta G^{\ominus}$ values from **M** to **M'** and then **M'** to **7** were +136 and -163 kJ mol^{-1}, respectively. The difference for rhodium and iridium thus appear to lie in the inability of the intermediate **M** to undergo oxidative addition to a Rh(V) species for rhodium.



Scheme 3.6

3.3 Conclusion

The reaction of $[Cp^*RhCl_2]_2$, **1b** with terminal alkynes in the presence of amines was found to give rhoda-pyrrole derivatives [Cp*Rh-CR(=CH{C(=NR')CH_2R})Cl], **15**. A reaction pathway for the formation of **15** has been proposed on the basis of experimental studies, including labelling studies, and further supported by computational studies. It was proposed that a vinylidene intermediate, **I**, was involved. Nucleophilic attack of amine at the vinylidene α-carbon, and subsequent alkyne insertion and enamine-imine rearrangement afforded **15**. We believe that the difference in reactivity between **1b** and its iridium analogue **1a** lies in the reduced tendency for rhodium to orthometallate via a Rh(V) species.

3.4 Experimental Section

3.4.1 General Procedure. The starting material 1b was prepared according to the published method.[13] FAB mass spectra were recorded in ESI mode on a Thermo Finnigan Mat95XP mass spectrometer. All other experimental procedures have been described in section 2.6.1.

Crystallographic studies. Diffraction quality crystals were grown either by slow diffusion of hexane into a dichloromethane solution (**15c**, **15k** and **16a**) or by slow cooling from MeOH (**15l**). X-ray data were obtained using the standard procedure as described in section 2.6.1.

The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light, non-hydrogen atoms. Hydrogen atoms were placed in calculated positions and refined with a riding model. The crystal of **15c** exhibited disorder of the benzyl group, which was modelled with two alternative sites, with occupancies summed to unity. A disordered methanol solvate was found in the crystal of **15l**. This was modelled with two alternative sites, with their occupancies summed

to unity. Appropriate restraints on the bond and thermal parameters were placed on the disordered parts. All non-hydrogen atoms were given anisotropic displacement parameters in the final model.

Computational studies. The LANL2DZ (Los Alamos Effective Core Potential Double-ζ) basis set together with polarisation functions are employed for the Rh atom, and the 6-311+G(2d,p) basis set for all the other atoms. All other procedures used for the energetics study (DFT calculation) have been described in section 2.6.1.

3.4.2 Formation of rhodapyrrole derivatives 15

In a typical reaction, to a solution of **1b** (40 mg, 65 μmol) and phenylacetylene (130 μL, 20-fold excess) in toluene (4 mL) was added aniline (12 μL, 130 μmol). The reaction mixture was then stirred at reflux overnight. The solvent was then removed under reduced pressure and the residue obtained was dissolved in the minimum amount of dichloromethane for chromatographic separation on silica gel TLC plates. Elution with hexane/ethylacetate (4:1, v/v) yielded **15a** as a yellow solid. Similar procedures were used with the other alkynes and anilines for **15b**-**15o**. The amount of reagents used, product formed (with yield) and, HRMS, FAB-Ms and elemental analysis for the products are given in the Table 3.4.

3.4.3 Preparation of Cp*RhCl$_2$(NH$_2$Ph), 16a

Aniline (10 μL, 0.105 mmol) and **1b** (30 mg, 0.048 mmol) were dissolved in dichloromethane (2 ml) and stirred for a few minutes, and then the solvent was removed under vacuum and the residue obtained was washed with hexane (1 ml) to give pure **16a** (37 mg, 96%). FAB Ms: 402 $[M+1]^+$. ^{1}H NMR: 1.41 (s, 15H, 5×CH_3, Cp*), 4.98 (bs, 2H, NH_2), 7.09 (t, $^3J_{HH}$ = 6.64 Hz, 1H, para), 7.27-7.32 (m, 4H, ortho and meta). $^{13}C\{^1H\}$ NMR: 9.05 (CH_3, Cp*), 94.06 (d, $^1J_{RhC}$ = 34.5 Hz, ring C, Cp*), 120.41, 124.62, 129.44 & 142.17 (C & CH aromatic).

3.4.4 Deuterium labelling experiments for 15

A sample of aniline (6 µL, 0.06 mmol) and a slight excess of phenylacetylene-*d* (20 µL, 0.18 mmol) were added using syringe to a suspension of **1b** (20 mg, 0.03 mmol) in toluene (3 mL). The mixture was degassed (3 cycles of freeze-pump-thaw) and then stirred at 110 ^{o}C for 12 h, after which the solvent was removed under vacuum and the crude product was characterized by ^{1}H NMR and HRMS.

Similarly, aniline (6 µL, 0.06 mmol) and aniline-d_7 (6 µL, 0.06 mmol) were reacted separately with pheneylacetylene (20 µL, 0.18 mmol) and **1b** (20 mg, 0.03 mmol) in the presence and absence of D_2O (50 µL), respectively, after which the solvent was removed under vacuum and the crude products characterized by ^{1}H NMR and HRMS. The amount of reagents used, product formed and, HRMS, FAB-Ms and ^{1}H NMR data for the products are given in the Table 3.3

Table 3.3. The reagents used, product formed, and ^{1}H NMR data for products **15**.

	FAB-Ms $[M+1]^+$, $[M-Cl+1]^+$	**HRMS (M-Cl+1)$^+$ Found (calc)**	**δ_H, ppm**
15a *-d*	571, 536	536.1686 (536.1809)	1.13 (s, 15H, Cp*), 3.74 (d, $^2J_{HH}$ =16.0 Hz, 1H, CH_2), 3.85 (d, 1H, CH_2), 7.11-7.21 (m, 5H, aromatic), 7.23-7.28 (m, 6H, aromatic), 7.30-7.38 (m, 2H, aromatic), 7.9 (d, $^3J_{HH}$ = 8.0 Hz, 2H, aromatic).
15a *-d_6*	576, 541	541.2126 (541.2123)	1.14 (s, 15H, Cp*), 3.72 (s, 0.5H, CH_2), 3.83 (s, 0.4H, CH_2), 6.45 (s, 1H, =CH), 7.12 (d, $^3J_{HH}$ = 6.9 Hz, 2H, aromatic), 7.17-7.28 (m, 6H, aromatic), 7.49 (d, $^3J_{HH}$ = 7.3 Hz, 2H, aromatic).
15a *-d_2*	572, 537	537.1868 (537.1872)	1.13 (s, 15H, Cp*), 6.46 (s, 1H, =CH), 7.11-7.21 (m, 5H, aromatic), 7.23-7.28 (m, 6H, aromatic), 7.30-7.38 (m, 2H, aromatic), 7.50 (d, $^3J_{HH}$ = 8.0 Hz, 2H, aromatic).

Table 3.4. Amount of reagents used, product formed, and elemental analyses, FAB mass and HRMS data for products **15**. In all experiments, amount of reagents used are: **1b** (40 mg, 0.065 mmol), anilines (0.13 mmol) and phenylacetylenes (1.3 mmol).

Amine	**Alkyne**	**Product (mg, %)**	**FAB-Ms**	**HRMS (M-Cl+1)$^+$ Found (calc)**	**Elemental analysis**
$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{32}H_{33}ClNRh$ **15a** (50, 68)	570 $[M+1]^+$, 535 $[M-Cl+1]^+$	535.1749 (535.1746)	Found: C, 67.28; H, 5.94; N, 2.64 Calc: C, 67.43; H, 5.84; N, 2.46
4-$CH_3C_6H_4NH_2$, **4d** (14 mg, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{33}H_{35}ClNRh$ **15b** (53, 70)	584 $[M+1]^+$, 549 $[M-Cl+1]^+$	549.1883 (549.1903)	Found: C, 68.07; H, 5.49; N, 2.10 Calc: C, 67.87; H, 6.04; N, 2.40
4-$CH_3OC_6H_4NH_2$, **4i** (16 mg, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{33}H_{35}ClNORh$ **15c** (56, 72)	600 $[M+1]^+$, 565 $[M-Cl+1]^+$	565.1839 (565.1852)	Found: C, 66.24; H, 5.99; N, 2.24 Calc: C, 66.06; H, 5.88; N, 2.33
4-$CH_3OC_6H_4NH_2$, **4i** (16 mg, 0.13 mmol)	*3*-CH_3-C_6H_4CCH, **3k** (166 µL, 1.30 mmol)	$C_{35}H_{39}ClNORh$ **15m** (56, 69)	628 $[M+1]^+$, 593 $[M-Cl+1]^+$	593.2146 (593.2165)	Found: C, 67.20; H, 6.43; N, 2.45 Calc: C, 66.93; H, 6.26; N, 2.23
4-$CH_3OC_6H_4NH_2$, **4i** (16 mg, 0.13 mmol)	*4*-CH_3-C_6H_4CCH, **3l** (164 µL, 1.30 mmol)	$C_{35}H_{39}ClNORh$ **15n** (52, 64)	628$[M+1]^+$, 593 $[M-Cl+1]^+$	593.2148 (593.2165)	Found: C, 67.05; H, 6.29; N, 2.31 Calc: C, 66.93; H, 6.26; N, 2.23
4-$CH_3OC_6H_4NH_2$, **4i** (16 mg, 0.13 mmol)	*4*-CH_3O-C_6H_4CCH, **3t** (168 µL, 1.30 mmol)	$C_{35}H_{39}ClNO_3Rh$ **15o** (56, 66)	660 $[M+1]^+$, 625 $[M-Cl+1]^+$	625.2048 (625.2063)	Found: C, 63.49; H, 5.79; N, 2.00 Calc: C, 63.69; H, 5.96; N, 2.12
4-$BrC_6H_4NH_2$, **4k** (22 mg, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{32}H_{32}BrClNRh$ **15d** (56, 67)	650 $[M+1]^+$, 614 $[M-Cl+1]^+$	613.0856 (613.0851)	
4-$ClC_6H_4NH_2$, **4n** (17 mg, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{32}H_{32}Cl_2NRh$ **15e** (47, 60)	604 $[M+1]^+$, 569 $[M-Cl+1]^+$	569.1342 (569.1357)	
$C_6H_5CH_2NH_2$, **4r** (12 µL, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{31}H_{39}ClNRh$ **15f** (44, 61)	584 $[M+1]^+$, 549 $[M-Cl+1]^+$	549.1901 (549.1903)	
$C_5H_{11}NH_2$, **4s** (15 µL, 0.13 mmol)	C_6H_5CCH, **3i** (130 µL, 1.30 mmol)	$C_{31}H_{39}ClNRh$ **15g** (40, 55)	564 $[M+1]^+$, 529 $[M-Cl+1]^+$	529.2200 (529.2216)	
$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	*3*-CH_3-C_6H_4CCH, **3k** (166 µL, 1.30 mmol)	$C_{34}H_{37}ClNRh$ **15h** (50, 64)	598 $[M+1]^+$, 563 $[M-Cl+1]^+$	563.2047 (563.2059)	

Table 3.4 continued…….

$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	*4*-CH_3-C_6H_4CCH, **3l** (164 µL, 1.30 mmol)	$C_{34}H_{37}ClNRh$ **15i** (48, 63)	598 $[M+1]^+$, 562 $[M-Cl+1]^+$	563.2047 (563.2059)	
$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	*4*-CH_3O-C_6H_4CCH, **3t** (168 µL, 1.30 mmol)	$C_{34}H_{37}ClNO_2Rh$ **15j** (56, 69)	630 $[M+1]^+$, 595 $[M-Cl+1]^+$	595.1949 (595.1958)	
$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	*4*-Br-C_6H_4CCH, **3v** (235 mg, 1.30 mmol)	$C_{32}H_{31}ClBr_2NRh$ **15k** (59, 63)	728 $[M+1]^+$, 692 $[M-Cl+1]^+$	690.9941 (690.9957)	
$C_6H_5NH_2$, **4a** (12 µL, 0.13 mmol)	*4*-Cl-C_6H_4CCH, **3x** (177 mg, 1.30 mmol)	$C_{32}H_{31}Cl_3NRh$ **15l** (58, 71)	638 $[M+1]^+$, 602 $[M-Cl+1]^+$	603.0985 (603.0967)	

Table 3.5. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for **15**.

	δ_H, ppm	$^{13}C\{^{1}H\}$, ppm
15a	1.13 (s, 15H, Cp*), 3.74 (d, $^{2}J_{HH}$ =16.0 Hz, 1H, CH_2), 3.85 (d, 1H, CH_2), 6.45 (s, 1H, =CH), 7.11-7.21 (m, 5H, aromatic), 7.23-7.28 (m, 6H, aromatic), 7.30-7.38 (m, 2H, aromatic), 7.49 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H, aromatic).	8.55 (CH_3, Cp*), 38.03 (CH_2), 97.23 (d, $^{1}J_{RhC}$ = 5.5 Hz, C, Cp*), 126.08, 126.46, 126.64, 127.24, 127.47, 128.82, 128.84, 133.06, 137.48, 148.61 and 149.86 (C & CH, aromatic & alkene), 181.15 (C=N), 216.84 (d, $^{1}J_{RhC}$ = 32.1 Hz, Rh-C).
15b	1.14 (s, 15H, Cp*), 2.33 (s, 3H, CH_3), 3.73 (d, $^{2}J_{HH}$ =16.0 Hz, 1H, CH_2), 3.85 (d, 1H, CH_2), 6.43 (s, 1H, =CH), 7.11-7.21 (m, 6H, aromatic), 7.24-7.29 (m, 6H, aromatic), 7.50 (d, $^{3}J_{HH}$ = 7.3 Hz, 2H, aromatic).	8.58 (CH_3, Cp*), 21.26 (CH_3), 37.99 (CH_2), 97.18 (d, $^{1}J_{RhC}$ = 6.6 Hz, C, Cp*), 126.48, 126.61, 127.19, 127.46, 128.82, 133.00, 135.68, 137.61, 147.38 and 148.65 (C & CH, aromatic & alkene), 181.12 (C=N), 216.11 (d, $^{1}J_{RhC}$ = 31.0 Hz, Rh-C).
15c	1.16(s, 15H, Cp*), 3.74 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.81 (s, 3H, OCH_3), 3.86 (d, 1H, CH_2), 6.45 (s, 1H, =CH), 6.86 (d, $^{3}J_{HH}$ = 7.8 Hz, 2H, aromatic), 7.13 (d, $^{3}J_{HH}$ = 6.8 Hz, 2H, aromatic), 7.18-7.22 (m, 2H, aromatic), 7.24-7.29 (m, 6H, aromatic), 7.51 (d, $^{3}J_{HH}$ = 7.6 Hz, 2H, aromatic).	8.63 (CH_3, Cp*), 37.99 (CH_2), 55.68 (OCH_3), 97.20 (d, $^{1}J_{RhC}$ = 5.7 Hz, C, Cp*), 126.47, 126.61, 127.21, 127.46, 128.76, 128.84, 132.96, 137.62, 143.34, 148.60 and 157.68 (C & CH, aromatic & alkene), 181.33 (C=N), 216.19 (d, $^{1}J_{RhC}$ = 31.0 Hz, Rh-C).
15d	1.16 (s, 15H, Cp*), 3.71 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.85 (d, 1H, CH_2), 6.48 (s, 1H, =CH), 7.10 (d, $^{3}J_{HH}$ = 7.3 Hz, 2H, aromatic), 7.18-7.29 (m, 8H, aromatic), 7.44-7.50 (m, 4H, aromatic).	8.67 (CH_3, Cp*), 38.02 (CH_2), 97.34 (d, $^{1}J_{RhC}$ = 5.8 Hz, C, Cp*), 119.39, 126.44, 126.81, 127.48, 127.56, 128.73, 128.96, 133.27, 137.22, 148.46 and 148.93 (C & CH, aromatic & alkene), 181.66 (C=N), 218.69 (d, $^{1}J_{RhC}$ = 31.6 Hz, Rh-C).
15e	1.15 (s, 15H, Cp*), 3.71 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.85 (d, 1H, CH_2), 6.48 (s, 1H, =CH), 7.09 (d, $^{3}J_{HH}$ = 7.3 Hz, 2H, aromatic), 7.18-7.31 (m, 10H, aromatic), 7.49 (d, $^{3}J_{HH}$ = 7.6 Hz, 2H, aromatic).	8.54 (CH_3, Cp*), 37.88 (CH_2), 97.20 (d, $^{1}J_{RhC}$ = 6.6 Hz, C, Cp*), 126.32, 126.68, 127.35, 127.42, 128.59, 128.80, 131.37, 133.11, 137.10 and 148.32 (C & CH, aromatic & alkene), 181.58 (C=N), 218.42 (d, $^{1}J_{RhC}$ = 32.1 Hz, Rh-C).

Table 3.5 continued…….

15f	1.31 (s, 15H, Cp*), 3.70 (s, 2H, CH_2), 5.20 (d, $^2J_{HH}$ = 16.9 Hz, 1H, CH_2), 5.34 (d, 1H, CH_2), 6.34 (s, 1H, =CH), 7.12-7.21 (m, 5H, aromatic), 7.23-7.32 (m, 6H, aromatic), 7.34-7.46 (m, 4H, aromatic).	9.35 (CH_3, Cp*), 38.15 (CH_2), 60.20 (CH_2), 97.36 (d, $^1J_{RhC}$ = 5.7 Hz, C, Cp*), 126.26, 126.45, 126.78, 127.02, 127.20, 127.46, 128.61, 128.88, 128.97, 129.14, 129.71, 133.04, 136.25, 138.99 and 148.92 (C & CH, aromatic & alkene), 184.21 (C=N), 215.56 (d, $^1J_{RhC}$ = 31.6 Hz, Rh-C).
15g	0.88 (t, $^3J_{HH}$=7.1 Hz, CH_3), 1.23-1.46 (m, 4H, 2 × CH_2) 1.39 (s, 15H, Cp*), 1.61-1.74 (m, 2H, CH_2), 2.08-2.11 (m, 1H, CH_2), 3.69-3.75 (m, 1H, CH_2), 3.83-3.95 (m, 3H, CH_2), 6.29 (s, 1H, =CH), 7.14-7.31 (m, 8H, aromatic), 7.48 (d, $^3J_{HH}$ = 8.3 Hz, 2H, aromatic).	9.20 (CH_3, Cp*), 14.42 (CH_3), 22.71, 29.70, 29.94, 36.59, 55.89 (5×CH_2), 96.72 (d, $^1J_{RhC}$ = 5.8 Hz, C, Cp*), 126.53, 126.79, 126.93, 127.39, 128.56, 128.94, 133.28, 137.19 and 148.53 (C & CH, aromatic & alkene), 180.50 (C=N), 212.51 (d, $^1J_{RhC}$ = 31.6 Hz, Rh-C).
15h	1.15 (s, 15H, Cp*), 2.29 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.71 (d, $^2J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.82 (d, 1H, CH_2), 6.46 (s, 1H, =CH), 6.92-7.03 (m, 5H, aromatic), 7.12-7.19 (m, 3H, aromatic), 7.26-7.28 (m, 2H, aromatic), 7.33 (s, 3H, aromatic).	8.55 (CH_3, Cp*), 21.58 and 21.64 (CH_3), 37.94 (CH_2), 97.23 (d, $^1J_{RhC}$ = 6.9 Hz, C, Cp*), 123.64, 125.79, 126.03, 127.34, 127.38, 128.04, 128.70, 129.77, 132.93, 136.82, 137.40, 138.42, 148.58 and 149.98 (C & CH, aromatic & alkene), 181.31 (C=N), 217.00 (d, $^1J_{RhC}$ = 31.8 Hz, Rh-C).
15i	1.13 (s, 15H, Cp*), 2.28 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.69 (d, $^2J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.79 (d, 1H, CH_2), 6.42 (s, 1H, =CH), 7.00 (d, $^3J_{HH}$ = 8.2 Hz, 3H, aromatic), 7.06 (d, $^3J_{HH}$ = 9.6 Hz, 4H, aromatic) 7.16 (t, $^3J_{HH}$ = 7.3 Hz, 2H, aromatic), 7.30-7.35 (m, 2H, aromatic), 7.38 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic).	8.60 (CH_3, Cp*), 21.24 and 21.55 (CH_3), 37.65 (CH_2), 97.18 (d, $^1J_{RhC}$ = 6.4 Hz, C, Cp*), 125.99, 126.53, 128.14, 128.69, 129.55, 132.79, 134.54, 136.17, 137.05, 145.76 and 149.95 (C & CH, aromatic & alkene), 181.40 (C=N), 217.03 (d, $^1J_{RhC}$ = 31.2 Hz, Rh-C).
15j	1.14 (s, 15H, Cp*), 3.67 (d, $^2J_{HH}$ = 15.6 Hz, 1H, CH_2), 3.75 (s, 3H, OCH_3), 3.76 (d, 1H, CH_2), 3.80(s, 3H, OCH_3), 6.41 (s, 1H, alkene), 6.77-6.82 (m, 5H, aromatic), 7.02 (d, $^3_{JHH}$ = 8.7 Hz, 2H, aromatic), 7.14-7.17 (m, 2H, aromatic), 7.30-7.37 (m, 2H, aromatic), 7.46 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic).	8.49 (CH_3, Cp*), 37.01 (CH_2), 55.35 (OCH_3), 97.10 (d, $^1J_{RhC}$ = 5.4 Hz, C, Cp*), 112.71, 114.13, 125.83, 127.87, 129.36, 129.49, 129.68, 132.28, 141.26, 149.81, 158.21 and 159.27 (C & CH, aromatic & alkene), 181.39 (C=N), 217.01 (d, $^1J_{RhC}$ = 30.8 Hz, Rh-C).

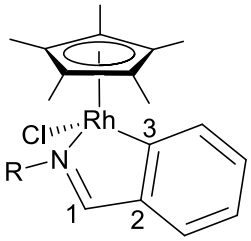
Table 3.5 continued…….

15k	1.15 (s, 15H, Cp*), 3.67 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.80 (d, 1H, CH_2), 6.39 (s, 1H, =CH), 6.97 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.18-7.21 (m, 2H, aromatic), 7.34-7.42 (m, 9H, aromatic).	8.64 (CH_3, Cp*), 37.42(CH_2), 97.40 (d, $^{1}J_{RhC}$ = 6.7 Hz, C, Cp*), 120.73, 121.24, 126.36, 127.99, 129.51, 130.55, 130.64, 131.98, 133.12, 136.16, 147.63 and 149.69 (C & CH, aromatic & alkene), 180.53 (C=N), 215.67 (d, $^{1}J_{RhC}$ = 31.5 Hz, Rh-C).
15l	1.17 (s, 15H, Cp*), 3.71 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.84 (d, 1H, CH_2), 6.41 (s, 1H, =CH), 7.04 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 6.77-6.82 (m, 5H, aromatic), 7.04 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.21-7.28 (m, 7H, aromatic), 7.30-7.37 (m, 2H, aromatic), 7.46 (d, $^{3}J_{HH}$ = 6.9 Hz, 2H, aromatic).	8.64 (CH_3, Cp*), 37.36 (CH_2), 97.39 (d, $^{1}J_{RhC}$ = 5.8 Hz, C, Cp*), 126.34, 127.68, 127.71, 127.88, 129.03, 129.54, 130.18, 132.65, 133.01, 133.15, 135.66, 147.16 and 149.70 (C & CH, aromatic & alkene), 180.63 (C=N), 215.74 (d, $^{1}J_{RhC}$ = 32.6 Hz, Rh-C).
15m	1.14 (s, 15H, Cp*), 2.27 and 2.32 (s, 6H, 2 x CH_3), 3.68 (d, $^{2}J_{HH}$ = 15.6 Hz, 1H, CH_2), 3.78 (s, 3H, OCH_3), 3.80 (d, 1H, CH_2), 6.42 (s, 1H, =CH), 6.84 (d, $^{3}J_{HH}$ = 8.2 Hz, 2H, aromatic), 6.91 (d, $^{3}J_{HH}$ = 7.3 Hz, 2H, aromatic), 6.98 (t, $^{3}J_{HH}$ = 8.5 Hz, 2H, aromatic), 7.11-7.15 (m, 2H, aromatic), 7.25 (d, $^{3}J_{HH}$ = 8.2 Hz, 3H, aromatic), 7.31 (s, 1H, aromatic).	8.62 (CH_3, Cp*), 21.63 (CH_3), 37.81 (CH_2), 55.66 (OCH_3), 97.19 (d, $^{1}J_{RhC}$ = 6.2 Hz, C, Cp*), 123.64, 125.71, 127.33, 127.98, 128.69, 129.68, 132.82, 136.79, 137.52, 138.39, 143.43, 148.53 and 157.64 (C & CH, aromatic & alkene), 181.43 (C=N), 216.32 (d, $^{1}J_{RhC}$ = 31.9 Hz, Rh-C).
15n	1.15 (s, 15H, Cp*), 2.29 and 2.32 (s, 6H, 2 x CH_3), 3.68 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.78 (d, 1H, CH_2), 3.80 (s, 3H, OCH_3), 6.41 (s, 1H, =CH), 6.84 (d, $^{3}J_{HH}$ = 7.8 Hz, 3H, aromatic), 7.00 (d, $^{3}J_{HH}$ = 8.2 Hz, 3H, aromatic), 7.06 (d, $^{3}J_{HH}$ = 8.2 Hz, 4H, aromatic), 7.38 (d, $^{3}J_{HH}$ = 7.8 Hz, 2H, aromatic).	8.67 (CH_3, Cp*), 21.24 and 21.54 (CH_3), 37.55 (CH_2), 55.69 (OCH_3), 97.15 (d, $^{1}J_{RhC}$ = 6.2 Hz, C, Cp*), 126.54, 128.13, 128.63, 129.54, 132.70, 134.67, 136.13, 136.99, 143.45, 145.75 and 157.63 (C & CH, aromatic & alkene), 181.55 (C=N), 216.45 (d, $^{1}J_{RhC}$ = 32.1 Hz, Rh-C).
15o	1.15 (s, 15H, Cp*), 3.65 (d, $^{2}J_{HH}$ = 16.0 Hz, 1H, CH_2), 3.73 (d, 1H, CH_2), 3.75 and 3.81 (s, 9H, 3 × OCH_3), 6.39 (s, 1H, =CH), 6.77-6.85 (m, 7H, aromatic), 7.02 (d, $^{3}J_{HH}$ = 8.7 Hz, 3H, aromatic), 7.46 (d, $^{3}J_{HH}$ = 8.2 Hz, 2H, aromatic).	8.70 (CH_3, Cp*), 37.04 (CH_2), 55.47 and 55.70 (OCH_3), 97.21 (d, $^{1}J_{RhC}$ = 6.2 Hz, C, Cp*), 112.84, 114.26, 128.02, 129.75, 132.30, 141.38, 143.43, 157.61, 158.32 and 159.37 (C & CH, aromatic & alkene), 181.68 (C=N), 216.44 (d, $^{1}J_{RhC}$ = 32.2 Hz, Rh-C).

Table 3.6. Crystal and refinement data for **15c**, **15k**, **15l** and **16a**.

Identification code	**15c**	**15k**	**15l**	**16a**
Empirical formula	$C_{33}H_{35}ClRhNO$	$C_{32}H_{31}Br_2ClRhN$	$C_{32}H_{32}Cl_3Rh$ N. CH_3OH	$C_{16}H_{22}Cl_2$ N Rh
Formula weight	599.98	727.76	670.88	402.16
Temperature, K	103 (2)	103 (2)	103 (2)	103 (2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/c$	P2(1)/n	P2(1)/n	$P\bar{1}$
a, Å	12.1461(7)	9.5480(7)	11.829(2)	7.4450(3)
b, Å	10.8587(6)	17.0504(9)	17.044(3)	9.3608(3)
c, Å	23.7126(15)	18.1105(13)	15.131(3)	13.0557(4)
β, deg	113.299(4)	102.218(2)	93.678(5)	93.353(2)°
Volume, $Å^3$	2872.4(3)	2881.6(3)	3044.2(9)	829.08(5)
Z	4	4	4	2
Density(calc) Mg/m^3	1.387	1.678	1.464	1.611
Abs coefficient, mm^{-1}	0.713	3.481	0.851	1.342
F(000)	1240	1448	1376	408
Crystal size, mm^3	0.40 x 0.20 x 0.02	0.24 x 0.22 x 0.14	0.28 x 0.20x 0.12	0.30 x 0.20 x 0.10
Reflections collected	37339	7778	30482	17191
Independent reflections	8495[R(int) = 0.0998]	7778[R(int) = 0.0000]	6228[R(int) = 0.1638]	5304 [R(int) = 0.0326]
Completeness (to θ, deg)	99.5 % (30.21°)	98.1 % (29.36°)	100.0 % (26.37°)	99.0 % (31.16°)
Max. and min transmission	0.9859 and 0.7635	0.6414 and 0.4888	0.9048 and 0.7965	0.8775 and 0.6889
Data / restraints / parameters	8495/99/404	7778/0/339	6228/13/363	5304 / 0 / 186
Goodness-of-fit on F^2	1.016	1.091	1.168	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0554, wR2 = 0.1203	R1 = 0.0360, wR2 =0.0875	R1 = 0.0832, wR2 = 0.2036	R1 = 0.0238, wR2 = 0.0538
R indices (all data)	R1 = 0.1119, wR2 = 0.1555	R1 = 0.0575, wR2 = 0.1067	R1 = 0.1625, wR2 = 0.2394	R1 = 0.0267, wR2 = 0.0550
Largest diff. peak and hole $e.Å^{-3}$	1.439 and -1.036	1.171 and -0.754	2.404 and -2.208	0.585 and -0.583

Table 3.7. Bond parameters for the earlier reported complexes **17a** and **17b**.



R= Ph (**17a**), -$(CH_2)_2$OMe (**17b**)

Bond parameter	**17a**	**17b**
Rh-Cl	2.399(1)	2.398(1)
Rh-N	2.115(3)	2.089(2)
Rh-C3	2.032(3)	2.027(2)
N-C1	1.281(4)	1.283(3)
C1-C2	1.434(4)	1.437(3)
C2-C3	1.399(5)	1.407(3)
N-Rh-C3	78.33(12)	78.73(7)

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Davies, D. L.; Al-Duaij, O.; Fawcett, J.; Giardiello, M.; Hilton, S. T.; Russell, D. R. *Dalton Trans.* **2003**, 4132-4138. (g) Li, L.; Jiao, Y.; Brennessel, W. W.; Jones, W. D. *Organometallics* **2010**, *29*, 4593-4605. (h) Li, L.; Brennessel, W. W.; Jones, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 12414-12419.

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Chapter 4: $[Cp^*RhCl_2]_2$-catalysed Formation of Ketimines and 1,2-Dihydroquinolines from the Reaction of Terminal Alkynes and Anilines

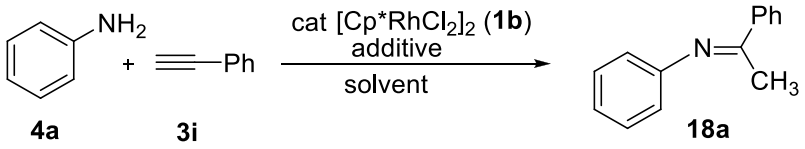
In the previous chapter, it was shown that the Rh(III) dimer $[Cp^*RhCl_2]_2$, **1b**, could form a rhodium metallacyclic complex via an alkyne hydroamination reaction. It therefore became of interest if it can also catalyse alkyne hydroamination. Intermolecular hydroamination of terminal alkynes is known to be catalysed by a number of metal complexes,[1] and the regioselective formation of aromatic ketimines via hydroamination of terminal alkynes with anilines has been achieved using ruthenium,[1a] and gold catalysts.[1j] Although several rhodium catalysts have also been used for the intramolecular cyclization of aminoalkynes,[2] and the intermolecular hydroamination of terminal alkynes,[3] the report by Beller *et.al.* appears to be the only one to-date which afforded Markovnikov addition products selectively.[4] That catalyst, however, was not effective for phenylacetylene, affording only a 10% yield of product because of competing oligomerisation.[4] Interestingly, all the rhodium catalysts reported have involved a Rh(I) species.

