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Large Scale Synthesis and Derivatization of Corannulene: The Smallest Buckybowl

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LARGE SCALE SYNTHESIS AND DERIVATIZATION OF CORANNULENE – THE SMALLEST BUCKYBOWL

By

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LARGE SCALE SYNTHESIS AND DERIVATIZATION OF CORANNULENE –

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Candidate for Degree of Master of Science

The major part of my thesis work includes large scale production of corannulene, $C_{20}H_{10}$, a bowl-shaped Polycyclic Aromatic Hydrocarbon. Over the road towards corannulene via tetramethylfluoranthene, we improved the existing multistep procedure as follows:

-Palladium catalyzed large scale debromination of tetrabromocorannulene was accomplished within thirty minutes of brief reflux, in contrast to original Zn/KI method which took weeks for completion.

Alternative palladium catalyzed ring closure methods where tested for synthesis of 1,6,7,10-tetramethylfluroanthene (25), key intermediate in corannulene production. A structurally similar system, 7,10-dimethylfluoranthene was synthesized by this new approach in low yield. Unfortunately, we did not succeed in the synthesis of 25 using similar methodology, since our attempts to produce the prerequisite 2,7-dimethyl-1-naphthylboronic acid failed.

Elaboration of corannulene core by coupling tetrabromocorannulene with *p*-methoxyphenylboronic acid and *p*-methoxycarbonylphenylboronic acid under Suzuki conditions resulted in formation of two vital intermediates which can be used to build capsules with corannulene caps.

DEDICATION

I would like to dedicate this research to my parents, sisters and brothers.

ACKNOWLEDGEMENTS

I sincerely thank Dr. Andrzej Sygula and Mrs. Renata Sygula for all their guidance (and patience) throughout my graduate education. I have benefited greatly from their valuable advice, writing skills and deep insights into the broad area of science. While writing this thesis, I think about the time I went to his office with no positive results and feeling depressed; at those times they both encouraged me and showed me other ways to deal with the current problems I was facing during my research. I really like Dr. Sygula's proverb "If I know what's going on in the reaction probably I would sit next to God". I really appreciate the way he changes a person's thinking in just a few minutes.

I would also like to thank Dr. Foster my graduate committee member and a great graduate coordinator. He welcomes every international student with a big smile and does his best to guide them in their hard times. I would also like to extend my sincere thanks to Dr. Michael Koscho for his constant and continuous helpful suggestions.

Big thanks are due to William Holmes for his help with mass spectrometry.

Further I would like to thank my Father for encouraging me time to time, my Mom, sister and family members for their love and care for me.

Finally I would like to thank all my friends out there who helped me to stay in high spirits and tried to pacify me when I was under pressure with chemistry and other problems.

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LIST OF ABBREVIATIONS

BBr_3	Boron tribromide
$B(OMe)_3$	Trimethylborate
Cs_2CO_3	Cesium carbonate
DBU	1,8-Diazabicyclo[5,4,0]-undec-7-ene
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMAc	Dimethylacetamide
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
ETSNa	Sodiumthioethoxide
FVP	Flash vacuum pyrolysis
IMes. HCl	1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride
IPA	Isopropyl alcohol
KO^tBu	Potassium-*ter*-butoxide
NBS	N-Bromosuccinimide
NHC	N-heterocylic carbenes
$Ni(dppe)Cl_2$	[1,2-bis(diphenylphosphino)ethane]nickel (II) chloride
NMP	1-Methyl-2-pyrrolidinone
OMe	Methoxy

MOM	Methoxymethyl
PPh_3	Triphenylphosphine
PCy_3	Tricyclohexylphosphine
P^tBu_3	Tri-t-butylphosphine
IMes. HCl	1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride
$Pd(PPh_3)_4$	Tetrakis(triphenylphosphine)palladium (0)
(IPr)Pd(allyl)Cl	Allylchloro[1,3-bis(2,6-di-i-propylphenyl)imidazol-2-ylidene]palladium(II)
$Pd_2(dba)_3$	Tris(dibenzylideneacetone)palladium (0)
$Pd(OAc)_2$	Palladium acetate
Tf_2O	Triflic anhydride
THF	Tetrahydrofuran

CHAPTER I

INTRODUCTION

Polycyclic Aromatic Hydrocarbons (PAHs), also called polyarenes, form a separate class of structurally similar organic compounds, usually characterized by the presence of fused benzene rings. PAHs are abundantly found in fossil fuels like coal and crude oil.[1] Not only their presence is detected in the air we breathe, the food we eat and the water we drink[2,3] but also in interstellar space.[4,5] Studies of polycyclic aromatic compounds have been long standing and an ongoing research effort have added new dimensions in the development of fuels, lubricants, chemicals and carbonaceous materials. The recent discovery of fullerenes resurged research activity in carbon rich compounds including PAHs even more.

Buckminsterfullerene (C_{60}), a new allotropic form of elemental carbon, is an important finding in the recent past. It was discovered in mid 1980's by H. W. Kroto, R. F. Curl and R. E. Smalley during their studies of nucleation in a carbon plasma formed by laser evaporation of graphite.[6,7] Named as the molecule of the year in 1991, it received tremendous prominence and a Nobel Prize was awarded to its discoverers. [8-10]

Carbon atoms in fullerenes or buckyballs are sp^2 hybridized and form geodesic cages. The foremost member of the fullerene family, buckminsterfullerene (C_{60}) exhibits a closed carbon framework with 20 hexagons and 12 pentagons (Figure 1). Its unusual curved structure attracted researchers from all branches of science with a belief that it could play a vital role in the emerging field of nanotechnology and material science. In addition, properties like low temperature superconductivity and its potential application in medicine as drug markers [11] motivated chemists further to explore this exotic class of carbon allotropes.

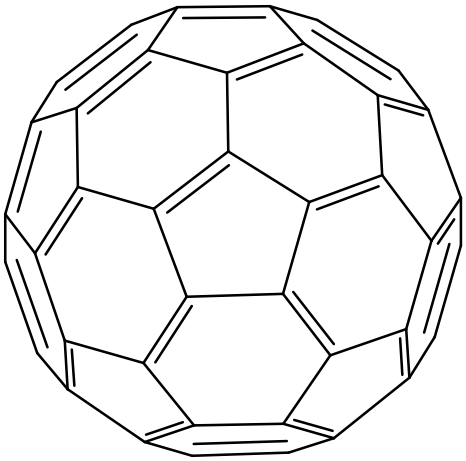
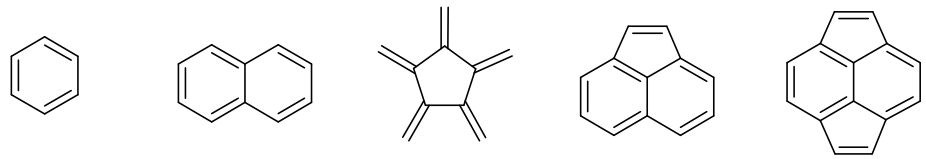


Figure 1: Buckminsterfullerene (C_{60}).

Despite significant efforts made by scientists worldwide, buckyballs have not received any widespread applications. However its discovery certainly sparked renewed interest in curved surfaced polycyclic aromatic hydrocarbons (PAHs) known as fullerene fragments or buckybowls.[12-20] Several familiar carbon frameworks may be identified as the substructures on the surface of C_{60} i.e. benzene (1), naphthalene (2), radialene (3),

acenaphthylene (4) and pyracylene (5) (Figure 2). [20] All molecules in Figure 2 are planar; curvature is attained only when a C_{20} fragment of fullerene is reached. These curved surface PAHs structurally related to fullerenes are called buckybowls. Bowl shaped PAHs have received considerable attention for variety of reasons such as:



1 **2** **3** **4** **5**

Figure 2: Substructures which map out on the surface of C_{60}.

a) It would be interesting to study at what stage of progression in size would these buckybowls exhibit fullerene like chemistry.

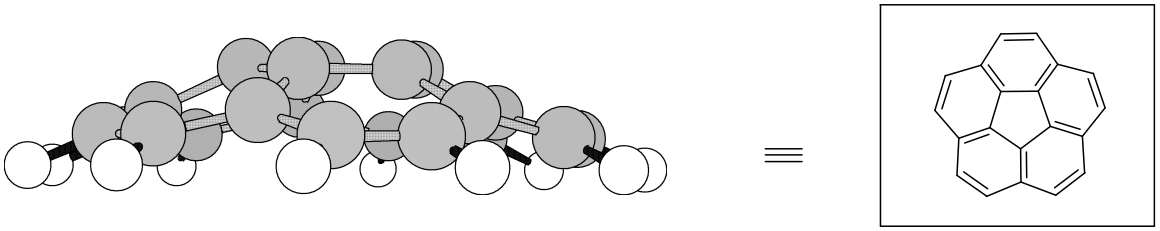
b) Unlike fullerene, these bowl shaped PAHs provide an opportunity to study convex vs. concave preferences for metal complex formation.

c) Alkali metal doped fullerenes act as superconductors at low temperature so one would wonder whether buckybowls would exhibit similar behavior.

d) Industrial production of C_{60} will generate huge fullerene "waste". During decomposition they may undergo fragmentation to form buckybowls and enter the environment. Hence in such a case knowledge about their physical and chemical properties would be important.

e) Buckybowls are potential substrates for the synthesis of fullerenes and nanotubes.

Thus due to above reasons and many more, significant research activities began in 1990's when buckybowls became more accessible. Reason (e) stated above needs further explanation. Presently, C_{60} is manufactured on a metric ton scale every year.[21-23] It is prepared either by vaporization of graphite in an electric arc or by combusting carbon rich materials. Higher fullerenes like C_{70}, C_{84} are found in small impurities in the C_{60} rich sooth formed by the vaporization of graphite. However, one thousand different isomeric fullerenes with 100 carbon atoms or less are possible by following the pentagon rule (no two pentagons abutting each other) and each may exhibit some remarkable properties.[24] To test these possibilities they should be synthesized and in this regard buckybowls could prove to be the best precursors in their total synthesis.



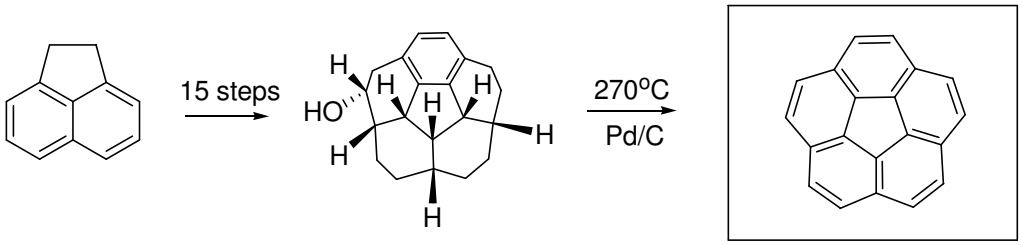
6

Figure 3: Corannulene (6).

The smallest buckybowl, corannulene ($C_{20}H_{10}$) (6, Figure 3), was first synthesized by Barth and Lawton in 1966 (Scheme 1).[25,26] In spite of its tedious 17 step synthesis, with an overall yield of 0.4%, several important results were reported:

a) The crystal structure determination of 6 confirmed a bowl shaped geometry. The bowl depth defined as the distance between the plane of five membered hub to the plane containing ten peripheral CH atoms was found to be 0.87 A^{o}.[27]

b) The ^{1}H NMR spectrum of 6 is remarkably simple exhibiting a singlet for all ten protons on the rim of corannulene confirming their identical environments.[25,26]



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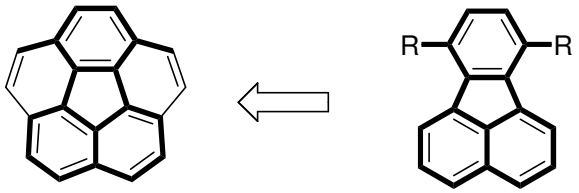
Scheme 1: First synthetic approach towards corannulene synthesis.

However, limited supply of corannulene hindered research activity for more than two decades after its first appearance in 1966. Numerous attempts to improve the synthesis of 6 using fluoranthene derivatives as starting materials ended in failures. Few were published and probably many went unnoticed.[28-31] Failures could be attributed to the strain (because of the bowl shape) present in product 6 when compared to strainless (planar) starting materials, usually 7,10-disubsituted fluoranthenes (Scheme 2).

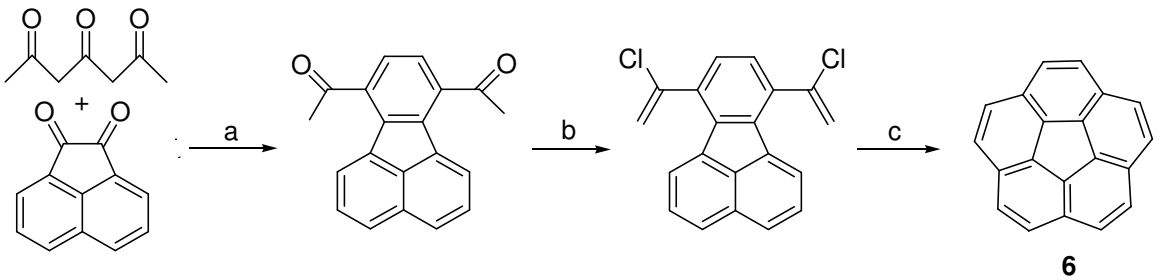


6 **7**

Scheme 2: 7,10-disubsituted derivatives of fluoranthene (**7**) as potential precursors for corannulene synthesis.

Hence, conventional intramolecular ring closure reactions effective for synthesis of planar PAHs are not feasible for synthesis of 6. Instead intermolecular processes like polymerization take place. In spite of many failures fluroanthene derivatives remained attractive precursors for synthesis of 6 due to presence of three six membered rings and a five membered ring present in right orientation (Figure 3).

In a groundbreaking effort Scott and his coworkers in 1991 successfully synthesized corannulene in an overall yield of 10-15% by using Flash Vacuum Pyrolysis (FVP) in the final step.[32] Eventually in 1997 the Scott group invented a convenient three step synthetic procedure starting from heptane-2,4,6-trione and using FVP at the end to obtain corannulene with 30% yield in the final step (Scheme 3).[33]



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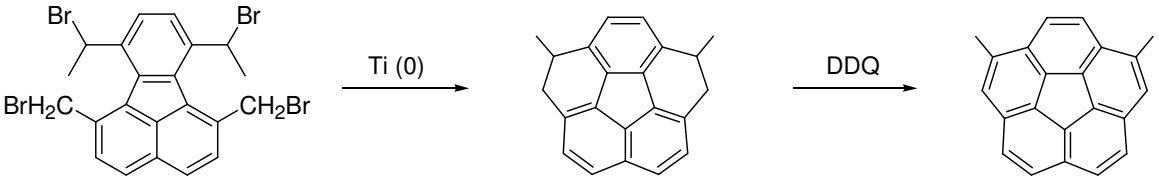
Scheme 3: Three step synthesis of corannulene using FVP

Success of FVP lies in its ability to deliver enough energy in the form of high temperatures (1000-1200 ^{o}C). These high temperatures assists in surmounting the high energy barrier needed for intramolecular ring closures to form strained curved surface buckybowls. In addition, gas phase conditions minimize possibilities for oligo – and/or polymerization. Later several other buckybowls were synthesized using FVP methods.[34-47] However, FVP has some limitations such as: a) Low yields, presumably due to the precursor's decomposition or polymerization before it enters the pyrolysis tube, b) Incompatibility with various functional groups which do not survive such drastic conditions and c) Synthesis of highly strained PAHs by FVP often require temperatures well above 1100 ^{o}C, which may result in technical difficulties like degradation of expensive quartz used in the FVP apparatus. Therefore, it was evident that solution phase methods are required for an efficient synthesis of buckybowls.

