Synthetic Efforts Towards New Stable Free Radicals

by

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B.Sc., University of Victoria, 2001

A Thesis Submitted in Partial Fulfillment of the
Requirements for the Degree of

MASTER OF SCIENCE

in the Department of Chemistry

Supervisor: Dr. Robin G. Hicks

ABSTRACT

A series of new 1,5-dimethyl-6-oxo-verdazyl radicals were prepared bearing either a hydroquinone or the 3,5-di-tertiary-butyl phenol substituent in the 3 position of the verdazyl ring as precursors to verdazyl / semiquinone diradical anions or verdazyl / phenoxyl diradicals. All radical precursor tetrazanes were characterized by ^1H / ^{13}C NMR and FTIR spectroscopies, MS, and elemental analysis. Oxidation of the tetrazane precursors with $NaIO_4$ or Ag^+ gave verdazyl radicals as microcrystalline solids. All verdazyl radicals were characterized by EPR, UV-visible, and FTIR spectroscopies, and high-resolution MS or elemental analysis. All attempts to oxidize the hydroquinone or phenol moieties were unsuccessful as was coordination chemistry with those verdazyls bearing a chelating *ortho*-hydroquinone.

Several molecules were synthesized as building blocks towards tris(2,6-disubstituted-4-pyridyl)methyl radicals where the substituents were ether chloro- or methoxy- groups. All of these building blocks (aldehydes, ester, alcohol, and ketone) were characterized by ^1H / ^{13}C NMR and FTIR spectroscopies, MS, and elemental analysis. All attempts to insert a third ring onto bis(2,6-dichloro-4-pyridyl)ketone to give the radical precursor triarylmethanol have been unsuccessful.

Supervisor: Dr. R. G. Hicks (Department of Chemistry)

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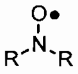

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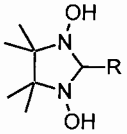

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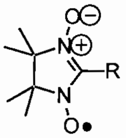

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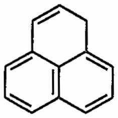

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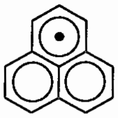

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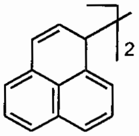

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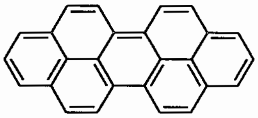

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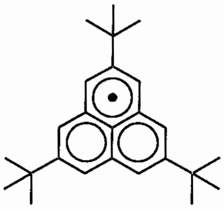

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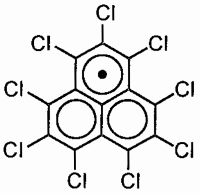

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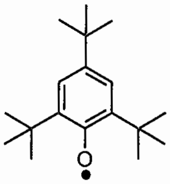

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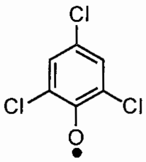

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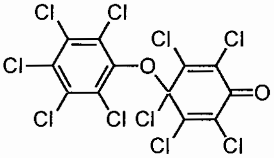

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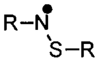

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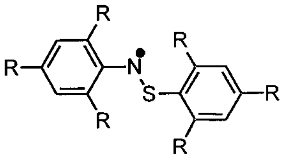

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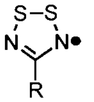

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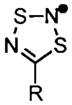

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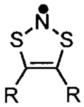

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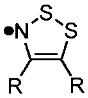

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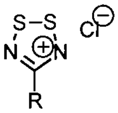

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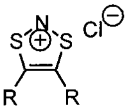

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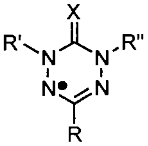

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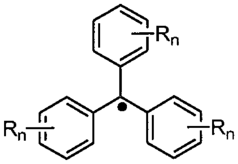

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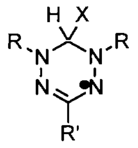
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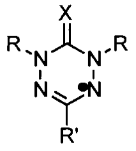
X = O, S

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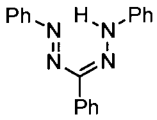
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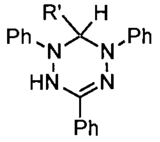
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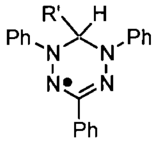
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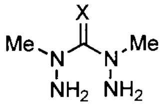
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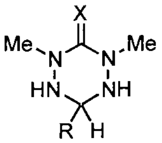
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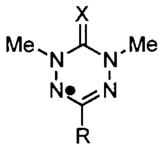
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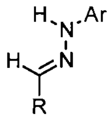
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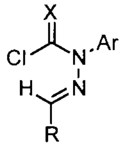
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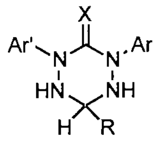
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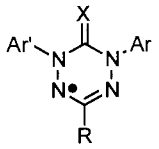
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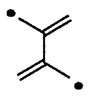
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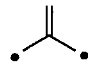
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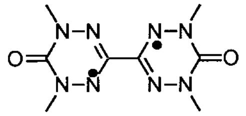
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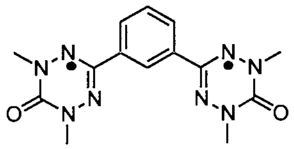
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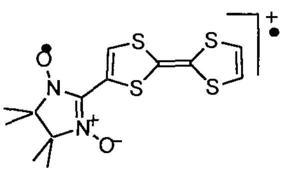

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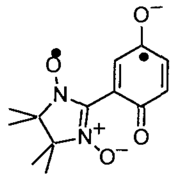

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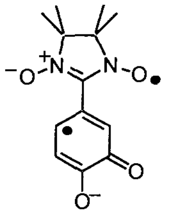

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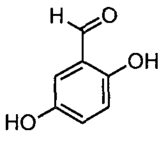

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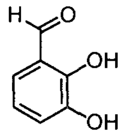

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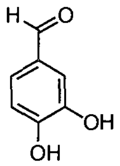

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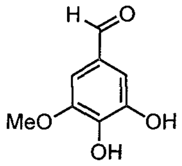

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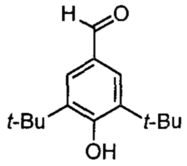

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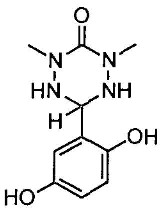

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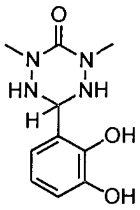

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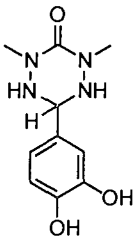

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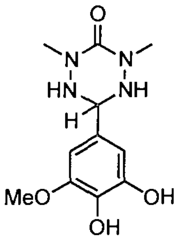

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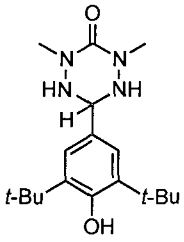

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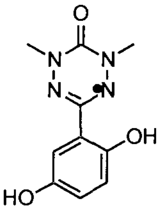

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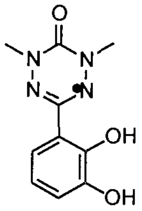

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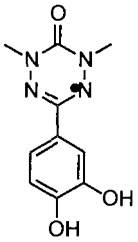

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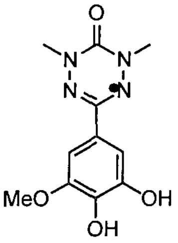

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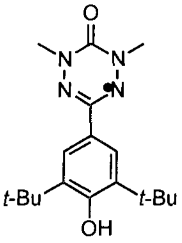

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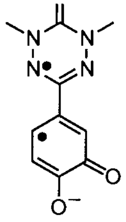

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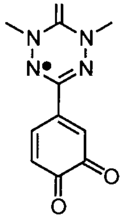

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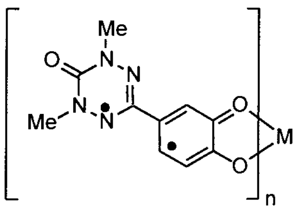

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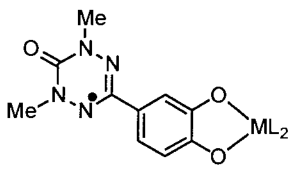

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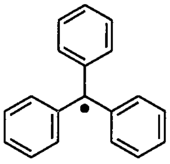

