NOTE TO USERS

SYNTHESIS OF 2,7-DISUBSTITUTED *N,N*-DIETHYL NAPHTHALENE-1,8-DICARBOXAMIDE DERIVATIVES BY DIRECTED *ortho* METALATION – CROSS COUPLING METHODOLOGY

by

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Abstract

Directed *ortho* Metalation (D*o*M) of the readily prepared *N,N*-diethyl naphthalene-1,8-dicarboxamide leads, after electrophilic quench, to 2- and 2,7-substituted *N,N*-diethyl naphthalene-1,8-dicarboxamide products as a function of the conditions. When the 2 and 2,7 substituents are halogens (*N,N*-diethyl-2 -iodonaphthalene-1,8-dicarboxamide, *N,N*-diethyl-2,7-dibromonaphthalene-1,8-dicarboxamide, *N,N*-diethyl-2,7-diiodonaphthalene-1,8-dicarboxamide, Suzuki-Miyaura Pd-catalyzed cross coupling methodology was employed to form 2-aryl and 2,7-diaryl-*N,N*-diethyl naphthalene-1,8-dicarboxamides. Treatment of *N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxamide leads to the mono fluorenone of *N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxamide by a Directed remote Metalation (DreM) reaction. The scope and limitations of these methodologies are presented. Different ratios of 2- and 2,7-deuterated products are obtained as a function of conditions and these results are discussed. Rotational barriers of the C-Ar bond rotation have been determined for N,N-diethyl naphthalene-1,8-dicarboxamide using VT NMR. The X-ray structure of *N,N*-diethyl-2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide is presented.

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To Mom, Dad and Andrew

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Abbreviations

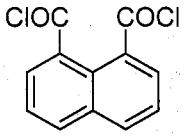
AcOH	acetic acid
Anhyd	anhydrous
Aq	aqueous
Ar	aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Boc	*tert*-butylcarbonyl
n-BuLi	n-Butyl Lithium
s-BuLi	s-Butyl Lithium
t-BuLi	t-Butyl Lithium
calcd	calculated
CIPE	Complex Induced Proximity Effect
CO_2	carbon dioxide
d	doublet
DCM	dichloromethane
dd	doublet of doublets
DME	Dimethoxyethane
DMF	*N,N*-dimethylformamide
DMG	Directed Metalation Group
DMSO	dimethyl sulfoxide
D*o*M	Directed *ortho* Metalation
dppe	diphenylphosphinoethane
dppb	diphenylphosphinobutane

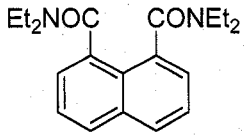
dppf	diphenylphosphinoferrocene
dppp	diphenylphosphinopropane
DreM	Directed remote Metalation
E^+	electrophile
EDG	electron donating group
EI	electron impact
Equiv	equivalents
Et_2O	diethyl ether
EWG	electron withdrawing group
GC	gas chromatograph
GC-MS	gas chromatograph-mass spectrometry
h	hour
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
IPA	isopropyl amine
iPr	isopropyl
IR	infrared
KEM	Kinetically Enhanced Metalation
KIE	Kinetic Isotope Effect
L	ligand
LDA	lithium diisopropyl amine
LG	leaving group

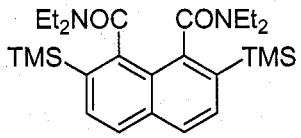
LRMS	low resolution mass spectrometry
m	multiplet
MeLi	methyllithium
min	minutes
mmol	millimole
MO	molecular orbital
MOM	methoxy methyl
Nd:Yag	type of laser
NGF	nerve growth factor
NMR	nuclear magnetic resonance spectroscopy
Nu	nucleophile
OAm	*N,N*-diethylcarbamate
OMe	methoxy
pd	pentet of doublets
Ph	phenyl
q	quartet
qd	quartet of doublets
qt	quartet of triplets
RCM	ring closing metathesis
rds	rate determining step
rt	room temperature
SAR	structure activity relationship
satd	saturated

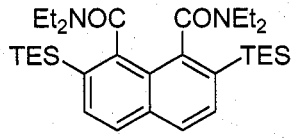
SM	starting material
t	time or triplet
Tc	temperature of coalescence
TBAF	tetrabutylamoniumflouride
TES	triethylsilane
TFA	triflouroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilane
TMEDA	*N,N,N`,N`*-tetramethylethylenediamine
TMS	trimethylsilane
UV	ultraviolet
VT-NMR	variable temperature NMR
yld	yield

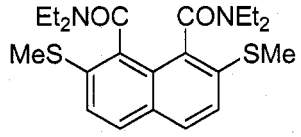
List of Experimental Procedures

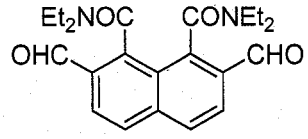


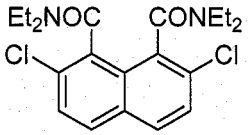


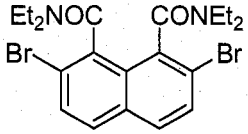


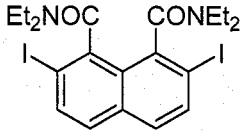


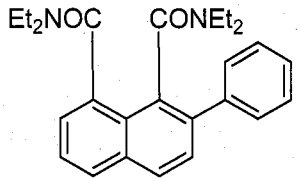


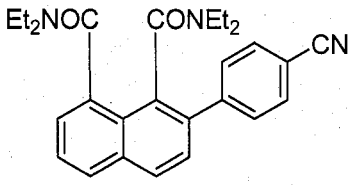


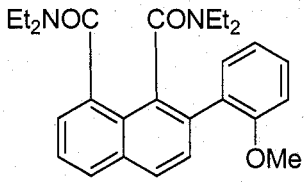


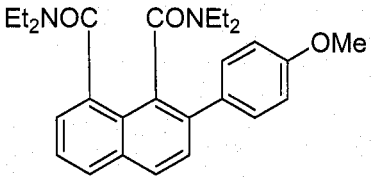


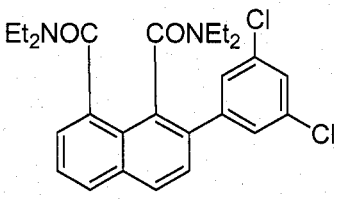


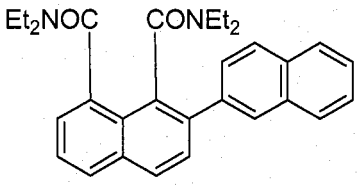


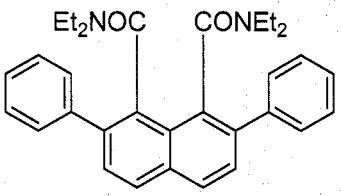


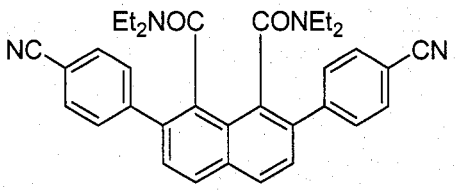


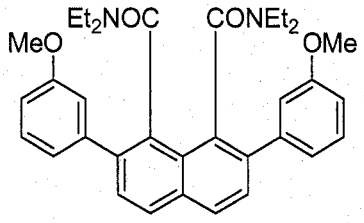


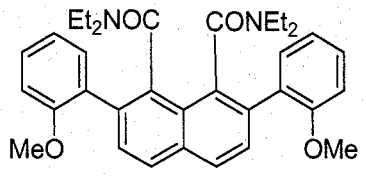


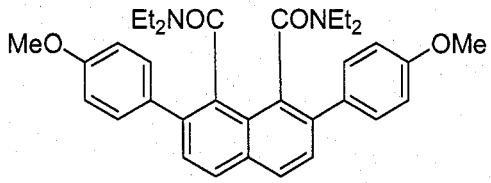


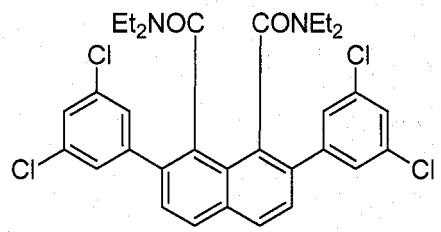


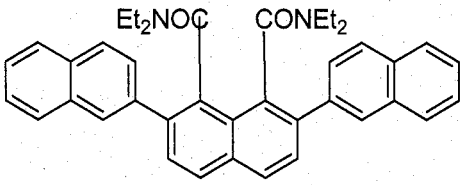


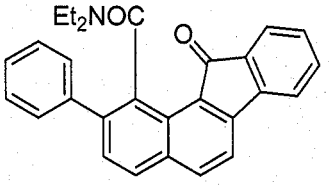


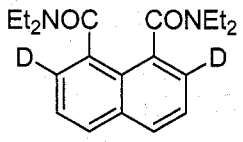








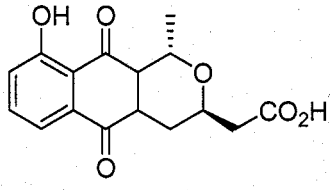




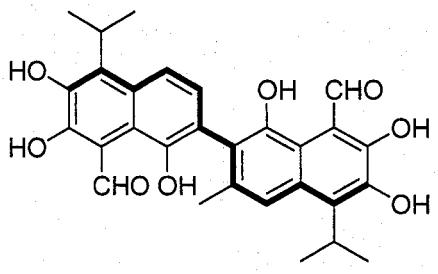
1 Introduction

1.1 The Synthesis of Naphthalene Derivatives

Simple naphthalene derivatives originate from coal tar distillation[1] and are the structural components of a variety of bioactive molecules and natural products. Some representative examples[2] of the latter include Nanaomycin A **1.1** which has antibacterial characteristics, gossypol **1.2**, of which (*R*)-gossypol is effective against tumor cells and HIV-1, whereas (*S*)-gossypol is active against herpes, influenza and Para influenza viruses, and finally Korupensamine A **1.3** which has been demonstrated to exhibit antimalarial activity.



1.1



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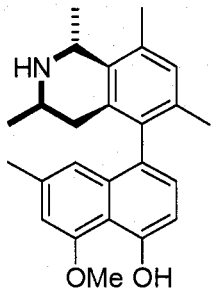
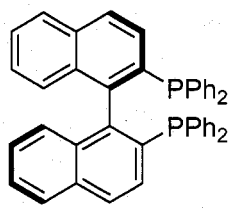


1.3

Recently, interest in naphthalenes has increased due to their significance as ligands, e.g. (R, R)-BINAP, **1.4**, developed by Noyori which, when complexed with Ru, is capable of effecting asymmetric hydrogenation.[3]

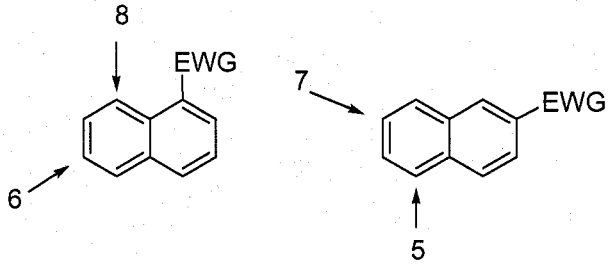


1.4

The synthesis of substituted naphthalenes has been accomplished via many different methods in past. These can be categorized as follows; normal electrophilic substitution, nucleophilic substitution, naphthalynes, free radical attack, formation of the naphthalene nucleus and, isomerizations. The facile reactivity of naphthalenes towards substitution, can be attributed to its nonsymmetrical nature, which in turn leads to more double bond character, hence more reactivity towards substitution.[1]

1.1.1 Electrophilic Substitution

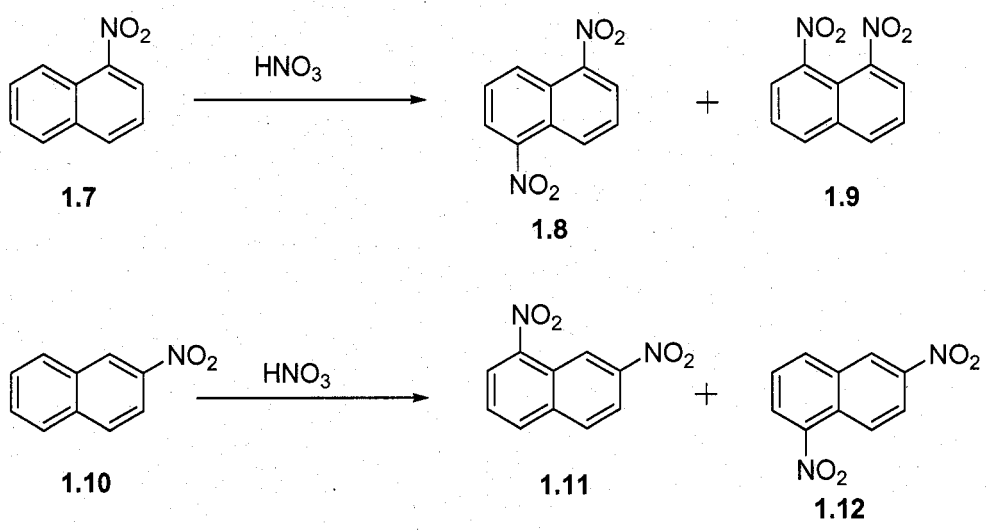
The reactivity of naphthalene is observed in electrophilic substitution. The positions on the ring at which the substitution occurs is dictated by the nature of the directing group. If the directing group is electron withdrawing (EWG), substitution occurs in the unsubstituted ring following the rules set forth in **1.5** and **1.6**.



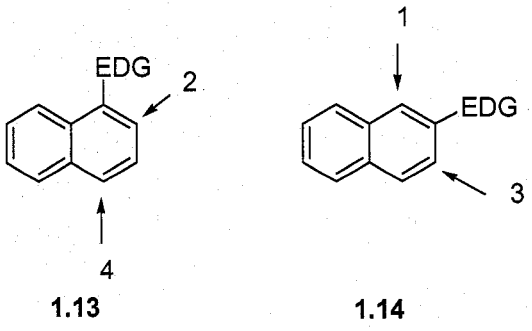
1.5 **1.6**

These rules can be applied to the nitration of nitronaphthalene[1] (**1.7** and **1.10**), where the nitration occurs in the remote ring. (**Scheme 1.1**)

Scheme 1.1

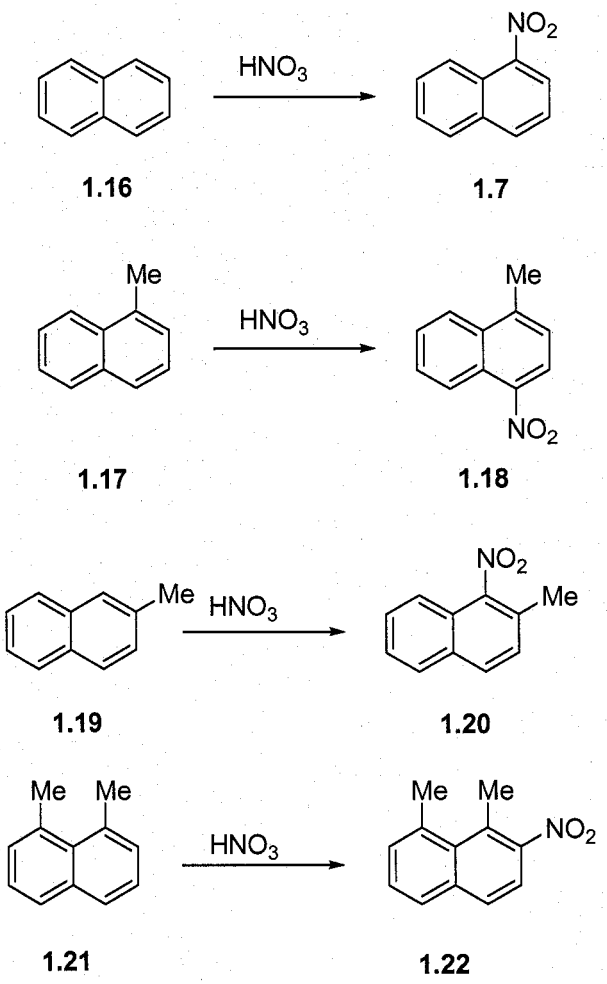


If the directing group is an electron donating group (EDG) the substitution occurs in the substituted ring and abides by normal *ortho* and *para* rules (**1.13** and **1.14**).



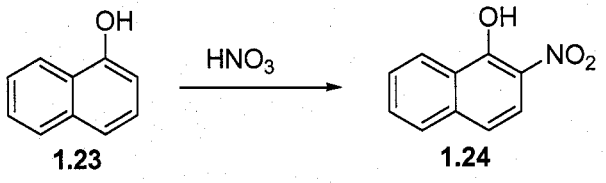
These rules can be observed in the simple nitration of naphthalene **1.16** and methylnaphthalene derivatives **1.17, 1.19,** and **1.21** (**Scheme 1.2**).[1]

Scheme 1.2



In the case of napthalenes containing a strong EDG, such as hydroxy-naphthalene **1.23**, the substitution occurs primarily at the *ortho* position **1.24**. (**Scheme 1.3**)[1]

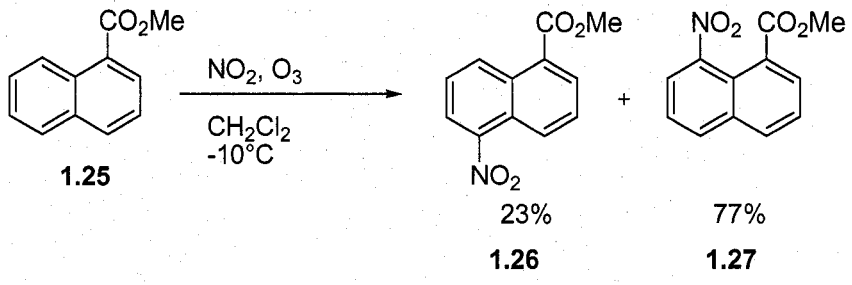
Scheme 1.3



Although electrophilic substitution occurs rapidly, due to the reactivity of the naphthalene core, the products listed above are the major products, and subsequent substitutions can occur.

Recently, one notable example has come to light which involves the nitration of naphthalenecarboxylate. Suzuki presented simple examples involving the substitution of naphthalene-1-carboxylate.[4] Before a discussion of these results can be presented, it must be noted that the substitution pattern of the major product is first dictated by the above rules, whereas the minor product's substitution pattern is dictated by steric hinderance. The following example presented by Suzuki, demonstrated this effect by the products which were produced when methyl naphthalene-1-carboxylate **1.25** was subjected to nitration conditions. (**Scheme 1.4**)

Scheme 1.4



1.25

23%

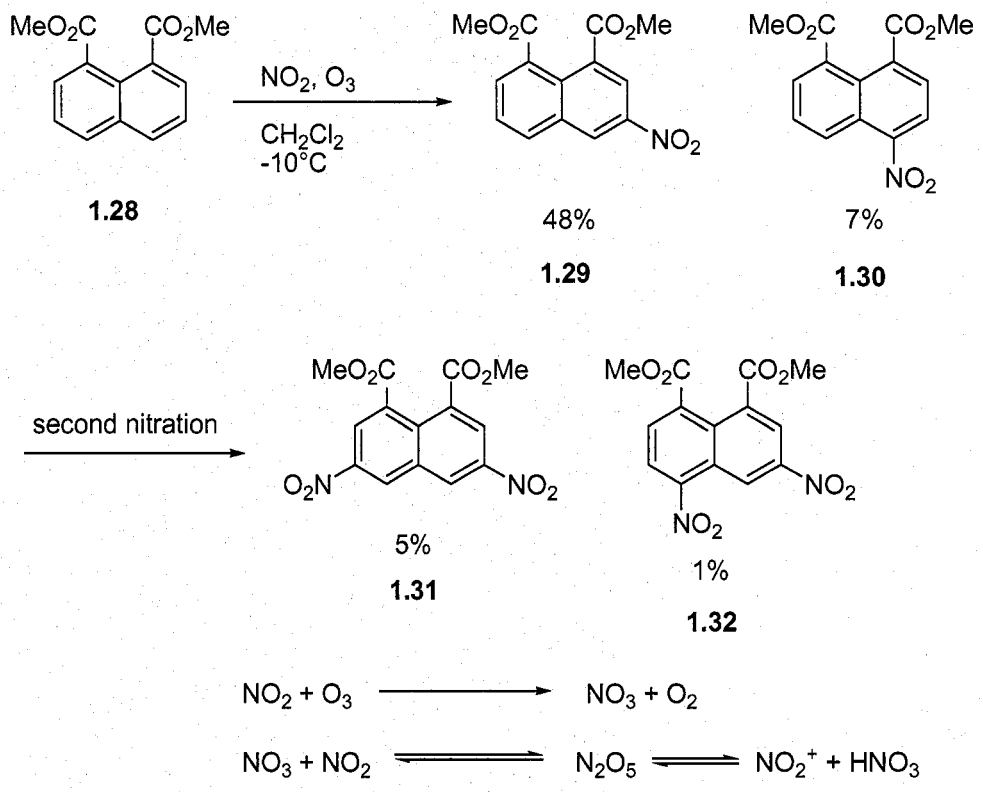
1.26

77%

1.27

Further, when the naphthalene-1,8-dicarboxylate **1.28** is subjected to nitration one obtains **1.29** and **1.30**, whereby **1.29** is the major product (based on the rules for electrophilic substitution of naphthalenes). The formation of minor products **1.31** and **1.32** can be logically explained due to the high reactivity of the nitration reagents and the steric hinderance at the *ortho* sites. (**Scheme 1.5**)

Scheme 1.5

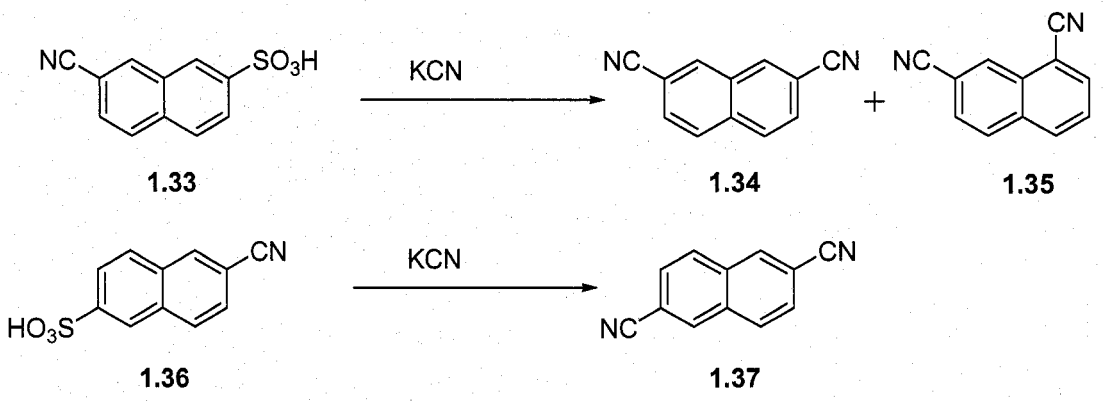


The major drawback to electrophilic substitution is the inability to prevent a mixture of compounds from forming. As well, the reactivity of the naphthalene allows for the second nitration to occur with little control over product formation.

1.1.2 Nucleophilic Substitution

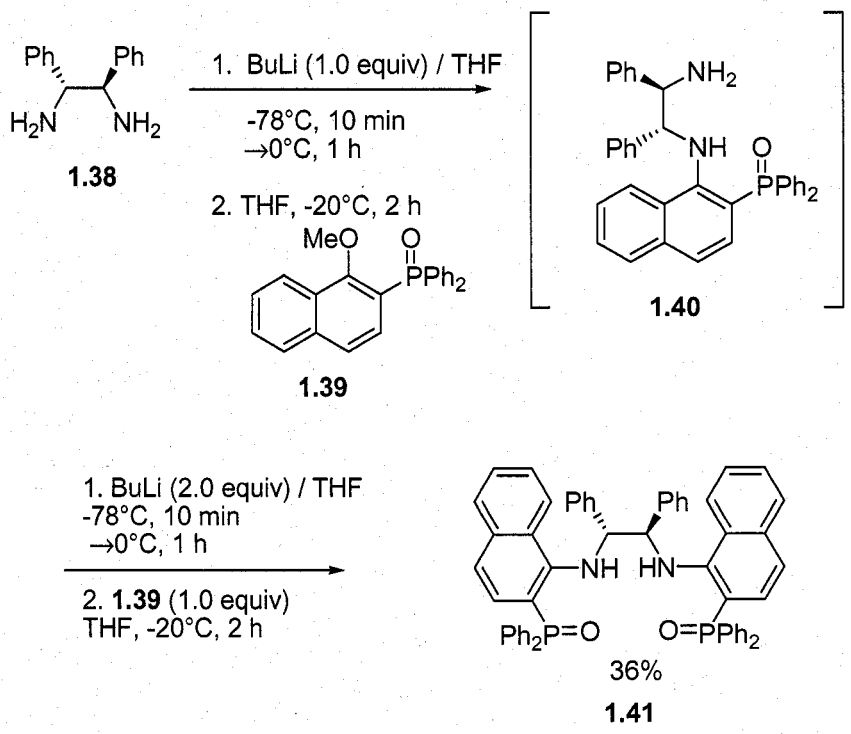
The utility of nucleophilic aromatic substitution, is not as versatile as it requires harsh conditions or the presence of a strong EWG. An early example involving the cine substitution of naphthalene sulphonic acids with potassium cyanide follows.[5] (**Scheme 1.6**)

Scheme 1.6



A modern example presented by Miyano[6] shows the utility of the nucleophilic substitution on the naphthalene core to form chiral phosphine ligands **1.41**.(**Scheme 1.7**)

Scheme 1.7

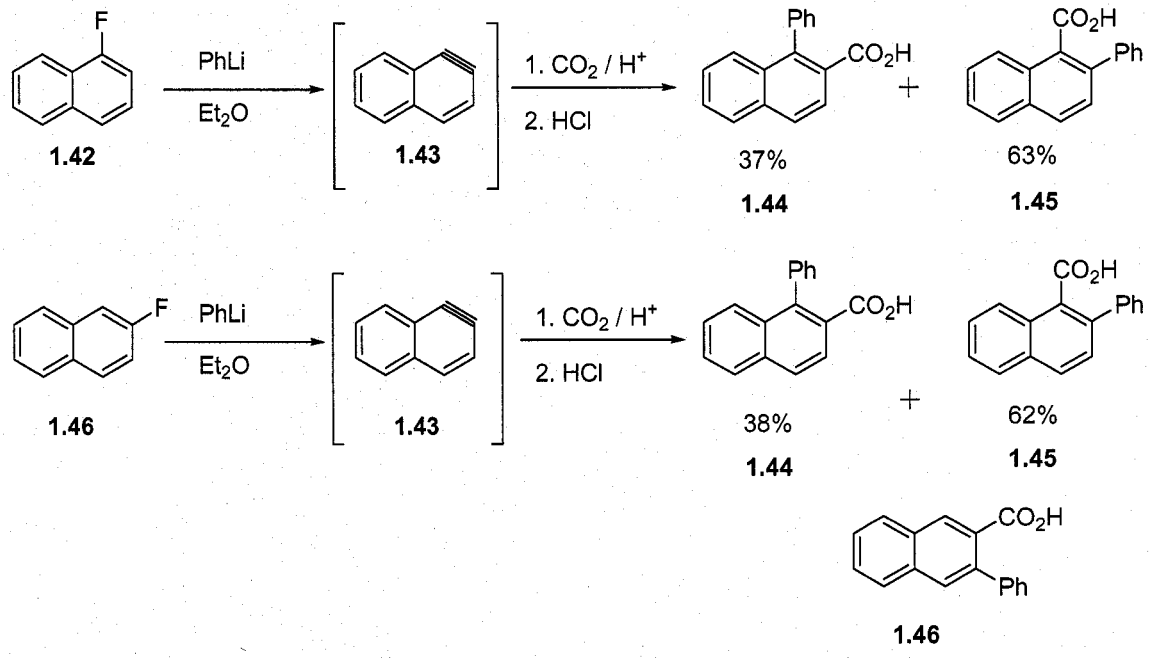


However, the viability of nucleophilic substitution is limited to the precursor availability.

1.1.3 Naphthalynes

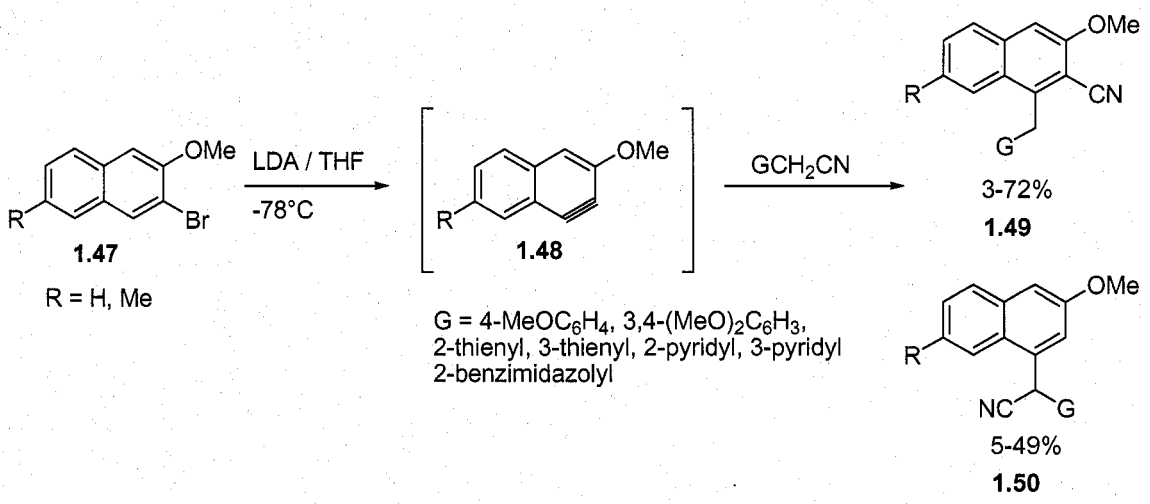
The formation of naphthalynes has been shown to be a versatile method in the synthesis of substituted naphthalenes. A representative case has been presented by Huisgen, in which 1-fluoronaphthalene **1.42** is reacted with phenyllithium resulting in a mixture of **1.44** and **1.45**.[7,8] However, when 2-fluoronaphthalene **1.46** is reacted with phenyllithium one obtains a mixture of 3 products. **1.44, 1.45** and **1.46** (**Scheme 1.8**)

Scheme 1.8



A modern example has been presented by Biehl[9] in which substituted 1-naphthalynes **1.48** are generated and quenched with various nitrile derivatives to form α-naphthylated nitriles **1.49** and **1.50**. (**Scheme 1.9**)

Scheme 1.9

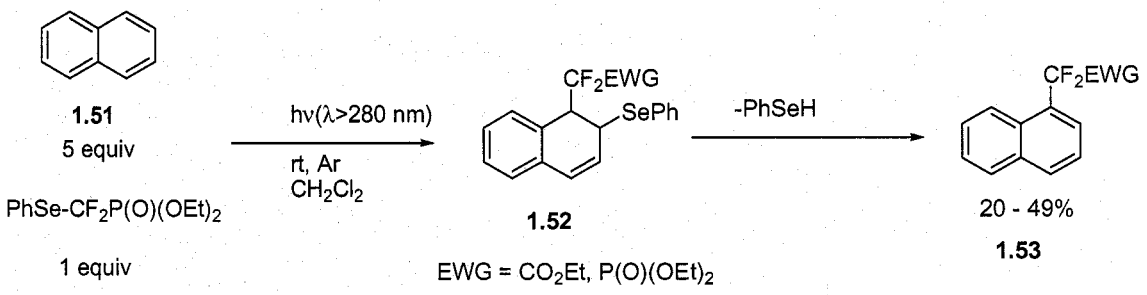


Zirconocene complexes of naphthalynes have also demonstrated synthetic utility for the synthesis of polysubstituted naphthalenes.[10] The major drawback to the use of naphthalynes is the limited substitution patterns which can be achieved.