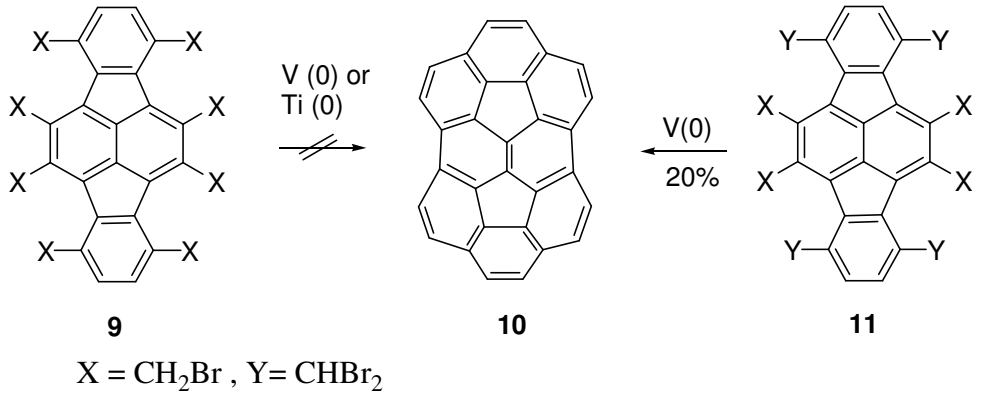
In 1996 the Siegel group reported a successful non-pyrolytic synthesis of 2,5-dimethylcorannulene (7).[48] The twofold intramolecular ring closure was achieved by low valent titanium reduction of 1,6-bis(bromomethyl)-7,10-bis(1-bromoethyl)fluroanthene (8). Subsequent dehydrogenation by 2,3-dichloro-5,6-dicyano-1,4-dibenzoquinone (DDQ) produced 2,5-dimethylcorannulene (7) in a combined two step yield of 18% (Scheme 4).



8 **7**

Scheme 4: Synthesis of dimethylcorannulene (**7**).

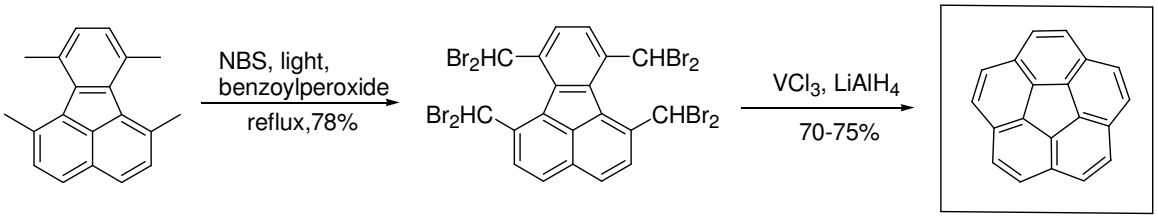
Successful formation of the corannulene framework in Scheme 4 was originally attributed to involvement of high energy organometallic intermediates. More recently, Sygula and Rabideau tried to use Siegel's methodology to synthesize semibuckminsterfullerene (10), but numerous attempts for a fourfold ring closure of 9 by using various reductive systems resulted in failures. [49] On the other hand dodecabromide 11 turned out to produce semibuckminsterfullerene with 20% yield upon reduction with vanadium (0) (Scheme 5).



Scheme 5: Nonpyrolytic synthesis of semibuckministerfullerene (10).

Due to close proximity of methyl groups the parent octamethyl hydrocarbon for 9 and 11 is strongly twisted as proven by X-ray structure determination.[50] This reflects a presence of significant strain in this molecule. Addition of bromine atoms further increases the steric strain. The strain is probably higher in 11 due to the presence of the additional four bromine atoms as compared to 9. Therefore, 11 undergoes intramolecular coupling to form semibuckminsterfullerene (10) more readily than 9.

The above results clearly suggested that: a) dibromomethyl groups are more likely to couple with bromomethyl groups to form a strained aromatic framework and b) the octahydrotetrabromo intermediate, if formed under these conditions, will rapidly lose HBr to produce fully aromatized product in a single step rather than two steps as seen in Siegel's approach for synthesis of 7. Indeed, corannulene (6) was formed from 1,6,7,10-tetrakis(dibromomethyl)fluoranthene (12) in a single step with high yield of 70-75% (Scheme 6). [51]

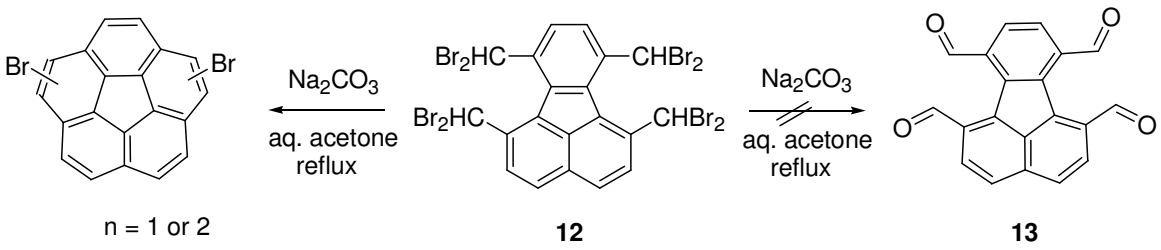


12 **6**

Scheme 6: Synthesis of corannulene (6) via treatement with low valent vanadium.

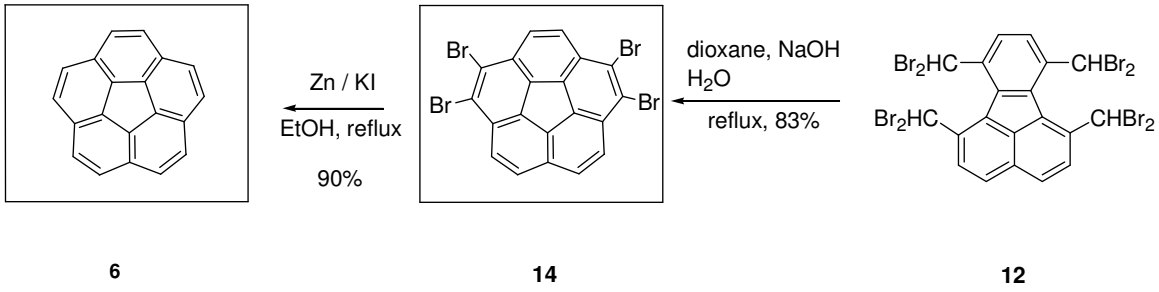
Encouraged by this success, Sygula's group started looking for an alternative synthesis of 6 which involves milder reaction conditions and uses inexpensive reagents resulting in better yields. Original McMurry coupling of dialdehydes or diketones to corresponding cycloalkenes appeared to be a feasible alternative.[52, 53] However, an attempt to convert octabromofluoranthene (12) to the tetraaldehyde (13) resulted in failure. Instead of a characteristic absorption peak from CHO, a complicated pattern of peaks in ^{1}H NMR from 7.1-8.1 ppm was observed. GC/MS and ^{13}C NMR analysis clearly indicated the unexpected formation of mixture of brominated corannulenes (Scheme 7).

Debromination using n-BuLi at -78 ^{o}C produced corannulene in 50-55% yield for the two steps combined.[54]



Scheme 7: Attempted base hydrolysis of 12 leading to unexpected corannulene core formation.

Replacing Na_2CO_3 by NaOH and aqueous acetone by aqueous dioxane with a brief reflux for 15 minutes produced 1,2,5,6-tetrabromocorannulene (14) as a single product with an impressive 83% yield.[55,56] 14 could be derivatized using different coupling agents or can be reduced to corannulene (6) using Zn / KI in ethanol resulting in an excellent yield of 90% in the final step (Scheme 8).[54-56]



Scheme 8: Large scale synthesis of tetrabromocorannulene (14) and corannulene (6).

Thus a convenient large scale synthesis of tetrabromocorannulene (14) followed by an easy reduction resulted in gram scale production of corannulene. The simplicity of this reaction makes it convenient and attractive to work with. This procedure does not

demand any high dilution techniques, does not involve any air sensitive organometallic reagents nor does it require any dry/degassed solvent or deoxygenated environment.

The above section has introduced reader to recent developments in the field of corannulene synthesis. The following chapters will focus my work on the synthesis of tetramethylfluoranthene, corannulene and its derivatives.

CHAPTER II

IMPROVED CORANNULENE SYNTHESIS

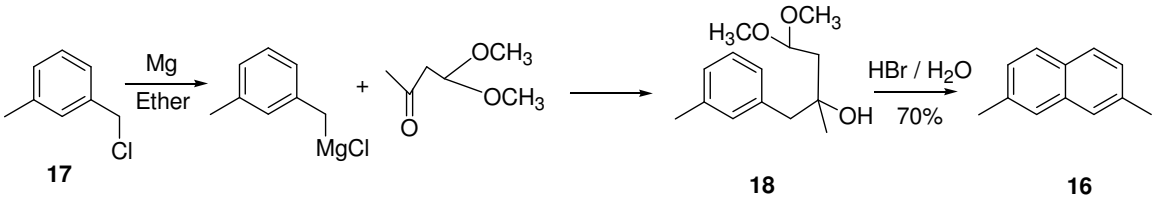
Introduction

Practical availability of corannulene (6) on a large scale following a simple three step synthesis starting from tetramethylfluoranthene (25) holds an enormous potential in advancement of this field towards synthesizing higher PAHs.[57] Unfortunately, 25 is not commercially available. By modification of an earlier scheme proposed by Buu-Hoi in 1942, [58] Siegel gained access to a key intermediate dimethylacenaphthaquinone (23) which can be used to produce 25.[59] This method involves use of toxic reagents such as selenium dioxide and requires ten tedious steps to arrive at the final product 25. A major part of my thesis work includes large scale production of 6 via 25. Therefore, several attempts were undertaken to improve the existing synthesis. In addition, this chapter also includes novel strategies attempted towards synthesizing tetramethylfluoranthene (25) using transition metal catalyzed coupling chemistry.

Results and Discussion

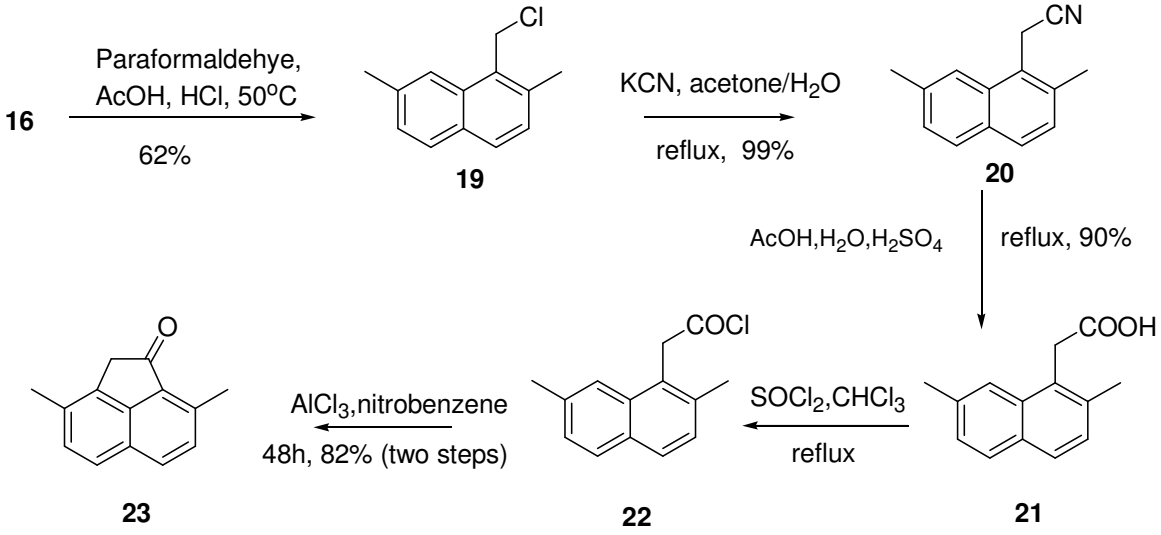
Synthesis of tetramethylfluoranthene.

2,7-dimethylnaphthalene (16) required to synthesize tetramethylfluoranthene (25) was readily prepared on a multigram scale following the reported procedures of Leitch and coworkers. [60] Quenching the Grignard reagent derived from 3-methylbenzylchloride (17) followed by cyclodehydration using Bradsher's reagent and subsequent purification via recrystallization in ethanol resulted in 70 % yield of 16 (Scheme 9). [60]



Scheme 9: Synthesis of 2,7-dimethylnaphthalene (**16**).

Formation of a five membered ring across 1,8 positions of 16, according to Siegel's approach is diagrammatically represented in Scheme 10. In contrast, developments and results obtained in our lab are discussed below.



Scheme 10: Siegel's approach towards synthesizing 3,8-dimethyl-1-acenaphthenone.

a) Chloromethylation of 2,7-dimethylnaphthalene at the α-position was achieved in an excellent yield of 98% by heating 16 with a mixture of paraformaldehyde, phosphoric acid and HCl in acetic acid as compared to 62% yield reported by the Siegel's group.

b) The nucleophilic substitution of chloride by cyanide failed to deliver high yield of 20 neither by Siegel's approach (acetone/H_2O) nor by the alternative methods (DMSO) used by our group in the past. For example, GC analysis revealed the presence of 15% of the starting material even after extended reaction times at 90°C in DMSO. In the present work we achieved 99% conversion with 90% isolated yield by switching the solvent system from DMSO to acetonitrile. The main

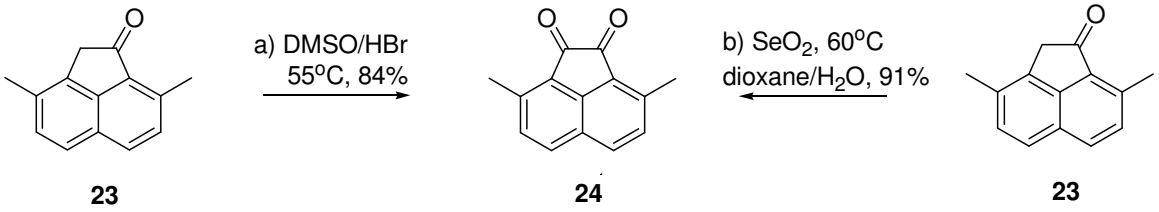
advantage of using acetonitrile is avoiding exposure to harmful solvents and tedious workup.

c) Hydrolysis of cyanide (20) gave the corresponding carboxylic acid (21) in 97% yield

d) Treatment of 21 with thionyl chloride in $CHCl_3$ delivered the corresponding acid chloride (22) in a yield of 98%, which underwent intramolecular ring cyclization in presence of Lewis acid to result in the formation of 3,8-dimethyl-1-acenaphthaquinone (23) in 97 % yield.

e) In comparison to Siegel's method where the reported yield was 82%, we achieved an improved yield of 95 % over two steps (from 21 to 23).

