Regiospecific Synthesis of Alkylphenanthrenes Using a Combined Directed *ortho* Metalation (DoM) - Suzuki-Miyaura Cross Coupling - Directed Remote Metalation (DreM) Methodology

By

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Abstract

A literature survey on the syntheses of phenanthrenes is reviewed. These syntheses have limitations, e.g. lack of regioselectivity and difficulty in preparation in multi-gram scale. Suzuki-Miyaura cross coupling reactions are discussed on various topics, i.e. bases, solvents, steric hindrance and tolerance of functional groups respectively. A combined directed *ortho* metalation (D*o*M) - Suzuki-Miyaura cross coupling route is used for regiospecific synthesis of alkylphenanthrenes. The highly pure alkylphenanthrenes, 1-methyl- (**128**), 1, 7-dimethyl- (**135**), 7-ethyl-1-methyl- (**145**) and 7-*t*-butyl-1-methylphenanthrene (**149**) have been synthesized in overall yield 21-36% and 4-7 steps. Carbonylative amination of triflates has been investigated, showing that inexpensive phenols can serve as a starting material for the preparation of N, N-diethylbenzamides, which, in turn, are potential point for the D*o*M chemistry.

Acknowledgements

First, I wold like to acknowledge my supervisor, Dr. Victor Snieckus, who gives me this chance to study the excited synthetic organic chemistry. During these two years of M.Sc. study, he has given me a lot of guidance, encouragement and care in my research and life.

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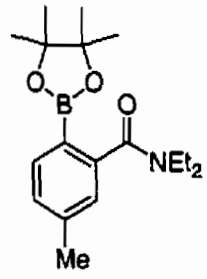
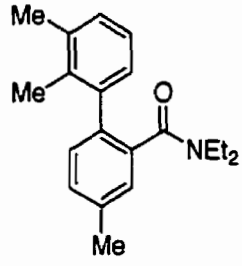
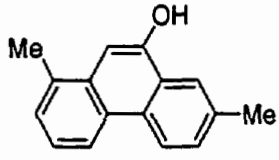
Abbreviations

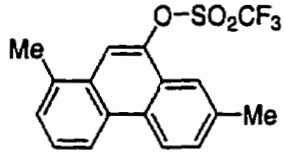
bda	bis(dibenzylideneacetone)
BOC	butoxycarbonyl
Bu	butyl
DME	dimethoxyethane
DMF	dimethyformide
DMSO	dimethylsulfoxide
dppe	diphenylphosphinoethane
dppf	diphenylphosphinoferrocene
dppp	diphenylphosphinopropane
LDA	lithium diisopropylamide
MOM	methoxymethoxy
PPA	polyphosphoric acid
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
TMSCl	chlorotrimethylsilane

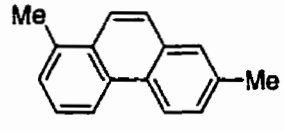
Specific Experimental Procedures

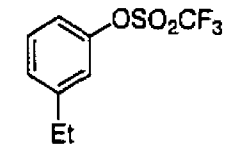


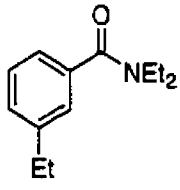


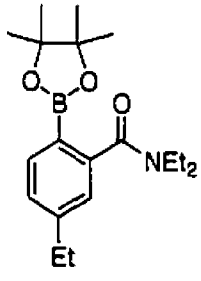


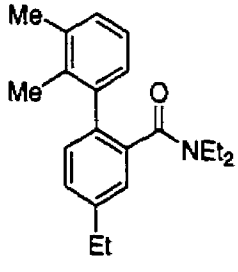


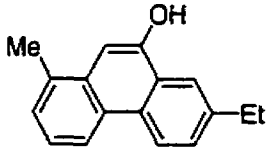










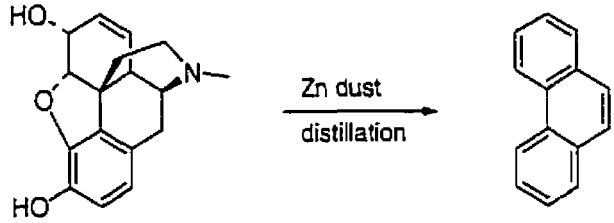


Chapter 1

Literature Survey on the Synthesis of Phenanthrenes

Phenanthrene was discovered concurrently and independently by Ostermayer and Fittig[1] and by Glaser[2] in 1872 as a constituent of coal tar. Subsequently, phenanthrenes became important degradation products obtained during the structural elucidation of morphine.[3] For example, zinc-dust distillation of morphine gives phenanthrene (**Scheme 1**). These early studies led to increased interest in the synthesis of phenanthrenes.

Scheme 1



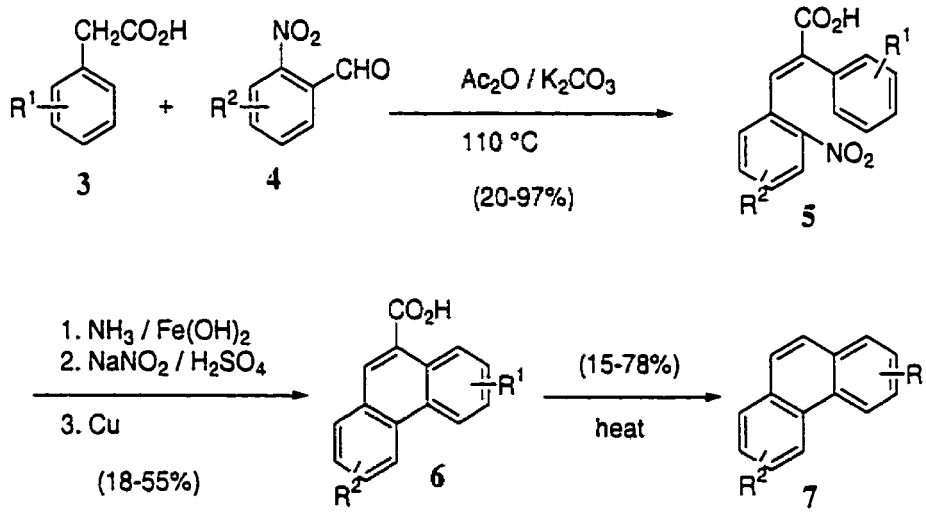
1 **2**

1.1 The Pschorr Synthesis

In 1896, Pschorr developed the first general method for the synthesis of phenanthrene derivatives to assist in the identification of the degradation of morphine alkaloids (**Scheme 2**).[4] The Pschorr synthesis[5, 6] involves reaction of **3** with **4** to give cinnamic acids **5** which upon reduction, diazotization, and cyclization under copper catalysis affords phenanthrene-9-carboxylic acids (**6**). Thermolysis of **6** yields the

phenanthrene derivatives **7**. Clearly, a deficiency in the Pschorr method is the formation of mixtures of isomers **7** using in C-2 or C-3 substituted phenyl acetic acids **3**.

Scheme 2



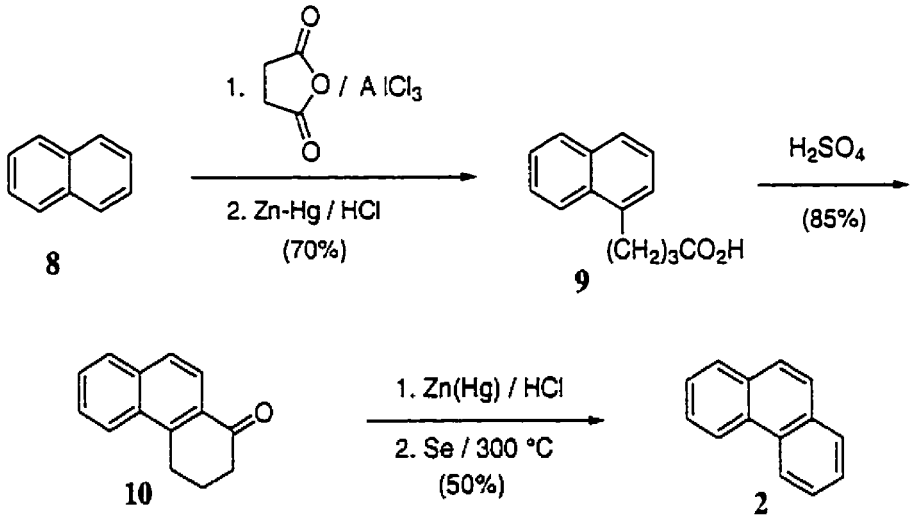
R^1 = Me, Et, NO_2, Cl, Br, OMe, CO_2H
R^2 = Me, OH, OMe, Cl, Br

1.2 The Friedel - Crafts Reaction

The naphthyl propionic acid **9**, obtained by Friedel-Crafts reaction of naphthalene **8** with succinic anhydride followed by Clemmensen reduction, upon a second Fridel-Crafts cyclization followed by aromatization leads to phenanthrene **2** (**Scheme 3**).[7]

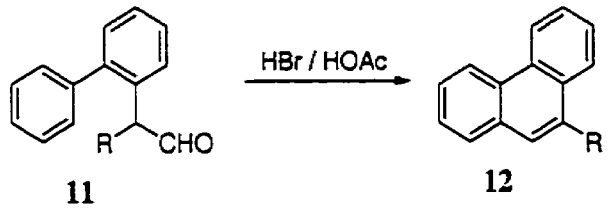
In a related Fridel-Crafts sequence, the aldehydes **11** undergo cyclization under HBr conditions to afford the phenanthrene derivatives **12** (**Scheme 4**).[8] If R is CN, the yield of this reaction is low.

Scheme 3



8 9 10 2

Scheme 4



11 12

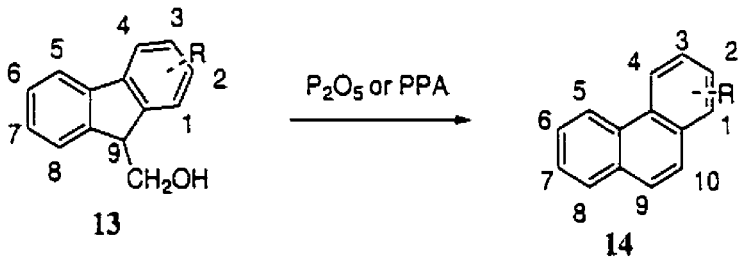
R = H (78%); Me (93%); Et (100%); CN (23%)

1.3 The Wagner - Meerwein Ring Expansion Route

In a widely used method, 9-hydroxymethofluorenes **13** undergo Wagner-Meerwein rearrangement in the presence of acidic reagents (e.g. PPA) to affords phenanthrenes **14** (**Scheme 5**).[9] The migratory aptitude of the benzo and substituted benzo groups of fluorenes in the Wagner-Meerwein rearrangement have been investigated using ^{14}C - labeled material (**Scheme 6**).[10] The electronic effects of the 3-

methyl and 3-methoxy groups in **15**, especially the latter, favor the migration of the substituted benzo group. The 1-methyl group has no effect, possibly because of the steric and electronic effects of the methyl cancelling each other in this position.[10]

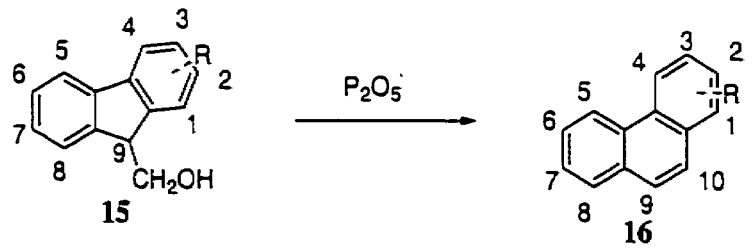
Scheme 5



13 **14**

R	Reagents	yld, %
H	P_2O_5	90
1-Me	P_2O_5	100
3-Me	P_2O_5	88
3-OMe	P_2O_5	93
2-F	PPA	64
4-Br	P_2O_5	47
2-NO_2	PPA	45

Scheme 6



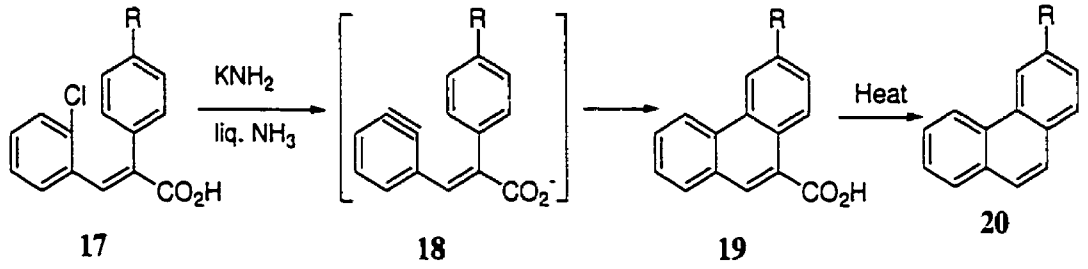
15 **16**

R	% ^{14}C at C-9	% ^{14}C at C-10
1-Me	50	50
3-Me	27	73
3-OMe	2	98

1.4 Intramolecular Benzyne Cyclization

A convenient synthesis of phenanthrenes by intramolecular benzyne cyclization has been developed (**Scheme 7**).[11] The *trans*-α-phenyl-2-chlorocinnamic acids **17**, readily prepared by Perkin condensation of phenylacetic acids with *o*-chlorobenzaldehyde, when treated with an excess of potassium amide in liquid ammonia gives phenanthrene-9-carboxylic acids **19** which, upon decarboxylation, affords phenanthrenes **20**.

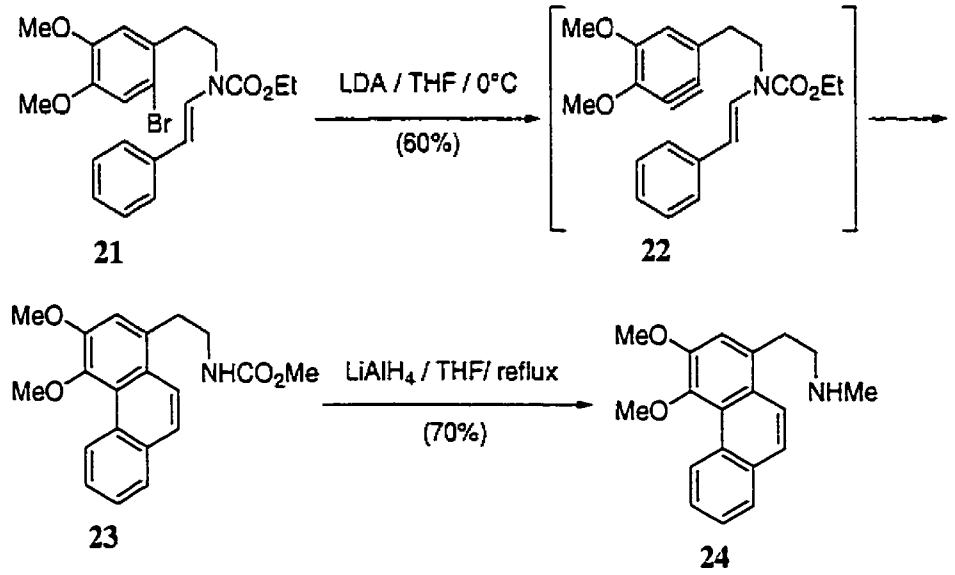
Scheme 7



17 **18** **19** **20**

R = H, (40%); OMe, (55%)

Scheme 8



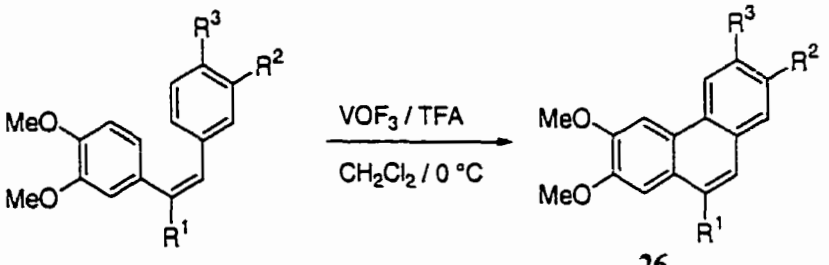
21 **22** **23** **24**

This intramolecular benzyne cycloaddition approach has been applied to the synthesis of phenanthrene alkaloids (**Scheme 8**).[12, 13] Compound **21**, when treated with LDA, affords the phenanthrene **23**, which, by reduction with $LiAlH_4$, is converted into **24**.

1.5 Oxidative Cyclization

Intramolecular oxidative cyclizations are well-known synthetic methods for the formation of aryl-aryl bonds.[13] Application of these reactions to the synthesis of phenanthrenes includes the oxidative coupling of stilbenes **25** using VOF_3 to afford the phenanthrenes **26** in high yield.[14] This method was used to synthesize a limited number of substituted phenanthrenes (**Scheme 9**).

