UNIVERSITY OF SOUTHAMPTON

PALLADIUM-CATALYSED SYNTHESIS OF AMIDINES AND IMIDATES

BY

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master of philosophy

FACULTY OF ENGINEERING, SCIENCE AND MATHEMATICS

DEPARTMENT OF CHEMISTRY

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This manuscript describes the work done by me while registered as a postgraduate student at the University of Southampton. The introduction (review) chapter describes the work done by Dr. Saluste, examples and procedures which are used from the literature have been clearly cited.

Om Sai Ram

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ABSTRACT

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PALLADIUM-CATALYSED SYNTHESIS OF AMIDINES AND IMIDATES

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Kali Kishore Redy. Tetala

A novel palladium-catalysed three-component synthesis of alkenyl amidines and imidates from alkenyl bromides, isonitriles and amines or alcohols was developed. The amidine synthesis utilised Cs_2CO_3 as the base and was limited to *tert*-butyl isonitrile. In the imidate synthesis NaO^tBu was the base and different isonitriles were successfully utilised. The (*E*) stereochemistry of the C=C group in alkenyl bromide was retained in the product. The stereochemistry of the imine double bond in two of the amidines was shown to be the thermodynamically more stable (*E*)-isomer by X-ray crystallography.

Abbreviations Listed in Alphabetical Order

Bu - Butyl

Cc - Column chromatography

CH_2Cl_2 - Dichloromethane

Cy - Cyclohexyl

°C - Degrees Celsius

d - doublet (related to NMR)

Dba - Dibenzylidene acetone

DFT- Density Function Theory

Dibal-H - Diisobutyl aluminium hydride

DMF - Dimethylformamide

Dppe - 1,2-bis -(diphenylphosphino)ethane

Dppf - $1,1^1$-bis -(diphenylphosphino)ferrocene

DPPFo -$1,1^1$-bis-(diphenylphosphino monoxide)ferrocene

Dppp - 1,3-bis -(diphenylphosphino)propane

EI - Electron ionisation

Eq - equivalent

Et - Ethyl

ES - ElectroSpray

GC - Gas chromatography

hr - hour

Hz - Hertz

J - Coupling constant (related to NMR)

m - multiplet (related to NMR)

Min - Minute

Me - Methyl

Mg - Magnesium

mL - millilitre

mol - mole

mmol - millimole

M. P - Melting point

MS - Mass Spectrometry

M/z - Mass to charge ratio (related to mass spectrometry)

NMR - Nuclear Magnetic Resonance

Ph - Phenyl

s - singlet (related to NMR)

Sec - secondary

t - triplet (related to NMR)

δ - Chemical shift

ppm - parts per million

MI - Molecular ion

CONTENTS

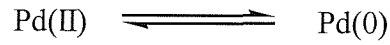
I dedicate this thesis to my parents

1. About Palladium-catalysis:

1.1. General:

The importance of organometallic[1] reagents in synthesis is increasing day by day and palladium-catalysts have numerous advantages[2,3,4,5] when compared to others. An advantage for synthetic chemist in using palladium-catalyst is the excellent functional group compatibility and the use of sp^2-halides as starting materials.

Palladium exists in two stable oxidation states- the +2 state and the zerovalent state, with redox interchange between two oxidation states.



Scheme 1. Redox interchange of palladium

Palladium(II)-complexes are electrophiles and tend to react with electron-rich organic compounds such as alkenes and arenes. Palladium(0)-complexes are strong nucleophiles and the key reaction is insertion into carbon-leaving group bonds.

In the palladium-catalysed reactions described in this thesis, isonitrile insertion plays a vital role, so in this chapter isonitrile insertion into palladium-carbon bond is discussed using information available in the literature. This chapter also deals with the palladium-catalysed tin free synthesis of amidines[6] and imidates.[7]

1.2. Isonitrile insertion into Palladium-carbon bonds:

Isonitriles are isoelectronic with carbon monoxide. They are stronger σ-donors and weaker π-acceptors than CO. The two resonance hybrid structures of isonitriles are outlined in scheme 2.

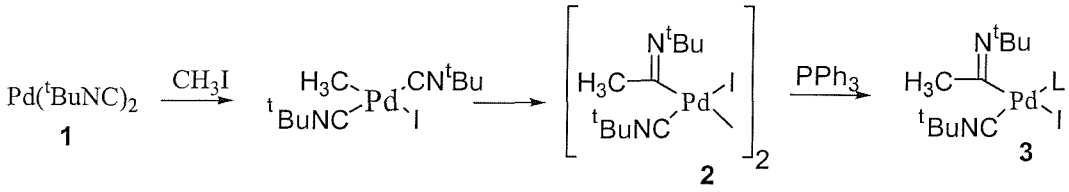
Scheme 2. Resonance hybrid structures of isonitriles

Isonitriles usually react with organopalladium complexes to give imidoyl compounds. Such insertions have also been observed with alkyl-, alkynyl-, and other organopalladium complexes.[8] Moreover, double, triple and polyinsertions of isonitriles are known from the literature.[8]

Isonitrile insertion has not been as extensively investigated as CO-insertion and there is much less information available.

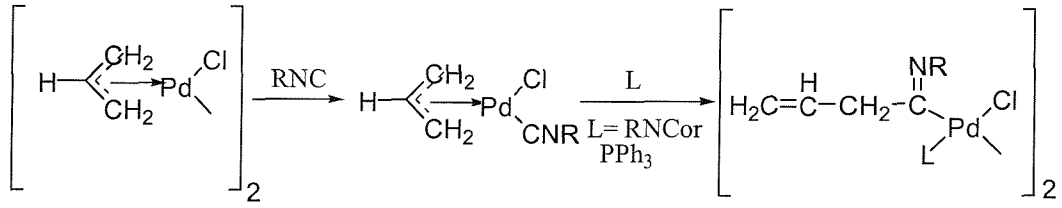
1.2.1. Isonitrile complexes of Palladium(II):

Synthesis of palladium-isonitrile complex **1**, followed by insertion into methyl iodide then migration of the isonitrile into the palladium-carbon bond[9] resulted in a *trans*-alignment of iodo **2** and α-iminoacyl groups **3** as shown in scheme 3.



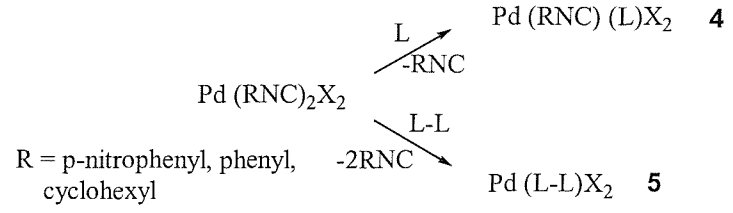
Scheme 3. Isonitrile insertion into Pd-C bond

The electronic properties[10] of different isonitriles (p-nitrophenyl, cyclohexyl and phenyl-isonitriles) were studied in the insertion into the palladium-carbon bond as shown in scheme 4. By comparing the results obtained[10] with those of cyclohexyl isonitrile, [11] the choice of R plays a vital role in the insertion reaction. The reaction is favoured when R is a strong electron-attracting group.



Scheme 4. Isonitrile insertion into Pd-C bond

Complexes of the type $Pd(RNC)_2X_2$ were reacted[12] with neutral monodentate ligands (L) and bidentate (L-L) phosphines, arsines and pyridine ligands as outlined in scheme 5.

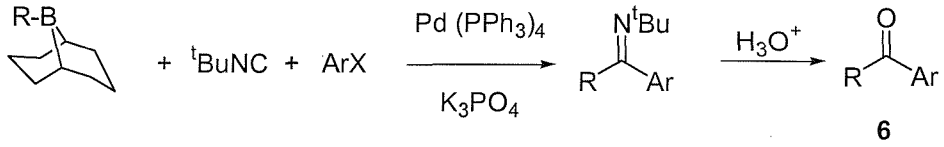


Scheme 5. Reaction of Pd complex with mono- and bi-dentate ligands

The reaction of phosphines proceed at milder conditions than arsines. Only the bidentate ligands are able to replace both isonitrile groups resulting in complex **5**, owing to the chelating nature of the entering groups. Pyridine and bipyridyl gave no substitution reactions. These facts show that the Pd(II)-CNR bond is particularly stable in such complexes.

1.2.2. Palladium-catalysed three component coupling incorporating isonitrile insertion:

Palladium-catalysed carbonylative[13] cross-coupling reaction of organoboron reagents, carbon monoxide and organic halides in presence of base resulted in ketones **6**. As isonitriles are isoelectronic with carbon monoxide, isonitriles replaced[14] CO in the reaction as shown in scheme 6.

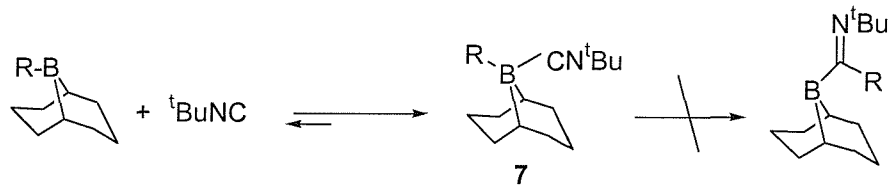


6

Scheme 6. Palladium-catalysed isonitrile cross-coupling

Best results were observed when equimolar amounts of ^{t}BuNC and 9-Alkyl-9-BBN were utilised. The reaction was unsuccessful with excess of isonitrile. It is not known why the increase of isonitrile prevents the reaction proceeding.

9-Alkyl-9-BBN was generated *in situ* by hydroboration of terminal alkenes. Subsequent reaction of the organoboron reagent with 1 equivalent isonitrile resulted in the complex **7**, [15] which may work as a buffer stock to reduce the concentration of free isonitrile to a minimum as shown in scheme 7. It is known that direct insertion of the isonitrile into the R-B bond does not occur.



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Scheme 7. Reaction of organoboron with isonitrile

A reasonable mechanism for the coupling shown in scheme 6 can be suggested as follows:

1. Oxidative addition of organic halide to Pd(0) complex.
2. Formation of iminoacyl Pd(II) halide by insertion of isonitrile.

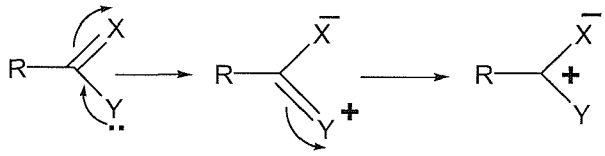
3. Alkyl group on boron was transferred to palladium with the aid of base.

4. Reductive elimination of imine.

1.3. Palladium-catalysed synthesis of amidines:

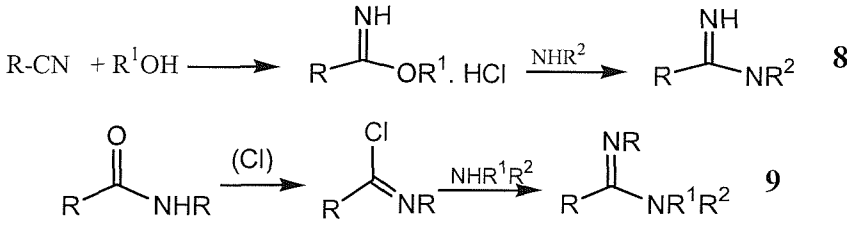
Amidines, the nitrogen analogues of carboxylic acids, are structural parts of numerous compounds of biological interest and form important medical and biochemical agents. [16]

Amidines are special cases of n-π conjugated heteroallylic systems, which are isoelectronic with allyl-anion, which have the mesomeric formula as shown in scheme 8.



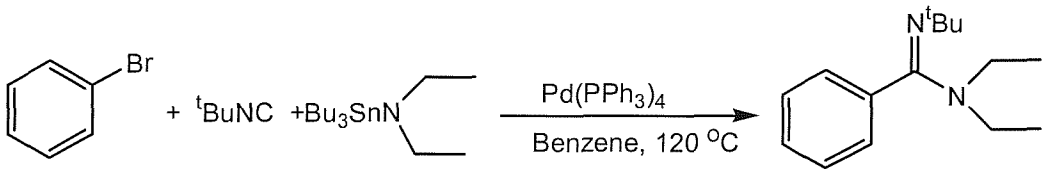
Scheme 8. Mesomeric formula

Previously amidines with general sturctures **8** and **9** were synthesised via a two step process involving moisture sensitive imidoyl esters or imidoyl chlorides as shown in scheme 9. The first process is the Pinner synthesis. [17]



Scheme 9. Two step amidine synthesis

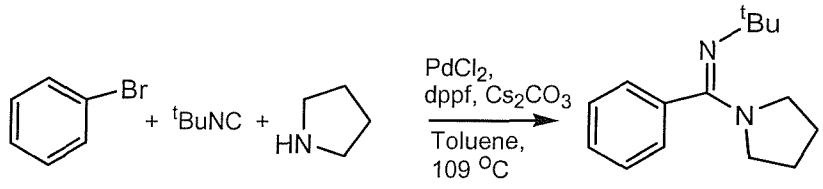
So, a single step route to these amidines would be of great interest and was carried out successfully by Kosugi et al., [18] where the amidine **10** resulted as outlined in scheme 10.



10

Scheme 10. Synthesis of amidines by coupling aryl bromide, *tert*-butyl isonitrile and tributyltin diethylamide

The main drawback of this reaction is the source of the amine. As tin is toxic it is best to avoid using a stannylated amine. Dr. Saluste successfully developed a tin free palladium-catalysed three component synthesis of amidines[6] as outlined in scheme 11.



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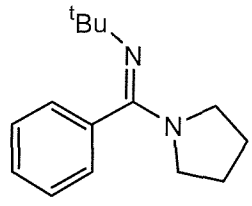
Scheme 11. Palladium-catalysed synthesis of amdines by coupling aryl bromide, *tert*-butyl isonitrile and amine

The author[2] believed that it is the *Z*-amidine **11**, which was synthesised through this procedure. Recently it was found to be the *E*-amidine **12** (see scheme 12) that was formed, which is thermodynamically more stable by 8 Kcal/mol (according to DFT calculations) than **11.**



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Scheme 12. Structure of *E*-amidine

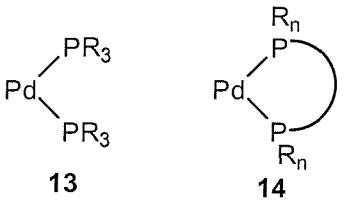
Section **1.3.3** to **1.5.2** deals with the establishment of reaction conditions for the formation of aryl amidines[6] and imidates[7] by the palladium-catalysed three component coupling. The coupling was attempted to the formation of imidates and thioimidates.

1.3.3.Influence of ligand, solvent, base, palladium source and aryl source:

Ligands:

Phosphine ligands can be either monodentate or bidentate

1. Monodentate ligands: Consists of single PR_3 units and require a ligand : palladium-ratio of 2:1 to form catalytically active PdL_2 species **13**.
2. Bidentate ligands: Consists of two phosphine groups and require a ligand : palladium-ratio of 1:1 to form the active intermediate **14**.



13 **14**

Scheme 13. Structures of mono- and bi-dentate phosphine ligand complexes

The best results were obtained with bidentate ligands. The ligands dppp and dppe are air-sensitive and more difficult to handle than dppf. Due to better results and greater stability, dppf was chosen as the ligand. Despite its cost dppf can also be synthesised in high yields through the literature procedure[19] thus avoiding the cost factor.

Solvents:

Solvents play an important role in palladium chemistry. Apart from the effects of solubility of the reactants and boiling point, the electronic co-ordinating effect of solvent molecules (like THF, dioxane and DMF) with the catalyst can often lead to changes in reactivity. [20] Toluene, THF, dioxane and DMF were tried in the synthesis of **12**. THF, which gave the most satisfactory results, had the disadvantage of having to be used in sealed tubes (109 °C). At 65 °C the reaction was unsuccessful with THF. Benzene was avoided due to its toxicity and low boiling point. Toluene and dioxane were therefore chosen as the solvents for these reactions.

Base:

In the palladium-catalysed synthesis of aryl amines[21] (tin free system) best results were obtained with NaO^tBu and Cs_2CO_3 as bases. In the palladium-catalysed synthesis of aryl amidines[6] Cs_2CO_3, NaO^tBu and excess of pyrrolidine (2 eq) instead of base were tried as bases with dppf and PPh_3 as ligands. Cs_2CO_3 was found to be the best base for the synthesis of **12**. The reactions were unsuccessful with excess of pyrrolidine. Higher yields were obtained with dried Cs_2CO_3.

Palladium source:

$Pd_2DBA_3.CHCl_3$ was the Pd(0) source utilised while optimising the reaction conditions. It should allow facile formation if the catalytically active $L_2Pd(0)$-species on addition of the appropriate phosphine ligand. It is well known that Pd(II) salts can be reduced to Pd(0) *in situ*[22] and thus be used as catalyst precursors. Palladium chloride, $Pd(OAc)_2$, $PdCl_2$.dppf and $Pd_2DBA_3.CHCl_3$ were tried. The results showed Pd(II) sources allowed for shorter reaction times and $PdCl_2$ with excess pyrrolidine was fastest. Unexpectedly ($PdCl_2$.dppf) gave poor results despite this complex being the expected intermediate in the pre-activation step. Addition of an extra equivalent of dppf improved the outcome of reaction, thus indicates that an extra phosphine may be necessary to reduce the Pd(II) complex to Pd(0) state.

Aryl source:

The established conditions for PhBr were tried on other phenyl sources (PhI, PhOTf, PhCl). After the reactions were performed the order of reactivity found to be PhOTf (2h, 100%) > PhBr (4h, 100%) > PhI (24h, 84.1%) > PhCl (no reaction).

1.3.4. Different isonitriles:

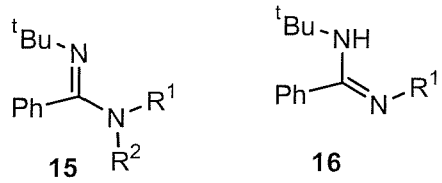
So far while establishing the reaction conditions the author[6] utilised ^{t}BuNC for these reactions. When tried to replace it with other isonitriles (^{n}BuNC, BnNC, & PhNC), the reaction failed, giving less than 5% conversion. The success of ^{t}BuNC may be due to its greater bulk, making it more stable towards polymerisation. Another hypothesis was that the isonitriles could deactivate the palladium catalyst by complexation. Slow addition of isonitriles with a syringe pump was performed to keep the isonitrile concentration low but with limited success, increasing the yield to around 30%.