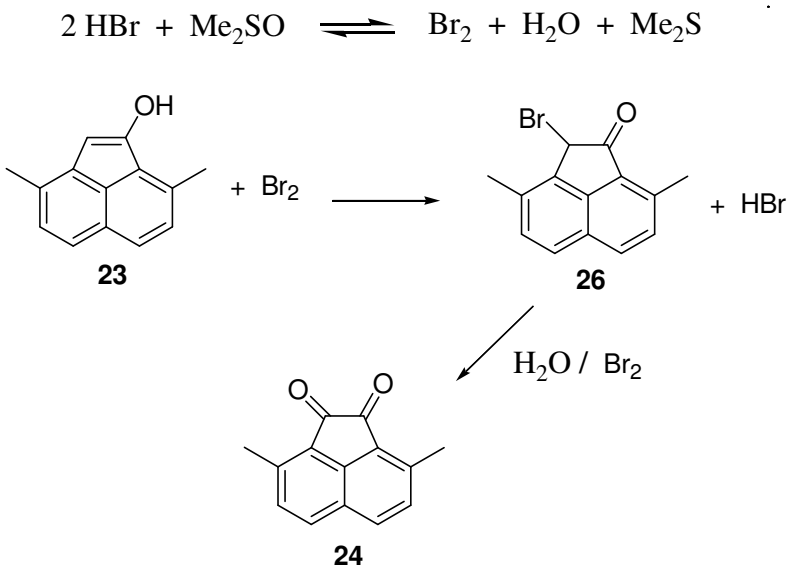
f) Transformation of 23 to 24 by Siegel's approach requires the use of toxic selenium dioxide, and involves a tedious work up. However, we achieved the similar transformation without the involvement of selenium dioxide. A comparison of both strategies is depicted in Scheme 11.



Scheme 11: Replacement of Selenium dioxide with HBr/DMSO.

Dropwise addition of HBr to a solution of 23 in DMSO at room temperature followed by warming the reaction mixture to 55°C for 1 hr gave diketone 24 in a comparative yield of 84%. Floyd et al. showed that in situ generated bromine is the

reactive species responsible for the oxidation of active methylene groups under these conditions.[61] Based on their findings we presume that the bromine produced by the reaction of HBr with DMSO (Scheme 12) α-brominates the ketone 23, which subsequently undergoes a series of reactions to produce 24.

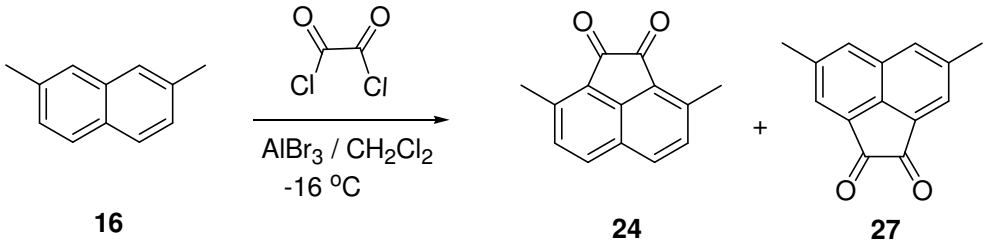


Scheme 12: Proposed mechanism for one pot oxidation of 23 to 24 using aq.HBr/DMSO.

Thus, diketone (24) was obtained in 75% overall yield in comparison to a modest yield of 41% obtained by Siegel's group.

Recent reports from Siegel's group suggested that diketone (24) can be synthesized directly from 2,7-dimethylnaphthalene (16) in one pot by treatment with oxalyl chloride and $AlBr_3$ in CH_2Cl_2 at -16°C in 32% yield. [62] The main advantage of this method is that it requires a shorter reaction time and excludes five steps of the Buu-Hoi/Siegel method in synthesizing 25. Therefore, attempts were made to reproduce these results in our lab. Surprisingly, all our attempts delivered an isomeric mixture of 24 and 27 in 1:1 ratio (Scheme 13). Attempts to control the regioselectivity failed, as did

attempts to efficiently separate the isomeric mixture. Thus, the lack of regioselectivity prompted us to direct our efforts back towards the classical method to synthesize 25.

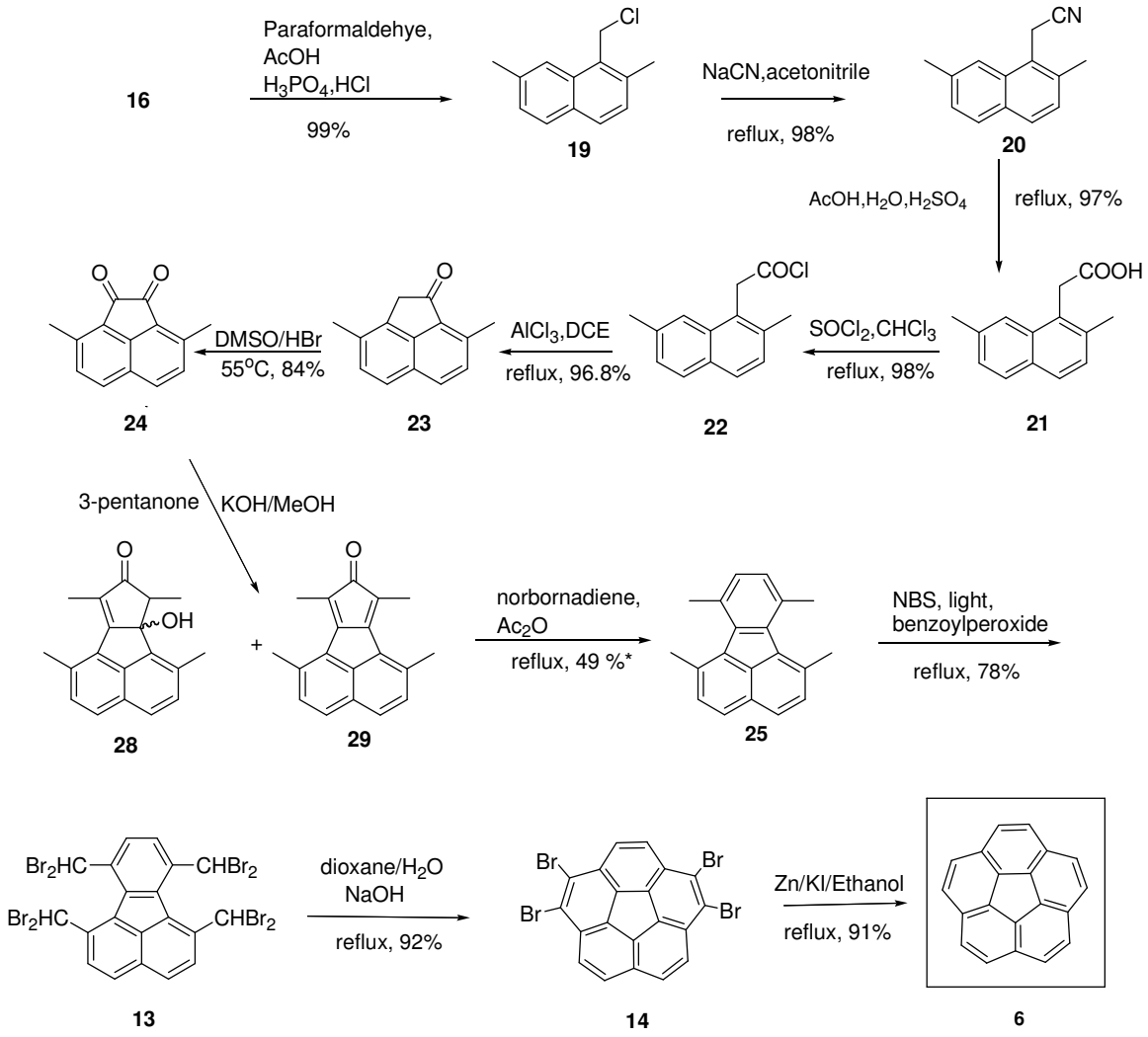


Scheme 13: One pot synthesis of 24 from 16.

With the first key intermediate dimethylacenaphthaquinone (24) in hand, the synthesis of tetramethylfluoranthene was performed as shown below:

a) A mixture of 28 and 29 was obtained by Knovenagel condensation of 24 with 3-pentanone in the presence of methanolic potassium hydroxide.

b) Diels-Alder reaction of 28 and 29 with norbornadiene (a masked acetylene equivalent) gave 1,6,7,10-tetramethylfluoranthene (25) in 49% yield over the two steps.



Scheme 14: A complete synthesis of corannulene via tetramethylfluoranthene.

A complete synthesis of 25 including the modifications with results obtained in our laboratory is provided in Scheme 14. In addition, Scheme 14 also provides three step synthesis of corannulene starting from tetramethylfluoranthene.

Solution phase methodology developed by Sygula's group allows one to prepare multigram quantities of corannulene employing common reagents. A three step synthesis of corannulene starting from tetramethylfluoranthene is performed as stated below:

a) Radical bromination of tetramethylfluoranthene with NBS in presence of catalytic amounts of benzoyl peroxide gave 1,6,7,10-tetrakis-(dibromomethyl)fluoranthene (12) in 78% yield.

b) The crucial ring closure step to produce tetrabromocorannulene was achieved by refluxing a solution of octabromofluoranthene in aqueous dioxane with NaOH for 15 minutes.

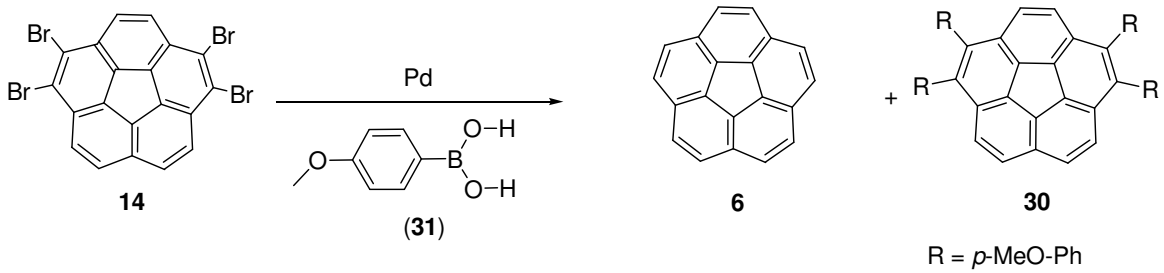
Our original trials to produce corannulene on a large scale by debromination of 14 using Zn/KI in ethanol met with only limited success. However, our attempts to solve the problem led us to discover a novel palladium catalyzed procedure capable of reducing 14 to 6 within minutes and in this case the scaling up was not a problem at all. This catalytic system is described in next part of the chapter.

Palladium catalyzed reduction of tetrabromocorannulene

Reduction of tetrabromocorannulene (14) to 6 by refluxing 14 with Zn/KI in ethanol turned out to be the most effective, low cost procedure available to date for synthesizing 6 on a small scale. However, in our present work we found that this reduction method required longer reaction times for complete conversions of 14 and afforded moderate to low yields of 6 on a larger, multigram scale. For example, GC analysis revealed incomplete debromination even after extended reaction time (from 6 hr to 2.5 weeks). Moreover, the presence of monobromocorannulene as a impurity in more than 10% and limited solubility of 6 in hexane further daunted the purification process via column chromatography. After complete separation, pure corannulene was obtained in 59% from tetrabromocorannulene. Due to clear limitations of that method, there was a

need for development of a more efficient dehalogenation process, which would deliver 6 in a shorter time on a large scale.

In a separate project, during our optimization efforts to find proper conditions for coupling tetrabromocorannulene with *p*-methoxyphenylboronic acid (31) under Suzuki coupling conditions using 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (IMes.HCl)/$Pd(OAc)_2$ as a catalyst, we observed formation of corannulene as a byproduct (Scheme 15). Therefore, we decided to exploit the possibility of using the same conditions for debromination of tetrabromocorannulene (14). Accordingly, we removed the coupling partner (31) from the reaction mixture and performed a series of trial reactions in various solvents.



Scheme 15: Formation of 6 as byproduct in Suzuki coupling of 14 with 31.

Among the seven solvents screened (benzene, toluene, NMP, DMF, DMAc, THF, IPA) the best yields were obtained in isopropanol. Aprotic polar solvents like THF, DMF, DMAc and NMP exhibited little propensity towards corannulene formation when compared to isopropanol (IPA). Also, formation of corannulene failed to occur in non-polar solvents.

The most crucial step towards formation of 6 is insertion of palladium between an aryl carbon and a halogen of tetrabromocorannulene. This step has been shown to be favored by the presence of electron-donating ancillary ligands such as tertiary phospines[63-65] and N-heterocyclic carbenes (NHC),[66-68] which make the metal center electron rich on coordination. Experiments conducted to test the catalytic efficiency of a catalyst with respect to different ligands generated in situ to debrominate 14 showed IMes. HCl to be the most suitable ligand among the series (PPh_3, PCy_3, PtBu3).

NHC-imidazolium ligand generated from IMes.HCl displayed an efficient conversion of 14 to 6 when refluxed in isopropanol, whereas the use of either PCy_3, PPh_3 or P^tBu_3 proved to be ineffective in mediating the catalytic dehalogenation.

Various palladium sources such as $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, $Pd_2(dba)_3$ and $Pd(OAc)_2$ were also tested. $Pd(OAc)_2$ was found to be the most effective palladium precursor generated in situ without any induction period. In contrast, the other palladium sources in the series displayed incomplete debromination even after extended reflux in isopropanol (IPA).

Investigation of the effect of various bases on the efficiency of reduction revealed that KO^tBu was the reagent of choice. Other inorganic bases such as Cs_2CO_3, K_3PO_4, KF and Na_2CO_3 required longer reaction times for complete consumption of 14 and afforded low yields of debrominated product 6.

Once $Pd(OAc)_2$/IMes. HCl with KO^tBu was selected as the most efficient catalytic system, efforts were directed on decreasing the catalyst load (Table 1). As

summarized in Table 1, excellent yields were obtained when 3 mol% of catalyst was used.

Table 1: Influence of $Pd(OAc)_2$/IMes.HCl salt ratio on debromination of tetrabromocorannulene.

Entry	$Pd(OAc)_2$	IMes.HCl	Yield %
1	10 mol%	10 mol%	55%
2	3 mol%	3 mol%	90%
3	1 mol%	1 mol%	80%

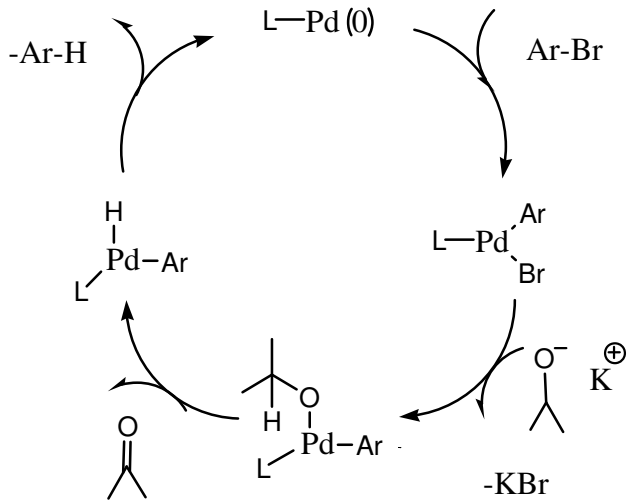
Nolan's group has introduced this catalytic system to organic chemistry. Based on their mechanistic suggestion we expect that debromination of 14 may follow a pathway as depicted in Scheme 16.[69-71] Moreover, we believe that the success of this reaction relies on several factors such as:

a) The use of KO^tBu as base, which plays a dual role: as a catalyst activator and as an in situ generator of isopropoxide anion.

b) Usage of isopropyl alcohol as solvent, which not only stabilizes the palladium complex, but also donates a hydrogen atom to the palladium center by a well known process called β-hydride transfer.[72]

c) IMes. HCl, a highly donating and sterically demanding ligand in comparison to tertiary phosphines, does not easily dissociate from the metal center and, as a result, excess of ligand is not required. Furthermore, it keeps palladium intact in solution and helps catalyzation process proceed towards completion within minutes.[73]

Thus, an efficient catalytic system has been introduced that proved to be equally potent in dehalogenation of tetrabromocorannulene and pentachlorocorannulene within minutes to form corannulene (6) under similar conditions. This method is a simple, low cost procedure that, in contrast to the Zn/KI method, is applicable to a large scale production of 6 from 14. In addition, this method does not require dry or degassed solvent which makes it quite practical for large scale synthesis.