4.1 Reaction of 1b with anilines and alkynes in the presence of additives

A test reaction using aniline **4a**, and phenylacetylene **3i**, in the presence of catalytic amounts of **1b** and NH_4PF_6 as an additive, gave the Markovnikov product *N*-(1-phenylethylidine)aniline regioselectively. The reaction probably first afforded the enamine which tautomerised to the more stable imine form. An optimization study showed that although a number of salt additives (AgOTf, $AgPF_6$, $AgSbF_6$, $LiPF_6$ and $NaPF_6$) could be employed, NH_4PF_6 was the most effective (Table 4.1). A control experiment using NH_4PF_6 alone did not catalyse the hydroamination reaction, pointing to a cationic rhodium complex as the active catalyst. In our subsequent studies, a

catalyst loading of 0.5 and 1.5 mol% of **1b** and NH_4PF_6, respectively, were used; although a higher catalyst loading did not improve the yield significantly, it appeared to accelerate the reaction. Changing the solvents to THF, methanol or isopropanol were ineffective for this transformation due to strong coordination to rhodium. Higher (>80 ^oC) temperatures gave slightly lower yields but the reaction failed to proceed at ambient temperature.

Table 4.1. Optimization study for **1b**-catalysed formation of ketimine.



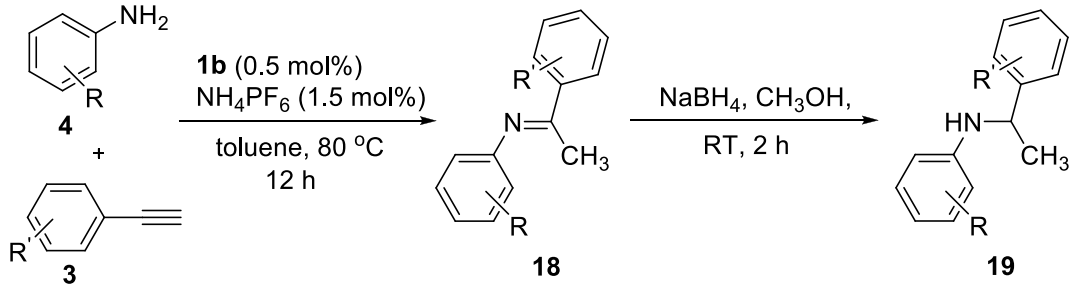
4a **3i** **18a**

S/No	Solvent	**1b** (mol %)	Additive (mol %)	T, °C	Yield (%)[b]
1	Toluene	1.0	NH_4PF_6 (2.0)	80	69
2	Toluene	1.0	NH_4PF_6 (3.0)	80	89
3	Toluene	1.0	NH_4PF_6 (5.0)	80	85
4	Toluene	1.0	$AgPF_6$ (3.0)	80	80
5	Toluene	1.0	$LiPF_6$ (3.0)	80	63
6	Toluene	1.0	$NaPF_6$ (3.0)	80	61
7	Toluene	1.0	Bu_4NPF_6(3.0)	80	-
8	Toluene	1.0	AgOTf (3.0)	80	81
9	Toluene	1.0	$AgSbF_6$ (3.0)	80	83
10	DCE	1.0	NH_4PF_6 (3.0)	80	84
11	THF	1.0	NH_4PF_6 (3.0)	60	-
12	IPA	1.0	NH_4PF_6 (3.0)	60	-
13	CH_3OH	1.0	NH_4PF_6 (3.0)	80	-
14	Toluene	1.5	NH_4PF_6 (4.5)	80	90
15	Toluene	1.0	NH_4PF_6 (3.0)	30	-
16	Toluene	1.0	NH_4PF_6 (3.0)	110	83
17	Toluene	0.5	NH_4PF_6 (1.5)	80	87
18	Toluene	0.2	NH_4PF_6 (0.6)	80	53
19	Toluene		NH_4PF_6 (3.0)	80	-

[a]Coditions: aniline (2.5 mmol), phenylacetylene (2.75 mmol), **1b**/additive in a solvent (10 mL), heated at 80 ^oC for 12 h. [b]Isolated yields.

The substrate scope has also been studied (Table 4.2), for both imines which were sufficiently stable for isolation (left column) and those which were reduced to the amine by $NaBH_4$ reduction and isolated as such (middle and right columns). We did not observe any anti-Markovnikov products, which may form via vinylidene

T**able 4.2**. Substrate scope study for isolated imine (left) and imine converted to, and isolated as, the amine (right).



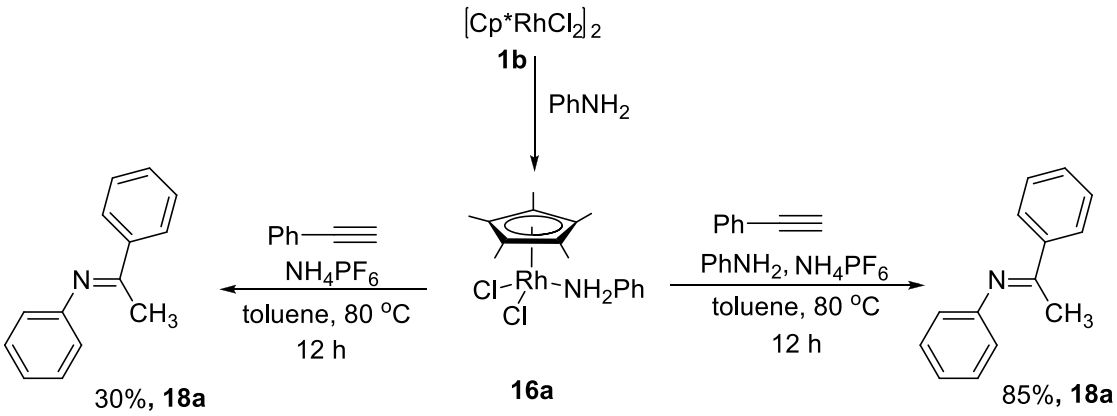
	R	**R'**	**Yield (%)**[b]			**R**	**R'**	**Yield (%)**[b]			**R**	**R'**	**Yield (%)**[b]
1	H	H	**18a** (89)		11	H	$C_{10}H_7$	**19a** (73)		21	H	*3*-F	**19k** (71)
2	H	*4*-CH_3	**18b** (90)		12	H	*2*-CH_3	**19b** (66)		22	H	*4*-F	**19l** (76)
3	H	*4*-OCH_3	**18c** (92)		13	H	*2*-CH_3,*4*-OCH_3	**19c** (78)		23	*3*-OCH_3	H	**19m** (68)
4	H	*4*-Cl	**18d** (84)		14	H	*3*-CH_3	**19d** (77)		24	*3,5*-$(OCH_3)_2$	H	**19n** (67)
5	*4*-CH_3	H	**18e** (91)		15	H	*4*-^{t}Bu	**19e** (79)		25	*4*-OCH_3	H	**19o** (83)
6	*4*-OCH_3	H	**18f** (93)		16	H	*4*-CH_2OH	**19f** (55)		26	*4*-Br	H	**19p** (78)
7	*4*-OCH_3	*3*-CH_3	**18g** (89)		17	H	*2*-OCH_3	**19g** (77)		27	*4*-Cl	H	**19q** (82)
8	*4*-OCH_3	*4*-CH_3	**18h** (91)		18	H	*3*-OCH_3	**19h** (61)		28	*4*-OCH_3	*2*-OCH_3	**19r** (76)
9	*4*-OCH_3	*4*-OCH_3	**18i** (93)		19	H	*4*-Br	**19i** (81)		29	*4*-OCH_3	*3*-OCH_3	**19s** (74)
10	*4*-OCH_3	*4*-Cl	**18j** (92)		20	H	*3*-Cl	**19j** (65)					

[a]Coditions: arylamine (2.5 mmol), arylalkyne (2.75 mmol), **1b** (0.5 mol%) and NH_4PF_6 (1.5 mol%) in toluene (10 mL), heated at 80 ^{o}C for 12 h. [b]Isolated yields.

rearrangement. Various substituents such as electron-donating, electron-withdrawing, -OH and -CH_2OH substituents on the alkyne and the aniline were tolerated. The reaction, however, failed to proceed with secondary anilines (*N*-methylaniline), aliphatic amines (1-pentylamine), or internal alkynes (diphenylacetylene).

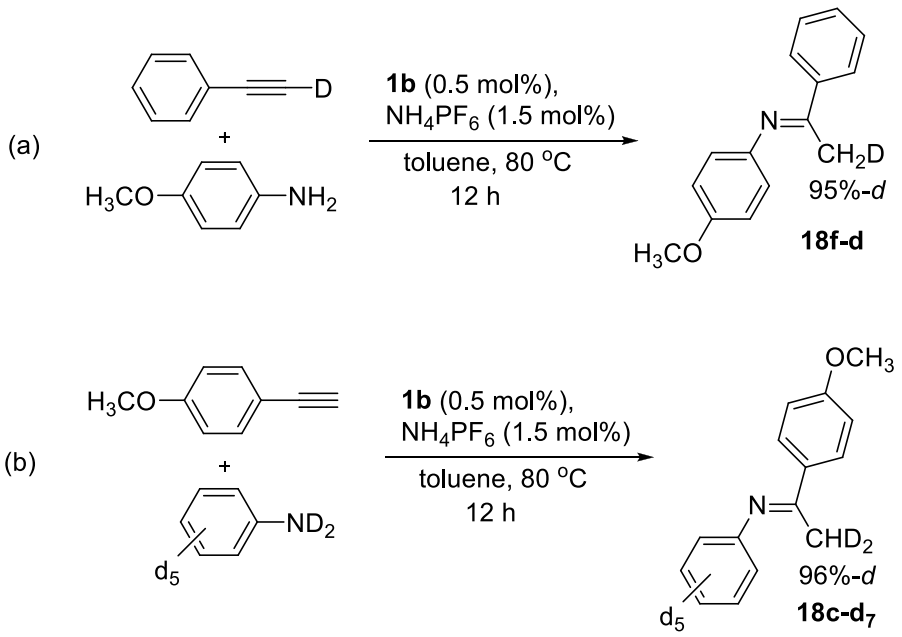
4.2 Mechanistic investigations into the formation of the ketimines 18

Oxidative addition of an N-H bond is a possible pathway for hydroamination, [2c, 3a-b] but it is commonly associated with the group 4 metals and lanthanides.[5] It is also an unlikely pathway here as it would involve the formation of an unfavourable Rh(V) species. Complex **1b** does not react with alkyne, NH_4PF_6, or both, even upon heating. However, it reacts rapidly at ambient temperature with aniline to form $Cp^*RhCl_2(NH_2Ph)$, **16a**, which cleanly catalyses the hydroamination reaction in the presence of NH_4PF_6 in a one-pot reaction (Scheme 4.1). Therefore, it is reasonable to assume that the cationic species $[Cp^*RhCl(NH_2Ph)]^+$, **P**, may be the active catalyst; it may be formed from **16a** via the loss of a chloride ion, assisted by NH_4PF_6.



Scheme 4.1

Isotopic labelling experiments employing (a) *4*-methoxyaniline and PhCCD, and (b) aniline-d_7 and *4*-methoxyphenyl acetylene, afforded **18f** with one, and **18c** with two, respectively, of the CH_3 protons being deuterated (Scheme 4.2). These results clearly indicate that the sources of the protons for the CH_3 protons are from the alkyne ≡CH and the aniline NH_2.



Scheme 4.2

A plausible reaction pathway that accounts for the above observations is shown in Figure 4.2. The free energeies for the various steps (for aniline and phenylacetylene) have been computed with DFT theory, and the free energy changes from **P** onwards are also given. The first step from **P** involves alkyne coordination, and the computed free energy change is slightly positive. The optimized structure of **Q** is shown in Figure 4.1, together with selected bond parameters. The structure is interesting and quite similar to that proposed for a similar cationic rhodium alkyne complex.[2e] The binding of the alkyne to the metal is so asymmetric that it is essentially a cationic metal-alkenyl complex; the Rh-C distance for the terminal carbon (2.219 Å) is reasonable for a Rh-C single bond while that for the non-terminal carbon (2.841 Å, *cf* sum of Van der Waals radii of ~2.25 Å) suggests that there is no Rh…C bonding interaction. In fact, the alkyne looks more like an allene; the phenyl ring plane is almost orthogonal to the Rh-C-H plane (dihedral angle of ~111^{o}). Steric repulsion cannot explain this asymmetry as this is not observed for similar metal-bound alkynes in which the metal centre is neutral, for example, intermediate **K** in chapter 3.

Presumably, it is the possibility of delocalisation of the positive charge into the phenyl group that favours this structure. This would also account for why the reaction worked with aryl but not with aliphatic alkynes. We have also computed the free energy for the step involving the coordination of solvent to intermediate **P**. For example, the $\Delta G^{\ominus}$ value for the binding of 2-propanol to **P** is -32 kJ mol^{-1} and this is consistent with the suppression of the reaction in coordinating solvents.

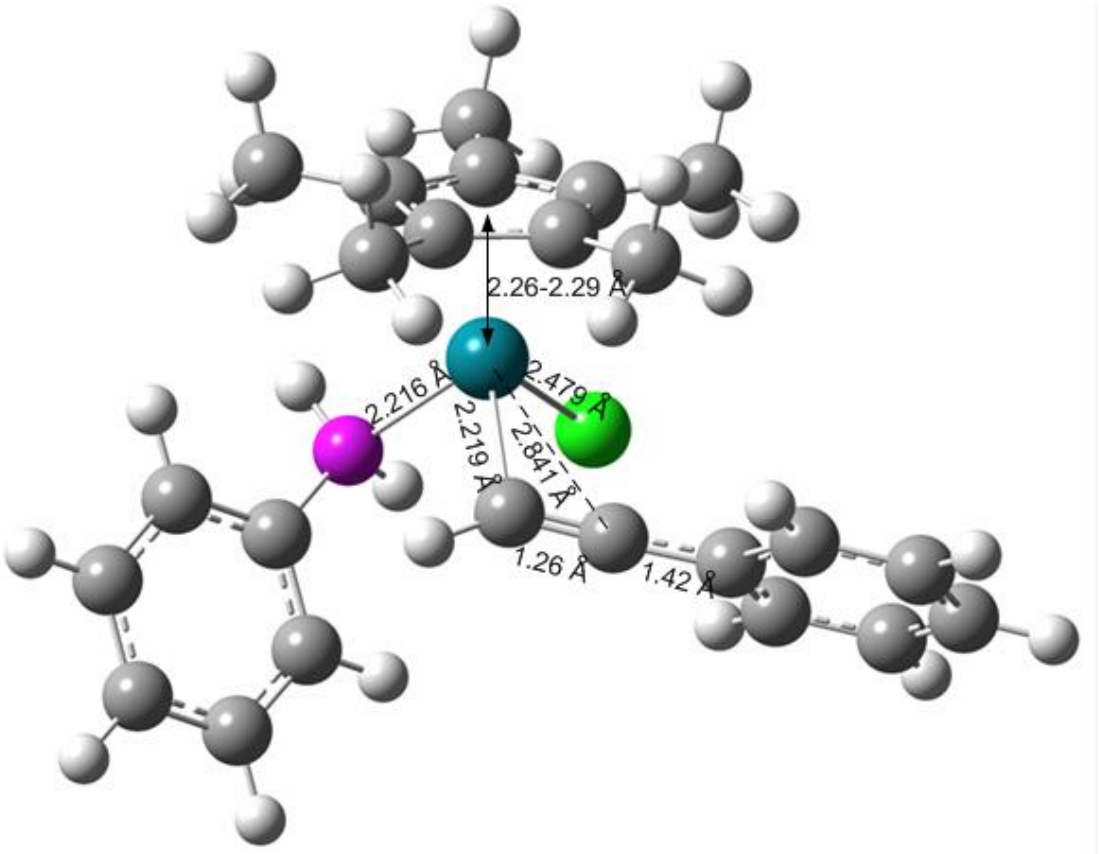


Figure 4.1. Computationally optimized geometry of intermediate **Q**.

The formation of intermediate **R** is the second step and involves direct migration of the Rh-bound aniline to the alkyne followed by external aniline coordination to rhodium.[1k] This process can occur either in a single step ($\Delta G^{\ominus}$ is -30 kJ mol^{-1}), or as two consecutive steps with $\Delta G^{\ominus}$ of -16 and -14 kJ mol^{-1}, respectively. We have also considered an alternative involving intermolecular nucleophilic attack by another aniline onto the coordinated alkyne to form an intermediate **R'** in which the

aniline group on the resulting enamine is trans to the rhodium and the computed $\Delta G^{\ominus}$ for this step is +24 kJ mol^{-1}. Although the computed $\Delta G^{\ominus}$ for this step is uphill, it cannot be ruled out at this point.

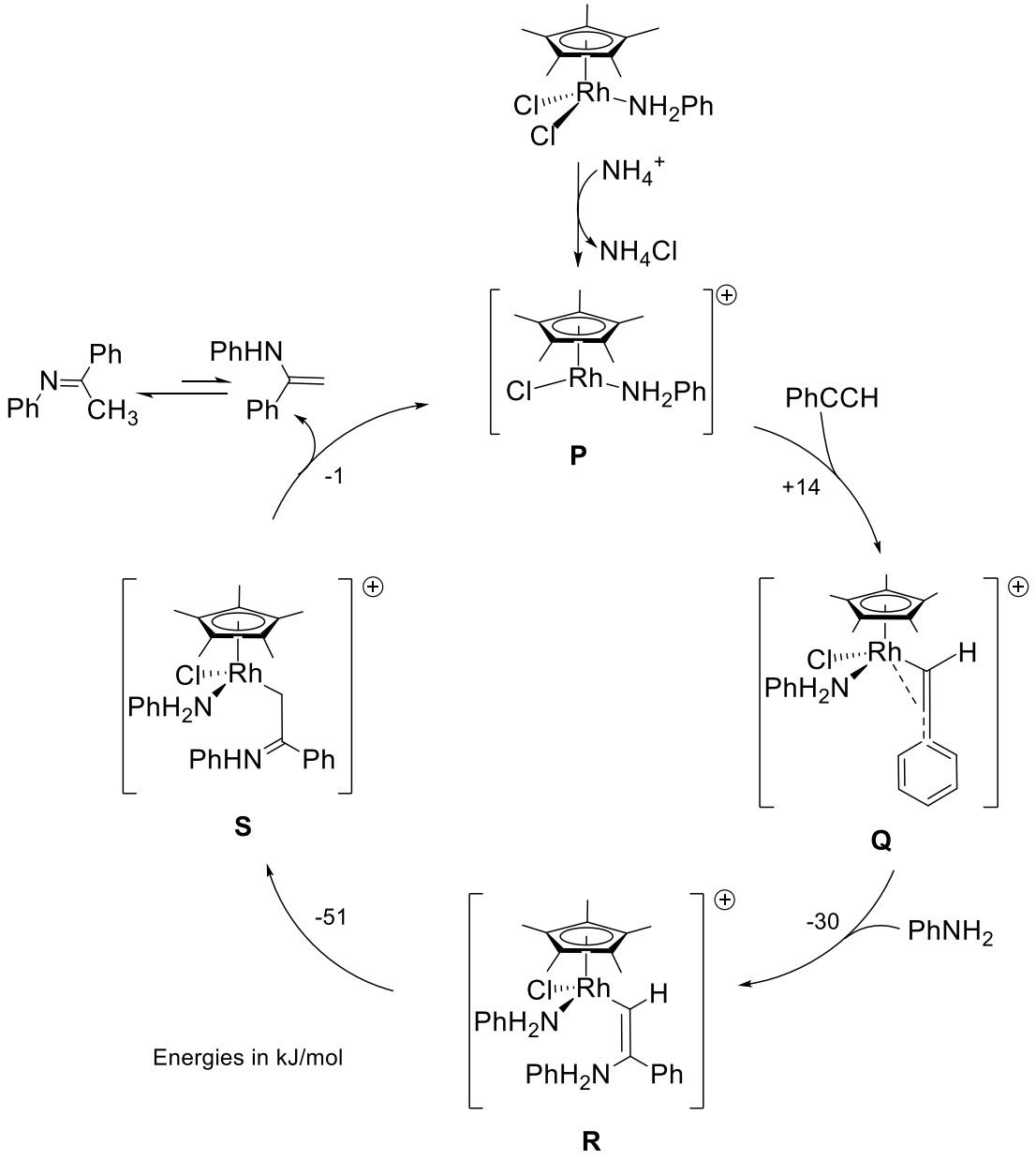


Figure 4.2. Proposed catalytic cycle for **1b**-catalysed hydroamination reaction.

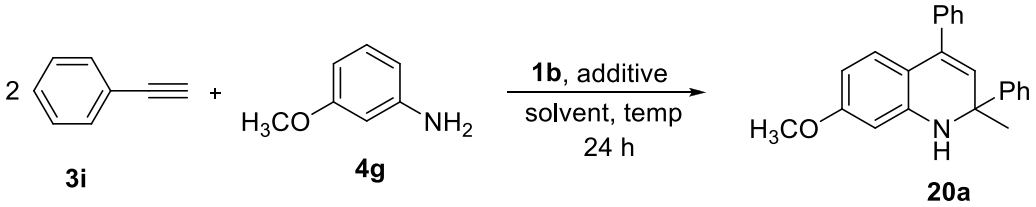
From **R** an enammonium-iminium rearrangement affords **S**. This has been shown to proceed via an intramolecular *1,3*-H shift,[6] and is consistent with our deuterium labelling experiments. The final step is the dissociation of enamine from **S** and regeneration of the assumed active catalyst. Tautomerization of the enamine to the

corresponding more stable imine also involves an intramolecular *1,3*-H shift,[7] which is again consistent with the deuterium labelling experiments.

4.3 Formation of 1,2-dihydroquinolines via alkyne hydroamination

In the course of the hydroamination study described above, a minor product was isolated along with the ketimine from the reaction between phenylacetylene, **3i** and 3-methoxyaniline, **4g**. This was identified as 7-methoxy-2-methyl-2,4-diphenyl-1,2-dihydroquinoline, **20a**. The identity of the product was established on the basis of NMR and mass spectroscopic data, and the structure was further confirmed by a single crystal X-ray crystallographic study (Figure 4.3).

Table 4.3. Reaction optimization table for the reaction **3i** + **4g** → **20a**.



3i **4g** **20a**

S/No	solvent	Catalyst mol %	Additives mol %	Temp °C	Yield (%)[b]
1	Toluene	2.0	NH_4PF_6 (5)	40	-
2	Toluene	2.0	NH_4PF_6 (5)	100	55
3	Toluene	3.0	NH_4PF_6 (5)	150	55
4	Toluene	5.0	NH_4PF_6 (7)	100	65
5	Toluene	2.0	NH_4PF_6 (12)	100	58
6	Toluene	2.0	Bu_4NPF_6(5)	100	-
7	Toluene	2.0	HBF_4(5)	100	86
8	Toluene	2.0	HBF_4(7)	100	77
9	Toluene	2.0	HBF_4(7)	100	66
10	Toluene	2.0	TFA(5)	100	70
11	Toluene	2.0	-	100	-
12	Toluene	1.0	HBF_4(5)	100	81
13	Toluene	-	HBF_4(5)	100	-
14	DCE	2.0	HBF_4(5)	100	78
15	THF	2.0	HBF_4(5)	100	-
16	IPA	2.0	HBF_4(5)	100	-
17	CH_3OH	2.0	HBF_4(5)	100	-

[a]Coditions: 3-methoxyaniline (1.0 mmol), phenylacetylene (2.1 mmol), **1b**/additive in a solvent (3 mL), heated at 100 °C for 24 h. [b]Isolate yields.

Substituted dihydroquinolines are important as they occur in a variety of natural products and pharmaceutical agents,[8] and similar reactions with various amines and alkynes have been reported to be facilitated by transition metals such as ruthenium,[9] gold,[10] silver,[11] zirconium,[12] and zinc.[13] An optimization study with **3i** and **4g** (Table 4.3) show that an increase in amount of catalyst (5 mol%) and/or NH_4PF_6 does not improve the yield much. The replacement of NH_4PF_6 with acids such as TFA or HBF_4, however, improves the yield dramatically. More coordinating solvents like THF, IPA or methanol, are detrimental. Control experiments involving either **1b** or HBF_4 alone show that both **1b** and HBF_4 are necessary.

The substrate scope for the reaction was also tested (Table 4.4). Both electron-donating and electron-withdrawing substituents on the phenylacetylene, as well as acid-sensitive groups like -OR and -OH, were tolerated. The reaction worked very well with aliphatic alkynes and various 3-alkoxyanilines too. Extending the methodology to other anilines (aniline and 3-methylaniline) gave, however, lower yield and the reaction failed with anilines which have electron-withdrawing substituents at the *meta*-position (3-chloroaniline), secondary aniline (*N*-methyl 3-methoxyaniline) and internal alkynes (diphenylacetylene).

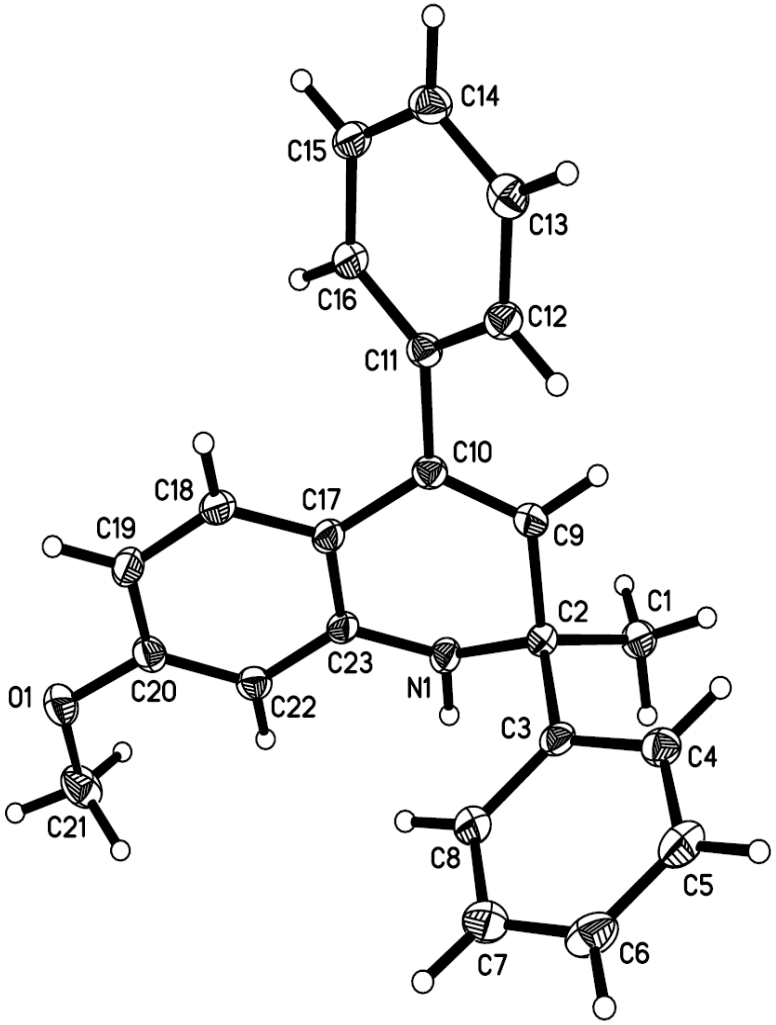
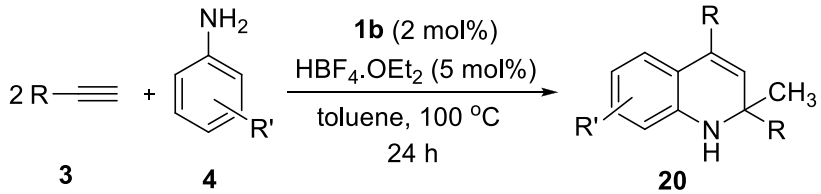


Figure 4.3. ORTEP plot of **20a**. Thermal ellipsoids are plotted at the 50% probability level. Selected bond lengths (Å) and angles (deg): N(1)-C(2), 1.461(2); C(2)-C(9), 1.513(2); C(9)-C(10), 1.346(2); C(17)-C(23), 1.404(2); N(1)-C(23), 1.381(2); C(23)-N(1)-C(2), 120.43(13), N(1)-C(2)-C(9), 107.30(12); C(2)-C(9)-C(10), 122.13(16); C(10)-C(17)-C(23), 117.86(14).

Table 4.4. Substrate scope study for 1,2-dihydroquinoline derivatives.



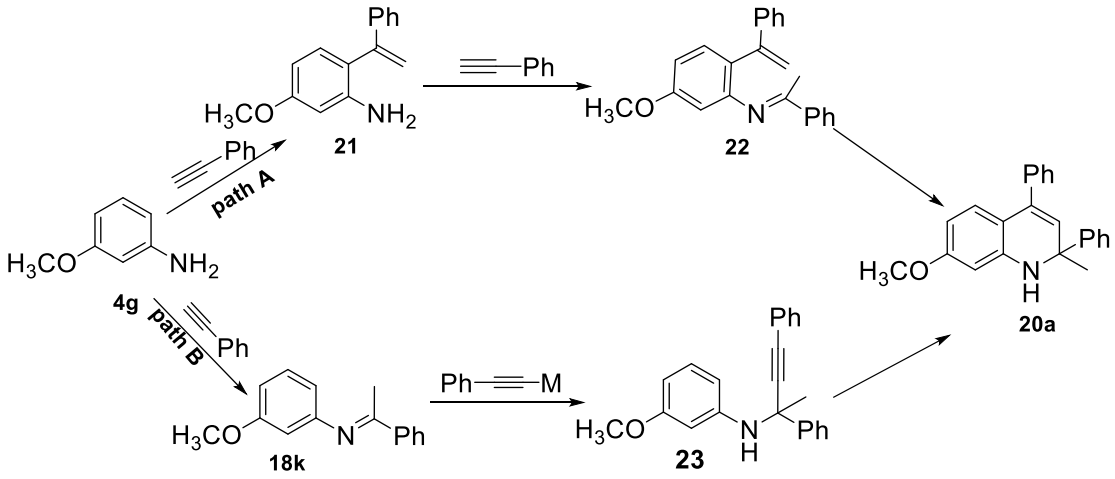
3 4 20

S/No	R	R'	Yield (%)[b]		S/No	R	R'	Yield (%)[b]
1	C_6H_5	*3*-OCH_3	**20a**, 86		14	F-*4*-C_6H_4	*3*-OCH_3	**20n**, 85
2	H_3C-*3*-C_6H_4	*3*-OCH_3	**20b**, 89		15	-$(CH_2)_2CH_3$	*3*-OCH_3	**20o**, 73
3	H_3C-*4*-C_6H_4	*3*-OCH_3	**20c**, 83		16	-$(CH_2)_4CH_3$	*3*-OCH_3	**20p**, 78
4	$CH_3(CH_2)_3$-*4*-C_6H_4	*3*-OCH_3	**20d**, 79		17	-$(CH_2)_5CH_3$	*3*-OCH_3	**20q**, 72
5	$(CH_3)_3C$-*4*-C_6H_4	*3*-OCH_3	**20e**, 78		18	-$(CH_2)_7CH_3$	*3*-OCH_3	**20r**, 71
6	$CH_3(CH_2)_4$-*4*-C_6H_4	*3*-OCH_3	**20f**, 87		19	-$(CH_2)_2$Ph	*3*-OCH_3	**20s**, 79
7	$HOCH_2$-*4*-C_6H_4	*3*-OCH_3	**20g**, 73		20	C_6H_5	*3*-OCH_2CH_3	**20t**, 83
8	HO-*3*-C_6H_4	*3*-OCH_3	**20h**, 71		21	C_6H_5	*3*-$OCH(CH_3)_2$	**20u**, 79
9	H_3CO-*4*-C_6H_4	*3*-OCH_3	**20i**, 89		22	C_6H_5	*3*-$O(CH_2)_5CH_3$	**20v**, 85
10	PhO-*4*-C_6H_4	*3*-OCH_3	**20j**, 83		23	C_6H_5	*3*-$OCH_2C_6H_5$	**20w**, 80
11	Br-*4*-C_6H_4	*3*-OCH_3	**20k**, 71		24	C_6H_5	*3,5*-OCH_3	**20x**, 72
12	Cl-*3*-C_6H_4	*3*-OCH_3	**20l**, 70		25	-$(CH_2)_3CH_3$	H	**20y**, 34[c]
13	Cl-*4*-C_6H_4	*3*-OCH_3	**20m**, 75		26	-$(CH_2)_3CH_3$	*3*-CH_3	**20z**, 57[c]

[a]Coditions: arylamine (1.0 mmol), alkyne (2.1 mmol), **1** (0.02 mmol) and HBF_4 (0.05 mmol) in toluene (3 mL), heated at 100 °C for 24 h. [b]Isolated yields. [c]30-40% ketimine was observed.