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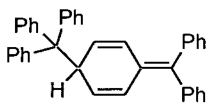

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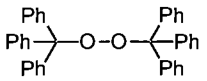

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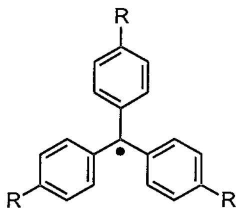
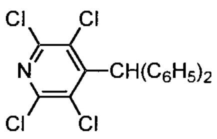


a) R = CH_3
b) R = *t*-butyl
c) R = NO_2

3.4



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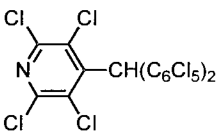

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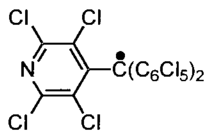

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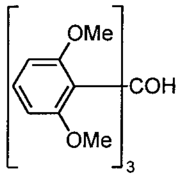

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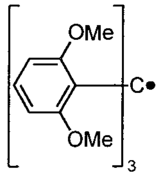

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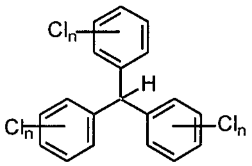

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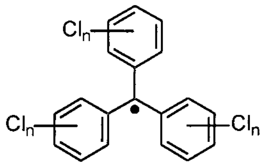

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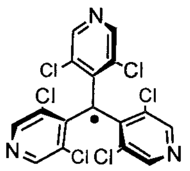

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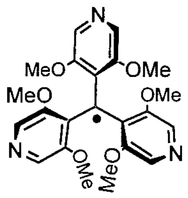

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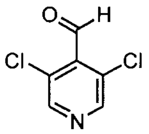

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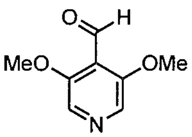

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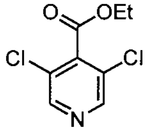

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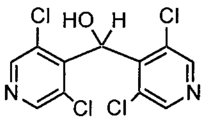

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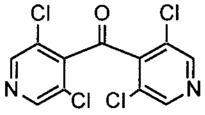

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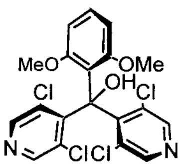

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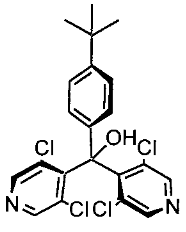

3.20

LIST OF ABBREVIATIONS

a	hyperfine coupling constant
Å	angstroms
AFM	antiferromagnetic
Ar	aromatic group or Argon
BCR	Ballester, Castener, and Riera
BMC	Ballester, Molinet, and Castener
Bu	butyl
BQ	benzoquinone
°C	degrees Celsius
CTH	5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane
Cat	catechol or catecholate
CI	chemical ionization
cm	centimeter
cm^{-1}	wavenumber
d	doublet
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano orthobenzoquinone
EI	electron impact
EPR	electron paramagnetic resonance
Et	ethyl
EtOAc	ethyl acetate

EtOH	ethanol
Et_2O	diethyl ether
FAB	fast atom bombardment
FM	ferromagnetic
G	Gauss
h	hours
HOMO	highest occupied molecular orbital
Hz	hertz
IR	infrared
KJ	Kilojoules
L	litres
LUMO	lowest unoccupied molecular orbital
Me	methyl
MeOH	methanol
min	minute(s)
MHz	megahertz
mL	millilitres
mp	melting point
MO	molecular orbital(s)
mol	mole
mmol	millimoles
MS	mass spectrometry
m/z	mass per charge

OAc	acetate
n-BuLi	*n*-butyl lithium
nm	nanometres
NMR	nuclear magnetic resonance
[O]	oxidation
pBQ	parabenzoquinone
Ph	phenyl
ppm	parts per million
py	pyridine
q	quartet
Q	quinone
RT	room temperature
s	seconds or singlet
SOMO	singly occupied molecular orbital
SQ	semiquinone
t	triplet
TEMPO	tetramethylpiperdine N-oxide
THF	tetrahydrofuran
*t*Bu	*tertiary*-butyl
TMEDA	N,N,N,N-tetramethylethylenediamine
UV-Vis	ultraviolet - visible
λ_{max}	wavelength of maximum electronic absorption
ε	molecular extinction coefficient

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Chapter 1

Introduction and Background

1.1 Stable Organic Free Radicals

Organic free radicals, molecules that have one or more unpaired electrons, differ substantially from the norms of electronic structure and bonding. Lewis observed that electrons tend to spin pair; an odd electron will combine with an electron of opposite spin to form a covalent bond.[1] This leads to an element having a distinct valence. In contrast, radicals are open-shell and subvalent; forming one less bond than usual. Atoms or molecules lacking a complete octet, or noble gas configuration, tend to be both unstable and very reactive.

Since Gomberg's discovery of the first free radical in 1900, many new radical species have been discovered and new techniques developed to probe and understand them. Free radical research has implications in many subfields of chemistry including, environmental[2,3], medicinal, materials[4-6], and mechanistic[7-10].

Stable radicals are a contradiction to the conventional view of free radicals as highly reactive, short-lived, transient intermediates. Instead, they have lifetimes on the order of hours to days in solution and days to years in the solid state.[11] They can be handled like any typical closed shell molecules and stored under ambient conditions with little or no decomposition.

All classes of stable free radicals rely on certain structural attributes that are responsible for their stability including steric bulk, lone-pair repulsion, or resonance delocalization. These attributes act to slow or prevent the typical pathways for free radical decomposition: dimerization, autooxidation, or H• (or R•) abstraction.

A common approach to stabilizing reactive species has been with steric bulk. The placement of large substituents around a radical centre suppresses its reactivity. This is frequently used with aromatic carbon-based radicals because of the inherent reactivity of a carbon centred radical and the energy gained through formation of a carbon-carbon bond (≈ 350 kJ/mol). Steric bulk imparts stability in two ways. This first acts to inhibit a major decomposition pathway, dimerization. Also, by shrouding the unpaired electron from attack by small molecules such as oxygen, the rate of autooxidation is also reduced.

Many classes of stable free radicals are based on catenated inorganic elements, the majority of spin density residing on atoms such as oxygen, nitrogen, or sulphur. The stability of these radicals is partially a result of lone pair repulsion, which helps prevent decomposition through dimerization. As Scheme 1.1 shows, for a nitroxide radical to dimerize, four electronegative atoms have to come together in a row which is a very unfavourable arrangement.

Scheme 1.1 Prevention of nitroxide radical dimer formation

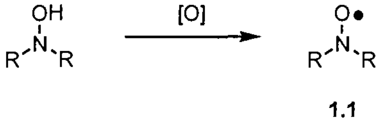
Most classes of stable radicals have the unpaired electron residing in an orbital of π-symmetry. Further delocalization into a conjugated π-system provides resonance stabilization by lowering the energy of the unpaired electron.

Stable and persistent are both terms commonly used with respect to certain classes of free radicals. Controversy over these terms arises due to their subjective nature. For the remainder of this thesis the term "stable" will refer to radicals that persist for several days in solution and can be isolated and/or stored in the solid state without appreciable decomposition.[11,12] Persistence of a radical depends on its environment.[11] This will refer to radicals that are long-lived enough for spectroscopic study but cannot be isolated in the solid state.

1.2 Survey of Stable Radicals

1.2.1 Nitroxide and Related Radicals

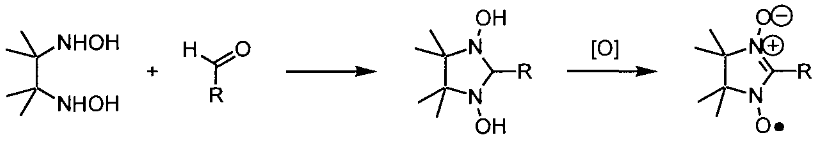
The first nitroxide radical was synthesized in 1901 by Piloty and Schwerin and has the added distinction of being the first isolated organic radical.[13,14] Nitroxides have been the most studied class of free radicals owing to their ease of synthesis and excellent stability. As a result, they have received the most attention in applications of free radicals (see Section 1.3). Oxidation of an N,N-disubstituted hydroxylamine with silver oxide or lead oxide gives the corresponding nitroxide radical **1.1** (Scheme 1.2). Many derivatives have since been prepared incorporating this simple radical fragment.[15]



Scheme 1.2 Formation of a nitroxide radical **1.1**

The stability of these radicals is due in part to delocalization of the unpaired electron over the nitrogen and oxygen atoms. EPR spectra show a strong *a*(^{14}N) coupling of 8 – 17 G. The R-groups present in structure **1.1** also affect the stability. Radicals containing an αH are prone to decomposition through a disproportionation to gives a nitrone and a hydroxylamine.[16]

Numerous other stable radicals have been prepared that are derivatives of the nitroxide. The most common of these are the nitronyl nitroxides, first synthesized in 1968 by Boocock and Ullman.[17] Condensing a bis(hydroxylamine) with an aldehyde gives the cyclic precursor **1.2** which upon oxidation affords radical **1.3**.