1.1.4 Substituted Naphthalenes via Free Radical Attack

Another method which has been presented in the literature, is the use of photochemically generated radicals for aromatic substitution of naphthalenes. Fuchigami[11] presented an interesting example whereby aryl-CF_2 bonds are formed by the photo-initiated bond cleavage of Se-CF_2 to form CF_2 radicals which attack naphthalene at the 1 position **1.52**. (**Scheme 1.10**)

Scheme 1.10



The utility of this reaction can be garnered by the bioactivity which difluoromethylene compounds have been demonstrated to have, particularly for the synthesis of stable phosphonate mimetics.[11] However, the viability of the reaction is hindered by the substitution patterns which can be achieved.

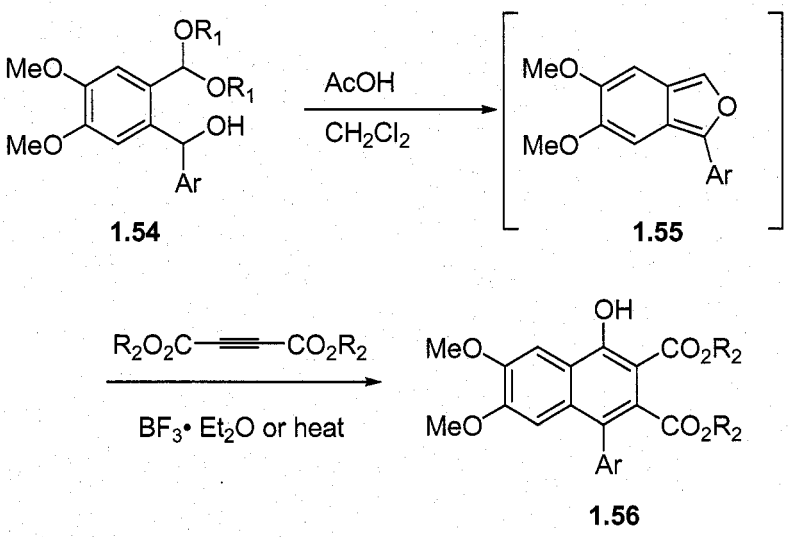
1.1.5 Synthesis of Substituted Naphthalenes via *de novo* Methods

The synthesis of substituted naphthalene via methods which involve building the naphthalene core up from various fragment pieces which dictate the substitution pattern, have demonstrated great synthetic utility.[2] In a recent review, de Koning has classified these syntheses into the following major categories: Diels-Alder, phthalide annulations, transition metal-mediated cyclizations, and isomerization reactions. The main thrust in recent years has focused on syntheses which involve transition metal mediated cyclizations. Representative examples will follow:

1.1.5.1 Synthesis of Naphthalenes via the Diels-Alder Reaction

The versatility of the Diel-Alder reaction for the preparation of substituted naphthalenes and naphthoquinones has been frequently demonstrated over the years.[12] In a representative case, Charlton[13] and coworkers showed that treatment of **1.54** with AcOH followed by trapping with acetylenes afforded, after basic workup, **1.56** in 39 to 80% yield.[13] (**Scheme 1.11**) These synthesized arylnaphthalene lignans were of interest as they possessed the possibility of being atropisomers which could posses different biological actives.

Scheme 1.11



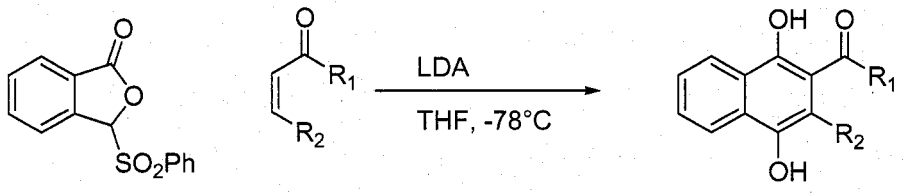
1.54 **1.55** **1.56**

R_1 = OMe, Ar = 4-pyridyl, R_2 = Me, 39%
R_1 = -CH_2-CH_2-, Ar = 3,4-methylenedioxyphenyl R_2 = Et, 80%

1.1.5.2 Synthesis of Naphthalenes via Phthalide Annulations

Another method with similarities to the Diels-Alder method is the phthalide annulation which was first demonstrated by Hauser.[14] One major advantage of using phthalide annulations is the strict regiocontrol which is attained by choosing the appropriate substituted phthalide and Michael acceptor. A general example presented by Hauser follows.[15] (**Scheme 1.12**)

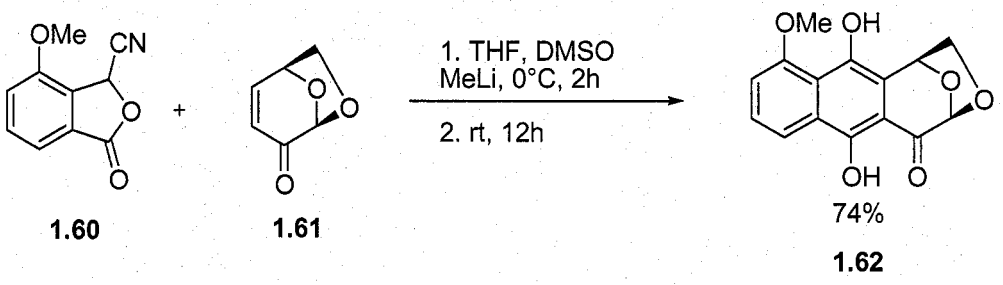
Scheme 1.12



1.57 **1.58** 29-86% **1.59**

This route has been applied to the synthesis of numerous natural products,[15] of which the synthesis of (-)-hongconin **1.62** is an example.[16] (**Scheme 1.13**)

Scheme 1.13

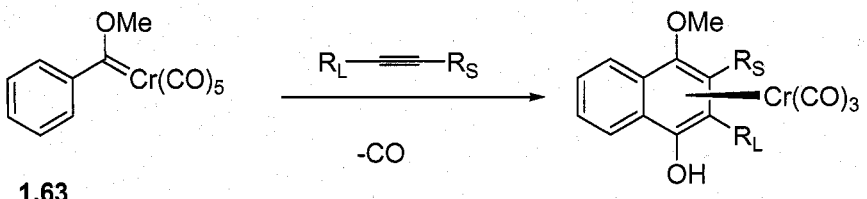


1.60 **1.61** **1.62**

1.1.5.3 Syntheses of Substituted Naphthalenes via Transition Metal Mediated Reactions

The synthesis of substituted naphthalenes via transition metal-mediated process have shown great promise over the years, and many new methods have been developed recently.[2] Transition metals which have been used for this purpose include, chromium, manganese, palladium, cobalt, ruthenium, nickel, copper, zinc, tin, and rhodium. Most notably, is the use of chromium in the Dötz cyclization.[17] The Dötz benzannulation is one of the older transition metal-mediated methods and has become a popular Fischer Carbene synthesis. (**Scheme 1.14**)

Scheme 1.14

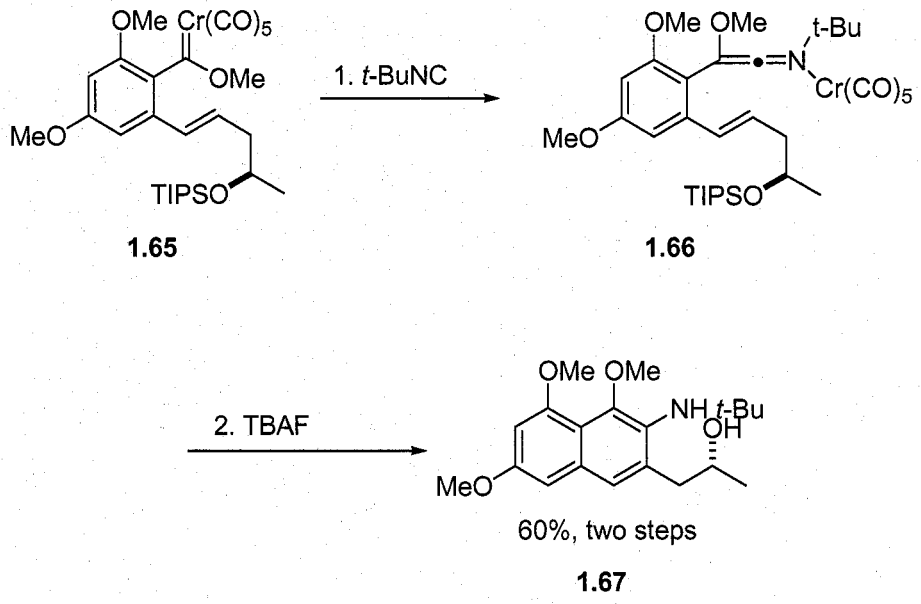


1.63 **1.64**

Two representative syntheses which employ transition metal-mediated processes which have been published recently are a modern version of the Dötz reaction presented by Merlic[18] and a ruthenium-catalyzed ring-closing metathesis presented by Huang.[19]

Merlic reported a chromium carbene assisted synthesis of aminonaphthalenes, designed as potential building blocks for Calphostins.[2] (**Scheme 1.15**)

Scheme 1.15

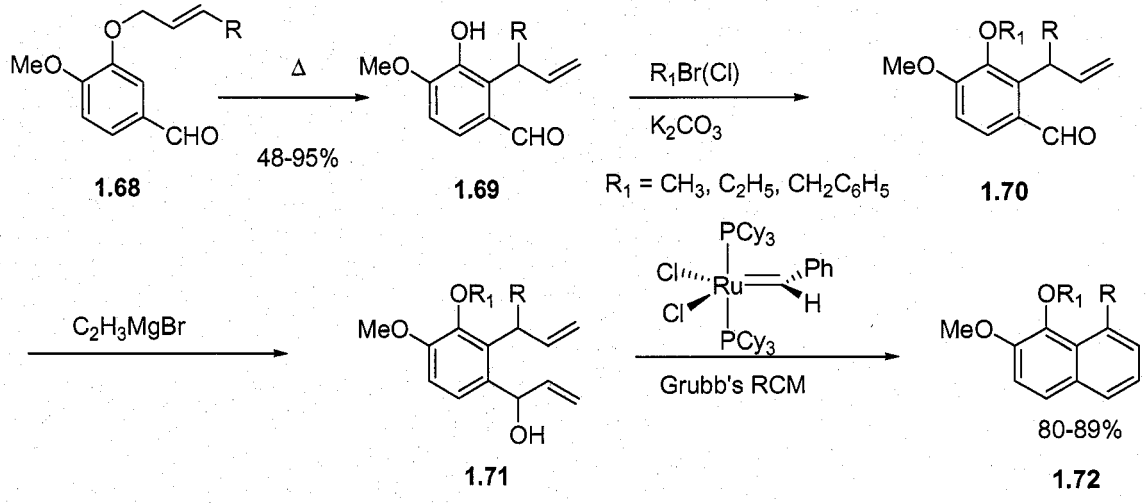


1.65 **1.66** **1.67**

The final structure **1.67**, contains a 1,8-disubstituted naphthalene, with substituents at positions, 2, 3, and 6. This process has been further applied to the synthesis of natural products.

Formation of the naphthalene nucleus using the versatile ring-closing metathesis (RCM) has also been presented as an effective method. In particular the synthesis of 1,8-disubstituted naphthalenes have been presented by Huang[19] and co-workers, whereby Grubb's catalyst is used to cyclize precursors such as **1.71** to 1,2,8-trisubstituted naphthalene derivatives such as **1.72**. (**Scheme 1.16**)

Scheme 1.16



This method demonstrates the advantage of using inexpensive starting materials such as **1.68** as well as the efficient reaction conditions which are employed for the RCM step.

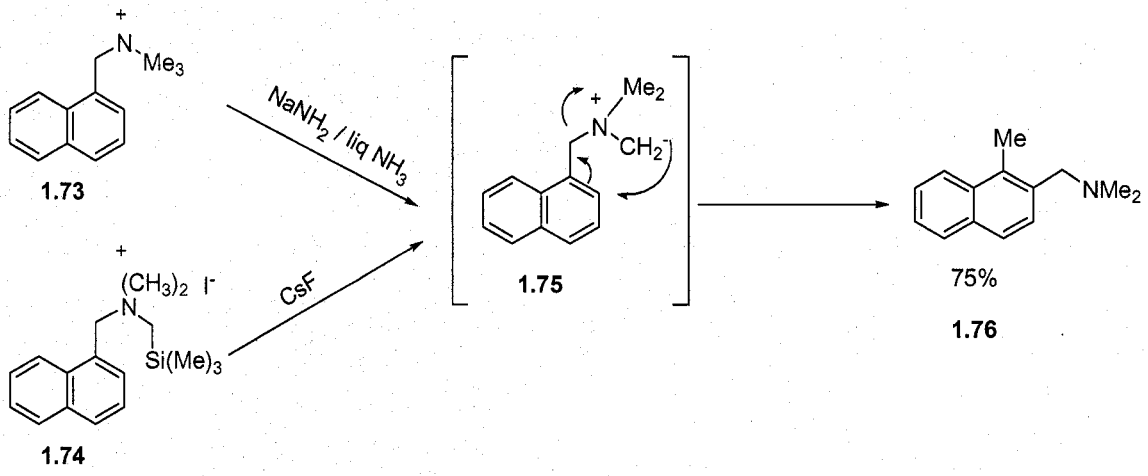
Other metals including manganese, palladium, cobalt, ruthenium, nickel and rhodium have been used as catalysts for the construction of substituted naphthalenes with great success.[2] One major drawback to the building of naphthalene cores from simple precursors is the limited diversity of products which can be achieved both in substitution pattern and substituents.

1.1.5.4 Synthesis of Substituted Naphthalenes via Isomerization of Naphthalene Precursors

The synthesis of substituted naphthalenes with the appropriate substitution pattern is a major issue which synthetic chemists have tried to address over the years. One such classical approach is the Sommelet-Hauser rearrangement of benzyl amonium ylides **1.75**

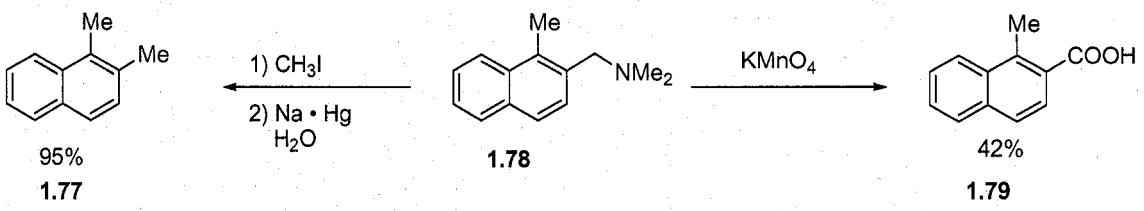
into *ortho*-methyl benzylamines **1.76**. Two syntheses involving this method have been presented in the literature.[20,21] (**Scheme 1.17**)

Scheme 1.17



The first synthesis was presented by Hauser, in which $NaNH_2$ was used to initiate the transformation of **1.73** to **1.76**.[20] The later method, was employed by Sato, using CsF to form the requisite ion by desilylation of **1.74**.[21] Hauser further demonstrated the ability to transform these products into 1,2-dimethyl **1.77** and 1-methyl, 2-carboxy substituted naphthalenes **1.79**.[14] (**Scheme 1.18**)

Scheme 1.18



Although this method allows one to substitute at the 1 and 2 positions, one major drawback is the limited substituents which can be placed in these positions.

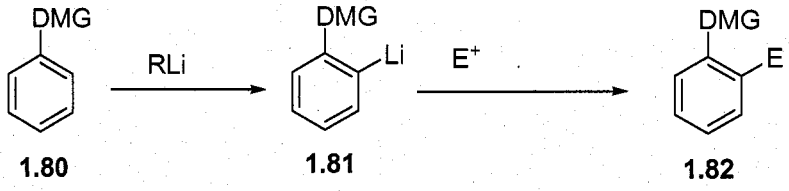
1.1.6 The Search for a Better Route

The routes presented thus far, although effective in attaining the desired products, limit one to certain substitution patterns, as well as limit one to the substituents. Hence, the Directed *ortho* Metalation (DoM) reaction in conjunction with the Suzuki-Miyaura Palladium Catalyzed Cross Coupling reaction was employeed to obtain 1,2,7,8 substituted naphthalenes.

1.2 Directed *ortho* Metalation

The Directed ortho Metalation (DoM)[22] reaction involves the deprotonation ortho to a heteroatom which contains a directed metalation group (DMG) by a strong base, **1.80**, usually an alkyllithium, to give an ortho-lithiated species **1.81** which is then treated with an electrophile to form a 1,2-disubstituted aromatic product **1.82**. (**Scheme 1.19**)

Scheme 1.19

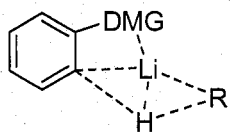


1.80 **1.81** **1.82**

The reaction was discovered independently by Gillman[23] and Wittig[24] in the late 1930's, whereby anisole was treated with *n*-butyllithium (*n*-BuLi) followed by a quench with CO_2 to give *ortho*-anisic acid. Since this initial discovery, many DMGs have been discovered and developed[25] and these have been classified according to: (a) carbon-based DMGs, including secondary[25, 26] and tertiary[27, 28] carboxamides, oxazoline,[27] and α-aminoalkoxide[29] functionalities, and (b) heteroatom-based DMGs such as sulfonamides,[25] sulfonates,[30] sulfoxides,[31] carbamoyloxy,[32] methoxy,[25] OMOM,[33] and NHt-Boc.[34] The D*o*M reaction has been used extensively as a means to prepare substituted aromatic compounds which are not easily accessible *via* classical synthetic methods.[28]

The mechanism of the D*o*M has been under considerable debate. Initial mechanistic studies by Roberts and Curtin[35] suggested prior coordination of RLi with the methoxy group in anisole to facilitate *ortho* metalation. Subsequently, this concept has

been explored by Meyers and Beak, and has been termed the complex-induced proximity effect (CIPE).[36] In a recent review,[37] Snieckus and Beak pose the question: does convincing evidence exist for the formation of these complexes (eg RLi·Anisole) on the reaction pathway? They postulate that the complex formation precedes proton transfer to the organolithium base. Alternative mechanisms have been proposed, the first by Schleyer being that the inductive effects of the DMG are responsible for an increase in the acidity of the *ortho* proton.[38] Schleyer states that it is not the precomplexation but the stabilization of the metal-substituent interaction of the rate-limiting transition structure **1.83** of the one step complexation/proton abstraction reaction.[38]

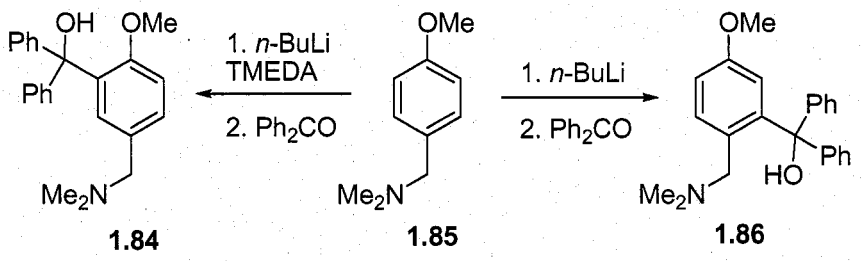


1.83

This is supported by Li NMR *ab initio* calculation studies, which show that the intermolecular complexation of the lithium cation with a Lewis base substituent in the transition structure drastically reduced the activation barrier for *ortho* lithiation.[39] Slocum postulated in subsequent work that the lone pairs on anisole are delocalized into the aromatic ring, hence causing the *ortho* proton to become more acidic.[40-43] Slocum found that when anisole is metalated with 2 equivalents of *n*-BuLi at 25°C in Et_2O and quenching with TMSCl, the reaction is very sluggish, and takes up to 24 h to obtain a yield of 85% of silylated product. However, when even catalytic amounts of TMEDA are added, the reaction is complete in under 0.5 h to give product in 95% yield. Slocum attributed these results to mean that coordination is not necessary to make the reaction proceed. Slocum states that the unshared electrons on the heteroatom are of the greatest

importance as their ground state gives rise to resonance structures in which the *ortho* protons have increased acidity. Slocum provides evidence for this argument in the example of metalation of *N,N*-dimethyl-*p*-methoxybenzylamine **1.85**, which, in the absence of TMEDA leads to exclusive metalation *ortho* to the dimethlyamino group **1.86**. However, in the presence of TMEDA, the metalation *ortho* occurs to the methoxy group **1.84**.[44] (**Scheme 1.20**)

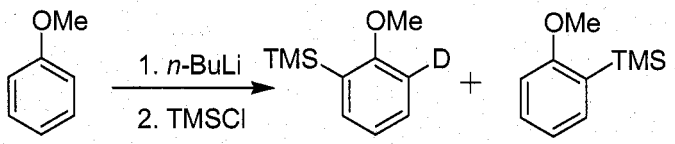
Scheme 1.20



1.84 **1.85** **1.86**

Stratakis[45] has determined the kinetic isotope effect (KIE) in the reaction **1.87** → **1.88** and **1.89**, on the basis of which he offered conclusions opposite to those expressed by Slocum and Schleyer. Thus, when 2-deuterioanisole is metalated with *n*-BuLi in the presence and absence of TMEDA, followed by a quench with TMSCl, a mixture of products **1.88** and **1.89** results, (**Scheme 1.21**) from which the KIE for inter and intra-molecular proton-deuterium exchange, $k_H/k_D \sim 3$, was determined. Consequently, one can show that the rate-determining step is the proton abstraction. However, it must be noted that the results obtained by Stratakis do not require or exclude the existence of a preequilibrium complex.

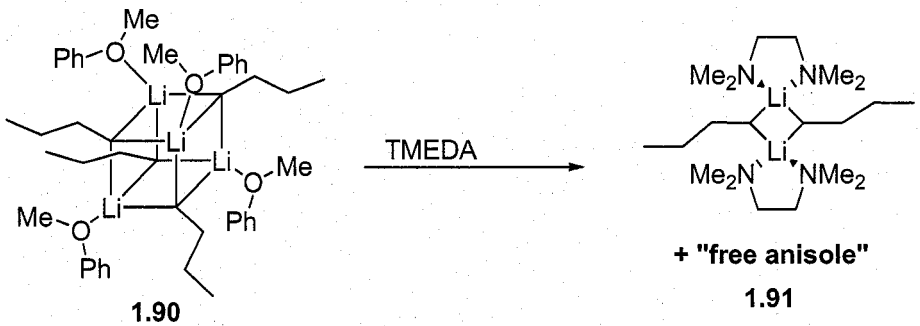
Scheme 1.21



1.87 **1.88** **1.89**

Schleyer has investigated the metalation of anisole with *n*-BuLi at -64°C using 2D heteronuclear NMR and semiempirical MO calculations. The NMR studies showed that, in the absence of TMEDA, the lithium tetramer **1.90** is formed. However, at this stage, there is no evidence of *ortho*-metalation. Upon addition of TMEDA, rapid metalation to form *ortho* lithiated anisole is observed, even at lower temperatures. On the basis of these observations, Schleyer proposed that a TMEDA-*n*-BuLi dimer anisole complex **1.91** is formed in low concentrations and argued that the observation of a complex does not necessarily mean that it is on the reaction pathway, and, subsequently, the absence of an observable complex does not preclude it from being on the reaction pathway. (**Scheme 1.22**)

Scheme 1.22[28]



1.90

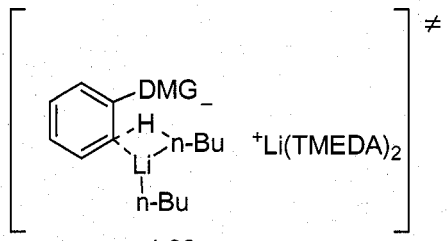
+ "free anisole"

1.91

Beak, on the other hand, has provided evidence that the *ortho*-lithiation of aryl carboxamides occurs by the CIPE mechanism.[46] For his interpretation of Schleyer's work, Beak noted that the definition of CIPE allows for, but does not require a

deprotonation to occur during the rate determining step. Hence, the argument that CIPE does not account for the more general "kinetically enhanced metalation" model is deemed invalid.[37] In order to provide supporting evidence for CIPE, Beak carried out extensive KIE studies to determine if one of the pathways is favoured over another. Despite this intensive study, no single pathway can be definitively identified as the "only" pathway. In the case of *N,N*-diisopropylbenzamide it was found that the reaction proceeds via a reversible complexation with the heteroatom of the DMG, followed by a slow deprotonation step. However, one cannot rule out a Kinetically Enhanced Mechanism.

Recently Collum questioned the meaning of "directed" in D*o*M.[38] Specifically, he questioned whether or not there are different mechanisms for different substrates? Is a CIPE actually involved in the reaction pathway? Can there be a cooperative influence if there are two DMG present on the ring in a *meta* orientation? Collum determined that the rate limited transition structures had the following stoichiometry, $[(\text{n-BuLi})_2(\text{TMEDA})_2(\text{Ar-H})]^{\neq}$ **1.92**.



1.92

These results together with *ab initio* studies lend support to the inductive effects and not to the CIPE concept as being the major effect in D*o*M: a) the rate law is independent of substrate. b) the *n*-BuL*i* dimer does not lend itself to coordination with the arene, c) in agreement with Schlosser, *ortho* selectivites can be attributed to pKa's.

Recently Clayden and Wheatley presented the first crystallographic evidence for the structure of *ortho*-lithiated aromatic tertiary amides.[47] The X-ray structures of *N,N*-diisopropylnaphthalene carboxamide and *N,N*-diisopropylbenzamide show (**Figure 1.1**) that the oxygen coordination of the lithium centre is maintained in the *ortho*-lithiated aromatic tertiary amide despite the deviation from coplanarity and that the $(LiC)_2$ ring is ideally suited to the stabilization of the metal by the amide carbonyl group.

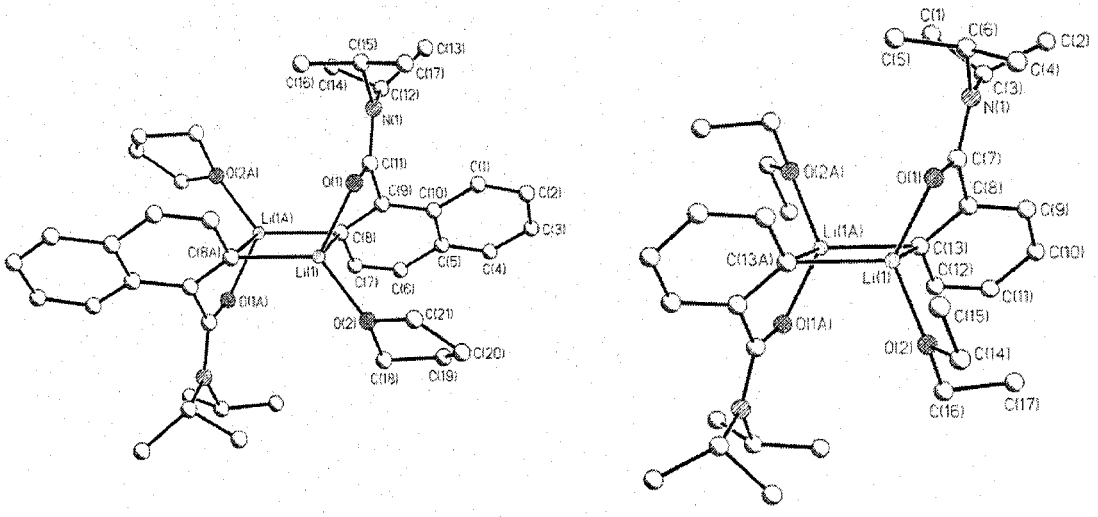
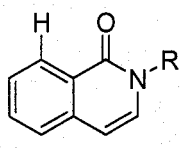
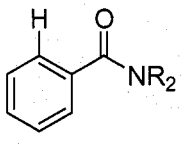


Figure 1.1: X-Ray Structures of *N,N*-diisopropyl-2-lithionaphthalene carboxamide-THF complex and *N,N*-diisopropyl-2-lithiobenzamide-diethyl ether complex [47]

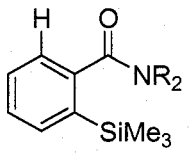
Hence stabilization of the ortho-Li species is achieved by the formation of bridged dimers which could not be achieved in single Li atom bridging between O and C atoms. The significance of planarity of the ortho metalation process has been demonstrated by Beak in kinetic studies on the series **1.93**, **1.94** and **1.95**.[37]



1.93



1.94



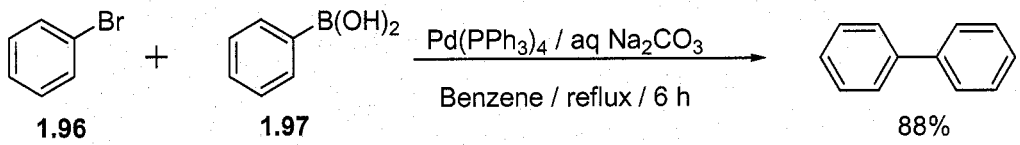
1.95

1.3 Transition Metal Catalyzed Cross Coupling Reactions

Transition metal catalyzed (primarily Ni, Pd, and Fe) cross coupling reactions have revolutionized the thought processes of synthetic chemists in the area of $sp^2 - sp^2$, $sp^2 - sp^3$, and recently sp^3-sp^2 and bond formation reactions. Palladium is a favourite metal for inducing C-C, C-N,[48] C-O,[49] and C-P[50] cross coupling reactions.[51] Most notably is the extensive development of the catalytic C-C bond coupling. This can be accomplished by using different aryl nucleophiles, such as aryl boron (Suzuki-Miyaura),[51] aryl-tin (Stille),[52,53] aryl-zinc (Negishi),[54] aryl-magnesium (Kumada), [55] and aryl-silicon (Hiyama)[56] species.