Scheme 9

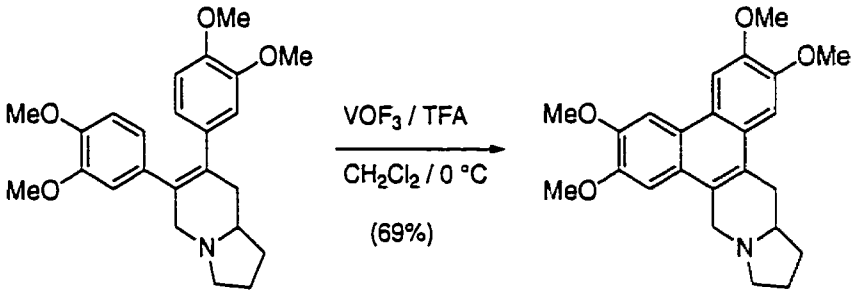


25 **26**

R^1	R^2, R^3	Yields %
CO_2Me	OMe, OMe	75
CO_2Me	$-OCH_2O-$	85
CN	$-OCH_2O-$	91

This reaction has also been used as a key step for the synthesis of the alkaloid (±)- tylophorine isolated from *Ficus septica*, a plant belonging to the Moraceae species (**Scheme 10**).[15]

Scheme 10

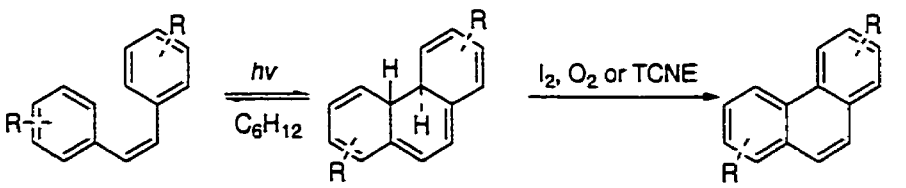


27 **28**

1.6 Photocyclization

On irradiation with ultraviolet light, stilbene **29** undergoes reversible photocyclization to give *trans*-4a, 4b-dihydrophenanthrene **30**, an intermediate that can be trapped oxidatively with hydrogen acceptors such as iodine, oxygen, or tetracyanoethylene to give phenanthrene **31** in high yield (**Scheme 11**). This reaction is one of the most widely used methods to prepare phenanthrenes with a variety of substituents (**Table 1**).[16, 17] However, it has many drawbacks such as a limited success on multigram scale and a lack of selectivity, yielding a mixture of isomers for C-3 substituted stilbenes **29** (entries 2, 3, 4, 7).

Scheme 11



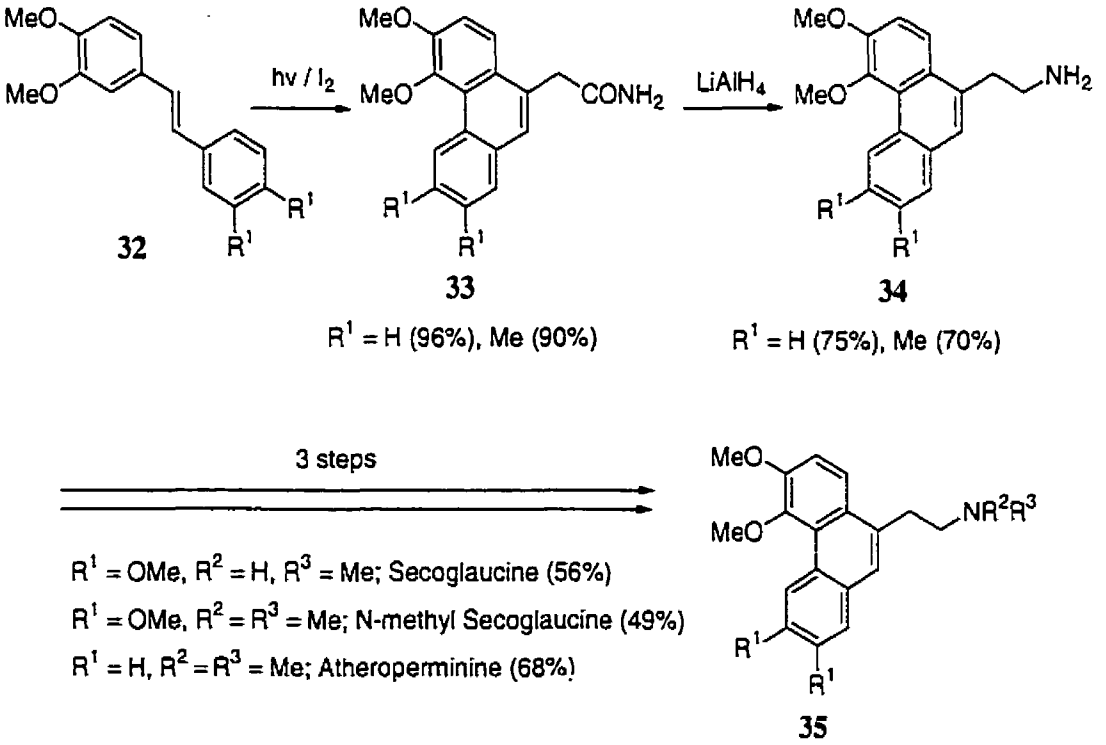
29 **30** **31**

Table 1. Photocyclization of Stilbenes to Phenanthrenes

Entry	Stilbene		Phenanthrene, yld, %
	R^1	R^1	
1	2-Me	H	1-Me (57)
2	3-Me	H	2-Me (31), 4-Me (29)
3	3-OMe	H	2-OMe (58), 4-OMe (15)
4	3-Me	3'-Me	2, 5-Dimethyl (54), 2, 7-Dimethyl (28)
			4, 5-Dimethyl (18)
5	4-OMe	4'-OMe	3, 6-Dimethoxy (79)
6	2-Br	H	1-Br (50%)
7	3-CN	H	2-CN (71), 4-CN (19)

The Mallory photocyclization method has been extensively applied to the synthesis phenanthrene alkaloids **35** (**Scheme 12**). For example, photocyclization of

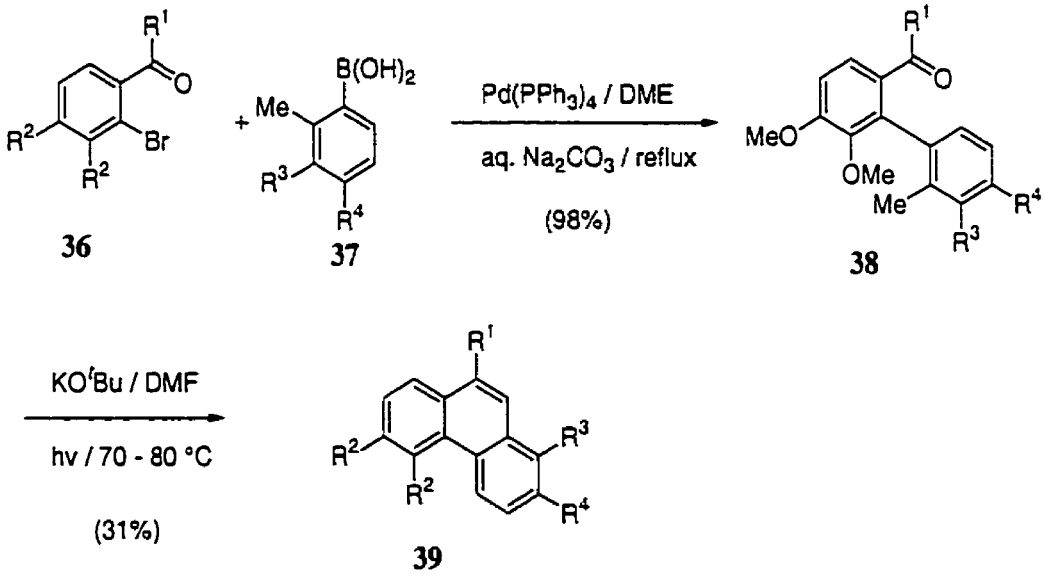
Scheme 12



stilbenes **32** affords amides **33**, which, upon reduction by $LiAlH_4$, yields amines **34**, which are readily transformed into the phenanthrene alkaloids **35**.[18]

A recent method for phenanthrene synthesis involves combined Suzuki-Miyaura cross coupling - photocyclization. Thus cross coupling of 2-bromobenzaldehydes **36** with *o*-tolylboronic acids **37** affords the phenanthrene precursors **38**, which, when heated with KO^{t}Bu in DMF with simultaneous mercury lamp irradiation, are converted into phenanthrenes **39** (**Scheme 13**).[19] It appears that oxygen substituents (entries 2, 3 and 4) on the aromatic rings facilitate phenanthrene formation. By using this methodology,

Scheme 13



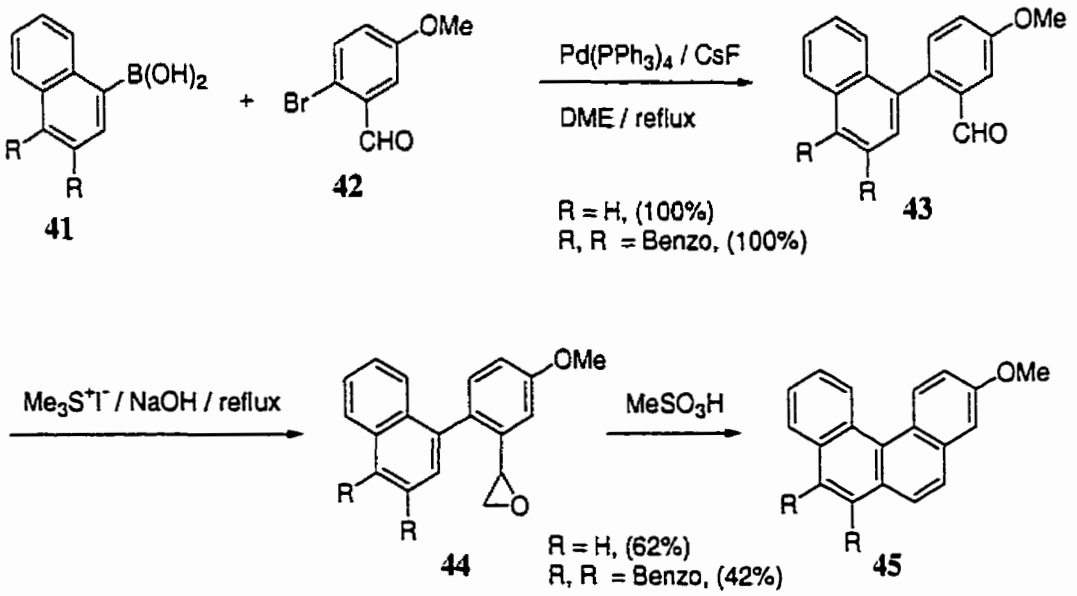
entry	R^1	R^2	R^3	R^4	biaryl, yld, %	phenanthrene, yld, %
1	H	H	H	H	98	31
2	OMe	H	H	H	86	62
3	OMe	Me	Me	H	96	70
4	OMe	H	H	OMe	72	61

phenanthrenes containing oxygen substituents in C-2, C-5 and C-6, as well as alkyl groups in C-1 and C-9 of the phenanthrene nucleus, were synthesized.

1.7 A Combined of Suzuki Cross Coupling - Acid-Catalyzed Cyclodehydration Route

A route which combines the Suzuki reaction with an acid-catalyzed cyclization method has been described (**Scheme 14**).[20] Thus, *ortho*-bromobenzaldehydes **42** are coupled with naphthalene-1-boronic acid **41** to afford the biaryl compounds **43**, which are converted into the epoxides **44** using $Me_3S^+I^-$. Acid-catalyzed cyclodehydration **X** with $MeSO_3H$ in CH_2Cl_2 affords the phenanthrenes **45** (**Scheme 14**).

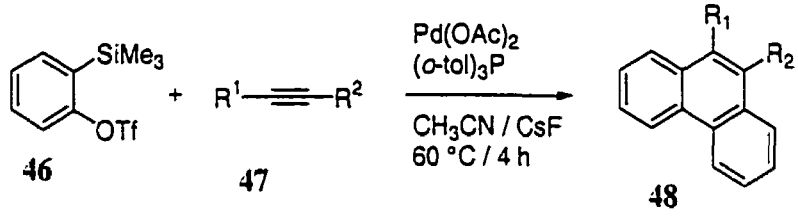
Scheme 14



1.8 Palladium Catalyzed Trimerization

A facile method for the synthesis of phenanthrenes by palladium catalyzed co-trimerization of benzyne with alkynes **47** has been described recently (**Scheme 15**).[21] Benzyne is generated in situ from **46** by the expedience of CsF. This reaction proceeds smoothly with tolerance of a number of functional groups. Obviously, a mixture of phenanthrene isomers would be obtained with substituents in **46**.

Scheme 15

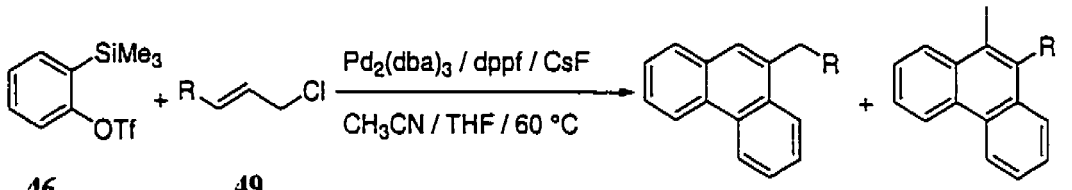


46 **47** **48**

R^1	R^1	yld, %
n-Pr	*n*-Pr	63
n-pentyl	*n*-pentyl	67
CH_2OCH_3	CH_2OCH_3	59
Ph	CH_3	67
Ph	CH_2CH_3	63
Ph	$COCH_3$	76

In another report, the CsF - generated benzyne has been found to be very reactive as a carbopalladation partner of π-allyl palladium chloride. Thus, reaction of allyl chlorides **49** with benzyne precursor **46** under palladium catalysis, gives mixtures of the phenanthrene derivatives **50** and **51** with very poor regioselectivity (**Scheme 16**).[22]

Scheme 16



46 **49** **50** **51**

R	yld, %	50:51
H	69	58:42
Me	66	70:30
Ph	56	

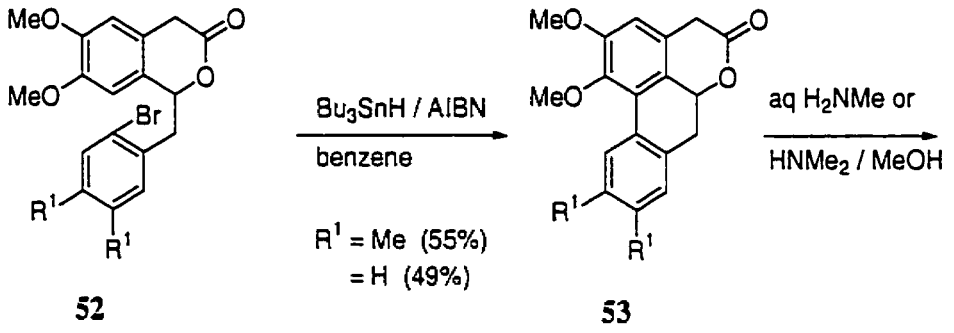
1.9 Radical Cyclization

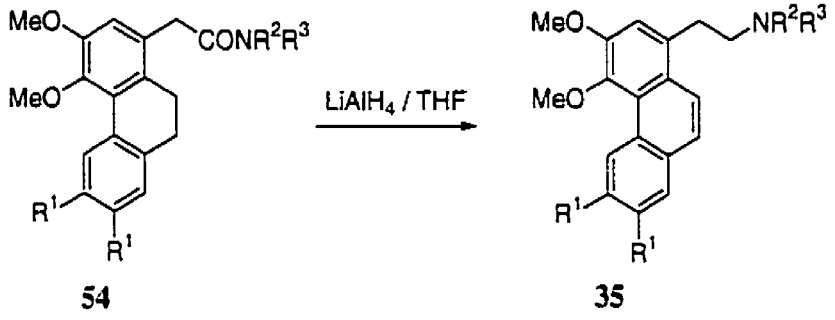
A radical cyclization path involving the conversion of the benzylisochromanones **52** to dibenzo[d, e, g]chromanones **53** which were then converted via **54** into phenanthrene alkaloids **35** has been described (**Scheme 17**).[23]

1.10 A Combined Ullmann - McMurry Coupling Route

Oxygenated phenanthrenes **58** have been prepared by a combined Ullmann - McMurry coupling route (**Scheme 18**).[24] Thus, the key 6, 6'-biphenyl-1, 1'-dicarboxaldehydes **57** are prepared by an ambient temperature Ullmann coupling. The subsequent McMurry condensation of **57** gives rise to the phenanthrenes **58** in medium to good yields (**Scheme 18**).