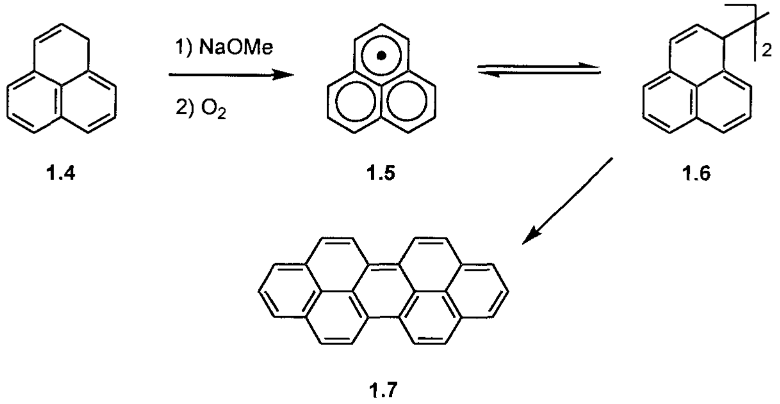
1.2 **1.3**

Scheme 1.3 Synthesis of nitronyl nitroxide **1.3**

Like the nitroxides, the nitronyl nitroxides display excellent stability and a variety of derivatives have been isolated with different R-group substituents. Stability is in part due to resonance delocalization of the unpaired electron across both N-O fragments. EPR spectra show a strong coupling to both ring nitrogens, *a*(^{14}N), of approximately 16 G.[18]

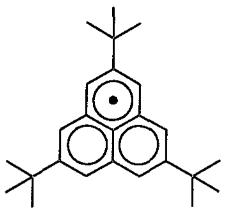
1.2.2 Phenalenyl Radicals

A class of purely carbon-based radicals, the phenalenyls, was first discovered in the 1950's.[19,20] The persistence of these radicals is solely a result of delocalization. The first radical of this class, **1.5**, was prepared from the precursor phenalene **1.4** by deprotonation followed by aerial oxidation (Scheme 1.4). Though a persistent species, radical **1.5** exists in an equilibrium with a σ-bound dimer (**1.6**), which is the only structure isolatable in the solid state. In solution, dimer **1.6** slowly disproportionates to give peropyrene **1.7** and other minor products.[21]



Scheme 1.4 Synthesis of phenalenyl radical **1.5** and decomposition products

More stable derivatives have since been synthesized utilizing steric bulk to prevent σ-dimer formation. In solution, **1.8** exists as a monomeric species though is still considered persistent as it forms a π-stacked dimer in the solid state.[22] **1.9**, on the other hand, is a fully stable derivative with no propensity to form either σ- or π-dimers.



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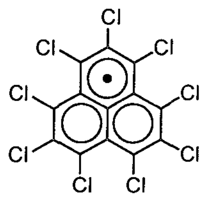

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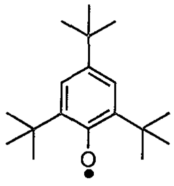
1.2.3 Phenoxyl Radicals

The idea of a phenoxyl radical was first proposed in the 1920's to rationalize the formation of certain diaryl peroxides.[23] It was not until 1953 that the first example of a stable phenoxyl (**1.10**) was discovered independently by Cook[24] and Muller[25]. **1.10** can be produced from the corresponding phenol with a range of inorganic oxidizing agents.[26]



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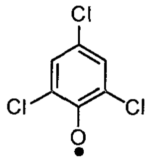

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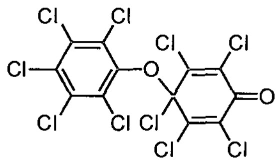
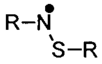


1.12

Some polyhalophenoxyl radicals, such as **1.11**, are also stable. In other cases, depending on the substitution pattern, they rapidly decompose. For example, the perchlorinated phenoxyl radical dimerizes to give 4,4-quinol ether **1.12** in both solution and the solid state.

1.2.4 Thiazyl Radicals

The thiazyls are a large class of free radicals based on an N-S fragment. The simplest of these are the thioaminyls, represented by the general structure **1.13**. They can be prepared by oxidation of the corresponding sulfenamide with PbO_2 and K_2CO_3. The stability of these radicals depends on the steric protection afforded by the nitrogen and sulphur bound substituents. Bulky aryl groups offer the most protection and provide additional stabilization through delocalization. Radicals **1.14**, with a variety of different R-groups, have been isolated in the solid state.[27,28]



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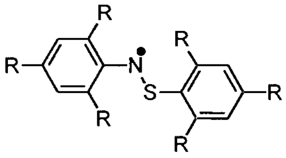
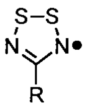


1.14

The heterocyclic thiazyls have received the most attention. Derivatives of **1.15**, **1.16**, and **1.17** have all been isolated in the solid state. A stable derivative of **1.18** was isolated very recently by Oakley *et al.*[29] Dithiadiazolyls **1.15** have been shown to form stacked π-dimer arrays. The propensity to dimerize can be reduced with the use of bulky substituents. 1,3,2-dithiazolyls also form π-stacked arrays in the solid state but do not dimerize.[30] Their solid state behavior has made them a focus in the study of molecular conductors.[29]



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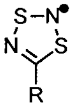

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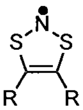

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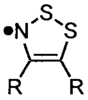
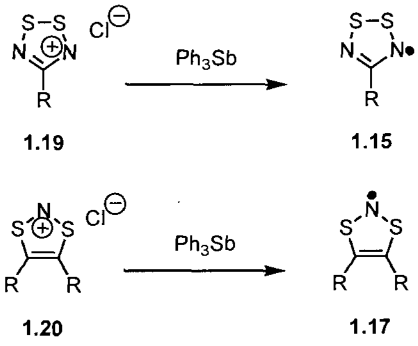


1.18

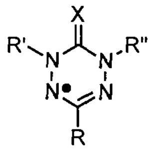
A variety of methods have been developed to construct the different ring systems of structures **1.15**, **1.16**, **1.17**, and **1.18**. In general, heterocyclic thioaminyl radicals are prepared by reduction of a dithiadiazolium (**1.19**) or dithiazolium (**1.20**) cation with triphenylantimony (Scheme 1.5). More recently, this has been achieved with decamethylferrocene as the reductant.



Scheme 1.5 Preparation of radicals **1.15** and **1.17**

1.2.5 Other Stable Radicals

Other classes of stable radicals are verdazyls **1.21** and triarylmethyl radicals **1.22**. Verdazyls radicals will be discussed in detail in Chapter 2 and triarylmethyl radicals in Chapter 3.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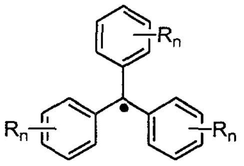
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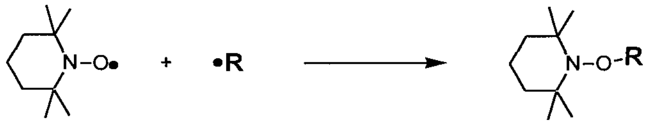
1.3 Uses of Stable Radicals

Diverse properties arising from the presence of an unpaired electron have made stable radicals very useful in a variety of applications. One of the interesting properties associated with the unpaired electron is magnetism. Because of their ubiquitous nature and technological importance, magnets have received a great deal of attention in both fundamental and applied sciences. Magnets have been traditionally composed of metals, metal oxides, or alloys. However, over the past two decades efforts have been towards molecule-based magnets.[4,6] Such materials incorporate stable radicals as building blocks in either a fully organic-based molecular solid or in conjunction with paramagnetic metal ions in a multidimensional coordination array. Molecule-based magnets would be made through low temperature, bench top synthetic methods and would share the physical properties of a molecular solid, including solubility, low density, and transparency. This makes them potentially easier to process and manipulate compared to their traditional counterparts, which are insoluble, dense and brittle. Though unlikely to replace traditional magnets, molecule-based magnets are of interest because of the potential of incorporating interesting electronic and / or optical properties into a magnetic material.