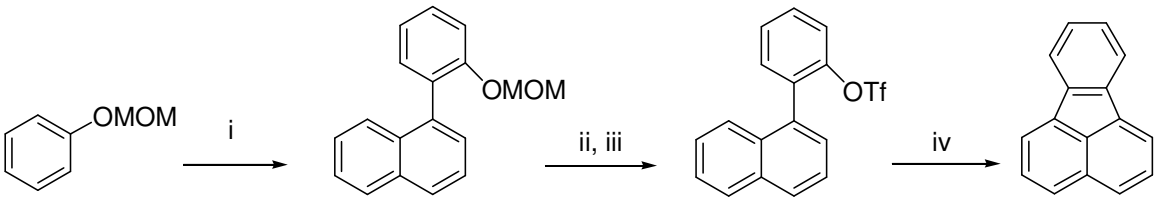
Ar = Tetrabromocorannulene (**14**), Ar-H = Corannulene (**6**)

Scheme 16: Proposed mechanism for activation of Pd(0) catalyst and subsequent reduction of 14 to 6.

Alternative methods to synthesize tetramethylfluoranthene

Siegel's methodology in synthesizing tetramethylfluoranthene (25) involves ten tedious steps, even after modifications. Such concerns were the motivation behind the current study to find a simpler method to synthesize 25.

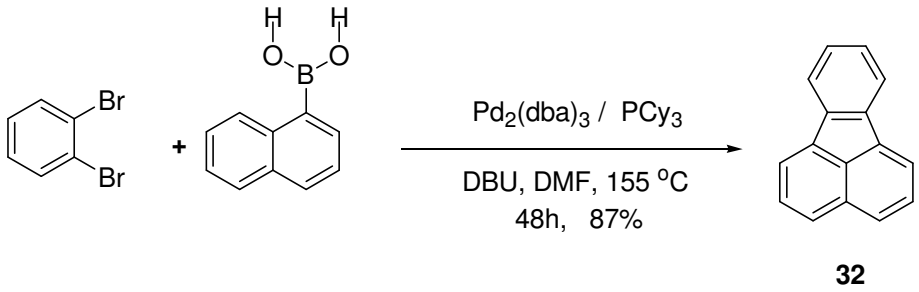
Early work by Rice and Cai demonstrated the ability of aryltriflates to undergo Heck-type intramolecular arylation reactions by closing the five membered ring to form fluoranthene (32) (Scheme 17).[74]



32

Scheme 17: Original synthesis of fluoranthene by Rice and Cai method.

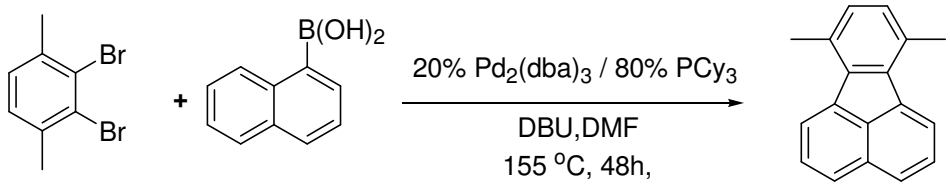
More recently, Scott and de Meijere showed the possibility of constructing fluoranthene nucleus in a single pot reaction, which they called "Suzuki-Heck cascade reaction".[75] Their novel strategy relied on the Suzuki coupling reaction to join two aryl rings, which is followed by an intramolecular Heck type ring closure using second bromine atom (Scheme 18).



32

Scheme 18: Suzuki-Heck cascade coupling leading to fluoranthene formation.

We decided to test the approach to synthesize 25. Anticipating steric problems caused by the presence of four methyl groups in tetramethylfluoranthene, we decided to test the methodologies first on synthesis of 33. If ring closure is successful in 33, it is more likely to be successful in 25 as well. Also, commercial availability of the boronic acid (34) made 33 a viable testing system (Scheme 19).

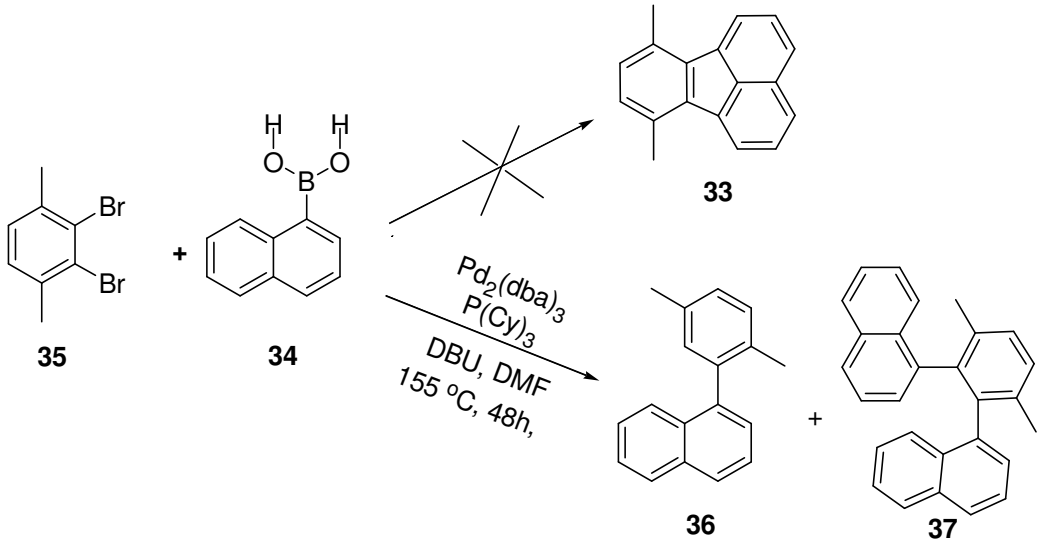


35 **34** **33**

Scheme 19: Schematic representation of Suzuki-Heck cascade for synthesis of dimethylfluoranthene.

The second substrate for the "cascade" synthesis of 33, 2,3-dibromo-*p*-xylene (35) was prepared according to the reported procedures by Gronowitz et al.[76] A series of test reactions were executed following the reported procedures by Scott et al. Unfortunately, this approach ended in failure. Analyses of the reaction mixtures by GC/MS showed the

presence of 36, resulting from incomplete ring closure product with loss of bromine atom, along with the twofold Suzuki coupling product 37 (Scheme 20).



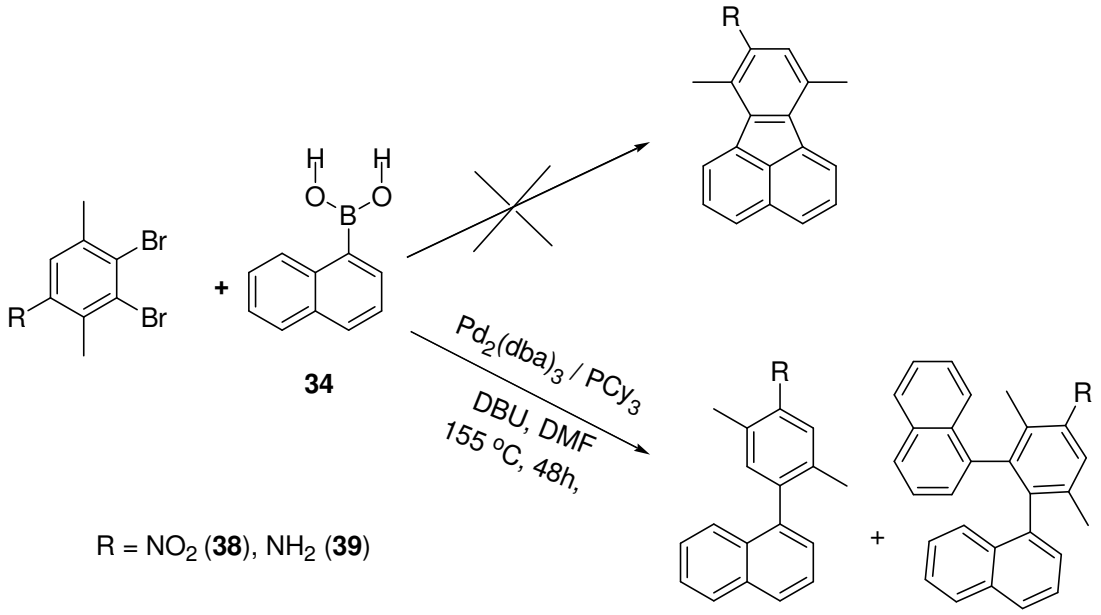
Scheme 20: Attempted synthesis of 33 following procedures of Scott et al.

Further attempts to promote ring closure either by raising the temperature (from 150 to 190°C) or lowering the temperature (from 155 to 120°C) in conjunction with different solvent mixtures of DMF and DMA, as well as employment of various palladium sources were also unsuccessful. Failures are probably due to the steric encumbrance of the additional methyl group near the palladium center which restricts the right orientation of coordination site for the ring closure.

The presence of 36 and 37 in the reaction mixture clearly shows that the second oxidative insertion of palladium between the aryl carbon and the second bromine atom is successful. However, due to steric hindrance the activation barrier needed for the five membered ring formation appears to be too high and, as a result, this process is too slow and instead competing reactions form the twofold Suzuki coupling product 37 and the

debrominated molecule 36. In order to suppress the formation of 37 and favor the formation of 33, the starting material 35 was modified. 2,3-dibromo-5-nitro-*p*-xylene (38) and 2,3-dibromo-5-amino-*p*-xylene (39) were synthesized and used as starting materials under similar conditions (Scheme 21).

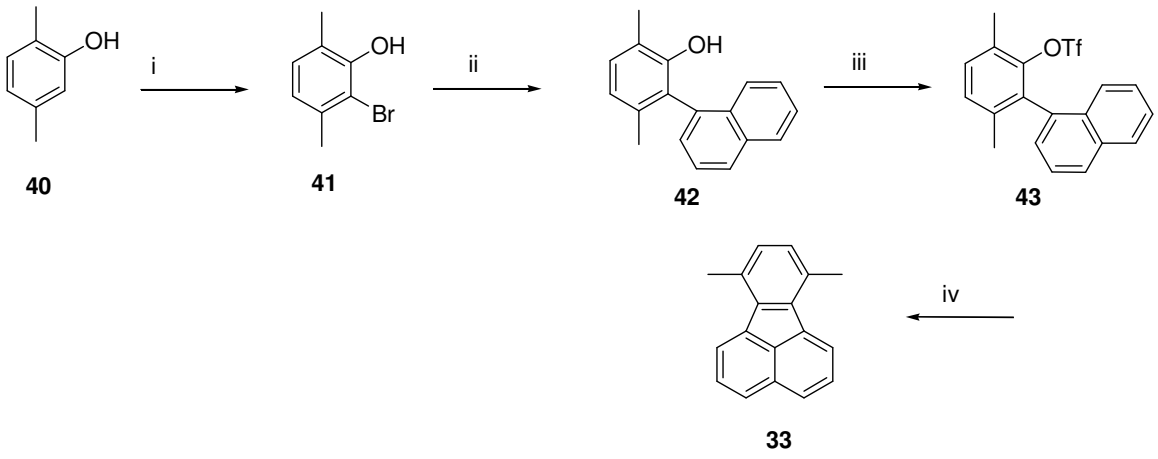
Unfortunately, these efforts were also unproductive. Similar incomplete ring closure product or double Suzuki coupling products were obtained. In addition, in the case of 38 the nitro group was reduced to an amino group under the reaction conditions.



Scheme 21: Suzuki-Heck cascade results on modified system using Scott's procedure.

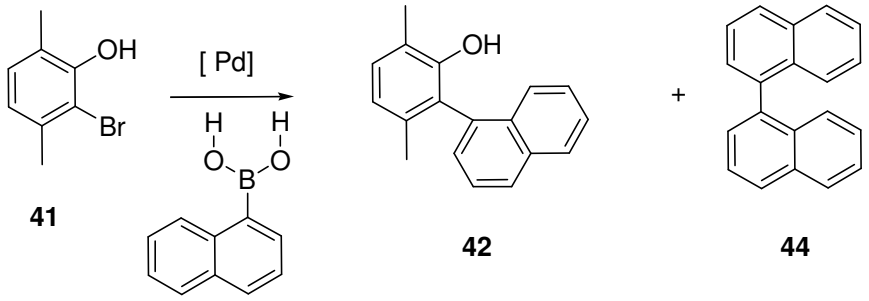
We also tested an alternative Rice approach starting from commercially available 2-hydroxy-*p*-xylene (40) (Scheme 22). 3-bromo-2-hydroxy-*p*-xylene (41) was prepared by addition of NBS to a solution of 40 in dichloromethane, in presence of catalytic amounts of diisopropylamine.[77,78] The reaction was found to be highly ortho-selective to the hydroxyl group in 40 since the hydrogen bonding between the hydroxyl group of 40

and intermediate N-bromodiisopropylamine generated in situ directs the bromine atom into the ortho position.



Scheme 22: Proposed synthesis of 7,10-dimethylfluoranthene using Rice and Cai method.

Surprisingly, Suzuki coupling of 41 with 1-naphthylboronic acid turned out to be a challenging step (Scheme 23). Table 3 summarizes our optimization trials for synthesis of 42.



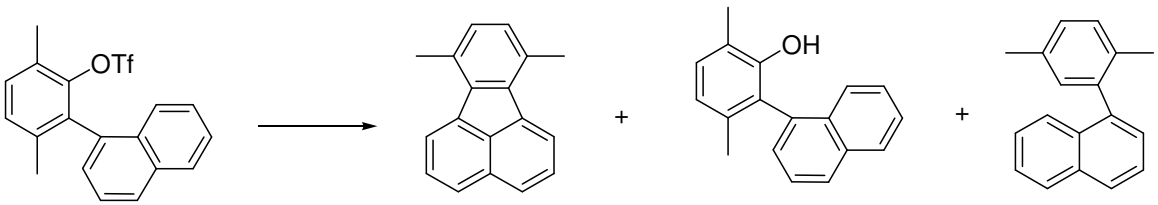
Scheme 23: Products obtained during optimization of Suzuki reaction.

Table 2: Optimization of Suzuki reaction towards formation of 42.

Entry	catalyst (mol %)	additive	base	solvent	temp (^{o}C)	time (h)	products	Ratio
1	$Pd(PPh_3)_4$, 3		Na_2CO_3	$PhCH_3$/EtOH H_2O	100	5	41, 42	7:3
2	$Pd(PPh_3)_4$, 5		Na_2CO_3	$PhCH_3$/EtOH H_2O	100	3	42, 44	1:1
3	$Pd(PPh_3)_2Cl_2$, 5		K_2CO_3	THF	80	3	42, 44	3:7
4	$Pd_2(dba)_3$, 20	PCy_3	Cs_2CO_3	DMF	100	3	41,44	9:1
5	$Pd(OAc)_2$, 20	PCy_3	Cs_2CO_3	Dioxane	80	5	42, 44	2:8

As can be seen from Table 3, the best results were obtained with 5 mol% $Pd(PPh_3)_4$ and 15 equivalents of Na_2CO_3 refluxed in a mixture of $EtOH/PhCH_3/H_2O$ (3:3:1), which gave 2-hydroxy-3-naphthyl-*p*-xylene (42) in 46% yield.[79] Treatment of 42 with 1.5 equivalents of triflic anhydride gave corresponding triflate derivative 43 in 77% yield. Unfortunately, attempts to complete the intramolecular ring closure with $Pd(PPh_3)_2Cl_2$ to give the corresponding 7,10-dimethylfluoranthene were unsuccessful. Instead of forming 33 we observed only 42 and 36 in reaction mixtures. None of our attempts such as: overloading of catalyst, addition of excess ligand to cease palladium precipitation and retaining completely dry conditions throughout the reaction process were successful.