Scheme 17

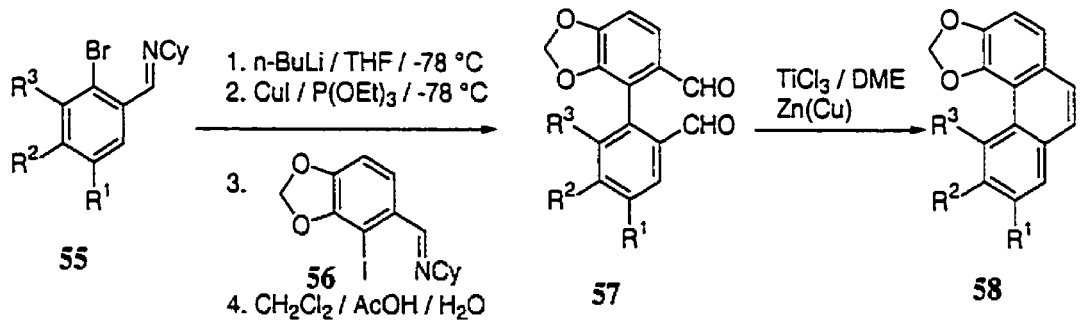




R^1 = OMe, R^2 = H, R^3 = Me (95%)
R^1 = OMe, R^2 = R^3 = Me (54%)
R^1 = H, R^2 = R^3 = Me (81%)

R^1 = OMe, R^2 = H, R^3 = Me; Secoglaucine (70%)
R^1 = OMe, R^2 = R^3 = Me; N-metyl Secoglaucine (69%)
R^1 = H, R^2 = R^3 = Me; Atheroperminine (68%)

Scheme 18



R^1 = H, R^2, R^3 = Benzo; biaryl **57a** (58%); phenanthrene **58a** (45%)
R^1, R^2, R^3 = H; biaryl **57b** (64%); phenanthrene **58b** (57%)
R^1 = OMe, R^2, R^3 = H; biaryl **57c** (70%); phenanthrene **58c** (45%)
R^1 = OMe, R^2 = OBn, R^3 = H; biaryl **57d** (44%); phenanthrene **58d** (failed)

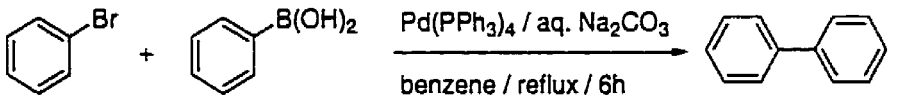
Chapter 2 Methodology

2.1 Suzuki-Miyaura Cross Coupling

During the past three decades, palladium mediated cross coupling reactions of organic electrophiles with an organo-boron (Suzuki-Miyaura)[25], -tin (Stille)[26], -zinc (Negishi)[27], -magnesium (Kumada)[28] and -silicon reagents[29], have proved to be extremely effective synthetic methods for aryl-aryl bond formation.[30]

Among these, the Suzuki-Miyaura cross coupling reaction **59** + **60** → **61** (**Scheme 19**) has received the widest application in both academic and industrial laboratories after its observation by Suzuki and Miyaura in 1981 (**Scheme 19**).[31] Organoboron compounds are nontoxic, stable and inert to water and oxygen, thus making them easy to handle. A drawback of the organoboron compounds is their difficult purification and characterization, although they may be converted into esters by treatment with pinacol or diethanolamine, which can be purified by column chromatography or recrystallization.[32]

Scheme 19

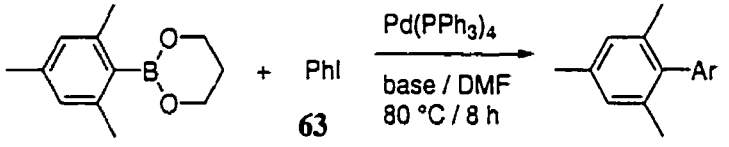


59 **60** (88%) **61**

2.1.1 Bases and Solvents

A number of bases and solvents have been effective for the Suzuki - Miyaura cross coupling reaction. However, the most commonly used base Na_2CO_3 is often ineffective with sterically hindered coupling partners.[33] Specially selected bases and solvents are needed for hindered coupling reactions. For example, when pinacolate of mesitylboronic acid is used, the reaction proceeds slowly because of steric hindrance during the transmetalation to palladium (II) halide. However, the addition of strong bases, e.g., aqueous NaOH or $Ba(OH)_2$ in benzene or DME exerts a remarkable acceleration on the coupling rate. Although weak bases give better results for less hindered arylboronic acids, the order of reactivity for mesitylboronic acids corresponds to the basic strength: $Ba(OH)_2 > NaOH > K_3PO_4 > Na_2CO_3 > NaHCO_3$ (**Scheme 20**).[34]

Scheme 20



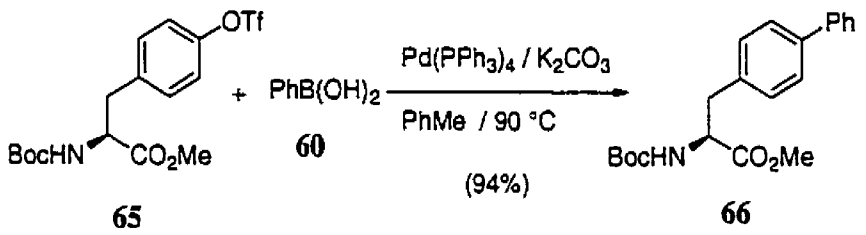
62 **64**

Base	yld, %
Na_2CO_3	50
K_3PO_4	70
NaOH	95
$Ba(OH)_2$	99

The reaction proceeds more rapidly in homogeneous conditions (aqueous base in DME). A combination of $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)_4$ and aqueous Na_2CO_3 in DME works

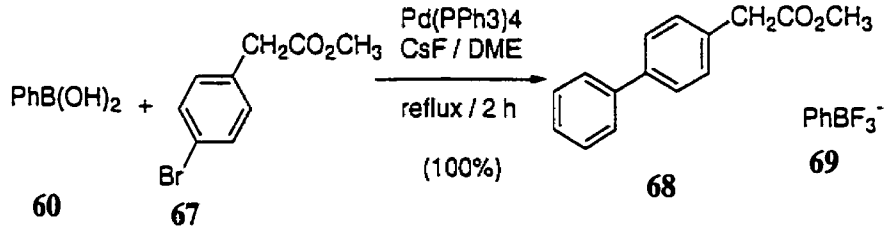
well in most cases.[32] Reasonable yields are also obtained under heterogeneous conditions. For example, K_2CO_3 suspended in toluene works well for base-sensitive substrates **65** in coupling with phenyl boronic acid to give **66** (**Scheme 21**).[35]

Scheme 21



Recently, fluoride salts have been found to be useful for the Suzuki - Miyaura cross-coupling reaction. Thus, coupling of phenylboronic acid **60** with 4-bromophenylacetate **67** under Pd catalysis using CsF gives the biaryl **68**. The species that undergoes transmetallation is assumed to be organo(trifluro)borate ion **69** (**Scheme 22**).[36]

Scheme 22



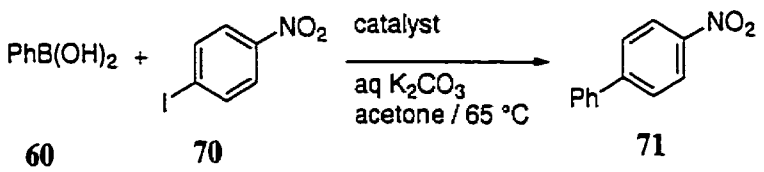
2.1.2 Catalysts

A very wide range of palladium (0) catalysts of Pd(II) precursors can be used for the Suzuki - Miyaura cross-coupling reaction. $Pd(PPh_3)_4$ is most commonly used, but

$PdCl_2(PPh_3)_2$ and $Pd(OAc)_2$ plus PPh_3 or other phosphine ligands are also efficient since they are stable to air and are readily reduced to the active Pd(0) complexes by phosphines added to the reactions.

Phosphine-based palladium catalysts are generally used since they are stable to long reaction times at elevated temperatures. However, high coupling reaction rates can be sometimes achieved by using palladium catalysts without a phosphine ligand such as $Pd(OAc)_2$ (**Scheme 23**).[37] Thus the reaction of phenylboronic acid **60** with 4-iodonitrobenzene **70** to afford 4-nitrobiphenyl **71** proceeds in 98% yield and is completed in 45 min (**Scheme 23**).

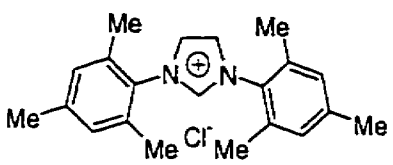
Scheme 23



60 **70** **71**

Catalyst	Time	yld, %
$Pd(PPh_3)_4$	8 h	23
$PdPdI(PPh_3)_2$	20 min	53
$Pd(OAc)_2$	45 min	98

Recently, some special ligands other than PPh_3 have been developed to realize the coupling of aryl chlorides with aryl boronic acids. These ligands include bulky phosphine

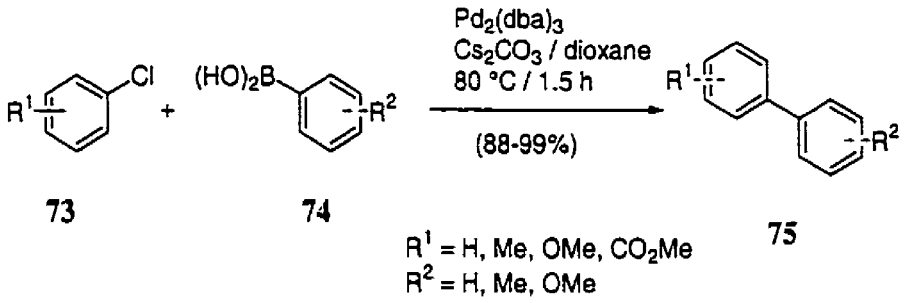


72

P^tBu_3[38] or phosphine-containing moiety (PCy_2)[39] and imidazolium salt (**72**).[40]

Using $Pd_2(dba)_3$ as catalyst, coupling of aryl chlorides **73** with aryl boronic acids **74** takes place in high yields to give **75** (**Scheme 24**).

Scheme 24

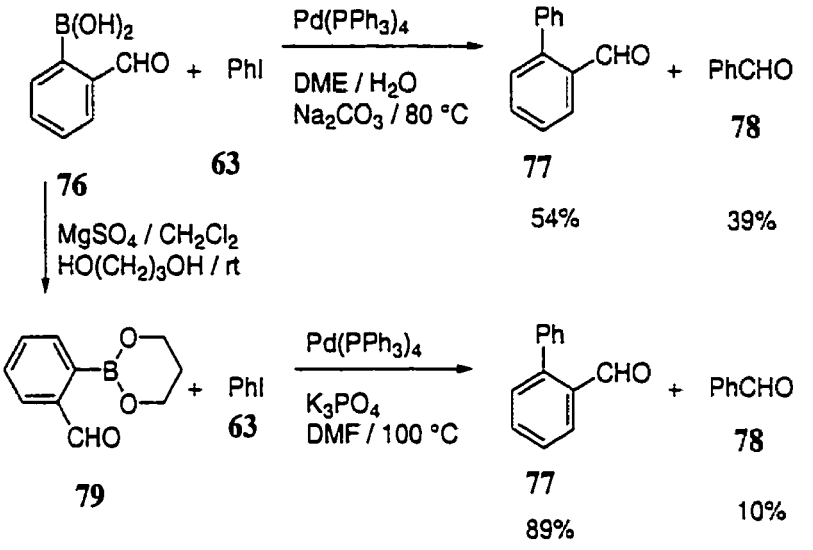


73 **74** **75**

2.1.3 Deboronation

Even if in the absence of great steric hindrance, the Suzuki - Miyaura reaction carried out under aqueous conditions, at times, gives undesirable results due to competitive hydrolytic deboronation. A kinetic study for the reaction of substituted arylboronic acids shows that electron-withdrawing substituents accelerate the deboronation.[41] For such boronic acids, an alternative procedure using the esters of boronic acids and anhydrous base gives better results. For example, the coupling of 2-formylboronic acid **76** with 2-idodotoluene **63** at 80 °C using an aqueous Na_2CO_3 in DME gives only 54% of the biaryl **77**. The yield of **77** can be improved to 89% by using the corresponding ester of boronic acid **79** and anhydrous K_3PO_4 suspended in DMF to give **77** in high yield (**Scheme 25**).

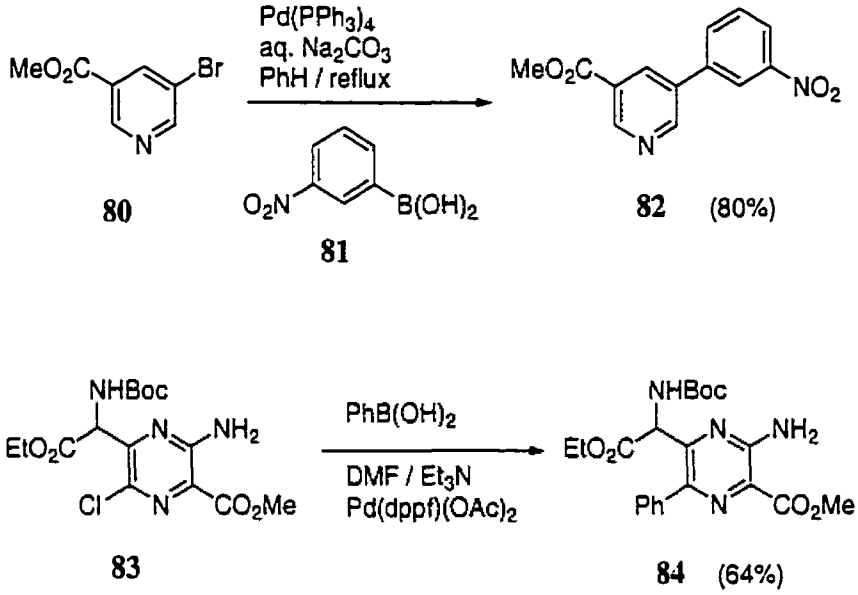
Scheme 25



2.1.4 Sensitive Functional Groups

The cross-coupling reaction of arylboronic acids is largely unaffected by the presence of water, tolerates a broad range of functionality, and yields no toxic byproducts. The reaction offers an additional advantage of being insensitive to the presence of *ortho*-functional groups or heteroaromatic rings in most cases.[42] Thus, coupling of methyl 5-bromonicotinate **80** (**Scheme 26**) with 3-nitrophenylboronic acid **81** gives 5-arylnicotinate **82** without hydrolysis of the ester group. In the same manner, multi-substituted pyrazinoate **83** may be coupled with phenylboronic acid **60** to yield arylpyrazinoate **84** in good yield.[43]

Scheme 26



2.1.5 Mechanism

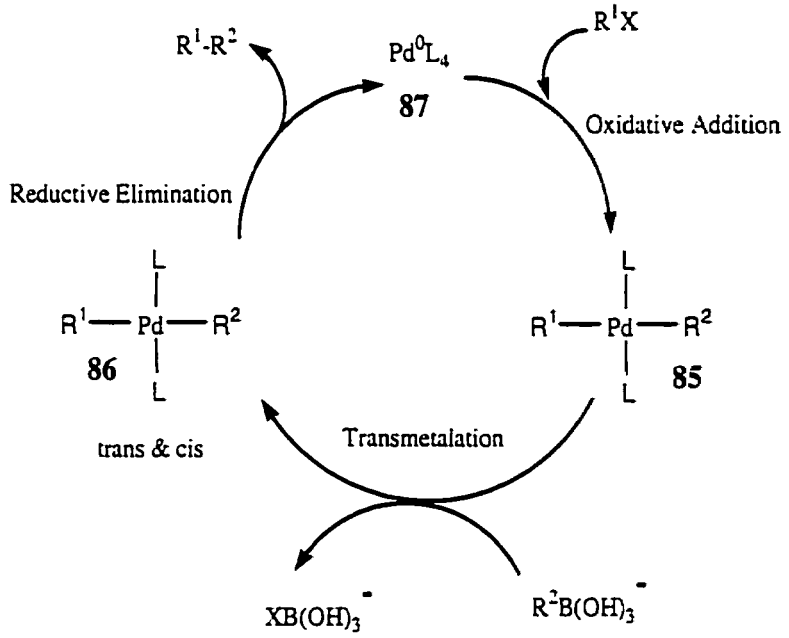
The mechanism of Suzuki - Miyaura cross-coupling reaction if far from being understood. A proposed catalytic cycle for the Suzuki - Miyaura cross-coupling reaction of organometallics, which involves an oxidative addition-transmetallation-reductive elimination sequence, is depicted in **Scheme 27**.[44] In the following discussion, a reasonable analogy to the mechanism of Stille cross coupling is utilized for that of Suzuki - Miyaura cross-coupling.

2.1.5.1 Oxidative Addition

Oxidative addition of 1-alkenyl, 1-alkynyl, allyl, benzyl and aryl halides (R^1X) to a palladium (0) complex affords a stable *trans*-σ-palladium (II) complex **85**.[45] The

reaction proceeds with complete retention of configuration for alkenyl halides and with inversion for allylic and benzylic halides. Alkyl halides having β-hydrogen are rarely useful because the oxidative addition step is very slow and may compete with β-hydride elimination from the σ-organopalladium (II) species **85**. The oxidative addition is often the rate-determining step in the catalytic cycle. The relative reactivity decreases in the order of I > OTf > Br >> Cl. Aryl and 1-alkenyl halides activated by the proximity of electron-withdrawing groups are more reactive to the oxidative addition than those with donating groups.

Scheme 27

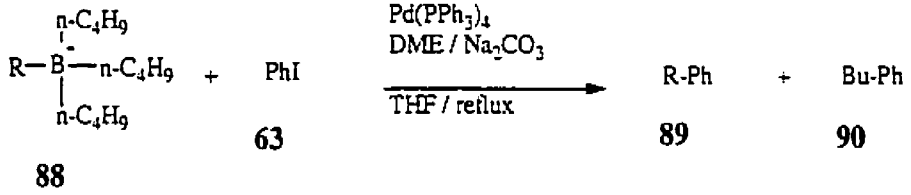


2.1.5.2 Transmetalation

It is apparent that the transmetaltion between organopalladium (II) halides and organoboron compounds does not occur readily due to the low nucleophilicity of organic

groups on a boron atom. However, this nucleophilicity can be enhanced by quaternization of the boron with negatively charged bases giving the corresponding complex **88**, which can undergo reaction directly with iodobenzene **63**. to give **89** and biphenyl **90** in excellent yields (**Scheme 28**).[25]

Scheme 28



R	yld. % (**89**/**90**)
$n\text{-}C_4H_9$	81
$CH_3CH{=}CH$	85 (45/55)
$C_4H_9C{\equiv}C$	98 (71/29)
Ph	79 (38/62)

Thus, formation of complex **88** indeed accelerates the transmetallation to the palladium (II) halides. Although there is no direct evidence that the boronate anions such as $RB(OH)_3^-$ are capable of effecting the transmetallation in the standard Suzuki-Miyaura process, it is quite reasonable to assume a similar effect of base for the transmetallation of organoboronic acids.