1.3.5. Establishing work-up conditions:

Purification of the aryl amidines on silica and alumina with different eluent systems was not successful, because teritary amidines are strongly basic compounds with pK_a-values of conjugate acids ranging from 10 to 12. Use of acetate resins[23] was also not successful. The tertiary amidines should be easily protonated, forming salts with weak acids. These salts should be soluble in aqueous layer, which could then be

washed with an appropriate organic solvent to remove organic impurities. Basification and extraction of the aqueous layer would then provide the amidines of good purity. Acetic acid (2.5% by volume in water) and KOH pellets and diethyl ether were chosen as acid, base and organic solvent respectively resulting in a method, which was successfully used. Kugelrohr distillation was used for further purification.

Aryl amidines synthesised through palladium-catalysed reaction were listed in Table 1. The amidines derived from secondary amines exist in **15** whereas amidines derived from primary amines (R^2 = H) exist in tautomeric form **16** as shown in scheme 14.



Scheme 14. Two forms of aryl amidines

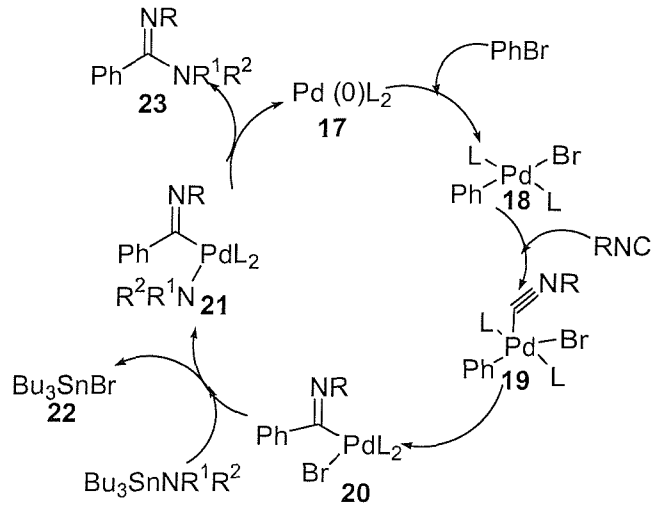
Table 1: Aryl amidines synthesised

ArX	Amine(R^1,R^2)	isonitrile	Time	temp	Yield
C_6H_5Br	-$(CH_2)_4$-	^tBu	4 h	109 °C	78%[a]
C_6H_5Br	Et, Et	"	6 h	"	61%[a]
C_6H_5Br	Bu, H	"	10 h	"	50%[b]
C_6H_5Br	Ph, H	"	20 h	"	45%[b]
p-$Me_2NC_6H_5Br$	-$(CH_2)_4$-	"	3 h	"	74%[a]
p-$MeCOC_6H_5Br$	-$(CH_2)_4$-	"	4 h	"	61%[a]

Conditions: 0.10 mmol $PdCl_2$, 2.6 mmol Cs_2CO_3, 0.20 mmol dppf, & 20 mL toluene. a. compound exist as **15**, b. compounds exists as **16.**

1.4. Mechanistic study:

The mechanism for palladium-catalysed synthesis of amidines has not been reported in literature until now. Considering the Stille coupling[24] together with the palladium-catalysed carbonylation/isonitrile insertion mechanism, a possible mechanism is shown in scheme 15.

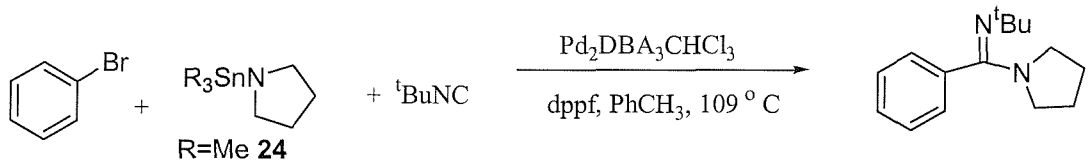


Scheme 15. Possible catalytic cycle for the synthesis of amidines

The steps are as follows:

1. PhBr undergoes oxidative addition with 14e⁻ $Pd(0)L_2$-species **17** resulting to 16e⁻ palladium(II) intermediate **18**.
2. Unstable 18e⁻ palladium-intermediate **19** was formed by isonitrile addition with **18**, followed by isonitrile migration into the Pd-Ph bond to give a stable 16e⁻ palladium(II)-intermediate **20**.
3. Transmetallation of tin with **20** proceeds in concerted fashion resulting in **21** and tributyltin bromide **22** as a by-product.
4. **21** undergoes reductive elimination forming **23** and re-generating **17**.

The reaction as shown in scheme 16 was attempted to find, whether transmetallation step was the rate-determining step with tridecane as an internal standard in GC monitoring these reactions.

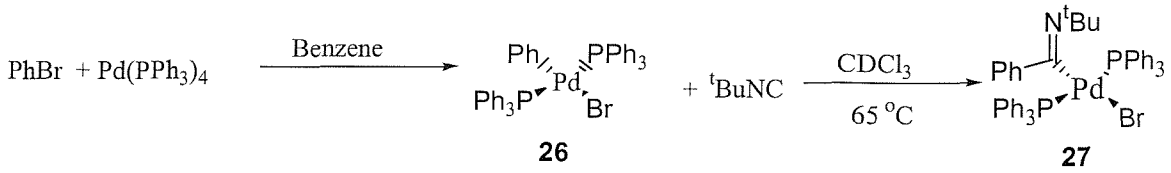


R=Me **24**
R=Bu **25**

Scheme 16. Reaction to find the rate determining step

The use of trimethyl analogue **24** gave a higher reaction rate indicating that transmetallation is the rate-limiting step of the catalytic cycle. In both cases, the reaction is very slow at start. This may mean that the slow formation of a catalytically active species is necessary for the reaction to take place.

An oxidative addition intermediate was generated through literature procedure and reaction with ^{t}BuNC resulted in **27** as outlined in scheme 17.



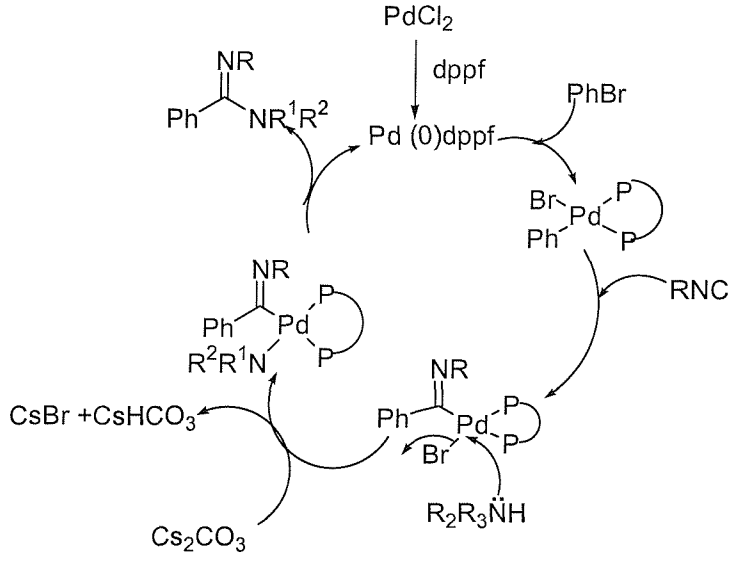
Scheme 17. Reaction of *tert*-butyl isonitrile with oxidative addition intermediate

The isonitrile inserted after 30 min, indicating that the isonitrile step is fast. The synthesis of **26**, required 20 h, which could indicate the oxidative addition step is slow. This data cannot be used for definite conclusion, as it doesn't mimic the chosen reaction system for the catalyst and palladium source. It has been generally assumed that the dibenzylidene acetone units of the complex are spectator ligands once replaced by the phosphines.

Two conclusions can be drawn from this investigation to date:

1. Isonitrile insertion is fast.
2. Transmetallation step is rate determining.

The palladium-catalysed synthesis of amines provides the closest analogy for tin-free palladium-catalysed synthesis of amidines. Taking the mechanism suggested for aryl amines[21] formation and from the discussion provided for tin system into account, a mechanism for tin free palladium-catalysed synthesis of amidines can be suggested [scheme 18].

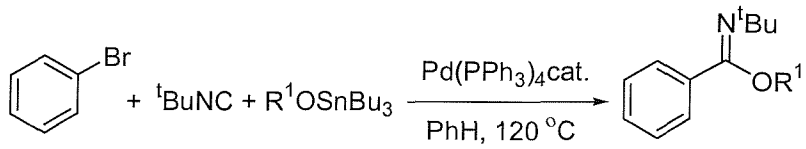


Scheme 18. Possible catalytic cycle for tin free palladium-catalysed synthesis of amidines

The steps of the catalytic cycle are similar to those in the tin system except for the transmetallation. It is replaced with the direct attack of the amine and the hydrobromic acid formed was neutralised by the base. Due to the electron withdrawing effect of palladium, the possibility that the attack occurs on the imino group cannot be excluded.

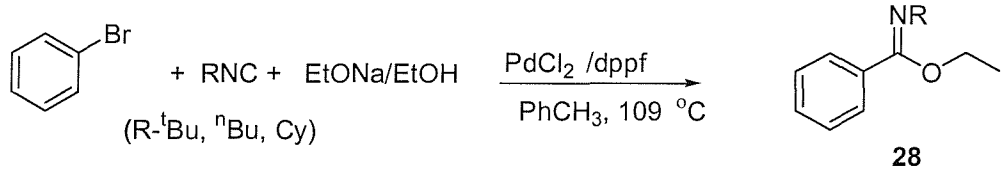
1.5. Synthesis of aryl imidates:

In 1986, Kosugi[18] reported the synthesis of imidates by coupling tin derivatives of alcohol with PhBr and ^{t}BuNC as shown in scheme 19.



Scheme 19. Synthesis of imidates by coupling tin derivatives of alcohol, arylbromide and *tert*-butyl isonitrile

A tin free methodology for the synthesis of imidates would be more advantageous. Dr. Saluste attempted to replace the amine with an alcohol in tin free synthesis of amidines under the same reaction conditions to synthesise aryl imidates, but faced longer reaction time (19 h). This is because alcohols are weaker nucleophiles than amines. He changed the base from Cs_2CO_3 to NaOEt/EtOH and K_2CO_3. NaOEt proved to be the best base and resulted in the desired aryl imidate as outlined in scheme 20.



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Scheme 20. Tin free palladium-catalysed synthesis of imidates

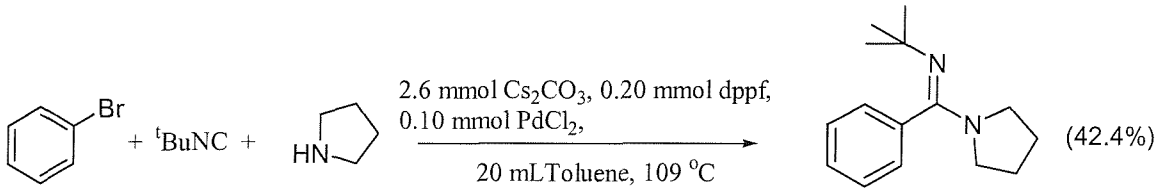
The reaction worked well with different isonitriles (Cy, ^{n}Bu) giving rise to desired compounds. Unexpectedly the formation of double inserted isonitrile products was observed. It was later found that only the sodium salts of aliphatic alcohols gave rise to double inserted products. The reason for this behaviour is not understood. Sodium ethoxide is a significantly better nuclephile than sodium phenoxide, but phenols are much more acidic than ethanol. This result suggested that the single *vs* double insertion may be pH-dependent. Electron neutral and electron rich aryl bromides tend to give double insertion, where as electron poor substrates preferred

single insertion. This is similar to palladium-catalysed carbonylation to amide and alpha-ketoamides, where the electronic nature of aromatic halides had the same influence as described above.

Chapter 2: Synthesis of amidines, imidates, α-amino imidates and sulfones

This chapter deals with extension to Dr. Saluste's work, [6,7] followed by an attempt to synthesise α-amino imidates and palladium-catalysed synthesis of aryl sulfones, which led to some interesting points.

2.1. Synthesis of (*E*) - (*N* - *tert*-butyl) - *N* - (1 - phenyl - 1 -tetra hydro - 1 *H* - pyrroyl methylidene) amine[6]



Scheme 22. Palladium-catalysed coupling of aryl bromide, *tert*-butyl isonitrile and pyrrolidine to synthesise amidine

The palladium-catalysed synthesis of amidines[6] using dppf as a ligand was complete in 4 h. However, in the same reaction an initiation period of 2 h was observed. In this period starting material and an intermediate were observed by GC. Attempts to identify the intermediate by EIMS were not successful. Initiation periods are normally caused by either a need to convert a pre-catalyst to an active catalyst, or the initial removal of an inhibitor.

2.1.1. Reducing the catalyst:

In the synthesis of the amidine the Pd(II) pre-catalyst must be reduced to a catalytically active Pd(0) species, which could cause the initiation period. The first step in our investigation involved reducing Pd(II) to Pd(0) by addition of 4 equivalents Dibal - H to $PdCl_2$ in the presence of 2 equivalents dppf followed by addition of the remaining reagents. This strategy was not successful as longer initiation and reaction times were needed before any product formation was observed.

2.1.2. Is dppfo the active catalyst:

It was suspected that the initiation period could be due to the mono-oxidation of dppf to dppfo, which might accompany reduction of Pd(II) to Pd(0) and could act as a much more active catalyst. Dppfo[25] was synthesised, but we could not avoid the presence of dppf around 20% in the product.

Duplicate reactions were performed using both dppf and dppfo at the same time using $Pd_2(dba)_3.CHCl_3$ and $PdCl_2$ as catalysts. The reactions containing dppfo were very slow thereby leading to the conclusion that dppfo was not a useful ligand.

2.1.3. Pre-inducing catalyst:

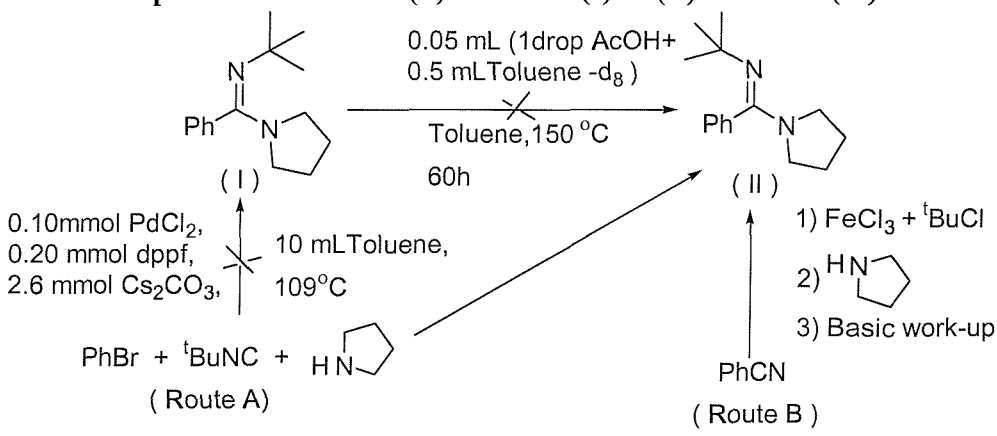
In an attempt to form an active catalyst which did not require an initiation period, we tried by pre-mixing $PdCl_2$, dppf, Cs_2CO_3 and pyrrolidine and heating for 2 h at 110 °C (the colour of the reaction mixture turned from dark yellow to dark brown after 10 min) before addition of PhBr and ^{t}BuNC, but after 5 h there was no conversion of starting material.

We tried to test for the presence of an active catalyst by adding additional PhBr and ^{t}BuNC to a reaction, which reached completion, but no conversion was observed.

2.1.4. Using Nickel catalyst:

We then tried nickel catalyst in the synthesis of amidine[6] instead of palladium. Four catalysts were tried each with $NiCl_2$ + 2 dppf; $Ni(PPh_3)_2Cl_2$ + 2 dppf; $NiCl_2$ + 2 dppf + 2 EtMgCl; Ni $(PPh_3)_2$ Cl_2 + 2 dppf + 2 EtMgCl; but all were unsuccessful.

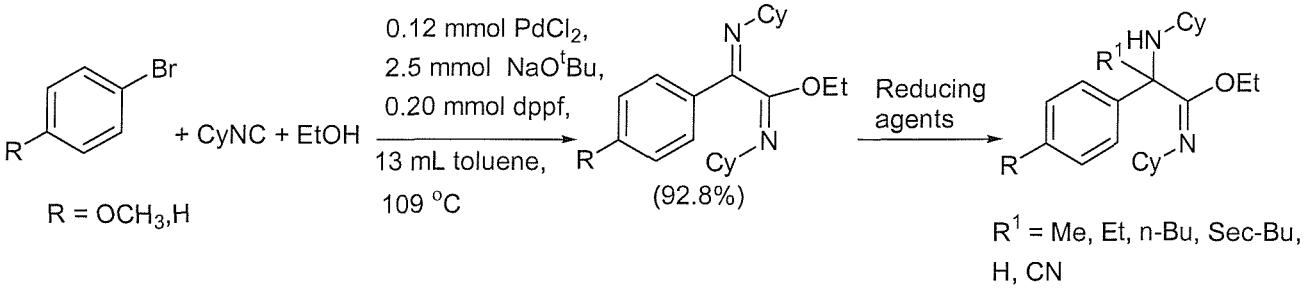
2. 2. Attempted conversion of (*Z*)- amidine (I) to (*E*)- amidine (II):



Scheme 23. Conversion of *Z*-amidine to *E*-amidine

Dr. Saluste[6] had thought that the (*E*)-amidine (II) was formed via an imidoyl chloride (Route B) and the (*Z*)-amidine (I) was formed by the palladium catalysed procedure. DFT calculations indicated that *E*-isomer is thermodynamically more stable by ~8 kcal/mol. We thus decided to look at the conversion of (I) to (II). At first heating of (I) was performed at 150 °C for 20 h in the absence of acid. No conversion of (I) to (II) was observed. Then 0.05 mL (1 drop AcOH + 0.5 mL toluene-d_8) solution was added to (I) and refluxed at 150 °C for 60 h, which was also unsuccessful. The low temperature NMR was performed for the palladium-catalysed compound, which indicated that it is the (*E*)-isomer and not the (*Z*)-isomer which is formed in this procedure. We concluded that the product Dr. Saluste characterised from the imidoyl chloride route was the hydrochloride salt, and that barrier to C-N rotation is much higher than for the free base.