Disappointed by the reaction outcome, we decided to try other combinations of palladium catalyst to achieve the intramolecular ring closure in 43 (Scheme 24). Table 4 describes our efforts towards formation of 33.



43 **33** **42** **36**

Scheme 24: Formation of 33 in the reaction mixture by Rice and Cai method.

Table 3: Screening of various palladium catalyst to promote intramolecular triflate ring closure.

Entry	catalyst (mol %)	additive	base	solvent	temp. (^{o}C)	time (h)	Product s
1	$Pd(PPh_3)_2Cl_2$, 10	LiCl	DBU	DMF	150	6	36,42
2	$Pd(PPh_3)_2Cl_2$, 10	LiI	DBU	DMF	150	6	36, 42
3	$Pd(PPh_3)_2Cl_2$, 10	PPh_3	DBU	DMF	150	6	36, 42
4	$Pd(PPh_3)_2Cl_2$, 10	LiI/PPh_3	DBU	DMF	150	6	36, 42
5	$Pd(PPh_3)_2Cl_2$, 10		DBU	DMF	150	6	42
6	$Pd_2(dba)_3$, 20	PCy_3	DBU	DMF	150	6	36, 42
7	$Pd(PPh_3)_4$, 10	LiCl	DBU	DMF	150	6	36, 42
8	$Pd(PPh_3)_4$, 5		Na_2CO_3	*	Reflux	6	43
9	$Pd(OAc)_2$, 30	PCy_3	DBU	DMAc	165	6	33, 36, 42

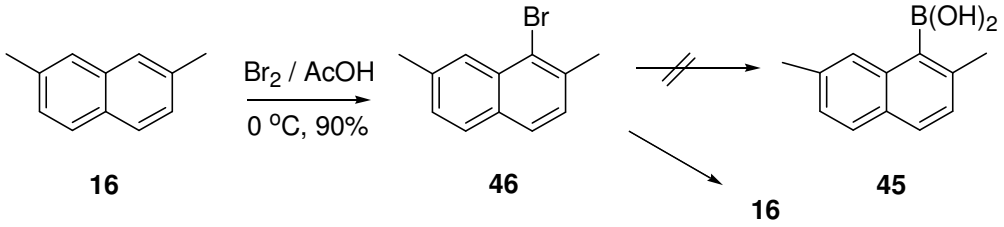
* (EtOH/$PhCH_3$/H_2O)

Interestingly, when $Pd(OAc)_2$ was used in combination with tricyclohexyl phosphine (PCy_3) and refluxed with 43 in DMAc for 4 hr, dimethylfluoranthene (33) was obtained, albeit in low yield, along with 36 and 42. Formation of 42 clearly suggested that there is a source of protons somewhere in the reaction mixture. Hence, in order to minimize or eliminate the possibility of such, all reagents along with the triflate derivative were kept in vacuum overnight prior to use. Unfortunately, all such attempts failed to improve the yield of 33. After purification 7,10-dimethylfluoranthene (33) was obtained in ca. 20% yield only. Again, low yields of 33 are presumably due to steric congestion caused by the methyl group. All failed attempts to suppress the formation of side product 32 clearly show that the reductive elimination step leading to formation of 33 is slow. However, results from Table 4 show that synthesis of 33 using $Pd(OAc)_2/PCy_3$ is possible but requires some optimization. Hence, with limited success in synthesizing 33, we directed our attention towards synthesis of tetramethylfluoranthene (25).

Following the modified procedures of Rice and Cai and using $Pd(OAc)_2/PCy_3$ as the catalyst for ring closure showed promising results in synthesizing 33. A similar approach such as coupling 3-bromo-2-hydroxy-p-xylene (41) with 2,7-dimethylnaphthaleneboronic acid (45) followed by an intramolecular Heck-type ring closure via triflate derivative was considered for the synthesis of 25. Unfortunately, the coupling partner 45 is not commercially available and had to be synthesized first.

1-bromo-2,7-dimethylnaphthalene (46) was successfully synthesized with complete regioselectivity by addition of bromine to a solution of 2,7-

dimethylnaphthalene in dichloromethane at 0°C. However, neither subsequent treatment of 46 with n-BuLi at -78°C [80] nor Grignard reagent derived from 46, under the conditions reported by Cammidge et al.[81] and Clews,[82] produced 45 when quenched with trimethylborate (Scheme 25). Several attempts to form 45 by using a slight excess of n-BuLi/magnesium and a large excess of trimethoxyborate failed to yield any of the desired product 45, and only debrominated product 16 was recovered from the reaction mixture.



Scheme 25: Attempted synthesis of 2,7-dimethyl-1-naphthylboronic acid.

Formation of debrominated product 2,7-dimethylnaphthalene (16) suggested that the first step involving lithiation or generation of Grignard reagent from 46 was successful. Unfortunately, once the reactive organometallic species are produced in situ, they are rapidly quenched by protons present somewhere in the reaction mixture. To eliminate such possibility, all reagents were additionally purified and dried under vacuum prior to their use. Similarly, solvents were freshly distilled before use. Unfortunately, these attempts did not prove to be beneficial.

Conclusions

In conclusion, we have disclosed an improved protocol for the synthesis of 2,7-dimethylacenaphthaquinone (24) in comparison to Buu-Hoi/Siegel method. 2,7-dimethylacenaphthaquinone is obtained in an overall yield of 75% when compared to a modest yield of 41% as reported by Siegel's group. Moreover, the oxidation of 3,8-dimethyl-1-acenaphthenone (23) was achieved in comparable yields without the use of selenium dioxide. Instead HBr/DMSO was employed to accomplish the work as depicted in Scheme 11.

A robust and reliable method for large scale reduction of tetrabromocorannulene was discovered. An optimum 1:1 ratio of $Pd(OAc)_2$/IMes. HCl favors the formation of catalytically active palladium species. When coupled with KO^tBu in isopropanol and refluxed for 30 minutes it generates corannulene as a single product in an excellent yield of 90%. This method appears to be simple and inexpensive, and the use of technical grade isopropyl alcohol makes it quite practical and amenable to large scale synthesis.

As $Pd(OAc)_2/PCy_3$ displayed promising results in closing the five membered ring in 7,10-dimethylfluoranthene Table 4, entry 9, a similar approach should be feasible in producing 25. However, our failed attempts to produce the prerequisite 2,7-dimethyl-1-naphthylboronic acid (45) clearly show that there is a need for a more robust borate reagent than trimethylborate.

CHAPTER III

DERIVATIZATION OF TETRABROMOCORANNULENE

Introduction

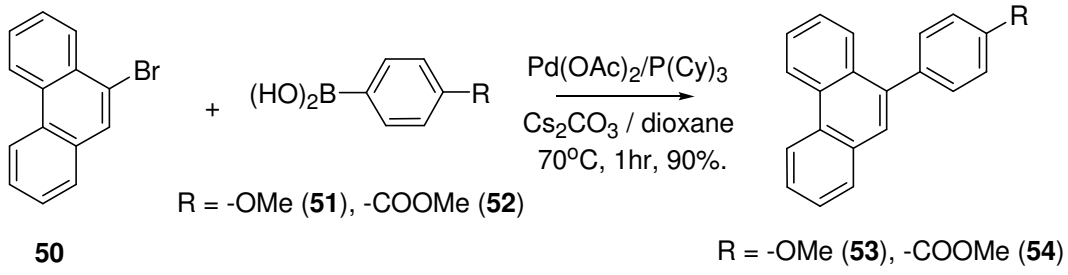
Non-planar polycyclic aromatic hydrocarbons exhibit unique physical and chemical properties and have attracted considerable attention.[13] For example, ($C_{20}H_{10}$) corannulene (**6**), which represents the polar cap of C_{60}, has extensively been studied since last decade. Several papers describing the synthesis of 6, its higher analogues and various derivatives have been published.[34-47] However, only few reports describe functionalization of the corannulene core utilizing tetrabromocorannulene as a synthon.[56] Therefore, the purpose of the current study was to increase the importance of tetrabromocorannulene not only as a precursor for corannulene but also as a potential substrate in synthesizing new PAH's using standard Suzuki coupling reactions. In this context two new derivatives 1,2,5,6-tetrakis(*p*-methoxyphenyl)corannulene (47), and 1,2,5,6-tetrakis(*p*-methoxycarbonylphenyl)corannulene (48) were synthesized.

In addition, the Suzuki-Heck cascade coupling reaction of 14 with 1-naphthylboronic acid was also attempted. This chapter mainly focuses on making derivatives of tetrabromocorannulene, which could be potentially used in production of corannulene capsules.

Results and Discussion

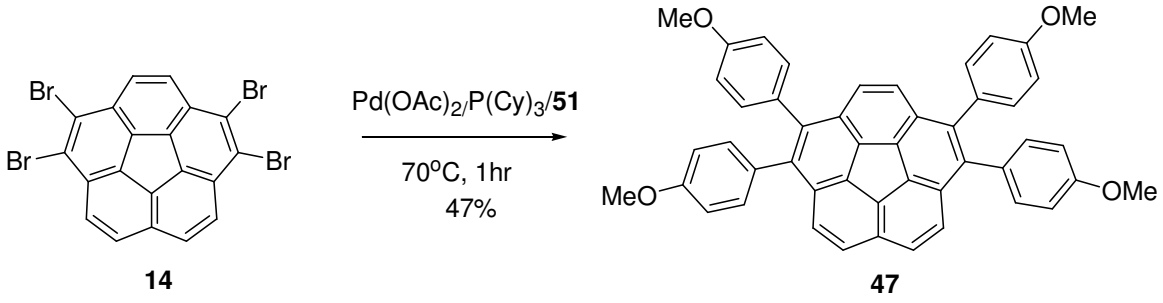
Derivatives of tetrabromocorannulene

Formation of a new carbon-carbon bond through the use of Suzuki cross-coupling methods has become an extremely powerful synthetic tool. Reactive partners like aryl iodides, bromides and triflates form an important pool of substrates for such methods, and have gathered huge attention since the last decade.[83] As Suzuki coupling appeared to be the method of choice to couple 14 with 51 and 52, we decided to perform a model study first using 9-bromophenanthrene (50) prior to the real synthesis of 47 and 48. The main purpose of performing a model reaction was a) to improve technical skills in Suzuki reactions, b) to check the feasibility of Suzuki cross coupling in presence of electron rich (*p*-methoxy) and electron deficient (*p*-COOMe) boronic acids and c) the commercial availability of 9-bromophenanthrene. Excellent results were obtained by coupling 50 with *p*-OMe phenylboronic acid (51) and *p*-carbomethoxy phenylboronic acid (52) using $Pd(OAc)_2/P(Cy)_3$ in a 1:1 ratio when heated at 70 ^oC for 1 hr (Scheme 26). Spectroscopic data for 53 and 54 were consistent with those reported in the literature.



Scheme 26: Test of Suzuki coupling for model system.

Delighted by the reaction outcome, we switched to the real system *i.e.,* tetrabromocorannulene 14. Suzuki coupling reactions were performed under similar conditions as shown in Scheme 27. As expected, the tetrasubsituted *p*-methoxyphenyl derivative of corannulene was readily obtained albeit in a modest yield of 47 %. The number of signals and the multiplicity of the ^{1}H NMR spectrum indicated the formation of the desired product 47. The chemical shifts of the six protons arising from the corannulene nucleus were slightly shifted upfield by 0.2 ppm when compared to corannulene, possibly due to the presence of the electron donating *p*-methoxy subsituents. Integration values suggested the presence of 22 aromatic protons which confirms tetrasubstitution of the corannulene core. The number of signals in ^{13}C NMR was found consistent with the expected structure. Mass spectroscopy also confirmed the presence of 47.

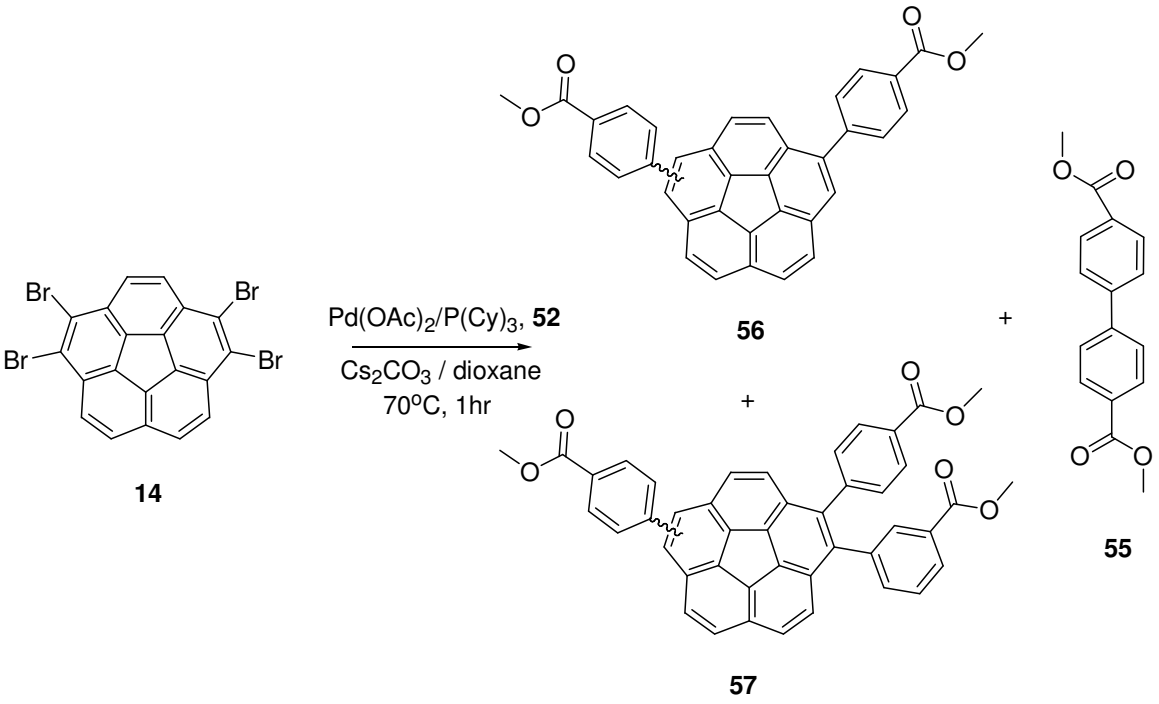


14 **47**

Scheme 27: Synthesis of 1,2,5,6-tetrakis(*p*-methoxyphenyl)corannulene from 14.

On the other hand, our preliminary attempts to derivatize 14 with *p*-methoxycarbonylphenylboronic acid (52) failed to produce the desired product 48 under similar conditions. Also, despite numerous attempts employing various palladium catalysts under different reaction conditions we did not observe any of the expected

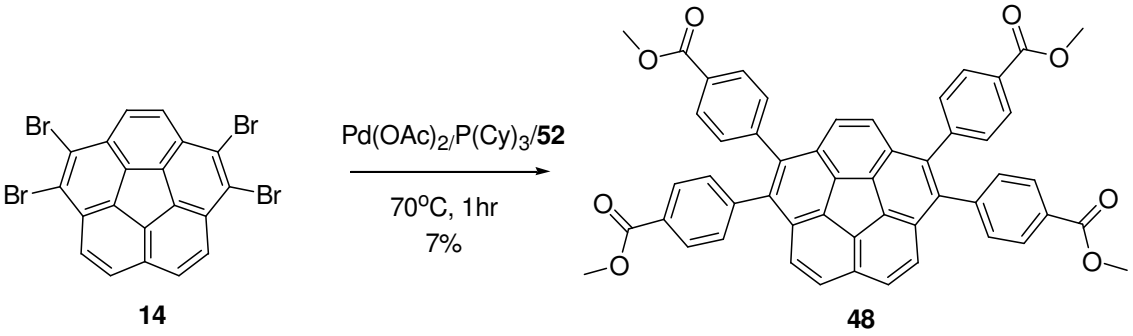
product 48. Instead, we identified formation of self coupled product 55 with traces of incomplete cross coupling products 56 and 57 (Scheme 28).