2.1.5.3 Reductive Elimination

Reductive elimination of organic partners from R^1-Pd(II)-R^2 (**86**, **Scheme 27**) regenerates the palladium (0) complex **X**.[46] The reaction takes place directly from

cis-R^1-Pd(II)-R^2, which is formed by isomerization from the trans R^1-Pd(II)-R^2 complex. The order of reactivity is diaryl- > (alkyl)aryl- > di(*n*-propyl)- > diethyl- > dimethylpalladium (II), suggesting participation by the π-orbital of the aryl group during the bond formation step. *Cis*-alkenyl and *cis*-arylpalladium (II) complexes **86**, which are intermediates in most cross-coupling reactions, directly eliminate organic partners from the four-coordinated complex to yield the product R^1-R^2 (nondissociative - nonassociateive mechanism) (**Scheme 27**).

2.1.6 Summary

The Suzuki - Miyaura cross coupling reaction has proved to be a very effective synthetic method leading to biaryl compounds, tolerating a number of functional groups. A variety of conditions combining different phosphine ligands, bases and solvents have been developed for hindered coupling partners. More recently, many aryl chlorides have been found to undergo successful coupling with aryl boronic acids using special phosphine ligands. However, the mechanism of the Suzuki - Miyaura reaction is far from being understood.

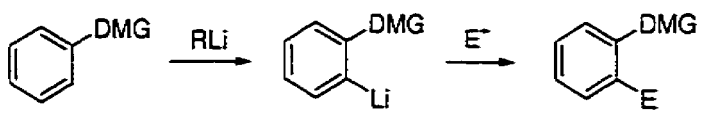
2.2. Combined DoM - Suzuki Cross Coupling Reactions

2.2.1 Introduction

In the transition metal catalyzed cross coupling reactions, the aryl metal species are usually prepared from the corresponding aryl bromide or iodide by metal-halogen exchange or metal insertion reactions. However, these routes are limited since the requisite intermediates are prepared by electrophilic bromination or iodination of substituted aromatic compounds which are always plagued by regiochemical control problems. It was envisaged that the directed *ortho* metalation (DoM) strategy could offer a general route to regiochemically defined aryl organometallics necessary for cross coupling reactions. Thus, the versatile DoM reaction would be connected to the palladium catalyzed cross coupling reaction for the regiospecific synthesis of unsymmetrical biaryls.

In the DoM process, an alkyllithium base-induced deprotonation of **91** containing a heteroatom directing metalation group (DMG) stabilizing the incipient negative charge by inductive effects, leads to the anion **92** which, in turn, undergoes reaction with an electrophile to give a 1, 2-disubstituted aromatic compound **93** (**Scheme 29**).

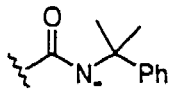
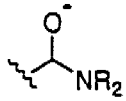
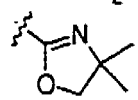
Scheme 29



91 **92** **93**

This process was discovered by Gilman[47] and Wittig[48] over sixty years ago on anisole (**91**, DMG = OMe). In the intervening years, a broad range of directed metalation groups (DMGs) have been found to efficiently direct the metalation process.[49, 50] Among these, the following DMGs are employed frequently in organic synthesis: carbon - based groups $CON^{-}R$[50, 51] $CONEt_2$,[52] $CON(Me)CH(TMS)_2$,[53, 54] $CON^{-}CH(Me)_2Ph$,[55] $CH(O^{-})NR_2$,[56] oxazoline,[57] etc. and heteroatom based groups, NHt-Boc,[58] $NHCOt$-Bu,[59] OMe,[50] OMOM,[60] $OCONR_2$,[61] $SO_2N^{-}R$,[50] SO_2NR_2,[50] $SO_2NHC(Me)_2Ph$,[55] $P(O)(t\text{-}Bu)_2$[62] (**Table 2**).

Table 2. Some Representative DMGs and E^{+}s

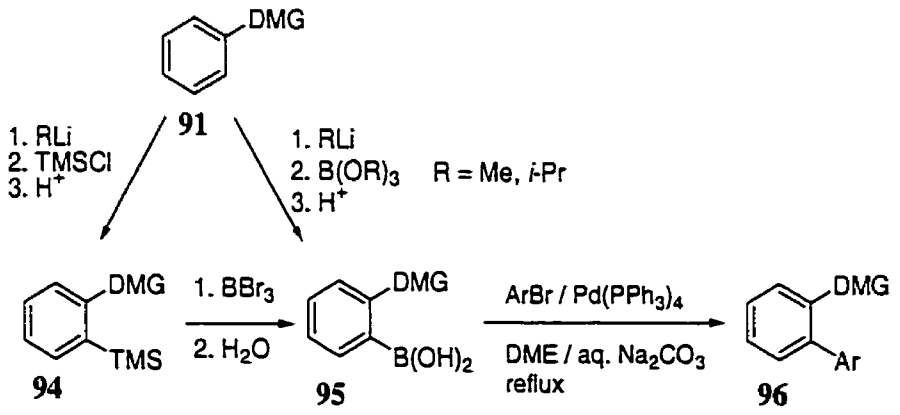
C-based DMG	reference	Hetatom-based DMG	reference
$CON^{-}R$	4, 5	$N^{-}t$-BOC	12
$CONEt_2$	6	$NCO^{-}t$-Bu	13
$CON(Me)CH(TMS)_2$	7, 8	OMe	4
	9	OCH_2OMe	14
		$OCONEt_2$	15
	10	$SO_2N^{-}R$	4
		SO_2NR_2	4
	11	$SO_2NHC(Me)_2Ph$	9
		$P(O)(t\text{-}Bu)_2$	16

The major significance of the D*o*M process is to conquer the problems of regiospecific preparation of polysubstitited aromatic compounds which was traditionally performed by classical, nonregiospecific processes such as the Friedel-Crafts reaction and the various other electrophile substitution methods (hal^{+}, NO_2^{+}).[63] In contrast, the D*o*M -

derived anion **92** may be trapped by a variety of electrophiles leading to the regiospecific formation of not only carbon, but also heteroatom substituted derivatives **93**.

In context of forming *ortho*-boron substituted derivatives via D*o*M chemistry, the key reaction for research described in this thesis, two methods have so far been established (**Scheme 30**). First, treatment of the DMG-containing substrate **91** with trialkyl borate followed by acidic hydrolysis gives the boronic acid.[64] An alternative method, compatible only for non-Lewis acid sensitive groups,[64] e.g., $CONEt_2$, $OCONEt_2$, involves ipso desilylation of silylated compounds **94** with BBr_3. In the few cases studied to date, the latter method gives higher yield and cleaner product. Thus the aryl boronic acids **95** are treated with aryl halides and a catalytic amount of $Pd(PPh_3)_4$ in DME and aqueous Na_2CO_3 solution, good to excellent yields of unsymmetrical biaryls **96** are obtained.[65, 66]

Scheme 30



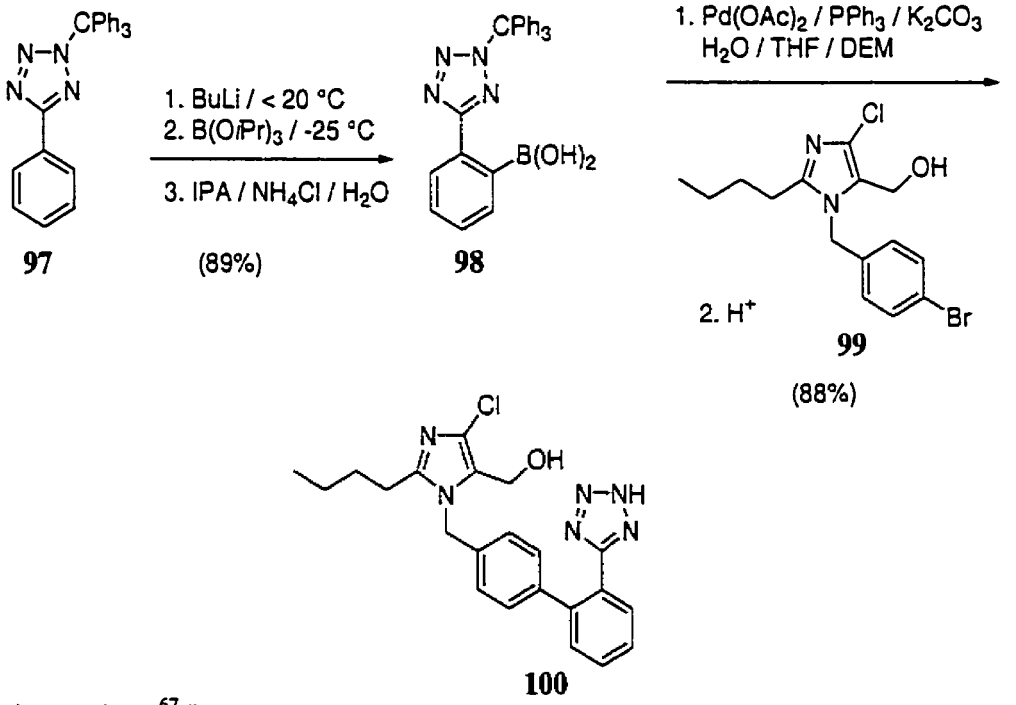
In this manner, the prologue of studies on the D*o*M - cross coupling connection was opened. The alliance of these two reactions stimulated the discoveries of novel synthetic methods and promoted the synthesis of a number of natural products. To a

certain extent thereby, the development of aromatic chemistry has been carried forward to a new plateau.

2.2.2 Applications

A highly efficient approach to the synthesis of the angiotensin II receptor antagonist Losartan® **100** using the Suzuki - Miyaura reaction was carried out by Larsen

Scheme 31

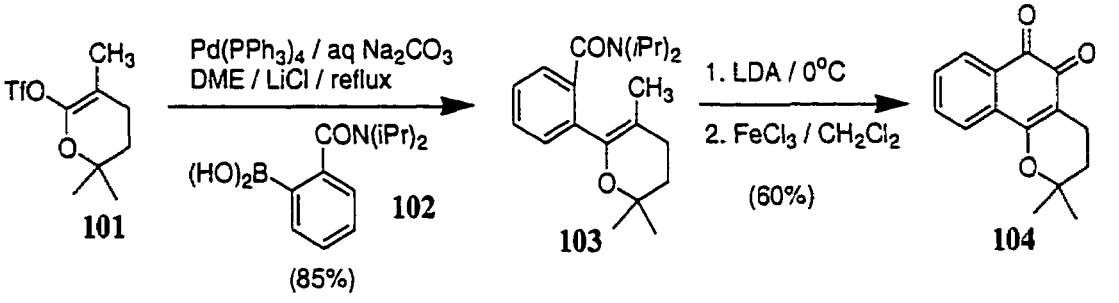


97 (89%) **98** **99** (88%) **100**

and coworkers.[67] Directed *ortho* metalation of phenyltetrazole **97** provided the key intermediate boronic acid **98** for Suzuki coupling with the bromide **99** to give the commercial drug Losartan® **100**. This process is currently carried out by Dupont Merck company on multikilogram scale.

A combined D*o*M – Suzuki-Miyaura cross coupling methodology was also used for the regiospecific construction of heteroring fused *o*-naphthoquinones as illustrated in the synthesis of the antimalarial / antitumor natural product β-lapachone **104** (**Scheme 31**).[68] The triflate **101** was subjected to Suzuki - Miyaura cross coupling with boronic acid **102** to afford the biaryl amide **103**, which, upon cyclization and oxidation gave β-lapachone **104**.

Scheme 31

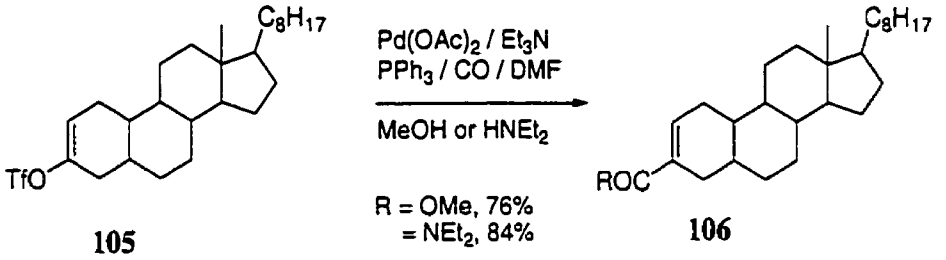


The ready availability of *ortho*-functionalized aryl boronic acid obtained by the D*o*M-boronation sequence provides a synthetic link to the cross coupling protocol. Thus the combined D*o*M-Suzuki-Miyaura cross coupling methodology has proved to be a promising method for the synthesis of unsymmetrical biaryl and heterobiaryls.[65]

2.3. Carbonylation of Triflates

Aryl and vinyl halides and triflates undergo palladium catalyzed carbonylation under mild conditions, offering a useful methods for esters, amides and carboxylic acids.[69] The first successful palladium catalyzed carbonylation of vinyl triflates was carried out by Cacchi and coworkers on steroidal system **105** to give α, β-unsaturated esters or amides **106** (**Scheme 32**).[70]

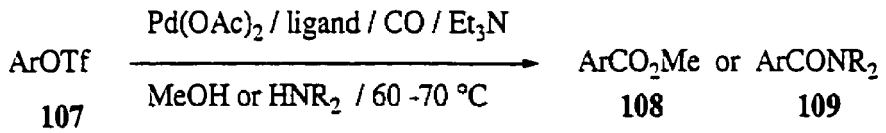
Scheme 32

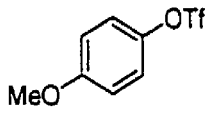
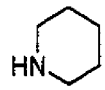
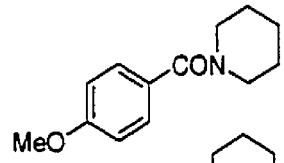
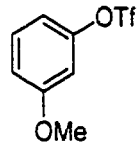
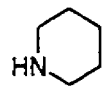
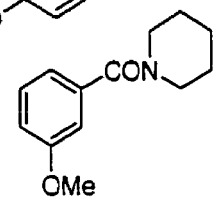
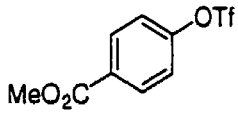
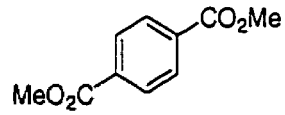
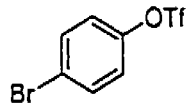
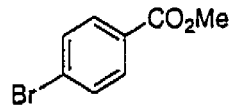
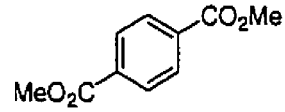
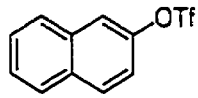
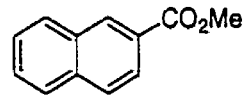
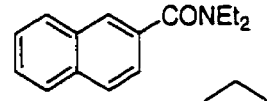
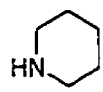
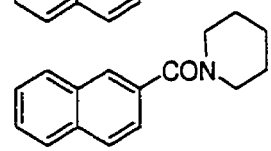
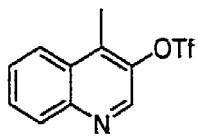
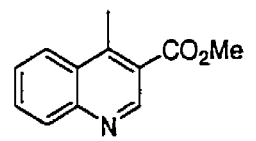


105 **106**

Cacchi also showed that carbonylation may be effected on aryl triflates under mild conditions to give esters **108** and amides **109** in good yields (**Table 3**).[71] 3- and 4-Methoxyphenyl triflates (entries 1 and 2) and 2-naphthyl triflate (entries 5, 6 and 7) undergo carbonylation in good yields using dppf as the ligand. The carbonylation reaction proceeds smoothly with tolerance of ester groups (entry 3). The triflate group performs better in carbonylation than the bromo group (entry 4). Carbonylation of heterocyclic compounds, e.g. quinoline, may also be achieved (entry 8). Besides dppf, another ligand dppp was found to afford ca. 500-fold rate enhancement compared to PPh_3 in the carbonylation reactions.[72]

Table 3. Carbonylation of Aryl Triflates

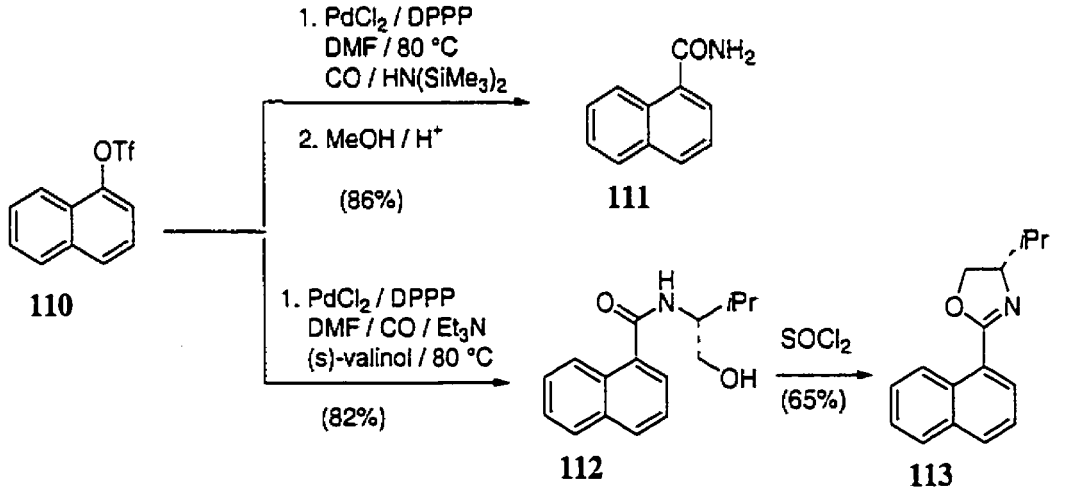


Entry	Triflates	Ligands	Alchols or Amines	Esters or Amides	Yields %
1		dppf			59
2		dppf			68
3		dppf	MeOH		77
4		dppf	MeOH		45
					27
5		PPh_3	MeOH		78
6			Et_2NH		80
7					70
8		dppf	MeOH		70