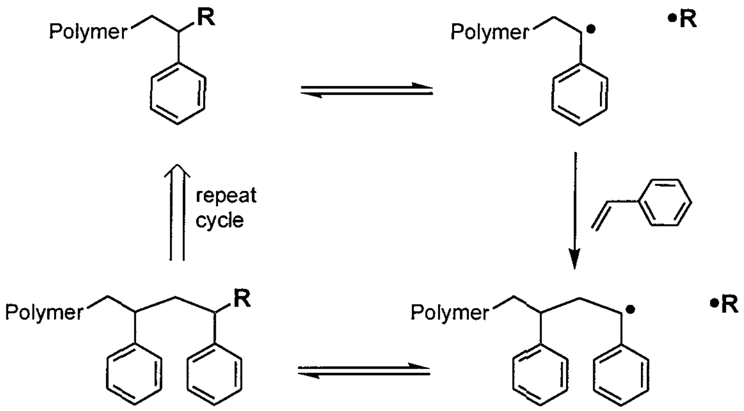
Stable radicals have been used extensively to study biological systems through electron paramagnetic resonance (EPR) spectroscopy, a technique first introduced in the 1960's by McConnell *et al.*[31] The radical serves as a "spin label" or "spin probe" which is attached to another molecule or macromolecule such as a protein. The EPR spectra of a labeled species can used to gain essential information about the environment and dynamics surrounding the label or to probe the different molecular environments within a complex system. By far the most popular family of radicals used for this purpose has been the nitroxides. These radicals have all of the requirements of a spin label most important of which is stability under a wide range of conditions, particularly those encountered in biological systems.

Stable radicals have also found utility in probing the kinetics and mechanisms of radical-induced polymerizations[32], radical rearrangements[7], and homolytic dissociations[10] as a so-called radical trap. A stable radical is added to a reaction under study to trap any reactive radical intermediates that are formed (Scheme 1.6). The result is a closed-shell species composed of a stable radical covalently bound to the radical intermediate fragment. This allows for detection and identification of species that would otherwise be too short-lived or in too low a concentration to observe.



Scheme 1.6 Trapping of a radical intermediate (R•) with TEMPO

Another use of stable radicals which is technologically important and has potential in industrial applications is living radical polymerization. This technique differs from conventional radical polymerization in that it utilizes a stable free radical to tune polymer structure, giving materials with low polydispersity, controlled molecular weights and defined chain ends.[33]



Scheme 1.7 General mechanism for living radical polymerization where R• is the stable radical

Scheme 1.7 shows a reversible termination of the growing polymer chain by a stable free radical. The labile bonding of the stable radical to the growing polymer effectively reduces the concentration of the reactive chain end which minimizes irreversible termination reactions.[33] The polymer, therefore, grows in a more controlled, predictable manner.

1.4 Thesis Objectives

As discussed in the previous sections, there are many reasons to study free radicals from purely scientific interest to application-based pursuits. The majority of work in this field has focused on a few classes of stable radicals, of which the nitroxides have been the most heavily investigated. Broadening the scope of research and expanding the chemistry of other stable radicals will help to improve on existing knowledge. This may lead to the synthesis of new classes of radicals, adding to those that were in the past discovered by accident. The ultimate goal of this field of work is the rational design of stable radicals with properties tuned to meet a particular need.

The goals of this thesis are to explore the targeted synthesis of new radical derivatives for specific purposes. Chapter 2 will present our attempts to synthesize diradicals composed of both a verdazyl and a semiquinone. The purpose of this work was to synthesize a new type of asymmetric diradical in order to investigate the exchange interactions between the two unpaired electrons. Thus, these molecules would serve as a fundamental model system for magnetic materials. Chapter 3 presents the work towards and attempts to synthesize new pyridine containing derivatives of the trityl radical. The purpose of using 4-pyridyl groups is to promote interactions between trityl radical and another spin carrier, such as a paramagnetic metal ion. The geometry of the target is such that it may serve as a building block in an extended coordination network. Conclusions and possible future directions of this work will be discussed at the end of each chapter.

Chapter 2

Synthetic Efforts Towards Verdazyl / Semiquinone Diradicals

2.1 Introduction

Verdazyls are a class of stable free radicals first discovered in the 1960's. The first examples, the Type I verdazyls (**2.1**), have a methylene group in the six position and phenyl groups at the one and five positions of the ring (numbering shown in Figure 2.1). These radicals have a half boat structure with the C6 methylene group approximately 0.59 Å out of the plane of the tetrazine ring.[34]

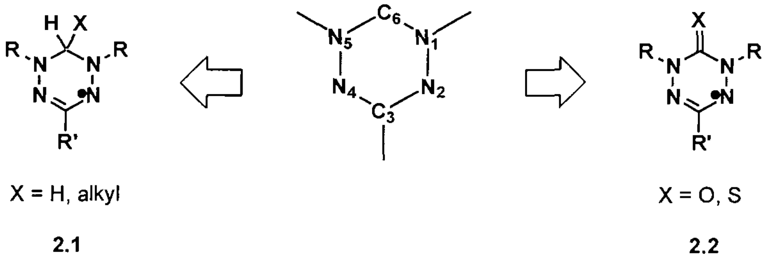


Figure 2.1 Type I (**2.1**) and Type II (**2.2**) verdazyl radicals with ring atom numbering scheme

Type II derivatives (**2.2**) have since been prepared which have a carbonyl or thiocarbonyl group in the six position.[35,36] Amide resonance between the carbonyl and the flanking nitrogen atoms give this type of verdazyl a planar geometry.

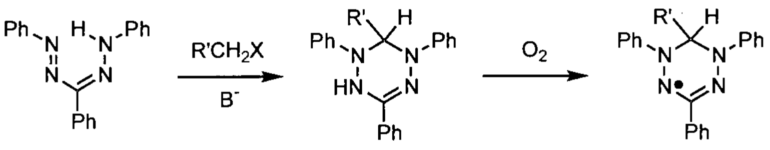
Since their discovery, little has been done to expand the available chemistry of this exceptionally stable radical species. Most work has been limited to minor modifications of ring substituents and characterization of the radicals. Several groups have reported the synthesis and characterization of simple verdazyl di- and triradicals.[37,38]

Coordination chemistry of verdazyls had not been investigated until 1997 when Brook *et al.* made the first metal complex of a previously studied verdazyl biradical (**2.13**).[39] This work was further expanded by Hicks *et al.* with the synthesis and coordination chemistry of a new class of verdazyl radicals based on oligopyridine structures.[40,41] No work has yet been done to investigate interactions between verdazyl radicals and a second spin-bearing species. This chapter describes attempts to synthesize verdazyl / semiquinone diradical anions.

2.2 Verdazyl Radicals

2.2.1 Synthesis

Verdazyls were discovered accidentally by Kuhn and Trischmann in 1963 during studies on the alkylation of formazans **2.3** (Scheme 2.1).[42] Reacting triarylformazan **2.3** with methyl iodide under strongly basic conditions gave a cyclized product, tetrazine **2.4**. Also referred to as a leucoverdazyl, tetrazine **2.4** was readily oxidized by atmospheric O_2 to give verdazyl radical **2.5**.

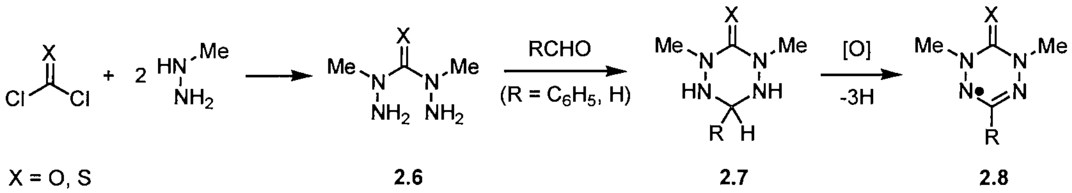


2.3 **2.4** **2.5**

Scheme 2.1 Preparation of verdazyl **2.5** from a formazan precursor **2.3**

The formazan route has since been used, with minor modifications, to synthesize a large number of verdazyl derivatives with different substituted aryl groups. The range of alkylating agents has also been expanded to incorporate alkyl and benzylic groups (R = C_6H_5 and *p*-BrC_6H_5) at C6.