Of all the palladium catalyzed cross coupling reactions noted, the Suzuki-Miyaura reaction has been shown to be the most versatile.[51] Since its discovery in 1979 by A. Suzuki and N. Miyaura,[57] the reaction has come to the forefront of cross-coupling methods due to the fact that the starting materials and byproducts are non-toxic and the organoboron compounds are easy to handle and are stable to water and oxygen. The Suzuki reaction was initially developed for the coupling of alkenylboranes with organic halides,[57] but, came into fruition when it was applied to the catalytic coupling of phenylboronic acid with haloarenes. The original studies showed that tetrakis(triphenylphosphine)palladium, $Pd(PPh_3)_4$ as the catalyst in a heterogeneous solvent system (aq Na_2CO_3 / benzene) provided the best results[58] (**Scheme 1.23**)

Scheme 1.23

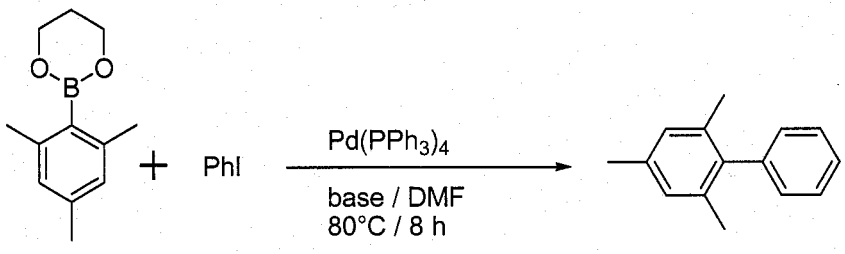


1.96 **1.97** **1.98**

1.3.1 Effect of the Base

Of the many different bases which have been explored for use in the Suzuki-Miyaura reaction; Na_2CO_3 has been identified as the most effective base. In the case of sterically hindered coupling partners, it has been found that stronger bases such as $Ba(OH)_2$ and K_3PO_4 are more effective in accelerating the catalytic cycle and giving better yields of biaryl products. The base is known to be involved in the coordination sphere of the palladium, more specifically the formation of the $ArPdL_2$ species from the $ArPdL_2$-X species.[59,60] Watanabe and Suzuki have shown that the relative strengths of bases parallel the rates of coupling for the reaction of mesitylboronic acid **1.99** arylhalides in the order $Ba(OH)_2 > NaOH > K_3PO_4 > Na_2CO_3 > NaHCO_3$ [61] (**Scheme 1.24**)

Scheme 1.24



1.99 **1.100**

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

Snieckus has demonstrated good results utilizing Na_2CO_3 in DME or K_3PO_4 in DMF for the synthesis of chlorodihydroxybiphenyls.[62] The addition of fluoride ions, most notably, CsF, to the Suzuki-Miyaura reaction has been discussed as another way of accelerating the reaction. [63]

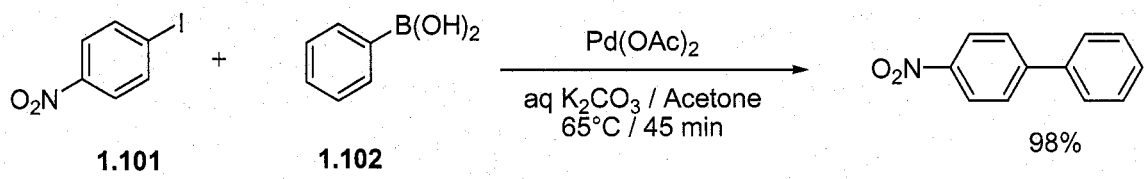
1.3.2 Effect of the Solvent

The effect of a solvent on the reaction is substrate dependent and may be dramatic. In general, it has been found that under homogeneous conditions (aqueous base in DME) the reaction tends to proceed at an accelerated rate. However, yields are still reasonable in heterogeneous solvent medium, such as K_2CO_3 suspended in toluene.[64] The advantage of using a heterogeneous solvent system over a homogeneous system is the ease of base and catalyst removal and, as such, the ability to scale up to industrial scale with relative ease. Recently there have been reports of solvent free Suzuki-Miyaura cross couplings, as well as aqueous conditions.[65,66,67]

1.3.3 Catalysts

Since the discovery of the Suzuki-Miyuara cross-coupling reaction, many different ligands have been used for the coupling of asymmetric aryl groups. Most notably $Pd(PPh_3)_4$ has been used as a catalyst, while $PdCl_2(PPh_3)_2$ and $Pd(OAc)_2$ with the addition of other phosphine ligands have also been used. These catalysts are stable in air and are easily reduced to the active Pd(0). However, despite these advantages, two side reactions have been observed: a) the coupling of the arylboronic acid and a phenyl group of the triphenylphosphine-stabilizing ligand[68] and b) the self-coupling of the arylboronic acids when the cross-coupling is sluggish.[69-71] Although the use of a ligand is normal in the Suzuki-Miyuara reaction, ligandless reactions have also been reported.[72,73] (**Scheme 1.25**)

Scheme 1.25



1.101 **1.102** **1.103**

Prior to 1998, the Suzuki-Myuara reaction was limited to the coupling of aryl boronic acids to arylbromides and aryliodides. Subsequently, numerous cases of the coupling of arylchlorides have been reported using electron rich ligands.[74] Recently, the cross coupling of arylfluorides has been reported.[75]

1.3.4 Deboronation

Although steric hinderence is known to cause decreases in yields of Suzuki-Miyaura cross coupling, there is the additional problem of hydrolytic cleavage of the boron-carbon bond when the reaction is carried out in water. A study was conducted to determine whether or not functional groups play a role in deboronation,[61] and it was concluded that electron-withdrawing substituents play a role in accelerating deboronation.

1.3.5 Mechanism

The initial mechanistic proposal[76] by Suzuki for the coupling of 1-alkenylboranes and bromoalkenes has been extended to the coupling of aryl groups. Suzuki proposed a mechanism based on the following observations: 1) only catalytic amounts of palladium are required, 2) coupling reactions are highly regio and stereospecific, 3) base is required for the successful coupling to occur, 4) small amounts of reduction products were detected and attributed to alkoxopalladium(II) intermediates, and 5) when 1-hexenyl-

1,2,3-benzodioxaborole is treated with allylic phenoxides in the absence of base, the coupled product is obtained. This result was interpreted to mean that the (Π-allylphenoxo)palladium(II) complex is involved in the coupling mechanism. As a result of these observations, the following was proposed as the mechanism for coupling of an aryl halide and aryl boronic acid. (**Figure 1.2**)

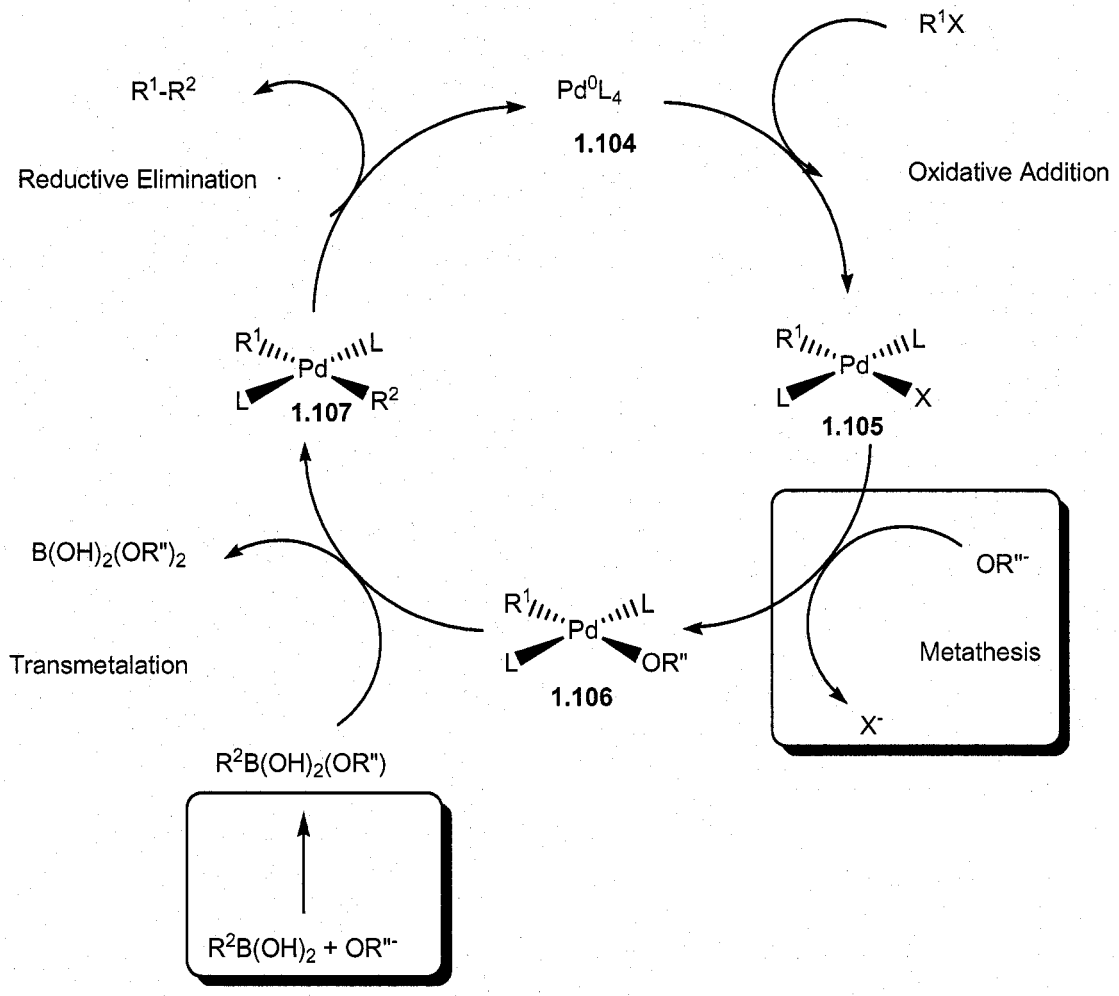


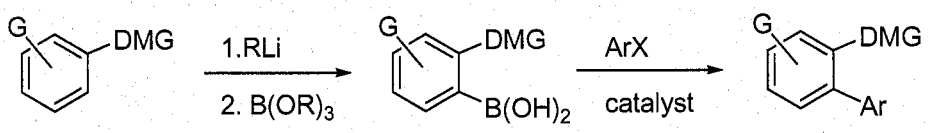
Figure 1.2: Suzuki-Miyaura Cross Coupling Reaction Catalytic Cycle[51]

Subsequently, Canary was able to prove the existence of the two key intermediates (**1.105** and **1.106**) using high resolution mass spectromety.[77] Since the initial proposal, Suzuki has suggested a metathesis step between the oxidative addition and transmetalation steps. For details of mechanistic evidence, see the review by Suzuki.[51, 78]

The Directed ortho Metalation - Cross Coupling: The convergence of two methods

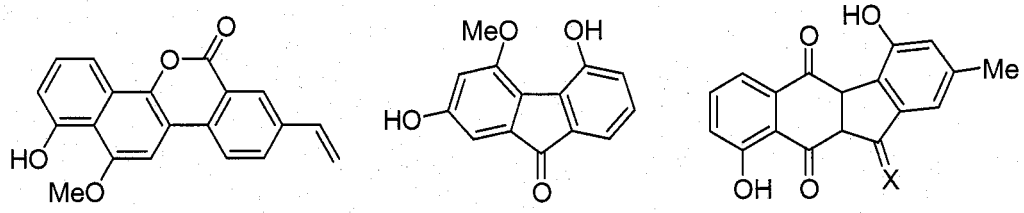
Shortly after the discovery of the Suzuki-Miyuara palladium catalyzed cross coupling reaction, Snieckus demonstrated its connection to D*o*M (**Scheme 1.26**).[28, 79-81] Thus, initially using amide DMG substrates **1.108**, metalation followed by $B(OR)_3$ quench afforded **1.109** which, upon subjection to Suzuki-Miyaura cross coupling conditions, furnished the biaryls **1.110** in good to excellent yields. A number of aryl,[82] heteroaryl,[83] and benzyl bromide[84, 85] were coupled, providing new regioselective routes to unsymmetrical biaryls.

Scheme 1.26



1.108 **1.109** **1.110**

Since this initial study, Snieckus has applied this methodology to the synthesis of a number of natural products (**Figure 1.3**) and the DoM-Cross Coupling sequence has seen use in large-scale industrial practice (**Scheme 1.27**)[86].



Defucogilvocarcin V
antibiotic and antitumor

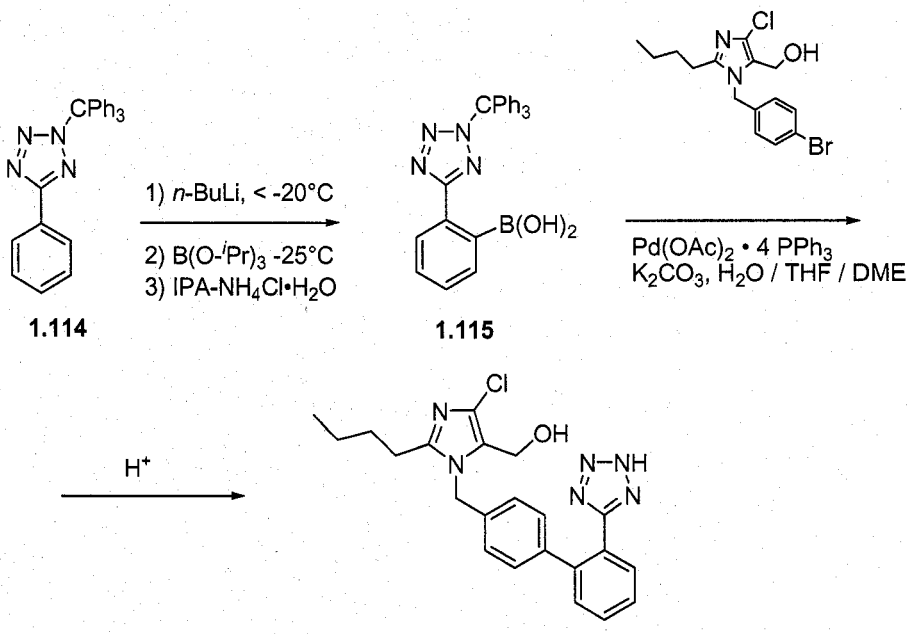
Dengibsin

X = N_2 (Prekinamycin)
X = O (Kinobscurinone)
antibiotic

1.111 **1.112** **1.113**

Figure 1.3: Natural Products Synthesized by DoM and Cross Coupling

Scheme 1.27



1.114

1.115

80%

1.116

Losartan (Angiotensin II Inhibitor)

1.4 The Directed Remote Metalation (DreM) Reaction

The directed remote metalation reaction (DreM) is a logical extension of the D*o*M reaction and was initially based on the CIPE. This remote metalation was initially proposed due to an interpretation of the X-ray structure of *m*-tetra-aryls using the CIPE concept.[87] The use of this reaction allows further functionalization or intramolecular cyclization of biaryl compounds. Thus, treatment of **1.117a** with *s-BuLi* leads to the formation of **1.118,** while treatment of **1.117b** under LDA conditions furnishes the DreM product **1.119, 1.120** (**Figure 1.3**).

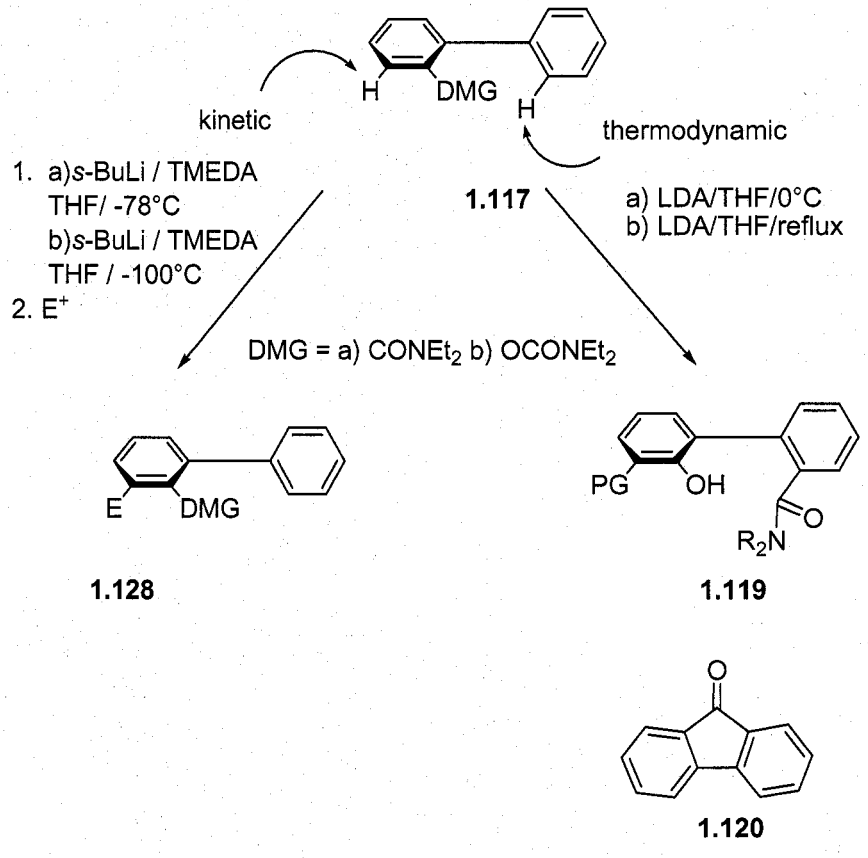
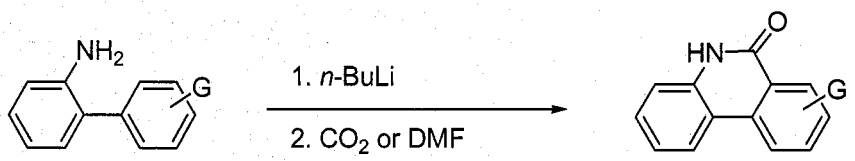


Figure 1.3: DreM vs D*o*M as a Function of Conditions[37]

However, as noted by Snieckus and Beak, although CIPE gives a good rationalization for this and related reactions, there is no definitive evidence for this effect.[37]

To the best of our knowledge, Narasimhan was the first to report a remote metalation example.[88, 89] The Indian group showed that when 2-aminobiphenyl **1.121** is treated with *n*-BuLi followed by a quench with either CO_2 or DMF, phenathridone **1.122** was obtained in 60 % yield. However, the reproducibility of these results has been questioned by Meyers.(**Scheme 1.28**)[90]

Scheme 1.28

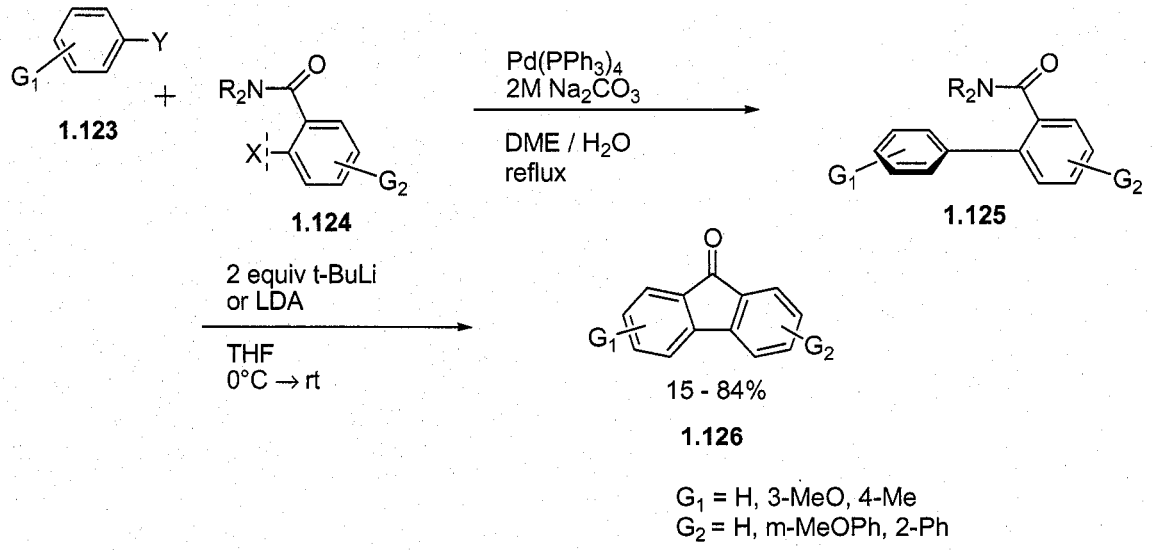


1.121 **1.122**

G = 7,8-OMe or 7,8-H

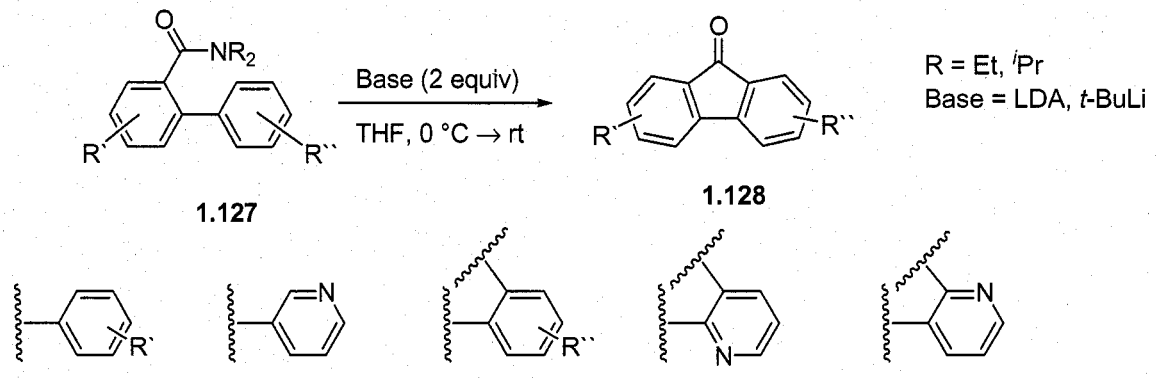
In 1991, Snieckus and Fu[87] showed that treatment of **1.125** with *t*-BuLi or LDA led to **1.126**. Since **1.125** originates from a Suzuki-Miyaura reaction, a connection between D*o*M and cross coupling was established (**Scheme 1.29**).

Scheme 1.29



Snieckus and Fu extended this reaction beyond simple biaryls to substituted and heteroatom biaryl systems to form more complex fluorenone derivatives **1.127 → 1.128** (**Scheme 1.30**). From these studies it was concluded that the regioselectivity is based on the acidity of the protons on the remote ring, which, in turn, is dictated by the presence of heteroatoms in the ring and the functional groups present.

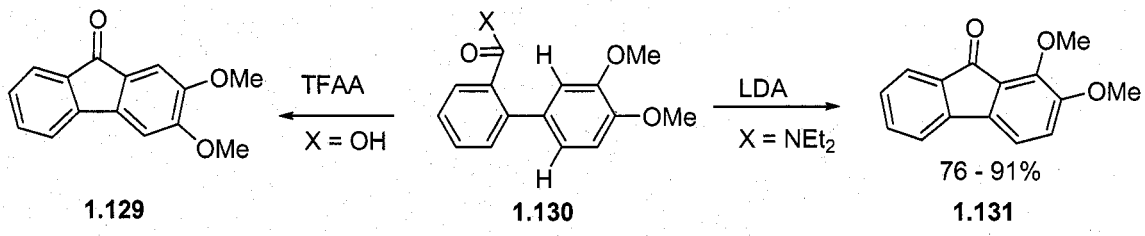
Scheme 1.30



Fluorenones are prepared by classical Friedel-Crafts chemistry and hence are regiochemically dependent on substituent effects, whereby electron withdrawing groups

diminish the yields obtained. Furthermore, Friedel-Crafts conditions are usually harsh, employing reagents such as thianole chloride,[91] polyphosphoric acid,[92] and methanesulfonic acid.[93] Ciske demonstrated the complementarities of Friedel-Crafts and DreM chemistry for the efficient synthesis of a series of methoxyfluorenones, **1.129** and **1.131** (**Scheme 1.32**) which were screened for protein kinase inhibitory activity.[94]

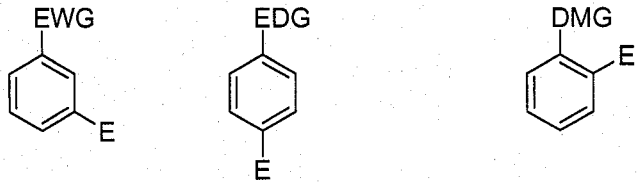
Scheme 1.32



1.129 **1.130** **1.131**

2 Aim of Thesis

Over the past 25 years, the Directed *ortho* Metalation (D*o*M) reaction has evolved as a new synthetic method for the preparation of substituted aromatic compounds which are not easily accessible by classical methods.[37, 81,95] When using the classical electrophilic substitution methodology, the *meta* (**2.1**) and *para* (**2.2**) positions are the favoured substitution sites, depending on the substituents present. The D*o*M methodology allows regioselective substitution *ortho* to the DMG (**2.3**) (**Figure 2.1**).



2.1 **2.2** **2.3**

Electrophilic Substitution

Directed *ortho* Metalation

DMG = Directing Metalating Group, EWG = Electron Withdrawing Group, EDG = Electron Donating Group

Figure 2.1: D*o*M vs Electrophilic Substitution

This thesis work was initiated from a discussion with Dr. G. Ross, Dept of Physiology, Queen's University, who was interested in 1,8-naphthalimides, **2.4a-b** as inhibitors of NGF (**Figure 2.2**) NGF has been implicated in Alzheimer's disease, epilepsy, stroke and pain. An increase in NGF levels has been found in arthritis patients. Hence, an inhibition of NGF production is thought to reduce pain.[96]

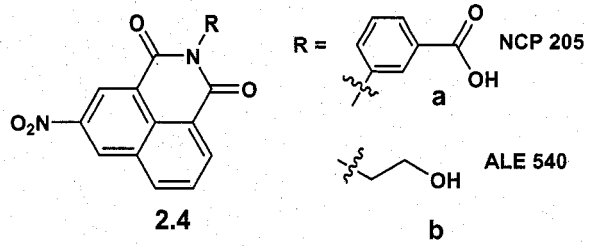
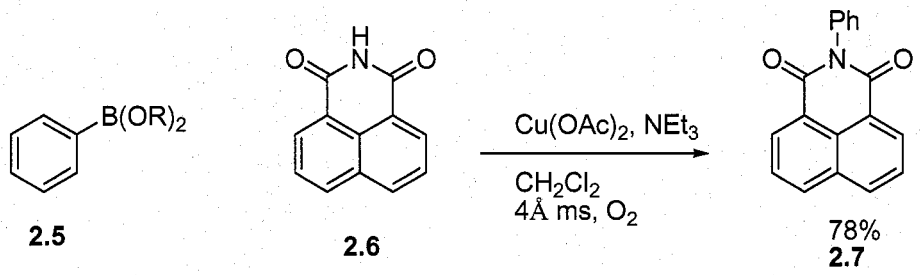


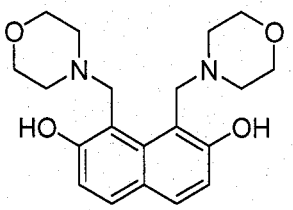
Figure 2.2: Potential Nerve Growth Factor Inhibitors

Recently Wasielewski presented the copper-promoted N-arylation of imides with phenyl boronic acid/esters.[97] (**Scheme 2.1**)

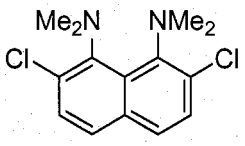
Scheme 2.1



For the preparation of derivatives which are not available by E^+ reactions, we considered the DoM chemistry of *N,N*-diethyl-naphthalene-1,8-dicarboxamide, either mono or dimetalation, to provide routes for new derivatives for SAR in inhibition studies. SciFinder Scholar® searches established that there are very few 1,2,7,8 substituted naphthalene derivatives which have been presented in the liturature. Furthermore only two compounds are commercially available with a 1,2,7,8 substitution pattern. (**Figure 2.3**)



2.8



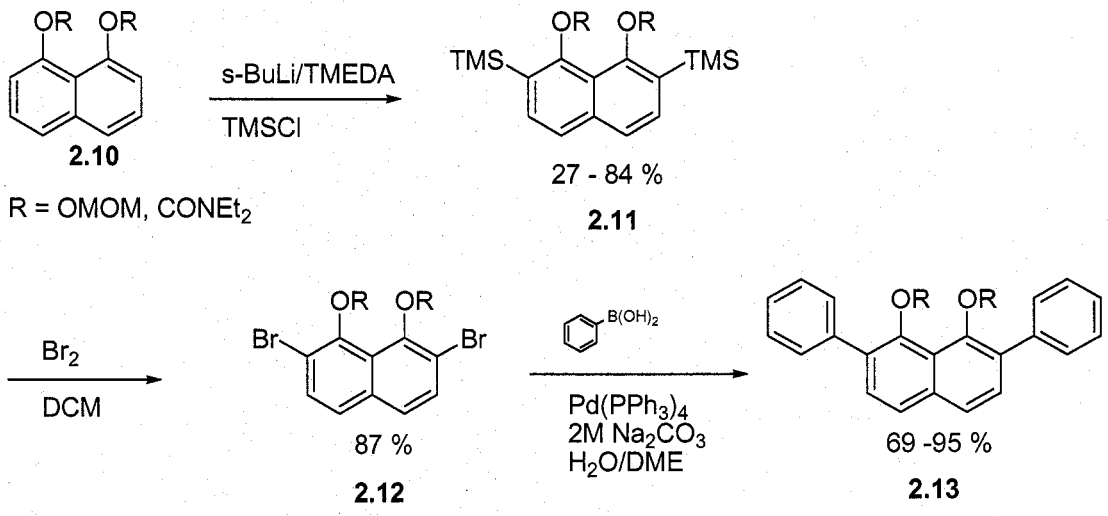
2.9

Figure 2.3: Commercially Available 1,2,7,8-Substituted Naphthalenes (Ambinter Screening Library)

It was hoped that transfer of knowledge gained from study of *N,N*-diethyl-naphthalene-1,8-dicarboxyamide to the naphthalene-1,8-diimide would be valuable for the preparation of derivatives more closely related to the inhibitors **2.4a** and **2.4b**. A brief review of 1,8-disubstituted-naphthalenes will be given.