2.3. Attempted synthesis of α - amino imidates:



Scheme 24. Synthesis of α-amino imidates from α-imino imidates

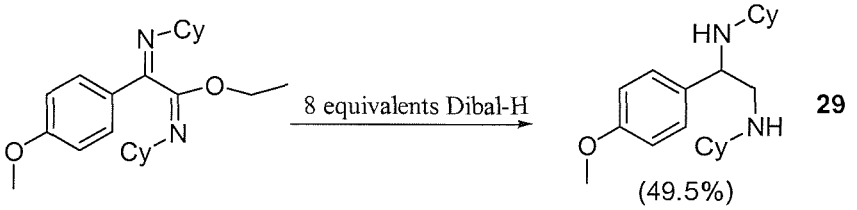
It would be of great interest to add nucleophiles[26] to the iminogroup of α-iminoimidate, [7] which are readily formed by palladium-catalysed reactions described to give α-amino imidates as shown in scheme 24.

The addition of organometallic reagents[27] to C=N bonds of imines or its derivatives (hydrazone, oxime) are well-known reactions, which have usually been carried out in THF.

Our attempts described below with a variety of organometallics were unsuccessful.

The reactions with EtMgCl, MeMgBr and $NaBH_4$ were unsuccessful with no loss of starting material. With ^{n}BuLi there was no loss of starting material, but with ^{S}BuLi there was loss of starting material, which might be due to deprotonation of cyclohexyl group.

Surprisingly, with the use of 8 equivalents $NaBH_3CN$ under acidic conditions, 8 equivalents Dibal-H, 8 equivalents $LiAlH_4$ and 10 equivalents selectride, all led to the starting material being reduced to the bis-amine **29** as shown in scheme 25.



Scheme 25. Synthesis of bis-amine from α-imino imidate

The development of addition of organometallics has been severely limited by the poor electrophilicity of the azomethine carbon. This limitation can be overcome by either

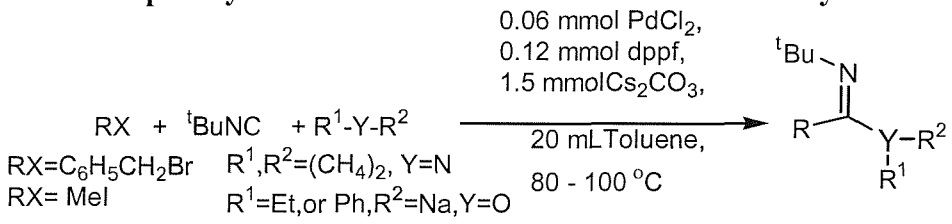
1). Activation of the C=N bond either by N-substitution with an electron withdrawing group or by N-coordinating Lewis acids.

2). Use of external ligands complexing the organometallic reagents

The use of Lewis acids ($AlCl_3$, $TiCl_4$, $In(OTf)_3$, $Yb(OTf)_3$) with allyltributyltin in 1:1 ratio were not successful in achieving the desired nucleophilic attack.

Attempts to complex the organometallic reagents by generating the zirconacycle[28] (Cp_2ZrCl_2 + EtMgX (X-Cl, Br) in 1:5 ratio were unsuccessful.

2.4. Attempted synthesis of amidines and imidates from benzyl bromide:



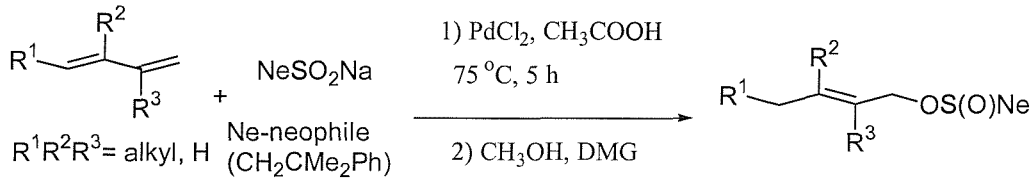
Scheme 26. Palladium-catalysed synthesis of benzyl / methyl amidines

In the palladium-catalysed synthesis of aryl amidines[6] and imidates, [7] replacing aryl group with benzyl, methyl, allyl and alkenyl halides would greatly enhance its versatility. Attempts at using methyl iodide and allyl bromide were unsuccessful presumably because direct nucleophilic attack dominates. Surprisingly, when benzyl bromide was utilised formation of benzyl amidine was observed by ES-MS but not by GC, which indicated the formation of amine only. This may be because amidines are strongly basic towards ES-MS. Attempts to isolate the amidine were unsuccessful.

In this thesis, we focussed our work on the synthesis of alkenyl amidines and imidates under the same reaction conditions, [6] which will be discussed in chapter 3.

2. 5. Synthesis of sulfones:

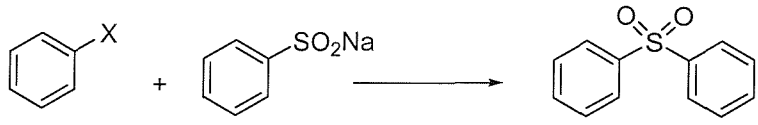
In 1978, the first communication[29] appeared concerning the potential use of palladium complex catalysts in the synthesis of higher sulfones from 1,3-dienes and arene sulfinic acids as shown in scheme 27.



Scheme 27. Coupling of alkene and sulfinic salts to synthesise sulfones

Based on this precedent, we decided to attempt the synthesis of aryl sulfones by coupling aryl sulfinic salts and aryl halides using a palladium catalyst.

Having synthesised the aryl sulfone independently to be used as a standard a series of reactions were set up to attempt the coupling shown in scheme 28. The conditions used are summarised in Table 2.



Scheme 28. Coupling of aryl halide and aryl sulfinic salts to synthesise aryl sulfones

Table 2: Different palladium sources, ligands and solvents utilised.

PhX	Pd-source	Ligand	Solvents
X = Br	$PdCl_2$	dppf [a]	Toluene
			DMF
			Dioxane
	Pd $(PPh_3)_4$	dppf [a]	Toluene
			DMF
			Dioxane
	Pd $(dba)_3.CHCl_3$	dppf [a]	DMF
		$(o\text{-Tolyl})_3P$ [b]	"
		$(o\text{-Tolyl})_3P$ [c]	"
X = I	Pd $(dba)_3.CHCl_3$	dppf [a]	DMF
		$(o\text{-Tolyl})_3P$ [b]	"
		$(o\text{-Tolyl})_3P$ [c]	"

Conditions: temp-100 °C, (a)- ligand (1 eq.); (b)- ligand (2 eq.); (c)- ligand (4 eq.) w.r.t to Pd-source.

Unfortunately none of the conditions reported proved to be successful.

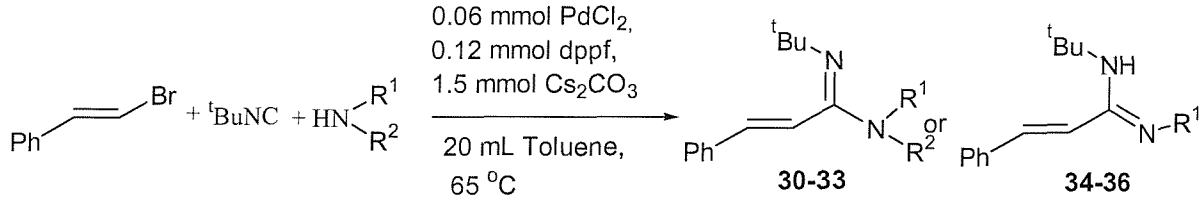
2.6. Conclusions:

1. Dppfo was not a useful ligand in the synthesis of aryl amidines.
2. Aryl amidines exist in the most thermodynamically stable E-isomer.
3. Reduction of α-iminoimidates led to the formation of bis-amines **29**, but nucleophilic attack could not be acheived.
4. Synthesis of benzyl, alkyl and allyl amidines and imidates under the same reaction conditions of aryl amidine/ imidate were unsuccessful.
5. Coupling of aryl halides and aryl sulfinic salts using palladium as a catalyst was unsuccessful.

Chapter 3: Synthesis of alkenyl amidines and imidates

This chapter deals with the palladium-catalysed synthesis of alkenyl amidines and imidates.

3.1. Synthesis of alkenyl amidines:



Scheme 29. Palladium-catalysed synthesis of alkenyl amidines

Initial optimisation of the coupling reaction between β-bromostyrene, *tert*-butyl isonitrile and pyrrolidine by GC indicated 65 °C as a reasonable temperature. β-Bromo styrene is commercially available as a mixture of *trans/cis* ~86/14 and was converted to *trans/cis* >99/1 through a literature procedure. [30] Primary and secondary amines utilised in these reactions are listed in Table 3.

Table 3: Alkenyl amidines synthesised

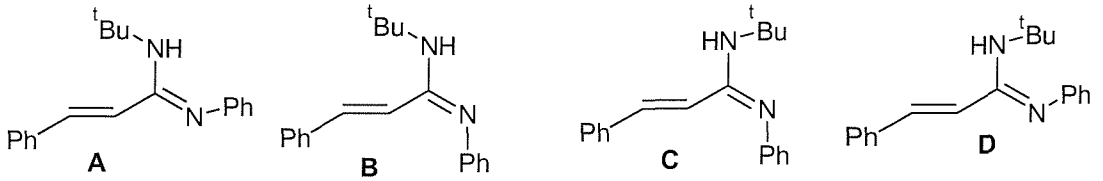
Amine (R^1, R^2)	Compound	Yield (%)	Time	Trans : Cis
-$(CH_2)_4$-	**30**	76.8	15 min.	>99 : 1
Et	**31**	61.2	"	~95 : 5
-$(CH_2)_2O(CH_2)_2$-	**32**	61.6	"	>98 : 2
-$(CH_2)_5$-	**33**	71.2	"	>98 : 2
Me, H	**34**	71.4	"	>99 : 1
Cy, H	**35**	71.2	"	100[a]
Ph, H	**36**	25.4	35 hr[c]	45 : 55[b]

a. *trans*-isomer w.r.t C=C bond, b. Mixture of *E*:*Z* w.r.t imine group, c. Temperature is 125 °C

As seen from Table 3, the reaction worked well with both primary and secondary amines. When aniline was the amine source, a little conversion of starting material to **36** was observed after 18 h stir at 65 °C. As aniline is much less nucleophilic than aliphatic amines the slow reaction was not surprising. However at

125 °C the reaction was complete after 35 h stirring. Compound **36** was formed as mixture of *E* : *Z* isomer of imine group in 45 : 55 ratio.

Compound **36** can exist in four possible structures **A, B, C** and **D** as shown in scheme 31. Out of the two rotomers **A** and **D**, **A** is stongly favoured over **D** this is because in **D** there is a steric clash between *tert*-butyl and phenyl groups. Out of the other two rotomers **B** and **C**, DFT calculations indicate that **C** is strongly favoured over **B**.



Scheme 31. Four possible structures for **36**

^{1}H-NMR shifts of the *tert*-butyl groups indicate that the amidines derived from primary amines exist in the tautomeric form (see scheme 31, compound **34-36**), as the singlet of the *tert*-butyl group has a distinctive upfield shift (~0.2 ppm) in compounds derived from primary amines when compared to secondary amines, as shown in Table 4.

Table 4: ^{1}H-NMR values of *tert*-butyl group

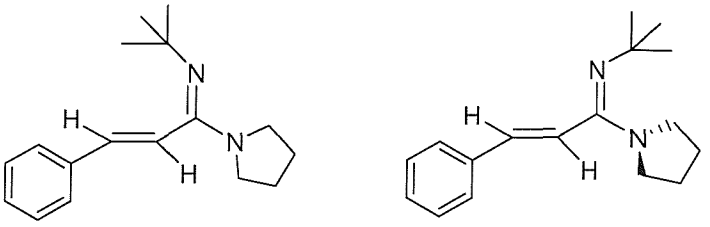
Compound	Sec. Amine (δ)	Compound	Pri. Amine (δ)
30	1.26 ppm	**34**	1.42 ppm
31	1.23 ppm	**35**	1.41 ppm
32	1.26 ppm	**36**	1.43 ppm
33	1.26 ppm		

There is clearly a second isomer i.e. the *cis*-isomer. The formation of *cis*-isomer was confirmed by comparing the ^{1}H-NMR of **30, 31** and **32** with different isomeric ratios as shown in Table 5. The coupling constant (*J*) for alkenyl protons in *trans/cis* of alkenyl amidines was expected to be 16/12 Hz, but found to be >16.5/12.5 Hz.

Table 5 : Comparison of ^{1}H-NMR values with different *Trans : Cis* ratio

Compound	Major isomer	Minor isomer	Ratio (*E*:*Z*) of PhCH=CHBr Precursor	
			~86 : 14	**>99 : 1**
30	6.72 (d, *J* = 16.8 Hz) 6.58 (d, *J* = 16.8 Hz)	6.34 (d, *J* = 12.8 Hz) 6.24 (d, *J* = 12.8 Hz)	90 :10	>99 : 1
31	6.66 (d, *J* = 16.6 Hz) 6.54 (d, *J* = 16.6 Hz)	6.48 (d, *J* = 12.8 Hz) 6.15 (d, *J* = 12.8 Hz)	91 : 9	~95 : 5
32	6.69 (d, *J* = 16.9 Hz) 6.61 (d, *J* = 16.9 Hz)	6.58 (d, *J* = 12.5 Hz) 6.09 (d, *J* = 12.5 Hz)	93 : 7	>98 : 2

3.2. Stereochemistry of amidines:



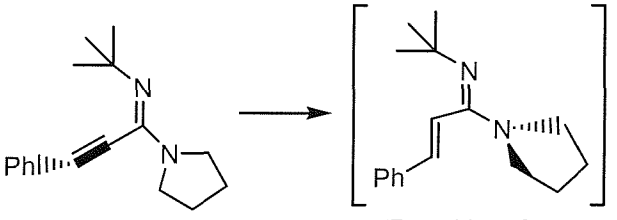
30A 30B

Scheme 32. *E*- and *Z*- isomers of **30**

In the palladium-catalysed synthesis of aryl amidines the *E*-isomer is formed but this is thought to be under thermodynamic control and not necessarily expected to be the same for alkenyl amidines.

We would expect the *E*-isomer to have a good overlap between the pyrrolidine nitrogen lone pair and the imine double bond. Therefore there will be a substantial barrier to rotation about the C-N bond due to partial double bond character. In the *Z*-isomer the steric clash between *tert*-butyl group and NCH_2 of pyrrolidine forces the pyrrolidine into a perpendicular configuration where NCH_2 of pyrrolidine are equal.

If a compound exists as a mixture of rapidly interconverting conformers they may be frozen out at low temperature. The low temperature NMR of **30** was performed. However it doesn't show freezing out of the rotomers. The barrier to rotation of the C-N bond is very low so that it is not freezing out at 213 K.



Transition State

Scheme 33. Compound **30** in Transition State

Conjugation of styrene with C=N in transition state, which is not possible in ground state, lowers the transition state energy.

X-Ray crystallography of **30** and **33** indicated the stereochemistry of the imine group exists in *E*- isomer.

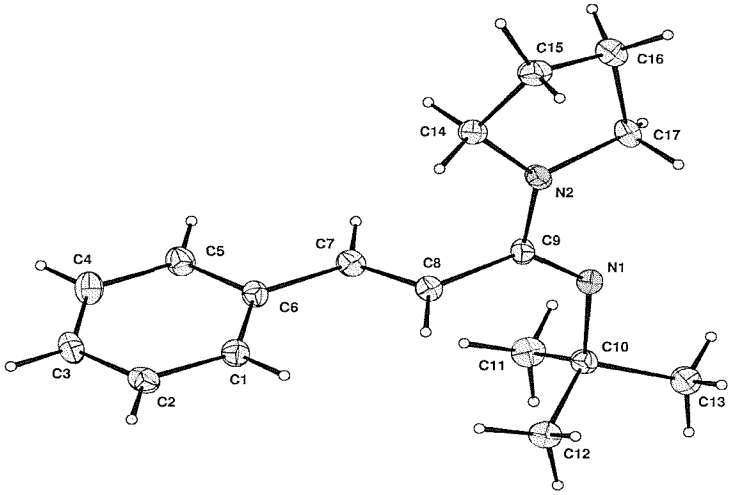


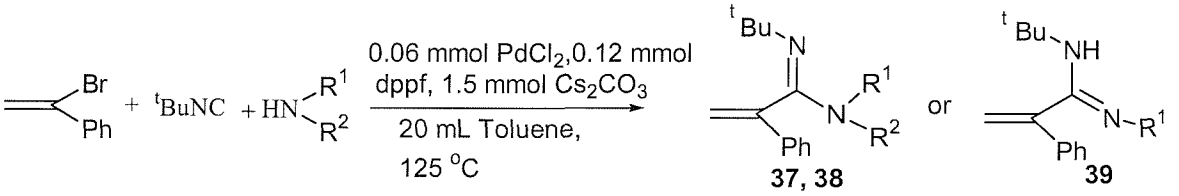
Figure 1: X-Ray crystallography of **30**

The bond length and dihedral angles for **30** was calculated. The angle between N_1-C_9-N_2-C_{17} was 179.8°, which indicates that there is an excellent overlap between pyrrolidine nitrogen lone pair and Imine group. The angle between N_1-C_9-C_8-C_7 was 105.6° indicates that there exists a little overlap between carbon- carbon double bond and imine group. The angle between C_8-C_7-C_6-C_1 was 3.0° which indicates that the excellent conjugation of C=C bond and phenyl group.