In the early 1980's Neugebauer and coworkers devised routes to 6-oxoverdazyls and 6-thioxoverdazyls, the former via a carbonic acid bis(1-methyl hydrazide) (**2.6**) precursor[43,44] or thiocarbonic acid bis(1-methyl hydrazide)[35] (Scheme 2.2).

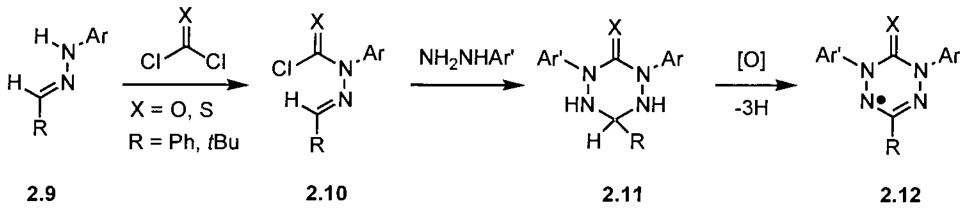


Scheme 2.2 Synthesis of the 6-oxoverdazyl radical **2.8** from bis(hydrazide) **2.6**

Bis(hydrazide) **2.6** is prepared by reacting two equivalents of 1-methylhydrazine with one equivalent of phosgene. At low temperatures the 1-methylhydrazine reacts exclusively through the N-methyl nitrogen. Two additional equivalents of 1-methylhydrazine are utilized to trap the hydrogen chloride produced as a hydrazine hydrochloride salt. Condensation of bis(hydrazide) **2.6** with an aldehyde gives the radical precursor 1,5-dimethyl-3-phenyl-1,2,4,5-tetrazane 6-oxide **2.7**, herein referred to as a tetrazane.[43] This route has the advantage of higher yields compared to the formazan method. A wide range of R-group substituents can be used and, for this reason, 6-oxoverdazyls have been the major focus of our work.

Oxidation of tetrazanes **2.7** to the corresponding 1,5-dimethyl-6-oxoverdazyls **2.8** can be achieved with $FeCl_3$ in formic acid[35] or $K_3Fe(CN)_6$ in basic water/DMF[36]. Many other organic and inorganic oxidants have since been used for a wide range of derivatives including *para*-benzoquinones, periodate, PbO_2, AgO, and Ag_2O.

The procedure via the bis(hydrazide) is limited to verdazyls with N-alkyl groups in the one and five positions of the ring. In the late 1980's Milcent *et al.* devised a new synthesis of the verdazyl precursor, 1,3,5-triphenyl-1,2,4,5-tetrazane 6-oxide.[45] This methodology was later used by Neugebauer to synthesize 6-oxo and 6-thioverdazyls that have two different N-phenyl substituents (Scheme 2.3).[46]



Scheme 2.3 Synthesis of the 6-oxoverdazyl radical **2.12** from hydrazone **2.9**

This synthesis starts from a hydrazone formed from the appropriate aldehyde and hydrazine. Reaction of a hydrazone **2.9** with phosgene or thiophosgene gives the 2-chloroformylhydrazone **2.10**, which is ring-closed with an aryl hydrazine to give tetrazane **2.11**. The tetrazanes are oxidized to the corresponding radicals as they were when made from bis(hydrazide) **2.6**.

2.2.2 Properties of Verdazyl Radicals

EPR spectra of verdazyl radicals are in general quite complex. The interaction of the unpaired electron with the four nearly equivalent nitrogen atoms of the tetrazine ring gives a dominant nine line EPR pattern.[47,48] Hyperfine coupling constants, *a*(N), are typically in the range of 5-7 Gauss, with the three coordinate nitrogens (N1, N5) being slightly larger than the two coordinate nitrogens (N2, N4). The unpaired electron resides almost exclusively in a delocalized π-system spanning the four ring nitrogens with a nodal plane bisecting the ring through C3 and C6 (Figure 2.2). Only a negligible amount of spin leaks on to the three and six positions of the ring through spin polarization effects. The EPR results have also been supported by molecular orbital calculations[49,50].

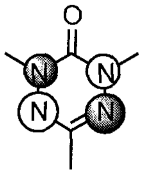


Figure 2.2 SOMO of the 6-oxoverdazyl radical

Additional hyperfine coupling is observed between the unpaired electron and the N-bound substituents. The complexity of the spectra of N,N'-dimethylverdazyls is increased by coupling to the six N-methyl protons; 5.3 – 5.5 Gauss for radical **2.8**.[36] The coupling to the N-methyl protons is a result of hyperconjugation, which allows spin transfer to the β-hydrogen.[51] In the spectrum of N,N'-diphenyl verdazyls **2.5**, the hyperfine coupling to the aromatic protons is usually too small to resolve, 0.17 to 0.36G as determined by ENDOR[36], resulting only in broadening of the nine line pattern imposed by the four nitrogens.

The electronic absorption spectra of verdazyl radicals show characteristic transitions in the visible region of the spectrum. Of these, it is the longest wavelength absorptions that are assigned as SOMO to LUMO transitions[52]. Type I verdazyl radicals **2.1**, which have a large degree of delocalization through N-phenyl substituents, have wavelengths of absorption maxima, or λ_{max}, between 650 and 750 nm. These derivatives are, as a result, typically green. Type II verdazyl radicals **2.2** have λ_{max} absorptions between 400 and 600 nm and are typically red, though, some derivatives are orange, maroon or brown. Increased conjugation at C3 for either Type I or Type II verdazyls leads to a bathochromic shift of λ_{max}.

2.3 Diradicals

One important branch of stable free radical research looks at molecules that contain two or more unpaired electrons. A molecule that is a diradical or polyradical gives rise to fundamental questions, beyond those of a simple monoradicals. How do the unpaired electrons interact with each other? What is the extent of this interaction?

Exchange interactions between two unpaired electrons depend on the relative energies of the two singly occupied molecular orbitals, or SOMOs. If two unpaired electrons reside in degenerate or near degenerate orbitals there are two possible spin state configurations, parallel and antiparallel (shown in Figure 2.3). In a low spin diradical, the coupling between unpaired electrons is antiferromagnetic (AFM) and the total spin is $S = 0$. This is said to have a singlet ground state. In a high spin diradical, the coupling between unpaired electrons is ferromagnetic (FM) and the total spin is $S = 1$. This is said to have a triplet ground state. If the ground state of a diradical is a singlet then the excited state will be a triplet and vice-versa. The strength of the interaction between the two unpaired electrons is represented by J, the exchange interaction. The magnitude of this interaction is proportional to the energy difference between the ground and excited states. If the interaction is ferromagnetic, then J is positive and if it is antiferromagnetic, then J is negative.

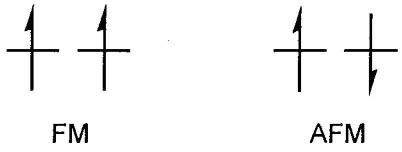


Figure 2.3 Diradical spin state configurations

As discussed in Chapter 1, a major class of stable free radicals are π radicals in which the unpaired electron resides in a delocalized π framework imparting their stability. It is through a common π system that a strong interaction between two unpaired electrons is observed in diradicals. If spin density from both unpaired electrons cannot reside on a common atom then the SOMOs are disjoint. An example of a disjoint diradical is tetramethyleneethane **2.13**. In this case, the unpaired electrons are confined to different parts of the molecule and the exchange interaction is relatively small. This makes the ground state difficult to predict because other factors such as conformation or weak interactions through σ-bonds can influence J. If spin density from both unpaired electrons overlaps on a common atom the then the SOMOs are non-disjoint, or coextensive. An example of a non-disjoint diradical is trimethylenemethane (**2.14**). The Pauli exclusion principle prohibits the unpaired spins from being antiparallel. The repulsion between the aligned spins keeps them apart, lowering their collective energy making ferromagnetic exchange a favourable arrangement. This assures a quantum mechanical exchange interaction that is ferromagnetic, resulting in a triplet ground state.