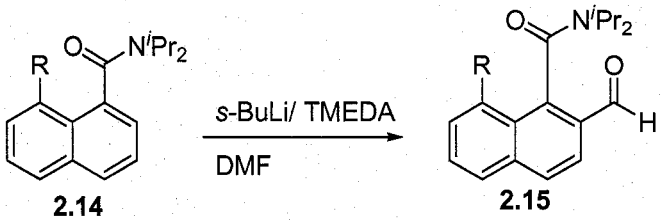
1,8-Disubstituted naphthalenes have recently been explored for the purpose of proton sponges,[98] ligands in transition metal catalysis,[99] and synthesis of cyclic oligophenylenes.[100] In the first D*o*M chemistry study of 1,8-disubstituted naphthalenes,[101]

Scheme 2.2



Wuest metalated the naphthalene 1,8-diOMOM and 1,8-diOAm derivatives **2.10** under standard conditions to form, after quench with TMSCl, the 2,7-bis(trimethylsilane) derivatives **2.11**.(**Scheme 2.2**) Double *ipso*-Br^+ induced desilylation gave the 2,7-dibromo derivative **2.12** which was subjected to standard Suzuki-Miyuara cross coupling conditions with phenyl boronic acid as a coupling partner to form the 2,7-diphenyl derivatives **2.13**. The ultimate purpose of this research was to form 1,8-diol ligands for coordination with $TiCl_4$ to form multidentate Lewis acids.[101, 102] This research has also been extended to studying the influence of the buttressing effect on basicity when alkoxy groups are introduced at the 2 and 7 positions.[103] Initial work involving naphthalene was reported by Snieckus [104]and Clayden.[105] Clayden[105] described an interesting example involving non-symmetrical 1,8-naphthalenes. (**Scheme 2.3**). Compound **2.14** was subjected to metalation and quenched with *N,N*-dimethylformamide to provide **2.15**.

Scheme 2.3

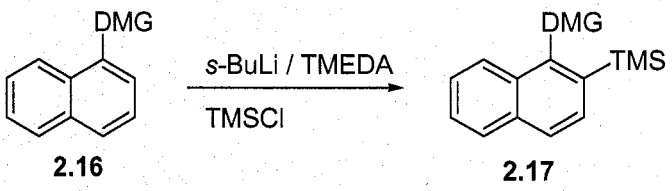


2.14 **2.15**

R = NMe_2 (86%), CH_2NMe_2 (60%), OMe (85%).

Mills[106] has shown that naphthalene amide **2.16** and O-carbamate **2.17** can easily be metalated and quenched with TMSCl to achieve 1,2-disubstituted systems, **2.17**. (**Scheme 2.4**)

Scheme 2.4



2.16 **2.17**

DMG = $CONEt_2$ (80%), $OCONEt_2$ (91%)

2.1 List of Aims

1) To synthesize *N,N*-diethyl-2,7-disubstituted naphthalene-1,8-dicarboxyamide derivatives using the DoM methodology.

2) To synthesize *N,N*-diethyl-2,7-diarylsubstituted naphthalene-1,8-dicarboxyamide derivatives using the Suzuki-Miyuara cross coupling approach.

3) To synthesize fluorenone systems from the *N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxyamide by DreM.

4) To gain preliminary insight into the formation of the 2-lithiated and 2,7-dilithiated species.

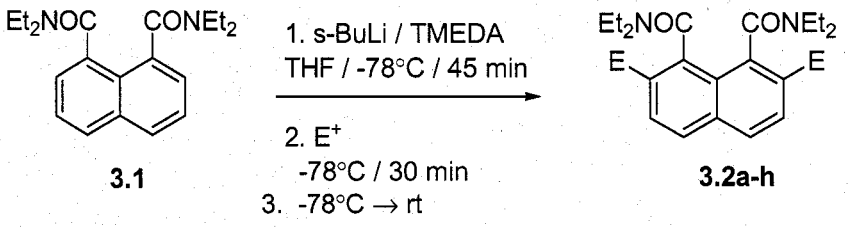
5) To determine the barrier to rotation of the amides of the *N,N*-diethyl naphthalene-1,8-dicarboxyamide and its 2,7-disubstituted derivatives.

3 Results and Discussion

3.1 Directed *ortho* Metalation Results

In order to provide new derivatives related to **2.4 a,b**, the *N,N*-diethyl-naphthalene-1,8-dicarboxyamide **3.1**, readily available from the corresponding anhydride (25¢ CDN/g), was tested in DoM chemistry. Initially, treatment of **3.1** with 2.2 equivalents of *s*-BuLi and quench with 2.2 equiv TMSCl provided a mixture of products **3.2a** and **3.9b** (analysis by GC-MS). As a result, the number of equivalents of base and electrophile were doubled to 4.4 equivalents. GC-MS analysis showed only the desired 2,7-disubstituted product which upon isolation by flash chromatography gave a 50% yield of **3.2a**. Once achieved, the conditions were applied to reactions with a variety of E^+ to give products **3.2a-i** (**Table 3.1**)

Table 3.1: Directed *ortho* Metalation of *N,N*-diethyl-naphthalene-1,8-dicarboxyamide (3.1) Synthesis of 2,7-disustituted-*N,N*-diethyl-naphthalene-1,8-dicarboxyamide (3.2a-h)



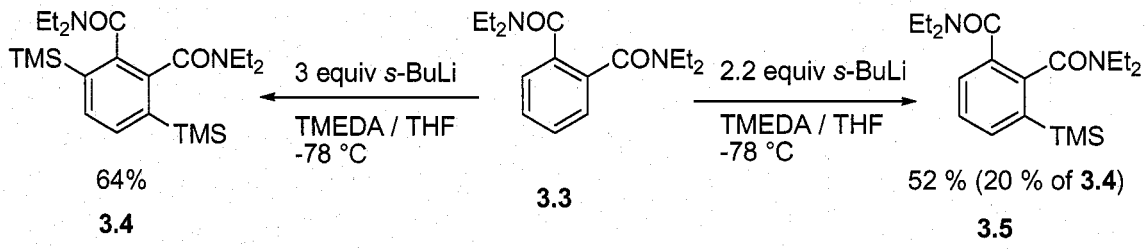
3.1 **3.2a-h**

Product	E^+	E	s-BuLi (equiv)	yld, %
3.2a	TMSCl	TMS	4.4	50
3.2b	TESCl	TES	2.2	31
3.2c	$(SMe)_2$	SMe	2.2	75
3.2d	DMF	CHO	2.2	40
3.2e	Cl_3CCCl_3	Cl	2.2	44
3.2f	Br_2	Br	*ispo*	77
3.2g	CF_3CH_2I	I	4.4	87
3.2h	CD_3OD	D	2.2	82

Reactions with several other E^+ proved unsuccessful. Hence, quenching the lithiated species with $(^iPrO)_3B$, F^+ salts, $ClCONEt_2$, MeI, 1,2-dibromoethane, iodine, TIPSCl, benzaldehyde and $ClSn^tBu_3$ resulted in decomposition. Presumably due to steric effects and/or the reactivity of the electrophile. The steric effects are caused both by the bulkiness of the E^+ as is the case with TIPSCl and $ClCONEt_2$ and the close proximity of the two amides to each other in **3.1**. The use of 4.4 equiv. of base was required in order to obtain high yields of the 2,7-bis(trimethylsilanyl) **3.2a** and 2,7-diiodo **3.2g** derivative.

This may be due to the necessary first coordination (CIPE)[37] of RLi reagents to the diamide before deprotonoation. Previous work[107] has shown that *N,N*-diethyl phthalamide **3.3**, when subjected to metalation using 2.2 equiv of *s*-BuLi and quenched with TMSCl, gives predominately the mono product **3.5**. (**Scheme 3.1**) However, when 3 equivalents of base were used, the bis product **3.4** was obtained exclusively. The wide range of yields of the isolated products shown in **Table 3.1** may be attributed to the steric and reactivity effects of the electrophile.

Scheme 3.1



In order to gain insight for the best conditions for the formation of 2,7-dilithiated and 2-monolithiated species of **3.1**, mechanistic studies were undertaken.

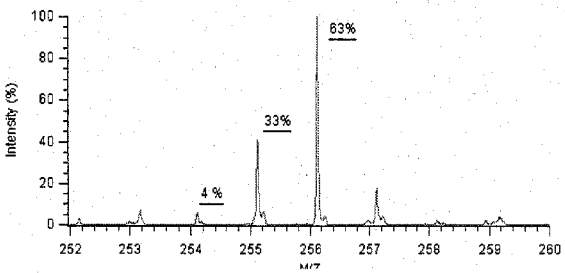
3.2 Mechanistic Studies

At the outset, two interesting questions arise: is the dianion **3.6** formed by sequential deprotonation or directly? In other words, with the addition of the lithium base, does one form a 2-lithiated species **3.7** which then shows enhanced acidity at C-7 such that a second deprotonation occurs rapidly or do the lithiated complexes form independently at each amide resulting in the formation of the 2-lithiated and the 2,7-dilithiated species respectively? Sequential deprotonation was resolved to be the more plausible route. Since it is plausible the acidity of the second *ortho* proton is increased

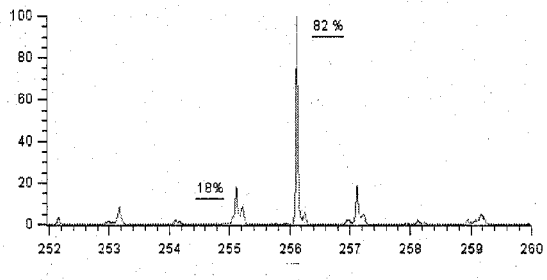
through inductive effects. In the presence of excess base and electrophile the mono substituted species can undergo a second deprotonation which, after E^+ quench, forms the 2,7-disubstituted product. The amounts of 2- and 2,7- products are a function of the amount of the respective anions present in solution when the electrophile is introduced. Since both the N,N-diethylnaphthalene-1,8-dicarboxamide (**3.1**) and the *N,N*-diethyl-1,2-phthalamide (**3.3**) have two DMGs in close proximity to each other, and therefore perhaps similar electronic and steric environments, similar reactivity effects may be expected (**Figure 3.1**). Compound **3.1** was treated with 1.1, 2.2, 3.3, and 4.4 equivalents of *s*-BuLi at -78 °C and the resulting lithiated species were stirred for 30 min and then quenched with 10 equiv of CD_3OD and allowed to warm to rt. Since the 1,8-naphthalene system is symmetrical, NMR studies do not allow determination of % deuterium incorporation as the signals for the 2-deuterated and 2,7-deuterated derivates show equivalent chemical shifts. Hence, it was decided that High Resolution Mass Spectrometry (HRMS) would be used to determine the relative amounts of deuterated product in the reaction mixtures. It should be noted, since there is fragment complexed with salt ions to form peaks which appear at the M^+ peak, it was decided to use the SM – NEt_2 peak (254). Further, when calculating the percent incorporation of deuterium, the effect of ^{13}C on the mass is incorporated in the calculations.

Figure 3.1: Mass Spectra of Deuterated Species of 3.1

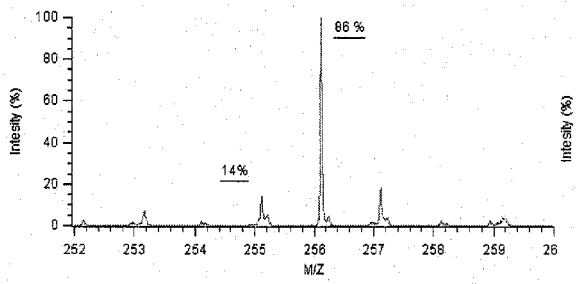
a) 1.1 Equivalents of Base



b) 2.2 Equivalents of Base



c) 3.3 Equivalents of Base



d) 4.4 Equivalents of Base

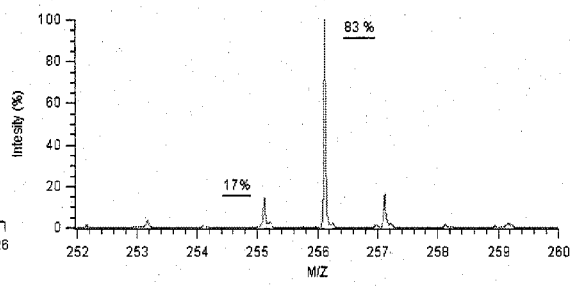


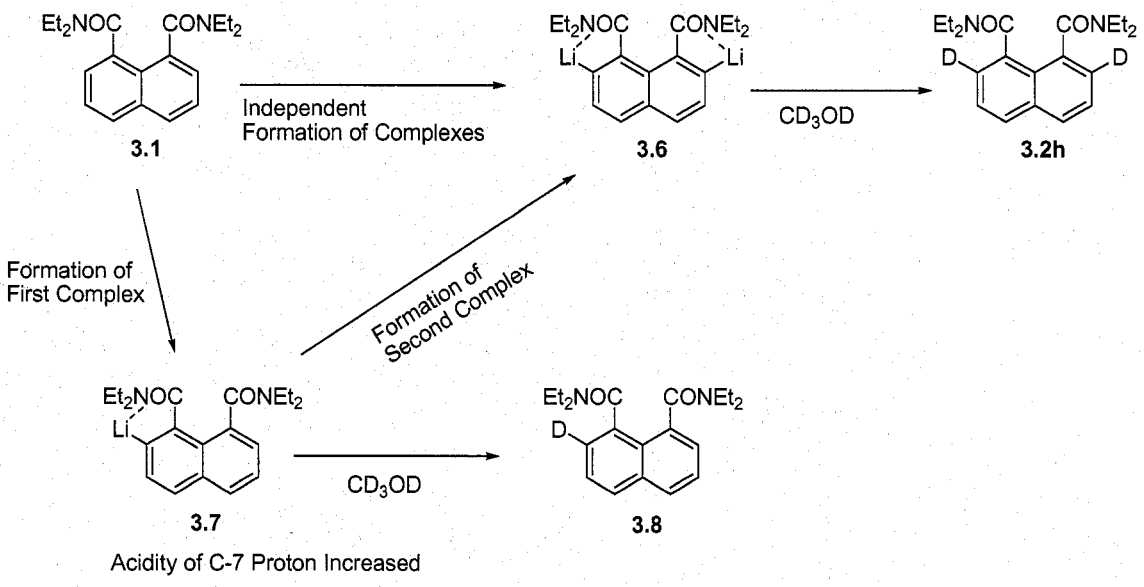
Table 3.2: Percent Incorperation of Deuterium as a function of Equivalents of Base

# of Equiv of *s*-BuLi	d-species (% incorporation)		
	d_0	d_1	d_2
1.1	4	33	63
2.2	0	18	82
3.3	0	14	86
4.4	0	17	83

When the compound **3.1** was treated with 1.1 equiv. of *s*-BuLi followed by excess of CD_3OD, the formation of a mixture of starting material (**3.1** (4%)), mono-(**3.8** (33%)) and bis-(**3.2h** (63%)) deuterated materials was formed. However, treatment of **3.1** with 2.2 equivalents of base followed by excess of CD_3OD, the 2,7-dideuterated product **3.2h** was

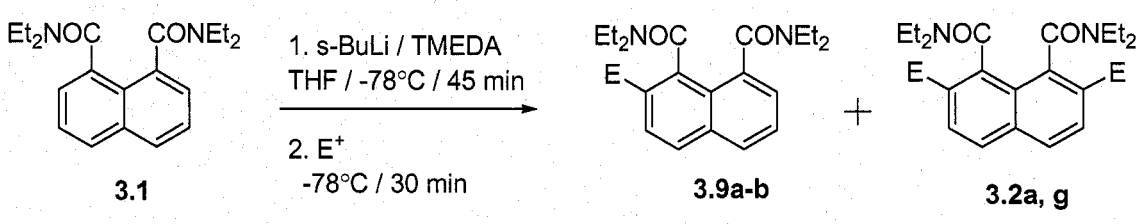
formed in 82% yield, with 18% 2-deuterated product. Based on these results, it is suggested that the deprotonation follows a two-step process, in which the second deprotonation is much faster than the initial deprotonation.

Scheme 3.2



Since, as noted above, mono deuterium incorporation was detected when a limited amount of base was added (1.1 equivalents), studies were undertaken to determine the conditions needed to selectively form the 2-substituted 1,8-naphthalene products **3.9 a-b** (**Table 3.3**)

Table 3.3: Directed ortho Metalation of N,N-diethyl-naphthalene-1,8-dicarboxyamide 3.1. Synthesis of 2-substituted- N,N-diethyl-naphthalene-1,8-dicarboxyamide 3.9a-b[108]



3.1 **3.9a-b** **3.2a, g**

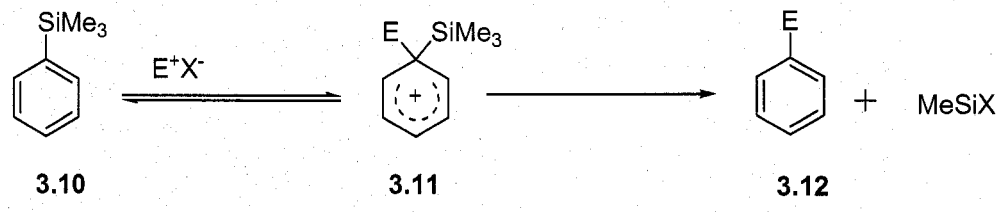
Product	E^+	E	s-BuLi (equiv)	yld, % **3.9**	**3.2**	**3.1**
3.9a	CF_3CH_2I	I	1.1	24	35	18
3.9b	TMSCl	TMS	1.1	15	25	38

As seen from **Table 3.3**, quench with CF_3CH_2I and TMSCl give a mixture of products similar to those observed in the deuteration study.

3.3 Electrophile-Induced ipso-desilylation

Since the formation of the 2,7-dibromo compound **3.2f** (**Table 3.1**) proved to be difficult by direct D*o*M reaction followed by quench using 1,2-dibromoethane as a Br^+ source, a different route was undertaken, this being electrophile-induced *ipso*-Bromo-desilylation. (**Scheme 3.3**).[109,110,111]

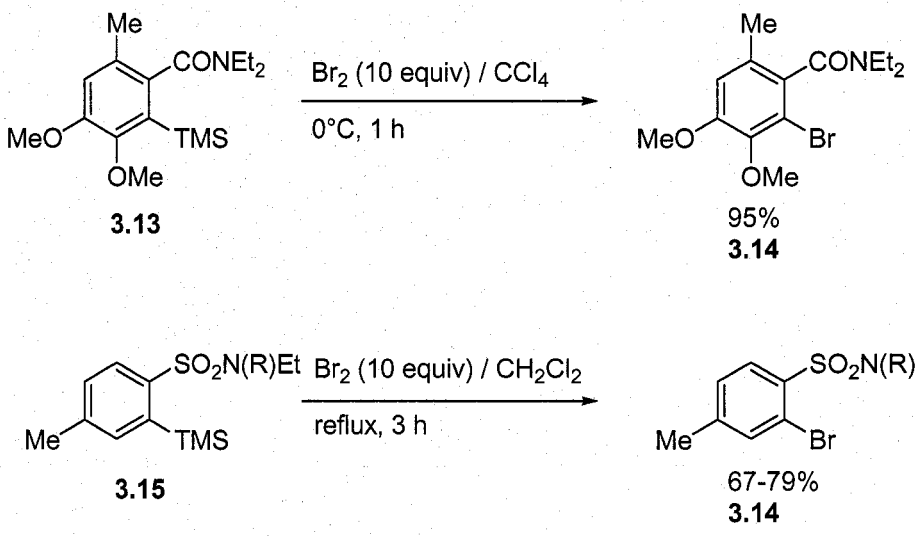
Scheme 3.3



3.10 **3.11** **3.12**

The D*o*M – *ipso*-bromo desilylation reaction has been used in past in our laboratories, notably by Mills **3.13** → **3.14**[112] and MacNeil **3.15** → **3.16**.[113] (**Scheme 3.4**)

Scheme 3.4

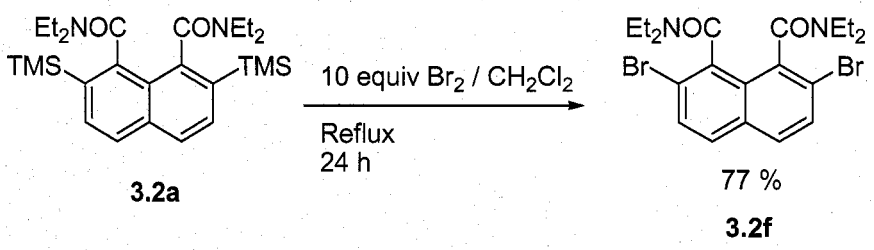


3.13 95% **3.14**

3.15 67-79% **3.14**

We found that treatment of **3.2a** with excess neat bromine in CH_2Cl_2 under refluxing conditions smoothly afforded the *ipso* substitution product **3.2f** in very good yield.[101] (**Scheme 3.5**)

Scheme 3.5



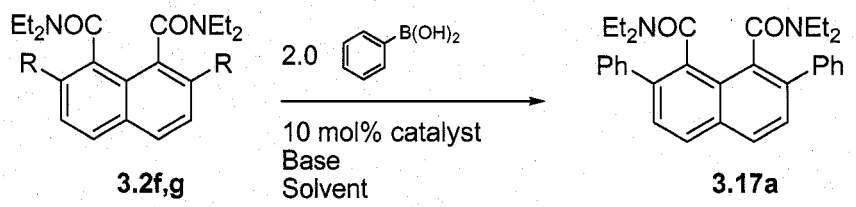
3.2a 77 % **3.2f**

The need for reflux conditions and extended reaction times could be attributed to the decreased rate of product formation, which can be in turn attributed to the mechanism of the ipso reaction; once the first electrophile attacks the ring, a delocalized carbocation is formed which can be further delocalized into the second ring, thus preventing a second attack from occurring.

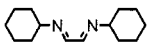
3.4 Suzuki-Miyaura Cross Coupling Reactions

The availability of the 2,7-dihalo and 2-halo substituted derivatives **3.2f, 3.2g (Table 3.1)** presented the opportunity to continue with the D*o*M-Cross Coupling Connection, a common theme in our laboratories.[80] Various conditions were investigated using the 2,7-dibromo derivative **3.2f** as a coupling partner but to no avail (**Table 3.3**). As is the common practice in our laboratories, the standard DME/H_2O conditions with $Pd(PPh_3)_4$ as the catalyst and Na_2CO_3 as the base were attempted. Since this reaction failed, it was decided to attempt to use the second most common conditions, which involves anhydrous DMF and K_3PO_4 as the base. This coupling was successful to give **3.17a** in 32 % yield. As expected, based on reactivity the corresponding iodo derivative **3.2g,** when subjected to the DMF/K_3PO_4 conditions, led to the formation of **3.17a** in 51 % yield. (**Table 3.4**)

Table 3.4: Suzuki-Miyaura Cross Coupling Conditions

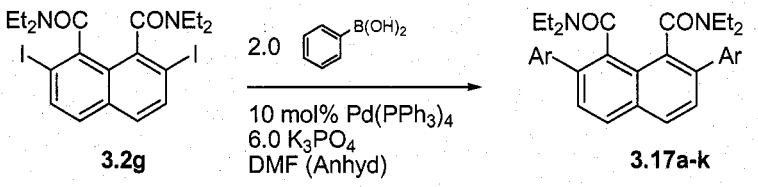


3.2f,g **3.17a**

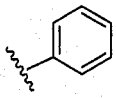
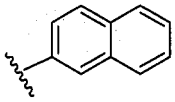
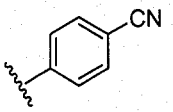
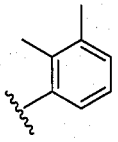
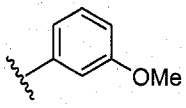
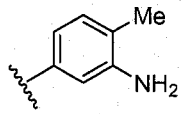
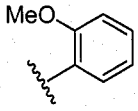
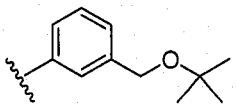
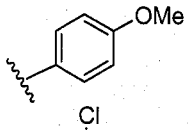
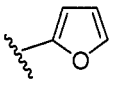
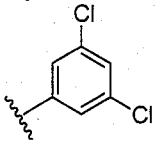
Entry	R= Halogen	Catalyst	Base	Solvent	Result
1	Br	$Pd(PPh_3)_4$	Na_2CO_3	DME/H_2O	X
2	Br	$Pd_2(dba)_3$ $[(tBu)_3PH]BF_4$	KF	Toluene	X
3	Br	$Pd(PPh_3)_4$	$Ba(OH)_2$	DMF	X
4	Br	$Pd(PPh_3)_4$	CsF	DMF	X
5	Br	$Pd(PPh_3)_4$	$CsCO_3$	DMF	X
6	Br	$Pd(PPh_3)_4$	K_3PO_4	DMF	32
7	Br	$Pd(PPh_3)_4$	K_3PO_4	Toluene	X
8	I	$Pd(PPh_3)_4$	K_3PO_4	DMF	51
9	Br	$Pd_2(dba)_3$ $P(o\text{-}tolyl)_3$	K_3PO_4	DMF	X
10	Br	$Pd_2(dba)_3$ dppb	K_3PO_4	DMF	X
11	Br	$Pd_2(dba)_3$ dppf	K_3PO_4	DMF	X
12	Br	$Pd_2(dba)_3$ 	K_3PO_4	DMF	X

X = No product isolated.

Table 3.5: Suzuki Cross-Coupling Reaction on N,N-diethyl-2,7-diiodonaphthalene-1,8-dicarboxamide (3.2g)



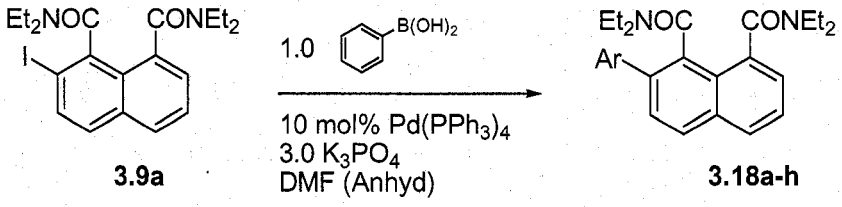
3.2g **3.17a-k**

entry	Ar =	yld %	entry	Ar =	yld %
a		51	g		29
b		50	h		no reaction
c		41	i		no reaction
d		56	j		no reaction
e		47	k		no reaction
f		45			

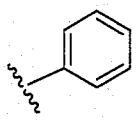
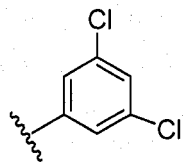
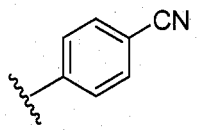
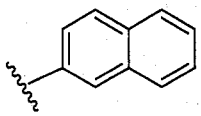
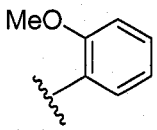
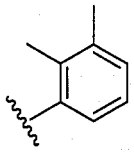
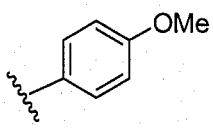
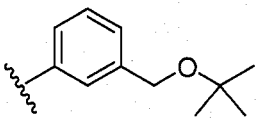
Using the diiodo derivative **3.2g** other boronic acids were subjected to Suzuki-Miyaura cross-coupling to give products **3.17a-g** (**Table 3.5**) in modest yields. However, attempts to form products **3.17h-k** failed with only decomposition of the starting material. These failed cases show that electronic and steric effects play an important role in these cross coupling reactions. On the other hand, the monoiodo bisamide **3.9a** underwent smooth

cross-coupling to give products **3.18a-f** in better yields (**Table 3.6**). This result is most likely due to the ability of the amides to adapt to preferred, less sterically encumbered arrangements, hence allowing for coupling to occur in a less hindered environment.

Table 3.6: Suzuki Cross-Coupling Reaction on N,N-diethyl-2-iodonaphthalene-1,8-dicarboxamide (3.9a)



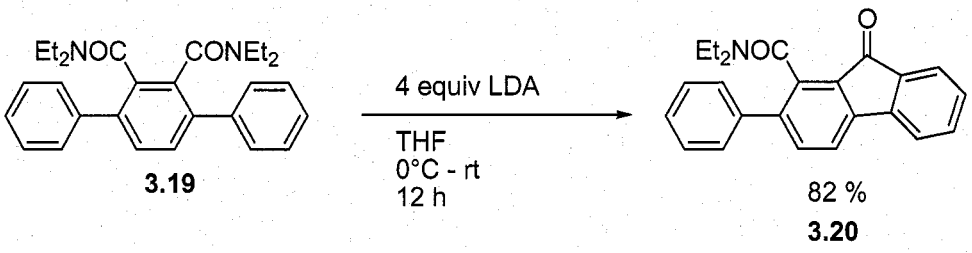
3.9a **3.18a-h**

a		85	**e**		44
b		80	**f**		67
c		43	**g**		no reaction
d		68	**h**		no reaction

3.5 Directed Remote Metalation

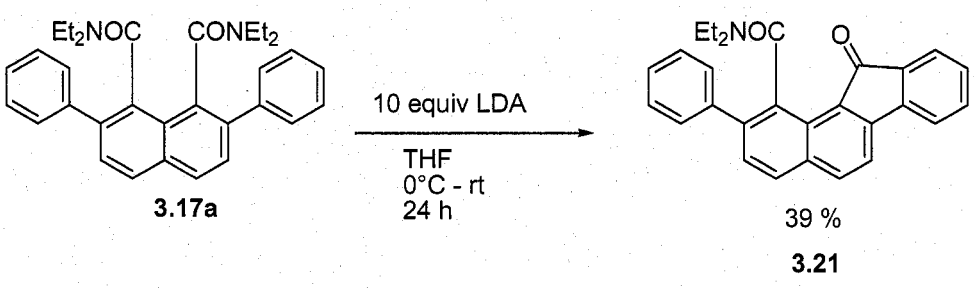
The availability of the *N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxamide **3.17a** allowed a test of the Directed Remote Metalation (DreM) (see **Section 1.4**). In an example of DreM pertinent to our **3.17a**, Fu and Snieckus showed that treatment of **3.19** with excess LDA led to the formation of **3.20** in 82% yield, indicating the inability to affect a second deprotonation – cyclization reaction.[82]

Scheme 3.6



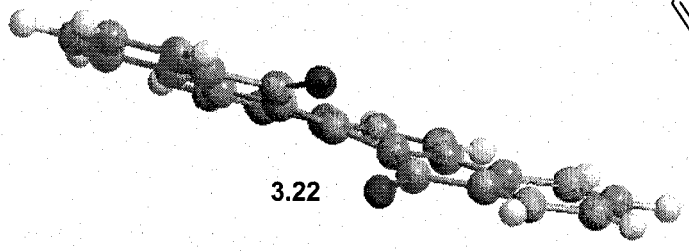
Based on these results, we tested the use of excess LDA and a longer reaction time for the reaction of the *N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxamide **3.17a** in an attempt to form the bis cyclized product.