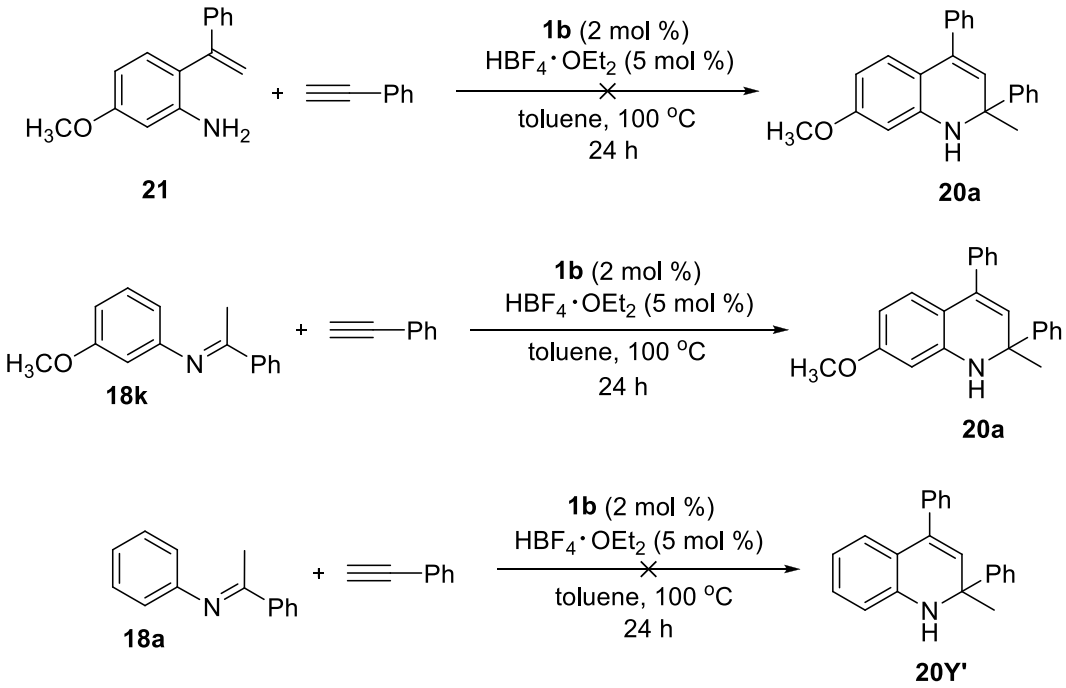
4.4 Mechanistic investigations into the formation of the 1,2-dihydroquinolines

A number of reaction pathways leading to the formation of **20** are possible, including the possibility that parts of the pathway may not involve metal-bound intermediates. In consideration of the latter, for instance, two possible pathways are depicted in Scheme 4.3. One involves an ortho alkenylation, a hydroamination, followed by a [3,3] sigmatropic shift (path A); both the hydroamination and ortho C-H bond insertion of arylamines have been well studied.[14] The second involves the formation and insertion of a metal-alkynyl species into an imine, followed by ortho C-H bond activated cyclization (path B).[10,11]



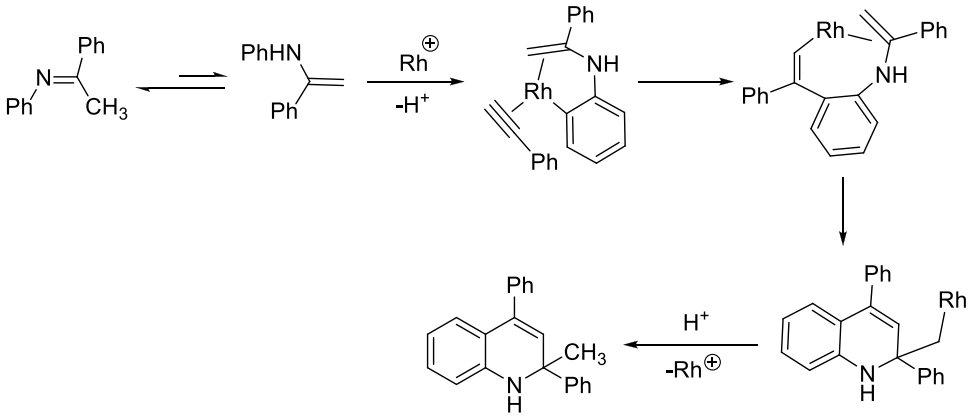
Scheme 4.3

These possibilities were tested out with the reactions shown in Scheme 4.4. The compound **21** failed to react with phenylacetylene to afford **20a** thus ruling out path A. The reaction of **18k** with phenylacetylene gave **20a**, whereas the reaction of **18a** did not afford any dihydroquinoline under identical conditions. It is expected that the step from **23** to **20a**, if involved, would be metal-catalysed and directed by the methoxy substituent on the aromatic ring.[9, 15] The failure of **18a** to react would thus be expected to occur at this step and hence a species analogous to **23** should be observable. Since this was not found to be so, path B is also unlikely.



Scheme 4.4

Since the catalytic system is capable of catalyzing both hydroamination reaction to ketimine (Scheme 4.7) and 1,2-dihydroquinoline formation via reaction between ketimine and alkyne (Scheme 4.4), we believe that the formation of 1,2-dihydroquinoline might have proceeded via formation of enamine intermediate followed by ortho C-H bond activation and alkyne insertion to afford **20a** (Scheme 4.5).[9a] Since this reaction works well only with 3-alkoxyanilines, it would suggest that if this is the correct pathway, then the ortho C-H activation of enamine may be rate-limiting.



Scheme 4.5

On the basis of the above arguments, we have proposed the reaction pathway shown in Figure 4.4. The pathway up to the formation of enamine is similar to what has been proposed above for the hydroamination reaction. Formation of the intermediate **T** may be envisaged as proceeding via an electrophilic substitution. The *meta*-alkoxy and NH_2 substituents on the aniline make the position ortho to the amine group electron-rich and thus favor substitution there. Displacement of the coordinated enaminyl alkene by an alkyne, followed by alkyne insertion, affords the intermediate **V**. A 1,2-alkene insertion of the enamine would give **W** which can then undergo protonolysis to yield the final product **20** and regenerate the active catalyst. We believe that the acidic condition helped shift the imine-enamine equilibrium towards the enamine via protonation of the nitrogen.[16]

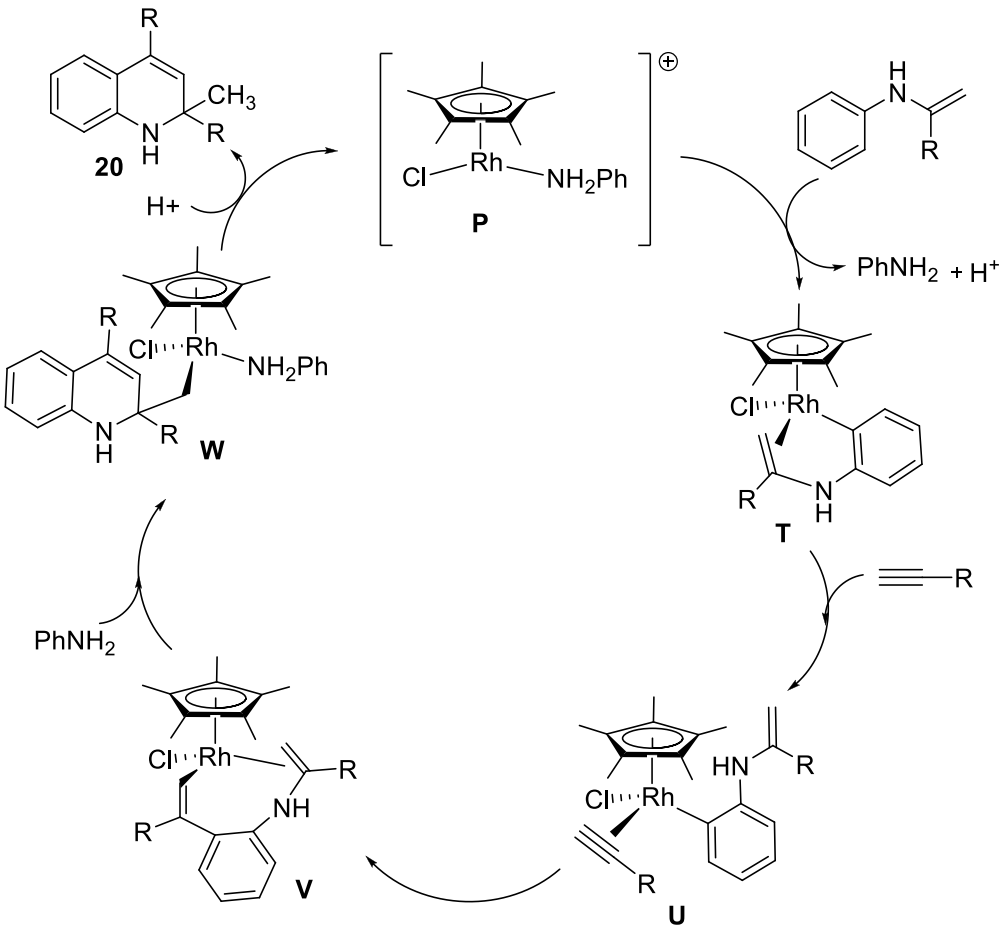
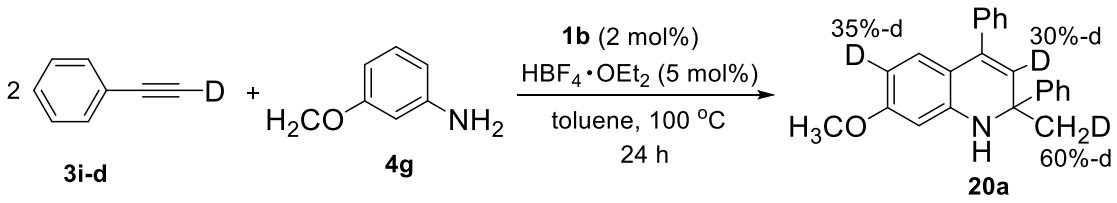


Figure 4.4. Proposed catalytic cycle for the formation of **20** catalysed by **1b**.

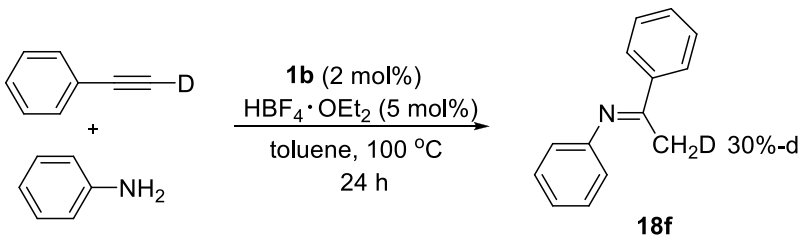
4.5 Deuteration of the aromatic ring in aniline

In an attempt to obtain some information on the reaction pathway above, a deuterium labelling experiment using phenylacetylene-*d* and **4g** gave **20a** which showed 30% and 60% deuteration of the alkene and one of the CH_3 protons, respectively (Scheme 4.6). Interestingly, 35% deuteration was also observed at the position para to the nitrogen in the aromatic ring.



Scheme 4.6

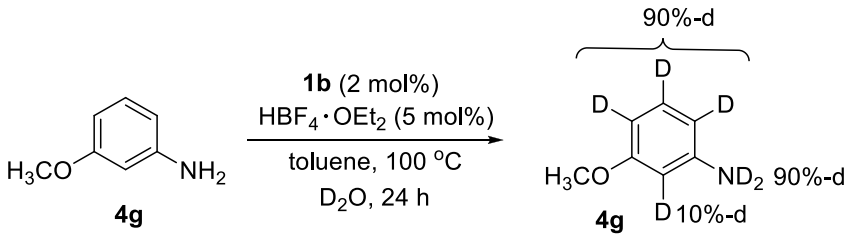
This latter observation suggested that the combination of **1b** and HBF_4 may have activated the para C-H bond in aniline, as well as the terminal ≡C-H bond. To test this, we reacted aniline with phenylacetylene-*d* in the presence of **1b**/HBF_4. This afforded the ketimine **18a** with 30% deuterium incorporation at the one of CH_3 group (Scheme 4.7). As has been described above, the same reaction with NH_4PF_6 as additive afforded **18a** with >90% deuterium incorporation at one of the CH_3 protons. These results clearly show that the reaction pathway with HBF_4 as the additive was different from that with NH_4PF_6 as additive, and that in the former, activation of the terminal ≡C-H bond occurs.



Scheme 4.7

A reaction between 3-methoxyaniline and D_2O in the presence of **1b**/HBF_4 afforded 3-methoxyaniline with essentially complete deuteration of the aromatic and

NH_2 protons (Scheme 4.8). This clearly indicates that the catalytic system of **1b**/HBF_4 can activate the aromatic C-H bonds in **4g**, and that the deuteration of **20a** in Scheme 4.6 occurred early in the reaction pathway leading to 1,2-dihydroquinoline formation, most probably of **4g** itself.



Scheme 4.8

4.5 Conclusion

In this chapter, the dimeric species $[Cp^*RhCl_2]_2$, **1b** was found to catalyse the hydroamination reaction of phenylacetylenes with anilines to give ketimines **18** in the presence of NH_4PF_6. Interestingly, it was also found that the reaction of 3-alkoxyanilines with terminal alkynes afforded 1,2-dihydroquinolines in the presence of **1b**/HBF_4. Reaction pathways for the formation of **18** and **20** have been proposed on the basis of labelling and computational studies (Figure 4.5).

Essentially, the proposed pathway leading to **18** involved the 16-electron cationic rhodium complex **P** as the active catalyst. Coordination of the alkyne **Q** followed by 1,2-insertion into the Rh-N bond led to the enammonium intermediate **R**. A rearrangement to **S** followed by cleavage of the Rh-C bond afforded the enamine which then tautomerized to the more stable imine **18**. In the presence of an acid, this final tautomerisation was inhibited and ortho C-H bond activation (electrophilic substitution) of the aniline moiety on the enamine occurred; this was favoured by a 3-alkoxy group on the aniline. Subsequent alkyne insertion, 1,2-migratory insertion into the enamine (**V** to **W**), and protonolysis afforded **20**. Additionally, it was found from the deuterium labelling studies, that the catalyst system also catalysed deuteration of the aromatic ring in aniline.

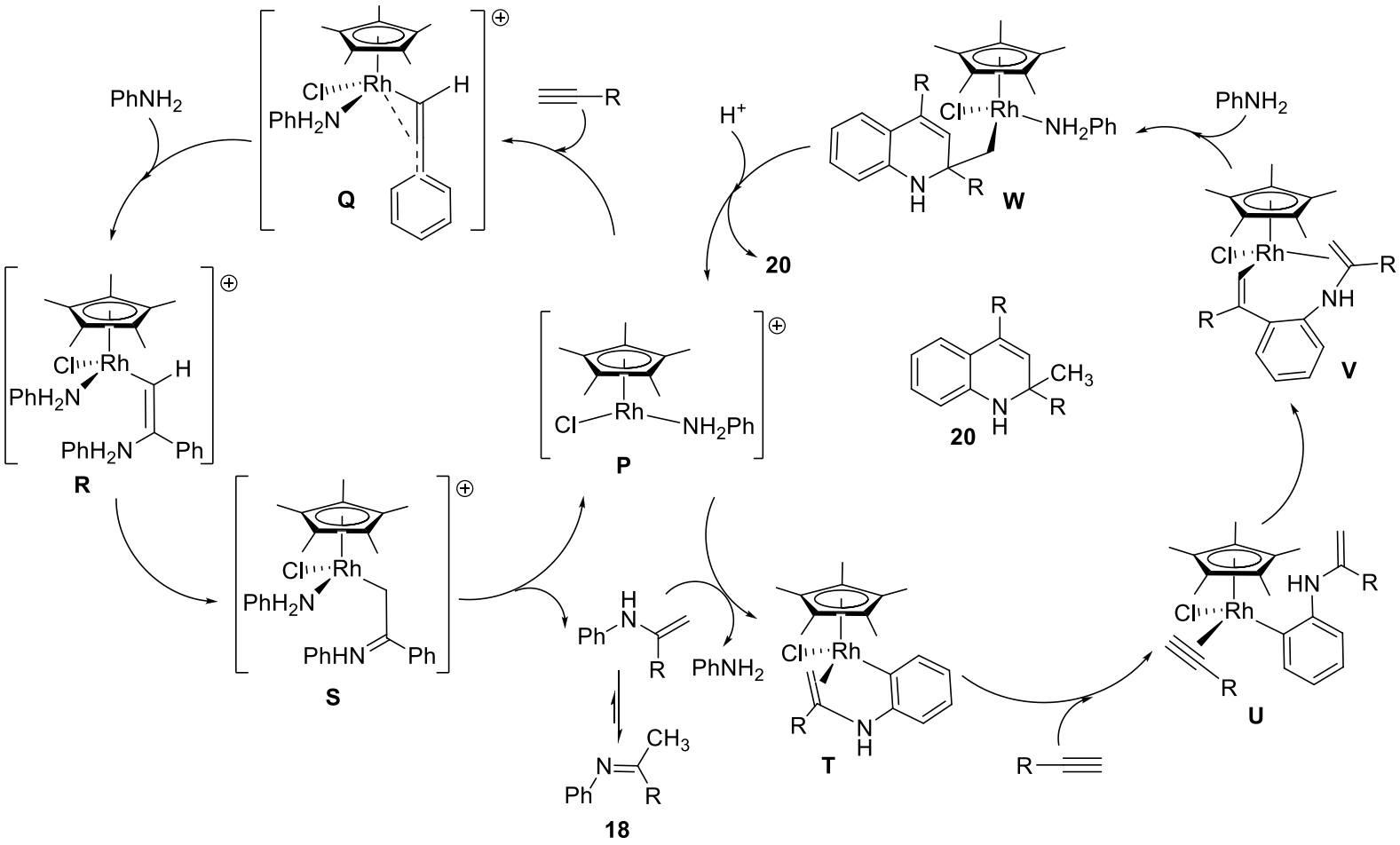


Figure 4.5. Combined catalytic cycles for **1b** catalysed hydroamination reactions towards **18** and **20**.

4.6 Experimental Section

4.6.1 General Procedure: GC/MS was recorded in EI mode on a Thermofinnigan DSQII mass spectrometer. All other experimental procedures have been described in section 2.6.1. Diffraction quality crystals were grown by slow diffusion of hexane into a dichloromethane solution. The reaction energetics were studied using the procedures described in section 2.6.1 without using polarization functions.

4.6.2 General procedure for the hydroamination of alkynes with anilines

In a typical experiment, aniline (240 µL, 2.5 mmol) and a slight excess of phenylacetylene (302 µL, 2.75 mmol) were added using syringe to a suspension of the **1b** (8.5 mg, 0.5 mol%) and NH_4PF_6 (6.7 mg, 1.5 mol%) in toluene (10 mL) in a carius tube under argon at room temperature. The mixture was degassed (3 cycles of freeze-pump-thaw) and then stirred at 80 ^oC for 12 h, after which the solvent was removed under vacuum and the crude product washed with chilled (-10 ^oC) dry hexane (3×5 mL). Similar procedures were used with the other alkynes and anilines for **18b**-**18j**. The amount of reagents used, product formed (with yield) and, HRMS and GC-MS for the products are given in the Table 4.5.

4.6.3 General procedure for the reduction of imines using $NaBH_4$

For reactions in which the imine is unstable, the crude imine product obtained from the hydroamination reaction was dissolved in dry methanol. To this was added sodium borohydride (1.2 eq) and the mixture stirred at room temperature for 2 h. The solvent was then evaporated and the residue was quenched with water and then extracted with ethyl acetate (3×15 mL). The combined extracts were dried over magnesium sulfate, and then the solvent was evaporated under reduced pressure. The crude amine product **19** was purified by column chromatography using ethyl acetate/hexane (15:85, v/v) as eluent. Similar procedures were used with the other

alkynes and anilines for **19b**-**19s**. The amount of reagents used, product formed (with yield) and, HRMS and GC-Ms for the products are given in the Table 4.5.

4.6.4 Reaction of 16a with phenylacetylene

In a carius NMR tube, aniline (5 µL, 0.048 mmol) and **1b** (15 mg, 0.024 mmol) were dissolved in $CDCl_3$ (0.5 ml), the ^1H NMR analysis showed the formation of **8a**. To this mixture was added NH_4PF_6 (12 mg, 0.072 mmol) and phenylacetylene (5 µL, 0.048 mmol) and then stirred at 60 ^oC for 8 h. Analysis by ^1H NMR spectroscopy showed the formation of the ketimine product in ≤ 30% yield. Aniline (50 µL, 0.538 mmol) and more phenylacetylene (55 µL, 0.538 mmol) were added and the mixture was again heated at 60 ^oC for 4 h. ^1H NMR analysis showed complete conversion to the ketimine product.

4.6.5 General procedure for the preparation of 1,2-dihydroquinolines

In a carius tube, **1b** (12 mg, 0.02 mmol) and $HBF_4 \cdot OEt_2$ (7 mg, 0.05 mmol) were dissolved in toluene (3 mL). To this suspension, *3*-methoxyaniline (123 mg, 1.0 mmol) and phenylacetylene (214 mg, 2.1 mmol) were added. The reaction mixture was heated at 100 ^oC for 24 h, and then the reaction solvent was rotary evaporated to give the crude product as brown oil. Purification using flash column chromatography on silica (5% V/V ethyl acetate/hexane as an eluent) gave *7*-methoxy-*2*-methyl-*2,4*-diphenyl-*1,2*-dihydroquinoline **20a** (281 mg, 86 %). Similar procedures were used with the other alkynes and anilines for **20b**-**20z**. The amount of reagents used, product formed (with yield) and HRMS for the products are given in the Tables 4.7 and 4.8.

4.6.6 General procedure for the preparation of 3-alkoxyanilines

In a 2-neck RB flask, *3*-nitrophenol (500 mg, 3.59 mmol) was dissolved in dry DMF (5 mL). To this solution *1*-iodoethane (316 µL, 3.95 mmol) and K_2CO_3 (496 mg, 3.59 mmol) were added and the reaction mixture was stirred at room temperature. The

reaction was monitored by TLC. After completion of the reaction, reaction solvent was removed under reduced pressure. Then the mixture was diluted with water and extracted with chloroform (3×15 mL), dried over $MgSO_4$ and the solvent evaporated to obtain crude 3-ethoxy nitrobenzene. In a *2*-neck RB flask, above obtained 3-ethoxynitrobenzene (500 mg, 3.0 mmol) was dissolved in absolute ethanol (10 mL), followed by the addition of acetic acid (560 µL). The reaction mixture was refluxed for 20 min. To the refluxing solution Fe powder (1.2 g, 21 mmol) was added portionwise, followed by $FeCl_3.6H_2O$ (135 mg, 0.48 mmol). The reaction was monitored by TLC, and after completion of the reaction, the mixture was filtered, diluted with ether (20 mL) and water (10 mL), and the layers separated. The aqueous layer was extracted with ether (3×15 mL), dried over $MgSO_4$, and the solvent was removed by evaporation. The crude product obtained was purified by silica gel (60-120 mesh) column chromatography. Similar procedures were used with the other alkyl and benzylhalides for **4u**-**4x**. The amount of reagents used, product formed (with yield) and HRMS for the products are given in the Table 4.6.

4.6.7 Synthesis of compound 21

3-methoxyaniline (615 mg, 5 mmol), phenylacetylene (510 mg, 5 mmol) and montmorillonite K-10 (500 mg) were placed in a round bottomed flask equipped with magnetic stirrer and reflux condenser. The reaction mixture then was heated at 140 ^oC for 12 hours and cooled to rt. The reaction mixture was filtered off, washed with diethylether (20 mL) and the solvent was removed by evaporation. The crude product obtained was purified by silica gel (60-120 mesh) column chromatography using hexane: ethyl acetate (90:10) as eluent to obtain pure **21** (618 mg, 55%). HRMS: Found (calc); 226.1232 (226.1232). ^1H NMR: 3.65 (bs, 2H, NH), 3.79 (s, 3H, OCH_3), 5.32 (d, $^2J_{HH}$ =1.4 Hz, 1H, CH_2), 5.74 (d, $^2J_{HH}$ =1.4 Hz, 1H, CH_2), 6.29 (s, 1H,

aromatic), 6.38 (d, $^{3}J_{HH}$ =8.7 Hz, 1H, aromatic), 7.03 (d, $^{3}J_{HH}$ =8.2 Hz, 1H, aromatic), 7.28-7.33 (m, 3H, aromatic), 7.36-7.39 (m, 2H, aromatic). $^{13}C\{^{1}H\}$ NMR: 55.36 (OCH_3), 101.48, 104.44, 116.20, 120.83, 126.96, 128.23, 128.72, 132.01, 140.32, 144.80, 146.93 and 160.49 (alkene & aromatic).

4.6.8 Reaction of 21 with phenylacetylene

In a carius tube, $[Cp^*RhCl_2]_2$ (10 mg, 0.016 mmol) and $HBF_4.OEt_2$ (7 mg, 0.04 mmol) were dissolved in toluene (3 mL). To this suspension, **21** (180 mg, 0.8 mmol) and phenylacetylene (91 mg, 0.85 mmol) were added. The reaction mixture was heated at 100^{o} C for 24 h and crude ^{1}H NMR analysis showed that there was no product formation.

4.6.9 Reaction of 18 with phenylacetylene

In a carius tube, $[Cp^*RhCl_2]_2$ (10 mg, 0.016 mmol) and $HBF_4{\cdot}OEt_2$ (7 mg, 0.04 mmol) were dissolved in toluene (3 mL). To this suspension, **18k** (180 mg, 0.8 mmol) and phenylacetylene (91 mg, 0.84 mmol) were added. The reaction mixture was heated at 100 ^{o}C for 24 h and then the reaction solvent was rotary evaporated to give the crude product as brown oil. Purification using flash column chromatography on silica (5% V/V ethyl acetate/hexane as an eluent) gave **20a** (55 mg, 86 %). Similar procedure was used with **18a** also.

4.6.10 Deuterium labelling experiments for 18

A sample of *4*-methoxyaniline (20 mg, 0.16 mmol) and a slight excess of phenylacetylene-*d* (19 µL, 0.18 mmol) were added using syringe to a suspension of **1b** (1 mg, 1 mol%) and NH_4PF_6 (1 mg, 3 mol%) in toluene (2 mL). The mixture was degassed (3 cycles of freeze-pump-thaw) and then stirred at 80 ^{o}C for 12 h, after which the solvent was removed under vacuum and the crude product was characterized by ^{1}H NMR and HRMS. HRMS: Found (calculated); 227.1286 (227.1295). ^{1}H NMR: 2.25 (s,

2H, CH_2D), 3.81 (s, 3H, OCH_3), 6.74 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 6.91 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic), 7.43-7.45 (m, 3H, aromatic), 7.94-7.97 (m, 2H, aromatic).

Similarly, aniline-d_7 (20 µL, 0.2 mmol) was reacted with *4*-methoxypheneylacetylene (29 µL, 0.22 mmol) in the presence of **1b** (1.2 mg, 1 mol%) and NH_4PF_6 (1 mg, 3 mol%) in toluene at 80 ^oC for 12 h, after which the solvent was removed under vacuum and the crude product was characterized by ^1H NMR and HRMS. HRMS: Found (calculated); 233.1673 (233.1671). ^1H NMR: 2.21 (s, 1H, CHD_2), 3.86 (s, 3H, OCH_3), 6.95 (d, $^3J_{HH}$ =7.3 Hz, 2H, aromatic), 7.94 (d, $^3J_{HH}$ =6.9 Hz, 2H, aromatic).

4.6.11 Deuterium labelling experiments for 20

In a carius tube, $[Cp^*RhCl_2]_2$ (6 mg, 0.01 mmol) and $HBF_4{\cdot}OEt_2$ (4 mg, 0.03 mmol) were dissolved in toluene (3 mL). To this suspension, *3*-methoxyaniline (60 mg, 0.5 mmol) and phenylacetylene-*d* (107 mg, 1.05 mmol) were added. The reaction mixture was heated at 100^o C for 24 h, then the reaction solvent was rotary evaporated and the crude product was characterized by ^1H NMR. ^1H NMR: 1.77 (s, 2.4H, CH_3), 3.76 (s, 3H, OCH_3), 4.23 (bs, 1H, NH), 5.52 (s, 0.7H, =CH), 6.14-6.16 (m, 1.7H, aromatic), 6.82-6.85 (m, 1H, aromatic), 7.22-7.26 (m, 1H, aromatic), 7.34-7.37 (m, 7H, aromatic), 7.57 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic). Similarly, aniline (46 mg, 0.5 mmol) was reacted with phenylacetylene-*d* (107 mg, 1.05 mmol) in the presence of **1b** /HBF_4 and the crude obtained was characterized by ^1H NMR.

In a carius tube, **1b** (6 mg, 0.01 mmol) and $HBF_4{\cdot}OEt_2$ (4 mg, 0.03 mmol) were dissolved in toluene (3 mL). To this suspension, *3*-methoxyaniline (60 mg, 0.5 mmol) and D_2O (0.5 mL) were added. The reaction mixture was heated at 100 ^oC for 24 h, then the reaction solvent was rotary evaporated and the crude product was characterized by ^1H NMR and HRMS.

Table 4.5. Amount of reagents used, product formed, and GC mass and HRMS data for products **18** and **19**. In all experiments, amount of reagents used are: anilines (2.5 mmol) and phenylacetylenes (2.75 mmol).

	Aniline	**Alkyne**	**Product (mg, %)**	**GC/MS (m/z)**	**HRMS $[M+H]^+$:**
1	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{14}H_{14}N$, **18a** (434 mg, 89%)	195 $[M]^+$, 180 $[M\text{-}CH_3]^+$	Found: 196.1128 Calc: 196.1126
2	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3-*4*-C_6H_4CCH, **3l** (348 µL, 2.75 mmol)	$C_{15}H_{16}N$, **18b** (470 mg, 90%)	209 $[M]^+$, 194 $[M\text{-}CH_3]^+$	Found: 210.1281 Calc: 210.1283
3	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3O-*4*-C_6H_4CCH, **3t** (356 µL, 2.75 mmol)	$C_{15}H_{16}NO$, **18c** (517 mg, 92%)	225 $[M]^+$, 210 $[M\text{-}CH_3]^+$	Found: 226.1233 Calc: 226.1232
4	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	Cl-*4*-C_6H_4CCH, **3x** (375 mg, 2.75 mmol)	$C_{14}H_{13}NCl$, **18d** (481 mg, 84%)	229 $[M]^+$, 214 $[M\text{-}CH_3]^+$	Found: 230.0736 Calc: 230.0737
5	CH_3-*4*-$C_6H_4NH_2$, **4d** (268 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{15}H_{16}N$, **18e** (475 mg, 91%)	209 $[M]^+$, 194 $[M\text{-}CH_3]^+$	Found: 210.1282 Calc: 210.1283
6	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{15}H_{16}NO$, **18f** (523 mg, 93%)	225 $[M]^+$, 210 $[M\text{-}CH_3]^+$	Found: 226.1233 Calc: 226.1232
7	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	CH_3-*3*-C_6H_4CCH, **3k** (355 µL, 2.75 mmol)	$C_{16}H_{18}NO$, **18g** (532 mg, 89%)	239 $[M]^+$, 224 $[M\text{-}CH_3]^+$	Found: 240.1387 Calc: 240.1388
8	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	CH_3-*4*-C_6H_4CCH, **3l** (348 µL, 2.75 mmol)	$C_{16}H_{18}NO$, **18h** (544 mg, 91%)	239 $[M]^+$, 224 $[M\text{-}CH_3]^+$	Found: 240.1387 Calc: 240.1388
9	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	CH_3O-*4*-C_6H_4CCH, **3t** (348 µL, 2.75 mmol)	$C_{16}H_{18}NO_2$, **18i** (593 mg, 93%)	255 $[M]^+$, 240 $[M\text{-}CH_3]^+$	Found: 256.1336 Calc: 256.1338
10	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	Cl-4-C_6H_4CCH, **3x** (375 mg, 2.75 mmol)	$C_{15}H_{15}NOCl$, **18j** (595 mg, 92%)	259 $[M]^+$, 244 $[M\text{-}CH_3]^+$	Found: 260.0841 Calc: 260.0842
11	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	$C_{10}H_7CCH$, **3h** (391 µL, 2.75 mmol)	$C_{18}H_{17}N$, **19a** (451 mg, 73%)	247 (M^+), 232 $[M\text{-}CH_3]^+$	Found: 248.1430 Calc: 248.1439
12	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3-*2*-C_6H_4CCH, **3j** (346 µL, 2.75 mmol)	$C_{15}H_{17}N$, **19b** (347 mg, 66%)	211 $[M]^+$, 196 $[M\text{-}CH_3]^+$	Found: 212.1440 Calc: 212.1439
13	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3-*2*-OCH_3-*4*-C_6H_3CCH, **3jt** (402 mg, 2.75 mmol)	$C_{16}H_{19}NO$, **19c** (470 mg, 78%)	241 $[M]^+$, 226 $[M\text{-}CH_3]^+$	Found: 242.1540 Calc: 242.1545

Table 4.5 continued…….