The use of dppp as the ligand is essential. It is not clear if this is due to the higher stability or its bidentate complexation ability leading to the necessary *cis*-configuration of the palladium complex prior to reductive elimination. Dppe may also be used as the ligand, but has been found to be inferior compared to dppp.[73]

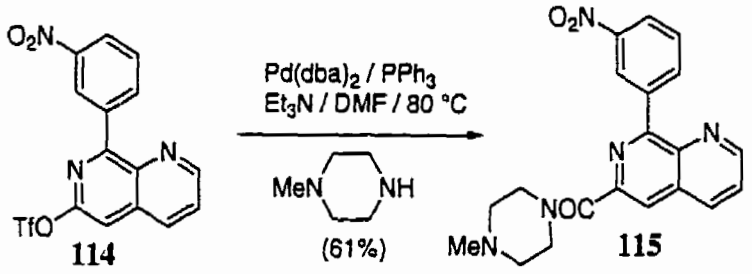
Aryl triflates **110** have also been shown to undergo palladium catalyzed carboamidation to give primary amides **111** in the presence of hexamethyldisilazane (HMDS) (**Scheme 33**).[74] Furthermore, carbonylation of aryl triflates **110** has also been used in synthesis of oxazolines **113** via the intermediate **112** (**Scheme 33**).[75]

Scheme 33



In a recent application, palladium-catalyzed carbonylation of triflate **114** in the presence of 4-methylpiperazine led to the amide **115**, a potent phosphodiesterase type 4D inhibitor (**Scheme 34**).[76]

Scheme 34


O2N
TfO
N
N
114
Pd(dba)2 / PPh3
Et3N / DMF / 80 °C
MeN
NH
(61%)
O2N
N
N
NOC
MeN
115

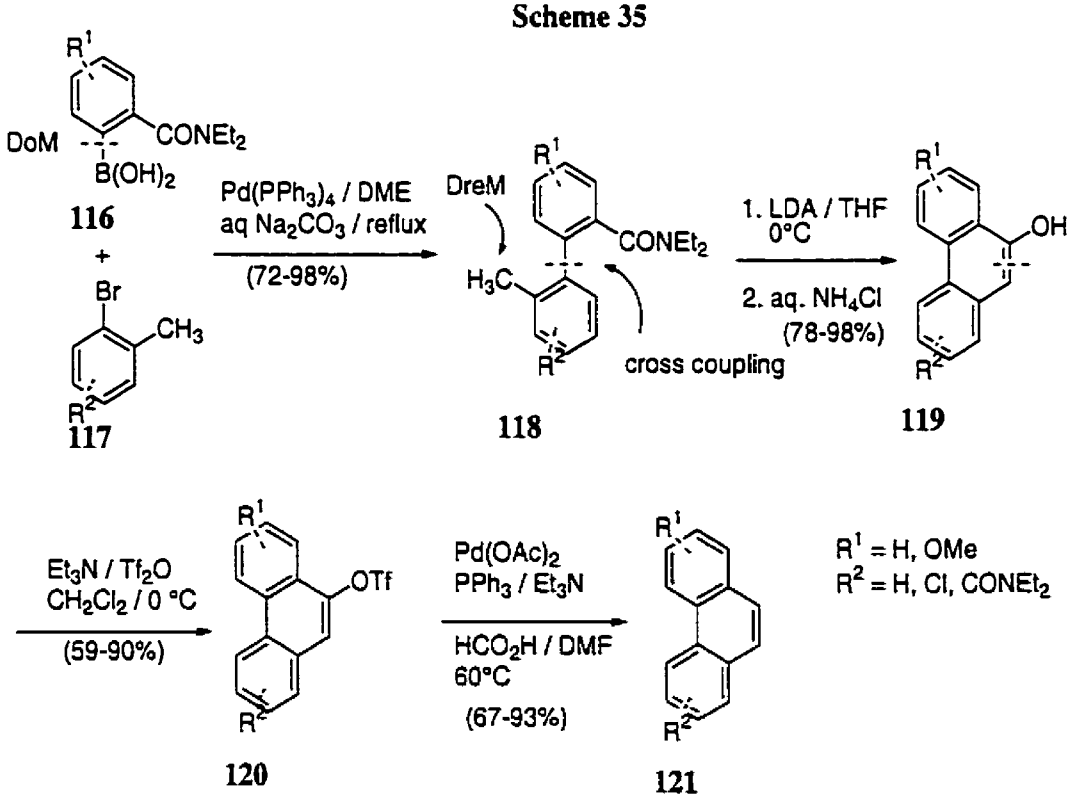
Chapter 3

Results and Discussion

3.1 Introduction

A general and regiospecific synthesis of phenanthrenes proceeding by a Directed *ortho* Metalation (D*o*M), Suzuki-Miyaura cross coupling, and Directed remote Metalation (DreM) sequence was developed in our group (**Scheme 35**).[77, 78] In this protocol, benzamide boronic acids **116** are coupled with ortho-bromotoluenes **117** under standard Suzuki-Miyaura conditions to give products **118**, which upon treatment with LDA, undergo DreM-mediated cyclization to the phenanthrols **119**. Conversion of **119** into the corresponding triflates **120** followed by Pd-catalyzed reduction using formic acid affords the phenanthrenes **121**. This synthetic strategy enjoys the advantages of the regiospecificity of D*o*M for the construction of benzamide boronic acids, the ready availability of starting materials, and the efficacy of the Suzuki-Miyaura reaction. This

Scheme 35



method has been used for the synthesis of a variety of substituted phenanthrenes **121** with functional groups such as Cl, OMe and $CONEt_2$, and served as a key step in synthesis of the natural product, gymnopusin.[79]

Alkylphenanthrenes are degradation products of a lot of natural product. For example, retene, 7-isopropyl-1-methylphenanthrene, which is a degradation product of abietic acid, is found toxic to the growth of fish.[80] In order to elucidate the structure-activity relationship of alkylphenanthrenes, a series of analytically pure alkylphenanthrenes were required for toxicity evaluation. The aim of this thesis work was to prepare alkylphenanthrenes, selected in consultation with our collaborators, Professors Peter Hodson and Stephen Brown using the regioselective approach devised in our laboratories (**Scheme 35**).

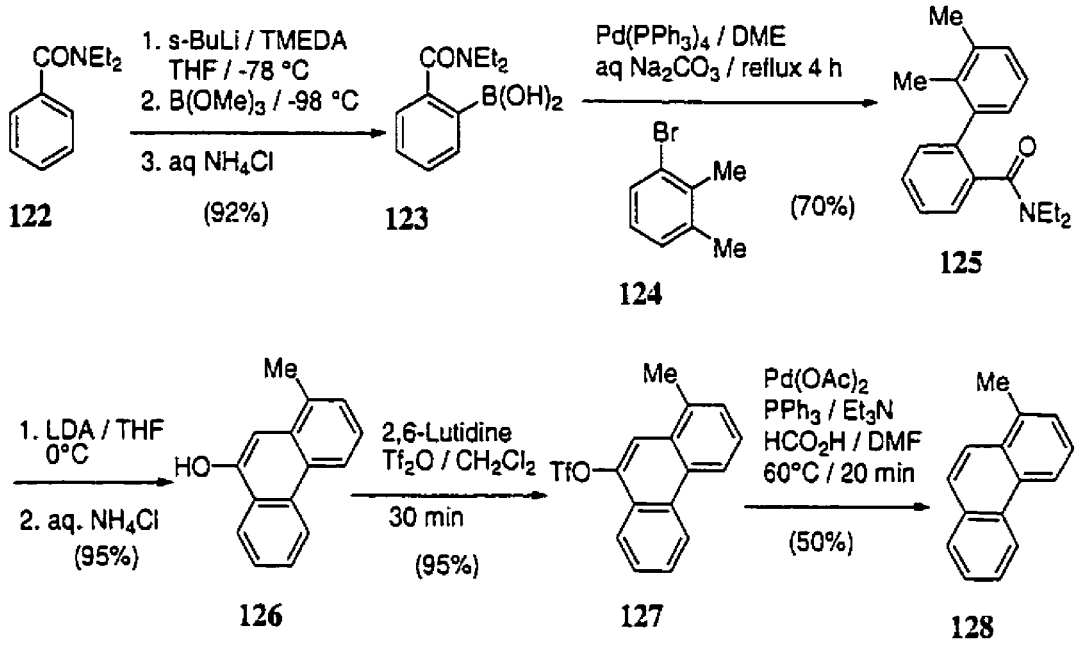
3.2 Synthesis of 1-Methylphenanthrene

The synthesis of 1-methylphenanthrene (**128**) started from N, N-diethylbenzamide **122**, which was subjected to metalation under standard conditions (*s*-BuLi / TMEDA / -78 °C / THF / 1 h) followed by quenching with trimethyl borate and acidic workup to afford the boronic acid **123**. Without purification, **123** was directly subjected, as the reactant in excess (1.4 equiv), to the Suzuki-Miyaura cross coupling reaction with *ortho*-bromoxylene **124** to give biaryl amide **125** in good yield (**Scheme 36**).

The biaryl amide **125**, upon treatment with 2.5 equiv of LDA underwent cyclization to afford 1-methyl-9-phenanthrol (**126**) in 95% yield. The compound **126** was

then converted into its triflate **127** which, under Pd-catalyzed hydrogenolysis in the presence of palladium catalyst and formic acid, afforded 1-methylphenanthrene (**128**) (**Scheme 36**) in medium yield. The overall yield (29%) is higher than that achieved by the Pschorr synthesis of **128** (21% overall yield in 4 steps)[81].

Scheme 36

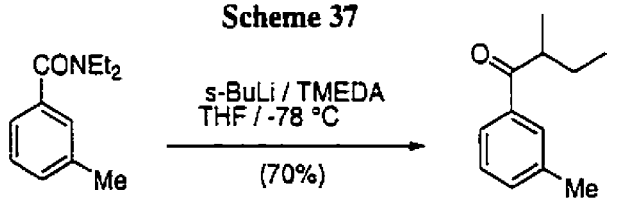


3.3 Synthesis of 1, 7-Dimethylphenanthrene

For the construction of 1,7-dimethylphenanthrene (**135**), the retrosynthetic analysis according to our strategy (**Scheme 37**) required the benzamide boronic acid **131** and the same aryl bromide **124** cross coupling partners. Metalation - boronation of **129**, the insecticide DEET, under standard D*o*M conditions at -78 °C afforded mainly (70%) the ketone condensation product **130**. However, at -98 °C, the reaction proceeded

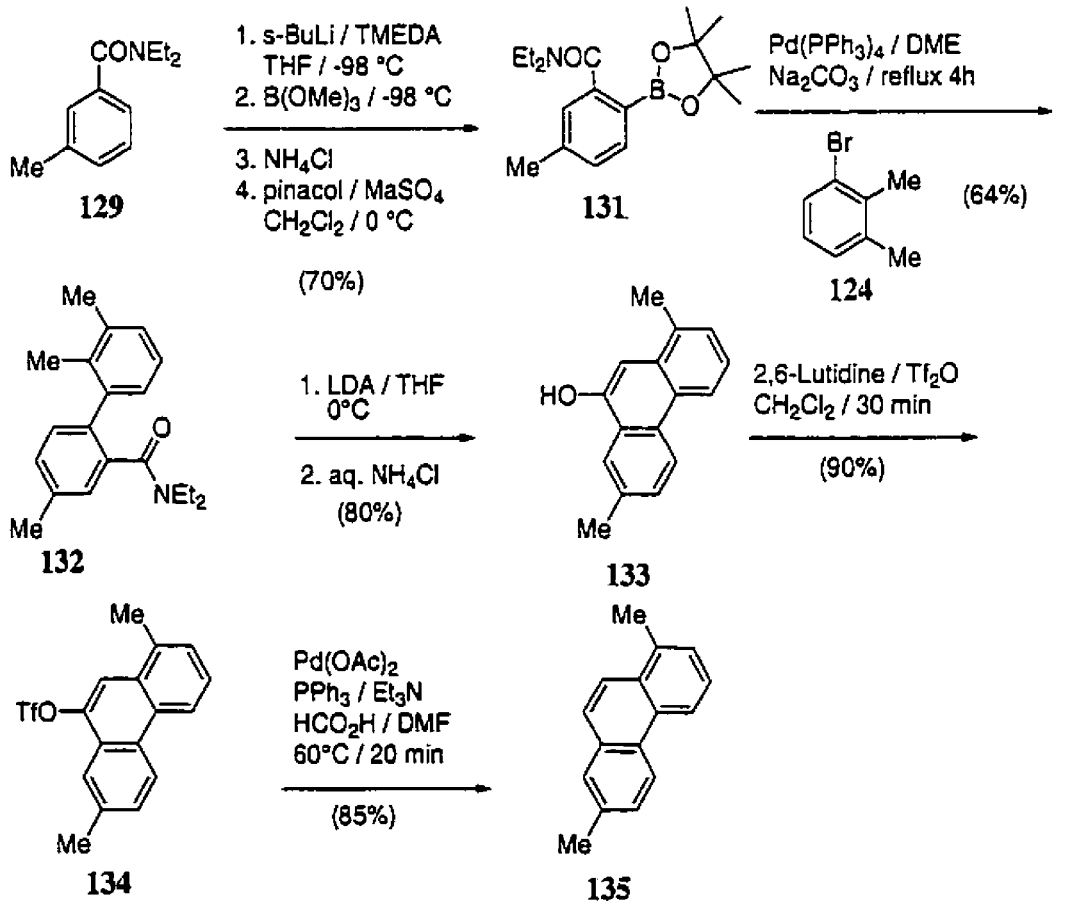
smoothly to give boronic acid, followed by treatment with pinacol to afford the boronate. The boronate **131** was subjected to Suzuki cross coupling with *o*-bromoxylene **124** to give biaryl **132**, which was then treated with LDA to afford the 9-phenanthrol **133**. Compound **133** was converted into its triflate **134** which, upon reductive hydrogenolysis, gave 1, 7-dimethylphenanthrene **135** in 5 steps and 27% overall yield (**Scheme 38**).

Scheme 37



129 **130**

Scheme 38



129 **131** **124**

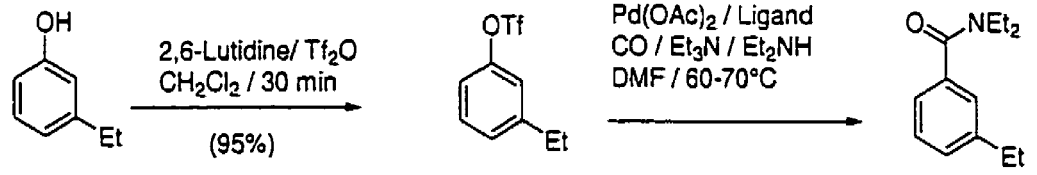
132 **133**

134 **135**

3.4 Synthesis of 7-Ethyl-1-methylphenanthrene

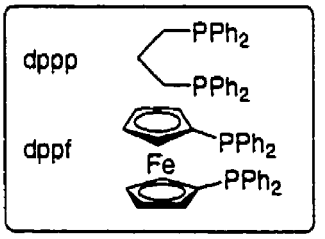
The synthesis of the homologues 7-ethyl-1-methylphanthrene (**145**) started from 3-ethylbenzamide **138**, which was obtained by carbonylation of 3-ethylphenyl triflate **137**,[82] itself prepared from the commercially available phenol **136** (**scheme 39**).[83]

Scheme 39



136 **137** **138**

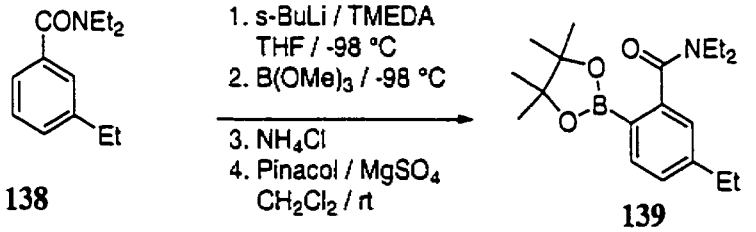
Ligand	time	yld, %
PPh_3	24h	25
dppp	4h	70
dppf	12h	62



This 3-ethylphenol **136** was converted into its triflate **137** in high yield using 2, 6-lutidine as the catalyst. Some problems were experienced with the carbonylative amination of the triflate **137** Three different ligands including PPh_3, dppf and dppp were tested. Precipitation took place quickly when PPh_3 was used. The yield was low and in this case, starting material was mostly recovered (72%). Bidentate dppp and dppf ligands behave much better than PPh_3, leading to good yields and completion of reactions with only trace amounts of starting material being detected by GC after conclusion of the reaction.

Carbonylation is a two-phase reaction. Therefore, it is important to ensure good mixing between CO and the solution, especially when the reaction is carried out on large scale. Using a balloon of CO above the solution led to poorer yield and longer reaction time. Bubbling CO into the solution provided higher yields of product under shorter reaction times.