Scheme 3.7

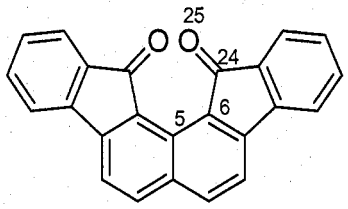


However, as with the *p*-terphenyl *o*-diamide **3.19**, it was found that treatment of **3.17a** with excess LDA leads only to mono cyclization product (**3.21**). When the structures **3.21** and **3.22** are energy minimized using the B3P86/6-311G(2d, 2p)//AM1 level of theory, the AM1 calculated structure for the bis fluorenone naphthalene **3.22** shows a dihedral angle (the angle by which the carbonyl is bent of plane from the plane of the naphthalene core) for the naphthalene ring to be 22° (atoms 25, 24, 6 and 5) (**Figure 3.2**). This suggests that there is too much strain for the bis flourenone to form.

Figure 3.2: AM1 Energy Minimized Structure of the bis fluorenone



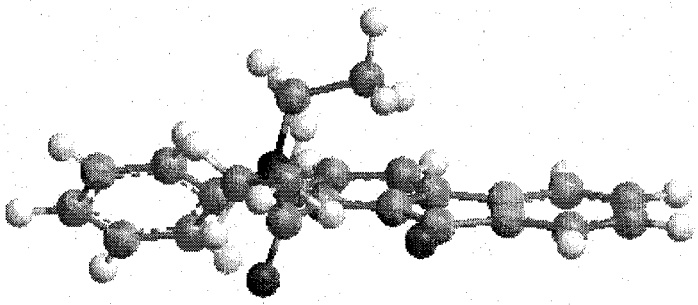
3.22



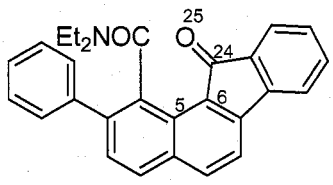
3.24

Comparison of the dihedral angle of 22° calculated for **3.24**, with that of the mono fluorenone naphthalene derivative **3.26**, which is 6° (atoms 25, 24, 6 and 5), shows a significant difference. However, the naphthalene core itself is flat. (**Figure 3.3**)

Figure 3.3: AM1 Energy Minimized Structure of the mono fluorenone



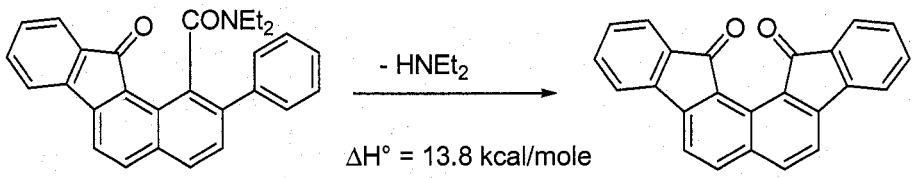
3.25



3.26

From these energy minimization calculations, it appears that the dihedral angle observed for the bis cyclized product **3.24** is too great for the existence of this molecule. This is most likely due to the proximity of the two carbonyls to each other in **3.24** and the resulting steric/electronic interference. Further, B3P86/6-311G(2d, 2p)//AM1 level of theory calculations for the second cyclization gives a value of $\Delta H° = 13.8$ kcal/mol. From this calculated value and the calculated angles, it can be postulated that the reaction is unfavourable in agreement with experimental results. This determination is based on the following reasoning. The $\Delta H°$ is the difference in energy between the starting material and product. The distribution of the moles of starting material vs. the product is based on the Boltzmann distribution which shows that $\Delta H°$ has a negative exponential effect on the formation of the product. Hence, without taking into account the $\Delta H^{\neq}$ one can say that 13.8 kcal/mole is a significant barrier to overcome.

Scheme 3.8



3.26 **3.24**

3.6 NMR Studies

X-ray structure analysis of **3.2a** (**Figure 3.4**) showed that the amides were perpendicular to the naphthalene ring and the carbonyls are pointing in opposite directions.

Figure 3.4: X-ray of *N,N*-diethyl 2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide (3.2a)

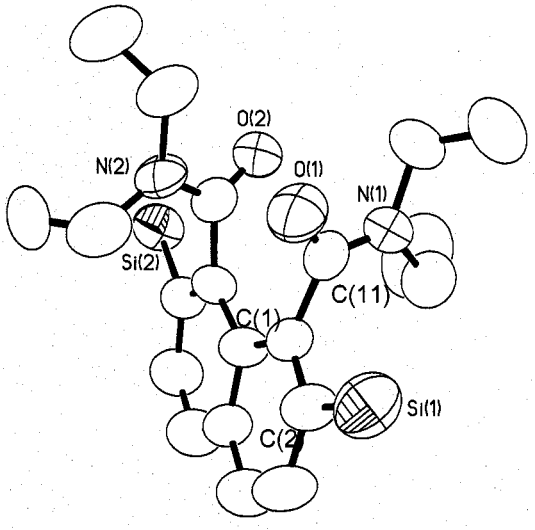


Table 3.7: Selected Bond lengths [Å](error limits) of N,N-diethyl-2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide (3.2a)

Si(1)-C(2)	1.899(4)
C(1)-C(11)	1.517(4)
C(11)-O(1)	1.236(3)
C(11)-N(1)	1.342(4)

Table 3.8: Selected Bond Angles [°] (error limits) of N,N-diethyl-2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide (3.2a)

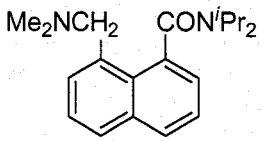
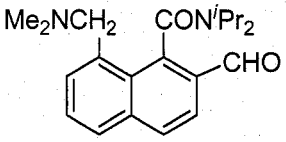
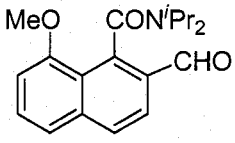
C(2)-C(1)-C(11)	116.8(3)
C(1)-C(2)-Si(1)	126.2(3)
O(1)-C(11)-C(1)	119.7(3)
N(1)-C(11)-C(1)	117.4(3)

From the bond angles noted in **Table 3.8** the following observations can be made regarding the X-ray structure of **3.2a**, the peri relationship of the two amides pushes them

outwards (116.8°) creating a smaller bond angle than the normal sp^2 carbon's orientation of 120°. This pushes the TMS groups downwards, thus giving a larger angle of 126.2°.

Variable temperature NMR studies were undertaken to determine the energy barrier to rotation. Previously Clayden reported activation energy barriers for the 1,8-peri-substituted naphthalene systems **3.30, 3.31, 3.32** (**Table 3.9**).[105]

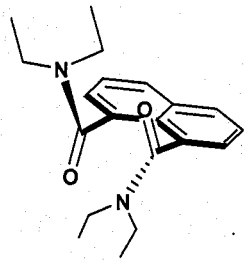
Table 3.9: Rotational Barriers of 1,8 peri-substituted naphthalenes[105]

Entry	$\Delta G^{\neq}$ kcal/mol
 **3.27**	21.8
 **3.28**	25.4
 **3.29**	29.2

Clayden demonstrated that the electronic effects between peri substituted groups is of much greater importance than the steric bulk of the substituent groups when one is concerned with the barrier to rotation of the two groups past each other. This is shown by the greater barrier to rotation in **3.29** vs **3.28** when the size of a OMe and Me_2NCH_2 groups are considered.[114]

Although rotational barriers of 1,8-naphthalene systems have been comprehensively studied over the years, [105,115,116,117] the availability of highly hindered compounds **3.31c** stimulated the investigation of rotational barriers in these derivatives.

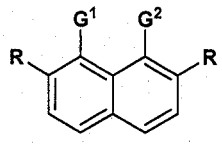
Figure 3.5: Rotation of the Diethyl Amides of *N,N*-diethyl naphthalene-1,8-dicarboxamide (3.2a)



3.30

Dynamic NMR analysis established that there were two spin systems present in the methylene region: one for the exchange of the protons caused by the rotation about the amide bond and the other for the rotation about the carbonyl aryl bond. Using the CH_3 decoupling mode, whereby the CH_3 shift which is associated with the CO-Ar rotation is decoupled, allowing for a simpler CH_2 region. (**Figure 3.6**) This allowed the coalescence temperature (T_c) to be determined for the amide slipage of **3.30**.

Table 3.10: ΔG‡(kcal/mol) comparison of naphthalene structures



3.31

Structure	G^1	G^2	$\Delta G^{\ddagger}$(kcal/mol)	T_c(°K)
3.31a	$CONEt_2$	H	15.1	309
3.31b	COPh	COPh	14.7	
3.31c	COAlkyl	COAlkyl	6.7 --> 9.0	
3.31d	$CONEt_2$	$CONEt_2$	18.2	368

R = Me, CO_2H, CO_2Me, H;[114]

Alkyl = Me, CH_2CH_3, CH_2Et, CH_2Pr^i, $CHMe_2$, CH_2Ph[115,118]

Rotational barriers for **3.31d** and known related systems are summarized in **Table 3.10**. As expected, the diethyl amide **3.31d** has a higher $\Delta G^{\ddagger}$ value than the corresponding ketone **3.31c**. This may be due to the steric bulk of the amides, which prevents the free rotation about the aryl-carbonyl bond (**Figure 3.5**). Further, in comparison to the 1-naphthalene amide **3.31a**, the barrier to rotation for the N,N-diethyl naphthalene-1,8-dicarboxamide **3.31d** is three times higher. In comparison to the 1,8-naphthalene phenone **3.31b**, the barrier to rotation in the N,N-diethyl naphthalene-1,8-dicarboxamide **3.31d** is higher. This is most likely due to the steric bulk of the amides in comparison to the phenone groups.

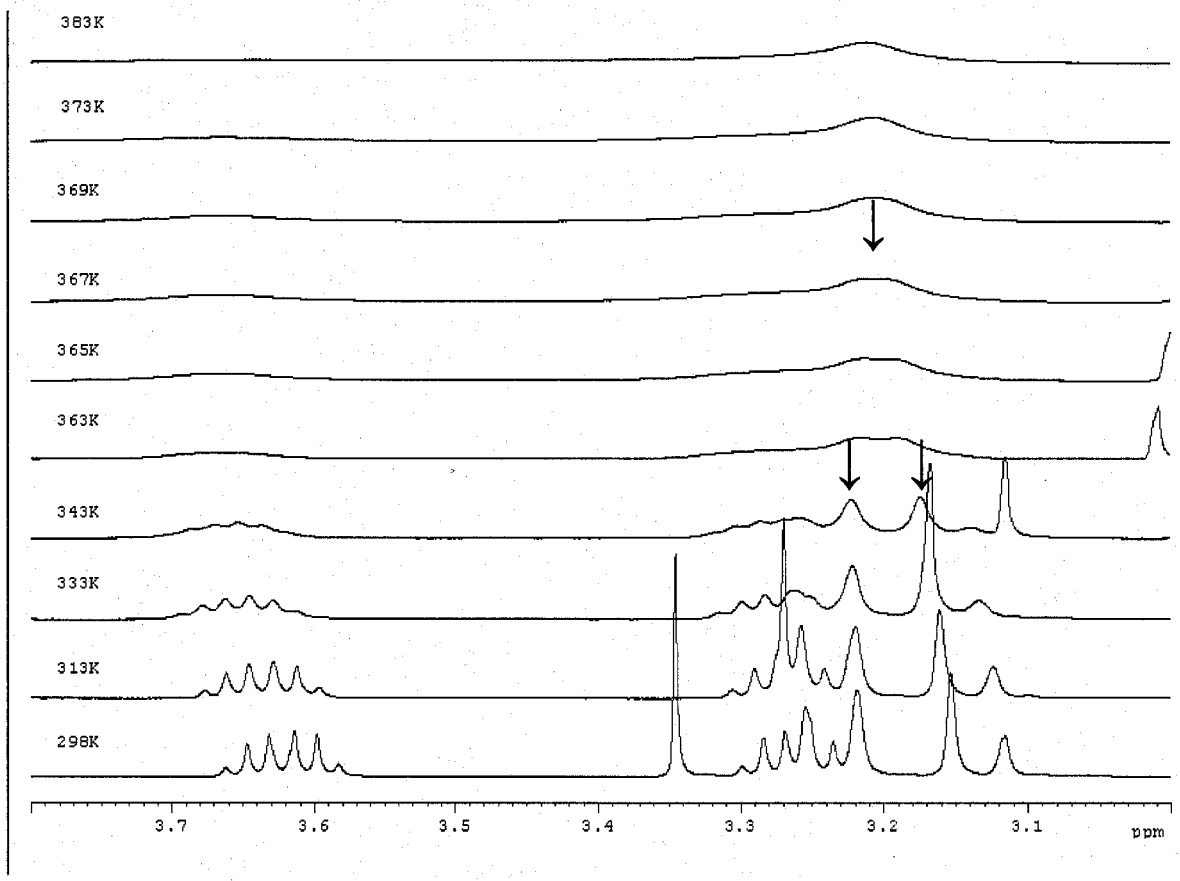


Figure 3.6: Variable Temperature NMR Spectra of *N,N*-diethyl naphthalene-1,8-dicarboxamide (3.1)

(↓= peaks used in calculation)

Further, VT NMR studies were attempted on the *N,N*-diethyl-2,7-dichloronaphthalene-1,8-dicarboxamide (**3.2e**) *N,N*-diethyl-2,7-diiodonaphthalene-1,8-dicarboxamide (**3.2g**) derivatives with no measurable result obtained. This is due to the steric and electronic effect of substituents being present at positions 2 and 7.

4 Conclusions

N,N-Diethyl naphthalene-1,8-dicarboxamide **3.1** was shown to undergo DoM using *s*-BuLi / TMEDA / THF / -78 °C / 30 min conditions to afford, after quench with a variety of electrophiles, 2,7-disubstituted products **3.2a-h** (**Table 3.1**) in good to excellent yields. On the other hand, attempts to establish conditions for the formation of 2-substituted products were less successful, yielding derivatives **3.9a-b** in low yields together with starting material and disubstituted products (**Table 3.2**).[108] The dibromo derivative **3.2f** was prepared conveniently by double ipso-deSi of the corresponding disilylated derivative **3.2a**.

A general protocol was established for the synthesis of 2-monoaryl (**3.18a-f**) and 2,7-diaryl derivatives (**3.17a-g**) by Suzuki-Miyaura cross coupling of the monoiodo **3.9a** and diiodo **3.2g** derivatives respectively (**Table 3.6 and 3.5** respectively). Using LDA, the directed remote metalation-cyclization of **3.17a** to the fluorenone **3.21** has been achieved (**Scheme 3.7**).

Also reported is a MS study of attempts to establish if the formation of the 2,7-disubstituted products occurs by a stepwise monolithiation or dilithiation process using deuterium quench experiments (**Scheme 3.2**). VT NMR studies of **3.1** has given a $\Delta G^{\neq} =$ 18.2 kcal/mol for the $\Delta G^{\neq}_{Ar\text{-}CO}$ barrier. The X-ray crystal structure of **3.2a** has been solved and shows that amides are pointing in opposite directions and are angled outwards.

5 Experimental

5.1 General Procedures

Melting points were determined using a Fisher Scientific hot stage apparatus and are uncorrected. Infrared spectra were obtained from a Bomen MB-100 FT IR spectrometer neat in KBr pellets or NaCl plates. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were obtained on a Bruker AV-300 intrument in $CDCl_3$ using TMS (for ^{1}H) or $CDCl_3$ (for ^{13}C) as the internal standard unless otherwise stated. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Bruker AV-400 intrument in $CDCl_3$ using TMS (for ^{1}H) or $CDCl_3$ (for ^{13}C) as the internal standard unless otherwise stated. The following abbreviations were used when assigning resonance multiplets ; s = singlet, d = doublet; t = triplet, q = quartet, m = multiplet. Low-resolution mass spectra were obtained on a Varian Chrompack Saturn GC/MS 2000, Agilent Technologies 5973 inert Mass Selective Detector, or Waters ZQ Single Quad Instrument equipped with an ESI/APcI multiprobe. High-resolution mass spectra were obtained on either a Applied Biosystems/MDS Sciex QSTAR XL (ESI, TurboIonspray, APCI, nanospray) with an Agilent HP1100 Cap-LC system or Waters/Micromass GC-TOF system with an Agilent HP6890 GC system. Reactions were monitored by TLC analysis (Merck 60-F254 precoated silica sheets)

All dry solvents used were purified under an argon atmosphere according to Perrin or purchased from commercial sources.[119] THF as freshly distilled from sodium benzophenone ketyl. *Sec*-butyllithium (hexanes solution) was purchased from Aldrich Chemical Company, stored in resealable containers and titrated periodically against *sec*-butanol with 1,10-phenathroline as an indicator.[120] All experiments were carried out

under argon in oven or flame dried glassware, using syringe-septum cap techniques. The temperature of -78°C was attained by combining dry ice and acetone and forming a slurry. Internal temperature readings were obtained using a Barnant Dual J stainless steel-sheathed thermocouple thermometer. *N,N,N'N'*-tetramethylethylenediamine (TMEDA) [CAS# 110-18-9] was purchased from Aldrich Chemical Company, and dried over KOH prior to use. All commodity chemicals were purchased from Aldrich Chemical Company.

The phrase "standard workup" refers to the addition of satd aq NH_4Cl solution, extraction with EtOAc x3. Followed by extraction of the organic layer with satd aq NaCl and drying of the organic layer with Na_2SO_4, subjection to filtration and concentration under reduced pressure, unless otherwise stated. In cases of using Br_2 as reagents, standard workup includes removal of excess Br_2 from the reaction mixture with satd aq $Na_2S_2O_3$.

General Procedure A: Directed *ortho* Metalation

A solution of the substrate (326 mg, 1.0 mmol) and TMEDA in THF (anhyd) (0.1 M, 5 mL), was precooled to -78 °C and treated dropwise with a solution of *s-BuLi* in hexanes (2.2-4.4 mmol, 1.4 M soln in hexanes). The resulting bright red solution was stirred at -78 °C for the time indicated, quenched with the appropriate electrophile and the whole was stirred at -78 °C for 30 min (unless otherwise stated). The resulting solution was processed following standard conditions (unless otherwise stated).

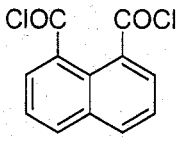
General Procedure B: Suzuki Reactions

A flamed-dried flask is cooled under an argon atmosphere and charged with the halogen cross coupling partner, aryl boronic acid (2.0 equiv), K_3PO_4 (3.0 equiv) and DMF (5 mL anhydrous). The mixture was degassed using a sonicator with argon bubbling through the solution. $Pd(PPh_3)_4$ (10 mol %), dispensed in a glove bag, was added and the system was purged with Ar for 15 min. The reaction mixture was heated at reflux for the time indicated, cooled to rt, and poured onto 5 x H_2O (25 - 30 mL). The aq phase was extracted with EtOAc (5 x) and the organic extract was washed with brine, dried (Na_2SO_4), subjected to filtration, and concentrated. The crude residue was purified by flash column chromatography (EtOAc/hexanes).

General Procedure C: Cyclization to benzofluorenones.

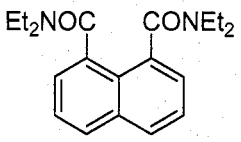
LDA (10 equiv) was prepared from *n*-BuLi (2.5 M in hexanes) and HN^iPr_2 in THF (~0.5 M) at 0 °C (ice/salt bath) and the resulting solution was added dropwise *via* a cannula to a solution of the amide in THF (~0.013 M) precooled to 0 °C. The reaction mixture was stirred for the time indicated and allowed to warm to rt and quenched with satd aq NH_4Cl solution. Standard workup followed by flash column chromatography (EtOAc/hexanes) afforded the product.

Naphthalene-1,8-dicarbonyl dichloride (4.1)



Compound **4.1** was prepared following a literature procedure.[121] 1,8-naphthalic anhydride [CAS# 81-84-5] (1.0 equiv) was combined with phosphorous pentachloride [CAS# 10026-13-8] (1.0 equiv) in phosphorous oxychloride [CAS# 10025-87-3] (10.0 equiv). Upon refluxing at 125 °C for 12 h, a dark brown solution was obtained. The solution was refluxed for 60 - 72 h under argon, cooled to rt and passed through a glass frit to remove phosphorous pentachloride. The excess phosphorous oxychloride was removed under reduced pressure and the remaining crystalline mass of **4.1** was stored under argon. Characterization was precluded as contact with moisture led to undesired products. Known data; mp 84-86 °C; bp 195 – 200 °C.

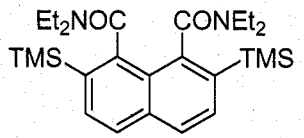
N,N-diethyl naphthalene-1,8-dicarboxamide (3.1)



To a solution of compound **4.1** in dry CH_2Cl_2 (100 mL) cooled to 0 °C was added triethylamine [CAS # 121-44-8] (2.0 equiv), while maintaining the temperature at 0 °C. Diethylamine [CAS# 109-89-7] (2.0 equiv) was added dropwise to the solution, maintaining the temperature at 0 °C. The resulting solution was stirred for 24 h allowing the temperature to rise to rt. Standard workup, followed by flash chromatography (1:1 EtOAc/ hexanes) afforded **3.1** (49% yield) as colourless crystals, mp 95-96 °C (hexanes); IR (KBr, neat) ν_{max} 2980, 2935, 1639, 1606, 1471 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ

7.89 (d, 2 H , J = 8.2 Hz), 7.49 (t, 2 H, J = 7.1 Hz), 7.39 (d, 2 H, J = 7.0 Hz), 3.74 (qd, 2 H, J = 7.2 Hz, J = 14.3 Hz), 3.46-3.10 (m, 6 H), 1.23 (t, 6 H, J = 7.2 Hz), 1.05 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, CCl_3) δ 171.8 , 135.6, 130.5, 126.5, 125.8, 78.1, 77.7, 77.3, 45.2, 40.2, 14.4, 13.9; MS m/z 326 (M^+, 3), 281 (1), 254 (100); HRMS calcd for $C_{20}H_{26}N_2O_2$: 326.2000, found: 326.1994.

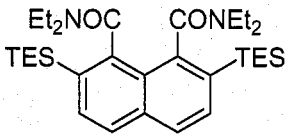
_N,N_-diethyl-2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide (3.2a)



Following General Procedure A using the following materials, [**3.1** (0.325 g, 1.0 mmol), *s-BuLi*,[CAS # 598-30-1] (3.16 mL 1.39 M, 4.4 mmol), TMEDA [CAS # 110-18-9] (0.66 mL, 4.4 mmol), and TMSCl [CAS# 75-77-4] (0.558 mL, 4.4 mmol) in THF (distilled) (5 mL)], followed by flash chromatography afforded **3.2a** (0.50 mmol, 50%) as crystalline cubes, mp 98-99°C (hexanes); IR (KBr, neat) ν_{max} 3036, 1636, 1471 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ7.80 (d, 2 H, J = 8.2 Hz), 7.71 (d, 2 H, J = 8.2 Hz), 3.94 (qd, 2 H, J = 7.3 Hz, J = 14.6 Hz), 3.26 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 2.73-2.30 (m, 4 H), 1.26 (t, 6 H, J = 7.9 Hz), 0.66 (t, 6 H, J = 7.2 Hz), 0.35 (s, 18 H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.3, 144.2, 140.7, 138.7, 131.9, 128.5, 71.8, 43.1, 42.8, 39.9, 26.6, 23.8, 13.5, 13.2, 12.9, 1.1; MS m/z (rel. intensity) 470 (M^+, 3), 455 (94), 399 (100), 354 (35), 324(35), 310(33), 282(6), 252 (6), 72(18); HRMS calcd for $C_{20}H_{41}N_2O_2Si_2$: 469.2716, found: 469.2707. X-Ray: $C_{26}H_{42}N_2O_2Si_2$, M= 470.80, orthorhombic, P2(1)2(1)2(1), a = 13.485(2) Å, b = 14.358(2) Å, c = 14.895(3) Å, α= 90°, β= 90°, γ = 90°, 2884.0(8) $Å^3$, Z= 4, D_c= 1.084 Mg/m^3 F(000) = 1024 , T= 298(2) K. Data were collected on a Bruker

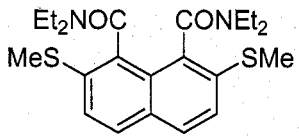
SMART CCD 1000 X-ray diffractometer with graphite-monochromated Mo K_α radiation (λ = 0.71073 Å), operating at 50 kV and 40 mA at 25 °C over 2θ ranges of 4.08 ~ 56.82°. The structure was solved by direct methods (SHELXTL version 5.10), corrected for Lorentz-polarization effects and refined by full-matrix least squares on F^2 resulting in final R, R_w and GOF (for 6913 data with $F > 4\sigma(F)$) of 0.0424, 0.0649 and 0.680 respectively for solution.

_N,N_-diethyl-2,7-bis(triethylsilanyl)naphthalene-1,8-dicarboxamide (3.2b)



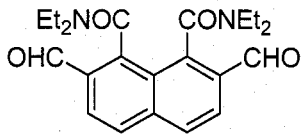
Following General Procedure A using the following materials, [**3.1** (0.326 g , 1.0 mmol), *s-BuLi*, (2.18 mL, 1.01 M, 2.2 mmol), TMEDA (0.33 mL, 2.2 mmol), and chlorotriethylsilane [CAS# 994-30-9] (0.4 mL, 3.0 mmol) in THF (distilled) (5 mL)], followed by flash chromatography afforded **3.2b** (0.31 mmol, 31%) as colourless crystals mp 91-92 °C (hexanes) IR (KBr, neat) ν_{max} 2935, 1628, 1434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ7.80 (d, 2 H, J = 8.2 Hz), 7.67 (d, 2 H, J = 8.2 Hz), 4.07 (qd, 2 H, J = 7.4 Hz, J = 14.7 Hz), 3.09 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 2.62 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 2.45 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 1.24 (t, 6 H, J = 7.3 Hz), 1.04-0.83 (m, 30 H), 0.66 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 140.9, 135.1, 133.1, 132.1, 127.4, 126.5, 42.6, 39.2, 12.6, 12.4, 7.5, 3.8, 3.6; MS m/z (rel. intensity) 555 (M^+, 95), 482 (99), 439(19), 366 (59) 248 (20) 72 (32); HRMS calcd for $C_{32}H_{54}N_2O_2Si_2$: 554.4724, found: 554.3729.

***N,N*-diethyl-2,7-dimethylthionaphthalene-1,8-dicarboxamide (3.2c)**



Following General Procedure A using the following materials, [**3.1** (0.325 g, 1.0 mmol), *s-BuLi*, (1.54 mL 1.43M, 2.2 mmol), TMEDA (0.33 mL, 2.2 mmol), and dimethyl sulfide [CAS# 75-18-3] (0.20 mL, 2.2 mmol) in THF (distilled) (5 mL)], followed by flash chromatography afforded **3.2c** (0.75 mmol, 75%) as pale yellow colourless crystals, mp 138-139 °C (hexanes); IR (KBr, neat) ν_{max} 2984, 1636, 1588, 1434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2 H, J = 8.6 Hz), 7.35 (d, 2 H, J = 8.3 Hz), 4.03 (qd, 2 H, J = 7.1 Hz, J = 14.4 Hz), 3.11-3.00 (m, 6 H), 2.46 (s, 6 H), 1.28 (t, 6 H, J = 7.1 Hz), 0.99 (t, 6 H, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 129.9, 129.5, 126.2, 124.3, 77.4, 77.1, 44.7, 39.9, 16.8, 13.3, 13.1; MS m/z (rel. intensity) 418 (M^+, 8), 346 (40), 318 (41), 298 (36), 272 (21), 247 (17), 72 (100); HRMS calcd for $C_{22}H_{30}N_2O_2S_2$: 418.1742, found: 418.1749.

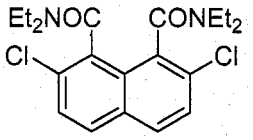
***N,N*-diethyl-2,7-diformylnaphthalene-1,8-dicarboxamide (3.2d)**



Following General Procedure A using the following materials; [**3.1** (0.325 g , 1.0 mmol), *s-BuLi*, (1.54 mL 1.43 M, 2.2 mmol), TMEDA (0.33 mL, 2.2 mmol), and DMF (0.17 mL, 2.2 mmol) in THF (distilled) (5 mL)], followed by flash chromatography, afforded **3.2i** (0.40 mmol, 40%) as colourless crystals, mp 160-162 °C (hexanes); IR (KBr, neat) ν_{max} 2970, 1689, 1637cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 2 H), 8.17 (d, 2 H, J = 8.7

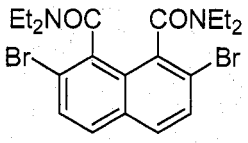
Hz), 8.00 (d, 2 H, 8.3 Hz), 4.01-4.11 (m, 2 H), 3.25 (qd, 2 H, J = 7.2 Hz, J = 14.3 Hz), 3.17-2.93 (m, 4 H) 1.37 (t, 6 H, J = 7.3 Hz), 0.94 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5, 165.9, 141.3, 139.3, 130.3, 125.7, 124.5, 45.2, 40.8, 13.4, 13.4; MS m/z (rel. intensity) 382 (M^+), 311 (67), 280 (32), 238 (100), 210 (25) 72 (71); HRMS calcd for $C_{22}H_{26}N_2O_4$: 382.1881, found: 382.1893.

_N,N_-diethyl-2,7-dichloronaphthalene-1,8-dicarboxamide (3.2e)



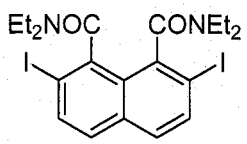
Following General Procedure A using the following materials, [**3.1** (0.326 g , 1.0 mmol), *s-BuLi*, (1.82 mL, 1.20 M, 2.2 mmol), TMEDA (0.33 mL, 2.2 mmol), and hexachloroethane [CAS# 67-72-1] (0.52g (in 2 mL), 2.2 mmol) in THF (distilled) (5 mL)], followed by flash chromatography afforded **3.2e** (0.44 mmol, 44%) as colourless crystals, mp 157-158 °C (hexanes); IR (KBr, neat) ν_{max} 2978, 1631, 1455 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, 2 H, J = 8.8Hz), 7.52 (d, 2 H, J = 8.8 Hz), 4.04 (qd, 2 H, J = 7.2 Hz, J = 14.3 Hz), 3.22-3.12 (m, 6 H), 1.35 (t, 6 H, J = 7.2 Hz), 1.13 (t, 6 H, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.4, 131.8, 131.2, 130.1, 128.0, 127.4, 44.6, 39.8, 30.9, 13.1, 12.9; MS m/z (rel. intensity) 396 ($[M+2]^+$, 21) 394 (M^+,12), 359 (3), 322 (7), 296 (13), 286 (49), 248 (32), 223 (14), 72 (100); HRMS calcd for $C_{20}H_{24}N_2O_2Cl_2$: 394.1215, found: 394.1223.