Scheme 28: Suzuki-Miyaura coupling of 14 with 52.

56 and 57 were identified by their MS data as di and tri-ester derivatives of corannulene. Due to limited amounts of 56 and 57 these compounds were not further characterized. We tried to minimize the amount of self coupling of boronic acid 52 by various techniques such as: (i) loading all components except 52 and stirring the reaction mixture for 20 minutes at 70°C, thereafter addition of 52 either dropwise or at once, (ii) adding a solution of 52 dropwise at a regulated flow through a period of 30 minutes, (iii) increasing or decreasing the temperature of the reaction with prolonged reaction times (up to 12 hrs), (iv) charging the reaction mixture with additional catalyst. However, all these attempts failed to promote the formation of desired coupling product 48.

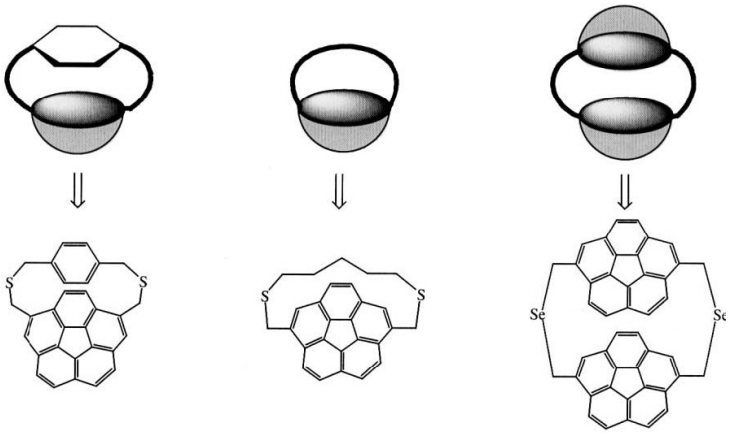
Hence, we decided to overload the reaction flask with huge excess of 52. Interestingly, by increasing the amount of 52 from 1.2 to 4 equivalents per bromine atom furnished 48 in 5 % yield along with 55, 56 and 57. As expected, ^{1}H NMR showed the presence of 22 aromatic protons on integration. The number of signals in the ^{13}C NMR was found consistent with the predicted structure. Mass Spectroscopy confirmed the molecular weight of the desired product 48. Unfortunately, we obtained 48 very recently, hence we were unable to optimize the reaction conditions further.



14 **48**

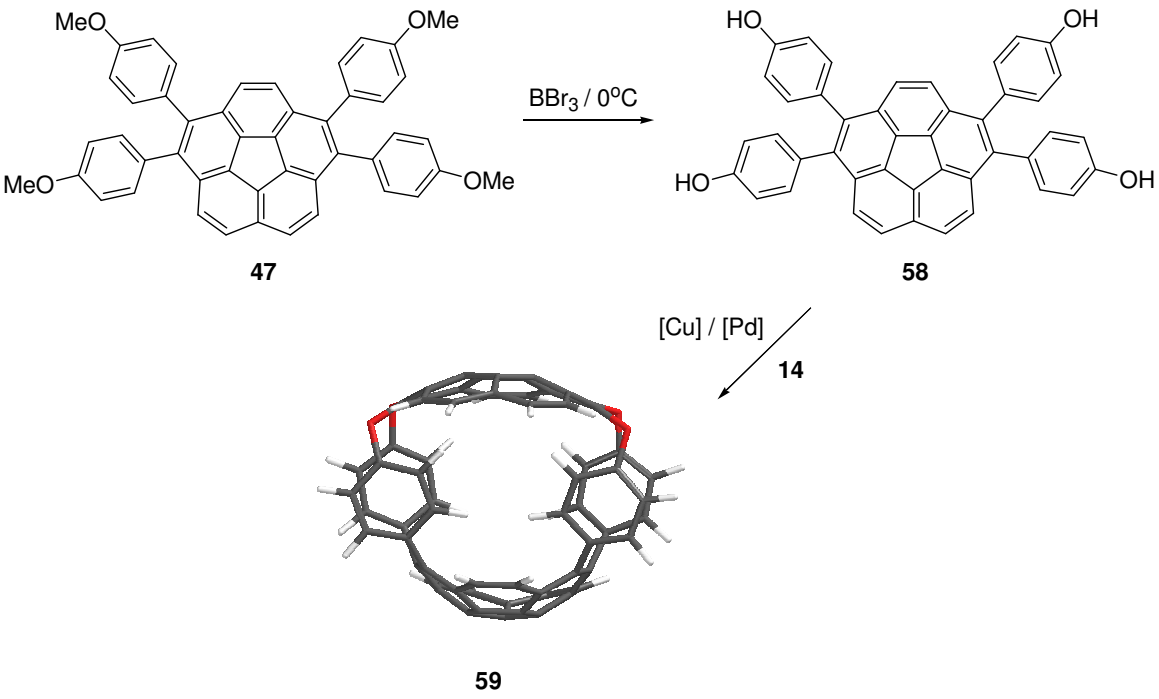
Scheme 29: Synthesis of 1,2,5,6-tetrakis(*p*-methoxycarbonylphenyl) corannulene from 14.

Inspired by an elegant work reported by Siegel's group in synthesizing corannulene based cyclophanes as depicted in Scheme 30,[84] we envisioned to construct capsules of corannulene involving tetrabromocorannulene and the two derivatives 47 and 48 synthesized in our laboratory.



Scheme 30: Cyclophane motifs: covered-basket, ansa-basket, basket-ball.[84]

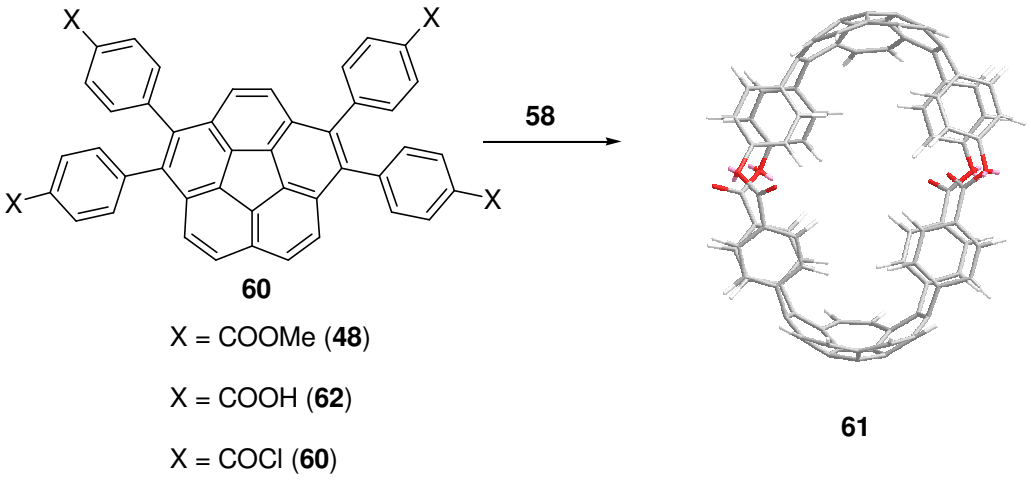
Possible ways to link two corannulene caps would by ether and ester linkages. Several reports describe formation of diaryl ethers by coupling aryl halides with phenols either by copper catalyzed Ulmann condensation [85-87] or palladium catalyzed C-O bond formation.[88] Thus, our synthetic plan which describes the possibility to build a corannulene capsule using 14 and 47 is outlined in Scheme 31.



Scheme 31: Proposed synthesis of corannulene capsule 59.

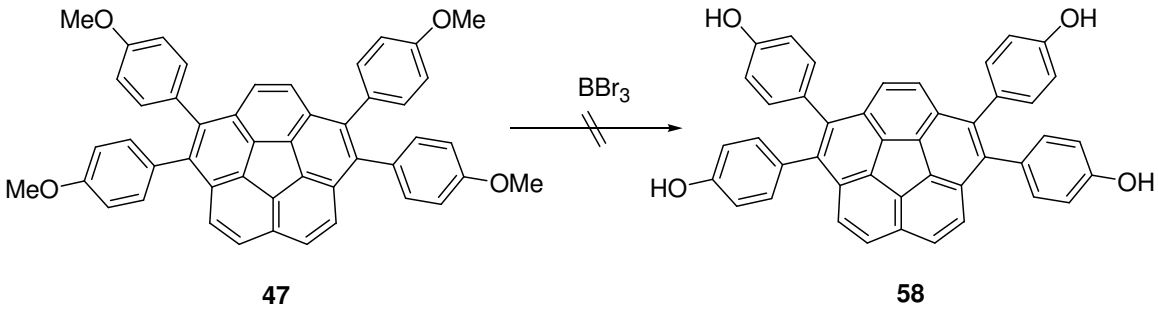
On the other hand, an ester linkage would result by coupling 58 with 1,2,5,6-tetrakis(*p*-benzoylchloro)corannulene (60) derived from 48 in formation of a second corannulene capsule (61). This approach is illustrated in Scheme 32.

According to our synthetic strategy outlined in Scheme 31, 47 should be converted to the tetraphenol 58. The standard method to cleave methyl aryl ethers requires addition of BBr_3 at low temperatures.



Scheme 32: Proposed synthetic plan to build corannulene capsule with ester linkage 61.

To our surprise none of our attempts such as: a) addition of 5 eq. of BBr_3 at -78°C, b) addition of 8 eq. of BBr_3 at -78°C, c) addition of 8 eq. of BBr_3 at 0°C and d) addition of 8eq. of BBr_3 at room temperature were successful in producing the desired product 58 (Scheme 33). Instead we observed formation of an isomeric mixture containing incompletely demethylated products. Furthermore, treatment of 58 with BBr_3 for longer reaction times at room temperature also proved to be unsuccessful. Also, limited availability of 48 hampered our progress towards synthesizing 61.

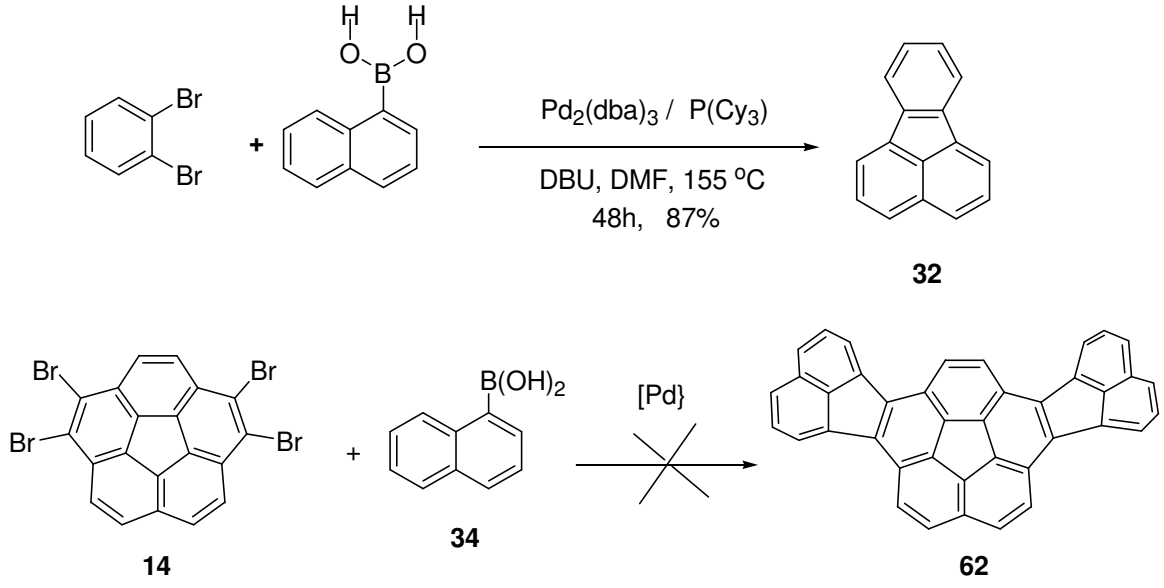


Scheme 33: Attempted cleavage of arylmethylether towards formation of 58.

Suzuki-Heck cascade coupling of tetrabromocorannulene

With a substantial amount of tetrabromocorannulene in hand, we tried to expand the aromatic framework of 6 by coupling 14 with 1-naphthylboronic acid (34), following the reported procedure by Scott et al.[75] Unfortunately, the conditions that led to the best outcome towards formation of fluoranthene were found to be ineffective in building 62 (Scheme 34). Increasing the amounts of catalyst (34) with subsequent increase in temperature (from 155 to 165°C) or using various mixtures of DMF and DMAc did not change the reaction outcome. All our attempts delivered a mixture of products, as observed by TLC. The product mixture was separated over silica gel and then analyzed by ^{1}H NMR. Unfortunately, the sample was still a mixture of products. Moreover, MS did not show the presence of 62 in the reaction mixture.

Similar results were obtained under microwave irradiation of the reaction mixture for 2 hrs.



Scheme 34: Attempted Suzuki-Heck cascade to synthesize 62.

Conclusions

In summary, we have successfully functionalized the corannulene core utilizing tetrabromocorannulene (14) as synthon, by coupling 14 with 51 under Suzuki conditions to produce 47 in a modest yield of 47 %. However, attempts to produce 48 by coupling 14 with 52 met with limited success only. Formation of huge amounts of the self coupling product 55 clearly shows that the cross coupling step is slow when compared to self coupling of boronic acids. An alternative would be to use a huge excess of boronic acid under the same conditions or by using a new and robust catalytic system which would promote the formation of 48 rather than 55.

As BBr_3 did not turn out to be a suitable method for demethylation of 47, other reagents such as ETSNa/DMF [89] and $PhSH/K_2CO_3$ [90] which react under basic conditions may be helpful in overcoming the problem.

Once the technical problems are resolved both 47 and 48 could be used in building corannulene capsules.

Even though the reported procedure by Scott et al. describe the formation of fluoranthene (32) in an excellent yield by coupling 1,2-dibromobenzene with 1-naphthylboronic acid (34), a similar attempt to reproduce their results by coupling 14 with 34 failed to produce diacenaphthene[1,2-a,g] corannulene (62).

CHAPTER IV

EXPERIMENTAL DETAILS

All experiments were carried in oven dried glassware with magnetic stirring unless otherwise stated. Commercially available solvents were used as received without any further treatment unless specified. 1,4-Dioxane, tetrahydrofuran and toluene were distilled from sodium/benzophenone ketyl; dichloromethane was distilled over $KOH/CaCl_2$ under nitrogen. All palladium salts and ligands including different derivatives of boronic acids except allylchloro[1,3-bis(2,6-di-i-propylphenyl)imidazol-2-ylidene]palladium (II) were purchased from Aldrich and the latter was purchased from Strem chemicals. They were all stored in either glove box or in desiccators before use. Preparative column chromatography was performed using silica gel (200-400 mesh) from Aldrich. Thin layer chromatography was performed on UV coated silica gel glass plates purchased from Sigma-Aldrich. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker model AMX-300 spectrophotometer operating at 300 MHz for proton and 75 MHz for carbon. Chemical shifts were reported in ppm downfield from TMS used as an internal standard. GC/MS and direct insertion probe method were used to determine the molar masses.