3.3. Different isonitrile:

Attempts to replace *tert*-butyl isonitrile with other isonitriles like n-butyl, cyclohexyl and benzyl isonitriles in the synthesis of alkenyl amidines were unsuccessful. In all these cases pyrrolidine was the amine source.

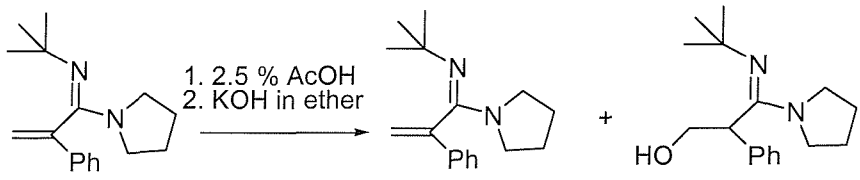
3.4. α-Bromo styrene as starting bromide:



Scheme 34. Synthesis of alkenyl amidines

Initial GC optimisation of the palladium-catalysed reaction between α-bromo styrene, *tert*-butyl isonitrile and pyrrolidine indicated 125 °C as the best temperature (see scheme 34).

The most surprising result in these reactions was the facile addition of water to the carbon-carbon double bond of **40** resulting in the formation of **41** (25 : 75 ratio of **40** : **41** by GC), during acid-base work-up where base was added immediately to the aqueous layer in presence of ether as shown in scheme 35.



Crude **(40)** **41**

Scheme 35. Acid-base work-up of **40** resulted to in **41**

At first different bases were tried to obtain **40** as a single product, as shown in Table 6.

Table 6: GC optimisation in acid-base work-up of 40

Work-up condition	**40 (%)**	**41 (%)**
AcOH+Conc.KOH	40	60
AcOH+$NaHCO_3$	----	100
AcOH+K_2CO_3	65	35
AcOH+2M NaOH	60	40

From these results, it was suspected that the attack of –OH group occured in acidic phase. To find this, **40** (crude) was left in acidic phase for few minutes followed by slow addition of base in presence of ether, which led to the formation of **40** (100%). This result shows that the –OH does not attack in the acidic phase. The result as well suggests that the -OH group was attacked by immediate addition of base to the aqueous layer.

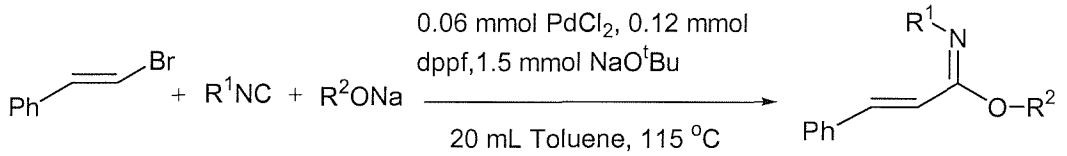
Both primary and secondary amines utilised in the reaction as shown in scheme 34 were listed in Table 7. The amidine synthesised from primary amine as amine source exists in tautomeric form (see scheme 34). In the crude form compound 38 was a mixture of **38** and compound **49** (see experimental, page 40). They were separated by column chromatography using petrol : ether (4.5:0.5+3% NEt_3). The attempts to replace *tert*-butyl isonitrile with ^{n}BuNC and CyNC were unsuccessful.

Table 7: Synthesis of alkenyl amidines from α-bromo styrene, ^{t}BuNC and amines

Amine (R^3, R^4)	Compound	Yield (%)	Time
$-(CH_2)_4-$	**37**	71.2	2h
$-(CH_2)_5-$	**38**	29.7	1h
H, Cy	**39**	52.7	50 min.

Conditions : 0.06 mmol $PdCl_2$, 0.12 mmol dppf, 1.5 mmol Cs_2CO_3, 6 mmol of amine, 1.2 mmol of α-bromostyrene, 1.8 mmol ^{t}BuNC, toluene(20 mL) and temp (125 °C).

3.5. Synthesis of alkenyl imidates:



Scheme 36. Synthesis of alkenyl imidates

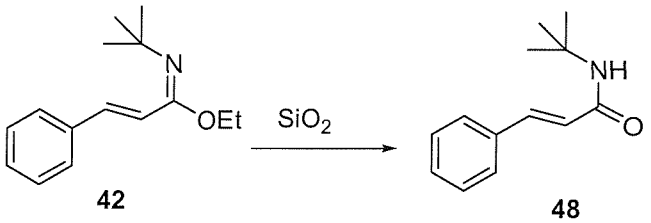
Initial GC optimisation of the palladium-catalysed reaction between β-bromo styrene, *tert*-butyl isonitrile and sodium ethoxide/ sodium phenoxide indicated 115 °C as the best temperature. The reaction worked with other isonitriles (see Table 8). Although the β-bromostyrene used for these reactions was of a mixture of *trans/cis* >99/1, no significant amount of the cis-isomer product was ever isolated.

Table 8: Compounds synthesised were listed

β-bromo styrene	Isonitrile (R^1)	Alcohol	Time	Yield (%)	Compound
"	^{t}BuNC	EtOH	1h 40 min	25	**48**[a]
"	"	PhONa	30 min	60	**43**[b]
"	^{n}BuNC	EtOH	1h 10 min	63.6[c]	**44+45**
"	"	PhONa	30 min	71.9	**46**[d]
"	CyNC	PhONa	1h	54.9	**47**[d]

a. *E*-isomer w.r.t C-N bond and **41** is not present b. *E*-isomer w.r.t imine group and **48** is not present, c. mix. of bis (65%)-& mono (35%)-inserted and **48** is not present, d. mix. of *E* : *Z* w.r.t imine group,

3.6. *tert*-butyl isonitrile:



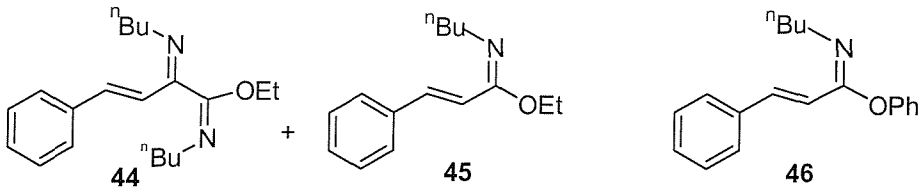
42 **48**

Scheme 37. Purification of **42** on silica gel led to **48**

Unexpectedly the purification of **42** on silica gel, led to the formation of **48**. Attempts to purify the crude product by Kugelrohr distillation were not successful in providing a pure sample of **42.**

The synthesis of **43** was suspected to be a mixture of *E*-and *Z*-isomers. However on further investigation it was found to be a mixture of **43** and **48**. Interestingly purification of the crude on silica gel led to the successive separation of **43**. From these observations, it can be concluded that **42** was much less stable towards purification than **43**. Double insertion of isonitrile was not observed for these compounds.

3.7. *n*-butyl isonitrile:



44 45 46

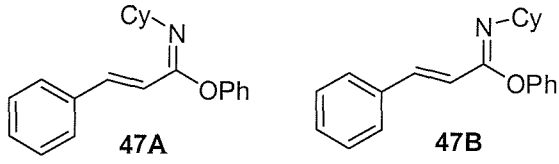
mixture of bis-and mono- inserted compound

Scheme 38. Alkenyl imidates synthesised by using n-butyl isonitrile

The synthesis of imidates, using ethanol and n-butyl isonitrile as sources of alcohol and isonitrile, provided some surprising results. The crude reaction mixture was found to be a mixture of product containing bis- and mono-inserted isonitrile compounds **44+45**, which was confirmed by GC-MS. Unfortunately the two products cannot be separated by flash column chromatography. The other reason not to repeat the purification was due to the potential for once again forming an amide. Therefore the compounds were reported as a mixture.

The use of sodium phenoxide and n-butyl isocyanide as sources of alcohol and isonitrile resulted in a mixture of *E*-and *Z*-isomer of imine group **46**. Double insertion of isonitrile was not observed for these compounds.

3.8. Cyclohexyl isonitrile:

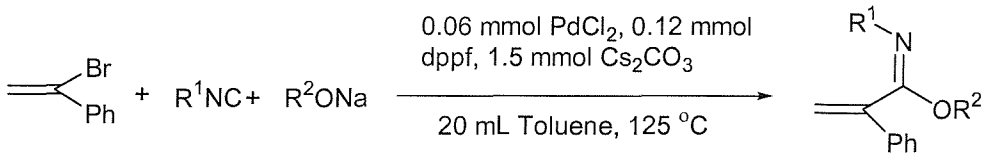


47A 47B

Scheme 39. *E*- & *Z*-isomers w.r.t imine group

The synthesis of imidates using sodium phenoxide and cyclohexyl isonitrile as sources of alcohol and isonitrile was successful and found to be a mixture of *E* and *Z*-isomers (see scheme 39). Unfortunately the reaction with ethanol as alcohol source didn't work. Double insertion of isonitrile was not found for these reactions.

3.9. α-Bromo styrene as bromide source:



Scheme 40. Synthesis of imidates by coupling α-bromostyrene, isonitrile and alcohol

Synthesis of imidates using α-bromo styrene was not successful. Different temperatures varying from 95 °C to 125 °C were tried. However even after 18h the starting bromide didn't disappear.

3.10. Conclusions:

1. Alkenyl bromides were successfully coupled with isonitrile and amines or alcohols to afford amidine and imidates.
2. X-Ray crystallography of **30** and **33** indicated the stereochemistry of amidine as the *E*- isomer.
3. Different isonitrile groups were successively utilised in the synthesis of imidates.
4. α-Bromostyrene was unsuccessful in replacing aryl bromide in the synthesis of imidates.
5. Purification of **42** on silica gel led to its conversion to **48**.
6. Attack of water on the carbon-carbon double bond of **40** can be restricted by slow addition of base to aqueous layer in presence of ether.

4. Experimental

4.A. General Experimental:

Unless otherwise stated, the following general experimental techniques apply to all procedures described below.

All reactions were carried out under an argon atmosphere using standard Schlenk techniques. Reaction solvents were dried over calcium hydride or sodium flakes before use. Toluene and THF were distilled from sodium/benzophenone under an argon atmosphere. Petrol refers to the fraction of petroleum ether which boils between 40 and 60 °C.

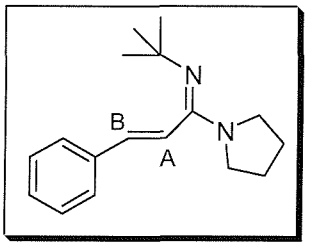
Thin layer chromatography (TLC) experiments were performed using petrol, ether, triethylamine, benzene, ethanol, CH_2Cl_2, and ethyl acetate as solvents, and were visualised under a 254nm uv lamp. ^1H and ^{13}C –NMR were recorded on Bruker AM300, AC300 or DPX400 Fourier transform spectrometers in $CDCl_3$ (stored over K_2CO_3) or toluene-d_8. Chemical shifts are expressed in units of ppm on the δ scale. ^1H-NMR spectra are reported as s, singlet; d, doublet; t, triplet; q, quartet; or m, multiplet. ^{13}C - NMR spectra are proton decoupled and reported as s, d, t, or q depending on the number of directly attached protons (0, 1, 2, 3 respectively as C, CH, CH_2, CH_3 as determined by DEPT experiment).

Low Resolution Mass spectra were recorded on Micromass platform II instrument using electron spray positive ion, in acetonitrile. High Resolution Mass spectra were recorded on Bruker Apex III using electron spray positive ion, in acetonitrile. Gas chromatography was carried out on a Hewlett Packard 6890 system with autosampler, passing through a 30 m, 5% methyl siloxane column, (HP-5) programmed starting at 80 °C up to 250 °C at 25 °C per min and holding for 4 min at 250 °C, 2 mL/min, He carrier gas. Microanalysis was performed by Medac Ltd.

UV-spectra were recorded on a Hewlett-packard 8452A Diode Array Spectrometer using two-way quartz cells. Kugelrohr-distillation was carried out with a Buchi 420851 oven. Melting points were determined in open capillary tubes using a Gallenkamp Electro thermal melting point apparatus.

4.2. Preparative

Synthesis of *tert*-butyl-[(*E*)-3-phenyl-1-pyrrolidin-1-yl-prop-2-en-(*E*)-ylidene] -amine 30



To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol) and $PdCl_2$ (0.01 g, 0.06 mmol) were added against a flow of argon, followed by *trans*-bromostyrene (0.21g, 1.2 mmol) and pyrrolidine (0.40 mL, 6 mmol). Dry degassed toluene (10 mL) was added followed by ^{t}BuNC (0.14 mL, 1.8 mmol). Another aliquot of toluene (10 mL) was added. The reaction mixture was heated at 65 °C for 15 min. GC indicated complete loss of *trans*-bromostyrene. After the reaction mixture was cooled to room temperature, ether (2×10 mL) was added and filtered to give a brown coloured solution. The ether layer was extracted into dil. AcOH (2.5 % in H_2O, 6×5 mL). Ether layer was discarded and aqueous layers were combined, to which ether (20 mL) was added, followed by KOH pellets. Ether layer was collected. Aqueous layers were extracted into ether (3×30 mL) and the combined ether layers were dried over $MgSO_4$. A yellow solid resulted by evaporation of the ether layer. Kugelrohr distillation (oven temp 120 –127 °C / 0.3 mm Hg) gave the title compound as a white solid (0.235 g, 76.8%), which is a mixture of *trans/cis* >99/1.

M.P: 74-77 °C (from ethanol).

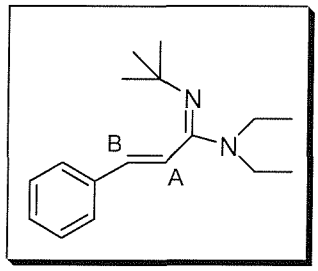
Major isomer (*Trans*):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.42-7.45 (2H, m, Ph), 7.29-7.40 (3H, m, Ph), 6.72 (1H, d, J = 16.8 Hz, H_B), 6.58 (1H, d, J = 16.8 Hz, H_A), 3.33 (4H, brm, 2xNCH_2), 1.84 (4H, brm, 2xCH_2), 1.26 (9H, s, 3xCH_3) ppm. **^{13}C-NMR ($CDCl_3$, 100 MHz):** δ = 153.80 (s, C=N), 135.45 (s, C-Ph), 132.84 (d, C_B), 127.76 (d, 2xC-Ph), 127.20 (d, C-Ph), 125.43 (d, C-Ph), 123.46 (d, C_A), 51.60 (s, $C(CH_3)_3$), 46.82 (t, 2xNCH_2), 31.46 (q, 3xCH_3),

24.24 (t, 2x$\underline{C}H_2$) ppm. **IR (cm^{-1}, neat):** 3058 (w), 3011 (w), 2968 (s), 2855 (m), 1644 (m), 1592 (s), 1441 (m), 1209 (s), 1020 (m), 1384 (m), 968 (s), 797 (s). **LR-MS (ES, m/z, %):** 257 (100, MH^+). **HR-MS (ES, MH^+):** $C_{17}H_{25}N_2$ calculated: 257.2012, found: 257.2012. **Elemental analysis** (%) Calculated: C 79.64, H 9.43, N 10.92; Observed: C 77.15, H 9.35, N 10.04; Calculated with 0.5 H_2O C 76.94, H 9.49, N 10.56. **UV/Vis (λ_{max}, nm):** 205 (ε = 6900), 268 (ε = 4600).

Minor isomer (*Cis*): Peaks from 90:10 mixture derived from 85:15 of *E*:*Z* bromostyrene. **^{1}H-NMR (400 MHz, $CDCl_3$):** δ = 6.34 (1H, d, *J* = 13 Hz, H_B), 6.24 (1H, d, *J* = 13 Hz, H_A), 1.35 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$):** δ = 133.24 (s, $\underline{C}$-Ph), 126.89 (d, 2x$\underline{C}$-Ph), 27.87 (q, 3x$\underline{C}H_3$) ppm.

Synthesis of (*E*)-N^1-*tert*-butyl-N,N-diethyl-3-phenyl-acrylamidine 31



The desired compound was synthesised from Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.21 g, 1.2 mmol), diethyl amine (0.43 mL, 6 mmol), and ^{t}BuNC (0.14 mL, 1.8 mmol) in dry degassed toluene (20 mL). The reaction mixture was heated at 65 °C for 15 min under argon. Work-up similar to compound **30** resulted in a brown coloured solution. Kugelrohr distillation (oven temp 115-125 °C / 0.3 mm Hg) gave the title compound as a colourless oil (0.19 g, 61.2%), which is a mixture of *trans/cis ~95/5*.

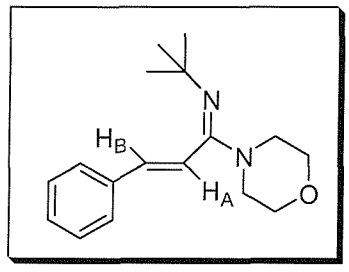
Major isomer (*Trans*):

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.43-7.45 (2H, m, Ph), 7.3-7.41 (3H, m, Ph), 6.66 (1H, d, J = 16.8 Hz, H_B), 6.54 (1H, d, *J* = 16.8 Hz, H_A), 3.29 (4H, q, *J* = 6.8 Hz, 2xCH_2), 1.23 (9H, s, 3xCH_3), 1.04-1.09 (6H, t, *J* = 6.8 Hz, 2xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 154.91 (s, $\underline{C}$=N), 136.42 (s, $\underline{C}$-Ph), 133.53 (d, $\underline{C}_B$), 128.80 (d, 2x$\underline{C}$-Ph), 128.16 (d, $\underline{C}$-Ph),

126.51 (d, 2x<u>C</u>-Ph), 124.20 (d, <u>C</u>$_A$), 52.61 (s, <u>C</u> $(CH_3)_3$), 41.87 (t, 2xN<u>C</u>H_2), 32.33 (q, 3x<u>C</u>H_3), 13.49 (t, 2x<u>C</u>H_2) ppm. **IR (cm^{-1}, neat)**: 2964 (m), 2899 (w), 2867 (w), 2356 (w), 1594 (s), 1356 (m), 1271 (m), 1198 (m), 1149 (w), 1080 (w), 1025 (w), 973 (w), 791 (m), 737 (m). **LR-MS (ES, m/z, %):** 259.3 (100, MH^+). **HR-MS (ES, MH^+):** $C_{17}H_{27}N_2$, calculated: 259.2169, found: 259.2168

Minor isomer (*Cis*): Peaks from 91:9 mixture derived from 85:15 of *E*:*Z* bromostyrene. **^{1}H-NMR (300 MHz, $CDCl_3$):** δ = 6.48 (1H, d, *J* = 12.8 Hz, H_B), 6.15 (1H, d, *J* = 12.8 Hz, H_A), 1.20 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 128.93 (d, 2x<u>C</u>-Ph), 31.72 (q, 3x<u>C</u>H_3) ppm.