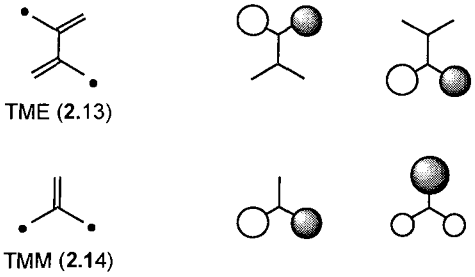
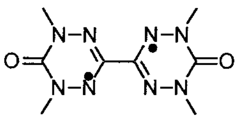


Figure 2.4 SOMOs of diradicals **2.13** and **2.14**

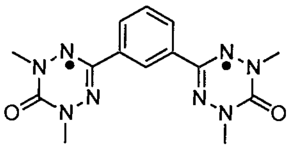
Studies on π-conjugated diradicals, such as trimethylenemethane (**2.14**)[53], tetramethyleneethane (**2.13**) and *meta*-dimethylenebenzene[54,55], have helped explain many of the phenomena discussed and the nature of diradical coupling units. All of these examples are very unstable and only observable at very low temperatures in a frozen matrix.

2.4 Heterospin Diradicals

In addition to those mentioned in the previous section, there have been a vast number of symmetric diradicals prepared and investigated. Those composed of stable radicals have a broader appeal in materials chemistry and towards potential applications. As a result, symmetric diradicals of almost every class of stable radical have been isolated including verdazyls **2.15** and **2.16**, both of which were found to have singlet ground states.[37,56]



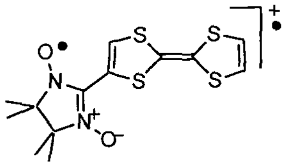
2.15



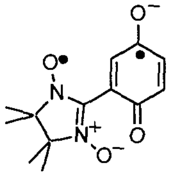
2.16

The previous section discussed the theory behind molecules that possess two unpaired electrons. One approach towards new types of diradicals is through the combination of entirely different spin carriers. The most common materials to fall under this category are coordination complexes of paramagnetic metal ions with paramagnetic ligands. Little work has gone into investigating and understanding interactions between two different organic spin carriers. These systems are more complex than those discussed in Section 2.3. The spin bearing orbitals are no longer degenerate or even near degenerate so interactions are dependent on the relative energies of the two SOMOs.

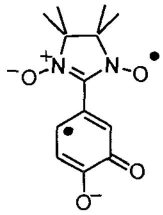
So far, investigations of heterospin diradicals have been limited to the two most commonly investigated classes of stable free radicals: the nitroxides and semiquinones. Sugawara *et al.* have coupled nitronyl nitroxide to the radical ions of both tetrathiafulvalene (**2.17**) and *para*quinone (**2.18**).[57] More recently, Shultz *et al.* have synthesized diradical anion **2.19** which instead has a *ortho*quinone fragment capable of binding to a metal centre.[58,59]



2.17



2.18



2.19

2.4.1 Semiquinone Radical Anions

As the second radical type the semiquinone radical anion was chosen. This is because of its stability, range of interesting properties and strong exchange interactions with other radical species. The semiquinones have been one of the most heavily investigated classes of stable free radicals over the last half century. Interest in this class of radicals is due to both their properties as related to materials research[60,61] and their prevalence in biological systems[62].

The semiquinone radical anion (SQ) is the central figure in a three-member redox chain (Figure 2.5). They can be formed through either a one electron reduction of a quinone (BQ) or a one electron oxidation of a hydroquinone dianion (Cat), both of which can be accomplished chemically or electrochemically.

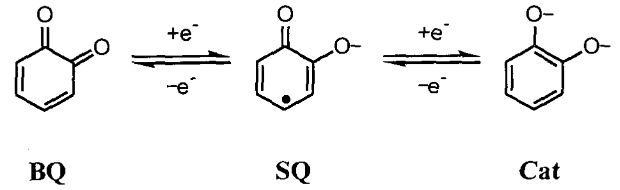


Figure 2.5 The possible oxidation states of an *ortho*-quinone

Reduction can be accomplished with ascorbic acid or sodium dithionite in protic solvents or with alkali metals or amalgams in ether solvents.[63] Depending on their ring substituents, quinones can also be reduced by zero valent transition metal sources to give semiquinone metal pi complexes[64,65] or σ,σ'-bound coordination complexes[66,67].

Ortho-quinones particularly, which have a bidentate chelating site have received an unprecedented amount of attention in the context of coordination chemistry of stable free radicals.[60,61] Certain metal complexes have been shown to exhibit valence tautomerism (Figure 2.6), a reversible intramolecular electron transfer triggered by external stimuli such as light, temperature or pressure.[68,69] This allows for switching between two different spin states with unique magnetic or conducting properties, which has spurred interest towards potential applications.[70]

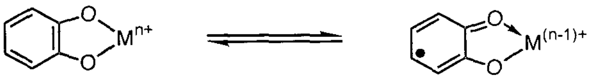


Figure 2.6 Valence tautomerism in a semiquinone metal complex

2.4.2 *Properties of Semiquinone Radical Anions*

The unpaired electron of the semiquinone radical resides in an orbital of π-symmetry delocalized over the ring and oxygen atoms. The EPR spectra depend on whether the oxygen atoms are *ortho* or *para* to each other and whether there are substituents on the ring.

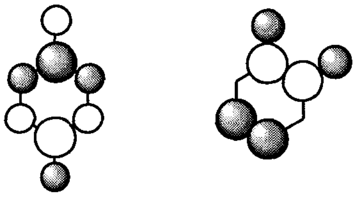


Figure 2.7 SOMOs of *para*- and *ortho*-semiquinones

In the case of *para*-semiquinone the SOMO is as shown in Figure 2.7. The unpaired electron interacts with the four equivalent protons with a hyperfine constant between 2.32 and 2.42 Gauss depending on the solvent.[63] Donor substituents cause a decrease in the hyperfine constant for a proton in the *ortho* position and an increase for the proton in the *para* position.[63]

The spectra of *ortho*-semiquinones differ from their *para* counterparts as is evidenced by the spin distribution of the SOMO (Figure 2.7). There are two pairs of equivalent protons to couple to the unpaired electron. Of these C4 and C5 are the positions with the largest spin density and a resulting hyperfine splitting of between 3.30 and 3.65 Gauss. This can be compared to C3 and C6, which couple more weakly at 0.95 to 1.50 Gauss.[63] The resulting spectrum of the unsubstituted *ortho*-semiquinone is a triplet of triplets.

Because of the ionic nature of the semiquinones, their EPR spectra also show hyperfine coupling to the cation present. For alkali metal ions this is generally quite small in the range of 0.5 – 0.6 Gauss.[71]

2.5 Results and Discussion

2.5.1 Synthesis of the Radical Precursor Tetrazanes

The synthetic approach towards radicals bearing a hydroquinone moiety was based on work by Neugebauer *et al.* outlined in Section 2.1.1, Scheme 2.2. By this methodology, aldehydes chosen contain different isomers of the required hydroquinones (Figure 2.8). Aldehyde **2.24** is a precursor to a phenoxyl radical, which were discussed in Chapter 1. All of the aldehydes used were available commercially.