14	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3-*3*-C_6H_4CCH, **3k** (355 µL, 2.75 mmol)	$C_{15}H_{18}N$, **19d** (406 mg, 77%)	211 $[M]^+$, 196 $[M\text{-}CH_3]^+$	Found: 212.1441 Calc: 212.1439
15	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	^{t}Bu-*4*-C_6H_4CCH, **3n** (490 µL, 2.75 mmol)	$C_{18}H_{23}N$, **19e** (500 mg, 79%)	253 (M^+), 238 $[M\text{-}CH_3]^+$	Found: 254.1906 Calc: 254.1909
16	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	$HOCH_2$-*4*-C_6H_4CCH, **3p** (363 mg,2.75 mmol)	$C_{15}H_{18}NO$, **19f** (312 mg, 55%)	227 $[M]^+$, 212 $[M\text{-}CH_3]^+$	Found: 228.1385 Calc: 228.1388
17	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3O-*2*-C_6H_4CCH, **3r** (355 µL, 2.75 mmol)	$C_{15}H_{18}NO$, **19g** (436 mg, 77%)	227 $[M]^+$, 212 $[M\text{-}CH_3]^+$	Found: 228.1389 Calc: 228.1388
18	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	CH_3O-*3*-C_6H_4CCH, **3s** (350 µL, 2.75 mmol)	$C_{15}H_{18}NO$, **19h** (346 mg, 61%)	227 $[M]^+$, 212 $[M\text{-}CH_3]^+$	Found: 228.1395 Calc: 228.1388
19	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	Br-*4*-C_6H_4CCH, **3v** (498 mg, 2.75 mmol)	$C_{14}H_{15}BrN$, **19i** (556 mg, 81%)	275 $[M]^+$, 260 $[M\text{-}CH_3]^+$	Found: 276.0384 Calc: 276.0388
20	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	Cl-*3*-C_6H_4CCH, **3w** (338 µL, 2.75 mmol)	$C_{14}H_{14}ClN$, **19j** (375 mg, 65%)	231 $[M]^+$, 216 $[M\text{-}CH_3]^+$	Found: 232.0892 Calc: 232.0893
21	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	F-*3*-C_6H_4CCH, **3y** (318 µL, 2.75 mmol)	$C_{14}H_{14}FN$, **19k** (381 mg, 71%)	215 $[M]^+$, 200 $[M\text{-}CH_3]^+$	Found: 216.1186 Calc: 216.1189
22	$C_6H_5NH_2$, **4a** (228 µL, 2.5 mmol)	F-*4*-C_6H_4CCH, **3z** (315 µL,2.75 mmol)	$C_{14}H_{14}FN$, **19l** (408 mg, 76%)	215 $[M]^+$, 200 $[M\text{-}CH_3]^+$	Found: 216.1191 Calc: 216.1189
23	CH_3O-*3*-$C_6H_4NH_2$, **4g** (281 µL,2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{15}H_{18}NO$, **19m** (386 mg, 68%)	227 $[M]^+$, 212 $[M\text{-}CH_3]^+$	Found: 228.1396 Calc: 228.1388
24	$(CH_3O)_2$-*3,5*-$C_6H_4NH_2$ **4h** (382 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL,2.75 mmol)	$C_{16}H19NO_2$, **19n** (430 mg, 67%)	257 $[M]^+$, 242 $[M\text{-}CH_3]^+$	Found: 258.1495 Calc: 258.1494
25	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{15}H_{18}NO$, **19o** (471 mg, 83%)	227 $[M]^+$, 212 $[M\text{-}CH_3]^+$	Found: 228.1387 Calc: 228.1388
26	Br-*4*-$C_6H_4NH_2$, **4k** (430 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{14}H_{15}NBr$, **19p** (536 mg, 78%)	275 $[M]^+$, 260 $[M\text{-}CH_3]^+$	Found: 276.0393 Calc: 276.0388
27	Cl-*4*-$C_6H_4NH_2$, **4n** (319 mg, 2.5 mmol)	C_6H_5CCH, **3i** (302 µL, 2.75 mmol)	$C_{14}H_{15}ClN$, **19q** (475 mg, 82%)	231 $[M]^+$, 216 $[M\text{-}CH_3]^+$	Found: 232.0895 Calc: 232.0893

Table 4.5 continued…….

28	CH_3O-*4*-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	CH_3O-*2*-C_6H_4CCH, **3r** (355 µL,2.75 mmol)	$C_{16}H_{20}NO_2$, **19r** (488 mg, 76%)	257 $[M]^+$, 242 $[M\text{-}CH_3]^+$	Found: 258.1494 Calc: 258.1494
29	CH_3O-4-$C_6H_4NH_2$, **4i** (308 mg, 2.5 mmol)	CH_3O-*3*-C_6H_4CCH, **3s** (350 µL, 2.75 mmol)	$C_{16}H_{20}NO_2$, **19s** (475 mg, 74%)	257 $[M]^+$, 242 $[M\text{-}CH_3]^+$	Found: 258.1494 Calc: 258.1494

Table 4.6. Amounts of reagents used and product formed and HRMS data for **4u**-**4x**. In all experiments, amount of other reagents used are: 3-nitrophenol (500 mg, 3.59 mmol) and alkylhalide (3.95 mmol).

	Alkyl halide	**Product yield (%)**	**HRMS $[M+H]^+$:**
1	Iodoethane (316 µL, 3.95 mmol)	*3*-ethoxyaniline, **4u**, (214 mg, 52%)	Found: 138.0916 Calc: 138.0919
2	*2*-bromopropane (316 µL , 3.95 mmol)	*3*-isopropoxyaniline, **4v**, (240 mg, 53%)	Found: 152.1072 Calc: 152.1072
3	*1*-bromohexane (583 µL, 3.95 mmol)	*3*-hexyloxyaniline, **4w**, (336 mg, 58%)	Found: 194.1545 Calc: 194.1545
4	Benzylbromide (470 µL, 3.95 mmol)	*3*-benzyloxyaniline, **4x**, (322 mg, 54%)	Found: 200.1076 Calc: 200.1075

Table 4.7. Amount of reagents used, product formed, and HRMS data for products **20**. All experiments carried out using **4g** (112 µl, 1.00 mmol) with alkynes (2.1 mmol).

	Alkyne	**Product (mg, %)**	**HRMS $[M+H]^+$:**			**Alkyne**	**Product (mg, %)**	**HRMS $[M+H]^+$:**
1	C_6H_5CCH, **3i** (230 µL, 2.1 mmol)	$C_{23}H_{21}NO$, **20a** (281 mg, 86%)	Found: 328.1710 Calc: 328.1701		11	Br-*4*-C_6H_4CCH, **3v** (378 mg, 2.1 mmol)	$C_{23}H_{19}Br_2NO$, **20k** (342 mg, 71%)	Found: 483.9899 Calc: 483.9912
2	CH_3-*3*-C_6H_4CCH, **3k** (270 µL, 2.1 mmol)	$C_{25}H_{25}NO$, **20b** (316 mg, 89%)	Found: 356.2024 Calc: 356.2014		12	Cl-*3*-C_6H_4CCH, **3w** (257 µL, 2.1 mmol)	$C_{23}H_{19}Cl_2NO$, **20l** (276 mg, 70%)	Found: 396.0926 Calc: 396.0922
3	CH_3-*4*-C_6H_4CCH, **3l** (266 µL, 2.1 mmol)	$C_{25}H_{25}NO$, **20c** (294 mg, 83%)	Found:356.2016 Calc: 356.2014		13	Cl-*4*-C_6H_4CCH, **3x** (285 mg, 2.1 mmol)	$C_{23}H_{19}Cl_2NO$, **20m** (296 mg, 75%)	Found: 396.0916 Calc: 396.0922
4	C_4H_9-*4*-C_6H_4CCH,**3m** (332 mg, 2.1 mmol)	$C_{31}H_{37}NO$, **20d** (347 mg, 79%)	Found: 440.2957 Calc: 440.2953		14	F-*4*-C_6H_4CCH, **3z** (240 µL, 2.1 mmol)	$C_{23}H_{19}F_2NO$, **20n** (308 mg, 85%)	Found: 364.1518 Calc: 364.1513
5	^{t}Bu-*4*-C_6H_4CCH, **3n** (378 µL, 2.1 mmol)	$C_{31}H_{37}NO$, **20e** (342 mg, 78%)	Found: 440.2951 Calc: 440.2953		15	$CH_3(CH_2)_2CCH$, **3b** (207 µL, 2.1 mmol)	$C_{17}H_{25}NO$, **20o** (189 mg, 73%)	Found: 260.2019 Calc: 260.2014
6	C_5H_{11}-*4*-C_6H_4CCH,**3o** (361 mg, 2.1 mmol)	$C_{33}H_{41}NO$, **20f** (406 mg, 87%)	Found: 468.3274 Calc: 468.3266		16	$CH_3(CH_2)_4CCH$, **3d** (275 µL, 2.1 mmol)	$C_{21}H_{33}NO$, **20p** (245 mg, 78%)	Found: 316.2662 Calc: 316.2640
7	$HOCH_2$-*4*-C_6H_4CCH **3p** (277 mg, 2.1 mmol)	$C_{25}H_{25}NO_3$, **20g** (282 mg, 73%)	Found: 388.1931 Calc: 388.1913		17	$CH_3(CH_2)_5CCH$, **3e** (294 µl, 2.1 mmol)	$C_{23}H_{37}NO$, **20q** (247 mg, 72%)	Found: 344.2948 Calc: 344.2953
8	HO-*3*-C_6H_4CCH, **3q** (288 µL, 2.1 mmol)	$C_{23}H_{21}NO_3$, **20h** (255 mg, 71%)	Found: 360.1602 Calc: 360.1600		18	$CH_3(CH_2)_7CCH$, **3f** (379 µL, 2.1 mmol)	$C_{27}H_{45}NO$, **20r** (283 mg, 71%)	Found: 400.3579 Calc: 400.3579
9	CH_3O-*4*-C_6H_4CCH, **3t** (272 µL, 2.1 mmol)	$C_{25}H_{25}NO_3$, **201** (344 mg, 89%)	Found: 388.1906 Calc: 388.1913		19	$PhCH_2CH_2CCH$, **3g** (295 µL, 2.1 mmol)	$C_{27}H_{29}NO$, **20s** (302 mg, 79%)	Found: 384.2326 Calc: 384.2327
10	PhO-*4*-C_6H_4CCH, **3u** (379 µL, 2.1 mmol)	$C_{35}H_{29}NO_3$, **20j** (424 mg, 83%)	Found: 512.2231 Calc: 512.2226		20			

Table 4.8. Amount of reagents used, product formed, and HRMS data for products **20**. All experiments carried out using aniline (112 µl, 1.00 mmol) with alkynes (2.1 mmol).

	Aniline	**Alkyne**	**Product (mg, %)**	**HRMS $[M+H]^+$:**
1	C_2H_5O-*3*-$C_6H_4NH_2$, **3u** (137 mg, 1.0 mmol)	PhCCH, **3i** (230 µL, 2.1 mmol)	$C_{24}H_{23}NO$, **20t** (283 mg, 83%)	Found: 342.1862 Calc: 342.1858
2	$(CH_3)_2CHO$-*3*-$C_6H_4NH_2$, **3v** (151 mg, 1.0 mmol)	PhCCH, **3i** (230 µL, 2.1 mmol)	$C_{25}H_{25}NO$, **20u** (280 mg, 79%)	Found: 356.2019 Calc: 356.2014
3	$C_6H_{13}O$-*3*-$C_6H_4NH_2$, **3w** (193 mg, 1.0 mmol)	PhCCH, **3i** (230 µL, 2.1 mmol)	$C_{28}H_{31}NO$, **20v** (301 mg, 76%)	Found: 398.2483 Calc: 398.2484
4	*3*-$PhCH_2O$-$C_6H_4NH_2$, **3x** (199 mg, 1.0 mmol)	PhCCH, **3i** (230 µL, 2.1 mmol)	$C_{29}H_{25}NO$, **20w** (322 mg, 80%)	Found: 404.2021 Calc: 404.2014
5	*3,5*-CH_3O-$C_6H_3NH_2$, **4h** (153 mg, 1.0 mmol)	PhCCH, **3i** (230 µL, 2.1 mmol)	$C_{24}H_{23}NO_2$, **20x** (257 mg, 72%)	Found: 358.1805 Calc: 358.1807
6	$C_6H_5NH_2$, **4a** (93 mg, 1.0 mmol)	$CH_3(CH_2)_3CCH$, **3c** (241 µL, 2.1 mmol)	$C_{18}H_{27}N$, **20y** (87 mg, 34%)	Found: 258.2221 Calc: 258.2222
7	*3*-CH_3-$C_6H_3NH_2$, **4b** (107 mg, 1.0 mmol)	$CH_3(CH_2)_3CCH$, **3c** (241 µL, 2.1 mmol)	$C_{19}H_{29}N$, **20z** (155 mg, 57%)	Found: 272.2373 Calc: 272.2378

Table 4.9. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for **18**, **19**, **20** and **4u-4x**.

	δ_H, ppm	$^{13}C\{^{1}H\}$, ppm
18a	2.22 (s, 3H, CH_3), 6.79 (d, $^3J_{HH}$ =8.5 Hz, 2H, aromatic), 7.07 (t, $^3J_{HH}$ =7.6 Hz, 1H, aromatic), 7.34 (t, $^3J_{HH}$ =8.0 Hz, 2H, aromatic), 7.43-7.46 (m, 3H, aromatic), 7.97 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic).	17.59 (CH_3), 119.56, 123.40, 127.35, 128.56 and 129.14 (CH, aromatic), 130.66, 139.65 and 151.87 (C, aromatic), 165.70 (C=N).
18b	2.20 (s, 3H, CH_3), 2.40 (s, 3H, $ArCH_3$), 6.78 (d, $^3J_{HH}$ =7.3 Hz, 2H, aromatic), 7.07 (t, $^3J_{HH}$ =7.6 Hz, 1H, aromatic), 7.24 (d, $^3J_{HH}$ =7.3 Hz, 3H, aromatic), 7.33 (t, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 7.86 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic).	17.53 (CH_3), 21.59 (Ar-CH_3), 119.68, 123.29, 127.36, 129.13 and 129.27 (CH, aromatic), 136.93, 140.92 and 152.05 (C, aromatic), 165.48 (C=N).
18c	2.20 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 6.78 (d, $^3J_{HH}$ =8.5 Hz, 2H, aromatic), 6.95 (d, $^3J_{HH}$ =9.1 Hz, 2H, aromatic), 7.07 (t, $^3J_{HH}$ =7.3 Hz, 1H, aromatic), 7.34 (t, $^3J_{HH}$ =7.3 Hz, 2H, aromatic), 7.94 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic).	17.35 (CH_3), 55.56 (OCH_3), 113.76, 119.77, 123.18, 129.00 and 129.08 (CH, aromatic), 132.36, 152.06 and 161.69 (C, aromatic), 164.71 (C=N).
18d	2.20 (s, 3H, CH_3), 6.77 (d, $^3J_{HH}$ =7.3 Hz, 2H, aromatic), 7.08 (t, $^3J_{HH}$ =8.0 Hz, 1H, aromatic), 7.34 (t, $^3J_{HH}$ =7.5 Hz, 2H, aromatic), 7.40 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic), 7.91 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic).	17.48 (CH_3), 119.52, 123.63, 128.76 and 129.21 (CH, aromatic), 136.76, 138.08 and 151.46 (C, aromatic), 164.54 (C=N).
18e	2.22 (s, 3H, CH_3), 2.33 (s, 3H, $ArCH_3$), 6.69 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic), 7.14 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.42-7.44 (m, 3H, aromatic), 7.95 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic).	17.51 (CH_3), 21.06 ($ArCH_3$), 119.58, 127.32, 128.53, 129.69 and 130.55 (CH, aromatic), 132.79, 139.82 and 149.21 (C, aromatic), 165.73 (C=N).
18f	2.23 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.74 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 6.89 (d, $^3J_{HH}$ =8.0 Hz, 2H, aromatic), 7.42-7.43 (m, 3H, aromatic), 7.94 (d, $^3J_{HH}$ =5.2 Hz, 2H, aromatic).	17.54 (CH_3), 55.68 (OCH_3), 114.42, 120.96, 127.30, 128.54 and 130.53 (CH, aromatic), 139.94, 144.99 and 156.12 (C, aromatic), 165.97 (C=N).
18g	2.22 (s, 3H, CH_3), 2.39 (s, 3H, $ArCH_3$), 3.80 (s, 3H, OCH_3), 6.73 (d, $^3J_{HH}$ =9.1 Hz, 2H, aromatic), 6.88 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic),7.25 (d, $^3J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.31 (t, $^3J_{HH}$ =7.5 Hz, 1H, aromatic), 7.69 (d, $^3J_{HH}$ =7.8 Hz, 1H, aromatic), 7.79 (s, 1H, aromatic).	17.63 (CH_3), 21.67 ($ArCH_3$), 55.68 (OCH_3), 114.42, 120.94, 124.53, 127.84, 128.43 and 131.31 (CH, aromatic), 138.26, 139.86, 144.97 and 156.09 (C, aromatic), 166.31 (C=N).

Table 4.9 continued…….

18h	2.22 (s, 3H, CH_3), 2.39 (s, 3H, $ArCH_3$), 3.80 (s, 3H, OCH_3), 6.74 (d, $^3J_{HH}$ =6.7 Hz, 2H, aromatic), 6.89 (d, $^3J_{HH}$ =6.7 Hz, 2H, aromatic), 7.23 (d, $^3J_{HH}$ =9.4 Hz, 2H, aromatic), 7.85 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic).	17.44 (CH_3), 21.57 (CH_3), 55.67 (OCH_3), 114.39, 120.99, 127.27 and 129.22 (CH, aromatic), 137.22, 140.73, 145.10 and 156.01 (C, aromatic), 165.81 (C=N).
18i	2.20 (s, 3H, CH_3), 3.80 (s, 3H, OCH3), 3.84 (s, 3H, OCH3), 6.72 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic), 6.88 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 6.93 (d, $^3J_{HH}$ =8.3 Hz, 2H, aromatic), 7.91 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic).	17.34 (CH_3), 55.59 and 55.67 (OCH_3), 113.78, 114.40, 121.14 and 128.97 (CH, aromatic), 132.50, 144.94, 156.03 and 161.63 (C, aromatic), 165.24 (C=N).
18j	2.21 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.72 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic), 6.89 (d, $^3J_{HH}$ =9.2 Hz, 2H, aromatic), 7.38 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic), 7.88 (d, $^3J_{HH}$ =8.7 Hz, 3H, aromatic).	17.42 (CH_3), 55.67 (OCH_3), 114.45, 120.99 and 128.68 (CH, aromatic), 136.42, 138.26, 144.49 and 156.29 (C, aromatic), 164.80 (C=N).
19a	1.69 (d, $^3J_{HH}$ =6.4 Hz, 3H, CH_3), 4.17 (bs, 1H, NH), 5.31 (q, $^3J_{HH}$ =6.9 Hz, 1H, CH), 6.51 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 6.67 (t, $^3J_{HH}$ =7.3 Hz, 1H, aromatic), 7.09 (t, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 7.43 (t, $^3J_{HH}$ =7.8 Hz, 1H, aromatic),7.52-7.61 (m, 2H, aromatic), 7.68 (d, $^3J_{HH}$ =6.8 Hz, 1H, aromatic), 7.77 (d, $^3J_{HH}$ =8.2 Hz, 1H, aromatic), 7.93 (d, $^3J_{HH}$ =7.8 Hz, 1H, aromatic), 8.19 (d, $^3J_{HH}$ =8.2 Hz, 1H, aromatic).	23.80 (CH_3), 49.66 (CH), 113.37, 117.43, 122.49, 122.81, 125.63, 126.08, 126.26, 127.65 and 129.35 (CH, aromatic), 130.90, 134.31, 140.13 and 147.29 (C, aromatic).
19b	1.50 (d, $^3J_{HH}$ =6.9 Hz, 3H, CH_3), 2.47 (s, 3H, $ArCH_3$), 4.03 (bs, 1H, NH), 4.70 (q, $^3J_{HH}$ =6.9 Hz Hz, 1H, CH), 6.47 (d, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 6.66 (t, $^3J_{HH}$ =7.3 Hz, 1H, aromatic), 7.11 (t, $^3J_{HH}$ =7.4 Hz, 2H, aromatic), 7.16-7.21 (m, 3H, aromatic), 7.45 (d, $^3J_{HH}$ =7.3 Hz, 1H, aromatic).	19.18 ($ArCH_3$), 23.18 (CH_3), 49.97 (CH), 113.20, 117.34, 124.84, 126.78, 126.85, 129.34 and 130.80 (CH, aromatic), 134.77, 142.95 and 147.45 (C, aromatic).
19c	1.51 (d, $^3J_{HH}$ =6.4 Hz, 3H, CH_3), 2.47 (s, 3H, $ArCH_3$), 3.82 (s, 3H, OCH_3), 4.02 (bs, 1H, NH), 4.68 (q, $^3J_{HH}$ =6.9 Hz, 1H, CH), 6.52 (d, $^3J_{HH}$ =8.2 Hz, 2H, aromatic), 6.70 (t, $^3J_{HH}$ =7.3 Hz, 1H, aromatic), 6.74-6.80 (m, 2H, aromatic), 7.16 (t, $^3J_{HH}$ =6.9 Hz, 2H, aromatic), 7.39 (d, $^3J_{HH}$ =8.7 Hz, 1H, aromatic).	19.32 ($ArCH_3$), 23.22 (CH_3), 49.47 (CH), 55.26 (OCH_3), 111.60, 113.18, 116.43, 127.22, 126.03 and 129.30 (CH, aromatic), 135.07, 136.20, 147.49 and 158.31 (C, aromatic).

Table 4.9 continued…….

19d	1.53 (d, $^{3}J_{HH}$ =7.32 Hz, 3H, CH_3), 2.36 (s, 3H, CH_3), 4.03 (bs, 1H, NH), 4.47 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.55 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 6.67 (t, $^{3}J_{HH}$ =7.6 Hz, 1H, aromatic), 7.06-7.25 (m, 6H, aromatic).	21.73 ($ArCH_3$), 25.22 (CH_3), 53.65 (CH), 113.43, 117.33, 123.04, 126.72, 127.85, 128.70 and 129.28 (CH, aromatic), 138.38, 145.43 and 147.56 (C, aromatic)
19e	1.39 (s, 9H, 3×CH_3), 1.58 (d, $^{3}J_{HH}$ =6.8 Hz, 3H, CH_3), 4.06 (bs, 1H, NH), 4.56 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.61 (d, $^{3}J_{HH}$ =8.3 Hz, 2H, aromatic), 6.73 (t, $^{3}J_{HH}$ =7.3 Hz, 1H, aromatic), 7.18 (t, $^{3}J_{HH}$ =7.3 Hz, 1H, aromatic), 7.18 (t, $^{3}J_{HH}$ =7.1 Hz, 2H, aromatic), 7.36-7.43 (m, 4H, aromatic).	24.90 (CH_3), 31.60 (3×CH_3), 34.61 (CMe_3) 53.13 (CH), 113.42, 117.29, 125.67, 125.72 and 129.29 (CH, aromatic), 142.23, 147.61 and 149.79 (C, aromatic).
19f	1.52 (d, $^{3}J_{HH}$ =6.8 Hz, 3H, CH_3), 1.95 (bs, 1H, OH), 4.06 (bs, 1H, NH), 4.50 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 4.63 (s, 2H, CH_2), 6.52 (d, $^{3}J_{HH}$ =8.9 Hz, 2H, aromatic), 6.66 (t, $^{3}J_{HH}$ =7.1 Hz, 1H, aromatic), 7.08-7.12 (m, 2H, aromatic), 7.30-7.38 (m, 4H, aromatic).	25.24 (CH_3), 53.37 (CH), 65.24 (CH_2), 113.46, 117.44, 126.19, 127.61 and 129.26 (CH, aromatic), 139.59, 144.94, and 147.35 (C, aromatic).
19g	1.52 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.92 (s, 3H, OCH_3), 4.17 (bs, 1H, NH), 4.89 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.55 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 6.64-6.69 (m, 1H, aromatic), 6.91-6.93 (m, 2H, aromatic), 7.12 (t, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 7.23 (t, $^{3}J_{HH}$ =4.3 Hz, 1H, aromatic), 7.35 (d, $^{3}J_{HH}$ =8.7 Hz, 1H, aromatic).	23.00 (CH_3), 48.24 (CH), 55.47 (OCH_3), 110.62, 113.41, 117.15, 120.96, 126.49, 127.84 and 129.22 (CH, aromatic), 132.86, 147.51 and 156.85 (C, aromatic).
19h	1.52 (d, $^{3}J_{HH}$ =6.7 Hz, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.04 (bs, 1H, NH), 4.48 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.54 (d, $^{3}J_{HH}$ =8.3 Hz, 2H, aromatic), 6.67 (t, $^{3}J_{HH}$ =6.5 Hz, 1H, aromatic), 6.78-6.80 (m, 1H, aromatic), 6.96-7.00 (m, 2H, aromatic), 7.10-7.14 (m, 2H, aromatic), 7.27 (t, $^{3}J_{HH}$ =7.6 Hz, 1H, aromatic).	25.18 (CH_3), 53.66 (CH), 55.32 (OCH_3), 111.83, 112.10, 113.43, 117.40, 118.36, 129.25 and 129.83 (CH, aromatic), 147.34, 147.44 and 160.07 (C, aromatic).
19i	1.46 (d, $^{3}J_{HH}$ =6.4 Hz, 3H, CH_3), 3.98 (bs, 1H, NH), 4.41 (q, $^{3}J_{HH}$ =6.8 Hz, 1H, CH), 6.45 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 6.65 (t, $^{3}J_{HH}$ =7.3 Hz, 1H, aromatic), 7.08 (t, $^{3}J_{HH}$ =7.8 Hz, 2H, aromatic), 7.23 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 7.41 (d, $^{3}J_{HH}$ =8.2 Hz, 2H, aromatic).	25.26 (CH_3), 53.20 (CH), 113.47, 117.69, 127.81, 129.33 and 131.90 (CH, aromatic), 120.64, 144.54 and 147.12 (C, aromatic).

Table 4.9 continued…….

19j	1.50 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 4.01 (bs, 1H, NH), 4.45 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.49 (d, $^{3}J_{HH}$ =7.8 Hz, 2H, aromatic), 6.67 (t, $^{3}J_{HH}$ =7.3 Hz, 1H, aromatic), 7.11(t, $^{3}J_{HH}$ =8.6 Hz, 2H, aromatic), 7.19-7.27 (m, 3H, aromatic), 7.37 (s, 1H, aromatic).	25.28 (CH_3), 53.44 (CH), 113.48, 117.75, 124.23, 126.22, 127.29, 129.36 and 130.18 (CH, aromatic), 134.72, 147.13 and 147.83 (C, aromatic).
19k	1.51 (m, $^{3}J_{HH}$ =6.8 Hz, 3H, CH_3), 4.02 (bs, 1H, NH), 4.47 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.50 (m, 2H, aromatic), 6.67 (m, 1H, aromatic), 6.89-6.94(m, 1H, aromatic), 7.08-7.16 (m, 4H, aromatic), 7.25-7.31 (m, 1H, aromatic).	25.24 (CH_3), 53.41 (CH), 112.89 (d, J_{CF}=22.03), 113.48, 113.96 (d, J_{CF}=21.07), 117.18, 121.65, 129.35, 130.36 (d, J_{CF}=8.63), 147.18, 148.52 and 163.46 (d, J_{CF}=247.17) (C & CH, aromatic).
19l	1.50 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 4.00 (bs, 1H, NH), 4.47 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.49 (m, 2H, aromatic), 6.65 (m, 1H, aromatic), 7.00 (m, 2H, aromatic), 7.09 (m, 2H, aromatic), 7.31-7.34 (m, 2H, aromatic).	25.42 (CH_3), 53.11 (CH), 113.52, 115.64 (d, J_{CF}=21.07), 117.64, 127.52 (d, J_{CF}=8.63), 129.34, 141.10 (d, J_{CF}=2.87), 147.31 and 161.93 (d, J_{CF}=245.26) (C & CH, aromatic).
19m	1.52 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.69 (s, 3H, OCH_3), 4.08 (bs, 1H, NH), 4.49 (q, $^{3}J_{HH}$ =6.6 Hz, 1H, CH), 6.08 (s, 1H, aromatic), 6.16 (d, $^{3}J_{HH}$ = 8.5 Hz, 1H, aromatic), 6.23 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.01 (t, $^{3}J_{HH}$ =8.2 Hz, 1H, aromatic), 7.21-7.39 (m, 5H, aromatic)	25.13 (CH_3), 53.65 (CH), 55.13 (OCH_3), 99.48, 102.55, 106.60, 125.98, 127.06, 128.82 and 129.99 (CH, aromatic), 145.35, 148.84 and 160.79 (C, aromatic).
19n	1.50 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.67 (s, 6H, 2×OCH_3), 4.05 (bs, 1H, NH), 4.47 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 5.71 (s, 2H, aromatic), 5.82 (s, 1H, aromatic), 7.22 (t, $^{3}J_{HH}$ =7.3 Hz, 1H, aromatic), 7.29-7.36 (m, 4H, aromatic).	25.08 (CH_3), 53.76 (CH), 55.27 (OCH_3), 89.90, 92.43, 126.00, 127.12, and 128.88 (CH, aromatic), 145.37, 149.40 and 161.74 (C, aromatic).
19o	1.46 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.76 (bs, 1H, NH), 4.38 (q, $^{3}J_{HH}$ =6.7 Hz, 1H, CH), 6.44 (d, $^{3}J_{HH}$ =9.1 Hz, 2H, aromatic), 6.67 (d, $^{3}J_{HH}$ =8.7 Hz, 2H, aromatic), 7.17-2.21 (m, 1H, aromatic), 7.26-7.34 (m, 4H, aromatic).	25.27 (CH_3), 54.34 (CH), 55.81 (OCH_3), 114.65, 114.87, 126.02, 126.94 and 128.74 (CH, aromatic), 141.70, 145.64 and 151.97 (C, aromatic).
19p	1.52 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 4.08 (bs, 1H, NH), 4.44 (q, $^{3}J_{HH}$ =6.4 Hz, 1H, CH), 6.36-6.40 (m, 2H, aromatic), 7.15-7.18 (m, 2H, aromatic), 7.24-7.26 (m, 1H, aromatic), 7.33-7.34 (m, 4H, aromatic)	25.16 (CH_3), 53.64 (CH), 115.05, 125.92, 127.22, 128.91 and 131.94 (CH, aromatic), 109.00, 144.78 and 146.34 (C, aromatic).

Table 4.9 continued…….