Synthesis of *tert*-butyl-[(*E*)-1-morpholin-4-yl-3-phenyl-prop-2-en-(*E*)-ylidene]-amine 32



To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.21 g, 1.2 mmol), morpholine (0.52 mL, 6 mmol) and ^{t}BuNC (0.14 mL, 1.8 mmol) were added against a flow of argon in dry degassed toluene (10 mL). Final amount of toluene (10 mL) was added to the reaction mixture and heated at 65 °C for 15 min. Work-up similar to compound **30** resulted in a dark yellow oil. Kugelrohr distillation (oven temp 140 –145 °C / 0.3 mm Hg) gave the title compound as a light yellow oil (0.201 g, 61.6%), which is a mixture of *trans/cis >98/2*.

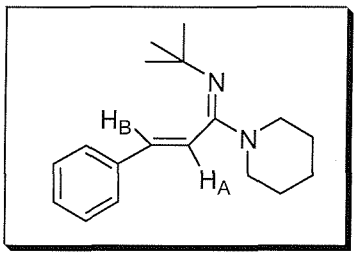
Major isomer (*Trans*):

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.44-7.47 (2H, m, Ph), 7.3-7.42 (3H, m, Ph), 6.69 (1H, d, *J* = 16.9 Hz, H_B), 6.61 (1H, d, *J* = 16.9 Hz, H_A), 3.7-3.74 (4H, m, 2xOCH_2), 3.23-3.26

(4H, m, 2xNCH$_2$), 1.26 (9H, s, 3xCH$_3$). **^{13}C-NMR (75 MHz, CDCl$_3$):** δ = 156.59 (s, C=N), 136.04 (s, C-Ph), 135.29 (d, C$_B$), 128.85 (d, 2xC-Ph), 128.61 (d, C-Ph), 126.71 (d, 2xC-Ph), 121.84 (d, C$_A$), 67.06 (t, 2xOCH$_2$), 52.87 (s, C(CH$_3$)$_3$), 47.62 (t, 2xNCH$_2$), 31.95 (q, 3xCH$_3$) ppm. **IR (cm^{-1}, neat)**: 2954 (s), 2855 (w), 1639 (m), 1592 (s), 1497 (w), 1450 (m), 1200 (m), 1114 (s), 1351 (m), 982 (m). **LR-MS (ES, m/z, %):** 273.3 (100, MH$^+$). **HR-MS (ES, MH$^+$):** $C_{17}H_{25}N_2O$ calculated: 273.1962, found: 273.1961.

Minor isomer (*Cis*): Peaks from 93:7 mixture derived from 85:15 of *E*:*Z* bromostyrene. **^{1}H-NMR (300 MHz, CDCl$_3$):** δ = 6.58 (1H, d, *J* = 12.5Hz, H$_B$), 6.09 (1H, d, *J* = 12.5 Hz, H$_A$), 3.44-3.50 (4H, m, 2xOCH$_2$), 3.30-3.90 (4H, m, 2xNCH$_2$), 1.25 (9H, s, 3xCH$_3$) ppm. **^{13}C-NMR (75 MHz, CDCl$_3$):** δ = 66.72 (t, 2xOCH$_2$), 31.44 (q, 3xCH$_3$)ppm.

Synthesis of *tert*-butyl-[(*E*)-3-phenyl-1-piperidin-1-yl-prop-2-en-(*E*)-ylidene]-amine 33

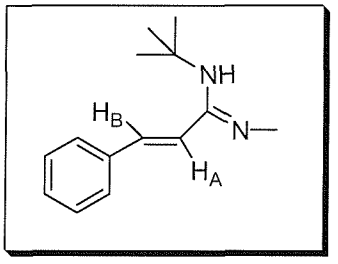


To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.21g, 1.2 mmol), and piperidene (0.51mL, 6 mmol) were added against a flow of argon followed by dry toluene (10 mL). Finally, ^{t}BuNC (0.14 mL, 1.8 mmol) was added followed by another aliquot of toluene (10 mL). The reaction mixture was heated at 65 °C for 15 min. GC indicated complete loss of *trans*-bromo styrene. Work-up similar to compound **30** resulted in a dark yellow gum. Kugelrohr distillation (oven temp 137 –142 °C / 0.3 mm Hg) gave the title compound as a colourless oil, which after few hours under vacuum resulted as a yellow solid (0.231 g, 71.2%), which is a mixture of *trans/cis >98/2*.

M.P: 76-79 °C (from hexane).

Major isomer (*Trans*):
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.44-7.47 (2H, m, Ph), 7.3-7.41 (3H, m, Ph), 6.67 (2H, s, H_B, H_A), 3.23-3.25 (4H, m, 2xNCH_2), 1.58 (6H, brm, 3xCH_2), 1.26 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 157.61 (s, C=N), 136.40 (s, C-Ph), 134.39 (d, C_B), 128.81 (d, 2xC-Ph), 128.34 (d, C-Ph), 126.70 (d, 2xC-Ph), 123.07 (d, C_A), 52.64 (s, $C(CH_3)_3$), 47.89 (t, 2xNCH_2), 32.10 (q, 3xCH_3), 26.10 (t, 2xCH_2), 25.20 (t, CH_2) ppm. **IR (cm^{-1}, neat)**: 3058 (w), 2961 (m), 2929 (m), 2856 (w), 2823 (w), 2360 (w), 1634 (m), 1593 (s), 1446 (m), 1371 (m), 1354 (m), 1259 (s), 1195 (s), 1125 (w), 1088 (s), 1024 (s), 972 (m), 797 (s), 741 (m). **LR-MS (ES, m/z, %):** 271.3 (100, MH^+). **HR-MS (ES, MH^+):** $C_{18}H_{27}N_2$ calculated: 271.2169, found: 271.2171. **Elemental analysis** (%) Calculated: C 79.95, H 9.69, N 10.35; Observed: C 77.24, H 9.65, N 9.71; Calculated with 0.5 H_2O C 77.37, H 9.74, N 10.03. **UV/Vis (λ_{max}, nm):** 207 (ε = 33,500), 268 (ε = 24,300). **Minor isomer (*Cis*):** Peaks from 90:10 mixture derived from 85:15 of *E*:*Z* bromostyrene.**^{1}H-NMR (300 MHz, $CDCl_3$):** δ = 6.52 (1H, d, *J* = 12.5 Hz, H_B), 6.13 (1H, d, *J* = 12.5 Hz, H_A), 1.23 (9H, s, 3xCH_3) ppm.

Synthesis of (*E*)-N-*tert*-butyl-N^1-methyl-3-phenyl-acrylamidine 34



To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.21 g, 1.2 mmol) and methylamine (0.18 mL, 6 mmol) were added against a flow of argon, followed dry degassed toluene (10 mL). Finally, ^{t}BuNC (0.14 mL, 1.8 mmol) was added, followed by another aliquot of toluene (10 mL). The reaction mixture was heated at 65 °C for 40 min. GC indicated complete loss of *trans*-bromostyrene. Work-up similar to compound **30** resulted to a brown coloured solution. Compound is decomposing while Kugelrohr distillation at 120-125°C. So, Purification on silica with petrol : ether (4.5 : 0.5 + 5 % NEt_3) gave the title compound as a brown oil (0.185 g, 71.4%), which is a mixture of *trans/cis >99/1*.

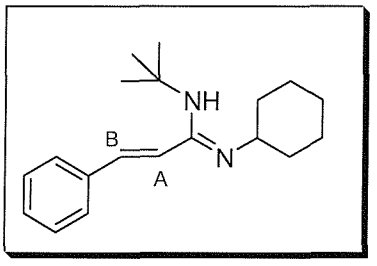
Major isomer (*Trans*):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.46-7.48 (2H, m, Ph), 7.30-7.39 (3H, m, Ph), 6.86 (2H, brs, H_B, H_A), 3.07 (3H, brs, NCH_3), 3.01(1H, s, NH), 1.42 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (100 MHz, $CDCl_3$):** δ = 156.35 (s, C=N), 136.48 (s, C-Ph), 134.48 (d, C_B), 129.16 (d, 2xC-Ph), 129.03 (d, C-Ph), 127.34 (d, 2xC-Ph), 122.40 (d, C_A), 51.33 (s, $C(CH_3)_3$), 36.79 (q, NCH_3), 30.13 (q, 3xCH_3) ppm. **IR (cm^{-1}, neat):** 2959 (s), 2907 (w), 2776 (w), 1644 (m), 1607 (m), 1495 (s), 1447 (m), 1385 (w), 1221(s), 1090 (w), 969 (m), 753 (s). **LR-MS (ES, m/z, %):** 217 (100, MH^+). **HR-MS (ES, MH^+):** $C_{14}H_{21}N_2$ calculated: 217.1699, found: 217.1702. **UV/Vis (λ_{max}, nm):** 220 (ε = 4300), 282 (ε = 6200).

Minor isomer (*Cis*):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.48 (1H, d, J = 12.3 Hz, H_B), 5.46 (1H, d, J =12.3 Hz, H_A), 1.23 (9H, s, 3xCH_3) ppm.

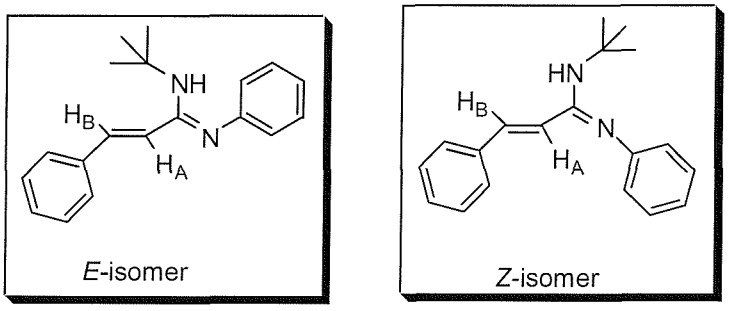
Synthesis of (*E*)-N-*tert*-butyl-N^1-cyclohexyl-3-phenyl-acrylamidine 35



To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), and $PdCl_2$ (0.01 g, 0.06 mmol) were added followed by *trans*-bromostyrene (0.21 g, 1.2 mmol) and cyclohexyl amine (0.6 mL, 6 mmol) under argon. Dry degassed toluene (10 mL) was added followed by ^{t}BuNC (0.14 mL, 1.8 mmol) against a flow of argon. Another aliquot of toluene (10 mL) was added. The reaction mixture was heated at 65 °C for 15 min. GC indicated the complete loss of *trans*-bromostyrene. Work-up similar to compound **30**, followed by Kugelrohr distillation (oven temp 137-142 °C / 0.3 mm Hg) gave the title compound as a colourless oil (0.231 g, 71.2%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.43-7.45 (2H, m, Ph), 7.29-7.39 (3H, m, Ph), 6.82 (2H, s, H_B, H_A), 3.40 (1H, s, NH), 3.35 (1H, tt, J = 4.0 Hz, 4.4 Hz -NCH), 1.44-1.76 (6H, m, 3xCH_2), 1.40 (9H, s, 3xCH_3), 1.27-1.35 (4H, m, 2xCH_2) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 151.54 (s, C=N), 136.27 (s, C-Ph), 133.27 (d, C_B), 128.75 (d, 2xC-Ph), 128.46 (d, C-Ph), 126.83 (d, 2xC-Ph), 121.81 (d, C_A), 56.53 (d, N CH (Cy)), 50.90 (s, C $(CH_3)_3$), 35.25 (t, 2xCH (Cy)), 29.17 (q, 3xCH_3), 26.16 (t, 2xCH (Cy)), 24.67 (t, 2xCH (Cy)) ppm. **IR (cm^{-1}, neat):** 3435 (w), 2919 (m), 2848 (w), 1643 (s), 1606 (s), 1488 (s), 1447 (s), 1355 (m), 1260 (m), 1223 (m), 1099 (m), 1018 (m), 974 (m), 799 (s), 757 (s). **LR-MS (ES, m/z, %):** 285.3 (100, MH^+). **HR-MS (ES, MH^+):** $C_{19}H_{29}N_2$ calculated: 285.2325, found: 285.2326. **UV/Vis (λ_{max}, nm):** 205 (ε = 45,000), 277 (ε = 38,600).

Synthesis of (*E*)-N-*tert*-butyl-3, N^1-diphenyl-acrylamidine 36

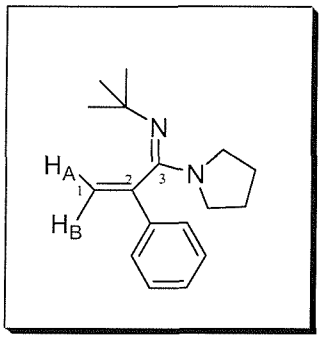


To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.21g, 1.2 mmol) and aniline (0.55 mL, 6 mmol) were added against a flow of argon. Dry degassed toluene (10 mL) was added followed by ^{t}BuNC (0.14 mL, 1.8 mmol). Another amount of toluene (10 mL) was added. The reaction mixture was refluxed at 125 °C for 35 hr. GC indicated the loss of *trans*-bromostyrene. Work-up similar to compound **30**, followed by Kugelrohr distillation (oven temp 137 – 142 °C / 0.3 mm Hg) gave the title compound as a colourless oil (0.12 g, 25.4%), which is a mixture of *Z* (55%)- and *E* (45%)- isomers.

It is difficult to assign *E*- and *Z*- isomers due to their 45 : 55 ratio. All δ values are reported together.

^{1}H-NMR* (400 MHz, $CDCl_3$): δ = 6.92 (2H, d, *J* = 6.5 Hz, Ph), 6.86 (1H, t, *J* = 6.6 Hz, Ph), 6.80 (1H, d, *J* = 16.3 Hz, H_B), 6.72 (2H, d, *J* = 7.2 Hz, Ph), 6.65 (2H, d, *J* = 7.2 Hz, Ph), 6.39 (1H, d, *J* = 16.3 Hz, H_A), 3.93 (1H, s, NH), 4.36 (1H, s, NH), 1.43 (9H, s, 3xCH_3), 1.36 (9H, s, 3xCH_3) ppm. *Signals of *Z*- and E-isomers overlapping at δ = 7.12-7.20 ppm. **^{13}C-NMR (100 MHz, $CDCl_3$):** δ = 151.37 (s, C=N), 149.78 (d, C=N), 133.58 (d), 132.55 (s), 129.37 (d), 128.78 (d), 128.75 (d), 128.64 (d), 127.08 (d), 122.56 (d), 121.95 (d), 121.18 (d), 50.47 (s), 28.48 (q), 27.92 (q) ppm. **IR (cm^{-1}, neat):** 3423 (w), 2961 (w), 1638 (s), 1586 (s), 1508 (s), 1485 (s), 1448 (m), 1387 (w), 1360 (w), 1258 (w), 1225 (w), 1197 (s), 1167 (w), 1069 9w), 1025 (w), 974 (w), 899 (w), 800 (w), 755 (m). **LR-MS (ES, m/z, %):** 279.2 (100, MH^+). **HR-MS (ES, MH^+):** $C_{19}H_{23}N_2$ calculated: 279.1856, found: 279.1860. **UV/Vis (λ_{max}, nm):** 204 (ε = 28,500), 268 (ε = 13,700).

Synthesis of *tert*-butyl-[2-phenyl-1-pyrrolidin-1-yl-prop-2-en-(*E*)-ylidene]-amine 37

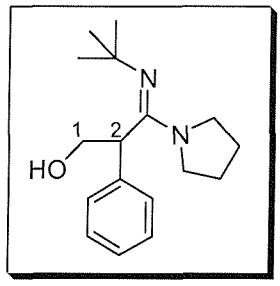


To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), α-bromostyrene (0.16 ml, 1.2 mmol) and pyrrolidine (0.4 mL, 6 mmol) were added against a flow of argon. Dry degassed toluene (10 mL) was added followed by

^{t}BuNC (0.14 mL, 1.8 mmol) against a flow of argon. Another aliquot of toluene (10 mL) was added. The reaction mixture was refluxed at 125 °C for 15 min. Work-up similar to compound **30**, followed by Kugelrohr distillation (oven temp 130-138 °C / 0.3 mm Hg) gave the title compound as a light yellow coloured oil (0.231 g, 71.2%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.43-7.46 (2H, m, Ph), 7.25-7.36 (3H, m, Ph), 5.92 (1H, s, H_A), 5.25 (1H, s, H_B), 3.23-3.31 (4H, m, 2xNCH_2), 1.78-1.82 (4H, m, 2xCH_2), 1.13 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 154.57 (s, C=N), 145.77 (s, C_2), 136.87 (s, C-Ph), 128.54(d, 2xC-Ph), 128.01(d, C-Ph), 125.65(d, 2xC-Ph), 114.39(t, C_1), 52.84(s, $C(CH_3)_3$), 46.73(t, 2xNCH_2), 32.63(q, 3xCH_3), 25.36(2xCH_2) ppm. **IR (cm^{-1}, neat):** 2962 (m), 2865 (w), 1595 (s), 1493 (w), 1375 (s), 1210 (s), 1028 (w), 906 (m), 781 (m). **LR-MS (ES, m/z, %):** 257.2 (100, MH^+). **HR-MS (ES, MH^+):** $C_{17}H_{25}N_2$, Calculated: 257.2012, found: 257.2011.