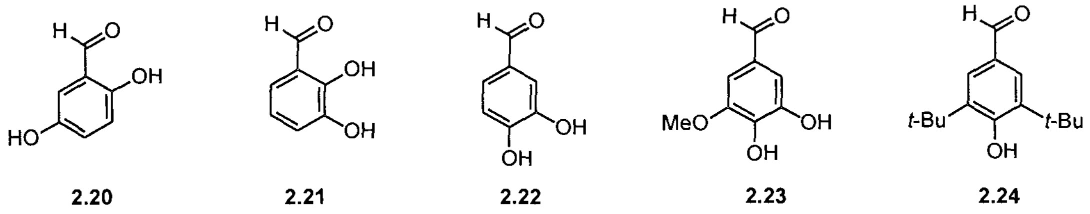
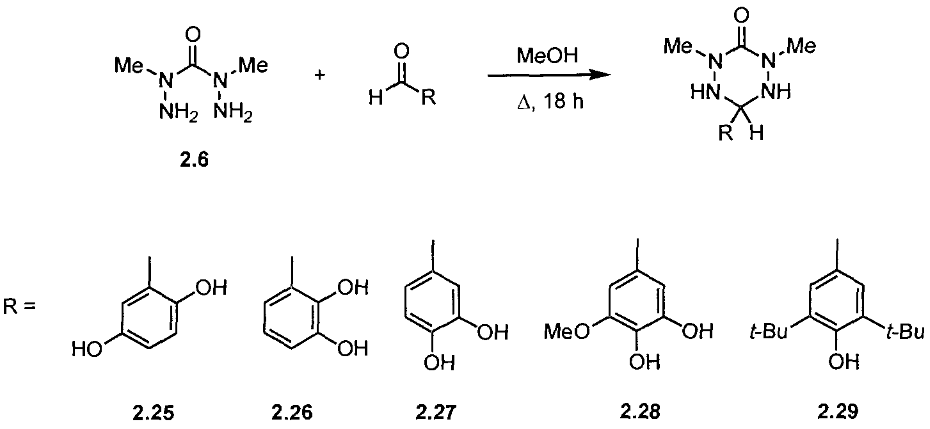


Figure 2.8 Aldehydes used in the synthesis of tetrazanes

The precursors to the verdazyl radicals, the tetrazanes, were synthesized by the application of standard procedures as outlined in Scheme 2.4.



Scheme 2.4 Synthesis of radical precursor tetrazanes

The synthesis of bis(hydrazide) **2.6** was first developed by Neugebauer[43] and later modified by our research group in order to avoid the use of phosgene gas[40]. Triphosgene (bis(trichloromethyl) carbonate) is a convenient electrophile to replace phosgene gas because as a solid it is easier and safer to work with. This reaction between triphosgene and 1-methylhydrazine at -78°C gave bis(hydrazide) **2.6** in excellent yield. The subsequent condensation of bis(hydrazide) **2.6** with the appropriate aldehyde gave the radical precursor tetrazane in yields in the range of 35 – 95 % (Scheme 2.4). To ensure cyclization to form the tetrazane, a dilute methanol solution of the aldehyde was added to a refluxing solution of bis(hydrazide) **2.6** in a minimum volume of methanol. If these steps were not taken, there was a possibilty of forming a bis(imine) byproduct (Figure 2.9). The tetrazanes were all purified by recrystallization.

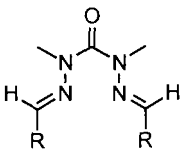


Figure 2.9 Possible bis(imine) byproduct

All tetrazanes were characterized by ^{1}H and ^{13}C NMR, FTIR, MS and elemental analysis. The detailed characterization of one representative example will be presented. The other derivatives share similar features common to the tetrazane moiety.

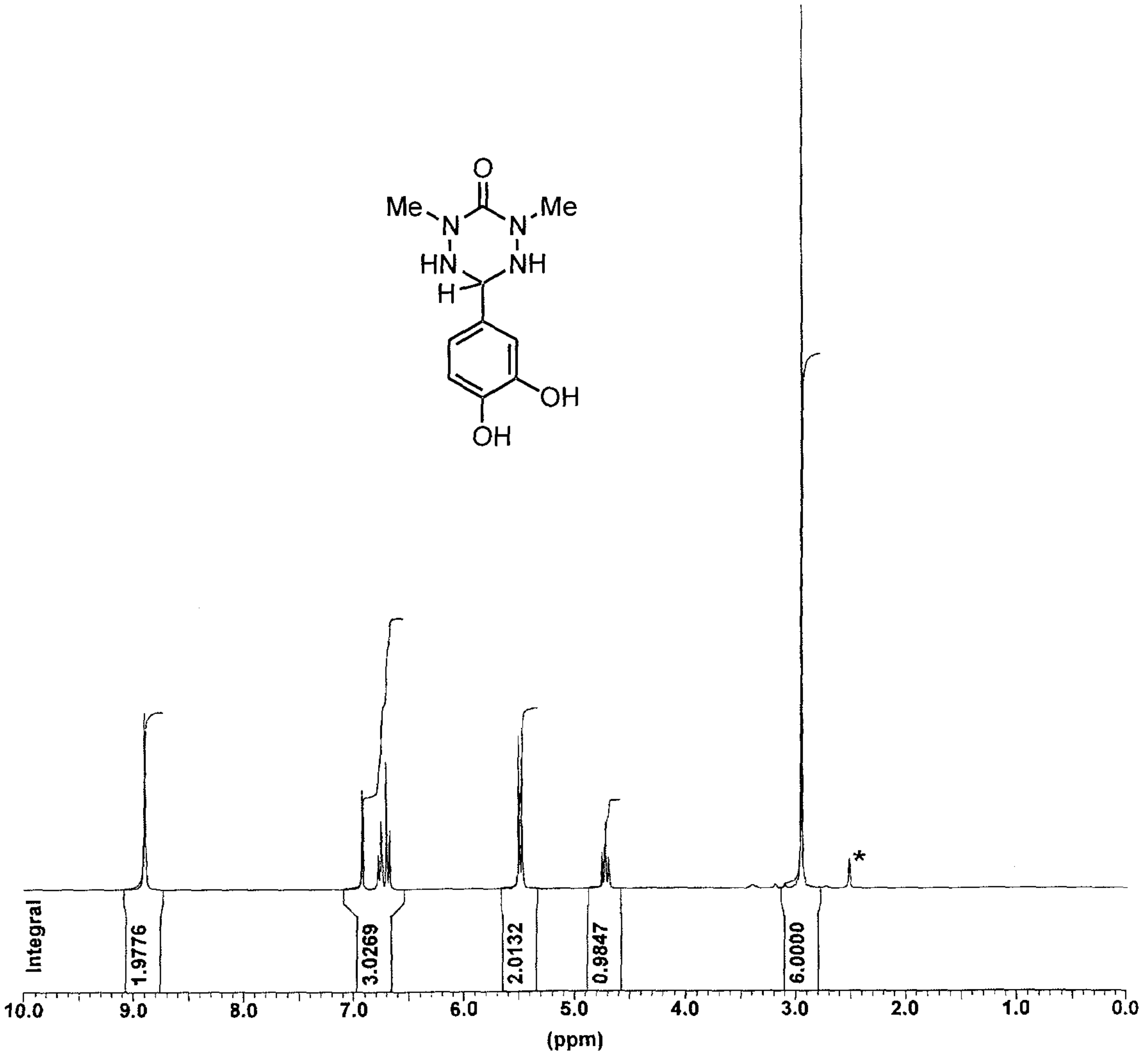


Figure 2.10 ^{1}H NMR spectrum of tetrazane **2.27** (starred peak is d_5-DMSO)

Figure 2.10 shows the ^{1}H NMR spectrum of tetrazane **2.27** in d_6-DMSO. The six equivalent protons of the two N-methyl groups show up as a singlet at 2.94 ppm. The peak of the C3 methine proton at 4.71 ppm is a triplet from coupling to the two equivalent protons on N2 and N4. The N2 and N4 protons appear as a doublet at 5.48 ppm. These three peaks are typical of the 1,5-dimethyl-1,2,4,5-tetrazane 6-oxide framework and similar chemical shifts are seen for all tetrazanes of this type. The remaining peaks are due to the 3,4-dihydroxyphenyl group attached at C3 of the tetrazane ring. In this structure the two chemically different hydroxyl protons form a singlet at 8.89 ppm likely due to having similar environments and fast exchange of the acidic protons. The hydroxyl proton shifts of these tetrazanes disappear when d$_4$-MeOH is used as an NMR solvent indicating that these protons are acidic.