3-hydroxy-3-methyl-4-(3-methylphenyl)-butanal dimethyl acetal *(18):*

A 1L three necked round bottom flask equipped with a nitrogen inlet and a mechanical stirrer was charged with 21.5 g of magnesium turnings and a pinch of iodine crystals in ether (15 mL). The violet color of iodine disappeared on adding a solution of 3-methylbenzylchloride (100g, 0.7 mol) in ether (450 mL) dropwise. Maintain the flow rate of 3-methylbenzylchloride as such that a brief reflux of ether solution is noticed. After additional 30 minutes of stirring, add a solution of 4,4,-dimethoxy-butan-2-one (83g, 0.62 mol) in ether (300 mL) dropwise to the Grignard reagent. After complete addition, the reaction mixture was heated under reflux for 30 min, cooled and kept aside for overnight stirring. Yellow reaction mixture was poured onto ice-cold aqueous ammonium chloride (2 L) and kept aside for 2 hr. The ether layer was separated, washed with water, dried and freed of solvent. The residue was distilled in vacuum to yield 224.36 g (44%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22-7.02 (m, 4H), 4.68 (t, J = 8.5Hz, 1H), 3.32 (s, 3H), 3.30 (s, 3H), 2.7 (s, 2H), 2.3 (s, 3H), 1.9-1.71 (m, 2H), 1.19 (s, 3H).

2,7-dimethylnaphthalene *(16):*

A 1L, one necked round bottom flask equipped with magnetic stirrer was charged with a solution of hydroxyl-acetal (130 g, 0.5 mol) in glacial acetic acid (500 mL) and 48% HBr (360 mL). The reaction contents were heated for 1 hr over steam bath with occasional stirring. After the required time, the flask was placed over ice-bath until the oil had completely crystallized. The solid obtained on cooling was filtered off with suction, washed with water, and finally recrystallized from ethanol to yield 59g (70%) of 2,7-dimethylnaphthalene as colorless flakes. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, J = 8.2Hz, 2H), 7.31 (d, J = 8.2, 2H), 7.07 (s, 2H), 2.80 (s, 3H), 2.71 (s, 3H).

2,7-dimethyl-1-chloromethylnaphthalene *(19) :*

To a 1L three necked round bottom flask, equipped with mechanical stirrer, a solution of 2,7-dimethylnaphthalene (63g, 0.40 mol) in acetic acid (225 mL) was transferred. Concentrated HCl (315 mL), 85% H_3PO_4 (135 mL) and paraformaldehyde (24.6g) were then added. The reaction mixture was gently heated at 55^oC (water bath) with stirring for 2 hr. The resulting mixture was poured into two liters of water and extracted with dichloromethane (200 mL). The organic phase was washed twice with Na_2CO_3 followed by water, dried over magnesium sulfate and concentrated under vacuum to result in 82g (99%) of pure 2,7-dimethyl-1-chloromethylnaphthalene. ^1H NMR (600 MHz, $CDCl_3$): δ 7.83 (s,1H), 7.70 (d, *J* = 8.4 Hz,1H), 7.68 (d, *J* = 8.4 Hz,1H), 7.28 (d, *J* = 8.4 Hz,1H), 7.23 (d, *J* = 8.4 Hz,1H), 5.05 (s, 2H), 2.56 (s, 3H), 2.55 (s, 3H).

2,7-dimethyl-1-naphthaleneacetonitrile *(20):*

A two necked round bottom flask equipped with a magnetic stirrer was charged with a mixture of 2,7-dimethyl-1-chloromethylnaphthalene (79g, 0.40 mol) and sodium cyanide (29g, 0.59 mol) in acetonitrile (400 mL). The reaction mixture was refluxed with stirring for 48 hrs. The resulting yellow solution was poured into 100 mL of water and allowed to stir at room temperature overnight. The solids were filtered off and the remaining aqueous phase was extracted with dichloromethane. DCM extracts were combined with solid, washed together with water, dried over magnesium sulfate, filtered and solvent was removed under reduced pressure to give in 74 g (98 %) of 2,7-dimethyl-1-naphthaleneacetonitrile. ^1H NMR (600 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.4Hz, 1H), 7.712 (d, *J* = 9Hz, 1H), 7.68 (s, 1H), 7.32 (d, *J* = 7.8Hz, 1H), 7.26 (d, *J* = 8.4Hz, 1H), 4.032 (s, 1H), 2.56 (s, 3H), 2.549 (s, 3H).

2,7-dimethyl-1-naphthaleneacetic acid *(21):*

Concentrated sulfuric acid (321 mL) was added carefully to a mechanically stirred solution of **20** (72 g, 0.36 mol) in a mixture of acetic acid (217 mL) and water (321 mL). After addition the reaction mixture was refluxed for 3 hours. Yellowish green color appeared with time. After 3 hours of reflux, contents were poured into water and left overnight with stirring. Greenish thick oily residue was separated out, extracted with dichloromethane, dried and rotovaped; yield; 76.65 g (97%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.69 (d, *J* = 8.4Hz, 1H), 7.64 (d, *J* = 7.8Hz, 1H), 7.24 (d, *J* = 7.8Hz, 2H), 4.09 (s, 1H), 2.509 (s, 1H), 2.50 (s, 1H).

2,7-dimethyl-1-naphthalene acid chloride *(22):*

A three necked round bottom flask equipped with a magnetic stirrer was charged with a mixture of 2,7-dimethyl-1-naphthaleneacetic acid (61.52 g, 0.28 mol) and thionyl chloride (68 mL, 0.93 mol) in chloroform (200 mL). The reaction mixture was kept at room temperature for 3 hours. Vigorous evolution of HCl gas was observed during the reaction. Once the evolution of gas ceased, the reaction mixture was gently heated for 1 h, then stirred overnight at room temperature. Solvent was evaporated to leave a residual dark oil; 65.9 g (98%), which was used further without further purification. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73-7.69 (m, 2H), 7.59 (s, 1H), 7.25-7.30 (m, 2H), 4.59 (s, 2H), 2.53 (s, 3H), 2.51 (s, 3H).

3,8-dimethyl-1-acenaphthenone *(23):*

Aluminum chloride (36.24 g, 0.27 mol) was added in portions for a period of 1 h to a mechanically stirred ice cold solution of 2,7-dimethyl-1-naphthalene acid chloride (49g, 0.21 mol) in dichloroethane (306 mL) under nitrogen. After addition of Lewis acid

the ice bath was removed and stirring was continued at room temperature for two hours, then gently refluxed for 1 h and finally left overnight at room temperature with stirring. The reaction mixture was quenched carefully by slow addition of 1:1 HCl solution, organic layer was washed twice with water (200 mL), dried over magnesium sulfate, filtered, and evaporated to yield a black oily material. The crude product was purified by column chromatography (silica gel, dichloromethane) to yield 40 g (97%) of monoketone (23) as yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4Hz, 1H), 7.68 (d, *J* = 8.4Hz, 1H), 7.38 (d, *J* = 8.4Hz, 1H), 7.34 (d, *J* = 8.4Hz, 1H), 3.65 (s, 2H), 2.80 (s, 3H), 2.45 (s, 3H).

3,8-dimethylacenapthaquinone *(24):*

Aqueous HBr (48%, 106 mL) was added dropwise to a solution of 23 (58.84 g, 0.3 mol) in 320 mL of DMSO at room temperature. Later the reaction mixture was gently heated at 55 ^{o}C with stirring for 75 minutes. The reaction was cooled and later quenched with 500 mL of water. Solid obtained was filtered and recrystallised from ethanol to yield 53g (84%) of 3,8-dimethylacenapthaquinone. ^{1}H NMR ($CDCl_3$): δ 8.04 (d, *J* = 8.1Hz, 2H), 7.51 (d, *J* = 8.4Hz, 2H), 2.86 (s, 6H).

1,6,7,10-tetramethylfluoranthene *(25):*

(I) A 20% solution of potassium hydroxide in methanol (4 mL) was added dropwise to a stirred solution of 22 (6.5 g, 0.03 mol) and 3-pentanone (8 mL) in methanol (48 mL). The solution was continued to stir at room temperature for 1 h, and kept overnight in refrigerator for precipitation. A gray colored solid which mostly contains diketone 29 was separated by filtration. The dark alcoholic filtrates consisting of a mixture 28 and 29 was concentrated under vacuum. The solid residue was washed twice

with water, acidified and was subjected to sonication for 2 hr and finally filtered. Both fractions were combined to give 7.73 g.

(II) 7.73 g of a mixture of 28 and 29 was transferred to a 250 mL round bottom flask charged with acetic anhydride (84 mL) and norbornadiene (19 mL). The reaction mixture was refluxed with stirring. Upon completion of the reaction, as judged by T.L.C (after ca. 12 h), excess norbornadiene was distilled off by heating the flask without a condenser under well working hood. The solution was cooled, poured into 200 mL of water and extracted with dichloromethane. The organic layer was washed twice with water, 5 % NaOH and again with water. The crude product was purified using column chromatography (toluene/cyclohexane, 4:1) to yield 4.0 g (49%) of tetramethyl-fluoranthene as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, *J* = 8.7Hz, 2H), 8.20 (s, 2H), 8.0 (d, *J* = 8.4Hz, 2H), 7.20 (s, 2H), 7.08 (s, 2H).

1,6,7,10-tetrakis(dibromomethyl)-fluoranthene *(12)*:

A three necked round bottom flask equipped with magnetic stirrer under nitrogen atmosphere was charged with 1,6,7,10-tetramethylfluoranthene (1.51 g, 0.005 mol), NBS (10 g, 0.056 mol) and benzoyl peroxide (53 mg). The reaction mixture was refluxed in benzene (160 mL) with irradiation with a sun lamp. The reaction progress was monitored by TLC. Aliquots after 6 hr of irradiation showed three major spots but after additional three hours there was only one major spot. The solvent was evaporated under reduced pressure and the orange solid washed well with water and extracted with dichloromethane, dried and evaporated to yield yellow solid (12) 4.05 g (78 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, *J*=8.7Hz, 2H), 8.20 (s, 2H), 8.0 (d, *J*=8.4Hz, 2H), 7.20 (s, 2H), 7.08 (s, 2H).

1,2,5,6-tetrabromocorannulene *(14):*

4.18 g of octabromofluoranthene (4.7 mmol) was refluxed in a mixture of dioxane (200 mL), water (80 mL) and 3 g of NaOH for 15 minutes. Originally formed dark red color faded with time. The reaction contents were cooled, poured into water (200 mL) and acidified with HCl. Yellowish brown insoluble solid was filtered and dried to yield 2.45 g (92 %) of 14. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96 (s, 2H), 7.96 (d, *J*=8.7Hz, 2H), 7.85 (d, *J*=8.1Hz, 2H).

Corannulene *(6):*

Method 1: 4% aq. HCl (4 mL) was added to a stirring solution of 14 (1 g, 1.76 mmol), KI (4.3 g), Zn (12 g) in ethanol (200 mL) and was refluxed for one week. The reaction progress was monitored by GC, which showed a gradual increase of 6 with time. Solvent was removed under reduced pressure and the product was extracted with dichloromethane, washed couple of times with water, dried and evaporated. Chromatography (silica gel, hexane / dichloromethane (5:1)) gave 0.45 g (59 %) of **6** as a pale yellow solid.

Method 2: A 250 mL two necked round bottom flask equipped with magnetic stirrer and a nitrogen inlet was charged with tetrabromocorannulene (14) (1 g, 1.76 mmol), $Pd(OAc)_2$ (3 mol%, 12 mg), IMes. HCl (3 mol%, 18 mg) and KO^tBu (2.96 g, 26.1 mmol). The reaction mixture was refluxed in isopropanol (90 mL) for 30 minutes (the originally formed yellowish brown color changed to dark brown). The reaction mixture was acidified with 1:1 aq. HCl solution and filtered. Solvent was evaporated under reduced pressure and the concentrated mixture was purified by flash

chromatography (dichloromethane/hexane (2:1)), gave 0.39 g (90%) of **6** as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (s, 10H).

3-bromo-2-hydroxy-p-xylene *(41):*

2-hydroxy-*p*-xylene (40) (10 g, 0.0818 mol) and diisopropylamine (545 μL) were dissolved in dichloromethane (50 mL) and the mixture was stirred at room temperature under nitrogen atmosphere for 5 minutes. A solution of NBS (21.85 g, 0.122 mol) in freshly distilled dichloromethane was added dropwise over 2hr and allowed to react for 3 hr. Upon completion of reaction, as monitored by TLC and GC, the solvent was removed under reduced pressure and the solid was washed with water, extracted with dichloromethane and dried to yield 41 as a yellowish white liquid 16.05 g (97%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.9 (d, *J* = 9Hz, 2H), 6.02 (d, *J* = 9Hz, 2H), 5.65 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 16.2, 22.7, 112.9, 121.6, 122.5, 129.1, 135.4, 150.2.

3-naphthyl-2-hydroxy-p-xylene *(42):*

A two necked 50 mL round bottom flask with nitrogen inlet was charged with 36 (500 mg, 2.48 mmol), 1-napthylboronic acid (500 mg, 2.9 mmol), $Pd(PPh_3)_4$ (5 mol%, 143 mg) and 4 g of Na_2CO_3. The reaction mixture was refluxed for 6 h in a mixture of ethanol (5 mL), toluene (5 mL) and water (2 mL). The solvent was removed under reduced pressure and the solid residue was washed with water, extracted with dichloromethane, dried and evaporated. The resulting white solid was recrystallized from ethanol to give 0.308 mg of 37 (46 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8Hz), 7.62-7.45 (m, 5H), 7.18 (d, *J* = 7.5Hz, 1H), 6.88 (d, *J* = 7.5Hz, 1H), 4.63 (s, 1H), 2.39 (s,

3H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.91, 19.81, 121.32, 121.49, 125.29, 125.38, 125.88, 125.91, 126.40, 126.74, 128.35, 128.42, 128.79, 130.10, 132.29, 134.13, 135.40, 151.42.

Triflate *(43):*

A solution of 3-napthyl-2-hydroxy-*p*-xylene (42) (250 mg, 1.01 mmol), dry 2,6-lutidine (230 µL, 2.02 mmol) in freshly distilled dichloromethane (10 mL) was cooled to -78 ^{o}C under atmosphere of nitrogen and treated dropwise with a solution of triflic anhydride (340 µL, 2.016 mmol) dissolved in dichloromethane (5 mL). The solution was slowly allowed to warm to 0^{o}C over a period of 3 h. Later the reaction mixture was quenched with water (10 mL) and extracted with dichloromethane. The organic fractions were combined, dried over magnesium sulfate and concentrated under vacuum. The crude product was purified by column chromatography (hexane/dichloromethane (1:1)) to give 276 mg of 38 (76%) as a colorless oil which solidified on standing. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (t, *J* = 8.5Hz, 2H), 7.56 (t, *J* = 7.8Hz, 1H), 7.50 (t, *J* = 7.08Hz, 1H), 7.41-7.36 (m, 3H), 7.30 (q, *J* = 8Hz, 2H), 2.49 (s, 3H), 1.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 17.31, 20.00, 115.73, 119.98, 125.17, 125.22, 125.85, 126.28, 128.27, 128.37, 128.69, 128.71, 129.66, 131.17, 131.85, 132.37, 133.62, 133.90, 138.06, 146.71.