Synthesis of 3-[(*E*)-*tert*-butylimino]-2-phenyl-3-pyrrolidin-1-yl-propan-1-ol 41

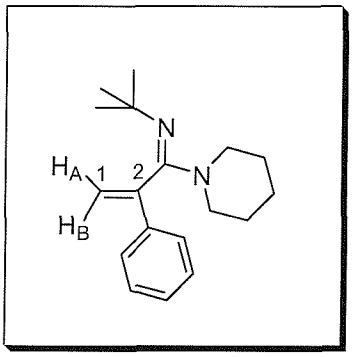


Compound 41 was obtained during work-up of compound 40. Purification on column with petrol : ether[(4 : 1) +5% NEt_3] resulted to a colourless oily compound (0.13 g, 25.4%).

^{1}H-NMR(300 MHz, $CDCl_3$): δ = 7.98 (1H, s, OH), 7.30-7.35 (2H, m, Ph), 7.23-7.28 (3H, m, Ph), 3.54 (1H, dd, J = 4.6 Hz, 10.1 Hz, H_1), 3.23 (1H, dd, J = 12.4 Hz, 10.0 Hz, H_1), 2.62-2.66 (3H, m, NCH_2+H_2), 2.51-2.54 (2H, m, NCH_2), 1.74-1.81 (4H, m, 2xCH_2), 1.35 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 172.11 (s, C=N), 139.93 (s, C-Ph), 128.46 (d, 2xC-Ph), 128.38 (d, 2xC-Ph), 126.79 (d, C-Ph), 59.38 (t, C_1), 53.70 (t, 2xNCH_2), 51.74 (d, C_2), 50.62 (s, $C(CH_3)_3$), 28.78 (q, 3xCH_3), 23.65 (t, 2xCH_2) ppm. **IR (cm^{-1}, neat):** 2973 (m), 2883 (w), 2360 (m), 1652 (w), 1613 (s), 1557 (w), 1450 (m), 1364 (m), 1224 (w), 1190 (m), 1098 (s), 785 (w),

755 (m). **LR-MS (ES, m/z, %):** 275.2 (MH^+).

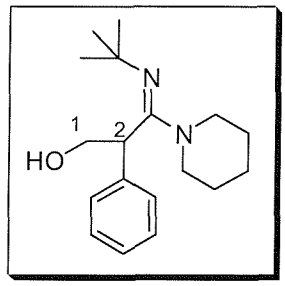
Synthesis of *tert*-butyl-[2-phenyl-1-piperidin-1-yl-prop-2-en-(*E*)-ylidene]-amine 38



To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), α-bromostyrene (0.16 mL, 1.2 mmol) and piperidene (0.51mL, 6 mmol) against a flow of argon. Dry degassed toluene (10 mL) was added followed by ^{t}BuNC (0.14 mL, 1.8 mmol) against a flow of argon. Another aliquot of toluene (10 mL) was added. The reaction mixture was refluxed at 125 °C for 50 min. Work-up similar to compound **30**, followed purification on silica with petrol : ether [(4.5 : 0.5) + 3% NEt_3] gave the title compound as a yellow coloured oil (0.11 g, 29.7%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.48-7.51 (2H, m, Ph), 7.25-7.36 (3H, m, Ph), 5.91 (1H, s, H_B), 5.22 (1H, s, H_A), 3.29-3.32 (4H, m, 2xNCH_2), 1.51-1.55 (2H, m, CH_2), 1.41-1.44 (4H, m, 2xCH_2), 1.11 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 154.66 (s, C=N), 43.75 (s, C_2), 136.38 (s, C-Ph), 127.44 (d, 2xC-Ph), 127.06 (d, C-Ph), 125.04 (d, 2xC-Ph), 114.07 (t, C_1), 44.90 (t, NCH_2), 51.89 (s, $C(CH_3)_3$), 31.35 (q, 3xCH_3), 25.16 (t, 3xCH_2), 24.16 (t, CH_2) ppm. **IR (cm^{-1}, neat):** 2962 (m), 2930 (m), 2852 (w), 1604 (s), 1494 (w), 1444(w), 1382 (m), 1275 (w), 1125 (m), 1018 (m), 907 (m), 781 (m), 703 (m). **LR-MS (ES, m/z, %):** 271.3 (100, MH^+). **HR-MS (ES, MH^+):** $C_{18}H_{27}N_2$ calculated: 271.2169, found: 271.2170.

Synthesis of 3-[(*E*)-*tert*-butylimino]-2-phenyl-3-piperidin-1-yl-propan-1-ol 49

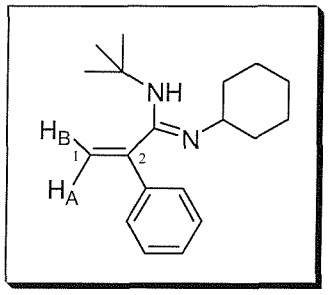


Compound 49 was obtained during work-up with 2.5% AcOH + KOH pellets. Kugelrohr distillation (oven temp 145-150 °C / 0.3mm Hg) gave the title compound as a colourless oil, re-crystallised from ethanol to a white solid (0.10 g, 28.9%).

M.P: 113-118 °C (from ethanol).

^{1}H-NMR(300 MHz, $CDCl_3$): δ = 8.61 (1H, s, OH), 7.34-7.27 (2H, m, Ph), 7.18-7.23 (3H, m, Ph), 3.57 (1H, dd, J = 13.0 Hz, 11.0 Hz, H_1), 2.93 (1H, dd, J = 13 Hz, 11.4 Hz, H_1), 2.62 (2H, brm, NCH_2), 2.45 (1H, dd, J = 3.7Hz, 13.0 Hz, H_2), 2.36 (2H, brm, NCH_2), 1.59-1.70 (4H, m, $2xCH_2$), 1.44-1.51 (2H, m, CH_2), 1.37 (9H, s, $3xCH_3$) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 172.28 (s, C=N), 139.79 (s, C-Ph), 128.68 (d, 2xC-Ph), 128.43 (d, 2xC-Ph), 126.73 (d, C-Ph), 62.66 (t, NCH_2), 54.12 (t, NCH_2), 50.61 (s, $C(CH_3)_3$), 49.03 (d, CH_2), 28.92 (q, $3xCH_3$), 26.16 (t, $3xCH_2$), 24.21 (t, $2xCH_2$) ppm. **IR (cm^{-1}, neat):** 3288 (m), 2934 (m), 1643 (s), 1549 (s), 1450 (m), 1358 (m), 1303 (w), 1268 (w), 1226 (m), 1154 (w), 1116 (m), 1033 (w), 910 (w), 858 (w), 780 (w), 743 (m). **LR-MS (ES, m/z, %):** 289.9 (100, MH^+). **HR-MS (ES, MH^+):** $C_{18}H_{29}N_2O$, Calculated: 289.2275, found: 289.2277. **Elemental analysis** (%) Calculated: C 74.96, H 9.78, N 9.71; Observed: C 74.16, H 9.80, N 9.54; Calculated with 0.2 H_2O C 74.03, H, 9.80, N 9.59.

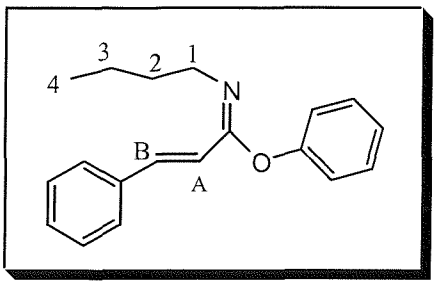
Synthesis of N-*tert*-butyl-N^1-cyclohexyl-2-phenyl-acrylamidine 39



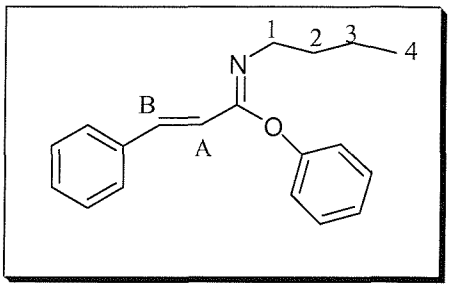
To dried Cs_2CO_3 (0.48 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), α-bromostyrene (0.16 mL, 1.2 mmol) and cyclohexyl amine (0.6 mL, 6 mmol) were added against a flow of argon. Dry degassed toluene (10 mL) was added followed by ^{t}BuNC (0.14 mL, 1.8 mmol) against a flow of argon. Another aliquot of toluene (10 mL) was added. The reaction mixture was refluxed at 125 °C for 15 min. Work-up similar to compound **30**, followed by Kugelrohr distillation (oven temp 183-186 °C / 0.3 mm Hg) gave the title compound as a light yellow coloured oil (0.18 g, 52.7%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.46-7.48 (2H, m, Ph), 7.32-7.37 (3H, m, Ph), 5.70 (1H, s, H_B), 5.15 (1H, s, H_A), 2.96 (1H, tt J = 9.0 Hz, 4.2 Hz, NCH), 1.07-1.69 (10H, m, 5xCH_2), 1.41 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 153.49 (s, $\underline{C}$=N), 144.65 (s, $\underline{C}_2$), 136.94 (s, $\underline{C}$-Ph), 128.55 (d, 2x$\underline{C}$-Ph), 128.08 (d, $\underline{C}$-Ph), 125.65 (d, 2x$\underline{C}$-Ph), 113.43 (t, $\underline{C}_1$), 58.15 (d, N$\underline{C}H_2$), 51.07 (s, $\underline{C}(CH_3)_3$), 35.23 (t, 2x$\underline{C}H_2$), 28.89 (q, 3x$\underline{C}H_3$), 26.10 (t, $\underline{C}H_2$), 24.48 (t, 2x$\underline{C}H_2$) ppm. **IR (cm^{-1}, neat):** 2926 (s), 2853 (m), 2360 (w), 1641 (s), 1493 (m), 1446 (m), 1402 (m), 1220 (m), 1028 (w), 909 (m), 752 (s). **LR-MS (ES, m/z, %):** 285.3 (100, MH^+). **HR-MS (ES, MH^+):** $C_{19}H_{29}N_2$, Calculated: 285.2325, found: 285.2325.

Synthesis of (E)-N-Butyl-3-phenyl-acrylimidic acid phenyl ester 46



***E*-isomer**



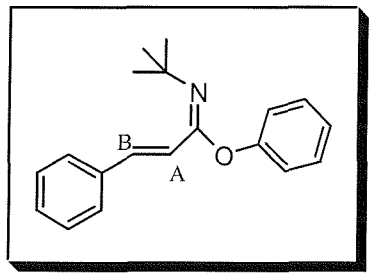
***Z*-isomer**

The title compound was synthesised from NaO^{t}Bu (0.14 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01g, 0.06 mmol), *trans*-bromostyrene (0.16 mL, 1.2 mmol), sodium phenoxide (6 mL of a 1M soln. in THF), and ^{n}BuNC (0.14 mL, 1.8 mmol) in dry toluene (20 mL). The reaction mixture was refluxed at 115 °C for 30 min. The reaction mixture was allowed to cool to room temperature before water (20 mL) was added. The organic layer was seperated and the aqueous solution was extracted into ether (3x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated to give a brown coloured oil. Kugelrohr distillation (oven temp 185-190 °C / 0.2 mm Hg) gave the title compound as a light yellow oil (0.241 g, 71.9%), which is a mixture of *E*- (65%) and *Z* (35%)- isomers.

Major isomer (*E*): ^{1}H-NMR* (400 MHz, $CDCl_3$): δ = 7.49 (1H, d, *J* = 16.6 Hz, H_B), 7.42 (2H, d, *J* = 7 Hz, Ph), 6.97 (1H, t, *J* = 7.4 Hz, Ph), 6.88 (2H, d, *J* = 7.7 Hz, Ph), 6.52 (1H, d, *J* = 16.6 Hz, H_A), 3.34 (2H, t, *J* = 7 Hz, H_1), 1.54 (2H, quintet, *J* = 7.2 Hz, H_3), 1.29 (2H, sept, *J* = 7.0 Hz, H_2) ppm. **Minor isomer (*Z*): ^{1}H-NMR*(400 MHz, $CDCl_3$):** δ = 7.32 (2H, d, *J* = 7 Hz, Ph), 7.12 (1H, d, *J* = 15.6 Hz, H_B), 7.02 (2H, d, *J* = 8.3 Hz, Ph), 6.78 (1H, d, *J* = 15.6 Hz, H_A), 3.40 (2H, t, *J* = 7 Hz, H_1), 1.45 (2H, quintet, *J* = 7.3 Hz, H_3) ppm. * **Peaks overlapping:** 7.14-7.31 (5H, m, Ph), 1.24-1.35 (2H, sept, *J* = 7.0 Hz, H_2), 0.83 (3H, t, *J* = 7.5 Hz, H_4) ppm. **Major isomer (*E*): ^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 155.35 (s, C=N or O-C(Ar)), 153.35 (s, C=N or O-C(Ar)), 138.75 (d, C_B), 135.37 (s, C-ph), 129.90 (d, 2xC-Ph), 128.72 (d,2xC- Ph), 129.17 (d, C-Ph), 127.41 (d, 2xC-Ph), 116.25 (d, 2xC-Ph), 121.72 (d, C-Ph), 122.65 (d, C_A), 47.99 (t, C_1), 32.85 (t, C_2), 20.56 (t, C_3), 13.92 (q, C_4) ppm.

Minor isomer (*Z*): ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 157.59 (s, C=N or O-C(Ar)), 153.81 (s, C=N or O-C(Ar)), 138.64 (d, C_B), 135.72 (s, C-Ph), 129.14 (d, 2xC-Ph), 128.87 (d, 2xC-Ph), 129.47 (d, C-Ph), 122.65 (d, 2xC-Ph), 121.88 (d, 2xC-Ph), 112.42 (d, C-Ph), 124.12 (d, C_A), 48.28 (t, C_1), 33.54 (t, C_2), 20.96 (t, C_3), 14.02 (q, C_4) ppm. **IR (cm^{-1}, neat):** 2928 (w), 2859 (w), 1644 (m), 1587 (w), 1490 (m), 1448 (w), 1240 (m), 1203 (s), 1189 (s), 1164 (s), 1075 (w), 1024 (w), 968 (m), 906 (m), 803 (w), 749 (s). **LR-MS (CI-MS):** 280 (MH^+). **HR-MS (ES, MH^+):** $C_{19}H_{22}N_1O$, Calculated: 280.1696, found: 280.1699. **UV/Vis (λ_{max}, nm):** 209 (ε = 15,500), 216 (ε = 14,800), 221 (ε = 14,200), 284 (ε = 15,900).

Synthesis of (*E*)-N-tert-butyl-3-phenyl-acrylimidic acid phenyl ester 43

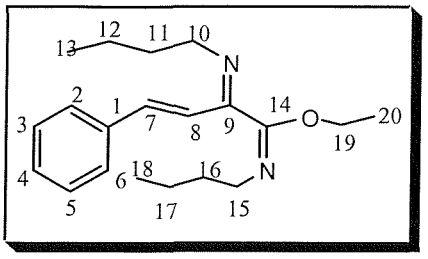


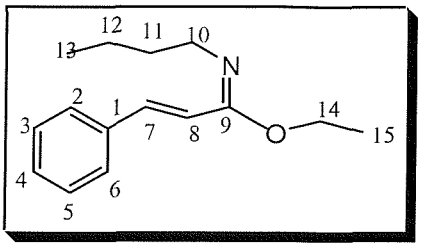
The title compound was synthesised from NaO^{t}Bu (0.14 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), *trans*-bromostyrene (0.16 mL, 1.2 mmol), sodium phenoxide (6 mL of a 1 M soln. in THF), and ^{t}BuNC (0.14 mL, 1.8 mmol) in dry toluene (20 mL). The reaction mixture was refluxed at 115 °C for 30 min. Work-up similar to compound **46**, followed by kugelrhor distillation (oven temp 180-185 °C / 0.33 mm Hg) gave the title compound as a light yellow oil (0.201 g, 60%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.27-7.35 (4H, m, Ph), 7.11 (1H, d, J = 16.3 Hz, H_B), 7.08 (1H, t, J = 7.4 Hz, Ph), 6.99 (2H, d, J = 7.7 Hz, Ph), 6.42 (1H, d, J = 16.3 Hz, H_A), 1.41 (9H, s, 3xCH_3) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 155.13 (s, C=N), 150.91 (s, C-Ph), 138.66 (d, C_B), 135.51 (s, C-Ph), 129.72 (d, 2xC-Ph), 128.93 (d, C-Ph), 127.29 (d, 2xC-Ph), 122.91 (d, C-Ph), 122.10 (d, C_A), 117.85 (d, 2xC-Ph), 54.82 (s, $C(CH_3)_3$), 30.34

(q, 3x$\underline{C}H_3$) ppm. **LR-MS (CI):** 280 (MH^+). **HR-MS (ES, MH^+):** $C_{19}H_{22}NO$, Calculated: 280.1696, found: 280.1699. **UV/Vis (λ_{max}, nm):** 216 (ε = 1200), 28 (ε = 2400).

4.14. Synthesis of (*E*)-N-butyl-2-[(*E*)-butylimino]-4-phenyl-but-3-enimidic acid ethyl ester 44+(*E*)- N-butyl-3-phenyl-acrylimidic acid ethyl ester 45





Bis-inserted (44) **Mono-inserted (45)**

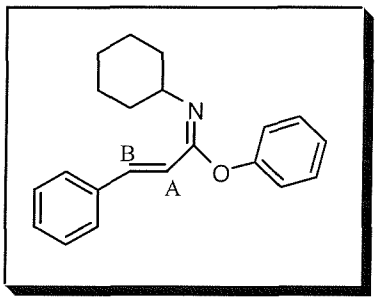
To NaO^tBu (0.14 g, 1.5 mmol), dppf (0.06g, 0.12 mmol), $PdCl_2$ (0.01g, 0.06 mmol), *trans*-bromostyrene (0.16 mL, 1.2 mmol) and sodium ethoxide (6 mL of a 1M soln. in ethanol) were added against a flow of argon. Then toluene (10 ml) was added followed by and ^{n}BuNC (0.14 mL, 1.8 mmol). Another aliquot of toluene (10 mL) was added and the reaction mixture was refluxed at 125 °C for 1h 10min. GC indicated the disappearance of the starting bromide. The reaction mixture was cooled to room temperature and ether (30 mL) was added, to which water was added and filtered to give a brown oil (0.299 g, 63.6%), which is a mixture of bis (73%)-and mono (27%)- inserted isocyanide.