19q	1.51 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 4.06 (bs, 1H, NH), 4.44 (q, $^{3}J_{HH}$ =6.4 Hz, 1H, CH), 6.40-6.44 (m, 2H, aromatic), 7.01-7.05 (m, 2H, aromatic), 7.22-7.34 (m, 5H, aromatic).	25.18 (CH_3), 53.73 (CH), 114.54, 125.93, 127.21, 128.90 and 129.08 (CH, aromatic), 121.94, 144.87 and 145.94 (C, aromatic).
19r	1.51 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.72 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.95 (bs, 1H, NH), 4.81 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.50-6.55 (m, 2H, aromatic), 6.72-6.76 (m, 2H, aromatic), 6.91-6.95 (m, 2H, aromatic), 7.23 (t, $^{3}J_{HH}$ = 8.0 Hz, 1H, aromatic), 7.36 (d, $^{3}J_{HH}$ =8.2 Hz, 1H, aromatic).	22.98 (CH_3), 49.02 (CH), 55.40 and 55.79 (OCH_3), 110.57, 114.65, 114.82, 120.90, 126.54 and 127.74 (CH, aromatic), 133.01, 141.79, 151.85 and 156.85 (C, aromatic).
19s	1.46 (d, $^{3}J_{HH}$ =6.9 Hz, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.76 (bs, 1H, NH), 4.35 (q, $^{3}J_{HH}$ =6.9 Hz, 1H, CH), 6.43-6.47 (m, 2H, aromatic), 6.65-6.68 (m, 1H, aromatic), 6.72-6.75 (m, 1H, aromatic), 6.91-6.94 (m, 2H, aromatic), 7.21 (t, $^{3}J_{HH}$ =8.0 Hz, 1H, aromatic).	25.23 (CH_3), 54.40 (CH), 55.26 & 55.82 (OCH_3), 111.81, 112.04, 114.64, 114.85, 118.37 and 129.75 (CH, aromatic), 141.72, 147.58, 151.99 and 160.02 (C, aromatic).
20a	1.77 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.23 (bs, 1H, NH), 5.52 (s, 1H, =CH), 6.14-6.16 (m, 2H, aromatic), 6.82-6.85 (m, 1H, aromatic), 7.22-7.26 (m, 1H, aromatic), 7.34-7.37 (m, 7H, aromatic), 7.57 (d, $^{3}J_{HH}$=7.8 Hz, 2H, aromatic).	30.35 (CH_3), 55.33 (C), 57.38 (OCH_3), 98.94, 102.76, 114.22, 125.53, 126.83, 126.99, 127.47, 127.51, 128.35, 128.61, 129.15, 135.56, 139.83, 144.76, 149.06 and 160.77 (C & CH, aromatic & alkene).
20b	1.84 (s, 3H, CH_3), 2.46 & 2.47 (s, 6H, 2xCH_3, Ar-CH_3), 3.83 (s, 3H, OCH_3), 4.30 (bs, 1H, NH), 5.61 (s, 1H, =CH), 6.22-6.26 (m, 2H, aromatic), 6.97 (d, $^{3}J_{HH}$=8.2 Hz, 1H, aromatic), 7.15 (d, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 7.22-7.37 (m, 5H, aromatic), 7.46 (d, $^{3}J_{HH}$=8.2 Hz, 1H, aromatic), 7.48 (s, 1H, aromatic).	21.54 & 21.81 (Ar-CH_3), 30.21 (CH_3), 55.18 (C), 57.24 (OCH_3), 98.85, 102.55, 114.13, 122.60, 126.15, 126.32, 126.73, 127.40, 127.63, 128.14, 128.41, 129.71, 135.36, 137.81, 137.98, 139.75, 144.71, 149.01 and 160.62 (C & CH, aromatic & alkene).
20c	1.81 (s, 3H, CH_3), 2.40 & 2.46 (s, 6H, 2xCH_3, Ar-CH_3), 3.81 (s, 3H, OCH_3), 4.28 (bs, 1H, NH), 5.58 (s, 1H, =CH), 6.19-6.23 (m, 2H, aromatic), 6.94 (d, $^{3}J_{HH}$=8.2 Hz, 1H, aromatic), 7.21-7.27 (m, 4H, aromatic), 7.34 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic), 7.52 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic).	21.08 & 21.32 (Ar-CH_3), 30.30 (CH_3), 55.19 (C), 56.98 (OCH_3), 98.86, 102.57, 114.29, 125.40, 126.67, 127.37, 128.95, 129.17, 135.21, 136.41, 136.87, 137.04, 144.78, 146.19 and 160.59 (C & CH, aromatic & alkene).

Table 4.9 continued…….

20d	0.95-1.01 (m, 6H, 2xCH_3), 1.37-1.46 (m, 4H, 2xCH_2), 1.59-1.71 (m, 4H, 2xCH_2), 1.78 (s, 3H, CH_3), 2.60-2.69 (m, 4H, 2xCH_2), 3.78 (s, 3H, OCH_3), 4.23 (bs, 1H, NH), 5.53 (s, 1H, =CH), 6.14-6.19 (m, 2H, aromatic), 6.91 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 7.18-7.26 (m, 4H, aromatic), 7.32 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 7.31 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 7.50 (d, $^3J_{HH}$=8.2 Hz, 2H, aromatic).	14.14 & 14.16 (CH_3), 22.58 (CH_2), 30.23 (CH_3), 33.77, 33.83, 35.33 and 35.57 (CH_2), 55.26 (C), 57.12 (OCH_3), 98.83, 102.56, 114.27, 125.45, 126.79, 127.42, 128.31, 128.53, 128.95, 135.16, 137.09, 141.52, 142.12, 144.80, 146.37 and 160.62 (C & CH, aromatic & alkene).
20e	1.36 (s, 9H, 3xCH_3), 1.40 (s, 9H, 3xCH_3), 1.80 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.24 (bs, 1H, NH), 5.54 (s, 1H, =CH), 6.15-6.20 (m, 2H, aromatic), 6.95 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic), 7.34-7.44 (m, 6H, aromatic), 7.32 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 7.54 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic).	30.17 (CH_3), 31.51 and 31.57 (CH_3), 34.54 and 34.69 (C), 55.24 (C), 57.04 (OCH_3), 98.79, 102.57, 114.20, 125.15, 125.25, 125.40, 126.84, 127.44, 128.71, 135.03, 136.84, 144.80, 146.06, 149.65, 150.29 and 160.61 (C & CH, aromatic & alkene).
20f	0.93-0.98 (m, 6H, 2xCH_3), 1.37-1.42 (m, 8H, 4xCH_2), 1.64-1.72 (m, 4H, 2xCH_2), 1.79 (s, 3H, CH_3), 2.61-2.70 (m, 4H, 2xCH_2), 3.78 (s, 3H, OCH_3), 4.24 (bs, 1H, NH), 5.54 (s, 1H, =CH), 6.15-6.19 (m, 2H, aromatic), 6.92 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic), 7.18-7.26 (m, 4H, aromatic), 7.32 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 7.51 (d, $^3J_{HH}$=8.2 Hz, 2H, aromatic).	14.19 (CH_3), 22.69 (CH_2), 30.19 (CH_3), 31.29, 31.34, 31.70, 35.59 and 35.82 (CH_2), 55.21 (C), 57.08 (OCH_3), 98.80, 102.52, 114.22, 125.42, 126.76, 127.37, 128.26, 128.48, 128.60, 128.73, 128.91, 135.12, 137.05, 141.51, 142.12, 144.77, 146.34 and 160.58 (C & CH, aromatic & alkene).
20g	1.60 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 4.46 & 4.53 (s, 4H, 2xCH_2), 5.49 (s, 1H, =CH), 5.97 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic), 6.23 (s, 1H, aromatic), 6.60 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 7.17-7.27 (m, 6H, aromatic), 7.43 (d, $^3J_{HH}$=8.2 Hz, 2H, aromatic).	31.14 (CH_3), 55.43 (C), 57.46 (OCH_3), 64.95 (OCH_2), 99.80, 103.44, 115.63, 126.29, 127.72, 127.88, 127.95, 129.85, 136.89, 140.21, 140.47, 141.63, 147.13, 149.84 and 161.89 (C & CH, aromatic & alkene).
20h	1.62 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.64 (bs, 1H, NH), 5.49 (s, 1H, =CH), 6.02 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 6.25 (s, 1H, aromatic), 6.58 (d, $^3J_{HH}$=7.3 Hz, 1H, aromatic), 6.69-6.75 (m, 4H, aromatic), 6.95 (d, $^3J_{HH}$=7.3 Hz, 2H, aromatic), 7.06-7.15 (m, 2H, aromatic).	31.15 (CH_3), 55.42 (C), 57.54 (OCH_3), 99.65, 103.37, 113.53, 114.16, 115.16, 115.46, 116.72, 117.48, 121.24, 127.36, 127.95, 130.13, 130.18, 136.96, 142.75, 147.01, 152.53, 158.15 and 161.91 (C & CH, aromatic & alkene).

Table 4.9 continued…….

20i	1.77 (s, 3H, CH_3), 3.77, 3.80 & 3.86 (s, 9H, 3xOCH_3), 4.31 (bs, 1H, NH), 5.51 (s, 1H, =CH), 6.15-6.21 (m, 2H, aromatic), 6.90-6.97 (m, 5H, aromatic), 7.34 (d, $^3J_{HH}$=8.2 Hz, 2H, aromatic), 7.52 (d, $^3J_{HH}$=8.7 Hz, 2H, aromatic).	30.08 (CH_3), 55.12 (C), 55.28 & 56.68 (OCH_3), 98.77, 102.52, 113.61, 113.67, 114.27, 126.54, 126.63, 127.24, 130.08, 132.11, 134.65, 141.33, 144.76, 158.35, 158.97 and 160.53 (C & CH, aromatic & alkene).
20j	1.76 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.19 (bs, 1H, NH), 5.49 (s, 1H, =CH), 6.13-6.17 (m, 2H, aromatic), 6.87 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 6.95-7.13 (m, 11H, aromatic), 7.31-7-37 (m, 6H, aromatic), 7.51 (d, $^3J_{HH}$=8.7 Hz, 2H, aromatic).	30.20 (CH_3), 55.19 (C), 56.99 (OCH_3), 98.93, 102.81, 114.10, 118.63, 119.10, 123.46, 126.68, 126.98, 127.38, 129.89, 130.43, 134.70, 134.81, 143.87, 144.65, 156.22, 156.77, 157.24, 157.32 and 160.76 (C & CH, aromatic & alkene).
20k	1.72 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.19 (bs, 1H, NH), 5.44 (s, 1H, =CH), 6.14-6.16 (m, 2H, aromatic), 6.76 (d, $^3J_{HH}$=9.6 Hz, 1H, aromatic), 7.19 (d, $^3J_{HH}$=7.8 Hz, 2H, aromatic), 7.38-7.49 (m, 6H, aromatic).	30.19 (CH_3), 55.38 (C), 57.09 (OCH_3), 99.12, 103.14, 113.75, 121.01, 121.63, 126.33, 127.31, 127.41, 130.78, 131.55, 131.68. 135.09, 138.50, 144.52, 147.93 and 161.01 (C & CH, aromatic & alkene).
20l	1.74 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.21 (bs, 1H, NH), 5.46 (s, 1H, =CH), 6.16-6.18 (m, 2H, aromatic), 6.78 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic), 7.20-7.34 (m, 6H, aromatic), 7.42 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 7.51 (s, 1H, aromatic).	30.21 (CH_3), 55.37 (C), 57.30 (OCH_3), 99.12, 103.24, 113.54, 123.80, 125.87, 126.41, 127.22, 127.34, 127.42, 127.77, 129.12, 129.65, 129.97, 134.25, 134.56, 141.44, 144.42, 150.95 and 161.04 (C & CH, aromatic & alkene).
20 m	1.73 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.20 (bs, 1H, NH), 5.45 (s, 1H, =CH), 6.15-6.17 (m, 2H, aromatic), 6.77 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic), 7.25-7.35 (m, 6H, aromatic), 7.46 (d, $^3J_{HH}$=8.7 Hz, 2H, aromatic).	30.16 (CH_3), 55.32 (C), 56.97 (OCH_3), 99.09, 103.06, 113.76, 126.41, 126.91, 127.35, 128.54, 128.65, 130.39, 132.80, 133.41, 134.91, 138.01, 144.51, 147.37 and 160.93 (C & CH, aromatic & alkene).
20n	1.76 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.21 (bs, 1H, NH), 5.46 (s, 1H, =CH), 6.15-6.19 (m, 2H, aromatic), 6.80 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 7.00-7.09 (m, 5H, aromatic), 7.30-7.34 (m, 2H, aromatic), 7.50-7.54 (m, 2H, aromatic).	30.16 (CH_3), 55.27 (C), 56.92 (OCH_3), 98.98, 102.92, 113.97, 115.22 (d, $^2J_{CF}$=21.07), 126.62, 127.23, 127.24 (d, $^2J_{CF}$=18.20), 130.59, 130.66, 134.71, 135.55, 144.52, 144.77, 160.84, 161.77 (d, $^1J_{CF}$=246.22) and 162.37 (d, $^1J_{CF}$=247.17) (C & CH, aromatic & alkene).

Table 4.9 continued…….

20o	0.90 (t, $^3J_{HH}$=7.3 Hz, 3H, CH_3), 0.97 (t, $^3J_{HH}$=7.3 Hz, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.34-1.49 (m, 4H, 2xCH_2), 1.55-1.60 (m, 2H, CH_2), 2.29-2.34 (m, 2H, CH_2), 3.62 (bs, 1H, NH), 3.75 (s, 3H, OCH_3), 5.09 (s, 1H, =CH), 6.00 (s, 1H, aromatic), 6.16 (d, $^3J_{HH}$=8.5 Hz, 1H, aromatic), 6.99 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic).	14.22, 14.72 and 17.75 (CH_3), 22.65, 30.30, 34.34 and 46.93 (CH_2), 54.79 (C), 55.19 (OCH_3), 98.47, 101.89, 114.35, 124.36, 124.52, 132.58, 145.53 and 160.15 (C&CH, aromatic & alkene).
20p	0.85 (t, $^3J_{HH}$=6.8 Hz, 3H, CH_3), 0.88 (t, $^3J_{HH}$=6.9 Hz, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.21-1.55 (m, 14H, 7xCH_2), 2.26-2.32 (m, 2H, CH_2), 3.58 (bs, 1H, NH), 3.72 (s, 3H, OCH_3), 5.06 (s, 1H, =CH), 5.97 (s, 1H, aromatic), 6.14 (d, $^3J_{HH}$=8.5 Hz, 1H, aromatic), 6.96 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic).	14.29, 14.34, 22.79, 22.88, 24.20, 28.33, 30.22, 32.06, 32.26, 32.52 and 44.40 (CH_3 &CH_2), 54.80 (C), 55.25 (OCH_3), 98.58, 101.96, 114.44, 124.32, 124.57, 132.91, 145.52 and 160.18 (C&CH, aromatic & alkene).
20q	0.86 (t, $^3J_{HH}$=6.8 Hz, 3H, CH_3), 0.89 (t, $^3J_{HH}$=6.9 Hz, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.25-1.56 (m, 18H, 9xCH_2), 2.28-2.34 (m, 2H, CH_2), 3.59 (bs, 1H, NH), 3.74 (s, 3H, OCH_3), 5.07 (s, 1H, =CH), 5.99 (s, 1H, aromatic), 6.15 (d, $^3J_{HH}$=8.5 Hz, 1H, aromatic), 6.97 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic).	14.30, 22.87, 22.91, 24.49, 28.59, 29.51, 29.99, 30.22, 31.97, 32.07, 32.28 and 44.46 (CH_3 &CH_2), 54.80 (C), 55.26 (OCH_3), 98.57, 101.95, 114.44, 124.31, 124.57, 132.89, 145.51 and 160.17 (C&CH, aromatic & alkene).
20r	0.88 (t, $^3J_{HH}$=7.3 Hz, 3H, CH_3), 0.89 (t, $^3J_{HH}$=6.9 Hz, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.26-1.59 (m, 26H, 13xCH_2), 2.29-2.35 (m, 2H, CH_2), 3.60 (bs, 1H, NH), 3.75 (s, 3H, OCH_3), 5.08 (s, 1H, =CH), 6.00 (s, 1H, aromatic), 6.16 (d, $^3J_{HH}$=8.5 Hz, 1H, aromatic), 6.99 (d, $^3J_{HH}$=8.2 Hz, 1H, aromatic).	14.33, 22.91, 24.54, 28.63, 29.54, 29.58, 29.73, 29.84, 30.23, 30.34, 32.10, 32.13, 32.29 and 44.46 (CH_3 &CH_2), 54.80 (C), 55.23 (OCH_3), 98.57, 101.95, 114.43, 124.30, 124.57, 132.89, 145.52 and 160.17 (C&CH, aromatic & alkene).
20s	1.27 (s, 3H, CH_3), 1.69-1.82 (m, 2H, CH_2), 2.53-2.61 (m, 1H, CH_2), 2.67-2.80 (m, 3H, CH_2), 2.88-2.93 (m, 2H, CH_2), 3.64 (bs, 1H, NH), 3.78 (s, 3H, OCH_3), 5.08 (s, 1H, =CH), 6.02 (s, 1H, aromatic), 6.23 (d, $^3J_{HH}$=8.5 Hz, 1H, aromatic), 7.10 (d, $^3J_{HH}$=8.7 Hz, 1H, aromatic), 7.15-7.34 (m, 10H, aromatic).	30.53, 31.28, 34.14, 34.92 and 46.12 (CH_3 &CH_2), 55.00 (C), 55.26 (OCH_3), 98.67, 102.24, 113.83, 124.22, 124.52, 125.78, 126.03, 128.50, 128.54, 128.72, 132.55, 142.25, 142.88, 145.46 and 160.37 (C&CH, aromatic & alkene).

Table 4.9 continued…….

20t	1.43 (t, $^{3}J_{HH}$=7.32 Hz, 3H, CH_3), 1.81 (s, 3H, CH_3), 4.02 (q, $^{3}J_{HH}$=7.3 Hz, 2H, CH_2), 4.26 (bs, 1H, NH), 5.57 (s, 1H, =CH), 6.17-6.20 (m, 2H, aromatic), 6.88 (d, $^{3}J_{HH}$=9.6 Hz, 1H, aromatic), 7.27 (t, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 7.35-7.42 (m, 7H, aromatic), 7.61 (d, $^{3}J_{HH}$=8.0 Hz, 2H, aromatic).	15.04 & 30.31 (CH_3), 57.30 (C), 63.37 (OCH_2), 99.48, 103.34, 114.09, 125.48, 126.72, 126.91, 127.40, 127.46, 128.29, 128.54, 129.11, 135.57, 139.83, 144.73 and 149.06, 160.10 (C & CH, aromatic & alkene).
20u	1.33 (d, $^{3}J_{HH}$=6.4 Hz, 6H, 2xCH_3), 1.77 (s, 3H, CH_3), 4.19 (bs, 1H, NH), 4.47-4.53 (m, 1H, CH) 5.51 (s, 1H, =CH), 6.11-6.14 (m, 2H, aromatic), 6.82 (d, $^{3}J_{HH}$=9.1 Hz, 1H, aromatic), 7.23 (t, $^{3}J_{HH}$=7.3 Hz, 1H, aromatic), 7.31-7.37 (m, 7H, aromatic), 7.57 (d, $^{3}J_{HH}$=7.8 Hz, 2H, aromatic).	22.36 (CH_3), 30.36 (CH), 57.37 (C), 69.77 (OCH), 100.76, 104.52, 114.00 125.54, 126.74, 126.94, 127.42, 127.47, 128.31, 128.58, 129.14, 135.58, 139.87, 144.75, 149.12 and 159.07 (C & CH, aromatic & alkene).
20v	0.95 (t, $^{3}J_{HH}$=6.4 Hz, 3H, CH_3), 1.37-1.47 (m, 6H, 3xCH_2), 1.79 (s, 3H, CH_3), 1.76-1.80 (m, 2H, CH_2), 3.94 (t, $^{3}J_{HH}$=6.9 Hz, 2H, CH_2), 4.23 (bs, 1H, NH), 5.53 (s, 1H, =CH), 6.16-6.17 (m, 2H, aromatic), 6.82-6.86 (m, 1H, aromatic), 7.25 (t, $^{3}J_{HH}$=6.4 Hz, 1H, aromatic), 7.32-7.39 (m, 7H, aromatic), 7.58 (d, $^{3}J_{HH}$=8.2 Hz, 2H, aromatic).	14.26 (CH_3), 22.82, 25.94, 29.48 (CH_2), 30.33 (CH_2), 31.80 (CH_2), 57.35 (C), 68.02 (OCH_2), 99.50, 103.44, 114.04, 125.53, 126.70, 126.95, 127.42, 127.48, 128.32, 128.58, 129.15, 135.62, 139.88, 144.72, 149.10 and 160.35 (C & CH, aromatic & alkene).
20 w	1.76 (s, 3H, CH_3), 4.21 (bs, 1H, NH), 5.01 (s, 2H, CH_2), 5.51(s, 1H, =CH), 6.19-6.21 (m, 2H, aromatic), 6.82 (d, $^{3}J_{HH}$=8.7 Hz, 1H, aromatic), 7.21-7.25 (m, 1H, aromatic), 7.29-7.42 (m, 12H, aromatic), 7.55 (d, $^{3}J_{HH}$=8.5 Hz, 2H, aromatic).	30.37 (CH_3), 57.42 (C), 70.07 (OCH_2), 99.90, 103.68, 114.44, 125.56, 126.96, 127.01, 127.48, 127.54, 127.68, 128.16, 128.36, 128.62, 128.77, 129.16, 135.58, 137.35, 139.81, 144.65, 149.03 and 160.03 (C & CH, aromatic & alkene).
20x	1.68 (s, 3H, CH_3), 3.29 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.35 (bs, 1H, NH), 5.53 (s, 1H, =CH), 5.79 (s, 1H, aromatic), 5.90 (s, 1H, aromatic), 7.17-7.31 (m, 8H, aromatic), 7.50 (d, $^{3}J_{HH}$=8.7 Hz, 2H, aromatic).	29.73 (CH_3), 55.18 (C), 55.35 & 56.46 (OCH_3), 90.12, 92.24, 104.10, 125.54, 126.29, 126.86, 127.33, 127.52, 128.26, 128.43, 135.00, 143.02, 146.67, 148.54, 158.16 and 161.36 (C & CH, aromatic & alkene).

Table 4.9 continued…….

20y	0.88-0.97 (m, 6H, 2×CH_3), 1.24 (s, 3H, CH_3), 1.26-1.58 (m, 10H, 5xCH_2), 2.35-2.39 (m, 2H, CH_2), 3.58 (bs, 1H, NH), 5.21 (s, 1H, =CH), 6.42 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 6.60 (t, $^3J_{HH}$=7.3 Hz, 1H, aromatic), 6.60 (t, $^3J_{HH}$=7.8 Hz, 1H, aromatic), 6.99 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic).	14.22 & 14.34 (CH_3), 22.87, 23.37, 26.72, 30.10, 30.78, 31.90 and 44.08 (CH_2), 54.61 (C), 112.97, 116.79, 120.64, 123.56, 126.74, 128.31, 133.18 and 144.13 (C&CH, aromatic & alkene).
20z	0.88-0.96 (m, 6H, 2×CH_3), 1.22 (s, 3H, CH_3), 1.25-1.55 (m, 10H, 5xCH_2), 2.22 (s, 3H, ArCH_3), 2.31-2.37 (m, 2H, CH_2), 3.65 (bs, 1H, NH), 5.15 (s, 1H, =CH), 6.26 (s, 1H, aromatic), 6.42 (d, $^3J_{HH}$=7.3 Hz, 1H, aromatic), 6.98 (d, $^3J_{HH}$=7.8 Hz, 1H, aromatic).	14.23 & 14.35 (CH_3), 21.51, 22.87, 23.37, 26.72, 30.10, 30.83, 31.96 and 44.07 (CH_2), 54.63 (C), 113.70, 117.69, 123.50, 125.75, 133.10, 138.24 and 144.03 (C&CH, aromatic & alkene).
4u	1.41 (t, $^3J_{HH}$= 7.1 Hz, 3H, CH_3), 3.60 (s, 2H, NH_2) 4.00 (q, $^3J_{HH}$= 7.1 Hz, 2H, OCH_2), 6.25-6.30 (m, 2H, aromatic), 6.34 (d, $^3J_{HH}$= 8.2 Hz, 1H, aromatic), 7.07 (t, $^3J_{HH}$= 8.0 Hz, 1H, aromatic).	14.93 (CH_3), 63.23 (OCH_2), 101.65, 104.57, 107.86 and 130.11 (CH, aromatic), 147.92 and 160.13 (C, aromatic).
4v	1.33 (d, $^3J_{HH}$= 6.4 Hz, 6H, 2×CH_3), 3.64 (s, 2H, NH_2) 4.50 (sep, $^3J_{HH}$= 6.4 Hz, 1H, CH), 6.24-6.34 (m, 3H, aromatic), 7.05 (t, $^3J_{HH}$= 8.0 Hz, 1H, aromatic).	22.29 (CH_3), 69.73 (OCH), 103.19, 106.00, 107.90 and 130.20 (CH, aromatic), 147.96 and 159.18 (C, aromatic).
4w	0.91 (t, $^3J_{HH}$= 6.9 Hz, 3H, CH_3), 1.31-1.35 (m, 4H, CH_2), 1.44 (q, $^3J_{HH}$=7.8 Hz. 2H, CH_2), 1.75 (q, $^3J_{HH}$=6.9 Hz, 2H, CH_2), 3.63 (s, 2H, NH_2), 3.91 (t, $^3J_{HH}$= 6.6 Hz, 2H, OCH_2), 6.24-6.33 (m, 3H, aromatic), 7.04 (t, $^3J_{HH}$= 8.0 Hz, 1H, aromatic).	14.25 (CH_3), 22.82, 25.95, 29.48 and 31.80 (CH_2), 67.99 (OCH_2), 101.89, 104.85, 107.92 and 130.24 (CH, aromatic), 147.91 and 160.53 (C, aromatic).
4x	3.65 (s, 2H, NH_2), 5.03 (s, 2H, OCH_2), 6.30-6.42 (m, 3H, aromatic), 7.07 (t, $^3J_{HH}$= 8.0 Hz, 1H, aromatic), 7.25-7.44 (m, 5H, aromatic).	70.02 (OCH_2), 102.22, 105.06, 108.39, 127.64, 128.06, 128.74 and 130.33 (CH, aromatic), 137.43, 147.98 and 160.21 (C, aromatic).

Table 4.10. Crystal and refinement data for **20a**.

Identification code	**20a**
Empirical formula	$C_{23}H_{21}NO$
Formula weight	327.41
Temperature, K	103(2)
Crystal system	Monoclinic
Space group	P2(1)/c
a, Å	5.9791(19)
b, Å	32.635(10)
c, Å	8.845(3)
β, deg	95.044(10)
Volume, $Å^3$	1719.2(9)
Z	4
Density (calculated) , Mg/m^3	1.265
Absorption coefficient, mm^{-1}	0.077
F(000)	696
Crystal size, mm^3	0.40 x 0.20 x 0.10
Reflections collected	18343
Independent reflections	5106 [R(int)=0.0454]
Completeness (to θ, deg)	99.3 % (30.25°)
Max. and min. transmission	0.9924 and 0.9700
Data / restraints / parameters	5106 / 0 / 232
Goodness-of-fit on F^2	1.092
Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.1468
R indices (all data)	R1 = 0.0929, wR2 = 0.1758
Largest diff. peak and hole, $e.Å^{-3}$	0.380 and -0.471

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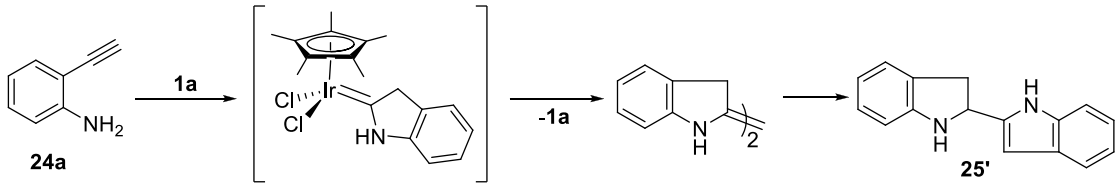
Chapter 5: $[Cp^*IrCl_2]_2$-Catalysed Formation of Indoles and 2,2'-Biindoles from 2-Alkynylanilines

As has been detailed in chapter 2, the reaction of $[Cp^*IrCl_2]_2$, **1a**, with an aniline and a terminal alkyne leads to the formation of an orthometallated iridium amino-carbene **7**. The proposed reaction pathway involves a hydroamination step. From that, it is possible that an intramolecular hydroamination with a 2-ethynylaniline, **24** may lead to an iridium amino-carbene which cannot undergo orthometallation as a result of ring strain but instead to dimerization and aromatization to afford a 2-(2-indolyl)indoline, **25'** (Scheme 5.1).



Scheme 5.1

5.1 Reaction of 1a with 2-ethynylanilines

The reaction of **1a** with 2-ethynylaniline afforded the 2-indolylindole (biindole), **25a**, instead. The biindole has been completely characterized, including by a single-crystal X-ray structural analysis (Figure 5.1). The biindole structural motif has been found in many naturally occurring alkaloids and biologically active molecules such as the tjipanazoles, staurosporine, *ent*-staurosporine, holyrine, arcyriaflavin, rebeccamycin and staurosporinone,[1] and has also been utilized in synthetic biologically active molecules like (-)-K252a.[2] The 2-indolylindoles are often prepared via the Madelung cyclization reaction from N-aryl oxamide derivatives,[3] intramolecular cyclization of the corresponding amino-diiynes,[4] or coupling of the corresponding indole derivatives.[5]

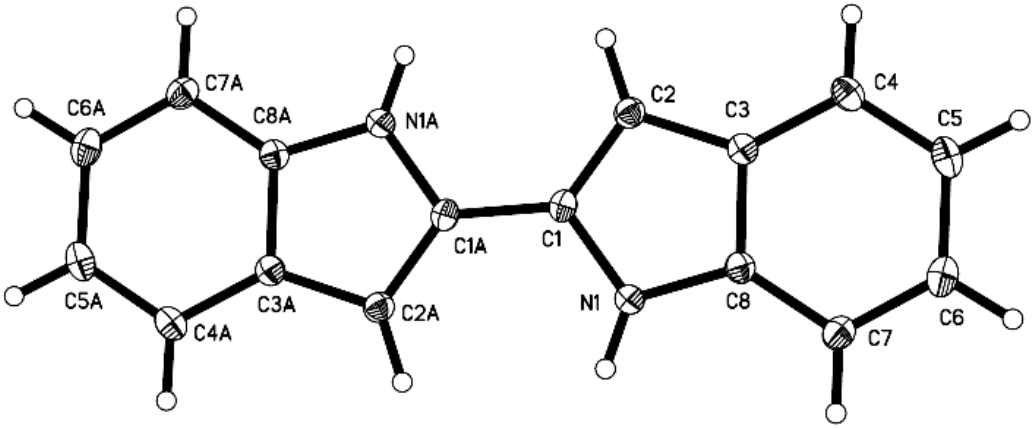
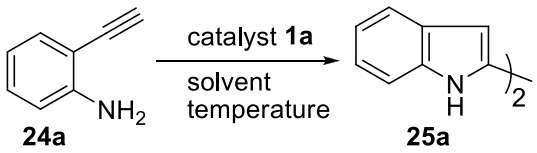


Figure 5.1. ORTEP plot of **25a**. Thermal ellipsoids are plotted at the 50% probability level. Selected bond lengths (Å) and angles (deg): N(1)-C(1), 1.3842(16); C(1)-C(2), 1.3821(16); C(2)-C(3), 1.4265(17); C(3)-C(8), 1.4189(16); N(1)-C(8), 1.3760(16); C(8)-N(1)-C(1), 109.38(10), N(1)-C(8)-C(3), 107.52(10); C(2)-C(1)-N(1), 108.82(10).

An optimisation study (Table 5.1) showed that the yield improved slightly with temperature (entries 1-3), and lower catalyst loading led to a slight lowering of the yield (entries 3-5). Although many solvents (DCE, toluene, THF, CH_2Br_2 and DMF) were effective for the reaction, acetonitrile was found to be the best (entries 4, 7, 9 and 11-13).

The substrate scope was investigated with various 2-ethynylanilines which could be synthesized by a straightforward synthetic route, i.e., Sonogashira cross-coupling and subsequent hydrolysis.[6] For example, the coupling reaction of 2-iodo-4-methylaniline with trimethylsilylacetylene followed by protodesilylation provided the desired substrate **24b** in an overall yield of 81% for the two steps. The substrate scope study showed excellent chemoselectivity; a wide range of functional groups (alkyls, halides, CN, NO_2 and esters) at the *4*-position of the aromatic ring were tolerated (Table 5.2). However, the reaction did not proceed with secondary alkynylanilines (*N*-methyl-2-ethynylaniline).