***N,N*-diethyl-2,7-dibromonaphthalene-1,8-dicarboxamide (3.2f)**



A solution of compound **3.2a** (1.30 g, 3 mmol) in CH_2Cl_2 (0.1 M) was treated dropwise with Br_2 (2.81 g, 4.4 equiv) at rt. The resulting solution was heated at reflux for 24 h, cooled to rt, decolourized with $Na_2S_2O_3$ and the whole was extracted with CH_2Cl_2 (30 mL x 3), dried (Na_2SO_4), and evaporated to dryness under reduced pressure. Recrystalization gave **3.2f** (2.1 mmol, 77%) as colourless needles, mp 174-175 °C (hexanes) IR (KBr, neat) ν_{max} 3074, 1649, 1469 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74-7.64 (m, 4 H), 4.04 (qd, 2 H, J = 7.3 Hz, J = 14.4 Hz), 3.25-3.05 (m, 6 H), 1.36 (t, 6 H, J = 7.2 Hz), 1.13 (t, 6 H, J = 7.2); ^{13}C NMR (75MHz, $CDCl_3$) δ 166.7, 134.6, 131.8, 131.1, 130.3, 121.8, 44.7, 39.9, 13.0, 12.8; MS m/z (rel. intensity) 484 ($[M+2]^+$, 1) 482 (M^+, 1), 412 (10), 384 (28), 332 (91), 233(14); HRMS calcd for $C_{20}H_{24}N_2O_2Br_2$: 482.0203, found: 482.0205.

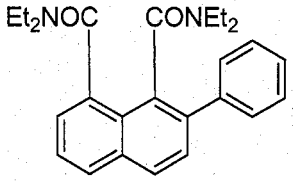
***N,N*-diethyl-2,7-diiodonaphthalene-1,8-dicarboxamide (3.2g)**



Following General Procedure A using the following materials, [**3.1** (0.326 g , 1.0 mmol), *s-BuLi*, (2.18 mL, 1.01 M, 2.2 mmol), TMEDA (0.33 mL, 2.2 mmol), and 2-iodo-1,1,1-triflouroethane [CAS# 353-83-3] (0.21 mL, 2.2 mmol) in THF (distilled) (5 mL)], followed by flash chromatography afforded **3.2g** (0.87 mmol, 87%) as a colourless crystals, mp 171-172 °C (hexanes); IR (KBr, neat) ν_{max} 2986, 1631, 1458 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, 2 H, J = 8.6 Hz), 7.40 (d, 2 H, J = 8.8 Hz), 3.93 (qd, 2 H, J

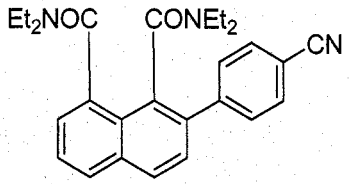
= 7.3 Hz, J = 14.5 Hz), 3.10 (qd, 2 H, J = 7.2 Hz, J = 14.3 Hz), 3.03 – 2.89 (m, 4 H), 1.30 (t, 6 H, J = 7.2 Hz), 1.03 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 138.8, 137.4, 132.6, 130.1, 127.0 97.1, 77.3, 77.0, 76.7, 44.6, 40.0, 13.0, 12.8; MS m/z (rel. intensity) 578 (M^+), 478 (12), 432 (11), 378 (56), 279 (5), 153 (11), 72 (100); HRMS calcd for $C_{20}H_{24}N_2O_2I_2$: 577.9914, found: 577.9927.

***N,N*-diethyl-2-phenylnaphthalene-1,8-dicarboxamide (3.18a)**



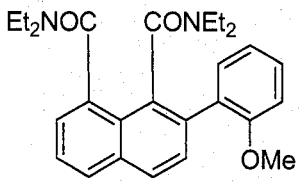
Following General Procedure B using the following materials, [**3.9a** (0.100 g, 0.22 mmol), 1.0 equiv phenyl boronic acid (0.65 g, 0.5 mmol), K_3PO_4 (0.325 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18a** (0.19 mmol, 85% yield) as an oil. IR (NaCl plates, neat) ν_{max} 2973, 1635, 1442 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (t, 2 H, J = 8.6 Hz), 7.57-7.49 (m, 4 H), 7.41-7.34 (m, 4 H), 3.87-3.81 (m, 2 H), 3.43 (qd, 1 H, J = 7.3 Hz, J = 14.6 Hz), 3.33-3.25 (m, 2 H), 3.08 (qd, 1 H, J = 7.3 Hz, J = 14.4 Hz), 2.82 (qd, 2 H, J = 7.2 Hz, J = 14.2 Hz), 1.34 (t, 3 H, J = 7.1 Hz), 1.15 (t, 3 H, J = 7.1 Hz), 0.77 (t, 3 H, J = 7.2 Hz), 0.68 (t, 3 H, J = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 140.4, 137.5, 135.7, 135.3, 133.9, 132.7, 131.9, 129.7, 129.7, 129.6, 128.4, 128.1, 128.0, 127.5, 126.7, 125.2, 45.0, 43.6, 39.9, 38.5, 13.8, 13.5, 12.6, 12.2; MS m/z (rel. intensity) 403($[M+1]^+$,72), 402(M^+, 34), 358(19), 330(100) 100(14); HRMS calcd for $C_{26}H_{30}N_2O_2$: 402.2307, found: 402.2305.

***N,N*-diethyl-2- (4-cyanophenyl)naphthalene-1,8-dicarboxamide (3.18b)**



Following General Procedure B using the following materials, [**3.9a** (0.100 g, 0.22 mmol), 1.0 equiv 4-cyanophenyl boronic acid (0.65 g, 0.5 mmol), K_3PO_4 (0.325 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18b** (0.17 mmol, 80% yield) as colourless crystals, mp 106-107 °C (hexanes); IR (KBr, neat) ν_{max} 2975, 2228, 1633, 1465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, 1 H, J = 8.5 Hz), 7.91 (d, 1 H, J = 8.2 Hz), 7.70 (s, 4 H), 7.54 (t, 1 H, J = 7.4 Hz), 7.44-7.39 (m, 2 H), 3.84-3.78 (m, 2 H), 3.39-3.21 (m, 3 H), 3.05 (qd, 1 H, J = 7.2 Hz, J = 14.4 Hz), 2.80 (qd, 2 H, J = 7.2 Hz, J = 14.3 Hz), 1.32 (t, 3 H, J = 7.1Hz), 1.13 (t, 3 H, J = 7.1 Hz), 0.77 (t, 3 H, J = 7.2 Hz), 0.69 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 168.4, 145.2, 135.6, 135.2, 134.2, 132.5, 131.8, 130.4, 130.0, 129.7, 127.4, 127.0, 126.2, 125.9, 125.8, 125.1, 118.8, 111.3, 44.8, 43.8, 39.7, 38.6, 13.7, 13.4, 12.7, 12.3; MS m/z (rel. intensity) 429(29), 428(M^+, 100), 355(33); HRMS calcd for $C_{27}H_{30}N_3O_2$: 428.2338, found: 428.2349.

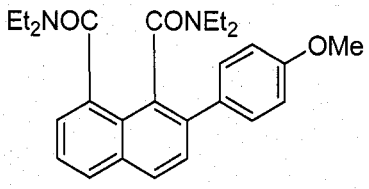
***N,N*-diethyl-2-(2-methoxyphenyl)naphthalene-1,8-dicarboxamide (3.18c)**



Following General Procedure B using the following materials, [**3.9a** (0.100 g, 0.22 mmol), 1.0 equiv 2-methoxyphenyl boronic acid (0.067 g, 0.44 mmol), K_3PO_4 (0.325 g,

3.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18c** (0.09 mmol, 43% yield) as colourless crystals, mp 143-144 °C (hexanes); IR (KBr, neat) ν_{max} 2967, 1636, 1460, 1276 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89-7.83 (m, 2 H), 7.50-7.46 (m, 3 H), 7.36-7.32 (m, 2 H), 6.97-6.94 (m, 2 H), 3.92-3.78 (m, 5 H), 3.42 (qd, 1 H, J = 7.3 Hz, J = 14.6 Hz), 3.29-3.16 (m, 3 H), 2.95 (qd, 1 H, J = 7.1 Hz, J = 14.3 Hz), 2.76-2.67 (m, 1 H), 1.32 (t, 3 H, J = 7.1 Hz), 1.13 (t, 3 H, J = 7.2 Hz), 0.78 (t, 3 H, J = 7.2 Hz), 0.65 (t, 3 H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ171.2, 168.7, 156.4, 135.5, 134.3, 133.9, 132.8, 132.1, 129.7, 129.5, 129.1, 128.6, 128.0, 126.7, 126.1, 125.0, 120.3, 110.2, 55.1, 44.9, 43.3, 39.8, 38.0, 13.8, 13.6, 12.7, 12.3; MS m/z (rel. intensity) 433($[M+1]^+$, 93), 388(58), 360(100), 332(24), 100(19); HRMS calcd for $C_{27}H_{32}N_2O_3$: 432.2413, found: 432.2425.

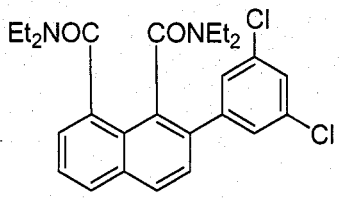
***N,N*-diethyl-2-(4- methoxyphenyl)naphthalene-1,8-dicarboxamide (3.18d)**



Following General Procedure B using the following materials, [**3.9a** (0.100 g, 0.22 mmol), 1.0 equiv 4-methoxyphenyl boronic acid (0.067 g, 0.44 mmol), K_3PO_4 (0.325 g, 3.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18d** (0.022 mole, 68% yield) as a colourless oil, IR (NaCl, neat) ν_{max} 2973, 1631, 1605, 1248, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20-8.18 (d, 2 H, J = 8.4 Hz), 7.91 (t, 2 H, J = 8.4 Hz), 7.40-7.37 (m, 2 H), 7.04 (d, 2 H, J = 8.4 Hz), 6.94 (d, 2 H, J = 8.6 Hz), 3.91 (s, 3 H), 3.87-3.81 (m, 5 H), 3.45-3.24 (m, 3 H), 3.07 (qd, 1 H, J = 7.2 Hz, J = 14.3 Hz), 2.84 (qd, 2 H, J = 6.9 Hz, J = 14.2 Hz), 1.34 (t, 3 H, J

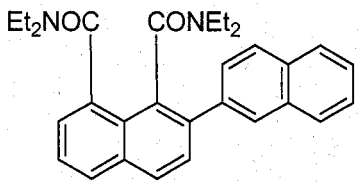
= 6.9 Hz), 1.14 (t, 3 H, J = 7.1 Hz), 0.84 (t, 3 H, J = 7.2 Hz), 0.70 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 169.1, 163.2, 159.3, 137.5, 137.1, 135.7, 135.3, 133.7, 132.9, 130.8, 129.6, 128.5, 126.7, 126.4, 125.9, 125.2, 125.0, 113.5, 55.4, 55.2, 45.0, 43.7, 39.8, 38.6, 13.5, 12.7; MS m/z (rel. intensity) 433(60), 432(M^+,40), 403 (38), 361(59) 360(100); HRMS calcd for $C_{27}H_{32}N_2O_3$: 432.2413, found: 432.2421.

_N,N_-diethyl-2-(di-3,5-dichlorophenyl)naphthalene-1,8-dicarboxamide (3.18e)



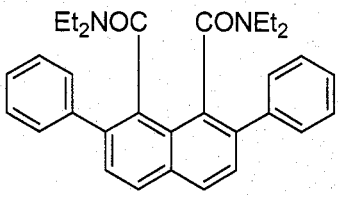
Following General Procedure B using the following materials, [**3.9a** (0.200 g, 0.22 mmol), 1.0 3,5-dichlorophenyl boronic acid (0.084 g, 0.44 mmol), K_3PO_4 (0.33 g, 3.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18e** (0.09 mmol, 44% yield) as colourless crystals, mp 67-68 °C (hexanes); IR (KBr, neat) ν_{max} 2970, 1638, 1423 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.90 (m, 2H), 7.55-7.39 (m, 6 H), 3.93-3.84 (m, 2 H), 3.41 (qd, 1 H, J = 7.3 Hz, J = 14.6 Hz), 3.31-3.21 (m, 2 H), 3.11 (qd, 1 H, J = 7.2 Hz, J = 14.4 Hz), 2.89 (qd, 1 H, J = 7.1 Hz, J = 14.2 Hz), 2.81 (qd, 1 H, J = 7.0 Hz, J = 14.1 Hz) 1.34 (t, 3 H, J = 7.1 Hz), 1.15 (t, 3 H, J = 7.2 Hz), 0.91 (t, 3 H, J = 7.2 Hz), 0.74 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 168.4, 143.3, 135.6, 134.7, 134.4, 134.3, 132.5, 132.3, 130.3, 129.7, 128.0, 127.6, 127.5, 127.0, 126.3, 125.8, 45.2, 44.1, 40.0, 39.0, 13.8, 13.7, 12.7, 12.5; MS m/z (rel. intensity) 471(M^+, 18), 400(80), 398(100); HRMS calcd for $C_{26}H_{38}Cl_2N_2O_2$: 471.1606, found: 471.1604.

***N,N*-diethyl-2-(2-naphthyl)naphthalene-1,8-dicarboxamide (3.18f)**



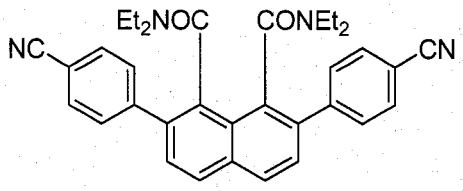
Following General Procedure B using the following materials, [**3.9a** (0.100 g, 0.22 mmol), 1.0 2-naphthyl boronic acid (0.076 g, 0.44 mmol), K_3PO_4 (0.33 g, 3.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.18f** (0.15 mmol, 67% yield) as colourless crystals, mp 133-134 °C (hexanes); IR (KBr, neat) ν_{max} 3054, 1634, 1460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1 H), 7.97-7.86 (m, 5 H), 7.70 (d, 1 H, J = 8.5 Hz), 7.60 (d, 1 H, J = 8.4 Hz), 7.53-7.49 (m, 3 H), 7.41 (d, 1 H, J = 7.0 Hz), 3.88 (qd, 1 H, J = 6.9 Hz, J = 14.0 Hz), 3.80 (qd, 1 H, J = 6.8 Hz, J = 13.9 Hz), 3.50 (qd, 1 H, J = 7.2 Hz, J = 14.6 Hz), 3.30 (qd, 2 H, J = 7.0 Hz, J = 14.2 Hz) 3.11 (qd, 1 H, J = 7.2 Hz, J = 14.4 Hz), 2.89-2.73 (m, 2 H), 1.35 (t, 3 H, J = 7.1 Hz), 1.18 (t, 3 H, J = 7.1 Hz), 0.62-0.57 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 137.8, 137.3, 135.6, 134.0, 132.5, 132.3, 129.7, 129.6, 128.6, 128.6, 128.3, 127.8, 127.6, 126.5, 126.3, 126.2, 125.6, 125.2, 45.1, 43.8, 39.9, 39.6, 13.8, 13.6, 12.6, 12.3; MS m/z (rel. intensity) 453.23($[M+1]^+$, 92) 408(68), 380(100), 100(16); HRMS calcd for $C_{30}H_{33}N_2O_2$: 452.2464, found: 452.2464.

***N,N*-diethyl-2,7-diphenylnaphthalene-1,8-dicarboxamide (3.17a)**



Following General Procedure B using the following materials, [**3.2g** (0.300 g, 0.52 mmol), 2.0 phenyl boronic Acid (0.156 g, 1.0 mmol), K_3PO_4 (0.488 g, 3.0 mmol) $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (5 mL)], followed by flash chromatography afforded **3.17a** (0.26 mmol, 51% yield) as colourless crystals, mp 150-151 °C (hexanes); IR (KBr, neat) ν_{max} 3051, 1634, 1492 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 2 H, J = 8.4 Hz), 7.56 (d, 4 H, J = 8.0 Hz), 7.50 (d, 2 H, J = 8.3 Hz), 7.41-7.35 (m, 6 H), 3.82 (qd, 2 H, J = 7.3 Hz, J = 14.5 Hz), 3.12 (qd, 2 H, J = 7.3 Hz, J = 14.4 Hz), 2.87 (qd, 2 H, J = 7.1 Hz, J = 14.2 Hz), 2.75 (qd, 2 H, J = 7.1 Hz, J = 14.0 Hz), 0.76 (t, 6 H, J = 7.3 Hz), 0.68 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 138.3, 132.9, 129.8, 129.3, 128.6, 127.9, 127.4, 126.3, 43.8, 38.5, 12.7, 12.3; MS m/z (rel. intensity) 478(M^+, 40), 434(24), 406(100); HRMS calcd for $C_{32}H_{34}N_2O_2$: 478.2617, found: 478.2617.

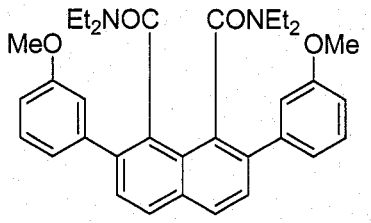
***N,N*-diethyl-2,7-di-(4-cyanophenyl)naphthalene-1,8-dicarboxamide (3.17b)**



Following General Procedure B using the following materials, [**3.2g** (0.200 g, 0.52 mmol), 2.0 equiv 4-cyanophenyl boronic acid (0.102 g,1.0 mmol), K_3PO_4 (0.65 g, 6.0

mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17b** (0.17 mmol, 50% yield) as colourless crystals, mp 239-240 °C (hexanes); IR (KBr, neat) ν_{max} 3093, 2223, 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, 2 H, J = 8.4 Hz), 7.71 (s, 8 H), 7.50 (d, 2 H, J = 8.4 Hz), 3.79 (qd, 2 H, J = 7.1 Hz, J = 14.3 Hz), 3.05 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 2.79 (qd, 4 H, J = 7.2 Hz, J = 14.0 Hz), 0.78 (t, 6 H, J = 7.2 Hz), 0.70 (t, 6 H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 145.1, 136.6, 133.5, 133.2, 131.7, 130.6, 129.8, 128.2, 126.0, 118.7, 111.5, 43.9, 38.7, 12.8, 12.3; MS m/z (rel. intensity) 528(M^+), 456 (22), 428(34), 382(46), 353 (56), 326(21), 72 (100); HRMS calcd for $C_{34}H_{32}N_4O_2$: 528.2537, found: 528.2525.

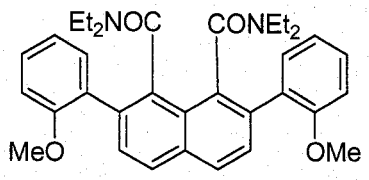
***N,N*-diethyl-2,7-(3-methoxyphenyl)naphthalene-1,8-dicarboxamide (3.17c)**



Following General Procedure B using the following materials, [**3.2g** (0.200 g, 0.52 mmol), 2.0 3-methoxyphenyl boronic acid (0.105 g, 0.69 mmol), K_3PO_4 (0.65 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17c** (0.14 mmol, 41% yield) as colourless crystals, mp 126-127 °C. IR (KBr, neat) ν_{max} 3056, 1599, 1467 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 2 H, J = 8.4 Hz), 7.51 (d, 2 H, J = 8.3 Hz), 7.32 (d, 2 H, J = 7.9 Hz), 7.16-7.12 (m, 4 H), 6.92 (d, 2 H, J = 8.2 Hz), 3.90-3.81 (m, 8 H), 3.20-3.17 (m, 2 H), 2.99-2.92 (m, 2 H), 2.81-2.74 (m, 2 H), 0.79 (t, 6 H, J = 7.1 Hz), 0.74 (t, 6 H, J = 7.2 Hz); ^{13}C NMR

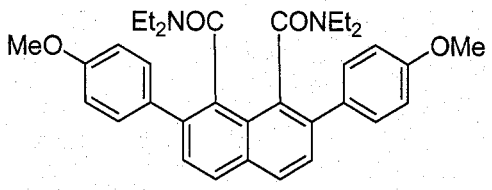
(100 MHz, CDCl3) δ 168.6, 159.1, 141.9, 138.1, 133.1, 132.3, 129.5 129.0, 128.5, 128.0, 126.4, 122.4, 115.3, 113.2, 55.4, 44.0, 38.5, 12.7, 12.3; MS m/z (rel. intensity) 539(42), 538(M^+, 17), 466(100); HRMS calcd for $C_{34}H_{38}N_2O_4$: 538.2832, found: 538.2841.

***N,N*-diethyl-2,7-di-(2- methoxyphenyl)naphthalene-1,8-dicarboxamide (3.17d)**



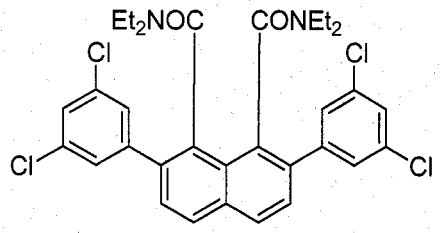
Following General Procedure B using the following materials, [**3.2g** (0.300 g, 0.52 mmol), 2.0 2-methoxyphenyl boronic acid (0.105 g, 0.69 mmol), K_3PO_4 (0.65 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17d** (0.19 mmol, 56% yield) as colourless crystals, mp 210-211 °C(hexanes); IR (KBr, neat) ν_{max} 3005, 1631, 1460 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ7.86 (d, 2 H, J = 8.4 Hz), 7.48 (t, 4 H, J = 9.7 Hz), 7.34 (t, 2 H, J = 7.3 Hz), 6.96 (t, 4 H, J = 6.9 Hz), 3.85-3.78 (m, 8 H), 3.26 (qd, 2 H, J = 7.1 Hz, J = 14.1 Hz), 3.05 (qd, 2 H, J = 7.1 Hz, J = 14.2 Hz), 2.67 (qd, 2 H, J = 6.9 Hz, J = 13.8 Hz), 0.82 (t, 6 H, J = 7.1 Hz), 0.60 (t, 6 H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.3, 132.9, 132.3, 129.6, 128.9, 127.8, 120.2, 110.0, 55.1, 43.7, 38.3, 12.9, 12.6; MS m/z (rel. intensity) 539($[M+1]^+$, 91), 466 (100), 438(22); HRMS calcd for $C_{34}H_{38}N_2O_4$: 538.2832, found: 538.2839.

***N,N*-diethyl-2,7-di-(4- methoxyphenyl)naphthalene-1,8-dicarboxamide (3.17e)**



Following General Procedure B using the following materials, [**3.2g** (0.200 g, 0.52 mmol), 2.0 4-methoxyphenyl boronic acid (0.105 g, 0.69 mmol), K_3PO_4 (0.65 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17d** (0.16 mmol, 47%yield) as colourless crystals, mp 176-177 °C (hexanes); IR (KBr, neat) ν_{max} 3056, 1634, 1608, 1440 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, 2 H, J = 8.4 Hz), 7.52-7.46 (m, 6 H), 6.94 (d, 4 H, J = 8.6 Hz), 3.87 – 3.84 (m, 8 H) 3.10 (qd, 2 H, J = 7.2 Hz, J = 14.2 Hz), 2.88 (qd, 2 H, J = 7.3 Hz, J = 14.5 Hz) 2.79 (qd, 2 H, J = 7.3 Hz, J = 14.3 Hz) 0.77 (dd, 12 H, J = 7.0 Hz, J = 12.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 131.0, 129.3, 128.6, 113.3, 55.4, 43.9, 38.6, 13.8, 12.6; MS m/z (rel. intensity) 538 (M^+, 9), 466 (100), 438 (42) 394 (30); HRMS calcd for $C_{34}H_{38}N_2O_4$ 538.2832, found: 538.2841.

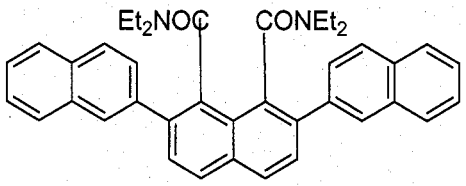
***N,N*-diethyl-2,7-di-(3,5-dichlorophenyl)naphthalene-1,8-dicarboxamide (3.17f)**



Following General Procedure B using the following materials, [**3.2g** (0.200 g, 0.52 mmol), 2.0 4-methoxyphenyl boronic acid (0.105 g, 0.69 mmol), K_3PO_4 (0.65 g, 6.0

mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17f** (0.16 mmol, 45% yield) as colourless crystals, mp 212-213 °C (hexanes); IR (KBr, neat) ν_{max} 3080, 1745, 1639, 1422 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, 2 H, J = 8.5 Hz), 7.48 (m, 6 H), 7.40 (s, 2 H), 3.92 (qd, 2 H, J = 7.1 Hz, J = 14.4 Hz), 3.15 (qd, 2 H, J = 7.2 Hz, J = 14.4 Hz), 2.95 (qd, 2 H, J = 7.2 Hz, J = 14.5 Hz), 2.78 (qd, 2 H, J = 7.1 Hz, J = 14.2 Hz), 0.84 (t, 6 H, J = 7.2 Hz), 0.79 (t, 6 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 134.6, 129.8, 128.3, 128.1, 127.7, 44.5, 39.2, 12.8, 12.7; MS m/z (rel. intensity) 614 (M^+, 22), 542(100), 72(30); HRMS calcd for $C_{32}H_{30}Cl_4N_2O_2$ 614.1061, found: 614.1040.

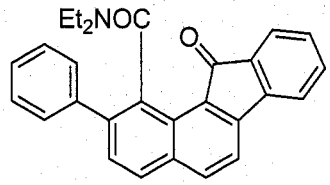
***N,N*-diethyl-2,7-di-(2-naphthyl)naphthalene-1,8-dicarboxamide (3.17g)**



Following General Procedure B using the following materials, [**3.2g** (0.200 g, 0.52 mmol), 2.0 2-naphthyl boronic acid (0.119 g, 0.69 mmol), K_3PO_4 (0.65 g, 6.0 mmol), $Pd(PPh_3)_4$ (10 mole%) in DMF [Degassed –Anhydrous (3 mL)], followed by flash chromatography afforded **3.17g** (0.01 mmol, 29% yield) as colourless crystals, mp 214-215 °C. IR (KBr, neat) ν_{max} 3054, 1631, 1467 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 2 H), 8.00 (d, 2 H, J = 8.4 Hz), 7.93-7.88 (m, 6 H), 7.73 (d, 2 H, J = 8.5 Hz), 7.62 (d, 2 H, J = 8.4 Hz), 7.53-7.52 (m, 4 H), 3.80 (qd, 2 H, J = 7.1 Hz, J = 14.2 Hz), 3.24 (qd, 2 H, J = 7.1 Hz, J = 14.4 Hz), 3.00 (qd, 2 H, J = 7.2 Hz, J = 14.5 Hz) 2.73 (qd, 2 H, J = 7.1 Hz, J = 14.1 Hz), 2.75-2.71 (m, 2 H), 0.69 (t, 6 H, J = 7.2 Hz), 0.52 (t, 6 H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 138.1, 133.1, 133.0, 132.5, 129.5, 128.9, 128.7, 128.4,

128.0, 127.6, 127.5, 126.6, 126.2, 126.2, 44.2, 38.7, 12.8, 12.5; MS m/z (rel. intensity) 579 ([M+1]$^+$, 27), 534(17), 506(100); HRMS calcd for $C_{40}H_{38}N_2O_2$: 578.2933, found: 578.2953.

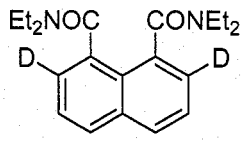
_N,N_-diethyl-11-oxo-2-phenyl-11H-benzo[_a_]fluorine carboxamide (3.21)



Following General Procedure C using the following materials [**3.17a** (0.300 g, 0.62 mmol), *n*-BuLi (3.1 mL, 2.27 M, 6.2 mmol) THF (50 mL) (36 hours, 0°C→ rt)] standard workup followed by flash chromatography (1:3 EtOAc:hexanes) afforded **3.24** (0.053 g, 39% yield) as bright orange crystals, mp 208-210 °C (hexanes; sublimes); IR (KBr, neat) ν_{max} 3052, 2363, 2345, 1708, 1619 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, 1 H, J = 8.2 Hz), 7.83 (d, 1 H, J = 8.5 Hz), 7.72 (d, 1 H, J = 8.1 Hz), 7.56-7.39 (m, 10 H), 7.29-7.24 (m, 1 H), 4.14 (qd, 1 H, J = 7.3 Hz, J = 14.9 Hz), 3.17 (qd, 1 H, J = 7.2 Hz, J = 14.4 Hz), 3.06 (qd, 1 H, J = 7.2 Hz, J = 14.3 Hz), 2.88 (qd, 1 H, J = 7.2 Hz, J = 14.3 Hz), 0.86 (t, 3 H, J = 7.2 Hz), 0.73 (t, 3 H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 148.6, 142.8, 140.5, 140.3, 137.0, 134.8, 134.0, 133.8, 132.0, 129.9, 129.5, 139.3, 129.7, 127.9, 127.6, 126.8, 124.0, 119.5, 118.6, 77.4, 77.1, 76.8, 43.3, 38.5, 12.5, 11.9; MS m/z (rel. intensity) 406(M$^+$, 94), 390(21), 333(100); HRMS calcd for $C_{28}H_{24}NO_2$: 406.1807, found: 406.1808.

Deuteration of *N,N*-diethyl-2,7-dideuteratednaphthalene-1,8-dicarboxamide (3.2h)

a) Using 1.1, 2.2, 3.3 and 4.4 equivalents of base



Following General Procedure A using the following materials, [**3.1** (0.325 g , 1.0 mmol), *s-BuLi*, [a) 1.1 mL 1.1 M, 1.1 mmol; b) 2.2 mL 1.1 M, 2.2 mmol; c) 3.3 mL 1.1 M, 3.3 mmol; d) 4.4 mL 4.4 M, 4.4 mmol], TMEDA [a) 0.17 mL, 1.1 mmol; b) 0.34 mL, 2.2 mmol; 0.51 mL, c) 3.3 mmol; d) 0.68 mL, 4.4 mmol], and CD_3OD [CAS# 811-98-3] (0.455 mL, 10 mmol) in THF (distilled) (5 mL)] HRMS used to determine percent incorporation of starting material (**3.1**), mono, and bis. Using peak intensities at [SM – NEt_2]$^+$ which corresponds to the following points; 254([SM-NEt_2]$^+$) 255([mono - NEt_2]$^+$) 265 ([bis - NEt_2]$^+$). Results are discussed in the Results and Discussion section.