Major Product (Bis- inserted):

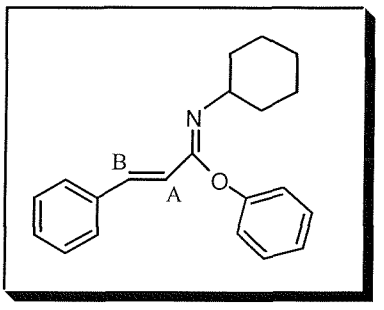
^{1}H-NMR* ($CDCl_3$, 300 MHz): δ = 4.27 (2H, q, J = 7Hz, H_{19}), 3.35 (2H, t, J = 7 Hz, H_{15}), 3.09 (2H, dt, J_1 = 3.5 Hz, J_2 = 4 Hz, H_{10}), 1.38 (4H, qt, J_1&J_2 = 7 Hz, H_{12}, H_{17}), 0.95 (6H, t, J = 7.4 Hz, H_{13}, H_{18}), 0.88 (3H, t, J = 7.3 Hz, H_{20}) ppm. **Minor Product (Mono- inserted): ^{1}H-NMR* (300 MHz, $CDCl_3$):** δ = 3.45 (2H, t, J =7.3 Hz, H_{10}), 4.15 (2H, q, J = 7.0 Hz, H_{14}) ppm. ***Peaks overlapping:** 7.46-7.51 (3H, m, Ph), 7.31-7.39 (2H, m, Ph), 6.87 (1H, d, J = 16.6 Hz, C_7), 6.76 (1H, d, J = 16.6 Hz, C_8) of both bis- and mono-inserted. **Major product: ^{13}C-NMR ($CDCl_3$, 75 MHz):** δ = 162.89 (s, $\underline{C}_{14}$), 155.71 (s, $\underline{C}_9$), 138.88 (d, $\underline{C}_7$), 135.67 (s, $\underline{C}_1$), 129.16 (d, $\underline{C}_8$), 128.79 (d, $\underline{C}_2$, $\underline{C}_6$), 127.42

(d, $\underline{C}_4$), 127.34 (d, $\underline{C}_3$, $\underline{C}_5$), 61.02 (t, $\underline{C}_{19}$), 54.78 (t, $\underline{C}_{15}$, $\underline{C}_{10}$), 49.21 (t, $\underline{C}_{11}$, $\underline{C}_{16}$), 32.87 (t, $\underline{C}_{12}$), 33.65 (t, $\underline{C}_{17}$), 20.55 (q, $\underline{C}_{13}$, $\underline{C}_{16}$), 13.94 (q, $\underline{C}_{20}$) ppm. **Minor Product: ^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 157.47 (s, $\underline{C}_9$), 137.39 (d, $\underline{C}_7$), 136.05 (s, $\underline{C}_1$), 129.04 (d, $\underline{C}_8$), 128.73 (d, $\underline{C}_2$, $\underline{C}_6$), 113.37 (d, $\underline{C}_4$), 127.36 (d, $\underline{C}_3$, $\underline{C}_5$), 67.91 (t, $\underline{C}_{14}$), 60.37 (t, $\underline{C}_{10}$), 48.03 (t, $\underline{C}_{11}$), 34.11 (t, $\underline{C}_{12}$), 20.71 (q, $\underline{C}_{13}$), 14.41 (q, $\underline{C}_{15}$) ppm. **IR (cm^{-1}, neat):** 3063 (w), 3026 (w), 2956 (m), 2929 (m), 2870 (w), 1670 (s), 1605 (m), 1448 (m), 1363 (w), 1283 (m), 1260 (w), 1183 (s), 1027 (m), 967 (m), 754 (s). **LR-MS (CI):** 232 (MH^+), 315 (MH+). **HR-MS (ES, MH^+):** $C_{20}H_{31}N_2O$, Calculated: 315.2431, found: 315.2432. **UV/Vis (λ_{max}, nm):** 206 (ε = 23,500), 220 (ε = 20,900), 225 (ε = 20,900), 284 (ε = 31,500).

Synthesis of (*E*)-N-cyclohexyl-3-phenyl-acrylimidic acid phenyl ester 47



***E*-isomer**



***Z*-isomer**

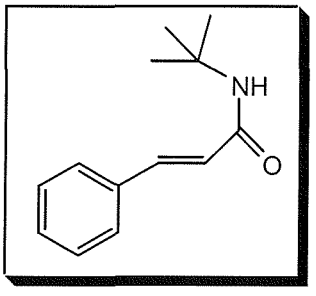
The desired compound was synthesised from NaO^tBu (0.14 g, 1.5 mmol), dppf (0.06 g, 0.12 mmol), $PdCl_2$ (0.01 g, 0.06 mmol), trans-bromostyrene (0.16 mL, 1.2 mmol). Sodium phenoxide (6 mL of a 1 M soln. in THF), and CyNC (0.2 mL, 1.8 mmol) in dry toluene (20 mL). The reaction mixture was refluxed at 115 °C for 1h. Work-up similar to compound **46,** followed by kugelrohr distillation (oven temp 200-206 °C / 0.2 mm Hg) gave the title compound as a yellow oil (0.201 g, 54.9%), which is a mixture of *E* (65%)- and *Z* (35%)- isomers.

Major isomer (*E*):

^{1}H-NMR* (400 MHz, $CDCl_3$): δ = 7.43 (2H, d, *J* = 7.1 Hz, Ph), 7.28 (1H, t, *J* = 7 Hz, Ph), 7.02 (1H, d, *J* = 16.1 Hz, H_B), 6.94 (1H, t, *J* = 7.3 Hz, Ph), 6.88 (2H, d, *J* = 7.8 Hz,

Ph), 6.48 (1H, d, J = 16.1 Hz, H_A), 3.61 (1H, tt, J_1= 10.4 Hz, J_2 = 5.1 Hz, NCH(Cy)) ppm. **Minor isomer (*Z*): ^{1}H-NMR* (400 MHz, $CDCl_3$):** δ = 7.45 (1H, d, J = 16.1 Hz, H_B), 7.25 (2H, d, J = 7.1 Hz, Ph), 6.96 (1H, t, J = 7.3 Hz, Ph), 6.98 (2H, d, J = 7.8 Hz, Ph), 6.75 (1H, d, J = 16.1 Hz, H_A), 3.48 (1H, tt, J_1 = 10 Hz, J_2 = 5 Hz, NCH(Cy)) ppm. ***Peaks overlapping:** 1.52-1.66 (4H, m, Cy), 1.11-1.39 (6H, m, Cy), 7.14-7.26 (m, Ph) of *Z* & *E*- isomers overlapping each other. **Major isomer (*E*): ^{13}C-NMR (100 MHz, $CDCl_3$):** δ = 154.78 (s, C=N), 150.93 (s, O-C(Ar)), 137.80 (d, C_B), 134.41 (s, C-Ph), 128.80 (d, 2xC-Ph), 128.02 (d, 2xC-Ph), 127.62 (d, 2xC-Ph), 126.30 (d, 2xC-Ph), 121.63 (d, C-Ph), 120.79 (d, C-Ph), 115.43 (d, C_A), 55.09 (d, NCH), 32.68 (t, 2xCH_2), 23.71 (t, 3xCH_2) ppm. **Minor isomer (*Z*): ^{13}C-NMR (100 MHz, $CDCl_3$):** δ = 154.42 (s, C=N or O-C(Ar)), 153.27 (s, C=N or O-C(Ar)), 137.49 (d, C_B), 134.81 (s, C-Ph), 128.31 (d, 2xC-Ph), 127.86 (d, 2xC-Ph), 127.78 (d, 2xC-Ph), 126.57 (d, 2xC-Ph), 122.49 (d, 2xC-Ph), 120.26 (d, C-Ph), 111.84 (d, C_A), 55.62 (d, NCH), 33.37 (t, 2xCH_2), 24.66 (t, 2xCH_2), 23.52 (t, CH_2) ppm. **IR (cm^{-1}, neat):** 2928 (s), 2854 (m), 1643 (s), 1589 9m), 1488 (m), 1447 (m), 1192 (s), 1159 (m), 1072 (m), 1022 (w), 970 (s), 911 (m), 800 (m). **LR-MS (CI-MS):** 306 (MH^+). **HR-MS (ES, MH^+):** $C_{21}H_{24}NO$, Calculated: 306.1853, found: 306.1856. **UV/Vis (λ_{max}, nm):** 217 (ε = 7,300), 284 (ε = 8,100).

Synthesis of (*E*)-N-tert-butyl-3-phenyl-acrylamide 48

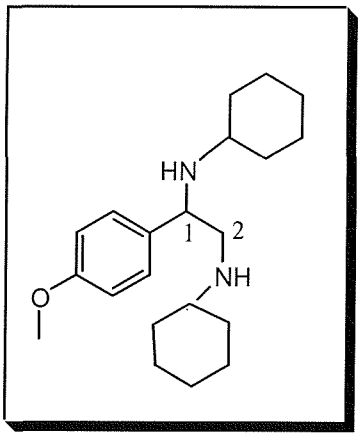


To NaO^{t}Bu (0.14 g, 1.5 mmol), dppf (0.06g, 0.12 mmol), $PdCl_2$ (0.01g, 0.06 mmol), *trans*-bromostyrene (0.16 mL, 1.2 mmol), sodium ethoxide (6 mL of a 1M soln. in ethanol), and ^{t}BuNC (0.14 mL, 1.8 mmol) in dry toluene (20 mL). The reaction mixture

was refluxed at 115 °C for 1h 40 min. Work-up similar to compound **46** resulted to a brown coloured oil. Purification on silica with petrol : ether in (4.5 : 0.5) ratio resulted to title compound as a yellow oil (0.06 g, 25%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.46-7.49 (2H, m, Ph), 7.33-7.41(3H, m, Ph), 7.57 (1H, d, J = 15.5 Hz, H_B), 6.35 (1H, d, J = 15.5 Hz, H_A), 5.59 (1H, s, NH), 1.44 (9H, s, 3xCH_3) ppm. **^{13} C-NMR (75 MHz, $CDCl_3$):** δ = 165.19 (s, C=O), 140.22 (d, C_B), 134.97 (s, C-Ph), 129.44 (d, C-Ph), 128.75 (d, 2xC-Ph), 127.70 (d, 2xC-Ph), 121.96 (d, C_A), 51.50 (s, $C(CH_3)_3$), 28.87 (q, 3xCH_3) ppm. **IR (cm^{-1}, neat):** 3270 (w), 3082 (w), 2963 (m), 2925 (w), 1735 (w), 1655 (m), 1617 (s), 1548 (s), 1448 (m), 1346 (s), 1224 (s), 1093 (m), 1027 (m), 985 (s), 868 (w), 798 (m), 766 (m), 733 (m). **LR-MS (CI):** 204 (MH^+). **HR-MS (ES, MH^+)**: $C_{13}H_{18}NO$, Calculated: 204.1383, found: 204.1384. **UV/Vis (λ_{max}, nm):** 206 (ε = 33,900), 217 (ε = 37,800), 223 (ε = 31,900), 272 (ε = 40,100).

Synthesis of N^1, N^2-dicyclohexyl-1-(4-methoxy-phenyl)-ethane-1,2-diamine 29



To the (*Z*, *E*)-*N*-cyclohexyl-2-cyclohexylimino-2-(4-methoxyphenyl)-acetimidic acid ethyl ester (0.50 g, 1.5 mmol) synthesised through Dr. Saluste procedure, [7] THF (3 mL) was added to a 50 mL Schlenk tube against a flow of argon, followed by Dibal-H (8 mL, 1.5 M in toluene) was added. Another aliquot of THF (5 mL) was added under

argon. The reaction mixture was refluxed at 90 °C for 16h. GC indicated loss of starting material. After cooling to room temperature ether (10 mL) was added followed by water (20 mL). Ether layer was collected and aqueous layer was treated with ether (5x10 mL). The combined ether layers were dried over $MgSO_4$ before evaporation. Purification on silica with petrol : ether (4 : 1 + 3% NEt_3) gave the title compound as a brown colour oil (0.15 g, 49.5%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.24 (2H, d, J = 8.8 Hz, Ph), 6.87 (2H, d, J = 8.5 Hz, Ph), 3.96 (1H, dd, J = 4.7 Hz, 10.9 Hz, H_1), 3.79 (3H, s, OCH_3), 2.93 (1H, dd, J = 4.7 Hz, 10.9 Hz, H_2), 2.82 (1H, dd, J = 4.7 Hz, 10.9 Hz, H_2), 2.56 (1H, brm, NCH(Cy)), 2.35 (1H, brm, NCH(Cy)), 1.53-1.98 (10H, m, 10xCH_2), 1.10-1.42 (10H, m, 10xCH_2) ppm. **^{13}C-NMR (75 MHz, $CDCl_3$):** δ = 159.10 (s, O-C(Ar)), 132.62 (s, C-Ph), 128.19 (d, 2xC-Ph), 114.14 (d, 2xC-Ph), 58.87 (t, NCH_2), 57.50 (d, NCH), 56.81 (d, NCH(Cy)), 55.26 (d, NCH(Cy)), 51.89 (q, OCH_3), 34.03 (t, CH_2), 32.27 (t, CH_2), 32.03 (t, CH_2), 31.93 (t, CH_2), 25.85 (t, CH_2), 25.62 (t, CH_2), 24.98 (t, CH_2), 24.83 (t, 2xCH_2), 24.61 (t, CH_2) ppm. **IR (cm^{-1}, neat):** 2926 (s), 2852 (m), 2359 (w), 1661 (w), 1609 (m), 1510 (s), 1449 (s), 1301 (w), 1245 (s), 1176 (m), 1118 (w), 1033 (m), 831 (s), 729 (s). **LR-MS (CI):** 331 (MH^+). **HR-MS (ES, MH^+):** $C_{21}H_{35}N_2O$, Calculated: 331.2744, found: 331.2741

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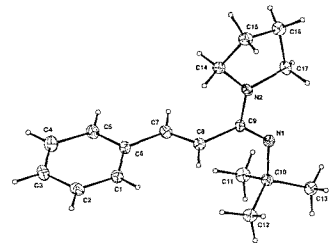
Table 1. Crystal data and structure refinement.



Identification code	**03sot085**
Empirical formula	$C_{17}H_{24}N_2$
Formula weight	256.38
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 8.8769(6) Å
	b = 10.7973(4) Å
	c = 15.7746(13) Å
Volume	1511.94(17) Å^3
Z	4
Density (calculated)	1.126 Mg / m^3
Absorption coefficient	0.066 mm^{-1}
$F(000)$	560
Crystal	Colourless Plate
Crystal size	0.32 x 0.14 x 0.04 mm^3
θ range for data collection	2.97 – 25.03°
Index ranges	$-10 \le h \le 10$, $-12 \le k \le 12$, $-18 \le l \le 18$
Reflections collected	10399
Independent reflections	2669 [R_{int} = 0.0738]
Completeness to θ = 25.03°	99.7 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2669 / 0 / 176
Goodness-of-fit on F^2	0.935
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0430, $wR2$ = 0.0882
R indices (all data)	$R1$ = 0.0802, $wR2$ = 0.1025
Absolute structure parameter	not reliably determined
Extinction coefficient	0.020(3)
Largest diff. peak and hole	0.156 and –0.160 e Å^{-3}

Diffractometer: *Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *asymmetric unit* sphere). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: *SORTAV* (R. H. Blessing, Acta Cryst. A**51** (1995) 33–37; R. H. Blessing, J. Appl. Cryst. **30** (1997) 421–426). **Structure solution**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). **Structure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Cameron - A Molecular Graphics Package. (D. M. Watkin, L. Pearce and C. K. Prout, Chemical Crystallography Laboratory, University of Oxford, 1993).

Special details: All hydrogen atoms were placed in idealised positions and refined using a riding model.

Table 2. Atomic coordinates [$\times 10^4$], equivalent isotropic displacement parameters [$Å^2 \times 10^3$] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
C1	1082(3)	7391(2)	1365(1)	28(1)	1
C2	1105(3)	8648(2)	1201(2)	30(1)	1
C3	1946(3)	9112(2)	538(2)	32(1)	1
C4	2791(3)	8317(2)	48(2)	35(1)	1
C5	2768(3)	7062(2)	214(2)	30(1)	1
C6	1908(3)	6576(2)	869(2)	25(1)	1
C7	1930(3)	5227(2)	1018(2)	29(1)	1
C8	1158(3)	4607(2)	1593(1)	27(1)	1
C9	1298(3)	3241(2)	1737(1)	24(1)	1
C10	−1053(2)	2580(2)	1052(1)	25(1)	1
C11	−732(3)	2775(2)	117(2)	35(1)	1
C12	−2039(3)	3633(2)	1385(2)	32(1)	1
C13	−1917(3)	1371(2)	1172(2)	37(1)	1
C14	3752(3)	3724(2)	2461(2)	29(1)	1
C15	4541(3)	2964(2)	3131(2)	35(1)	1
C16	4408(3)	1654(2)	2802(2)	39(1)	1
C17	2857(3)	1607(2)	2388(2)	34(1)	1
N1	366(2)	2376(2)	1526(1)	25(1)	1
N2	2560(2)	2903(2)	2170(1)	31(1)	1

Table 3. Bond lengths [Å] and angles [°].