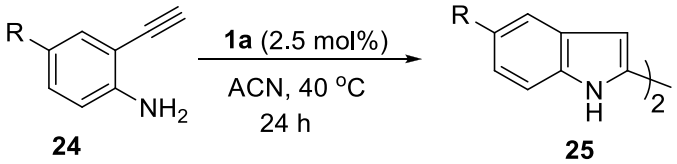
Table 5.1. Optimization study for the conversion of 24a to 25a.



S/No	1a (mol %)	Solvent	T, (°C)	t, (h)	Yield (%)[b]
1	5	DCE	40	12	77
2	5	DCE	50	12	82
3	5	DCE	80	12	86
4	2.5	DCE	80	12	81
5	1	DCE	80	12	71
6	2.5	DCE	40	24	79
7	2.5	toluene	80	12	75
8	2.5	toluene	110	12	78
9	2.5	THF	60	12	77
10	2.5	CH_3OH	60	12	-
11	2.5	ACN	80	12	91
12	2.5	CH_2Br_2	80	12	70
13	2.5	DMF	80	12	60
14	2.5	ACN	40	24	89

[a]The cyclization of **24a** (0.5 mmol) was carried out in the presence of **1a** in a solvent (5 mL) at various temperature. [b]Isolated yields.

Table 5.2. Substrate scope study for the conversion of 24 to 25.

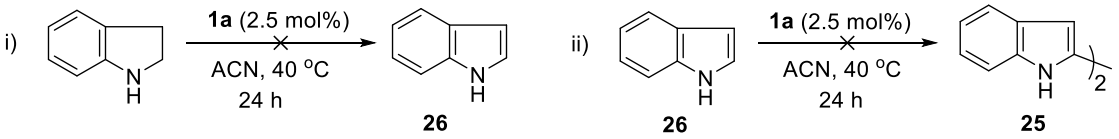


S/No	R	Yield (%)[b]		S/No	R	Yield (%)[b]
1	H	**25a**, 89[c]		6	NO_2	**25f**, 89
2	CH_3	**25b**, 81		7	CN	**25g**, 73
3	^{t}Bu	**25c**, 79		8	COOMe	**25h**, 79
4	Br	**25d**, 86		9	COOEt	**25i**, 87
5	Cl	**25e**, 84[c]				

[a]The cyclization of **24** (0.5 mmol) was carried out in the presence of **1a** (0.0125 mmol) in acetonitrile (5 mL) at 40 °C for 24 h. [b]Isolated yields. [c]Molecular structures determined by single-crystal X-ray crystallographic analyses.

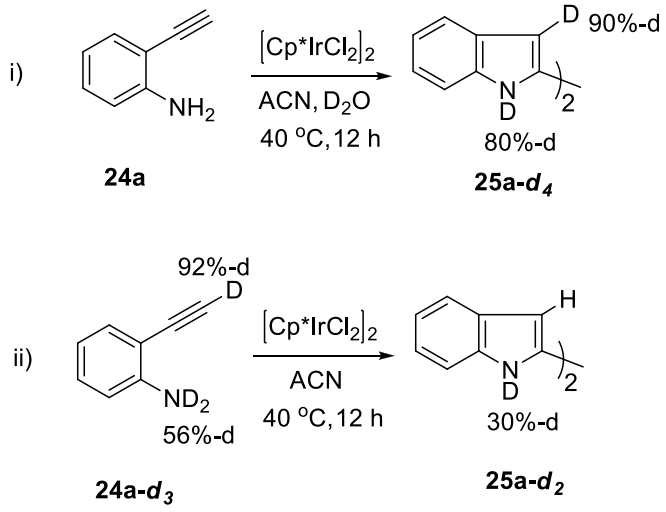
5.2 Mechanistic investigations into the formation of the biindoles

Under similar conditions as those above, indoline and indole failed to react with **1a** in separate reactions to afford indole **26** (via dehydrogenation reaction) or the biindole **25a** (via oxidative coupling), respectively (Scheme 5.2). These results indicated that the reaction did not proceed via the formation and subsequent dehydrogenation of 2-(2-indolyl)indoline **25'** or the formation and subsequent oxidative coupling of indole.



Scheme 5.2

Isotopic labelling experiments employing (a) *2*-ethynylaniline and D_2O, and (b) d_3-ethynylaniline alone, afforded **25a** with two and none, respectively, of the 3 and 3' protons of biindole being deuterated (Scheme 5.3). These results clearly pointed to cleavage and loss of alkyne ≡C-H and adventitious water as the source for the protons at the 3 and 3' positions in the biindole, and are consistent with the formation of a vinylidene intermediate via an intermolecular deprotonation-protonation steps as have been proposed earlier in chapters 2 and 3 in the reaction pathway.[7]



Scheme 5.3

A proposed reaction pathway that accounts for these observations is shown in Figure 5.2; the energetics for the various steps (for *2*-ethynylaniline) have also been computed with density functional theory, and the computed free energy changes ($\Delta G^{\ominus}$, in kJ mol^{-1}) are also given. The initial steps up to the formation of the vinylidene intermediate **B'** follows that which we have proposed earlier for many reactions of **1a** with functionalised alkynes.[7] The next step involves an intramolecular attack of the amino group at the vinylidene α-carbon together with elimination of HCl, leading to cyclization into an indolyl, to the intermediate **X**.

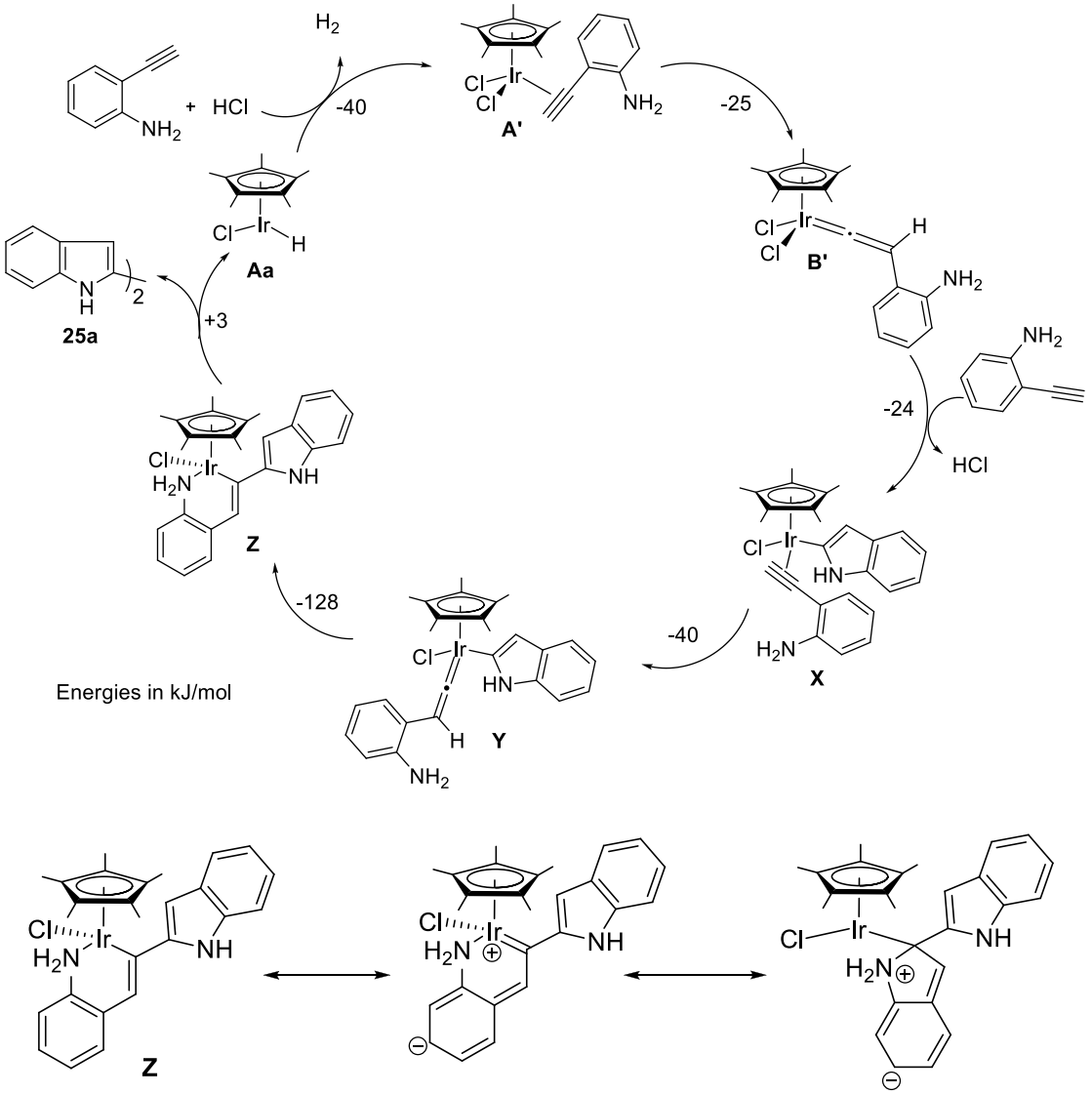


Figure 5.2. Proposed catalytic cycle for the formation of **25** catalysed by **1a**.

The alkyne in the computationally optimized structures of **A'** and **X** are asymmetrically coordinated; the non-substituted end is closer to the metal than the substituted end (Rh-C bond lengths of 2.159 and 2.426 Å in **A'**, and 2.169 and 2.282 Å in **X**, respectively) and this may be attributed to the asymmetrical nature of the alkyne, where the bulkier substituent on the alkyne is oriented further away from the metal center. Rearrangement of the coordinated ethynylaniline to a vinylidene (**Y**), followed by 1,2-migratory insertion of the indolyl gives **Z**. From the intermediate **Z**, we believe that it undergoes a Meisenheimer-type rearrangement (bottom of Figure 5.2) to afford the bisindole and the hydrido species **Aa**. The latter can be converted back to **1a** via reaction with HCl. Similar iridium hydrido species are known to react with HCl to afford the corresponding iridium chloride complex.[8]

The computationally optimized structure of **Z**, together with selected bond parameters, is shown in Figure 5.3. It contains an iridacycle with an Ir-C bond length of 2.054 Å, which is similar to the corresponding bond lengths in the iridacycles **12b** and **13e** (2.002(8) and 2.015(6) Å, respectively) which have been crystallograhically characterised. In these compounds, there is considerable double bond character in the Ir-C bond, suggesting a certain degree of aromaticity in the iridacycles. This aromaticity may be the driving force for the rearrangement to **Z**.

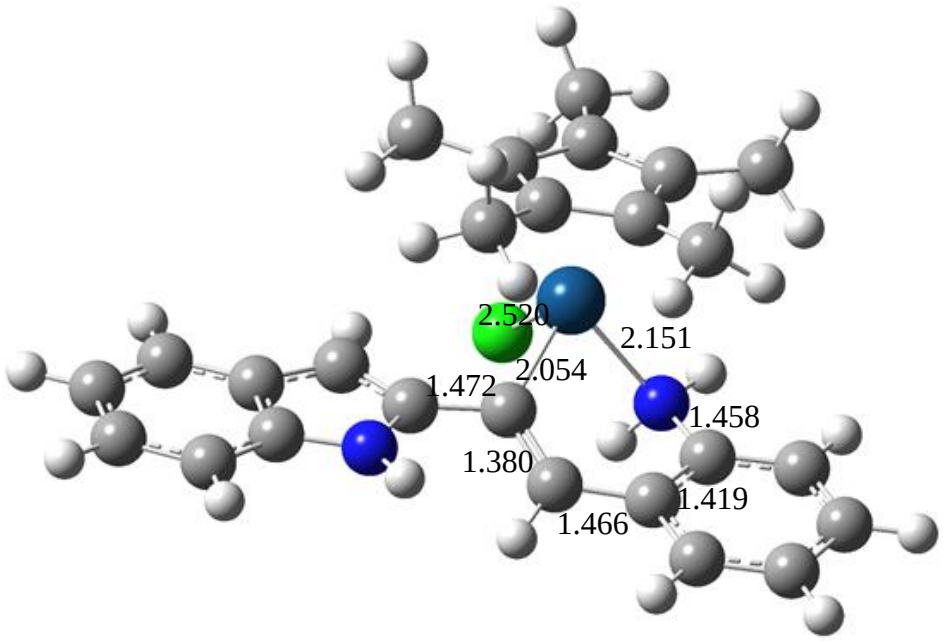
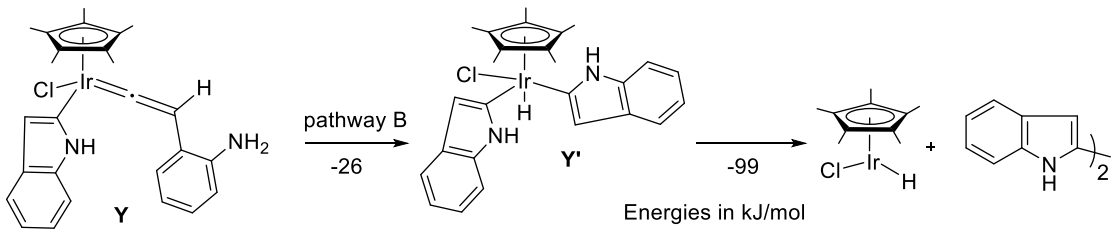


Figure 5.3. Computationally optimized geometry, with selected bong lengths (Å), of intermediate **Z**.

An alternative pathway from **Y** which we have also considered is that depicted in Scheme 5.4, in which the vinylidene undergoes a cyclisation similar to that in the step from **B'** to **X**, to form the di-indolyl intermediate **Y'**. Reductive elimination from here would also result in biindole and **Aa**, and the free energies associated with this pathway are also reasonable, although the iridium(V) species **Y'** is sterically crowded and its formation of **Y'** is energetically less favoured than for **Z**.



Scheme 5.4

Two side products were also isolated from the reaction of **24a**; the indole **26** (2%), and a new compound **27** (3%) (Figure 5.4). The structure of **27** was proposed on the basis of its spectroscopic characteristics. It's ^{1}H NMR spectrum shows two singlet resonances, at 2.33 and 4.02 ppm, which could be assigned to a =C-CH_3 and benzylic

CH_2 protons, respectively. The corresponding ^{13}C resonances appeared at 8.71 and 29.00 ppm, respectively, in the $^{13}C\{H\}$ NMR spectrum, and the correlations confirmed by a DEPT-135 NMR spectrum. The NH_2 and NH protons gave rise to two broad singlet resonances at 4.28 and 7.92 ppm, respectively, in the ^{1}H NMR spectrum. Peaks at m/z 236 and 237 in the GC-MS and HRMS were consistent with $[M]^+$ and $[M+1]^+$ ions, respectively.

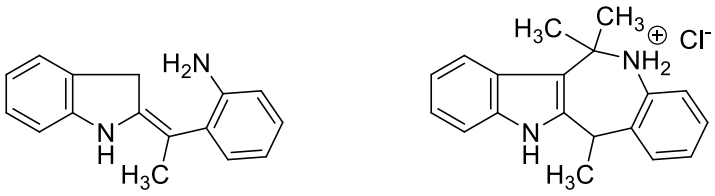
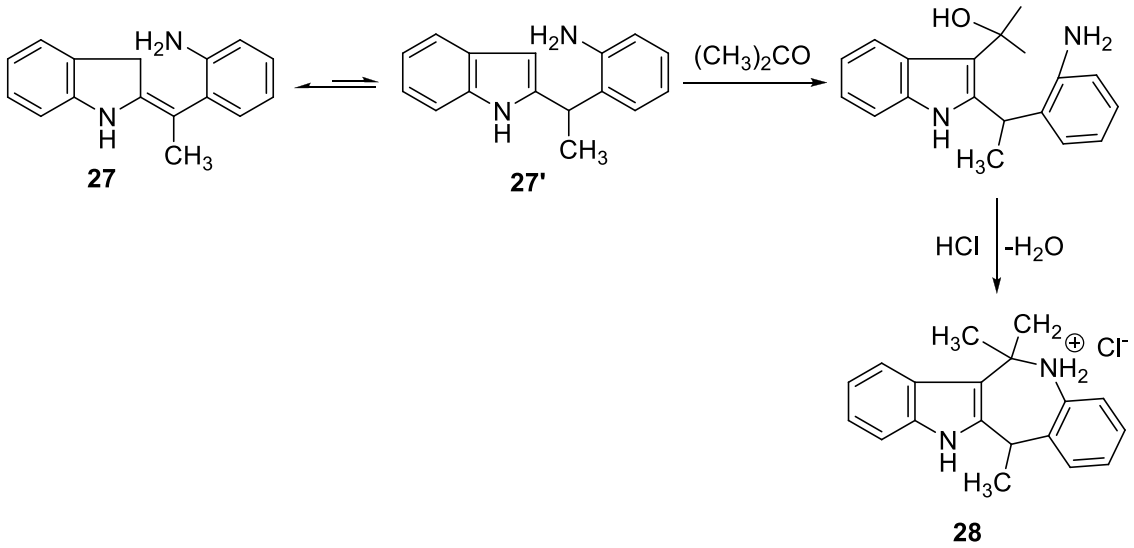


Figure 5.4. Molecular structure of **27** and **28**.

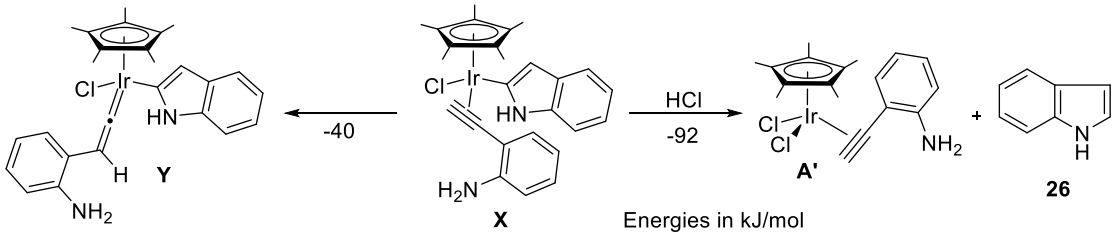
During an attempt at growing a crystal of **27** from acetone as its HCl salt, white crystals were obtained, which upon a single-crystal X-ray crystallographic study, turned out to be compound **28**, presumably resulting from a rearrangement of **27** to **27'** followed by reaction with acetone (Scheme 5.5).



Scheme 5.5

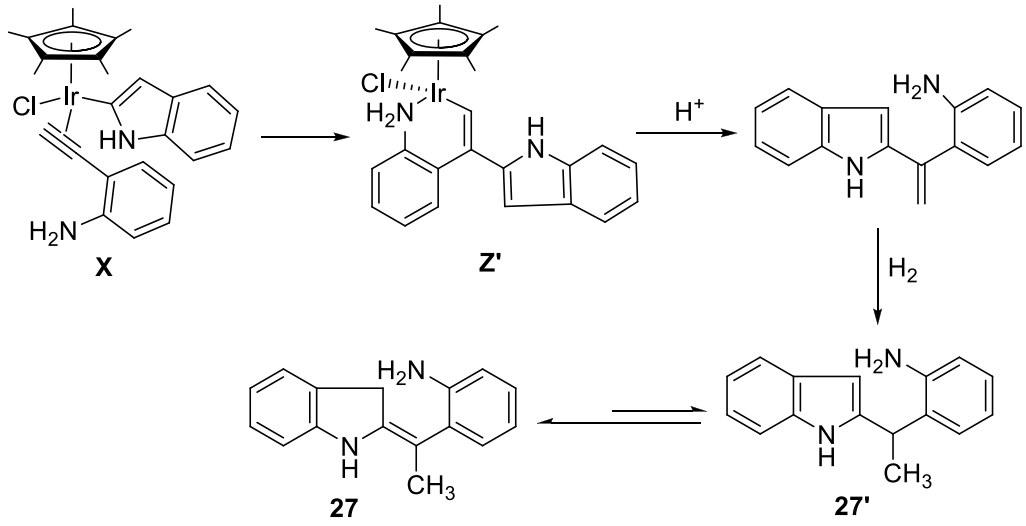
The computed free energy change for protonolysis of the indolyl ligand in **X** to form the indole **26** is more favourable than for the vinylidene rearrangement from **X** to

Y (Scheme 5.6). Presumably, this protonolysis is less favoured in the absence of a proton source in the aprotic solvents used.



Scheme 5.6

Compound **27** could have been derived from a 1,2-alkyne insertion,[9] instead of a vinylidene rearrangement, from **X** to form **Z'**; an isomer of **Z** in which the indolyl was substituted on the α- rather than the β-carbon of the alkenyl ligand. Protonolysis and decoordination would afford an alkene intermediate, which could undergo subsequent reduction and isomerization to form **27** (Scheme 5.7). The reduction of the alkene compound could have been by the iridium hydride species **Aa**.



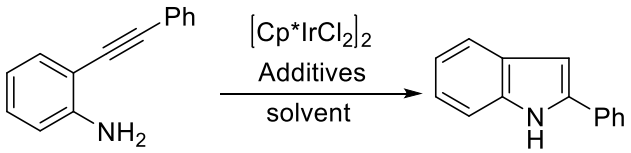
Scheme 5.7

5.3 Reaction of 1a with internal 2-alkynylanilines

The above catalytic formation of bisindole is not possible for alkynylanilines with an internal alkyne. Nevertheless, it was found that the use of a salt additive

enabled cyclisation of, for example, 2-(phenylethynyl)aniline (**24j**) to 2-phenylindole (**29a**) in 76% yield (Table 5.3).

Table 5.3. Identification of catalytic system for the intramolecular cyclization of 2-ethynylaniline.



24j **29a**

S/No	1a (mol %)	Additives (mol %)	solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	5	-	Acetonitrile-d_3	60	12	76
2	5	$NaBF_4$ (10)	Acetonitrile-d_3	60	4	95
3	5	$NaBF_4$ (10)	Toluene-d_8	60	18	89
4	5	$NaBF_4$ (10)	Chloroform-d_3	60	30	30
5	5	$NaBF_4$ (10)	THF-d_8	60	24	76
6	5	$NaBF_4$ (10)	Methanol-d_4	60	4	95
7	2	$NaBF_4$ (4)	Acetonitrile-d_3	60	8	93
8	1	$NaBF_4$ (2)	Acetonitrile-d_3	60	8	59
9	2	$NaBF_4$ (4)	Acetonitrile-d_3	40	8	96
10	2	NH_4PF_6 (4)	Acetonitrile-d_3	40	8	78
11	2	NH_4BF_4 (4)	Acetonitrile-d_3	40	8	83
12	2	$NaPF_6$ (4)	Acetonitrile-d_3	40	8	67
13	-	$NaBF_4$ (4)	Acetonitrile-d_3	40	8	-

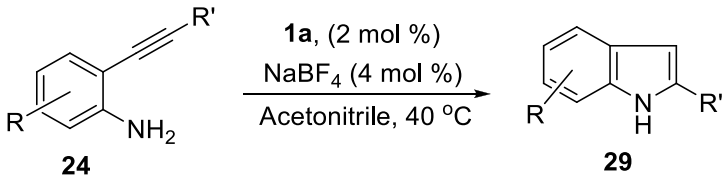
[a]The cyclization of **24j** (0.5 mmol) was carried out in the presence of **1a** / additive in a solvent (5 mL) at various temperature with various time. [b]Yields reported are NMR yields, with 1,3,5-trimethoxybenzene as internal standard.

An optimization study showed that the reaction was more effective in the more polar solvents methanol or acetonitrile (entries 2-6). The catalyst loading could be effectively lowered from 5 to 2 mol% without detriment to the yield, but further lowering to 1 mol% afforded a significantly lower yield (entries 2, 7 and 8). A number of different additives ($NaPF_6$, $NaBF_4$, NH_4BF_4 or NH_4PF_6) could be employed (entries 9-12), although $NaBF_4$ showed the best catalytic activity; the additive $NaBF_4$ alone did not catalyse the reaction (entry 13).

Similar cyclisations have been demonstrated with several metal systems such as Pd,[10] Au,[11] In,[12] Zn,[13] Pt,[14] and Rh,[15] although they have drawbacks such as higher

catalyst loading,[13] high temperature,[10,11c,12-14] or the need for protection of the amino group.[13] Several iridium catalysts have also been reported to catalyse this reaction,[15a-b,16] but the functional group tolerance of the reaction has apparently been tested for only two catalytic systems, both of which showed very limited functional group compatibility.[16b-c] For example, Liu et. al. reported the iridium catalysed intramolecular cyclization of aminoalkynes,[16b] but their catalyst failed with alkynylanilines with electron-withdrawing substituent on the aniline moiety. Similarly, that reported by Fukuzawa was not effective for alkynylanilines with electron-withdrawing substituent on the alkyne moiety.[16c] In our system, a substrate scope study showed that the reaction worked well for both electron-withdrawing and -donating substituents on the aniline, as well as for sterically crowded 2-ethynylaniline (Table 5.4).

Table 5.4. Substrate scope study for intramolecular cyclization of internal 2-ethynylanilines.



24 **29**

S/No	R	R'	Yield (%)[b]
1	H	C_6H_5	**29a**, 90
2	*4*-CH_3	C_6H_5	**29b**, 92
3	*4*-$C(CH_3)_3$	C_6H_5	**29c**, 93
4	*4*-Cl	C_6H_5	**29d**, 91
5	*4*-NO_2	C_6H_5	**29e**, 89
6	*4*-CO_2Et	C_6H_5	**29f**, 92
7	*4*-CO_2Et, *6*-C_2Ph	C_6H_5	**29g**, 85
8	H	^nBu-*4*-C_6H_5	**29h**, 87
9	H	Cl-*4*-C_6H_5	**29i**, 81
10	H	^nBu	**29j**, 91

[a]Conditions: 2-alkynylaniline (0.5 mmol), **1a** (0.01 mmol) and $NaBF_4$ (0.02 mmol) in acetonitrile (3 mL), heated to 40 ^oC for 8 h.
[b]Isolated yields.

With ethynylaniline, however, the reaction in the presence of NH_4PF_6 as additive afforded a mixture of indole and bisindole in a 20:80 ratio. With 20 mol% of $AgPF_6$ as additive, the yield of indole improved dramatically (80%), but a 5 mol% of the additive was ineffective. A control experiment using $AgPF_6$ alone showed, however, that Ag^+ can catalyse the reaction and hence the formation of indole was not pursued further.

5.4 Reaction pathway for the formation of 2-substituted indoles

The intramolecular cyclization of internal alkynylanilines to give the indoles can proceed with or without $NaBF_4$ as an additive, with respective yields of 93 and 76%, although the reaction time was reduced substantially in the presence of $NaBF_4$. These results suggest that the formation of iridium cationic species may be involved. The proposed reaction pathway to **29** involving a cationic iridium species as the active catalyst is shown in Figure 5.5, and it is similar to that proposed for rhodium catalysed hydroamination in chapter 4.

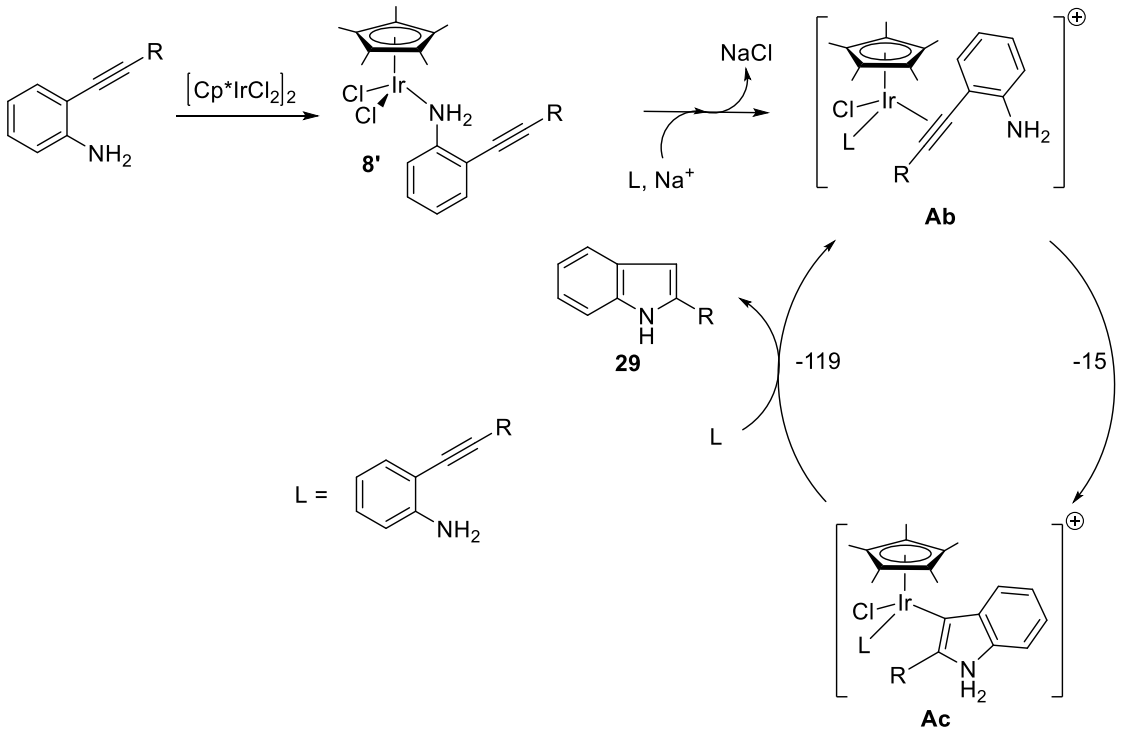


Figure 5.5. Proposed catalytic cycle for **1a** catalysed formation of indoles.

Presumably, the intermediate **Ab** is formed via alkynylaniline coordination to **1a** followed by loss of a chloride ion. The optimized structure of **Ab** is shown in Figure 5.6, together with selected bond parameters. The structure is essentially the same as that of the cationic rhodium alkyne complex **Q** in chapter 4, with a very asymmetric bonding of the alkyne to the metal centre (the bond distances of 2.150 and 2.832 Å, respectively, for Ir-C(CH_3) and Ir-C(Ph)). The alkyne is thus more like an allene, with the phenyl ring plane almost orthogonal to the Ir-C-CH_3 plane (dihedral angle of ~121^o).

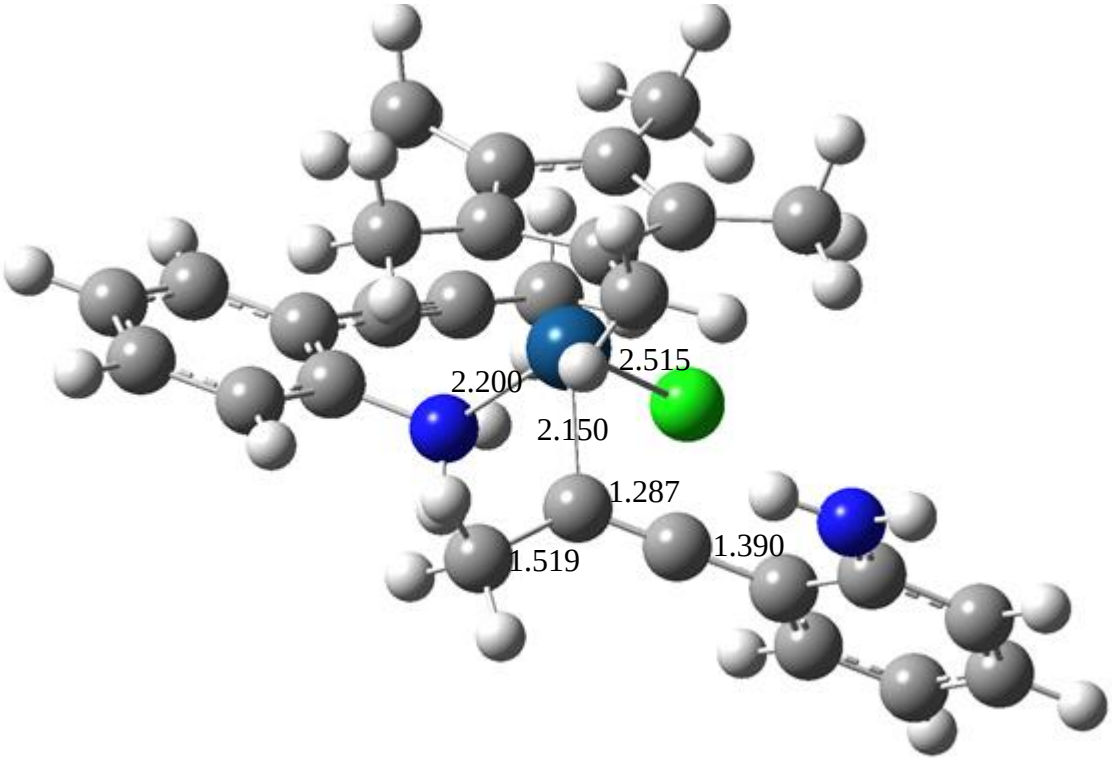


Figure 5.6. Computationally optimized structure of intermediate **Ab**.