Scheme 40

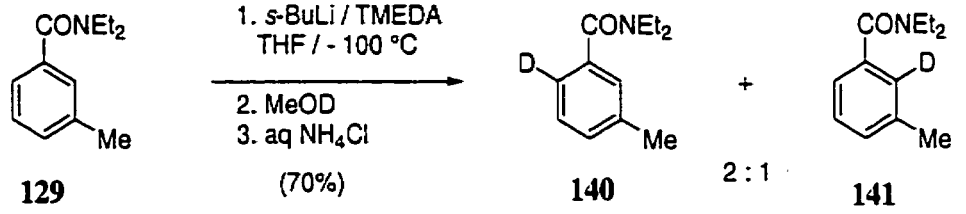


138 **139**

(76%)

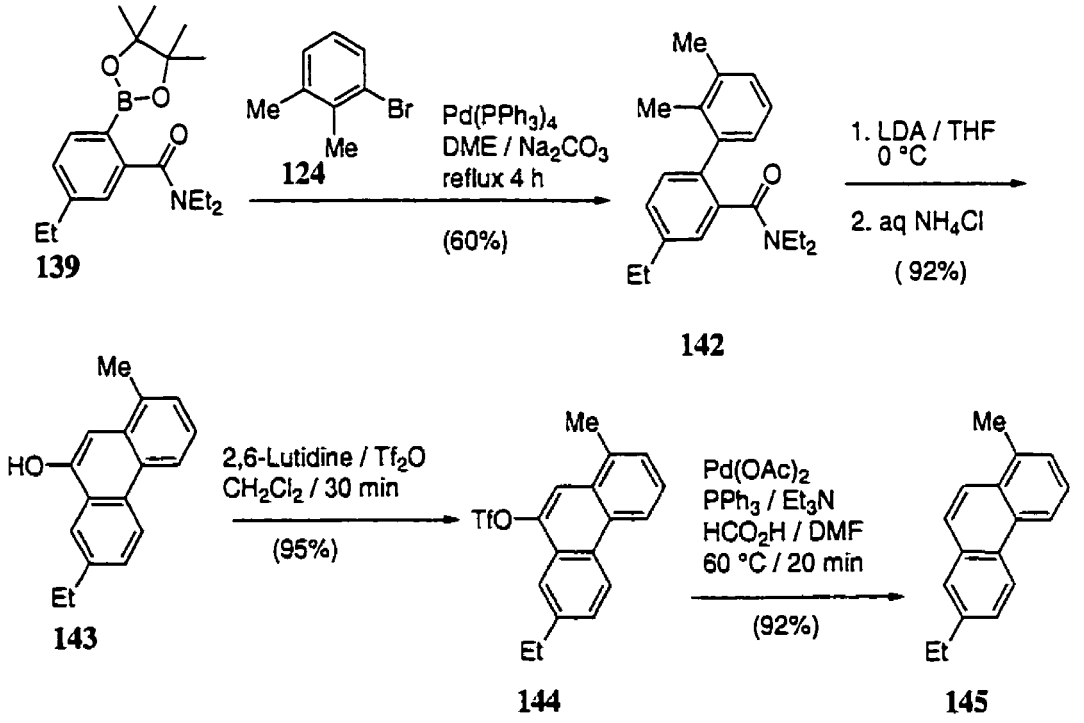
In the next step, a study of the metalation of 3-ethylbenzamide **138** was undertaken. Thus, D*o*M of **138** under the low temperature conditions used previously for **129** (**Scheme 40**) followed by boronation and treatment with pinacol led to the formation of boronate **139**. Thus D*o*M of **138** took place exclusively on C-6. This result is different from Beak's observation that metalation of 3-methylbenzamide **129** under similar conditions but followed by MeOD quench yielded the two isomers **140** and **141** in the ratio of 2:1 (**Scheme 41**).[84] The difference in regioselectivity may be understood by the size of the electrophile: trimethyl borate is larger than MeOD. Therefore, it is more difficult for trimethyl borate to access to C-2 in **Scheme 40** than MeOD to C-2 (**Scheme 41**), resulting in the production of only one isomeric boronate **139** for the former reaction.

Scheme 41



In the next step, the boronate **139** was subjected to Suzuki-Miyaura cross coupling with o-bromoxylene **X** under normal conditions to afford the biaryl amide **142** (**Scheme 42**). Treatment of **142** with LDA yielded the 9-phenanthrol **143** in high yield. Conversion to its triflate **144** followed by hydrogenolysis, afforded 7-ethyl-1-methylphenanthrene (**145**) in high yield and > 98% purity (HPLC analysis) (**Scheme 42**). This concluded that the synthesis of 7-ethyl-1-methylphenthrene in 6 steps with an overall yield of 36%.

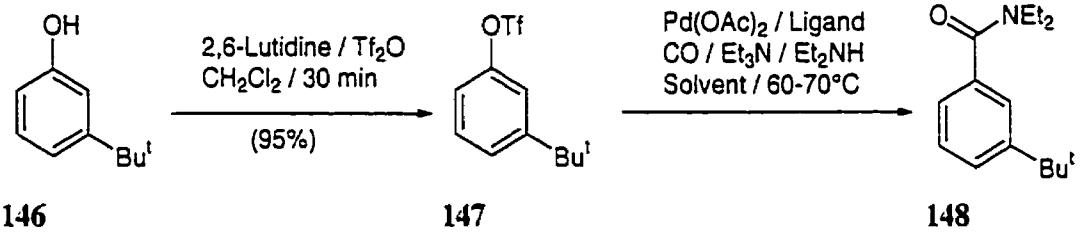
Scheme 42



3.5 Synthesis of 7-*t*-Butyl-1-methylphenanthrene

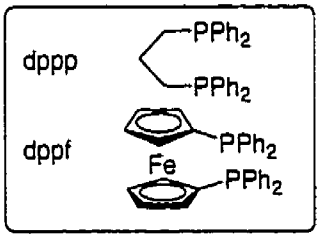
In pursuit of the same strategy for the synthesis of 7-*t*-butyl-1-methyl-phenanthrene (**149**), we envisaged the preparation of the requisite benzamide **148** by the carbonylative amidation of **147**, which, in turn, was available in high yield from the commercial phenol (**146**, **Scheme 43**). However, the reaction **147** --> **148** proceeded only in low yields using several sets of conditions, including the ligands which provided high yields in the analogous sequence for **138** (**Scheme 43**).

Scheme 43



146 **147** **148**

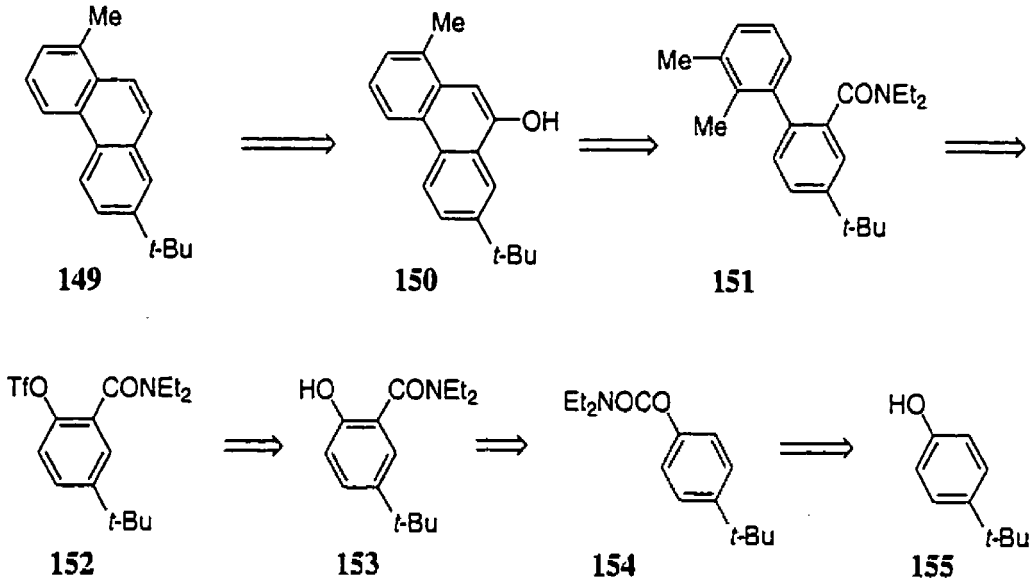
Ligand	Solvent	Reation Time	Yld, %
dppp	DMF	24h	20
dppf	DMF	24h	22
dppp	DMSO	48h	25
dppf	DMSO	48h	27



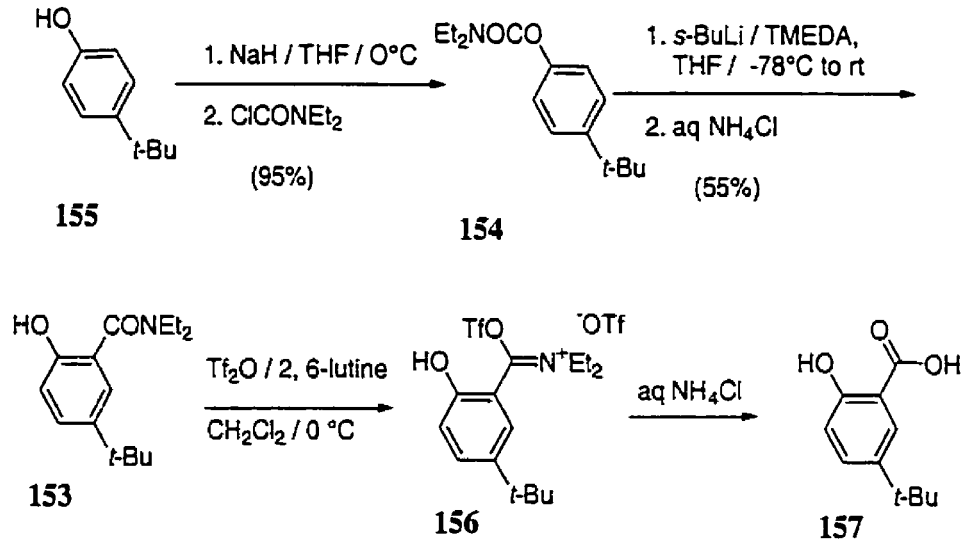
Therefore, a variation in the approach to starting coupling partners was pursued (**Scheme 44**). Dissection of **149** via the DreM route cascades to the phenanthrol **150** and thence to the biaryl amide **151**, which was envisaged to be derived from the coupling of *ortho*-bromoxylene (**124**) and the benzamide triflate **152**, readily available from the phenol **153**. Compound **153** was expected to be derived from the O-carbamate **154** by an

anionic Fries rearrangement.[85] The starting point would be the inexpensive phenol **155**. Thus 4-*t*-butylphenol **155** (**Scheme 45**) was readily converted into **154.** The latter, upon treatment with s-BuLi / TMEDA at –78 °C, and the intermediate lithium species allowed to undergo the Fries anionic rearrangement, gave compound **153** in good yield (**Scheme 45**).[85]

Scheme 44



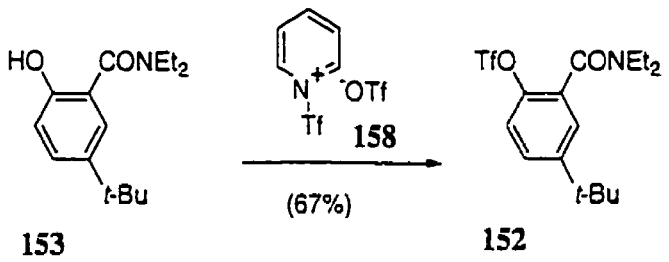
Scheme 45



To prepare **152**, phenol **153** was treated with Tf_2O using 2, 6-lutidine as the catalyst; however, the yield was lower than 20%. A possible explanation is that Tf_2O attack the carboxamate group to form compound **156**, which may be converted into benzoic acid **157** upon workup (**Scheme 45**).[86]

However, using pyridine as catalyst, compound **152** was obtained in good yield. Presumable, pyridine is less hindered than 2, 6-lutidine, therefore forming the reactive triflating reagent **158**, which leads to a good yield of product **152** (**Scheme 46**).[87]

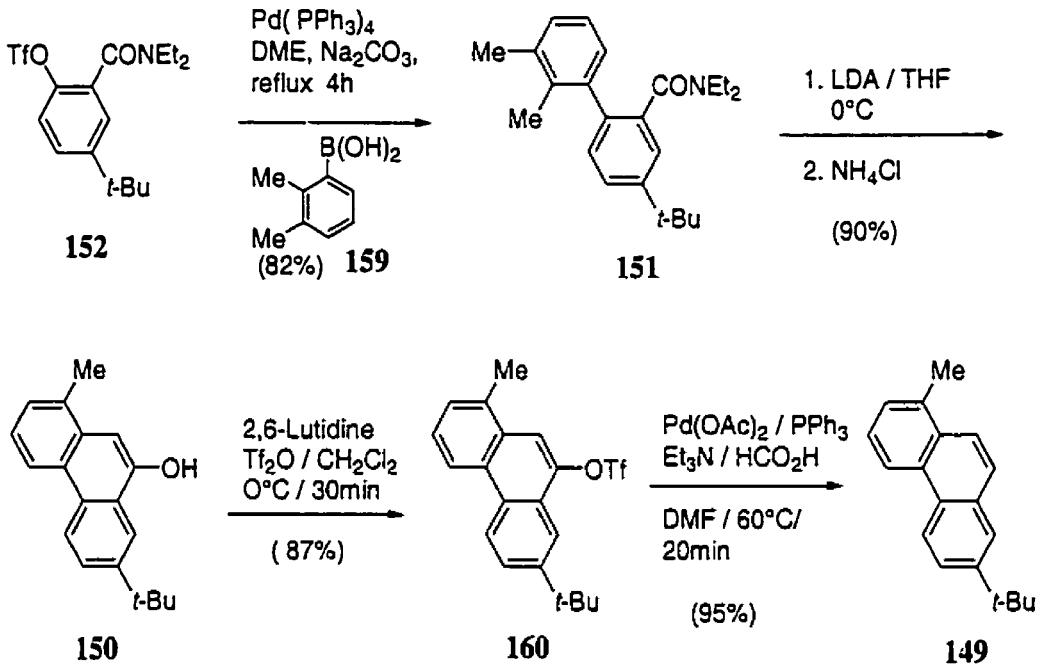
Scheme 46



153 **152**

In the next step, compound **152** underwent Suzuki-Miyaura coupling with the boronic acid **159** to form the biaryl carboxamate **151** in very good yield. Compound **151** was cyclized with LDA to yield the 9-phenanthrol, which was converted to **160**, and thence to 7-t-butyl-1-methylphenanthrene **149** by the triflation - reduction protocol (**Scheme 47**). Thus, the synthesis of 7-*t*-butyl-1-methylphenanthrene **149** was accomplished in 7 steps with an overall yield of 21%. The purity of **149** was established as 99% (HPLC analysis).

Scheme 47



3.6 Summary

The highly pure alkylphenanthrenes, 1-methyl- (**128**), 1, 7-dimethyl- (**135**), 7-ethyl- 1-methyl- (**145**), and 7-*t*-butyl-1-methylphenanthrenes (**149**) have been successful synthesized by a combined D*o*M - Suzuki-Miyaura cross coupling - DreM methodology in overall yields 29% (4 steps), 27% (5 steps), 36% (6 steps) and 21% (7 steps) respectively. Therefore this methodology contributes an effective and general method for regiospecific synthesis of substituted phenanthrenes. Carbonylative amination of triflates have been investigated, showing that inexpensive phenols can serve as a useful starting material for the preparation of N, N-diethylbenzamides (**Scheme 39**), which, in turn, are potential starting point for the D*o*M chemistry.

Experimental Section

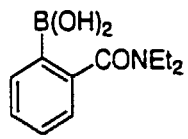
A Lithiation of Benzamides. A solution of the benzamide (1.00 mmol), dissolved in anhydrous THF (2 ml) was added dropwise to a stirred solution of 1:1 s-BuLi-TMEDA complex in anhydrous THF (3 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 1 h and treated with an excess of $B(OMe)_3$ (2 mmol) followed by warming to ambient temperature overnight. A few drops of saturated aqueous NH_4Cl solution was added and the THF was removed in vacuo. The residue was taken up to normal workup to afford the crude product.

B Cross Coupling Reaction of Arylboronic Acids with Aryl Halides or Aryl Triflates. A mixture of $Pd(PPh_3)_4$ (0.04 mmol) and aryl halide or aryl triflate (1 mmol) in DME (3 mL) was stirred at room temperature for 10 min. The solution of aryl boronic acid (1.4 mmol) dissolved in a minimum amount of ethanol and DME (2 mL) was added, followed by the addition of 2 M aqueous Na_2CO_3 solution (3 mL). The resulting mixture was heated at reflux overnight and cooled to rt. The resulting black misture was subjected to filtration, the residue was washed with Et_2O, and the filtrate was concentrated to dryness in vacuo. Normal workup followed by flash chromatography afforded the coupled product.

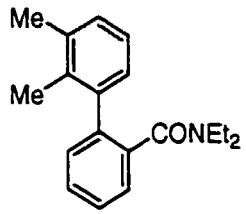
C Synthesis of 9-Phenanthrols To a solution of LDA (2.50 mmol) in THF (8 mL) was added the solution of 2'-methylbiphenylcarboxamide (1.00 mmol) in THF (2 mL) at 0 °C. The resulting mixture was stirred at rt for 30 min to give a brown or black

solution which became colorless upon the addition of a few drops of NH_4Cl solution. The reaction mixture was concentrated in vacuo. Normal workup followed by flash column chromatography afforded the product.