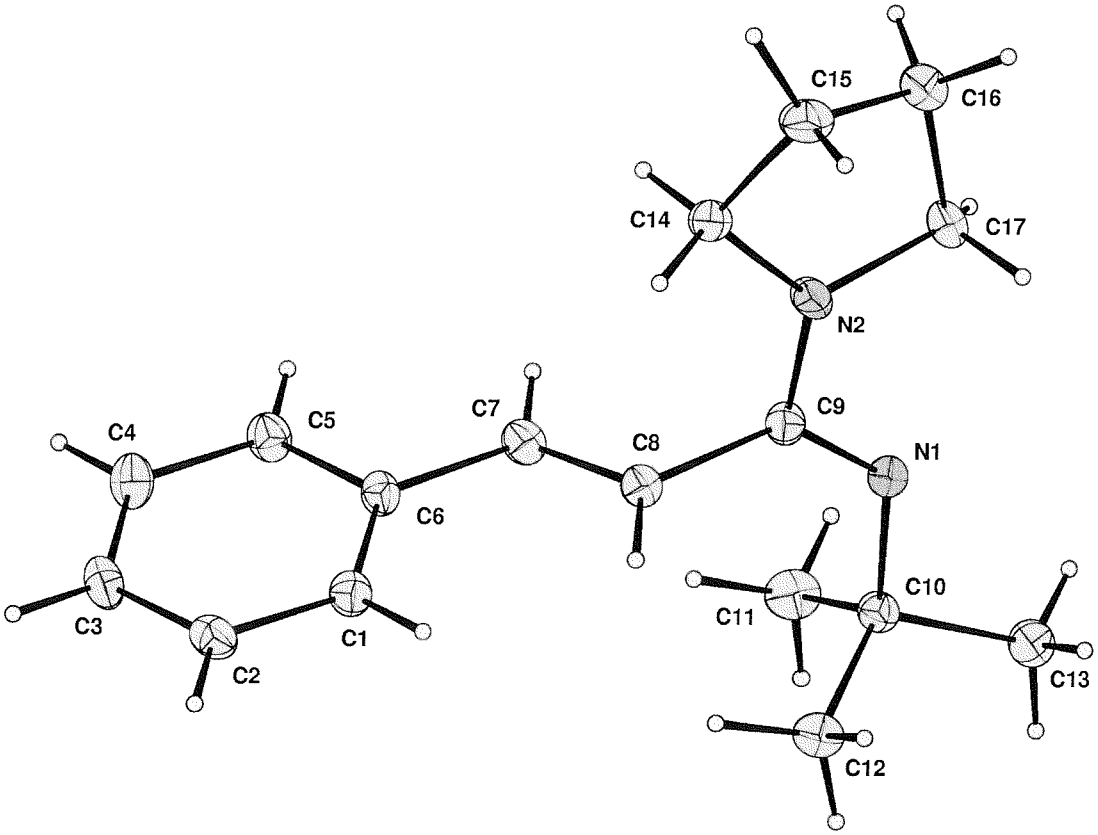
C1–C2	1.382(3)	C9–N2	1.363(3)
C1–C6	1.387(3)	C10–N1	1.481(3)
C2–C3	1.378(3)	C10–C11	1.518(3)
C3–C4	1.378(3)	C10–C13	1.526(3)
C4–C5	1.381(3)	C10–C12	1.527(3)
C5–C6	1.387(3)	C14–N2	1.455(3)
C6–C7	1.476(3)	C14–C15	1.510(3)
C7–C8	1.320(3)	C15–C16	1.511(3)
C8–C9	1.497(3)	C16–C17	1.524(3)
C9–N1	1.291(3)	C17–N2	1.464(2)
C2–C1–C6	120.6(2)	N1–C10–C13	103.78(17)
C3–C2–C1	120.4(2)	C11–C10–C13	109.45(19)
C4–C3–C2	119.7(2)	N1–C10–C12	115.13(18)
C3–C4–C5	119.7(2)	C11–C10–C12	109.76(19)
C4–C5–C6	121.4(2)	C13–C10–C12	107.86(19)
C1–C6–C5	118.10(19)	N2–C14–C15	103.06(17)
C1–C6–C7	122.8(2)	C14–C15–C16	103.4(2)
C5–C6–C7	119.0(2)	C15–C16–C17	104.43(19)
C8–C7–C6	127.2(2)	N2–C17–C16	103.37(17)
C7–C8–C9	124.1(2)	C9–N1–C10	124.61(18)
N1–C9–N2	117.55(18)	C9–N2–C14	126.33(17)
N1–C9–C8	128.3(2)	C9–N2–C17	121.48(17)
N2–C9–C8	114.10(19)	C14–N2–C17	112.19(18)
N1–C10–C11	110.55(18)		

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$]. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + \cdots + 2\,h\,k\,a^*\,b^*\,U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	29(1)	27(1)	27(1)	2(1)	−4(1)	−2(1)
C2	31(1)	25(1)	34(2)	−3(1)	−4(1)	5(1)
C3	41(2)	22(1)	34(2)	6(1)	−7(1)	−2(1)
C4	42(2)	33(1)	30(2)	7(1)	3(1)	−4(1)
C5	36(2)	26(1)	28(1)	0(1)	3(1)	2(1)
C6	28(1)	22(1)	24(1)	1(1)	−4(1)	−2(1)
C7	31(1)	24(1)	31(1)	−1(1)	0(1)	3(1)
C8	26(1)	23(1)	31(1)	1(1)	0(1)	1(1)
C9	26(1)	20(1)	27(1)	3(1)	4(1)	−1(1)
C10	24(1)	23(1)	27(1)	1(1)	−3(1)	0(1)
C11	35(2)	39(1)	31(2)	−1(1)	−1(1)	0(1)
C12	30(2)	34(1)	32(2)	0(1)	−2(1)	3(1)
C13	31(2)	30(1)	50(2)	4(1)	−9(1)	−3(1)
C14	24(1)	23(1)	41(2)	−2(1)	−3(1)	0(1)
C15	27(2)	37(1)	42(2)	0(1)	−5(1)	1(1)
C16	34(2)	31(1)	52(2)	7(1)	−5(1)	3(1)
C17	35(1)	20(1)	49(2)	4(1)	0(1)	3(1)
N1	24(1)	23(1)	30(1)	2(1)	0(1)	−1(1)
N2	26(1)	19(1)	48(1)	3(1)	−10(1)	0(1)

Table 5. Hydrogen coordinates [$\times 10^4$] and isotropic displacement parameters [$Å^2 \times 10^3$].

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
H1	506	7088	1812	33	1
H2	551	9185	1540	36	1
H3	1941	9956	422	39	1
H4	3376	8625	−394	42	1
H5	3341	6531	−120	36	1
H7	2556	4763	669	34	1
H8	485	5046	1931	32	1
H11A	−235	3556	38	53	1
H11B	−1663	2772	−194	53	1
H11C	−96	2120	−87	53	1
H12A	−2132	3564	1989	48	1
H12B	−3019	3582	1130	48	1
H12C	−1585	4413	1244	48	1
H13A	−1340	698	942	55	1
H13B	−2867	1422	882	55	1
H13C	−2088	1232	1765	55	1
H14A	3340	4480	2699	35	1
H14B	4433	3935	2002	35	1
H15A	4049	3051	3677	42	1
H15B	5588	3207	3186	42	1
H16A	4477	1061	3263	47	1
H16B	5193	1478	2392	47	1
H17A	2870	1090	1885	41	1
H17B	2106	1292	2779	41	1


C15
C16
C14
C17
N2
C9
C7
C5
C4
C8
N1
C6
C10
C11
C3
C1
C2
C13
C12

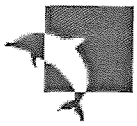
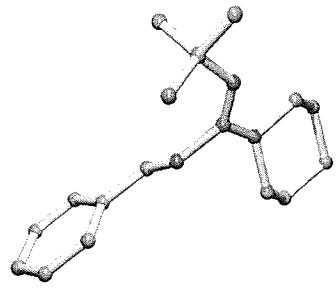


Table 1. Crystal data and structure refinement.



Identification code	**03sot0107**
Empirical formula	$C_{18}H_{26}N_2$
Formula weight	270.41
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 31.1911(10) Å
	b = 11.0411(3) Å β = 92.5650(10)°
	c = 19.1354(5) Å
Volume	6583.3(3) Å^3
Z	16 (4 molecules)
Density (calculated)	1.091 Mg / m^3
Absorption coefficient	0.064 mm^{-1}
$F(000)$	2368
Crystal	Colourless Plate
Crystal size	0.35 × 0.20 × 0.02 mm^3
θ range for data collection	2.92 – 25.03°
Index ranges	$-37 \le h \le 37$, $-9 \le k \le 13$, $-22 \le l \le 22$
Reflections collected	19980
Independent reflections	11597 [R_{int} = 0.1145]
Completeness to θ = 25.03°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9987 and 0.9780
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11597 / 0 / 733
Goodness-of-fit on F^2	0.945
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0789, $wR2$ = 0.1831
R indices (all data)	$R1$ = 0.1914, $wR2$ = 0.2396
Largest diff. peak and hole	0.318 and –0.284 e Å^{-3}

Diffractometer: *Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *asymmetric unit* sphere). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: *SORTAV* (R. H. Blessing, Acta Cryst. A**51** (1995) 33–37; R. H. Blessing, J. Appl. Cryst. **30** (1997) 421–426). **Structure solution**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). **Structure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Cameron - A Molecular Graphics Package. (D. M. Watkin, L. Pearce and C. K. Prout, Chemical Crystallography Laboratory, University of Oxford, 1993).

Special details: All hydrogen atoms were placed in idealised positions and refined using a riding model.

Table 2. Atomic coordinates [× 10^4], equivalent isotropic displacement parameters [$Å^2$ × 10^3] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
N1A	242(1)	3070(2)	3751(2)	29(1)	1
N2A	493(1)	2660(2)	2663(2)	32(1)	1
C1A	1080(1)	7281(3)	3931(2)	38(1)	1
C2A	1166(1)	8507(3)	3915(2)	40(1)	1
C3A	969(1)	9227(3)	3404(2)	44(1)	1
C4A	679(1)	8724(3)	2927(2)	41(1)	1
C5A	586(1)	7501(3)	2946(2)	35(1)	1
C6A	791(1)	6755(3)	3447(2)	29(1)	1
C7A	705(1)	5447(3)	3478(2)	33(1)	1
C8A	445(1)	4808(3)	3058(2)	27(1)	1
C9A	393(1)	3463(3)	3113(2)	27(1)	1
C10A	−129(1)	3703(3)	4032(2)	34(1)	1
C11A	−166(1)	3432(3)	4805(2)	42(1)	1
C12A	−192(1)	2064(3)	4933(2)	38(1)	1
C13A	191(1)	1457(3)	4619(2)	44(1)	1
C14A	221(2)	1756(3)	3852(2)	43(1)	1
C15A	718(1)	2898(3)	2013(2)	35(1)	1
C16A	547(1)	3953(3)	1568(2)	43(1)	1
C17A	1198(1)	3069(4)	2190(2)	56(1)	1
C18A	650(2)	1743(3)	1581(2)	59(1)	1
N1B	2600(1)	1856(2)	1038(2)	31(1)	1
N2B	2104(1)	2367(2)	171(2)	31(1)	1
C1B	1963(1)	−2473(3)	516(2)	34(1)	1
C2B	1852(1)	−3685(3)	564(2)	41(1)	1
C3B	1502(1)	−4033(4)	941(2)	45(1)	1
C4B	1274(1)	−3163(4)	1288(2)	47(1)	1
C5B	1386(1)	−1955(3)	1245(2)	41(1)	1
C6B	1731(1)	−1583(3)	863(2)	31(1)	1
C7B	1844(1)	−285(3)	843(2)	31(1)	1
C8B	2179(1)	199(3)	547(2)	29(1)	1
C9B	2271(1)	1540(3)	560(2)	31(1)	1
C10B	2687(1)	1154(3)	1685(2)	36(1)	1
C11B	2406(1)	1566(3)	2267(2)	39(1)	1
C12B	2449(2)	2924(3)	2392(2)	44(1)	1
C13B	2389(1)	3634(3)	1710(2)	34(1)	1
C14B	2679(1)	3152(3)	1164(2)	32(1)	1
C15B	1799(1)	2158(3)	−432(2)	33(1)	1
C16B	1343(1)	2092(4)	−172(2)	49(1)	1
C17B	1887(1)	1043(3)	−881(2)	37(1)	1
C18B	1843(1)	3282(3)	−888(2)	46(1)	1

N1C	4795(1)	6925(2)	1319(2)	29(1)	1
N2C	4527(1)	7326(2)	2393(2)	32(1)	1
C1C	4432(1)	2472(3)	1922(2)	31(1)	1
C2C	4336(1)	1252(3)	1909(2)	35(1)	1
C3C	4013(1)	812(3)	1453(2)	40(1)	1
C4C	3798(1)	1603(3)	1007(2)	41(1)	1
C5C	3896(1)	2825(3)	1021(2)	33(1)	1
C6C	4213(1)	3283(3)	1475(2)	27(1)	1
C7C	4308(1)	4588(3)	1491(2)	28(1)	1
C8C	4544(1)	5185(3)	1964(2)	31(1)	1
C9C	4619(1)	6527(3)	1942(2)	27(1)	1
C10C	5154(1)	6258(3)	1037(2)	35(1)	1
C11C	5209(1)	6554(3)	269(2)	43(1)	1
C12C	5267(1)	7917(3)	171(2)	41(1)	1
C13C	4899(2)	8591(3)	489(2)	43(1)	1
C14C	4846(2)	8239(3)	1245(2)	40(1)	1
C15C	4278(1)	7119(3)	3024(2)	31(1)	1
C16C	3805(1)	6965(3)	2817(2)	44(1)	1
C17C	4438(1)	6063(3)	3490(2)	40(1)	1
C18C	4348(2)	8280(3)	3449(2)	55(1)	1
N1D	2694(1)	7099(2)	−1233(2)	33(1)	1
N2D	2987(1)	7452(2)	−131(2)	30(1)	1
C1D	3106(1)	2635(3)	−705(2)	35(1)	1
C2D	3199(1)	1415(3)	−773(2)	36(1)	1
C3D	3476(1)	1033(3)	−1265(2)	42(1)	1
C4D	3659(1)	1873(3)	−1697(2)	45(1)	1
C5D	3569(1)	3087(3)	−1634(2)	41(1)	1
C6D	3292(1)	3498(3)	−1131(2)	31(1)	1
C7D	3195(1)	4797(3)	−1082(2)	35(1)	1
C8D	2975(1)	5343(3)	−613(2)	38(1)	1
C9D	2889(1)	6681(3)	−614(2)	33(1)	1
C10D	2327(1)	6424(3)	−1540(2)	38(1)	1
C11D	2251(2)	6732(3)	−2301(2)	52(1)	1
C12D	2187(2)	8097(3)	−2399(2)	55(1)	1
C13D	2562(2)	8768(3)	−2047(2)	45(1)	1
C14D	2636(2)	8415(3)	−1301(2)	45(1)	1
C15D	3260(1)	7216(3)	501(2)	31(1)	1
C16D	3156(1)	6071(3)	912(2)	40(1)	1
C17D	3180(2)	8295(3)	979(2)	50(1)	1
C18D	3727(1)	7209(4)	310(2)	55(1)	1

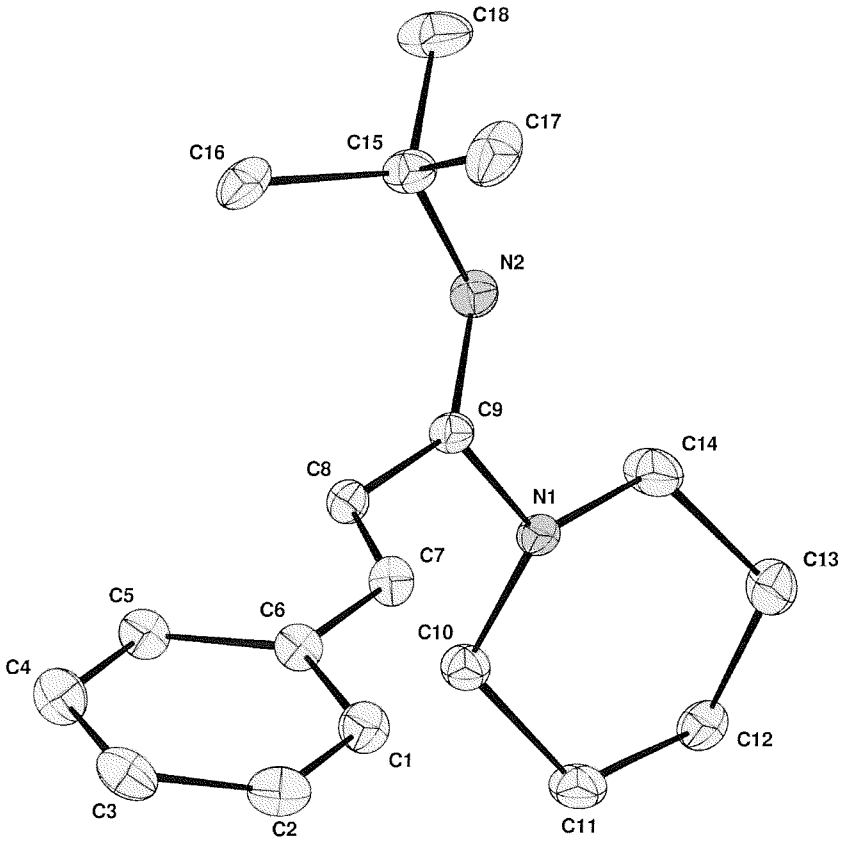


Figure 1. One of the 4 independent molecules in the asymmetric unit.

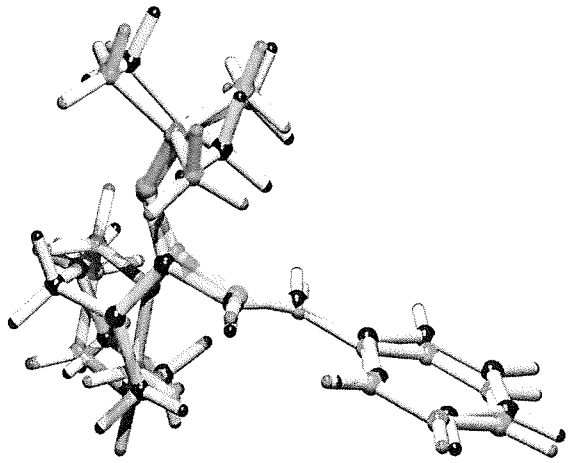


Figure 2. Fit of two of the four molecules in the asymmetric unit.