From the intermediate **Ab**, a hydroamination reaction via nucleophilic attack of amine onto the coordinated alkyne would form **Ac**, and the computed free energy change for this step is -15 kJ mol^{-1}. Loss of a proton and protonolysis at the alkenyl-iridium bond would give the indole, and recoordination of an alkynylaniline would regenerate **Ab**. The overall $\Delta G^{\ominus}$ value for these last steps is -119 kJ mol^{-1}.

The reaction of 2-ethynylaniline with **1a** or **1a**/NH_4PF_6 afforded biindole or a mixture of indole and biindole, respectively, whereas internal 2-alkynylanilines gave indole in the presence of **1a**/$NaBF_4$. Taken together, it suggests that the formation of iridium cationic species tends to lead to the formation of indole derivatives. We believe that both the reactions began with a common intermediate, in which an alkyne is coordinated. From there, a vinylidene rearrangement followed by nucleophilic attack of amine at vinylidene α-carbon leads to biindole formation, whereas intramolecular nucleophilic attack of amine onto the coordinated alkyne leads to indole formation. We think that the different pathway taken depends on whether a neutral or cationic iridium species is involved, as well as the nature of the alkyne moiety. With internal alkynes, the vinylidene rearrangement is not possible, and with a cationic species, nucleophilic attack at the coordinated alkyne is favoured.

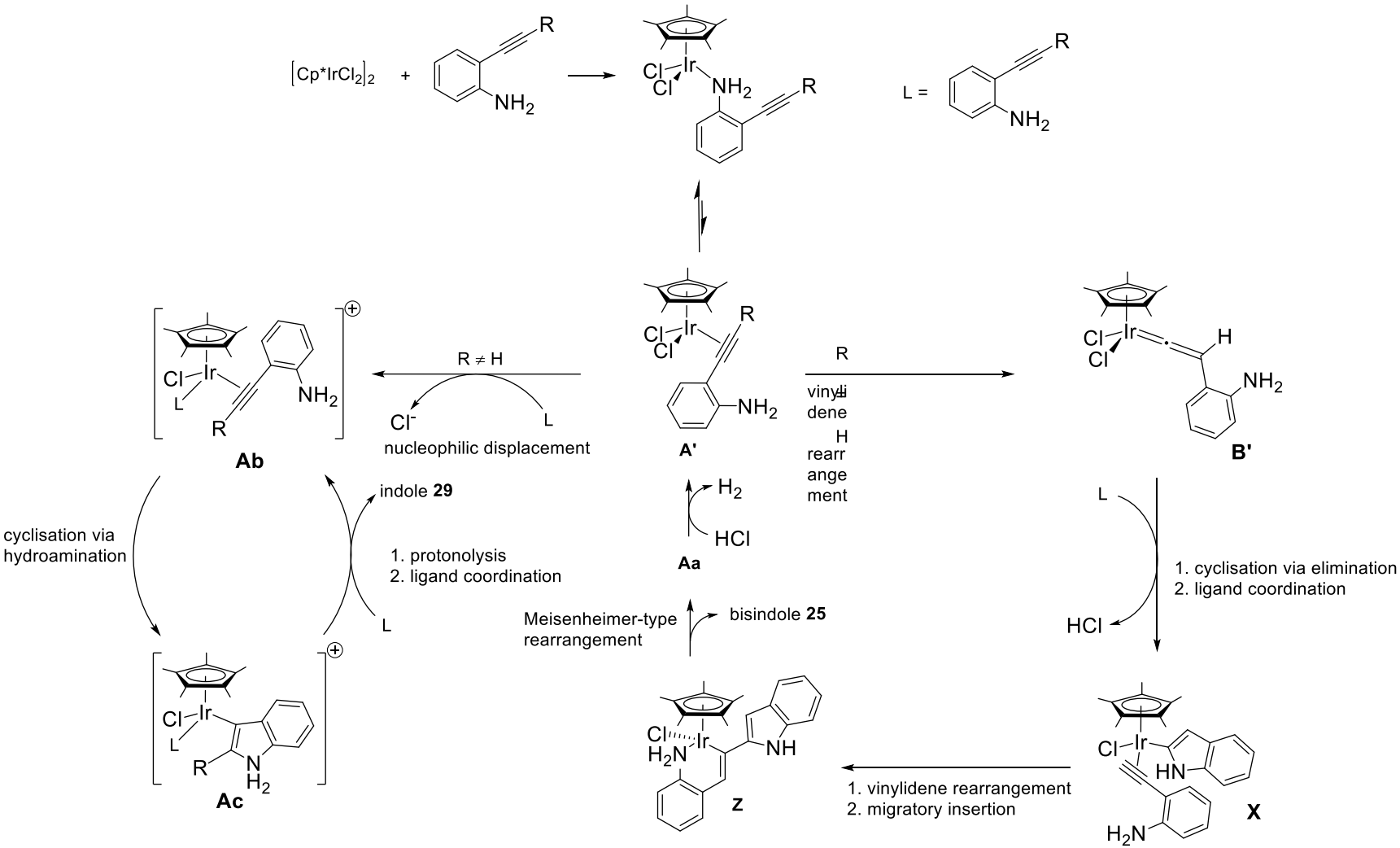
5.5 Conclusions

The complex **1a** was found to be an effective catalyst for the intramolecular hydroamination of terminal aminoalkynes to afford biindoles **25**. In the presence of a salt additive, it catalysed the cyclisation of internal alkynylanilines to form indoles **29**. The reaction pathways to both **25** and **29** have been studied experimentally via labelling experiments, as well as computationally, and they are presented in Scheme 5.8.

A common intermediate **A'**, corresponding to coordination of the alkynylaniline via the alkyne moiety, was proposed. For terminal alkynylanilines, a vinylidene rearrangement (to **B'**) is favoured. An intramolecular nucleophilic attack at vinylidene carbon, resulting in an HCl elimination and cyclisation, together with coordination of a second alkynylaniline, leads to intermediate **X**. A second vinylidene

rearrangement followed by a migratory insertion gives **Z**, which subsequently eliminates the biindole.

In the case of internal alkynylanilines, this vinylidene rearrangement is not feasible, and the use of additives leads to a cationic iridium species via loss of a chloride ligand. In this cationic species **Ab**, the alkyne moiety is bound asymmetrically, and the computational results suggest that it is almost allene-like. Nevertheless, nucleophilic attack of amino group onto the coordinated alkyne leads to the formation of intermediate **Ac**, which cleaves the Ir-C bond to afford the indole. The results suggest that this pathway is favoured not only for internal alkynylanilines but also in the presence of salt additives and in polar solvents.


[Cp*IrCl2]2
L =
A'
B'
Ab
Ac
Aa
Z
X
R ≠ H
Cl-
nucleophilic displacement
vinylidene
H
rearrangement
H2
HCl
indole 29
1. protonolysis
2. ligand coordination
cyclisation via
hydroamination
1. cyclisation via elimination
2. ligand coordination
Meisenheimer-type
rearrangement
bisindole 25
1. vinylidene rearrangement
2. migratory insertion

Scheme 5.8

5.6 Experimental Section

5.6.1 General procedure. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded either in acetone-d_6 or in DMSO-d_6 for **25** and in $CDCl_3$ for **29** on a JEOL ECA400 or ECA400SL spectrometer. All other experimental procedures have been described in section 2.6.1. Diffraction quality crystals were grown by slow diffusion of hexane into a acetone solution. The reaction energetics were studied using the procedures described in section 2.6.1 without using polarization functions.

5.6.2 General procedure for the preparation of 2-ethynylanilines

In an oven dried 2-neck RB flask were placed $PdCl_2(PPh_3)_2$ (88 mg, 0.125 mmol), CuI (24 mg, 0.125 mmol) and THF (5 mL). To this suspension, *2*-iodo-*4*-methylaniline (582 mg) and triethylamine (702 µL, 5.0 mmol) were added. The reaction mixture was degassed by bubbling with argon for 15 min. Trimethylsilylacetylene (390 µL, 2.75 mmol), was then added, and the reaction mixture was stirred at RT. After complete consumption of the *2*-iodoanilines (~2 h, by TLC), the reaction mixture was filtered through celite, and the solvent was rotary evaporated to obtain the crude product.

The crude product obtained was then dissolved in methanol (10 mL), K_2CO_3 (345 mg, 3.59 mmol) added and then, stirred at RT for 2h. The methanol was then removed by rotary evaporattion, the residue redissolved in water (10 mL), and the product extracted with diethyl ether (3×15 mL). The crude product obtained was purified by silica gel (60-120 mesh) column chromatography using ethylacetate/ hexane (1:9, V/V) as eluent to give pure *2*-ethynyl-*4*-methylaniline, **24b** (265 mg, 81%). Similar procedures were used with the other alkynes and anilines to obtain **24b-i**. The amount of reagents used, product formed (with yield) and HRMS for the products, are given in the Table 5.6.

5.6.3 Formation of biindole derivatives 25

In a 50 mL carius tube, *2*-ethynylaniline **24a** (58 mg, 0.5 mmol) and **1a** (10 mg, 0.0125 mmol) were dissolved in acetonitrile (5 mL). The reaction mixture was then degassed (3 x freeze-pump-thaw) and stirred at 40 °C for 24h. The solvent was then removed under reduced pressure and the crude product obtained was washed with cold (-30 °C) dichloromethane (2 mL) to afford **25a** as a brown solid.

Similar procedures were used with the other alkynylanilines to obtain **25b-i**. The amount of reagents used, product formed (with yield) and HRMS for the products, are given in the Table 5.7.

5.6.4 Formation of indole derivatives 29

In a carius tube, $[Cp^*IrCl_2]_2$ (8 mg, 0.01 mmol), $NaBF_4$ (2 mg, 0.02 mol%) and *2*-(phenylethynyl)aniline (97 mg, 0.5 mmol) were dissolved in dry acetonitrile (3 mL). The reaction mixture was stirred at 40^o C for 8 h, and then the reaction solvent was removed by rotary evaporation to give the crude product. Purification of the crude product by silica gel (60-120 mesh) column chromatography using ethylacetate/ hexane (1:9, V/V) as eluent gave pure *2*-phenylindole, **29a**. Similar procedures were used with the other alkynylanilines to obtain **29b-j**. The amount of reagents used, product formed (with yield) and HRMS for the products, are given in the Table 5.7.

5.6.5 Deuterium labelling experiments for 25

A sample of *2*-ethynylaniline (58 mg, 0.5 mmol) with D_2O (200 µL) and *2*-ethynylaniline-d_3 (58 mg, 0.5mmol) alone were added to **1a** (10 mg, 0.0125 mmol) in acetonitrile (3 mL) in two separate experiments. The mixtures were degassed (3 cycles of freeze-pump-thaw) and then stirred at 40 ^{o}C for 24 h, after which the solvents were removed under vacuum and the crude products were characterized by ^{1}H NMR spectroscopy.

Table 5.5. Amounts of reagents used and product formed. In all experiments, amount of reagents used are: 2-iodoanilines (2.5 mmol), alkyne (2.75 mmol), $PdCl_2(PPh_3)_2$ (88 mg, 0.125 mmol , CuI (24 mg, 0.125 mmol), Alkyne (702 µl, 5.0 mmol) and K_2CO_3 (345 mg, 3.59 mmol).

	2-iodo anilines	**Alkyne**	**2-alkynylanilines Yield (%)**	**HRMS $(M+H)^+$:**
1	I-*2*-CH_3-*4*-C_6H_3-NH_2 (582 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	C_9H_9N, **24b**, (265 mg, 81%)	Found: 132.0813 Calc: 132.0813
2	I-*2*-$C(CH_3)_3$-*4*-C_6H_3-NH_2 (687 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	$C_{12}H_{15}N$, **24c**, (329 mg, 76%)	Found: 174.1287 Calc: 174.1283
3	I-*2*-Br-*4*-C_6H_3-NH_2 (742 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	C_8H_6BrN, **24d**, (429 mg, 88%)	Found: 195.9753 Calc: 195.9762
4	I-*2*-Cl-*4*-C_6H_3-NH_2 (632 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	C_8H_6ClN, **24e**, (320 mg, 85%)	Found: 152.0271 Calc: 152.0267
5	I-*2*-NO_2-*4*-C_6H_3-NH_2 (660 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	$C_8H_6N_2O_2$,**24f**, (320mg, 79%)	Found: 163.0508 Calc: 163.0508
6	I-*2*-CN-*4*-C_6H_3-NH_2 (610 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	$C_9H_6N_2$, **24g**, (216 mg, 61%)	Found: 143.0615 Calc: 143.0609
7	I-*2*-CO_2Me-*4*-C_6H_3-NH_2 (692 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	$C_{10}H_9NO_2$,**24h**, (381mg, 87%)	Found: 176.0704 Calc: 176.0712
8	I-*2*-CO_2Et-*4*-C_6H_3-NH_2 (725 mg, 2.5 mmol)	$(CH_3)_3SiCCH$ (390 µL)	$C_{11}H_{11}NO_2$,**24i**, (326 mg, 69%).	Found: 190.0874 Calc:190.0868
9	I-*2*-C_6H_4-NH_2 (547 mg)	C_6H_5CCH (300 µL)	$C_{14}H_{11}N$, **24j**, (400 mg, 83%)	Found: 194.0970 Calc:194.0970
10	I-*2*-CH_3-*4*-C_6H_3-NH_2 (582 mg)	C_6H_5CCH (300 µL)	$C_{15}H_{13}N$, **24k**, (378 mg, 73%)	Found: 208.1124 Calc:208.1126
11	I-*2*-$C(CH_3)_3$-*4*-C_6H_3-NH_2 (687 mg)	C_6H_5CCH (300 µL)	$C_{18}H_{19}N$, **24l**, (485 mg, 78%)	Found: 250.1595 Calc:250.1596
12	I-*2*-Cl-*4*-C_6H_3-NH_2 (632 mg)	C_6H_5CCH (300 µl)	$C_{14}H_{10}ClN$,**24m**, (454 mg, 80%)	Found: 228.0579 Calc:228.0580
13	I-*2*-NO_2-*4*-C_6H_3-NH_2 (660 mg)	C_6H_5CCH (300 µL)	$C_{14}H_{10}N_2O_2$, **24n**, (470 mg, 79%)	Found: 239.0827 Calc:239.0821
14	I-*2*-CO_2Et-*4*-C_6H_3-NH_2 (725 mg)	C_6H_5CCH (300µL)	$C_{17}H_{15}NO_2$, **24o**, (589 mg, 89%)	Found: 266.1183 Calc:266.1181
15	I-*2,6*-CO_2Et-*4*-C_6H_3-NH_2 (908 mg)	C_6H_5CCH (300 µL)	$C_{25}H_{19}NO_2$, **24p**, (693 mg, 76%)	Found: 366.1492 Calc:366.1494
16	I-*2*-C_6H_4-NH_2 (547 mg)	nBu-*4*-C_6H_4CCH (350 µL)	$C_{18}H_{19}N$, **24q**, (467 mg, 75%)	Found: 250.1597 Calc:250.1596
17	I-*2*-C_6H_4-NH_2 (547 mg)	Cl-*4*-C_6H_4CCH (374 mg)	$C_{14}H_{10}ClN$, **24r**, (431 mg, 76%)	Found: 228.0581 Calc:228.0580
18	I-*2*-C_6H_4-NH_2 (547 mg)	$CH_3(CH_2)_3CCH$ (318 µL)	$C_{12}H_{15}N$, **24s**, (307 mg, 71%)	Found: 174.1284 Calc: 174.1283

Table 5.6. Amounts of reagents used and product formed. In all experiments, amount of reagents used are: 2-ethynylanilines (0.5 mmol) and **1a** (10 mg, 0.0125 mmol) for **25**, and **1a** (8 mg, 0.01 mmol) and $NaBF_4$ (2 mg, 0.02 mmol) for **29**.

	2-ethynylanilines	**Product (mg, %)**	**HRMS $[M+H]^+$: Found (calc)**		**2-ethynylanilines**	**product (mg, %)**	**HRMS $[M+H]^+$: Found (calc)**
1	HC_2-*2*-$C_6H_4NH_2$ **24a**, (58 mg)	$C_{16}H_{12}N_2$**, 25a**, (48 mg, 83%)	233.1086 (233.1079)	10	PhC_2-*2*-$C_6H_4NH_2$ **24j**, (96 mg)	$C_{14}H_{11}N$, **29a**, (86 mg, 90%)	194.0973 (194.0970)
2	HC_2-*2*-CH_3-*4*-$C_6H_3NH_2$ **24b**, (66 mg)	$C_{18}H_{16}N_2$, **25b**, (54 mg, 81%)	261.1398 (261.1392)	11	PhC_2-*2*-CH_3-*4*-$C_6H_3NH_2$ **24k**, (103 mg)	$C_{15}H_{13}N$, **29b**, (95 mg, 92%)	208.1123 (208.1126)
3	HC_2-*2*-$(CH_3)_3C$-*4*-$C_6H_3NH_2$ **24c**, (86 mg)	$C_{24}H_{28}N_2$ **, 25c**, (78 mg, 79%)	345.2328 (345.2331)	12	PhC_2-*2*-$(CH_3)_3C$-*4*-$C_6H_3NH_2$ **24l**, (125 mg)	$C_{18}H_{19}N$, **29c**, (115 mg, 93%)	250.1593 (250.1596)
4	HC_2-*2*-Br-*4*-$C_6H_3NH_2$ **24d**, (97 mg)	$C_{16}H_{10}Br_2N_2$, **25d**,(81 mg, 86%)	388.9295 (388.9289)	13	PhC_2-*2*-Cl-*4*-$C_6H_3NH_2$ **24m**, (113 mg)	$C_{14}H_{10}ClN$,**29d**, (103 mg, 91%)	228.0583 (228.0580)
5	HC_2-*2*-Cl-*4*-$C_6H_3NH_2$ **24e**, (76 mg)	$C_{16}H_{10}Cl_2N_2$, **25e**, (61 mg, 84%)	301.0288 (301.0299)	14	PhC_2-*2*-NO_2-*4*-$C_6H_3NH_2$ **24n**, (119 mg)	$C_{14}H_{10}N_2O_2$,**29e**, (105 mg, 89%)	239.0821 (239.0821)
6	HC_2-*2*-NO_2-*4*-$C_6H_3NH_2$ **24f**, (81 mg)	$C_{16}H_{10}N_4O_4$, **25f**, (72 mg, 89%)	323.0766 (323.0780)	15	PhC_2-*2*-CO_2Et-*4*-$C_6H_3NH_2$ **24o**, (132 mg)	$C_{17}H_{15}NO_2$, **27f**, (121 mg, 92%)	266.1182 (266.1181)
7	HC_2-*2*-CN-*4*-$C_6H_3NH_2$ **24g**, (71 mg)	$C_{18}H_{10}N_4$, **25g**, (52 mg, 73%)	283.0981 (283.0984)	16	$(PhC_2)_2$-*2,6*-CO_2Et-*4*-$C_6H_3NH_2$, **24p**, (182 mg)	$C_{25}H_{19}NO_2$, **29g**, (155 mg, 85%)	366.1495 (366.1494)
8	HC_2-*2*-CO_2Me-*4*-$C_6H_3NH_2$ **24h**, (88 mg)	$C_{20}H_{16}N_2O_4$, **25h**, (67 mg, 79%)	349.1195 (349.1188)	17	nBu-C_6H_4-C_2-*2*-$C_6H_4NH_2$ **24q**, (125 mg)	$C_{18}H_{19}N$, **29h**, (108 mg, 87%)	250.1596 (250.1596)
9	HC_2-*2*-CO_2Et-*4*-$C_6H_3NH_2$ **24i**, (95 mg)	$C_{22}H_{20}N_2O_2$, **25i**, (67 mg, 87%)	377.1507 (377.1501)	18	Cl-C_6H_4-C_2-*2*-$C_6H_4NH_2$ **24r**, (113 mg)	$C_{14}H_{10}ClN$, **29i**, (92 mg, 81%)	228.0582 (228.0580)
				19	$CH_3(CH_2)_3$-C_2-*2*-$C_6H_4NH_2$ **24s**, (87 mg)	$C_{12}H_{15}N$, **29j**, (78 mg, 91%)	250.1599 (250.1596)

Table 5.7. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for **24**, **25**, **26**, **27** and **29**.

	δ_H, ppm	$^{13}C\{^{1}H\}$, ppm
24b	2.20 (s, 3H, CH_3), 3.35 (s, 1H, ≡CH), 4.11 (bs, 2H, NH_2), 6.62 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 6.96 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.14 (s, 1H, aromatic).	20.42 (CH_3), 81.00 (≡C), 82.35 (≡CH) 114.72, 131.19, 132.85, (CH, aromatic), 106.84, 127.28 and 146.40 (C, aromatic).
24c	1.26 (s, 9H, 3 x CH_3), 3.36 (s, 1H, ≡CH), 4.11 (bs, 2H, NH_2), 6.66 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 6.96 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.34 (s, 1H, aromatic).	32.26 (CH_3), 35.04 (C), 81.39 (≡C), 82.06 (≡CH) 114.50, 127.71, 129.35, (CH, aromatic), 106.37, 140.95 and 146.35 (C, aromatic).
24d	3.41 (s, 1H, ≡CH), 4.25 (bs, 2H, NH_2), 6.58 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.22 (d, $^{3}J_{HH}$ = 8.9 Hz, 1H, aromatic), 7.42 (s, 1H, aromatic).	79.43 (≡C), 83.80 (≡CH), 116.00, 133.18, 134.89, (CH, aromatic), 108.65, 108.92 and 147.76 (C, aromatic).
24e	3.40 (s, 1H, ≡CH), 4.21 (bs, 2H, NH_2), 6.61 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.08 (d, $^{3}J_{HH}$ =8.7 Hz, 1H, aromatic), 7.27 (s, 1H, aromatic).	79.56 (≡C), 83.66 (≡CH), 115.65, 130.40, 132.03, (CH, aromatic), 108.10, 122.24 and 147.34 (C, aromatic).
24f	3.46 (s, 1H, ≡CH), 4.96 (bs, 2H, NH_2), 6.68 (d, $^{3}J_{HH}$ = 9.1 Hz, 1H, aromatic), 8.05 (d, $^{3}J_{HH}$ = 9.2 Hz, 1H, aromatic), 8.26 (s, 1H, aromatic).	78.37 (≡C), 84.47 (≡CH), 113.16, 126.64, 129.55, (CH, aromatic), 105.97, 135.62 and 153.68 (C, aromatic).
24g	3.44 (s, 1H, ≡CH), 4.47 (bs, 2H, NH_2), 6.69 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.36 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.58 (s, 1H, aromatic).	78.39 (≡C), 84.42 (≡CH), 114.20, 133.85 and 137.10, (CH, aromatic), 100.09, 106.93 and 151.90 (C, aromatic), 119.42 (C≡N).
24h	3.39 (s, 1H, ≡CH), 3.83 (s, 3H, CH_3), 4.71 (bs, 2H, NH_2), 6.65 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.80 (d, $^{3}J_{HH}$ = 8.5 Hz, 1H, aromatic), 8.02 (s, 1H, aromatic).	51.94 (OCH_3), 79.67 (≡C), 83.18 (≡CH) 113.44, 132.01, 135.08, (CH, aromatic), 105.92, 119.35 and 152.37 (C, aromatic), 166.67 (C=O).
24i	1.36 (t, $^{3}J_{HH}$ = 7.3 Hz, 3H, CH_3), 3.39 (s, 1H, ≡CH), 4.31 (q, $^{3}J_{HH}$ =7.3 Hz, 2H, OCH_2), 4.71 (bs, 2H, NH_2), 6.67 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.83 (d, $^{3}J_{HH}$ =8.5 Hz, 1H, aromatic), 8.04 (s, 1H, aromatic).	14.61 (CH_3), 60.76 (OCH_2), 79.78 (≡C), 83.13 (≡CH) 113.47, 132.07, 135.08, (CH, aromatic), 105.97, 119.92 and 152.24 (C, aromatic), 166.21 (C=O).
24j	4.84 (bs, 2H, NH_2), 6.75-6.81 (m, 2H, aromatic), 7.14 (t, $^{3}J_{HH}$ =7.6 Hz, 1H, aromatic), 7.31-7.40 (m, 4H, aromatic), 7.53-7.56 (m, 2H, aromatic).	85.82 and 95.15 (≡C) 109.00, 115.29, 119.03, 123.40, 128.46, 128.56, 129.91, 131.73, 132.42 and 146.67 (C&CH, aromatic).

Table 5.7 continued…….

24k	2.26 (s, 3H, CH_3), 4.15 (bs, 2H, NH_2), 6.66 (d, $^3J_{HH}$ =8.2 Hz, 1H, aromatic), 6.97 (d, $^3J_{HH}$ =8.0 Hz, 1H, aromatic), 7.21 (s, 1H, aromatic), 7.34-7.38 (m, 3H, aromatic), 7.53-7.56 (m, 2H, aromatic).	20.44 (CH_3), 86.32 and 94.60 (≡C) 108.12, 114.73, 123.58, 127.37, 128.30, 128.54, 130.77, 131.61, 132.39 and 145.64 (C&CH, aromatic).
24l	1.30 (s, 9H, 3 x CH_3), 4.18 (bs, 2H, NH_2), 6.70 (d, $^3J_{HH}$ =8.7 Hz, 1H, aromatic), 7.20 (d, $^3J_{HH}$ =8.5 Hz, 1H, aromatic), 7.33-7.36 (m, 3H, aromatic), 7.40 (s, 1H, aromatic), 7.54-7.56 (m, 2H, aromatic).	31.60 (CH_3), 34.10 (C), 86.66 and 94.36 (≡C) 107.68, 114.50, 123.62, 127.30, 128.32, 128.89, 131.66, 141.07 and 145.61 (C&CH, aromatic).
24m	4.27 (bs, 2H, NH_2), 6.65 (d, $^3J_{HH}$ =8.7 Hz, 1H, aromatic), 7.09 (d, $^3J_{HH}$ =8.9 Hz, 1H, aromatic), 7.33-7.37 (m, 4H, aromatic), 7.50-7.53 (m, 2H, aromatic).	84.80 & 95.80 (≡C) 105.50, 115.64, 122.49, 123.04, 128.67, 128.79, 129.89, 131.57, 131.74 and 146.57 (C&CH, aromatic).
24n	5.02 (bs, 2H, NH_2), 6.70 (d, $^3J_{HH}$ =9.2 Hz, 1H, aromatic), 7.36-7.40 (m, 3H, aromatic), 7.52-7.55 (m, 2H, aromatic), 8.03 (d, $^3J_{HH}$ =9.2 Hz, 1H, aromatic), 8.29 (s, 1H, aromatic).	83.37 and 96.33 (≡C) 113.09, 122.24, 126.15, 128.77, 128.94, 129.23, 131.83, 138.87 and 150.03 (C&CH, aromatic).
24o	1.37 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 4.33 (q, $^3J_{HH}$ =7.3 Hz, 2H, OCH_2), 4.69 (bs, 2H, NH_2), 6.70 (d, $^3J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.35-7.37 (m, 3H, aromatic), 7.52-7.54 (m, 2H, aromatic), 7.83 (d, $^3J_{HH}$ =8.5 Hz, 1H, aromatic), 8.08 (s, 1H, aromatic).	14.62 (CH_3), 60.73 (OCH_2), 85.00 and 95.27 (≡C), 107.32, 113.48, 120.03, 123.09, 128.65, 128.70, 131.65, 131.72, 134.54, 151.57 and 166.35 (C&CH, aromatic).
24p	1.39 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 4.35 (q, $^3J_{HH}$ =7.3 Hz, 2H, OCH_2), 4.69 (bs, 2H, NH_2), 7.36-7.39 (m, 6H, aromatic), 7.53-7.56 (m, 4H, aromatic), 8.06 (s, 1H, aromatic).	14.62 (CH_3), 60.93 (OCH_2), 84.61 and 95.62 (≡C), 107.16, 119.66, 122.89, 128.70, 128.88, 131.78, 134.26, 152.07 and 165.81 (C&CH, aromatic).
24q	0.93 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 1.32-1.40 (m, 2H, CH_2), 1.55-1.63 (m, 2H, CH_2), 2.61 (t, $^3J_{HH}$ =7.8 Hz, 2H, CH_2), 4.62 (bs, 2H, NH_2), 6.75-6.82 (m, 2H, aromatic), 7.11-7.15 (m, 3H, aromatic), 7.37 (d, $^3J_{HH}$ =7.8 Hz, 1H, aromatic), 7.45 (d, $^3J_{HH}$ =6.4 Hz, 2H, aromatic).	14.16 (CH_3), 22.52, 33.62 and 35.80 (CH_2), 85.06 & 95.41 (≡C), 109.40, 115.36, 119.13, 120.57, 128.68, 129.70, 131.64, 132.34, 143.64 and 146.40 (C&CH, aromatic).

Table 5.7 continued…….

24r	4.27 (bs, 2H, NH_2), 7.36-7.39 (m, 6H, aromatic), 6.74 (t, $^3J_{HH}$ =7.3 Hz, 1H, aromatic), 7.16 (t, $^3J_{HH}$ =7.8 Hz, 2H, aromatic), 7.32-7.38 (m, 3H, aromatic), 7.46 (d, $^3J_{HH}$ =8.7 Hz, 2H, aromatic).	87.10 & 93.72 (≡C), 107.05, 114.58, 118.19, 121.97, 128.88, 130.15, 132.34, 132.80, 134.32 and 147.99 (C&CH, aromatic).
24s	0.94 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 1.43-1.52 (m, 2H, CH_2), 1.56-1.64 (m, 2H, CH_2), 2.46 (t, $^3J_{HH}$ =6.9 Hz, 2H, CH_2), 4.14 (bs, 2H, NH_2), 6.65-6.71 (m, 2H, aromatic), 7.07 (t, $^3J_{HH}$ =8.2 Hz, 1H, aromatic), 7.24 (d, $^3J_{HH}$ =6.9 Hz, 2H, aromatic).	13.84 (CH_3), 19.54, 22.25 and 31.21 (CH_2), 96.10 (≡C), 109.50, 114.61, 118.36, 128.96, 132.22 and 147.32 (C&CH, aromatic).
25a	6.93 (s, 2H, aromatic), 7.02 (t, $^3J_{HH}$ = 7.6 Hz, 2H, aromatic), 7.12 (t, $^3J_{HH}$ =7.6 Hz, 2H, aromatic), 7.41 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.56 (d, $^3J_{HH}$ = 7.8 Hz, 2H, aromatic), 10.71 (s, 2H, NH).	99.50, 111.82, 120.55, 121.03 and 122.82 (CH, aromatic), 129.98, 132.38 and 138.21 (C, aromatic).
25b	2.38 (s, 6H, 2 x CH_3), 6.81 (s, 2H, aromatic), 6.94 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.28 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.33 (s, 2H, aromatic), 10.55 (s, 2H, NH).	21.55 (CH_3), 98.91, 111.50, 120.66 and 124.36 (CH, aromatic), 129.31, 130.29, 132.60 and 136.55 (C, aromatic).
25c	1.36 (s, 18H, 6 x CH_3), 6.87 (s, 2H, aromatic), 7.23 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.32 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.56 (s, 2H, aromatic), 10.55 (s, 2H, NH).	32.27 (CH_3), 35.05 (C), 99.41, 111.31, 116.80 and 121.04 (CH, aromatic), 129.92, 132.64, 136.37 and 143.08 (C, aromatic).
25d	6.94 (s, 2H, aromatic), 7.24 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.38 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.44 (s, 2H, aromatic), 11.00 (s, 2H, NH).	99.62, 113.74, 123.49 and 125.69 (CH, aromatic), 113.42, 131.69, 133.24 and 136.96 (C, aromatic).
25e	6.95 (s, 2H, aromatic), 7.12 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.42 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.58 (s, 2H, aromatic), 11.00 (s, 2H, NH).	99.68, 113.27, 120.34 and 123.07 (CH, aromatic), 125.85, 131.00, 133.45 and 136.69 (C, aromatic).
25f	7.30 (s, 2H, aromatic), 7.62 (d, $^3J_{HH}$ = 9.2 Hz, 2H, aromatic), 8.09 (d, $^3J_{HH}$ = 8.9 Hz, 2H, aromatic), 8.60 (s, 2H, aromatic), 11.78 (s, 2H, NH).	102.60, 112.36, 118.20 and 118.70 (CH, aromatic), 129.05, 134.70, 141.41 and 142.99 (C, aromatic).
25g	7.14 (s, 2H, aromatic), 7.49 (d, $^3J_{HH}$ = 8.5 Hz, 2H, aromatic), 7.57 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 8.18 (s, 2H, aromatic), 12.31 (s, 2H, NH).	100.07, 112.45, 124.95 and 126.02 (CH, aromatic), 101.76, 128.13, 132.83 and 138.92 (C, aromatic), 120.64 (C≡N).