D Synthesis of Triflates The solution of aromatic hydroxy compound (1.00 mmol) and 2, 6-lutidine or pyridine (1.2 mmol) in CH_2Cl_2 (10 mL) was stirred for 5 min at 0 °C followed by addition of triflic anhydride (1.20 mmol). The resulting mixture was stirred at room temperature for 30 min. A few drops of aqueous NH_4Cl solution were added and the solvent was removed in vacuo. Normal workup followed by flash chromatography afforded the product.

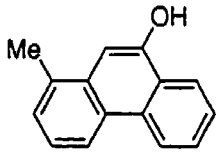


2–(N, N-Diethylcarboxamido)phenylboronic acid (123) According to method A, to a solution of N, N-diethylbenzamide (1.77 g, 10.0 mmol), s-BuLi (9.60 mL of 1.25M solution ,12.0 mmol), and TMEDA (1.07 mL, 1.39g, 12.0 mmol) was added $B(OMe)_3$. Normal workup afforded 2.03g (92%) of product as a viscous oil which was used in corss coupling reactions without any further purification.

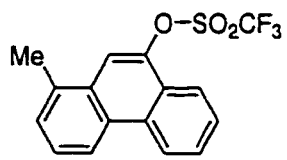


N, N-Diethyl 2', 3'-dimethylbiphenyl-2-carboxamide (125) According to method B, 1-bromo-2, 3-dimethylbenzene (1.36 mL, 1.85 g, 10.0 mmol) was coupled with 2-(N, N-diethylcarboxamido)phenylboronic acid (3.09 g, 14 mmol) in the presence of $Pd(PPh_3)_4$ (0.185 g, 0.16 mmol). Normal workup followed by flash chromatography (1:5) afforded 2.30 g (82%) of product as a colorless crystal. mp 68 –69 °C (EtOAc); IR (neat) 1632 cm^{-1}

[1]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.59 (s, 2H), 0.80 (s, 3H), 2.01 (s, 3H), 2.19 (s, 3H), 2.40 - 3.30 (br, 3H), 3.65 (s, 1H), 6.90 - 7.15 (m, 4H), 7.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 14.0, 17.5, 20.9, 38.2, 42.8, 117.3, 118.9, 124.9, 127.5, 127.9, 128.6, 129.5, 130.1, 131.2, 135.0, 137.1, 137.6, 170.3; MS EI *m/z* (rel. int.) 281 (M^+, 100), 209 (20), 181 (13), 165 (47), 74 (30) HRMS *m/z* calcd for $C_{19}H_{23}NO$, 281.1780, found 281.1776.

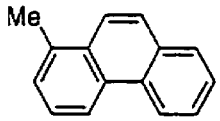


1-Methyl-9-phenanthrol (126) According to method C, treatment of N, N-Diethyl 2', 3'-dimethylbiphenyl-2-carboxamide (2.81 g, 10 mmol) with LDA (25.0 mmol) for 30 min followed by acidification, normal workup and flash chromatography (hexane) afforded 1.98 g (95%) of product as a colorless crystal. mp 194 – 197 °C (CH_2Cl_2); IR (KBr) 3307 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.61 (s, 3H), 7.34 (q, 1H, J = 7.8), 7.39 (d, 1H, J = 6.8), 7.67 (m, 2H), 8.31 (d, 1H, J = 7.4), 8.53 (d, 1H, J = 7.8), 8.77 (d, 1H, J = 7.6), 10. 39 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 20.5, 102.3, 121.7, 123.3, 123.9, 126.1, 128.0, 128.7, 132.2, 132.6, 132.9, 151.9; MS EI *m/z* (rel. int.) 208 (M^+, 100), 178 (17), 165 (38), 152 (5), 89 (5), 76 (5) HRMS *m/z* calcd for $C_{15}H_{12}O$, 208.0888, found 208.0890.

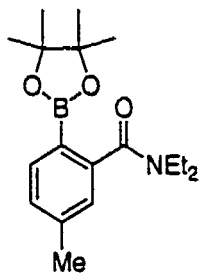


1-Methylphenanthryl-9 trifluoromethanesulfonate (127) According to method D, to a solution of 1-methyl-9-phenanthrol (1.04 g, 5.00 mmol) and 2, 6-lutidine (0.69 ml, 0.64 g, 6.00

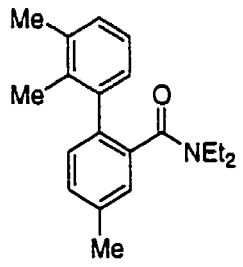
mmol) in CH_2Cl_2 was added triflic anhydride (1.01 ml, 1.69 g, 6.00 mmol). Normal workup followed by flash chromatography (hexane) afforded 1.62 (95%) g of product as a colorless crystal. mp 60 –61 °C (EtOAc);IR (KBr) 1416, 1206, 1139 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.72 (s, 3H), 7.49 (s, 1H), 7.57 (t, 1H, J = 7.2), 7.71 - 7.77 (m, 2H), 7.91 (s, 1H), 8.15 - 8.21 (m, 1H), 8.47 (d, 1H, J = 6.9), 8.63 - 8.68 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 114.8, 119.5, 121.2, 121.9, 123.7, 125.4, 127.8, 128.0, 129.1, 129.8, 130.1, 132.6, 135.8, 144.7; MS EI *m/z* (rel. int.) 340 (M^+, 55), 207 (49), 179 (100), 152 (5), 69 (8) HRMS *m/z* calcd for $C_{16}H_{11}F_3O_3S$, 340.0381, found 340.0387.



1-Methylphenanthrene (128) The stirred mixture of 1-Methylphenanthryl-9 trifluoromethanesulfonate (0.340 g, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3, (10.5 mg, 0.04 mmol) Et_3N (0.303 g, 3.00 mmol) and HCO_2H (0.08 ml, 92 mg, 2.00 mmol) in DMF (10 mL) was heated at 60 – 70 °C for 30 min. After which, it was cooled down to room temperature and added water. The resulting aqueous solution was extracted with Et_2O. The combined organic layer was dried (Na_2SO_4) and concentrated to dryness, followed by flash chromatography (hexane) afforded 96 mg (50%) of product as a colorless crystal. mp 118 – 119 °C (hexane); IR (neat) 1598 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.87 (s, 3H), 7.56 (d, 1H, J = 7.2), 7.63 – 7.69 (m, 3H), 7.88 (d, 1H, J = 9.2), 8.01 (d, 1H, J = 9.2), 8.04 (t, 1H, J = 9.2), 8.69 (d, 1H, J = 8.1), 8.81 (d, 1h, J = 8.1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 121.4, 123.4, 123.5, 126.7, 127.1, 127.2, 128.3, 129.0, 130.9, 131.3, 132.2, 135.4; MS EI *m/z* (rel. int.) 192 (M^+, 100), 165 (23), 150 (4), 139 (4), 95 (28), 83 (24)

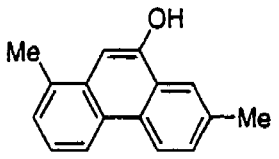


Pinacolo[2-(N, N-diethylcaarboxamido)-4-methylphenyl]boronate (131) According to method A, to a solution of N, N-diethyl 3-methylbenzamide (1.91 g, 10.0 mmol), s-BuLi (9.60 mL of 1.25M solution ,12.0 mmol), and TMEDA (1.07mL, 1.39 g, 12.0 mmol) was added $B(OMe)_3$ (2.73 mL, 2.50 g, 24.0 mmol). Normal workup afforded thick oil which was stirred with pinacol (2.83 g, 24.0 mmol) and Mg_2SO_4 in dry CH_2Cl_2. After filtered and concentrated, the crude product was purified by flash chromatography (1:3) to afforded 2.21 g (70%) of product as a colorless oil. IR (neat) 1633, 1432, 1350 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 7.2), 1.15 (s, 12H), 1.20 9t, 3H, J = 7.2), 2.20 (s, 3H), 3.02 (q, 2H, J = 7.2), 3.41 (q, 2H, J = 7.2), 6.90 (s, 1H), 7.02 (d, 1H, J = 8.1), 7.56 (d, 1H, J = 8.1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 14.4, 22.3, 25.5, 38.8, 43.6, 84.2, 123.1, 126.8, 129.2, 136.2, 141.7, 144.1, 172.5; MS EI *m/z* (rel. int.) 316 (M^+, 25), 302 (13), 259 (100), 218 (18), 174 (18), 144 (18), 177 (18), 83 (7), 55 (4); HRMS *m/z* calcd for $C_{18}H_{27}BNO_3$, 316.2093, found 316.2084.

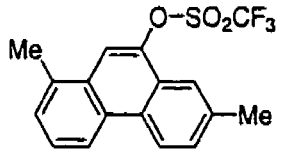


N, N-Diethyl 3, 2' 3'-trimethylbiphenyl-2-carboxamide (132) According to method B, 1-bromo-2, 3-dimethylbenzene (1.36 ml, 1.85 g, 10.0 mmol) was coupled with Pinacolo[2-(N, N-diethylcaarboxamido)-4-methylphenyl]boronate (3.16 g, 10 mmol) in the presence of $Pd(PPh_3)_4$ (0.185g, 0.16 mmol). Normal workup followed by flash chromatography (1:5) afforded 1.89 g (64%) of product as a colorless crystal. mp 66 – 68 °C (EtOAc); IR (neat) 1630 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.65 (br, 3H), 0.75 – 1.00 (br, 3H), 2.28 (s, 3H), 2.48 (s, 3H), 2.50 – 3.30 (br, 4H), 3.65 – 3.85 (s, 1H), 6.98 –

7.23 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 13.9, 17.4, 20.8, 21.3, 38.0, 42.7, 124.7, 127.4, 129.2, 130.0, 130.9, 131.6, 136.9, 137.1, 170.4; MS EI *m/z* (rel. int.) 295 (M^+, 35), 222 (100), 177 (48), 180 (57), 165 (65), 74 (47); HRMS *m/z* calcd for $C_{20}H_{25}NO$, 295.1936, found 295.1932.

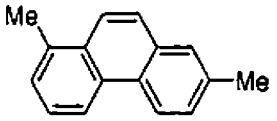


1, 7-Dimethyl-9-phenanthrol (133) According to method C, treatment of N, N-Diethyl 3, 2', 3'-dimethylbiphenyl-2-carboxamide (2.95 g, 10 mmol) with LDA (25.0 mmol) for 30 min followed by acidification, normal workup and flash chromatography (hexane) afforded 1.78 g (80%) of product as a colorless crystal. mp 203 – 205 °C (CH_2Cl_2); IR (KBr) 3351 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 2.54 (s, 3H), 2.59 (s, 3H), 7.20 (s, 1H), 7.30 – 7.39 (m, 2H), 7.51 (d, 1H, J = 9.0), 8.07 (s, 1H), 8.49 (d, 1H, J = 9.0), 8.65 (d, 1H, J = 9.0); ^{13}C NMR (75 MHz, DMSO-d_6) δ 20.9, 22.4, 102.5, 121.8, 123.1, 124.0, 124.2, 126.4, 126.8, 128.6, 129.9, 130.4, 132.4, 133.0, 136.6, 151.9; MS EI *m/z* (rel. int.) 222 (M^+, 100), 207 (7), 194 (13), 179 (41), 110 (3), 89 (3) ; HRMS *m/z* calcd for $C_{16}H_{14}O$, 222.1045, found 222.1040

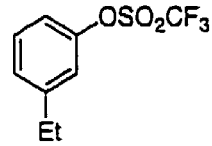


1, 7-Dimethylphenanthryl-9 trifluoromethanesulfonate (134) According to method D, to a solution of 1, 7-dimethyl-9-phenanthrol (1.11 g, 5.00 mmol) and 2, 6-lutidine (0.69 mL, 0.64 g, 6.00 mmol) in CH_2Cl_2 was added triflic anhydride (1.01 ml, 1.69 g, 6.00 mmol). Normal workup followed by flash chromatography (hexane) afforded 1.42 (90%) g of

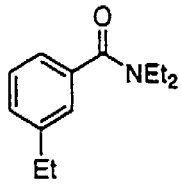
product as a colorless crystal. mp 74 – 75 °C (EtOAc); IR (KBr) 1421, 1215, 1140 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.64 (s, 3H), 2.75 (s, 3H), 7.49 (d, 1H, J = 7.2), 7.57 – 7.64 (m, 2H0, 7.72 (s, 1H0, 7.74 (s, 1H), 8.53 (d, 1H, J = 8.4), 8.63 (d, 1H, J = 8.4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 22.5, 115.0, 121.4, 121.7, 123.9, 125.8, 128.0, 128.9, 129.8, 130.6, 130.8, 136.0, 138.4, 144.9; MS EI *m/z* (rel. int.) 354 (M^+, 38), 221 (39), 193 (100), 178 (20), 69 (7); HRMS *m/z* calcd for $C_{17}H_{13}O_3F_3S$, 354.0538, found 354.0545.



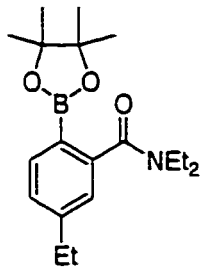
1, 7-Dimethylphenanthrene (135) The stirred mixture of 1, 7-dimethylphenanthryl-9 trifluoromethanesulfonate (0.354 g, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3, (10.5 mg, 0.04 mmol) Et_3N (0.303 g, 3.00 mmol) and HCO_2H (0.08 mL, 92 mg, 2.00 mmol) in DMF (10 mL) was heated at 60 – 70 °C for 30 min. After which, it was cooled down to room temperature and added water. The resulting aqueous solution was extracted with Et_2O. The combined organic layer was dried (Na_2SO_4) and concentrated to dryness, followed by flash chromatography (hexane) afforded 175 mg (85%) of product as a colorless crystal. mp 83 – 84 °C (hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (s, 3H0, 2.78 (s, 3H), 7.43 –7.58 (m, 3H), 7.71 (s, 1H), 7.75 (d, 2H, J = 9.1), 7.90 (d, 1H, J = 9.1), 8.70 (d, 1H, J = 8.4), 8.62 (d, 1H, J = 8.4); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 21.9, 121.2, 123.4, 126.5, 126.9, 127.8, 128.8, 129.0, 130.9, 131.0, 132.3, 135.3, 136.6; MS EI *m/z* (rel. int.) 206 (M^+, 100), 192 (18), 179 96), 166 (6), 152 (5), 102 (6), 88 (5); HRMS *m/z* calcd for $C_{16}H_{14}$, 206.1096, found 206.1090.



3-Ethylphenyl trifluoromethanesulfonate (137) According to method D, to a solution of 3-ethylphenol (1.22 g, 10.00 mmol) and 2, 6-lutidine (1.40 ml, 1.28 g, 12.00 mmol) in CH_2Cl_2 (100 mL) was added triflic anhydride (2.01 ml, 3.38 g, 12.00 mmol). Normal workup followed by flash chromatography (hexane) afforded 2.28 g (90%) of product as a colorless oil. IR (neat) 1424, 1214, 1143 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, 3H, J = 8.4), 2.73 (q, 3H, J = 8.4), 7.14 (s, 1H), 7.19 – 7.34 (m, 2H), 7.38 (t, 1H, J = 15.0); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 28.9, 118.8, 119.2, 129.4, 130.4, 147.6, 150.1; MS EI *m/z* (rel. int.) 254 (M^+, 100), 174 (75), 121 (47), 91 (90), 77 (22), 65 (8)

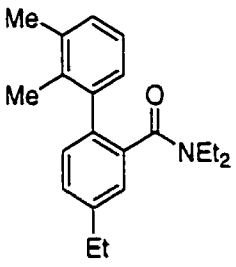


N, N-Diethylbenzamide (138) The stirred mixture of 3-Ethylphenyl trifluoromethanesulfonate (0.254 g, 1.00 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), DPPF (33 mg, 0.06 mmol) Et_3N (.42 ml, 0.303 g, 2.00 mmol) and Et_2NH (2.06 ml, 1.46 g, 20.0 mmol) in DMF (10 ml) was heated at 60 ~ 70 °C for 12 h to afford yellow oil. IR (neat) 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 – 1.10 (br, 1H), 1.17 (t, 3H, J = 7.2), 2.60 (q, 2H, J = 7.2), 3.17 (s, 2H), 3.48 (s, 2H), 7.08 –7.27 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 14.6, 15.7, 29.1, 39.5, 43.6, 123.7, 126.7, 128.9, 137.6, 144.7, 171.8; MS EI *m/z* (rel. int.) 205 (M^+, 58), 176 (7), 133 (100), 105 (28), 77 (17)



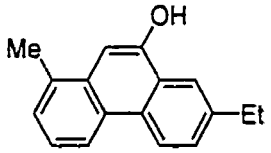
Pinacolo[2-(N, N-diethylcaarboxamido)-4-ethylphenyl]boronate (139) According to method A, to a solution of N, N-diethyl 3-ethylbenzamide (2.05 g, 10.0mmol), s-BuLi (9.60 ml of 1.25M solution

,12.0mmol), and TMEDA (1.07ml, 1.39g, 12.0mmol) was added $B(OMe)_3$ (2.73 ml, 2.50 g, 24.0 mmol). Normal workup afforded thick oil which was stirred with pinacol (2.83 g, 24.0 mmol) and Mg_2SO_4 in dry CH_2Cl_2. After filtered and concentrated, the crude product was purified by flash chromatography (1:3) to afforded 2.51 g (76%) of product as a colorless oil. IR (neat) 1635, 1432, 1354 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, 3H, J = 7.5), 1.20 (t, 6H, J = 8.1), 1.28 (s, 2H), 2.63 9q, 2H, J = 7.5), 3.14 (q, 2H, J = 8.1), 3.55 (q, 2H, J = 8.1), 7.06 (s, 1H), 7.15 – 7.22 (m, 2H), 7.72 (d, 2H, J = 7.5); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9, 14.1, 15.6, 25.2, 38.5, 43.3, 83.9, 125.4, 127.7, 135.9, 143.9, 149.9, 171.0; MS EI *m/z* (rel. int.) 331 (M^+, 21), 273 (100), 232 (16), 188 (6), 158 (7), 105 (8), 55 (4); HRMS *m/z* calcd for $C_{19}H_{30}BNO_3$, 331.2319, found 331.2321.