7,10-dimethyfluoranthene *(33):*

An oven-dried 10 mL two necked flask under nitrogen atmosphere was charged with a mixture of **38** (20 mg, 0.052 mmol), $Pd(OAc)_2$ (4 mg, 0.0156 mmol), $P(Cy)_3$ (17 mg, 0.054 mmol), DBU (0.1 mL) in DMAc (2 mL) and was allowed to reflux for 6 h. The reaction mixture was then cooled, diluted with 5 mL of dichloromethane, washed

twice with 10 mL each of 10% HCl, and with 5 mL of aq. $NaHCO_3$ and water. Drying over magnesium sulfate, followed by evaporation of solvent under reduced pressure gave the crude product. Column chromatography on silica gel gave 6 mg of **33** (20%) as brownish white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.1 Hz, 2H), 7.85 (d, *J* = 8.1Hz, 2H), 7.66 (t, *J* = 7.8 Hz, 2H), 7.10 (s, 2H), 2,7 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.3, 20.3, 123.0, 126.2, 127.8, 129.8, 129.9, 131.9.

1,2,5,6-tetrakis(p-methoxyphenyl)corannulene *(47):*

An oven dried 100 mL round bottom equipped with magnetic stirrer under nitrogen flow was charged with a mixture of $Pd(OAc)_2$ (8 mg, 10 mol%), finely powdered tetrabromocorannulene (200 mg, 0.35 mmol), $P(Cy)_3$ (10 mol%, 10 mg), and Cs_2CO_3 (506 mg, 4 eq.). The reaction mixture was dissolved in 16 mL of anhydrous dioxane and heated gently at 70^{o}C for 1 hr. The reaction progress was monitored by TLC. Upon completion of the reaction, the contents were diluted with water and acidified using 1:1 HCl solution. Black solid obtained by filtration was purified quickly through a pad of silica gel. Purification by column chromatography on silica gel (dichloromethane/hexane (2:1)) yielded the tetraderivative of corannulene (47) as yellow solid (113.7 mg, 47%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, *J* = 9Hz, 2H), 7.64-7.62 (m, 4 H), 7.72-7.20 (m, 8H), 6.87 (m, 8H), 3.84 (s, 6H), 3.83 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.16, 113.14, 127.01, 127.14, 127.22, 130.20, 130.27, 130.88, 130.93, 132.58, 133.95, 134.92, 135.10, 138.26, 138.53, 158.24 MS (EI) M+ found 674.4.

1,2,5,6-tetrakis(p-methoxycarbonylphenyl)corannulene *(48):*

A two necked 50 mL round bottom flask equipped with nitrogen inlet and a magnetic stirrer was charged with $Pd(OAc)_2$ (10 mol%, 4 mg), finely powdered

tetrabromocorannulene (100 mg, 0.176 mmol), $P(Cy)_3$ (10 mol%, 5 mg), *p*-methoxycarbonylphenylboronic acid (506 mg, 2.8 mmol) and Cs_2CO_3 (228 mg, 0.7 mmol). The reaction mixture was dissolved in 4 mL of anhydrous dioxane and heated at 70^{o}C for 1 hr. Upon completion of the reaction, as judged by TLC, the contents were cooled, diluted with water and acidified with 1:1 HCl. Black solid residue obtained was filtered and allowed to pass through a pad of silica gel with dichloromethane. The crude product was purified by column chromatography (dichloromethane/hexane (5:1)) to yield 7 mg (5 %) of (48) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98-7.94 (m, 8H), 7.82 (d, *J* = 9Hz, 2H), 7.57-7.53 (m, 4H), 7.33-7.31 (m, 8H), 3.93 (s, 6H), 3.92 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ {52.1, 127.01, 127.10, 127.72, 128.88, 128.96, 129.09, 129.57, 130.0, 131.42, 134.23, 135.21, 137.91, 138.36, 143.0, 166.83.

REFERENCES

1) Simonei, B. R. T. *Hand Environ. Chem.* 1998, *3*, 175-221.

2) Grimmer, G. *Environmental Carcinogens* [(Boca Rator, Eds.), CRC Press, Fla., 1983)] Chapter: Polycyclic Aromatic Hydrocarbons.

3) Schaket, B. *Mutat. Res.* 1999, *424*, 143-153.

4) Becker, L. *Astrophysics and Space Science Library* 1999, *236*, 377-398.

5) Heymann, D. *Astrophys. J.* 1997, *489*, L111-L114.

6) Kroto, H. W., Heath, J. R. O'Brian, S. C., Curl, R. F. and Smalley, R. E., *Nature*, 1985, *318*, 162-163.

7) Gerhardth, P.; Loeffler, S.; Homann, K. H. *Chem. Phys. Lett*. 1987, *137*, 306-310.

8) Curl, R. F., *Angew. Chem., Int. Ed. Engl.*, 1997, *36*, 1566-1567.

9) Kroto, R.; *Angew. Chem., Int. Ed. Engl.,* 1997, *36*, 1578-1593.

10) Smalley, R. E., *Angew. Chem., Int. Ed. Engl.,* 1997, *36*, 1594-1603.

11) Friedman, S. M.; Decamp, D. L.; Sijbesma, R. P.; Srdanov. G.; Wudl, F.; Kenyon, G. L. *J. Am. Chem. Soc.* 1993, *115*, 6506-6509.

12) Scott, L. T.; Bronstein, H. E.; Preda, D. V.; Anselms, R. B. M.; Bratcher, M. S.; Hagen, S. *Pure Appl. Chem.* 1996, *68*, 291-300.

13) Rabideau, P. W.; Sygula, *A. Acc. Chem. Res.,* 1996, *29*, 235-242.

14) Ansems, R. B. M.; Scott, L. T. *J. Am. Chem. Soc.* 2000, *121*, 2719-2724.

15) Diederich, F.; Rubin, Y. *Angew. Chem. Int. Ed. Engl.* 1992, *31*, 1101-1106.

16) Mehta, G.; Rao, H. S. P. *Tetrahedron* 1998, *54*, 13325-13370.

17) Mehta, G.; Rao, H. S. P. *Advances in Strain in Organic Chemistry* (Eds.: Halton, B.), Jai Press, London, 1997, *6*, 139-187.

18) Scott, L. T.; *Angew. Chem. Int. Ed.* 2004, *116*, 5102-5116.

19) Sygula, A.; Rabideau, P. W. in *Carbon-Rich Compounds* (Haley, M.; Tykwinski, R, Ed.), Wiley, Weinheim, 2006, chapter 12, 529-565.

20) Rabideau, P. W.; Sygula, A. *Advances in Theoretical Interesting Molecules* [(Randolph. P. T, Ed.), Jai Press, Connecticut, 1995] chapter1, 1-36.

21) Tremblay, J. F. *Chem. Eng. News* 2003, 81 (32), 13-14.

22) Takehara, H.; Yamamoto, T.; (Mitsubishi Chemical Corp., Japan), JP 2003160317, 2003**.**

23) Yamamoto, T.; Takehara, H.; Takakura, T. (Mitsubishi Chemical Corp., Japan), JP 2003232505, 2003. See also www.m-agaku.co.jp/english/rel/2001/120302.htm.

24) Fowler, P. W.; Manolopoulos, D. E. *Atlas of Fullerenes*, Oxford University, Oxford, 1995.

25) Barth, W. E.; Lawton, R. G. *J. Am. Chem. Soc.* 1966, *88*, 380-381.

26) Lawton, R. G.; Barth, W. E. *J. Am. Chem. Soc.* 1971, *93*, 1730-1745.

27) Hanson, J. C.; Nordman, C. E. *Acta Crystallogr. Sect. B.* 1976, *32*, 1147-1153.

28) Craig, J. T.; Robins, M. D. W. *Aust. J. Chem.* 1968, *21*, 2237-2245.

29) Jacobson, R. H. Ph.D. Dissertation, University of California, Los Angeles, 1986.

30) Davy, J. R.; Iskander, M. N.; Resis, J. A. *Tetrahedron Lett.* 1978, 4085-4088.

31) Shen, D. Ph.D. Dissertation, University of California, Los Angeles, 1990.

32) Scott, L. T.; Hashemi, M. M.; Meyer, D. T.; Warren, H. B. *J. Am. Chem. Soc.* 1991, *113*, 7082-7084.

33) Scott, L. T.; Cheng, P. C.; Hashemi, M. M.; Bratcher, M. S.; Meyer, D. T.; Warren, H. B. *J. Am. Chem. Soc*. 1997, *119*, 10963-10968.

34) Borchardt, A.; Fuchicello, A.; Kilway, K. V.; Baldrige, K. K.; Siegel, J.S. *J. Am. Chem. Soc.* 1992, *114*, 1921-1923.

35) Zimmermann, G.; Neuchter, U.; Hagen, S.; Nuechter, M. *Tetrahedron Lett.* 1994, *35*, 4747-3440.

36) Liu, C. Z.; Rabideau, P. W. *Tetrahedron Lett.* 1996, *37*, 3437-3440.

37) Mehta, G.; Panda, G. *Tetrahedron Lett.* 1997, *38*, 2145-2148.

38) Hagen, S.; Christoph, H.; Zimmermann, G. *Tetrahedron* 1995, *51*, 6961-6970.

39) Abdourazak, A. H.; Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* 1993, *115*, 3010-3011.

40) Bratcher, M. S.; Scott, L. T. Abstracts of Papers, 207th National Meeting of the American Chemical Society, San Diego, CA.

41) Bratcher, M. S. Ph.D. Dissertation, Boston College, 1996**.**

42) Mehta, G.; Sarma, P. V. V. S. *Chem. Commun.* 2000, 19-20.

43) Rabideau, P. W.; Abdourazak, A. H.; Folsom, H. E.; Marcinow, Z.; Sygula, A. *J. Am. Chem. Soc.* 1994, *116*, 7891-7892.

44) Abdourazak, A. H.; Marcinow, A. Z.; Sygula, A.; Sygula, R.; Rabideau, P. W. *J. Am. Chem. Soc.* 1995, *117*, 6410-6411.

45) Clayton, M. D.; Rabideau, P. W. *Tetrahedron Lett.* 1997, *38*, 741-744.

46) Scott, L. T.; Bratcher, M. S.; Hagen, S. *J. Am. Chem. Soc.* 1996, *118*, 8743-8744.

47) Ansems, R. B.M.; Scott, L. T. *J. Am. Chem. Soc.* 2000, *122*, 2719-2724.

48) Seider, T. J.; Baldridge, K. K.; Siegel, J. S. *J. Am. Chem. Soc.* 1996, *118*, 2754-2755.

49) Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* 1998, *120*, 12666-12667.

50) Sygula, A.; Fronczek, F. R.; Rabideau, P. W. *Tetrahedron Lett*. 1997, 5095-5098.

51) Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* 1999, *121*, 7800-7803.

52) Baumstark, A. L.; Bechara, E. J. H.; Semigran, M. J. *Tetrahdron Lett.,* 1976, 3265-3266.

53) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem.* 1978, *43*, 3255-3266.

54) Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* 2000, *122*, 6323-6324.

55) Sygula, A.; Xu, G.; Marcinow, Z.; Rabideau, P. W. *Tetrahedron* 2001, *57*, 3637-3644.

56) Xu, G.; Sygula, A.; Marcinow, Z.; Rabideau, P. W. *Tetrahedron Lett*. 2000, *41*, 9931-9934.

57) Sygula, A.; Sygula, R.; Rabideau, P. W. *Org. Lett.* 2005, *7*, 4999-5001.

58) Buu-Hoi; Cagniant, P. *Revue. Scientifique* 1942, *80*, 130-134.

59) Borchardth, A.; Hardcastle, K.; Gantzel, P.; Siegel, J. S. *Tetrahedron Lett*. 1993, *34*, 273-276.

60) Wolinska-Mocydlarz, J.; Canonne, P.; Leitch, L. C. *Synthesis* 1974, 566-568.

61) Floyd, M. B.; Du, M. T.; Fabio, P. F.; Jacob, L. A.; Johnson, B. D. *J. Org. Chem.* 1985, *50*, 5022-5027.

62) Jones, C. S.; Elliott, E.; Siegel, J. S. *Synlett*, 2004, *1*, 187-191.

63) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* 1999, *38*, 2411-2413.

64) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* 1998, *37*, 3387-3388.

65) Littke, A. F.; Fu, G. C. *J. Org. Chem.* 1999, *64*, 10-11.

66) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* 1999, *121*, 9889-9890.

67) Grasa, A. G.; Nolan, S. P. *Org. Lett.* 2001, *3*, 119-122.

68) Lee, H. M.; Nolan, S. P. *Org. Lett.* 2000, *2*, 1307-1310.

69) Navarro, O.; Kelly, R. A.; Nolan, S. P. *J. Am. Chem. Soc.* 2003, *125*, 161194-16195.

70) Singh, R.; Viciu, M. S.; Kramareva, N.; Navarro, O.; Nolan, S. P. *Org. Lett.* 2005, *7*, 1829-1832.

71) Viciu, M. S.; Grasa, G. A.; Nolan, S. P. *Organometallics,* 2001, *20*, 3607-3612.

72) Tsuji, J. *Palladium Reagents and Catalysts*, Wiley, 2004, Chapter 1, 14-15.

73) Hermann, W. A.; Goosen, L. T.; Kocher, C. *Angew. Chem. Int. Ed. Engl.* 1996, *35,* 2805-2807.

74) Rice, J. E.; Cai, Z. W. *Tetrahedron Lett.*, 1992, *33*, 1675-1678.

75) Wegner, H. A.; Scott, L. T.; de Meijere, A. *J. Org. Chem.* 2003, *68*, 883-887.

76) Gronowitz, S.; Hansen, G. *Arkiv Kemi,* 1967, *27*, 145-151.

77) Shizu, F.; Hisao, E.; Atsushi, O.; Atsushi, O.; Akiko, N. *Bull. Chem. Soc. Japan,* 1993, *66*, 1576-1579.

78) Hisao, C. E.; Katsumi, T.; Hideo, S. *Toso Kenkyu Hokoku*, 1993, *37*, 109-116.

79) Anderson, N. G.; Maddaford, S. P.; Keay, B. A. *J. Org. Chem.* 1996, *61*, 9556-9559.

80) Pathak, R.; Vandayar, K.; Otterlo, W. A. L.; Michael, J. P.; Fernandes, M. A.; de Kaning, C. B. *Org., Biomol. Chem.*, 2004, *2*, 3504-3509.

81) Cammidge, A. N.; Crepy, K. V. L. *Tetrahedron*, 2004, *60*, 4377-4386.

82) Clews, J.; Curtis, A. D. M.; Malkin, H. *Tetrahedron*, 2000, *56*, 8735-8746.

83) Littke, A. F.; Dai, C.; Fu, G. *J. Am. Chem. Soc.* 2000, *122*, 4020-4028 and references therein.

84) Seiders, T. J.; Baldridge, K. K.; Siegel, J. S. *Tetrahedron*, 2001, *57*, 3737-3742.

85) Ghosh, R.; Samuelson, A. G. *New J. Chem.,* 2004, *28*, 1390-1393 and references therein.

86) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.,* 2001, *3*, 4315-4317.

87) Xu, L. W.; Xia, C. G.; Li, J. W.; Hu, X, X. *Synlett* 2003, *13*, 2071-2073.

88) Harkal, S.; Kumar, K.; Michalik, D.; Zapf, A.; Jackstell, R.; Rataboul, F.; Riermeier, T.; Monsees, A.; Beller, M. *Tetrahedron Lett.* 2005, *46*, 3237-3240 and references therein.

89) Fentrill, G. I.; Mirrington, R. N. *Tetrahedron Lett.*, 1970, 1327-1328.

90) Nayak, M. K.; Chakraborti, A. K. *Tetrahedron Lett.*, 1997, *38*, 8749-8752.