Table 5.7 continued…….

25h	3. 85 (s, 6H, 2 x OCH_3), 7.11 (s, 2H, aromatic), 7.48 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.76 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 8.29 (s, 2H, aromatic), 12.08 (s, 2H, NH).	51.81 (OCH_3), 100.24, 111.17, 121.09 and 122.83 (CH, aromatic), 123.06, 128.02, 132.55 and 139.76 (C, aromatic), 167.20 (C=O).
25i	1.34 (t, $^3J_{HH}$ =7.4 Hz, 6H, 2 x CH_3), 4.32 (q, $^3J_{HH}$ =7.3 Hz, 4H, 2xOCH_2), 7.11 (s, 2H, aromatic), 7.49 (d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 7.77(d, $^3J_{HH}$ = 8.7 Hz, 2H, aromatic), 8.29 (s, 2H, aromatic), 12.06 (s, 2H, NH).	14.43 (CH_3), 60.23 (OCH_2), 100.19, 111.10, 121.37 and 122.72 (CH, aromatic), 123.05, 127.99, 132.52 and 139.72 (C, aromatic), 166.70 (C=O).
26	6.54 (s, 1H, aromatic), 7.13-7.25 (m, 3H, aromatic), 7.39 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.68 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 8.09 (bs, 1H, NH).	
27	2.33 (s, 3H, CH_3), 4.02 (s, 2H, CH_2), 4.28 (bs, 2H, NH_2), 6.80-6.87 (m, 2H, aromatic), 7.09-7.17 (m, 5H, aromatic), 7.51-7.53 (m, 1H, aromatic), 7.92 (bs, 1H, NH).	8.71 (CH_3), 29.00 (CH_2), 108, 124.95, 129.27, 131.79, 135.68 and 142.68 (C, aromatic), 110.69, 117.52, 118.43, 119.28, 120.79, 121.61, 128.36 and 130.77 (CH, aromatic).
29a	6.84 (s, 1H, aromatic), 7.14 (t, $^3J_{HH}$ = 7.5 Hz, 1H, aromatic), 7.21 (t, $^3J_{HH}$ = 7.5 Hz, 1H, aromatic), 7.34 (t, $^3J_{HH}$ = 7.6 Hz, 1H, aromatic), 7.40-7.47 (m, 3H, aromatic), 7.66 (t, $^3J_{HH}$ = 8.9 Hz, 1H, aromatic), 8.33 (s, 1H, NH).	100.19, 111.11, 120.48, 120.88, 122.57, 125.37, 127.92, 129.24, 129.46, 132.56, 137.01 and 138.08, (C & CH, aromatic).
29b	2.46 (s, 3H, CH_3), 6.75 (s, 1H, aromatic), 7.02 (d, $^3J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.28-7.33 (m, 2H, aromatic), 7.43 (t, $^3J_{HH}$ = 7.8 Hz, 3H, aromatic), 7.66 (d, $^3J_{HH}$ = 8.0 Hz, 2H, aromatic), 8.30 (s, 1H, NH).	21.68 (CH_3), 99.67, 110.82, 120.45, 124.15, 125.26, 127.74, 129.18, 129.60, 129.72, 132.75, 135.44 and 138.38, (C & CH, aromatic).
29c	1.44 (s, 9H, 3 × CH_3), 6.81 (s, 1H, aromatic), 7.28-7.37 (m, 3H, aromatic), 7.44 (t, $^3J_{HH}$ = 7.8 Hz, 2H, aromatic), 7.66 (d, $^3J_{HH}$ = 7.6 Hz, 3H, aromatic), 8.28 (s, 1H, NH).	32.10 (CH_3), 34.80 (C) 100.23, 110.64, 116.65, 120.89, 125.29, 127.71, 129.18, 129.29, 132.81, 135.21, 138.22 and 143.35 (C & CH, aromatic).
29d	6.75 (s, 1H, aromatic), 7.12 (d, $^3J_{HH}$ = 8.7 Hz, 1H, aromatic), 7.30-7.35 (m, 2H, aromatic), 7.44 (t, $^3J_{HH}$ = 7.6 Hz, 1H, aromatic), 7.58 (s, 1H, aromatic), 7.65 (d, $^3J_{HH}$ = 8.0 Hz, 2H, aromatic), 8.52 (s, 1H, NH).	99.57, 112.16, 120.06, 122.65, 125.41, 125.91, 128.26, 129.26, 130.45, 132.03, 135.36 and 139.51, (C & CH, aromatic).

Table 5.7 continued…….

29e	6.96 (s, 1H, aromatic), 7.38-7.50 (m, 4H, aromatic), 7.70 (d, $^3J_{HH}$ = 7.3 Hz, 2H, aromatic), 8.10 (d, $^3J_{HH}$ = 9.2 Hz, 1H, aromatic), 8.58 (s, 1H, aromatic), 8.92 (s, 1H, NH).	101.78, 111.08, 117.86, 118.13, 125.65, 128.77, 128.99, 129.48, 131.27, 139.97, 141.39 and 142.41 (C & CH, aromatic).
29f	1.42 (t, $^3J_{HH}$ = 7.1 Hz, 3H, aromatic), 4.40 (q, $^3J_{HH}$ = 7.2 Hz, 2H, aromatic), 6.88 (s, 1H, aromatic), 7.33 (t, $^3J_{HH}$ = 7.5 Hz, 1H, aromatic), 7.41-7.46 (m, 3H, aromatic), 7.69 (d, $^3J_{HH}$ = 8.0 Hz, 2H, aromatic), 7.89 (d, $^3J_{HH}$ = 8.7 Hz, 1H, aromatic), 8.38 (s, 1H, aromatic), 8.89 (s, 1H, NH).	14.67 (CH_3), 60.82 (OCH_2), 100.95, 110.88, 122.70, 123.59, 123.81, 125.47, 128.29, 129.28, 130.43, 132.01 139.54 and 139.67 (C & CH, aromatic), 167.98 (C=O).
29g	1.43 (t, $^3J_{HH}$ = 7.1 Hz, 3H, aromatic), 4.41 (q, $^3J_{HH}$ = 7.2 Hz, 2H, aromatic), 6.91 (s, 1H, aromatic), 7.35-7.48 (m, 6H, aromatic), 7.63 (d, $^3J_{HH}$ = 6.4 Hz, 2H, aromatic), 7.71 (d, $^3J_{HH}$ = 7.8 Hz, 2H, aromatic), 8.11 (s, 1H, aromatic), 8.37 (s, 1H, aromatic), 8.85 (s, 1H, NH).	14.63 (CH_3), 61.02 (OCH_2), 84.85 & 94.05 (≡C), 101.73, 106.05, 123.05, 123.13, 123.98, 125.64, 127.16, 128.58, 128.69, 128.88, 129.31, 131.66, 131.93 and 139.73 (C & CH, aromatic), 167.18 (C=O).
29h	0.96 (t, $^3J_{HH}$ = 7.3 Hz, 3H, aromatic), 1.34-1.44 (m, 2H, CH_2), 1.60-1.67 (m, 2H, CH_2), 2.65 (t, $^3J_{HH}$ = 7.8 Hz, 2H, CH_2), 6.78 (s, 1H, aromatic), 7.09-7.19 (m, 2H, aromatic), 7.25 (d, $^3J_{HH}$ = 8.2 Hz, 2H, aromatic), 7.39 (d, $^3J_{HH}$ = 8.4 Hz, 1H, aromatic), 7.56-7.62 (m, 3H, aromatic), 8.34 (s, 1H, NH).	14.08 (CH_3), 22.60, 28.16 & 31.48 (CH_2), 99.61, 110.50, 119.77,119.94, 121.10, 129.05, 136.02 and 140.22 (C & CH, aromatic).
29i	6.80 (s, 1H, aromatic), 7.11-7.22 (m, 2H, aromatic), 7.39 (d, $^3J_{HH}$ = 8.2 Hz, 3H, aromatic), 7.55-7.63 (m, 3H, aromatic), 8.36 (s, 1H, NH).	100.56, 111.24, 120.61, 120.89, 122.83, 126.50, 129.33, 129.37, 131.07, 133.57, 136.88 and 137.13 (C & CH, aromatic).
29j	0.98 (t, $^3J_{HH}$ = 7.3 Hz, 3H, aromatic), 1.40-1.49 (m, 2H, CH_2), 1.68-1.76 (m, 2H, CH_2), 2.76 (t, $^3J_{HH}$ = 7.8 Hz, 2H, CH_2), 6.26 (s, 1H, aromatic), 7.08-7.16 (m, 2H, aromatic), 7.30 (d, $^3J_{HH}$ = 7.8 Hz, 1H, aromatic), 7.56 (d, $^3J_{HH}$ = 7.8 Hz, 1H, aromatic), 7.82 (s, 1H, NH).	14.18 (CH_3), 22.58, 33.75 & 35.60 (CH_2), 99.55, 111.08, 120.35, 120.68, 122.28, 125.28, 129.27, 129.55, 129.98, 136.93, 138.32 and 142.89 (C & CH, aromatic).

Table 5.8. Crystal and refinement data for **25a**, **25e** and **28**.

Identification code	**25a**	**25e**	**28**
Empirical formula	$C_{16}H_{12}N_2$	$C_{16}H_{10}Cl_2N_2$	$C_{19}H_{21}ClN_2$
Formula weight	232.28	301.16	312.83
Temperature, K	103(2)	103(2)	203(2)
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	P2(1)/c	P-1	C2/c
a, Å	5.8302(3)	7.1284(8)	18.1943(4)
b, Å	7.3449(3)	8.2155(8)	9.3463(2)
c, Å	13.0907(7)	11.4719(11)	20.5337(5)
β, deg	91.283(3)	88.984(3)	95.2730(10)
Volume, $Å^3$	560.43(5)	632.33(11)	3476.97(14)
Z	2	2	8
Density (calculated) , Mg/m^3	1.376	1.582	1.195
Absorption coefficient, mm^{-1}	0.082	0.501	0.218
F(000)	244	308	1328
Crystal size, mm^3	0.12 x 0.08 x 0.04	0.24 x 0.18 x 0.16	0.40 x 0.38 x 0.28
Reflections collected	2134	5921	3558
Independent reflections	2134 [R(int) = 0.0000]	5921 [R(int) = 0.0000]	3558 [R(int) = 0.0000]
Completeness (to θ, deg)	99.1 % (33.16°)	98.9 % (25.00°)	100.0 % (26.37°)
Max. and min. transmission	0.9967 and 0.9902	0.9241 and 0.8891	0.9414 and 0.9178
Data / restraints / parameters	2145 / 0 / 83	5921 / 0 / 190	3558/0/206
Goodness-of-fit on F^2	1.043	1.046	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0498, wR2 = 0.1212	R1 = 0.0470, wR2 = 0.1117	R1 = 0.0366, wR2 = 0.1009
R indices (all data)	R1 = 0.0667, wR2 = 0.1316	R1 = 0.0692, wR2 = 0.1225	R1 = 0.0415, wR2 = 0.1107
Largest diff. peak and hole, $e.Å^{-3}$	0.513 and -0.206	0.575 and -0.548	0.325 and -0.250

5.7 References

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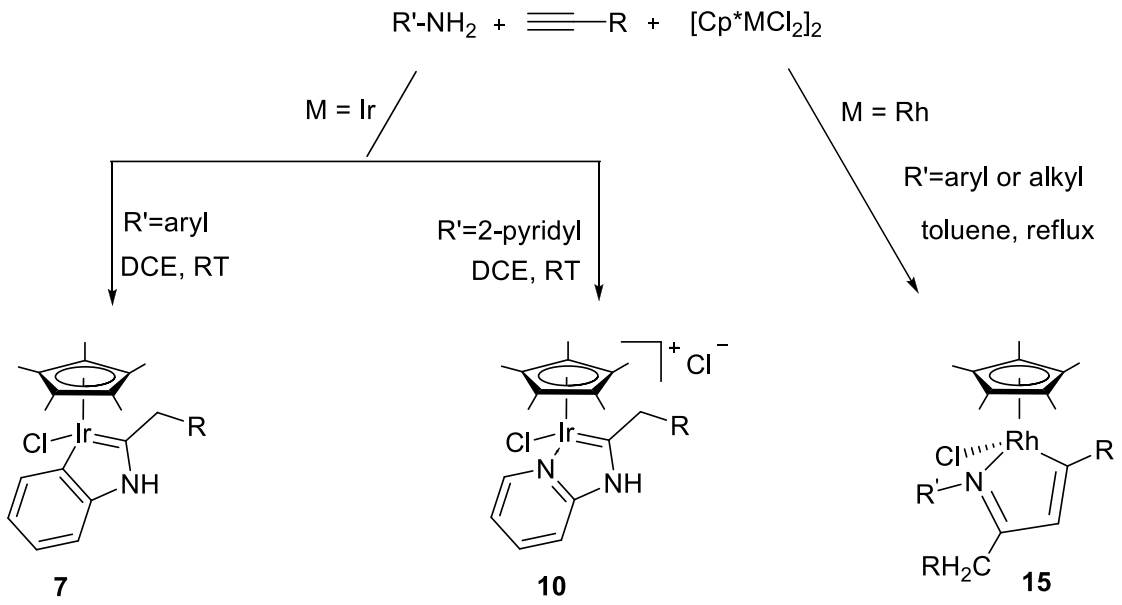
Chapter 6: Overall conclusion

As set out in chapter 1, the primary aim of this project was to examine alkyne activation by iridium and rhodium complexes. Three sets of reactions were investigated:

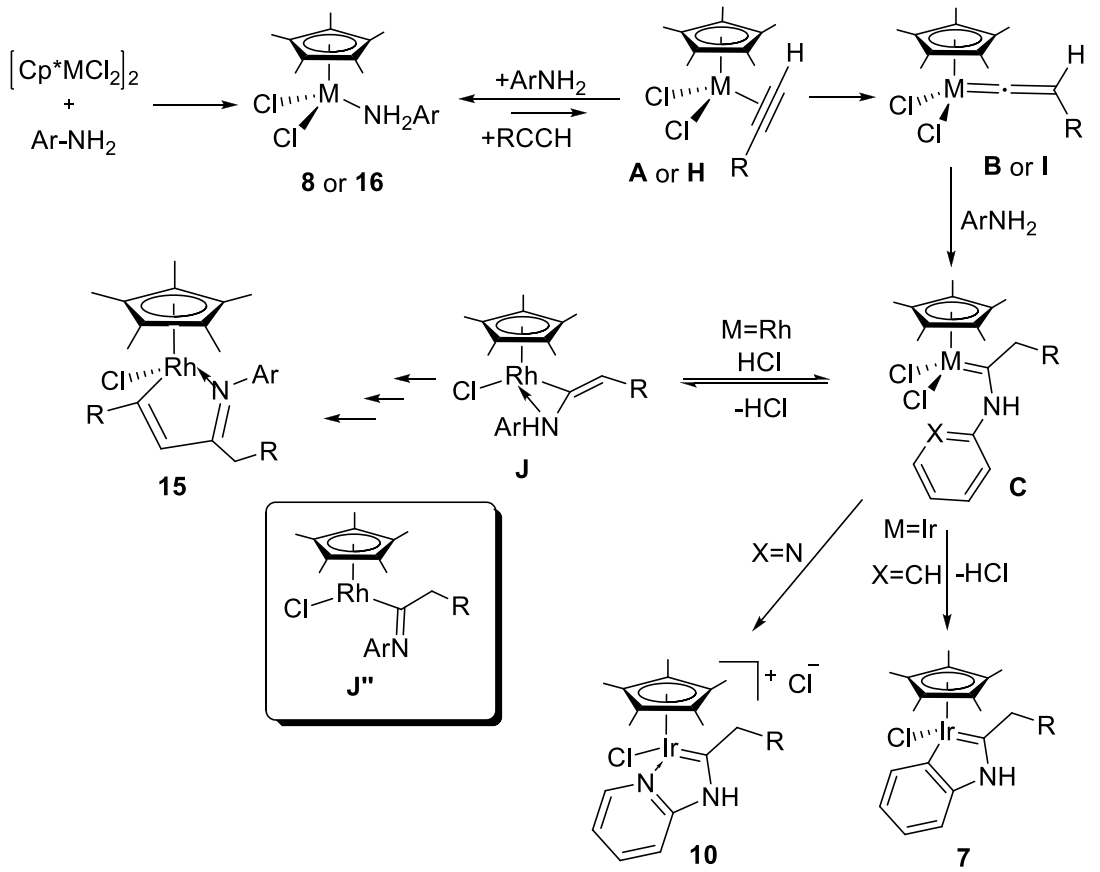
1) The reaction of $[Cp^*MCl_2]_2$ (M=Ir, **1a**, or Rh, **1b**) with alkynes and amines,
2) The reaction of $[Cp^*RhCl_2]_2$, **1b**, with alkynes and anilines in the presence of additives, and
3) The reaction between $[Cp^*IrCl_2]_2$, **1a**, and 2-alkynylanilines.

It was found that the neutral dinuclear complexes $[Cp^*MCl_2]_2$, **1**, reacted with amines and alkynes to form various metallacyclic complexes via hydroamination (Schem 6.1). Thus the reaction of **1a** with a terminal alkyne and an aniline or 2-aminopyridine gave the orthometallated iridium amino-carbene **7** or cationic iridium amino-carbene **10**, respectively. These ambient temperature reactions proceeded smoothly with both aliphatic and aromatic terminal alkynes, but not with internal alkynes or aliphatic amines. Similarly, the reaction of **1b** with a terminal alkyne and an amine led to a rhodapyrrole **15**. This reaction required a higher temperature (refluxing toluene), and although it worked with both aliphatic and aromatic amines, it failed to proceed with aliphatic and internal alkynes.



Scheme 6.1

Reaction pathways to these complexes have been proposed on the basis of computational and experimental investigations (Scheme 6.2), and it is suggested that the initial steps are similar. These are: (i) initial cleavage of the dinuclear species through binding of an amine to form **8** or **16**; (ii) this is in equilibrium with an alkyne-bound species (**A** or **H**), which (iii) undergoes rearrangement to a vinylidene complex; and finally (iv) nucleophilic attack by an amine at the α-carbon gives a carbene complex type **C**. The reason for reactions involving aliphatic amines failing with the Ir complex **1a** may lie in the equilibrium (ii): The Ir-N bond for these amines may be more stable than the corresponding Rh-N bond, and hence this equilibrium lies very much on the amine complex side.[1]

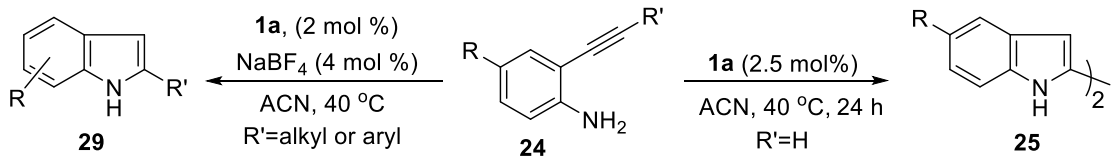


Scheme 6.2

From **C**, two competing pathways are available. One involves orthometallation (for aniline) or ligand substitution (for 2-aminopyridine), to give the corresponding final products **7** or **10**, respectively. Whether orthometallation or ligand substitution occurs may be attributed to the ease of ligand substitution vs orthometallation. The other pathway is the elimination of HCl to the metalla-aziridine intermediate **J**, presumably via formation of the 16-electron **J''**.[2] It is possible that this pathway favoured in the Rh case because orthometallation would involve an unfavourable Rh(V) intermediate.

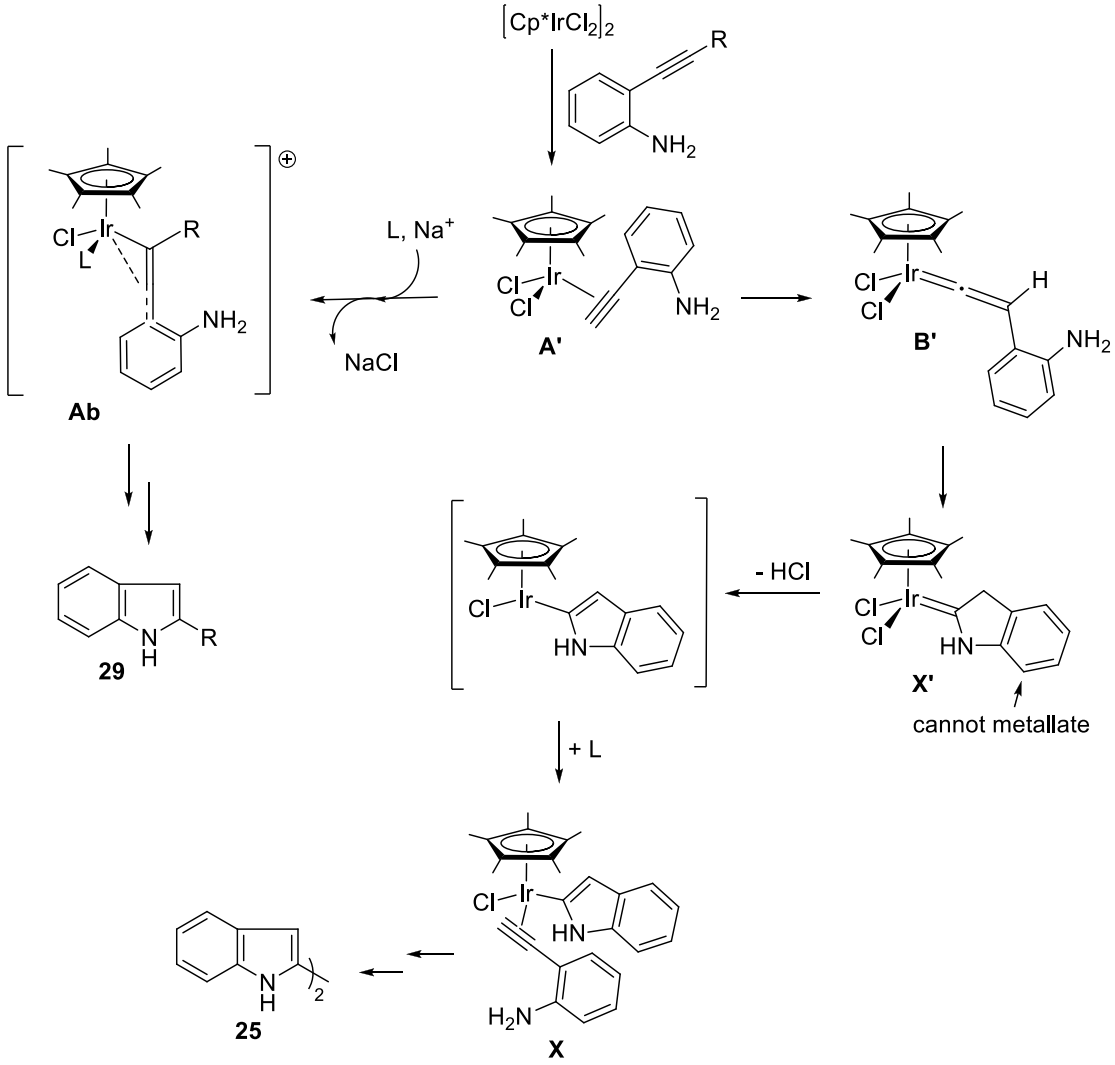
The inhibition of orthometallation may also be the reason behind the observation that **1a** catalysed the cyclisation of 2-ethynylaniline **24** to the biindole **25** (Scheme 6.3). In this case, orthometallation of the resulting carbene ligand in **X'** was inhibited by ring strain (Scheme 6.4). Thus a stable iridacycle could not be formed and

instead, complex **1a** turned into a catalyst. A similar disruption of the pathway occurred in the formation of 2-substituted indoles **29** from internal 2-alkynylanilines catalysed by **1a**; formation of the vinylidene intermediate is not possible with internal alkynes.



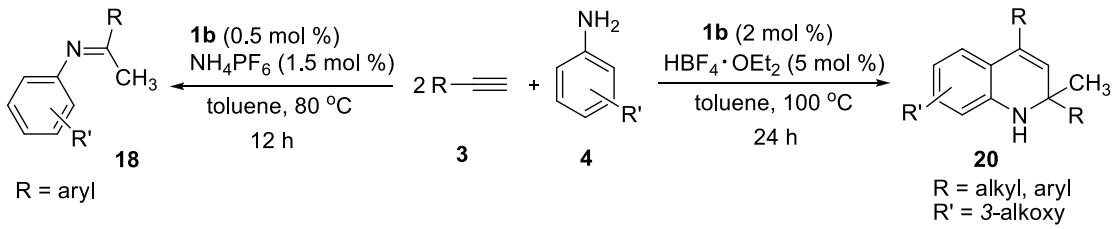
Scheme 6.3

The requirements for the formation of **25** and **29** did differ, however, in one important respect, which was that the latter required a salt additive which led to a different reaction pathway. The divergence in pathway begins from the alkyne-coordinated intermediate **A'**. In the absence of a salt additive and a terminal alkynylaniline, this step is followed by the vinylidene rearrangement as above, which leads ultimately to the biindole. For internal alkynylanilines, rearrangement to a vinylidene is not possible, and a polar environment favours substitution of a chloride ligand by another molecule of alkynylaniline to form a cationic complex **Ab**. The computationally optimised structure of **Ab** suggests that the alkyne moiety is allene-like, and intramolecular nucleophilic attack of the amine group leads ultimately to the indole.



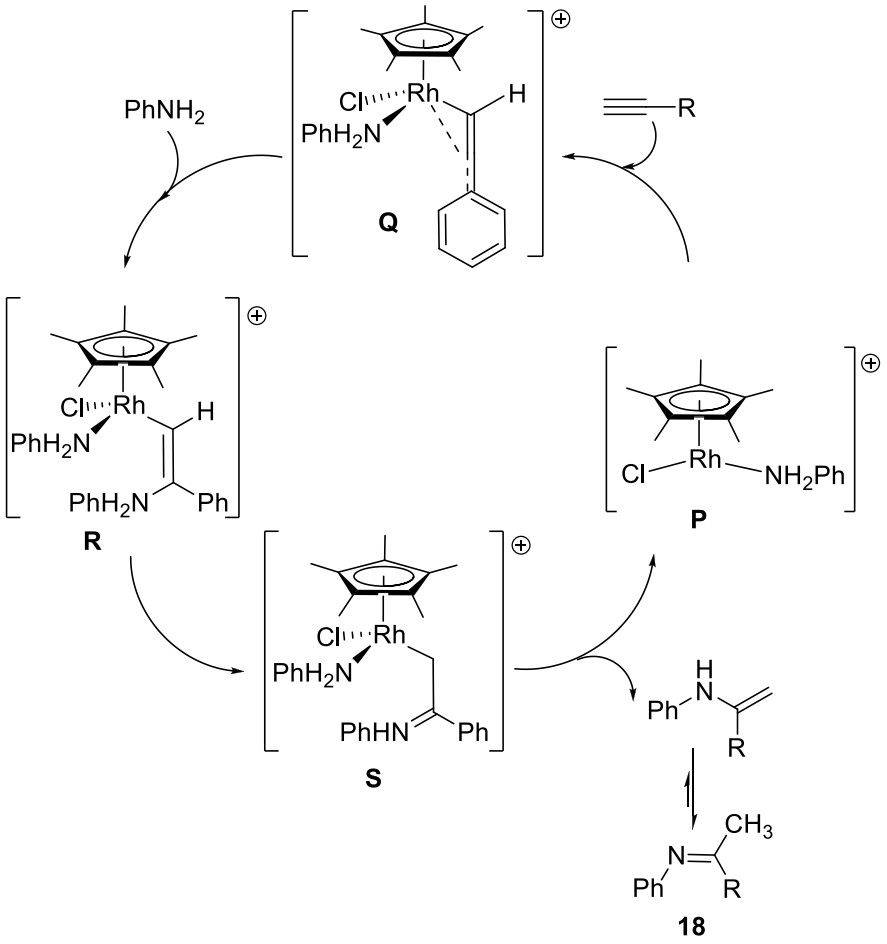
Scheme 6.4

Cationic intermediates were also proposed for the reaction pathways leading to the **1b**-catalysed formation of ketimine **18** from the reaction of an aniline and a terminal aromatic alkyne in the presence of NH_4PF_6, and 1,2-dihydroquinoline **20** from the reaction of a 3-alkoxyaniline and a terminal alkyne in the presence of HBF_4, respectively (Scheme 6.5).



Scheme 6.5

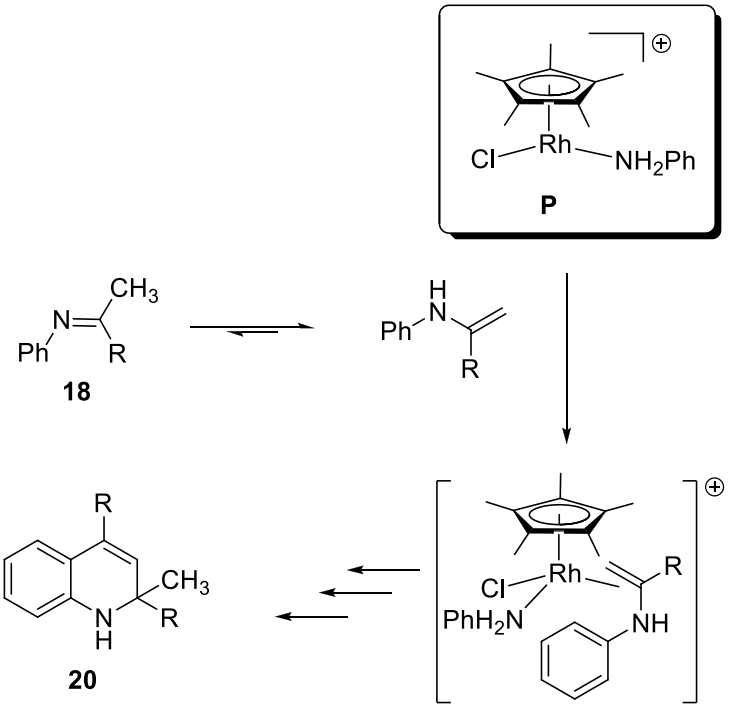
It is proposed that both reactions share the same 16-electron cationic species $[Cp^*RhCl(NH_2Ph)]^+$, **P**, as the active catalyst, which is formed from **1b** by the displacement of a chloride by aniline. This is expected to be favoured by the polar environment in the presence of a salt or acid additive. With the salt, the reaction follows a similar pathway to that above, culminating in the formation of an imine (Scheme 6.6); the iridium analogue **1a** can also catalyse the same reaction in the presence of NH_4PF_6, albeit less effectively.[3]



Scheme 6.6

With the acid additive, the crucial difference is that the acid favours the imine-enamine equilibrium towards the enamine and thus promotes enaminyl-alkene assisted ortho C-H bond activation by **P** to give the intermediate **T** (Scheme 6.7) This critical step is also facilitated by a *meta*-alkoxy substituent on the aniline, and leads eventually

to **20**, and the intermediary of the enamine in this reaction has been verified experimentally.



Scheme 6.7

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