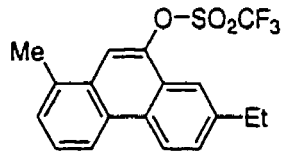


N, N-Diethyl 3-ethyl-2' 3'-dimethylbiphenyl-2-carboxamide (142) According to method B, 1-bromo-2, 3-dimethylbenzene (1.36 ml, 1.85 g, 10.0 mmol) was coupled with Pinaco[2-(N, N-diethylcaarboxamido)-4-ethylphenyl]boronate (3.31 g, 10 mmol) in the presence of $Pd(PPh_3)_4$ (0.185g, 0.16 mmol). Normal workup followed by flash chromatography (1:5) afforded 1.85 g (60%) of product as a viscous oil. IR (neat) 1634 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.68 (s, 3H), 0.75-1.04 (br, 3H), 1.28 (t, 3H, J = 7.8), 2.08 (s, 3H), 2.27 (s, 3H), 2.72 (q, 2H, J = 7.8), 2.75-3.30 (br, 4H), 3.73 (s, 1H), 6.96-7.25 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 14.1, 15.6, 17.6, 20.9, 28.8, 38.2, 42.8, 125.4, 126.8, 128.0, 129.4, 130.1, 135.1, 137.2, 143.5, 170.8; MS EI *m/z* (rel. int.) 309

(M^+, 100), 280 (13), 237 (15), 209 (8), 178 (18), 165 (15), 74 (35); HRMS *m/z* calcd for $C_{21}H_{27}NO$, 309.2093, found 309.2086.

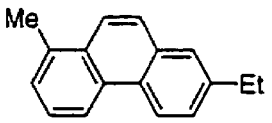


7-Ethyl-1-methyl-9-phenanthrol (143) According to method C, treatment of N, N-Diethyl 3-ethyl-2', 3'-dimethylbiphenyl-2-carboxamide (3.09 g, 10 mmol) with LDA (25.0 mmol) for 30 min followed by acidification, normal workup and flash chromatography (hexane) afforded 2.24 g (95%) of white powder. mp 192 – 195 °C (CH_2Cl_2); IR (neat) 3306 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, J = 8.1), 2.60 (s, 3H), 2.84 (q, 2H, J = 8.1), 7.25 (s, 1H), 7.28-7.38 (m, 2H), 7.51 (d, 1H, J = 8.4), 8.12 (s, 1H), 8.47 (d, 1H, J = 8.1), 8.63 (d, 1H, J = 8.1); ^{13}C NMR (75M Hz, $CDCl_3$) δ 16.4, 20.5, 29.2, 102.1, 121.5, 123.7, 124.0, 126.1, 126.6, 127.4, 128.2, 128.4, 130.4, 132.2, 132.7, 142.5, 151.8; MS EI *m/z* (rel. int.) 236 (M^+, 100), 221 (65), 207 (10), 193 (15), 179 (10), 165 (4), 89 (3). HRMS *m/z* calcd for $C_{17}H_{16}O$, 236.1201, found 236.1205.

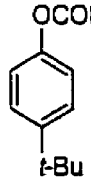


7-Ethyl-1-methylphenanthryl-9 trifluoromethanesulfonate (144) According to method D, to a solution of 7-ethyl-1-methyl-9-phenanthrol (1.18 g, 5.00 mmol) and 2, 6-lutidine (0.69 ml, 0.64 g, 6.00 mmol) in CH_2Cl_2 was added triflic anhydride (1.01 mL, 1.69 g, 6.00 mmol). Normal workup followed by flash chromatography (hexane) afforded 1.20 g (95%) of product as a colorless crystal. mp 61 – 62 °C (EtOAc); IR (neat) 1421, 1208, 1135 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 3H), 2.75 (q, 2H, J = 7.5), 7.48 (d, 1H, J = 7.2),

7.57-7.66 (m. 2H), 7.91 (s, 1H), 7.97 (s, 1H), 8.52 (d, 1H, J = 9.0), 8,64 (d, 1H, J = 9.0) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7, 20.1, 29.4, 114.7, 120.1, 121.1, 121.4, 123.7, 129.3, 129.5, 130.2, 130.7, 135.7, 144.3, 144.7; MS EI *m/z* (rel. int.) 368 (M^+, 35), 235 (45), 207 (100), 192 (18), 165 (3), 69 (7); HRMS *m/z* calcd for $C_{18}H_{15}F_3O_3F$, 368.0684, found 368.0688.

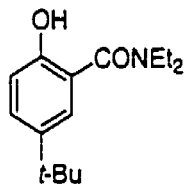


7-Ethyl-1-methylphenanthrene (145) The stirred mixture of 7-ethyl-1-methylphenanthryl-9 trifluoromethanesulfonate (0.368 g, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3, (10.5 mg, 0.04 mmol) Et_3N (0.42 ml, 0.303 g, 3.00 mmol) and HCO_2H (0.08 ml, 92 mg, 2.00 mmol) in DMF (10 ml) was heated at 60 – 70 °C for 30 min. After which, it was cooled down to room temperature and added water. The resulting aqueous solution was extracted with Et_2O. The combined organic layer was dried (Na_2SO_4) and concentrated to dryness, followed by flash chromatography (hexane) afforded 202 mg (92%) of product as a colorless crystal. mp 92 – 93 °C (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (t, 3H, J = 7.5), 2.84 (s, 3H), 2.96 (q, 2H, J = 7.5), 7.48-7.65 (m, 3H), 7.78 (s, 1H), 7.81 (d, 1H, J = 9.0), 8.01 (d, 1H, J = 9.0), 8.63 (d, 1H, J = 9.0), 8.69 (d, 1H, J = 9.0); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1, 20.4, 29.2, 121.2, 123.2, 123.4, 126.5, 127.0, 127.2, 127.7, 127.8, 129.2, 130.8, 130.9, 132.3, 135.2, 142.9; MS EI *m/z* (rel. int.) 220 (M^+, 100), 205 (73), 189 (15), 178 (3), 165 (3), 101 (4); HRMS *m/z* calcd for $C_{17}H_{16}$, 220.1252, found 220.1255.



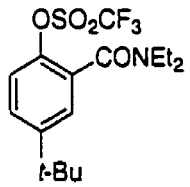
N, N-Diethyl 4-*tert*-butylphenyl carbamate (154) To sodium hydride (0.48 g, 60%, 12 mmol) in anhydrous THF (20 ml) was added 4-tert-

butylphenol (1.50 g, 10 mmol). After stirring for 1 h, hydrogen evolution ceased. Diethylcarbamyl chloride (1.51 ml, 1.62 g, 12 mmol) was added and stirred at room temperature for 2 h. Normal workup followed by recrystallization in CH_2Cl_2 afforded 1.49 g (60%) of product as a colorless crystal. mp 77 – 78 °C (CH_2Cl_2); IR (neat) 1706, 1480, 1402, 1277, 1211cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 6H), 1.34 (s, 9H), 3.43 (s, 4H), 7.04-7.10 (m, 2H), 7.36-7.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 14.6, 31.8, 34.7, 42.2, 42.6, 121.4, 126.4, 148.1, 149.6, 154.8; MS EI *m/z* (rel. int.) 249 (M^+, 35), 163 (2), 146 (2), 135 (3), 100 (100), 72 (7) HRMS *m/z* calcd for $C_{15}H_{23}NO_2$, 249.1729, found 249.1736.

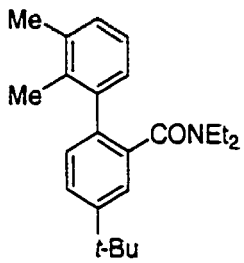


N, N-Diethyl 4-*tert*-butyl-2-hydroxybenzamide (153) A solution of N, N-Diethyl 4-*tert*-butylphenyl carbamate (2.49 g, 10.0 mmol), dissolved in anhydrous THF (20 ml) was added dropwise to a solution of s-BuLi (9.6 ml of 1.25 M solution, 12.0 mmol) and TMEDA (1.07 ml, 1.39 g, 12.0 mmol) in andydrous THF (30 ml) at –78 C. The resulting mixture was stirred at –78 C for 1 h and increased to room temperature overnight. Normal workup followed by recrystallizaion in CH_2Cl_2 afforded 1.37 g (55%) of product as a colorless crystal. mp 133 – 135 °C (CH_2Cl_2); IR (neat) 3142, 1595, 1268cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28(s, 3H), 1.29(s, 9H), 1.33 (s, 3H), 3.51(q, 4H, J = 7.2), 6.92 (d, 1H, J = 17.1), 7.27 (d, 1H, J = 5.0) 7.34 (dd, 1H, J = 17.1, J = 5.0); ^{13}CNMR (75 MHz, $CDCl_3$) δ13.8, 31.8, 34.4, 42.5, 117.6, 118.1, 124.3, 129.6, 141.4, 156.4, 172.2; MS EI *m/z* (rel. int.) 249 (M^+, 31), 234

(72), 177 (76), 161 (100), 133 (16), 105 (20), 72 (38) HRMS *m/z* calcd for $C_{15}H_{23}NO_2$, 249.1729, found 249.1719.

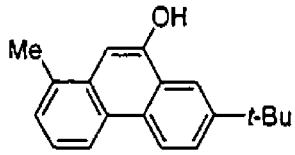


4-*tert*-Butyl-2-(N, N-diethylcarboxamido)phenyl trifluoromethanesulfonate (152) According to method D, to a solution of N, N-Diethyl 4-*tert*-butyl-2-hydroxybenzamide (2.49 g, 10.0 mmol) and pyridine (0.97 ml, 0.95 g, 12.0 mmol) in CH_2Cl_2 was added triflic anhydride (2.01 ml, 3.38 g, 12.0 mmol). Normal workup followed by flash chromatography (1:5) afforded 2.48 g (65%) of product as a colorless oil. IR (neat) 1645, 1426, 1215 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (t, 3H, J = 7.2), 1.17 (t, 3H, J = 7.2), 1.30 (s, 9H), 3.16 (q, 2H, J = 7.2), 3.40 –3.70 (br, 2H), 7.23 9d, 1H, J = 8.6), 7.37 (d, 1H, J = 2.1), 7.40 (dd, 1H, J = 8.6, 2.1); ^{13}C NMR ($CDCl_3$) δ 12.7, 14.2, 31.4, 35.1, 39.5, 43.3, 118.8, 121.5, 125.8, 128.0, 130.7, 143.3, 152.1, 166.2; MS EI *m/z* (rel. int.) 382 (M^+, 71), 309 (100), 233 (38), 161 (73), 72 (69) HRMS *m/z* calcd for $C_{16}H_{22}F_3NO_4S$, 381.1222, found 381.1234.

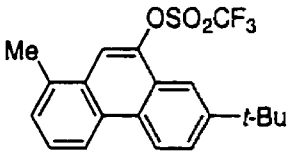


N, N-Diethyl 3-*tert*-butyl-2' 3'-trimethylbiphenyl-2-carboxamide (151) According to method B, 2, 3-dimethylphenylboronic acid (1.50 g, 10.0 mmol) was coupled with 4-*tert*-Butyl-2-(N, N-diethylcarboxamido)phenyl

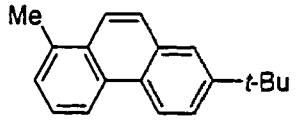
trifluoromethanesulfonate (3.82 g, 10 mmol) in the presence of $Pd(PPh_3)_4$ (0.185g, 0.16 mmol). Normal workup followed by flash chromatography (1:5) afforded 2.76 g (82%) of product as a viscous oil. IR 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.69 (t, 3H, J = 7.2), 0.90 (br, 3H), 1.35 (s, 9H), 2.10 (s, 3H0, 2.27 (s, 3H), 2.50 – 3.30 (br, 3H), 3.60 –3.90 (br, 3H), 6.80 – 7.43 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 12.2, 13.8, 24.1, 31.6, 34.9, 38.3, 124.4, 125.4, 126.5, 127.6, 128.4, 129.3, 134.7, 137.1, 142.6, 150.3, 151.6, 155.5, 171.1; MS EI *m/z* (rel. int.) 337 (M^+, 97), 322 (7), 264 (100), 250 (37), 209 (40), 181 (12), 165 (17), 74 (32) HRMS *m/z* calcd for $C_{23}H_{31}NO$, 337.2406, found 337.2398.



7-*tert*-Butyl-1-methyl-9-phenanthrol (150) According to method C, treatment of N, N-Diethyl 3-*tert*-butyl-2', 3'-dimethylbiphenyl-2-carboxamide (3.37 g, 10 mmol) with LDA (25.0 mmol) for 30 min followed by acidification, normal workup and flash chromatography (hexane) afforded 2.38 g (90%) of white powder. mp 165 – 168 °C (CH_2Cl_2); IR (KBr) 3466 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (s, 9H), 2.63 (s, 3H), 5.81 (s, 1H), 7.20 (s, 1H), 7.38 – 7.45 (m, 2H), 7.81 (dd, 1H, J = 8.1, 2.1), 8.36 (d, 1H, J = 2.1), 8.49 (d, 1H, J = 8.1), 8.64 (d, 1H, J = 9.0); ^{13}C NMR ($CDCl_3$) δ 20.6, 31.1, 35.7, 103.4, 118.4, 121.3, 123.6, 124.3, 125.5, 126.2, 127.3, 128.2, 130.5, 131.9, 133.4, 149.9, 150.3; MS EI *m/z* (rel. int.) 264 (M^+, 100), 250 (50), 232 (13), 221 (22), 194 (13), 179 (12), 165 (9), 11 (8) HRMS *m/z* calcd for $C_{19}H_{20}O$, 264.1514, found 264.0888.



7-*tert*-Butyl-1-methylphenanthryl-9 trifluoromethanesulfonate (160) According to method D, to a solution of 7-*tert*-butyl-1-methyl-9-phenanthrol (1.32 g, 5.00 mmol) and 2, 6-lutidine (0.69 ml, 0.64 g, 6.00 mmol) in CH_2Cl_2 was added triflic anhydride (1.01 ml, 1.69 g, 6.00 mmol). Normal workup followed by flash chromatography (hexane) afforded 1.72 g (87%) of product as a colorless crystal. mp 103 – 104 °C (EtOAc); IR (KBr) 1423, 1207, 1139 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61 (s, 9H), 2.73 (s, 3H0, 7.45 (d, 1H, J = 7.2), 7.56 (t, 1H, J = 8.4), 7.88 9dd, 1H, J = 9.0, 1.8), 7.93 (s, 1H), 8.27 (d, 1H, J = 1.8), 8.44 (d, 1H, J = 8.1), 8.66 (d, 1H, J = 9.0); ^{13}C NMR ($CDCl_3$) δ 20.0, 31.6, 35.5, 114.7, 117.6, 119.4, 121.1, 123.6, 125.1, 126.9, 127.7, 128.7, 129.6, 130.1, 130.6, 135.6, 144.9, 151.2; MS EI *m/z* (rel. int.) 396 (M^+, 68), 381 (14), 263 (100), 236 (75), 220 (32), 205 (16), 179 (8), 69 (11) HRMS *m/z* calcd for $C_{20}H_{19}F_3O_3S$, 396.1007, found 396.1008.



7-*tert*-Butyl-1-methylphenanthrene (149) The stirred mixture of 7-ethyl-1-methylphenanthryl-9 trifluoromethanesulfonate (0.396 g, 1.00 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3, (10.5 mg, 0.04 mmol) Et_3N (0.42 ml, 0.303 g, 3.00 mmol) and HCO_2H (0.08 ml, 92 mg, 2.00 mmol) in DMF (10 ml) was heated at 60 – 70 °C for 30 min. After which, it was cooled down to room temperature and added water. The resulting aqueous solution was extracted with Et_2O. The combined organic layer was dried (Na_2SO_4) and concentrated to dryness, followed by flash chromatography (hexane) afforded 248 mg (95%) of product as a colorless

crystal. mp 126 – 127 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 1.74 (s, 9H), 2.96 (s, 3H), 7.64 (d, 1H, J = 7.4), 7.74 (t, 1H, J = 7.5), 7.93 (dd, 1H, J = 8.6, 1.8), 7.98 (d, 1H, J = 9.3), 8.14 (d, 1H, J =9.2), 8.77 (d, 1H, J = 8.6), 8.82 (d, 1H, J = 8.8); ^{13}C NMR ($CDCl_3$) δ 20.5, 32.0, 35.3, 121.7, 123.7, 125.8, 126.9, 127.9, 128.2, 129.4, 131.2, 131.5, 132.6, 135.6, 150.0; MS EI *m/z* (rel. int.) 248 (M^+, 100), 234 (95), 218 (10), 205 (13), 189 (7), 178 (3)) HRMS *m/z* calcd for $C_{19}H_{20}$, 248.1565, found 248.1564.

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