Variable Temperature NMR Experiments

A sample of compound **3.1** was dissolved in deuterated DMSO. 2D ^{1}H (600 MHz) NMR spectra were first obtained to determine the nature of the splitting pattern for the CH_2 groups of the *N,N*-diethyl amides. Dynamic NMR experiments were performed on the Bruker AV-400 with CH_3 decoupling. Spectra were obtained at the following temperatures; 298K, 313K, 333K, 343K, 363K, 365K, 367K, 369K, 373K, 383K. Coalescence of the AB system was observed at 368°K. Hence using standard calculations, a value of $\Delta G^{\neq}$ = 18.2kcal/mol was determined. In order to determine the

barrier to rotation – the equation presented by Sandström[122] was used. Where k is defined as follows;

$$k = \Pi\sqrt{\frac{(\Delta\upsilon)^2 + 6(J_{AB})^2}{2}}$$

$\Delta\upsilon$ is defined as the difference in coupling constants according to the following equation.

$$\Delta\upsilon = \left|(l_1 - l_4)(l_2 - l_3)\right|^{1/2}$$

J_{AB} is the coupling constant between the AB system.

T_c is the temperature of coalescence.

$\Delta G^{\neq}_{Ar\text{-}CO}$ is the activation energy for the barrier to rotation of the carbonyl-aromatic bond.

The value of k was then substituted into the Eyring equation in order to determine the $\Delta G^{\neq}_{Ar\text{-}CO}$.

$$\Delta G^{\neq}_{Ar-CO} = 0.01914 \times T_c \times \left[10.319 + \log_{10}\left(\frac{T_c}{k}\right)\right]$$

Data

PPM	Hz
3.26	1303.66
3.22	1288.46
3.16	1265.05
3.12	1250.04

Calculation as follows:

1) Analyze AB → J_{AB} = 15Hz

2) $k = \Pi\sqrt{\frac{(\Delta\upsilon)^2 + 6(J_{AB})^2}{2}}$

$$\Delta\upsilon = \left|(l_1 - l_4)(l_2 - l_3)\right|^{1/2}$$

$$\Delta\upsilon = \sqrt{(1303.66 - 1250.04)(1288.46 - 1265.05)}$$

$$\Delta\upsilon = \sqrt{(53.6)(23.41)}$$

$\Delta\upsilon = 35.4\text{Hz}$

$$k = \Pi\sqrt{\frac{2603.16}{2}}$$

$k = 113.34\ \text{s}^{-1}$

$$\Delta G^{\neq}_{Ar-CO} = 0.01914 \times T_c \times \left[10.319 + \log_{10}\left(\frac{T_c}{k}\right)\right]$$

$$\Delta G^{\neq}_{Ar-CO} = 0.01914 \times 368 \times \left[10.319 + \log_{10}\left(\frac{368}{113.34}\right)\right]$$

$\Delta G^{\neq}_{\text{Ar-CO}} = 18.2\ \text{kcal / mol}$

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7 Appendices

7.1 Apendix 1 Single Crystal X-Ray Data for 3.2a (aw32) Prepared by Wang, Ruiyao, Dept of Chemistry, Queen's University

A crystal of the compound (colorless, plate-shaped, size 0.1 x 0.1 x 0.1mm) was mounted and sealed on a glass fiber with epoxy glue. Data collection was performed on a Bruker SMART CCD 1000 X-ray diffractometer with graphite-monochromated Mo K_α radiation ($\lambda = 0.71073$ Å), operating at 50 kV and 40 mA at 25 °C over 2θ ranges of 4.08 ~ 56.82°. No significant decay was observed during the data collection.

Data were processed on a Pentium PC using the Bruker AXS Windows NT SHELXTL software package (version 5.10).[1] Neutral atom scattering factors were taken from Cromer and Waber.[2] The raw intensity data were converted (including corrections for scan speed, background, and Lorentz and polarization effects) to structure amplitudes and their esd's using the program SAINT, which corrects for *Lp* and decay. Absorption corrections were applied using program SADABS. The crystal is orthorhombic space group $P2_12_12_1$, based on the systematic absences, *E* statistics and successful refinement of the structure. The structure was solved by direct methods. Full-matrix least-square refinements minimizing the function $\sum w (F_o^2 - F_c^2)^2$ were applied to the compound. All non-hydrogen atoms were refined anisotropically. The positions for all hydrogen atoms were calculated, and their contributions were included in the structure factor calculations with isotropic thermal parameters 1.2 times that of the attached carbon atoms (1.5 times for methyl hydrogens).

Convergence to final $R_1 = 0.0424$ and $wR_2 = 0.0649$ by using 6913 independent reflections and 298 parameters were achieved,[3] with the largest residual peak and hole to be 0.155 and – 0.134 e/Å^3, respectively. Crystallographic data, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters,

and torsion angles are given in Table 1 to 6. The molecular structure and the cell packing are shown in Figures 1 and 2.

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[1] *SHELXTL NT: Crystal Structure Analysis Package, version 5.10*; Bruker AXS Inc.: Madison, WI, 1999.

[2] Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, UK, 1974; Vol. 4, Table 2.2 A.

[3] $R_1 = \Sigma \, | \, |Fo| - |Fc| \, | \, / \, \Sigma \, |Fo|$

$wR_2 = \{\Sigma \, [w \, (Fo^2 - Fc^2)^2] \, / \, \Sigma \, [w(Fo^2)^2]\}^{1/2}$

($w = 1 \, / \, [\sigma^2(Fo^2) + (0.075P)^2]$, where $P = [\text{Max} \, (Fo^2, 0) + 2Fc^2] \, / \, 3$)

Table 1. Crystal data and structure refinement for aw23

Identification code	aw23	
Empirical formula	C26 H42 N2 O2 Si2	
Formula weight	470.80	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 13.485(2) Å	α= 90°.
	b = 14.358(2) Å	β= 90°.
	c = 14.895(3) Å	γ = 90°.
Volume	2884.0(8) Å^3	
Z	4	
Density (calculated)	1.084 Mg/m^3	
Absorption coefficient	0.146 mm^{-1}	
F(000)	1024	
Crystal size	0.1 x 0.1 x 0.1 mm^3	
Theta range for data collection	2.04 to 28.41°.	
Index ranges	-17<=h<=17, -17<=k<=19, -18<=l<=19	
Reflections collected	21062	
Independent reflections	6913 [R(int) = 0.0672]	
Completeness to theta = 28.41°	97.0 %	
Absorption correction	Empirical (Bruker SADABS)	
Max. and min. transmission	1.0000 and 0.8889	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6913 / 0 / 298	
Goodness-of-fit on F^2	0.680	
Final R indices [I>2sigma(I)]	R1 = 0.0424, wR2 = 0.0649	
R indices (all data)	R1 = 0.2034, wR2 = 0.0844	
Absolute structure parameter	0.39(11)	
Largest diff. peak and hole	0.155 and -0.134 e.Å^{-3}	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for aw23. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1)	2443(1)	5472(1)	7943(1)	99(1)
Si(2)	8515(1)	4258(1)	8277(1)	83(1)
C(1)	4583(3)	5136(2)	7986(2)	59(1)
C(2)	3726(3)	5189(2)	7493(3)	76(1)
C(3)	3794(3)	4987(2)	6557(3)	92(1)
C(4)	4678(3)	4760(2)	6173(2)	90(1)
C(5)	5552(3)	4680(2)	6667(3)	68(1)
C(6)	5510(3)	4813(2)	7618(2)	59(1)
C(7)	6377(3)	4601(2)	8120(2)	57(1)
C(8)	7281(2)	4398(2)	7703(2)	66(1)
C(9)	7275(3)	4352(2)	6758(3)	80(1)
C(10)	6450(3)	4460(2)	6265(2)	88(1)
C(11)	4535(3)	5488(2)	8945(3)	68(1)
C(12)	5032(3)	6601(2)	10070(2)	112(1)
C(13)	4297(3)	7277(3)	10373(3)	201(3)
C(14)	5315(3)	6961(2)	8442(3)	106(1)
C(15)	6407(3)	7147(3)	8431(4)	171(2)
C(16)	1991(2)	4443(3)	8601(3)	148(2)
C(17)	1589(3)	5675(3)	6981(2)	144(2)
C(18)	2405(3)	6528(2)	8650(3)	147(2)
C(19)	6375(2)	4551(2)	9135(2)	61(1)
C(20)	5776(3)	3815(2)	10493(2)	104(1)
C(21)	6444(3)	3180(3)	11005(2)	151(2)
C(22)	5478(4)	3026(3)	9012(3)	116(2)
C(23)	5894(6)	2250(4)	9046(5)	117(3)
C(23A)	4531(5)	2852(4)	8886(5)	109(3)
C(24)	8512(2)	3553(2)	9311(2)	113(1)
C(25)	9375(2)	3666(2)	7480(2)	125(1)
C(26)	9000(3)	5438(2)	8518(2)	106(1)
N(1)	4956(2)	6315(2)	9121(2)	80(1)
N(2)	5931(2)	3810(2)	9510(2)	74(1)
O(1)	4112(2)	5018(2)	9526(2)	91(1)
O(2)	6806(2)	5152(2)	9574(1)	81(1)

Table 3. Bond lengths [Å] and angles [°] for aw23.

Si(1)-C(18)	1.847(3)
Si(1)-C(17)	1.861(3)
Si(1)-C(16)	1.875(3)
Si(1)-C(2)	1.899(4)
Si(2)-C(24)	1.843(3)
Si(2)-C(26)	1.851(3)
Si(2)-C(25)	1.864(3)
Si(2)-C(8)	1.882(3)
C(1)-C(2)	1.372(4)
C(1)-C(6)	1.442(4)
C(1)-C(11)	1.517(4)
C(2)-C(3)	1.426(4)
C(3)-C(4)	1.361(4)
C(4)-C(5)	1.394(4)
C(5)-C(10)	1.387(4)
C(5)-C(6)	1.431(4)
C(6)-C(7)	1.421(4)
C(7)-C(8)	1.399(4)
C(7)-C(19)	1.512(4)
C(8)-C(9)	1.409(4)
C(9)-C(10)	1.342(4)
C(11)-O(1)	1.236(3)
C(11)-N(1)	1.342(4)
C(12)-C(13)	1.459(4)
C(12)-N(1)	1.475(3)
C(14)-N(1)	1.455(4)
C(14)-C(15)	1.497(5)
C(19)-O(2)	1.229(3)
C(19)-N(2)	1.343(3)
C(20)-N(2)	1.480(3)
C(20)-C(21)	1.492(4)
C(22)-C(23)	1.249(6)
C(22)-C(23A)	1.315(7)
C(22)-N(2)	1.479(4)
C(18)-Si(1)-C(17)	107.04(17)
C(18)-Si(1)-C(16)	109.84(18)
C(17)-Si(1)-C(16)	108.96(17)
C(18)-Si(1)-C(2)	113.74(16)
C(17)-Si(1)-C(2)	108.99(17)
C(16)-Si(1)-C(2)	108.17(15)
C(24)-Si(2)-C(26)	109.97(16)
C(24)-Si(2)-C(25)	106.43(15)
C(26)-Si(2)-C(25)	108.75(17)
C(24)-Si(2)-C(8)	115.84(16)
C(26)-Si(2)-C(8)	107.63(14)
C(25)-Si(2)-C(8)	108.04(15)
C(2)-C(1)-C(6)	123.0(3)
C(2)-C(1)-C(11)	116.8(3)
C(6)-C(1)-C(11)	120.1(3)
C(1)-C(2)-C(3)	117.2(3)
C(1)-C(2)-Si(1)	126.2(3)
C(3)-C(2)-Si(1)	116.6(3)
C(4)-C(3)-C(2)	121.0(4)

C(3)-C(4)-C(5)	122.6(4)
C(10)-C(5)-C(4)	122.0(4)
C(10)-C(5)-C(6)	119.5(4)
C(4)-C(5)-C(6)	118.5(4)
C(7)-C(6)-C(5)	117.4(3)
C(7)-C(6)-C(1)	125.6(3)
C(5)-C(6)-C(1)	117.0(3)
C(8)-C(7)-C(6)	121.9(3)
C(8)-C(7)-C(19)	115.8(3)
C(6)-C(7)-C(19)	122.3(3)
C(7)-C(8)-C(9)	116.6(3)
C(7)-C(8)-Si(2)	126.2(3)
C(9)-C(8)-Si(2)	117.0(3)
C(10)-C(9)-C(8)	123.1(3)
C(9)-C(10)-C(5)	120.9(3)
O(1)-C(11)-N(1)	122.8(4)
O(1)-C(11)-C(1)	119.7(3)
N(1)-C(11)-C(1)	117.4(3)
C(13)-C(12)-N(1)	115.7(3)
N(1)-C(14)-C(15)	116.7(4)
O(2)-C(19)-N(2)	123.1(3)
O(2)-C(19)-C(7)	119.8(3)
N(2)-C(19)-C(7)	117.0(3)
N(2)-C(20)-C(21)	114.6(3)
C(23)-C(22)-C(23A)	105.8(6)
C(23)-C(22)-N(2)	118.2(5)
C(23A)-C(22)-N(2)	128.1(6)
C(11)-N(1)-C(14)	124.7(3)
C(11)-N(1)-C(12)	117.6(3)
C(14)-N(1)-C(12)	117.7(3)
C(19)-N(2)-C(22)	125.2(3)
C(19)-N(2)-C(20)	118.1(3)
C(22)-N(2)-C(20)	116.3(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for aw23. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	71(1)	114(1)	112(1)	9(1)	-10(1)	10(1)
Si(2)	65(1)	101(1)	81(1)	-10(1)	-2(1)	3(1)
C(1)	69(3)	58(2)	50(2)	8(2)	-4(2)	-5(2)
C(2)	74(3)	87(2)	66(3)	3(2)	-16(2)	1(2)
C(3)	83(3)	114(3)	77(3)	4(2)	-32(3)	-4(3)
C(4)	88(3)	117(3)	66(3)	-7(2)	-7(3)	7(3)
C(5)	70(3)	75(2)	60(3)	3(2)	-11(3)	-3(2)
C(6)	60(2)	74(2)	45(2)	2(2)	2(2)	-7(2)
C(7)	61(2)	62(2)	49(2)	-5(2)	-4(2)	-9(2)
C(8)	70(3)	72(2)	56(2)	-1(2)	3(2)	-1(2)
C(9)	71(3)	100(2)	69(3)	-2(2)	11(2)	-8(2)
C(10)	96(3)	110(3)	57(2)	-1(2)	13(3)	1(3)
C(11)	71(3)	60(2)	74(3)	5(2)	-13(2)	11(2)
C(12)	162(4)	100(3)	75(3)	-29(2)	-25(3)	29(3)
C(13)	286(6)	192(4)	125(4)	-71(3)	-48(4)	164(5)
C(14)	150(4)	71(2)	97(3)	14(2)	-8(3)	-15(3)
C(15)	137(4)	134(3)	241(6)	51(4)	7(5)	-44(3)
C(16)	75(3)	184(4)	184(4)	65(4)	6(3)	-15(3)
C(17)	83(3)	205(4)	144(4)	19(3)	-28(3)	16(3)
C(18)	94(3)	155(3)	192(4)	-52(3)	-26(4)	43(3)
C(19)	52(2)	70(2)	60(3)	7(2)	4(2)	10(2)
C(20)	136(4)	109(3)	68(3)	31(2)	11(3)	4(3)
C(21)	196(5)	172(4)	84(3)	37(3)	4(4)	57(4)
C(22)	151(5)	105(3)	92(3)	32(3)	-29(4)	-61(4)
C(23)	163(9)	62(5)	126(7)	-22(5)	-25(7)	23(5)
C(23A)	114(7)	87(5)	125(7)	9(5)	31(7)	-22(5)
C(24)	94(3)	124(3)	120(3)	26(2)	-8(3)	22(3)
C(25)	74(3)	175(3)	127(3)	-60(3)	-6(3)	11(3)
C(26)	97(3)	124(3)	98(3)	-12(2)	-12(2)	-21(2)
N(1)	106(3)	71(2)	62(2)	-10(2)	-11(2)	11(2)
N(2)	94(2)	81(2)	48(2)	18(2)	11(2)	0(2)
O(1)	100(2)	98(2)	75(2)	15(1)	23(2)	10(2)
O(2)	94(2)	79(2)	69(2)	-7(1)	-14(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for aw23.

	x	y	z	U(eq)
H(3A)	3227	5011	6203	110
H(4A)	4699	4655	5558	108
H(9A)	7871	4243	6462	96
H(10A)	6481	4386	5645	106
H(12A)	4977	6049	10442	134
H(12B)	5687	6862	10168	134
H(13A)	4399	7409	10998	301
H(13B)	3643	7026	10288	301
H(13C)	4364	7841	10032	301
H(14A)	4975	7550	8524	127
H(14B)	5127	6722	7858	127
H(15A)	6561	7568	7950	256
H(15B)	6759	6573	8345	256
H(15C)	6602	7421	8992	256
H(16A)	1347	4577	8843	222
H(16B)	2444	4317	9083	222
H(16C)	1951	3910	8215	222
H(17A)	1811	6205	6644	216
H(17B)	931	5789	7202	216
H(17C)	1583	5135	6600	216
H(18A)	2632	7053	8308	220
H(18B)	2825	6443	9163	220
H(18C)	1737	6637	8845	220
H(20A)	5094	3642	10616	125
H(20B)	5871	4445	10712	125
H(21A)	6306	3234	11635	226
H(21B)	7122	3348	10894	226
H(21C)	6334	2549	10816	226
H(22A)	5661	3207	8399	139
H(23A)	5548	1819	8666	176
H(23B)	5885	2025	9653	176
H(23C)	6568	2309	8847	176
H(23D)	4460	2316	8506	163
H(23E)	4222	3380	8607	163
H(23F)	4221	2732	9455	163
H(24A)	8259	2943	9180	169
H(24B)	8098	3847	9752	169
H(24C)	9176	3503	9538	169
H(25A)	9129	3053	7349	188
H(25B)	10021	3620	7747	188
H(25C)	9416	4020	6935	188
H(26A)	9014	5796	7974	159
H(26B)	9659	5390	8757	159
H(26C)	8578	5740	8948	159

Table 6. Torsion angles [°] for aw23.

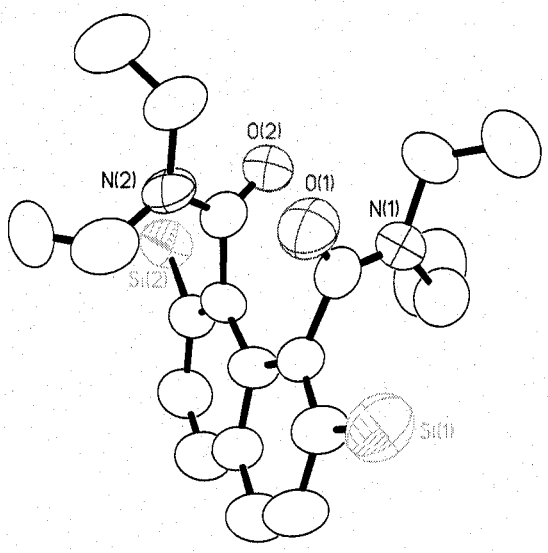
C(6)-C(1)-C(2)-C(3)	-5.5(4)
C(11)-C(1)-C(2)-C(3)	171.2(3)
C(6)-C(1)-C(2)-Si(1)	172.6(2)
C(11)-C(1)-C(2)-Si(1)	-10.6(4)
C(18)-Si(1)-C(2)-C(1)	50.1(3)
C(17)-Si(1)-C(2)-C(1)	169.4(3)
C(16)-Si(1)-C(2)-C(1)	-72.3(3)
C(18)-Si(1)-C(2)-C(3)	-131.8(3)
C(17)-Si(1)-C(2)-C(3)	-12.4(3)
C(16)-Si(1)-C(2)-C(3)	105.9(3)
C(1)-C(2)-C(3)-C(4)	-0.5(5)
Si(1)-C(2)-C(3)-C(4)	-178.9(3)
C(2)-C(3)-C(4)-C(5)	2.3(6)
C(3)-C(4)-C(5)-C(10)	-179.1(3)
C(3)-C(4)-C(5)-C(6)	2.0(5)
C(10)-C(5)-C(6)-C(7)	-7.5(4)
C(4)-C(5)-C(6)-C(7)	171.5(3)
C(10)-C(5)-C(6)-C(1)	173.6(3)
C(4)-C(5)-C(6)-C(1)	-7.5(4)
C(2)-C(1)-C(6)-C(7)	-169.3(3)
C(11)-C(1)-C(6)-C(7)	14.1(4)
C(2)-C(1)-C(6)-C(5)	9.6(4)
C(11)-C(1)-C(6)-C(5)	-167.1(3)
C(5)-C(6)-C(7)-C(8)	8.9(4)
C(1)-C(6)-C(7)-C(8)	-172.2(3)
C(5)-C(6)-C(7)-C(19)	-169.1(3)
C(1)-C(6)-C(7)-C(19)	9.8(5)
C(6)-C(7)-C(8)-C(9)	-4.1(4)
C(19)-C(7)-C(8)-C(9)	174.0(3)
C(6)-C(7)-C(8)-Si(2)	171.6(2)
C(19)-C(7)-C(8)-Si(2)	-10.2(4)
C(24)-Si(2)-C(8)-C(7)	44.6(3)
C(26)-Si(2)-C(8)-C(7)	-78.9(3)
C(25)-Si(2)-C(8)-C(7)	163.8(3)
C(24)-Si(2)-C(8)-C(9)	-139.7(2)
C(26)-Si(2)-C(8)-C(9)	96.8(3)
C(25)-Si(2)-C(8)-C(9)	-20.4(3)
C(7)-C(8)-C(9)-C(10)	-2.5(5)
Si(2)-C(8)-C(9)-C(10)	-178.6(3)
C(8)-C(9)-C(10)-C(5)	3.8(6)
C(4)-C(5)-C(10)-C(9)	-177.5(3)
C(6)-C(5)-C(10)-C(9)	1.3(5)
C(2)-C(1)-C(11)-O(1)	74.5(4)
C(6)-C(1)-C(11)-O(1)	-108.7(4)
C(2)-C(1)-C(11)-N(1)	-105.0(4)
C(6)-C(1)-C(11)-N(1)	71.8(3)
C(8)-C(7)-C(19)-O(2)	71.7(4)
C(6)-C(7)-C(19)-O(2)	-110.2(4)
C(8)-C(7)-C(19)-N(2)	-105.3(3)
C(6)-C(7)-C(19)-N(2)	72.9(4)
O(1)-C(11)-N(1)-C(14)	-169.3(3)
C(1)-C(11)-N(1)-C(14)	10.1(5)
O(1)-C(11)-N(1)-C(12)	8.6(5)
C(1)-C(11)-N(1)-C(12)	-171.9(3)

C(15)-C(14)-N(1)-C(11)	-115.6(4)
C(15)-C(14)-N(1)-C(12)	66.4(4)
C(13)-C(12)-N(1)-C(11)	-101.5(4)
C(13)-C(12)-N(1)-C(14)	76.6(5)
O(2)-C(19)-N(2)-C(22)	-174.4(4)
C(7)-C(19)-N(2)-C(22)	2.4(5)
O(2)-C(19)-N(2)-C(20)	12.7(5)
C(7)-C(19)-N(2)-C(20)	-170.4(3)
C(23)-C(22)-N(2)-C(19)	110.4(6)
C(23A)-C(22)-N(2)-C(19)	-105.3(6)
C(23)-C(22)-N(2)-C(20)	-76.7(7)
C(23A)-C(22)-N(2)-C(20)	67.6(7)
C(21)-C(20)-N(2)-C(19)	-106.7(4)
C(21)-C(20)-N(2)-C(22)	79.8(4)

Symmetry transformations used to generate equivalent atoms:

Figure 1. Molecular Structure of aw23 (The hydrogen atoms and the methyl groups on -TMS are omitted for clarity!).

a)



b)

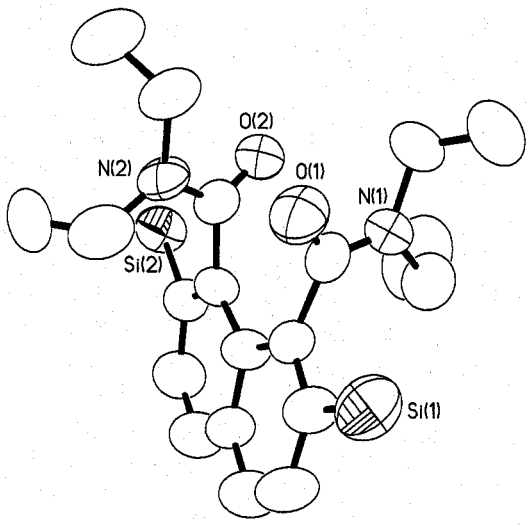
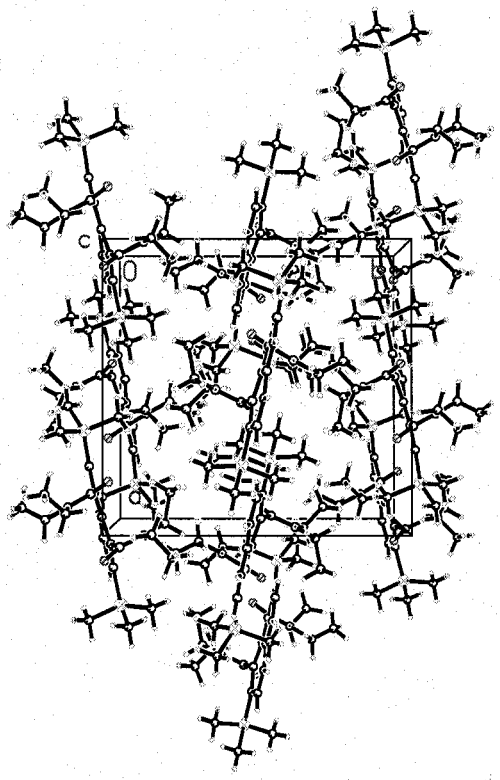


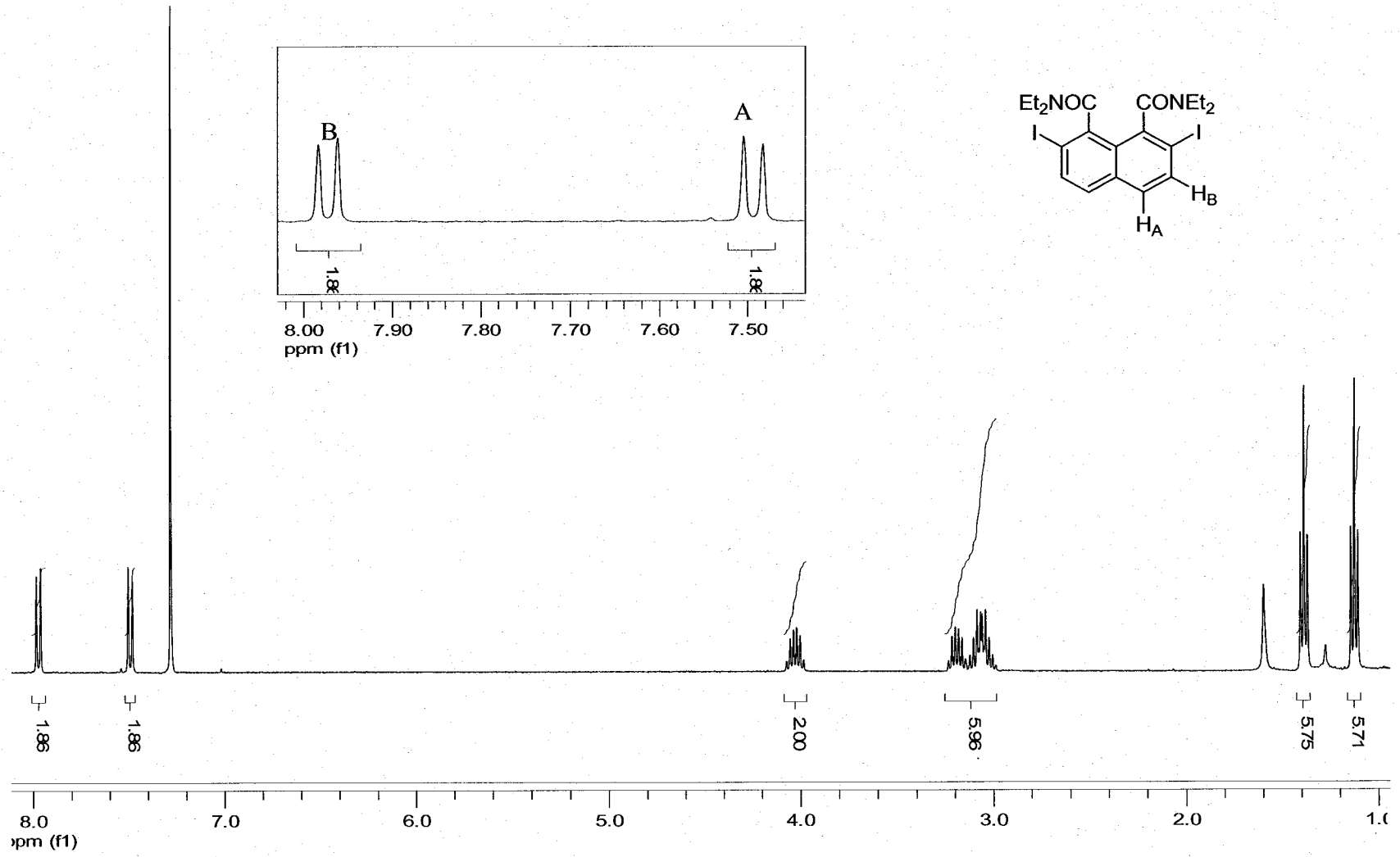
Figure 2. Cell Packing of aw23.

a)

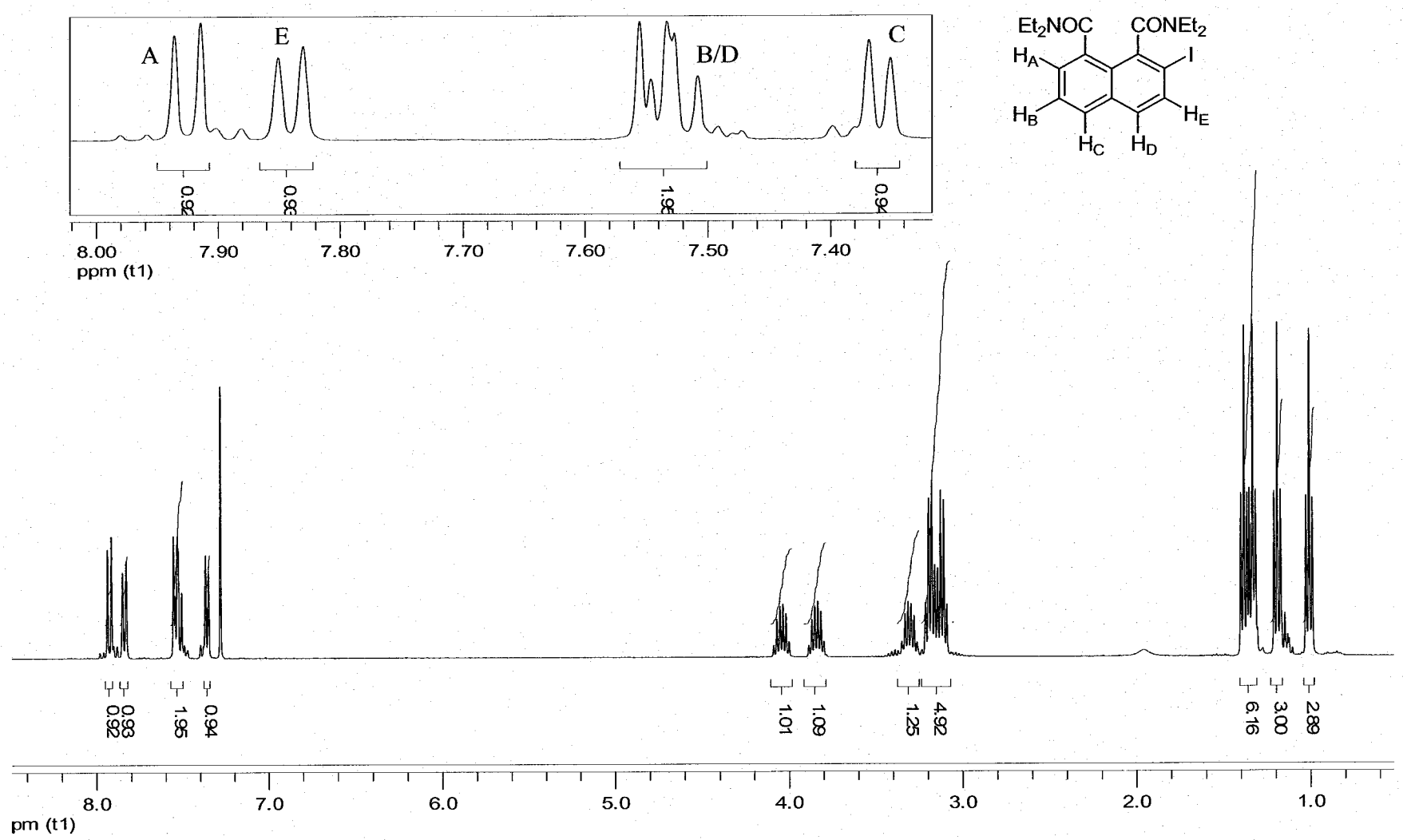


7.2 Appendix 2: Representative ^{1}H NMR Spectra

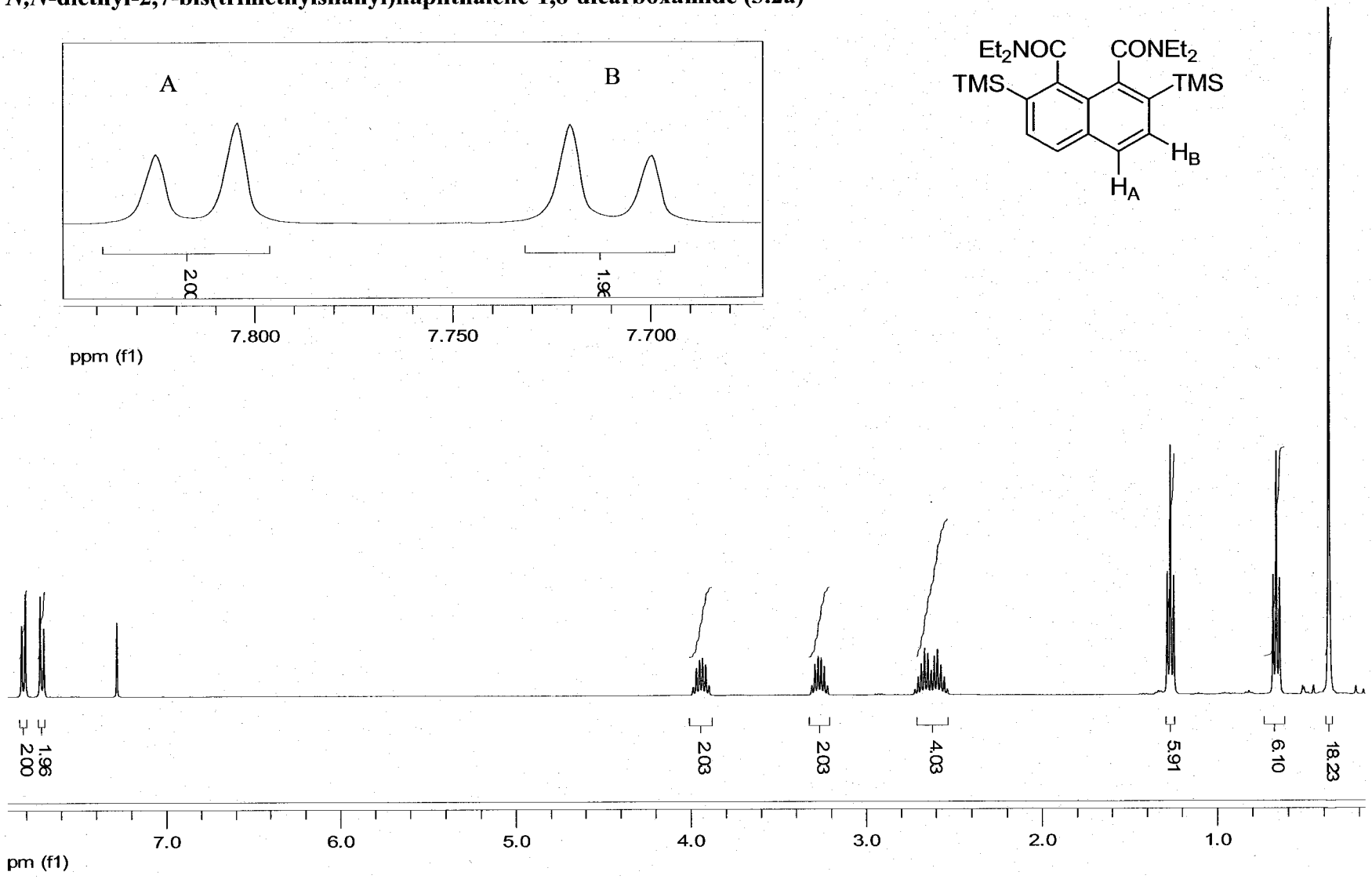
***N,N*-diethyl-2,7-diiodonaphthalene-1,8-dicarboxamide (3.2g)**



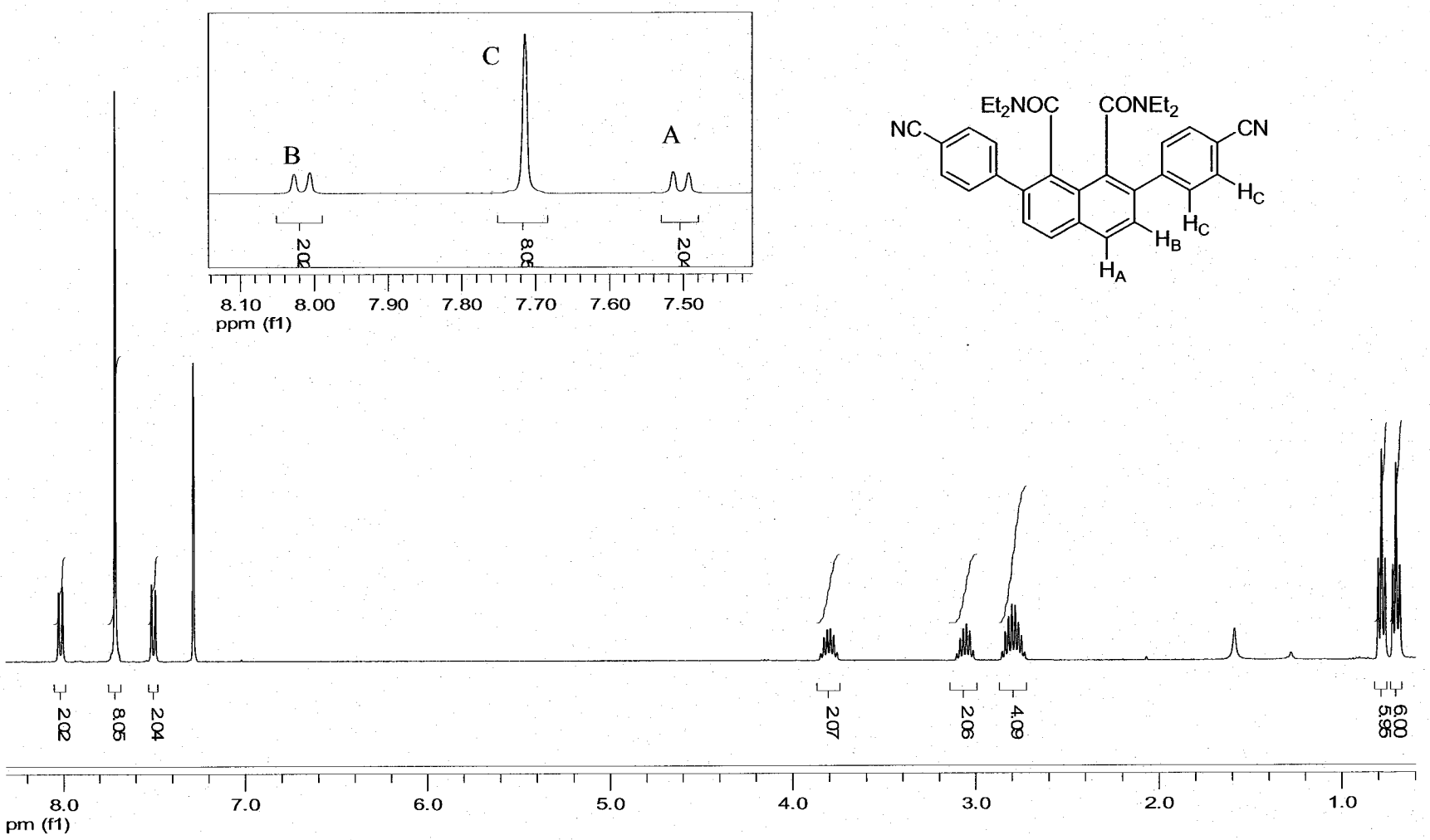
***N,N*-diethyl-2-moniodonaphthalene-1,8-dicarboxamide (3.9a)**



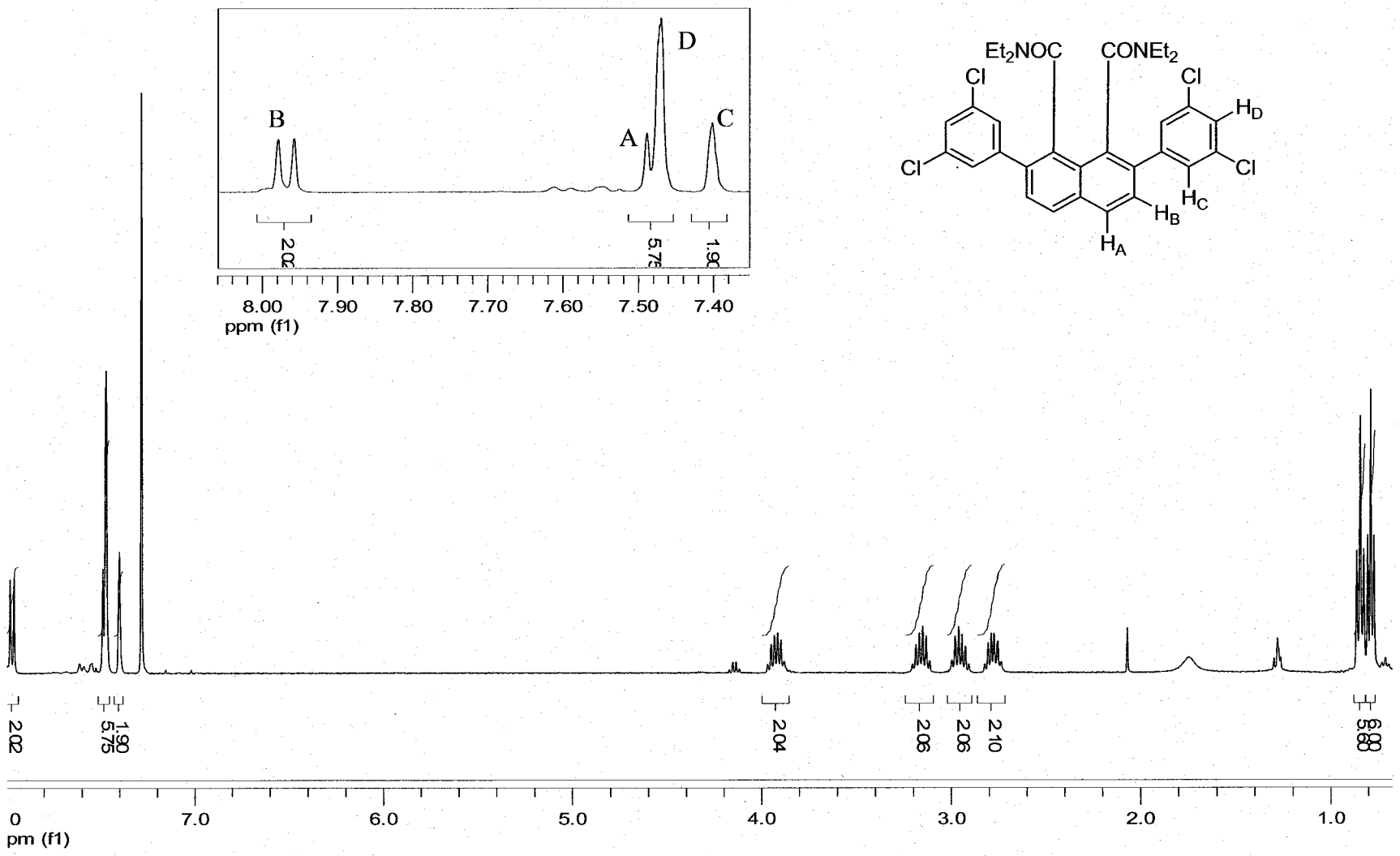
_N,N_-diethyl-2,7-bis(trimethylsilanyl)naphthalene-1,8-dicarboxamide (3.2a)



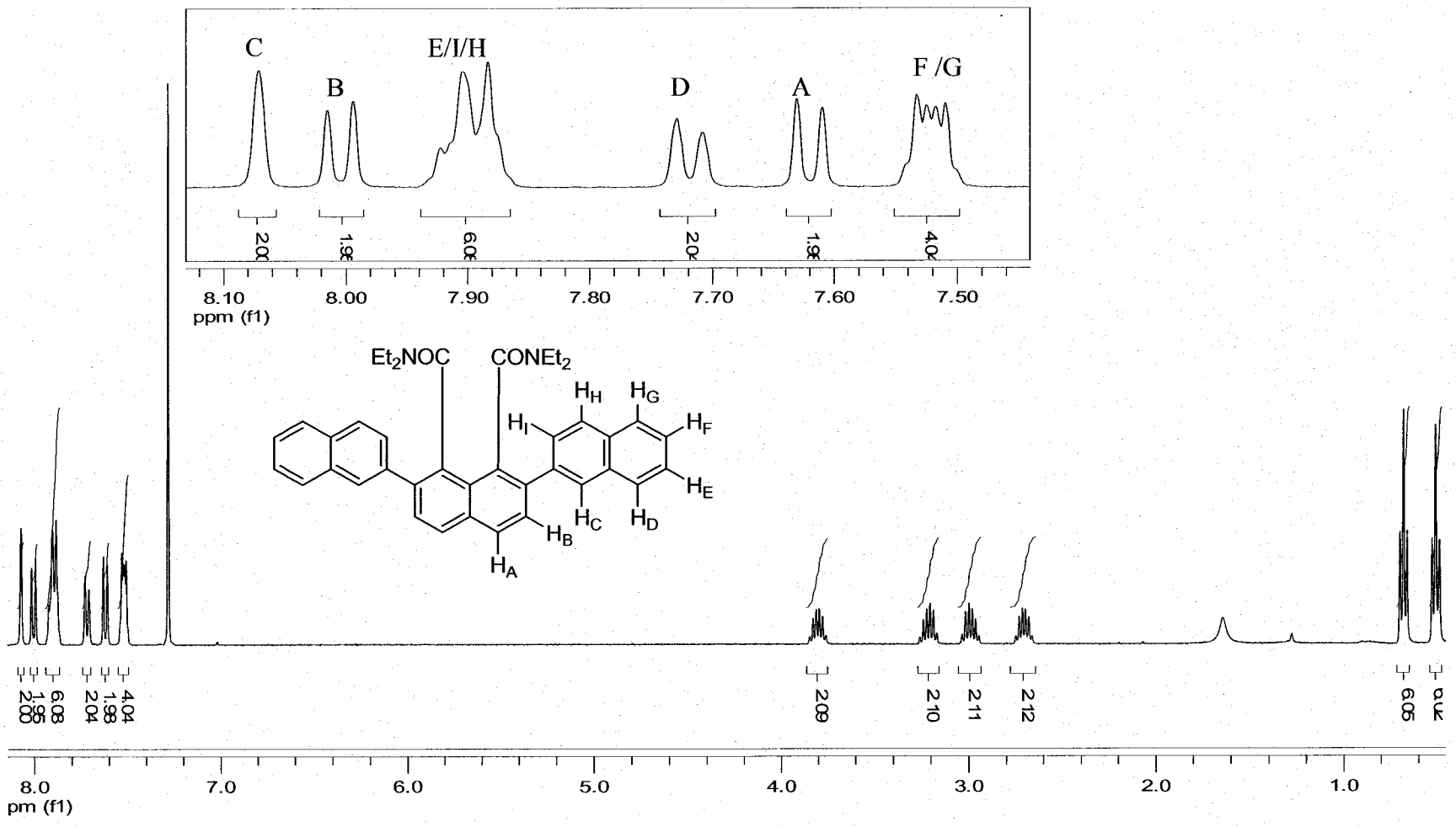
***N,N*-diethyl-2,7-di-(4-cyanophenyl)naphthalene-1,8-dicarboxamide (3.17b)**



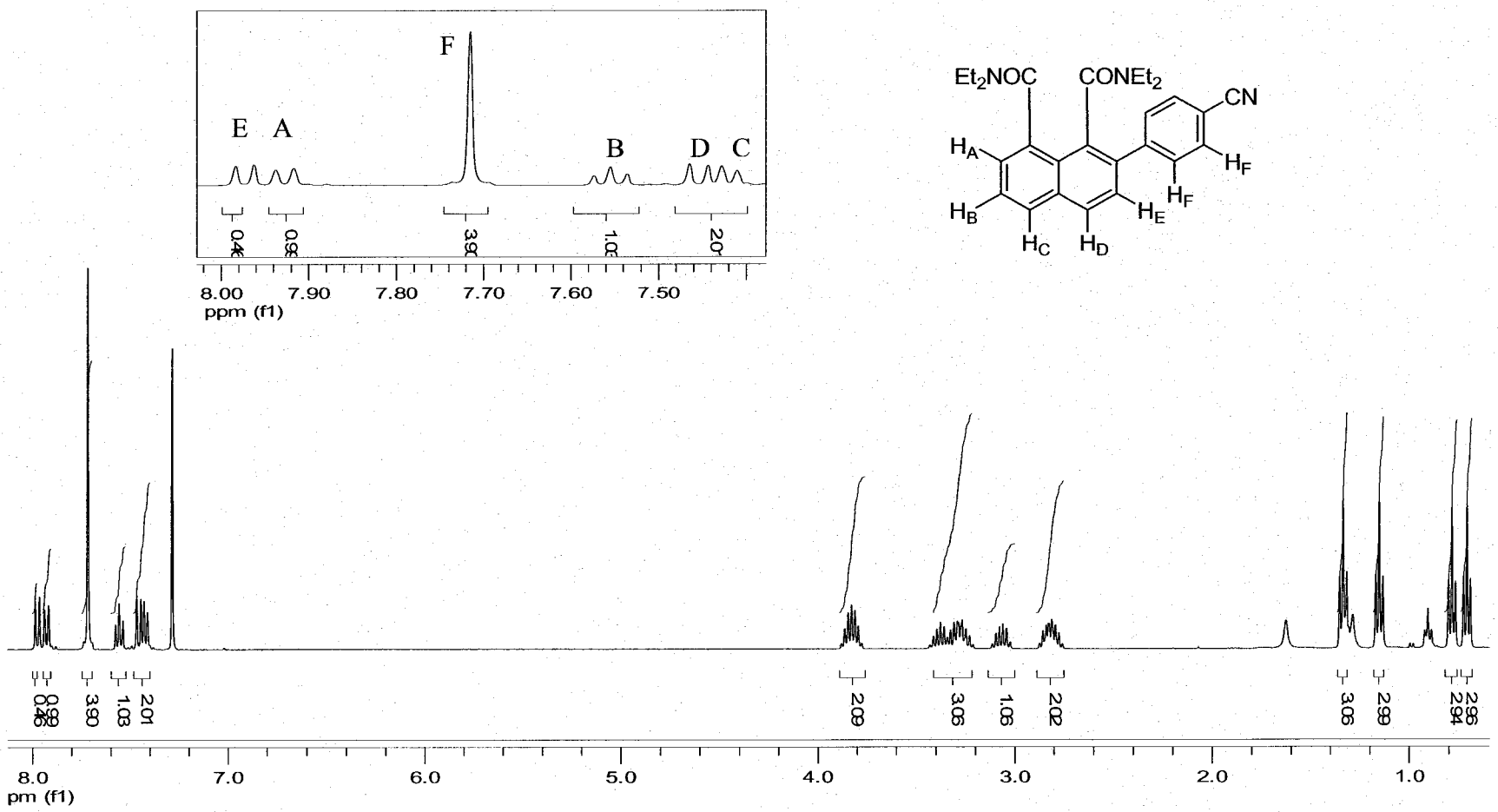
_N,N_-diethyl-2,7-di-(3,5-dichlorophenyl)naphthalene-1,8-dicarboxamide (3.17f)



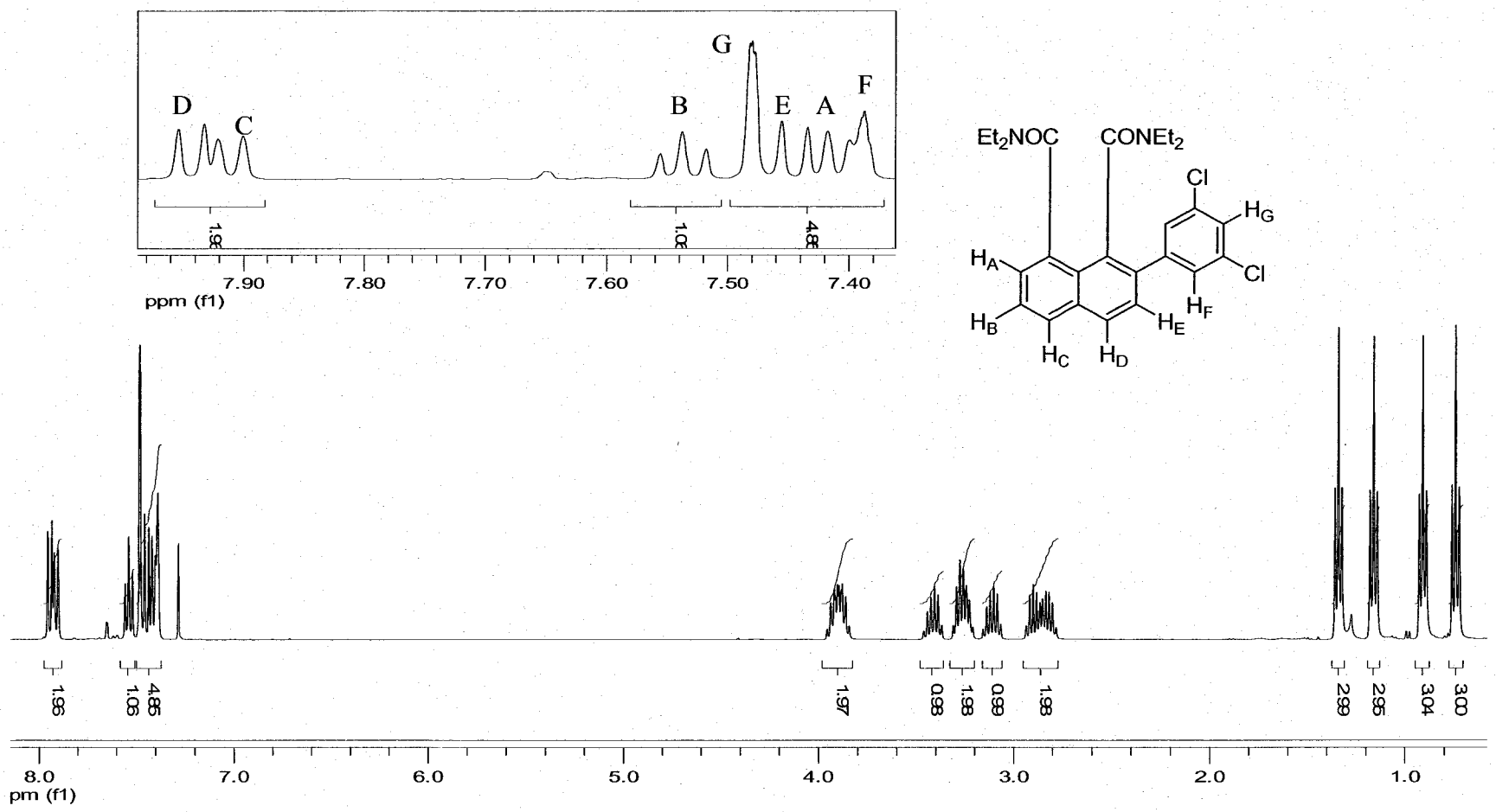
***N,N*-diethyl-2,7-di-(2-naphthyl)naphthalene-1,8-dicarboxamide (3.17g)**



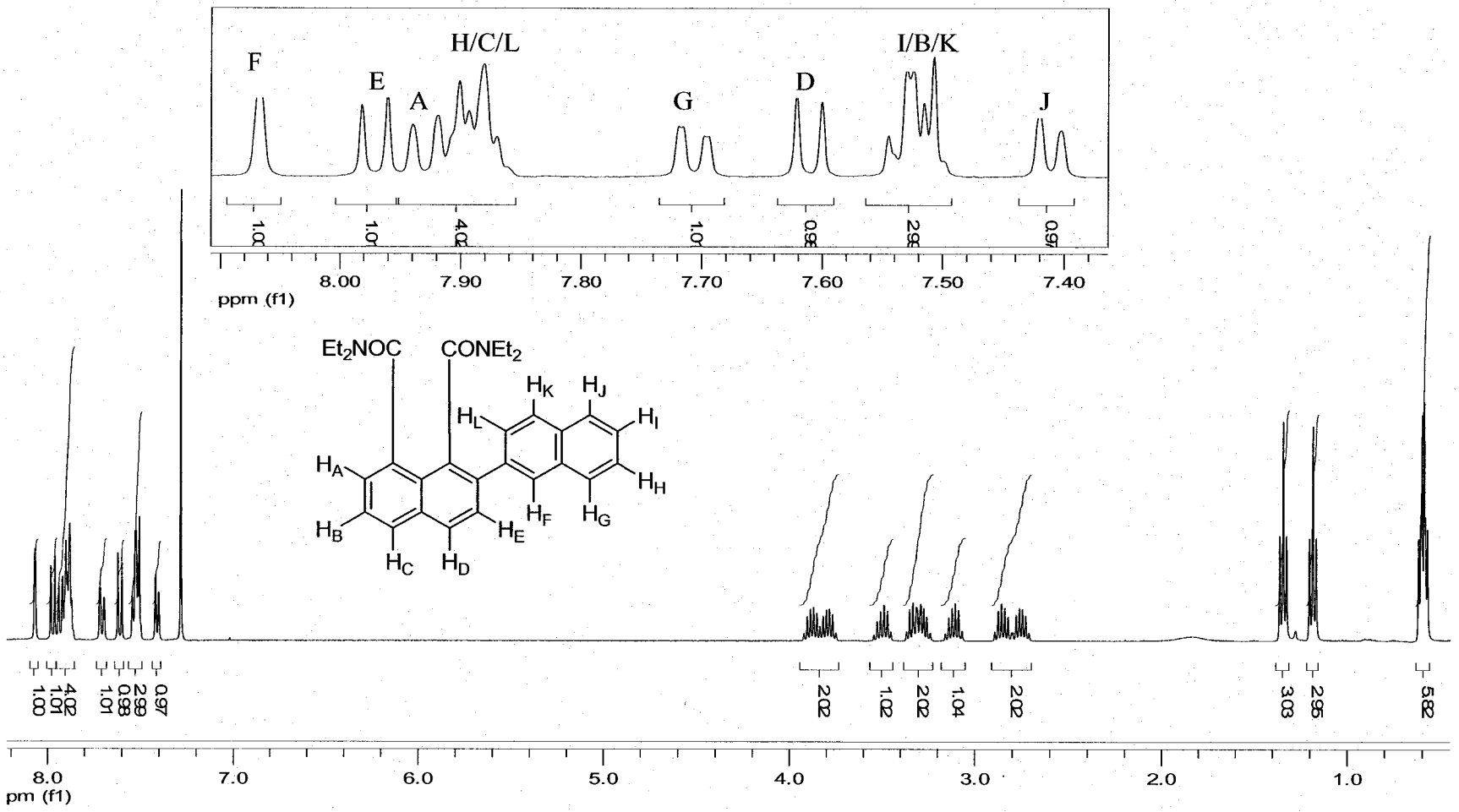
***N,N*-diethyl-2-(4-cyanophenyl)naphthalene-1,8-dicarboxamide (3.18b)**



***N,N*-diethyl-2-(di-3,5-dichlorophenyl)naphthalene-1,8-dicarboxamide (3.18e)**



***N,N*-diethyl-2-(2-naphthyl)naphthalene-1,8-dicarboxamide (3.18f)**



***N,N*-diethyl-11-oxo-2-phenyl-11H-benzo[*a*]fluorene carboxamide (3.24)**