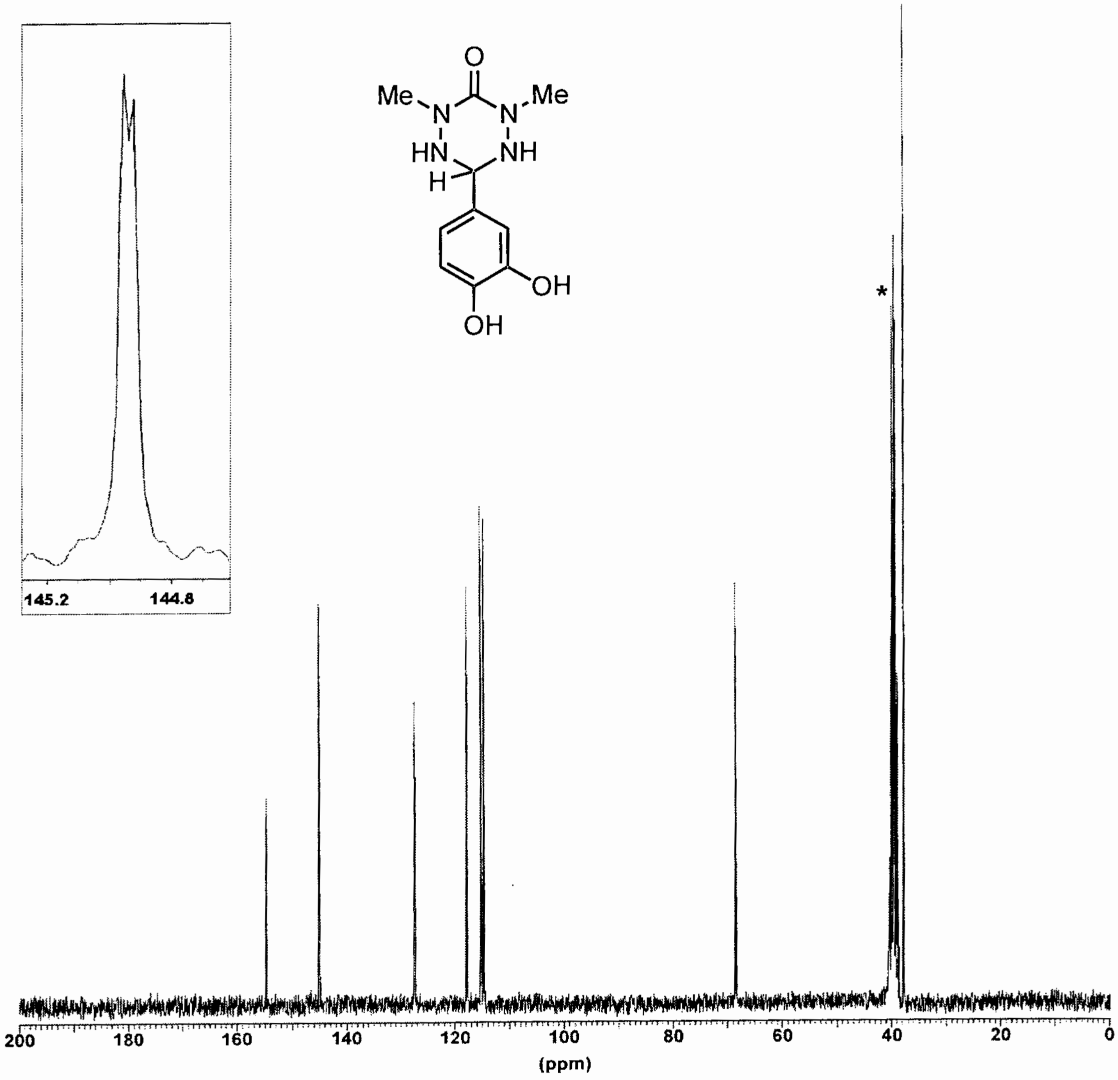


Figure 2.11 ^{13}C NMR spectrum of tetrazane **2.27** (starred peak is d$_6$-DMSO) and expansion (inset)

Figure 2.11 shows the ^{13}C NMR spectrum of tetrazane **2.27** in d_6-DMSO. There are nine peaks as expected for the nine chemically different carbons of tetrazane **2.27**. The N-methyl carbons are at 37.7 ppm slightly downfield for a typical methyl group due to deshielding by a nitrogen atom. The methine carbon, C3, is also deshielded showing up at 68.5 ppm. The carbonyl carbon, C6, structurally resembles urea because it is flanked by two nitrogens. As a result, it is the furthest downfield shift at 154.6 ppm. The remaining shifts are in the range for a substituted benzene ring.

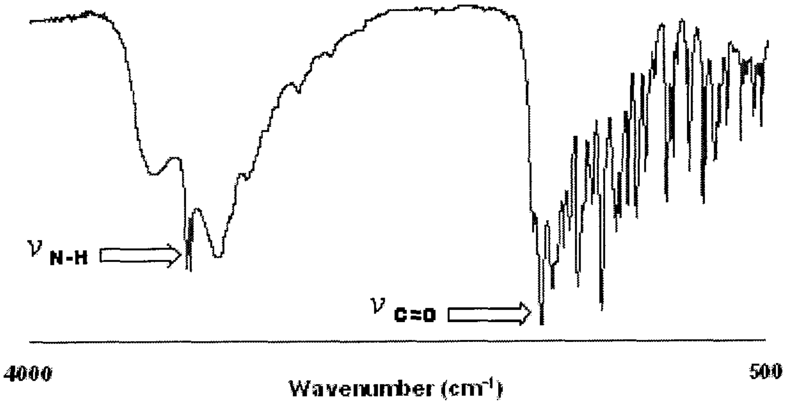


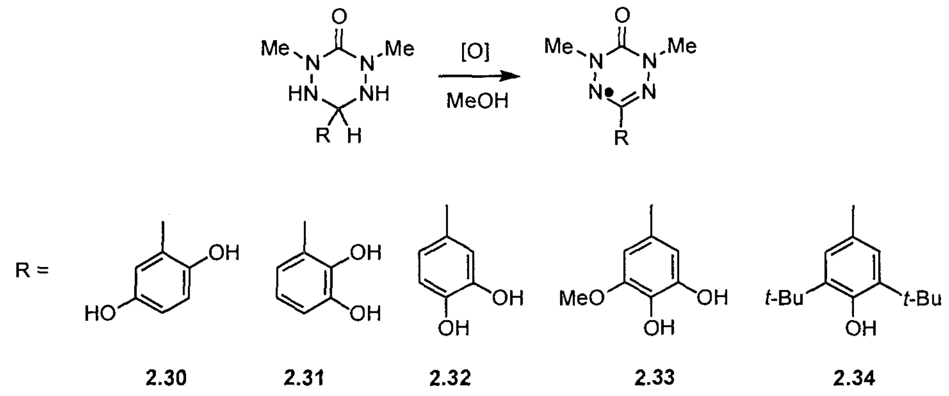
Figure 2.12 FTIR spectrum of tetrazane **2.27** (KBr disc)

Figure 2.12 shows the FTIR spectrum of tetrazane **2.27** recorded as a pressed KBr disc. There are two main diagnostic functional groups common to all of the tetrazanes investigated. The first feature is the strong amine N-H stretches at 3264 and 3242cm^{-1}. The second is the strong carbonyl ($\nu_{C=O}$) stretch at 1571cm^{-1}, which is in the expected range for a carbonyl with a reduced bond order from conjugation to two nitrogen lone pairs.

Both mass spectrometry and elemental analysis confirmed the molecular formulas of all the tetrazanes. The EI mass spectrum of tetrazane **2.27** shows the parent ion, (M^+), with a mass to charge ratio of 238. This corresponds to the expected molecular mass and thus supports the molecular formula.

2.5.2 Synthesis of Verdazyl Radicals

A range of organic and inorganic oxidants were used to convert the tetrazanes to the corresponding verdazyl radicals and were chosen based on previous work in our group. Generally IO_4^- and Ag_2O were used giving the verdazyl radical in yields ranging from 30 – 80 %. Ag_2CO_3 / celite (also known as Fetizon's reagent) and *p*-BQ were also used successfully. Over-oxidation was a common problem so reaction times were generally kept below 20 min except when Ag_2O was used, which was stirred for several hours. The solubility of the tetrazanes investigated was limited to very polar solvents: MeOH, DMF or DMSO. Radicals either did not form in DMSO or DMF to an appreciable extent or were unstable depending on the oxidant used, so oxidations were performed in MeOH. Purification of the radicals was accomplished by column chromatography. Radicals **2.30**. **2.31**, **2.32**, **2.33**, and **2.34** are stable for several months in the solid state and from days to weeks in solution.



Scheme 2.5 Oxidation of tetrazanes to verdazyl monoradicals.

The verdazyl radicals were characterized by EPR, FTIR and UV/vis spectroscopies, MS, and elemental analysis or high resolution MS. As with the tetrazanes discussed in the previous section, the verdazyl radicals investigated here all share similar spectroscopic properties. The detailed characterization of one representative example will be presented. The other derivatives share similar features common to the verdazyl moiety.

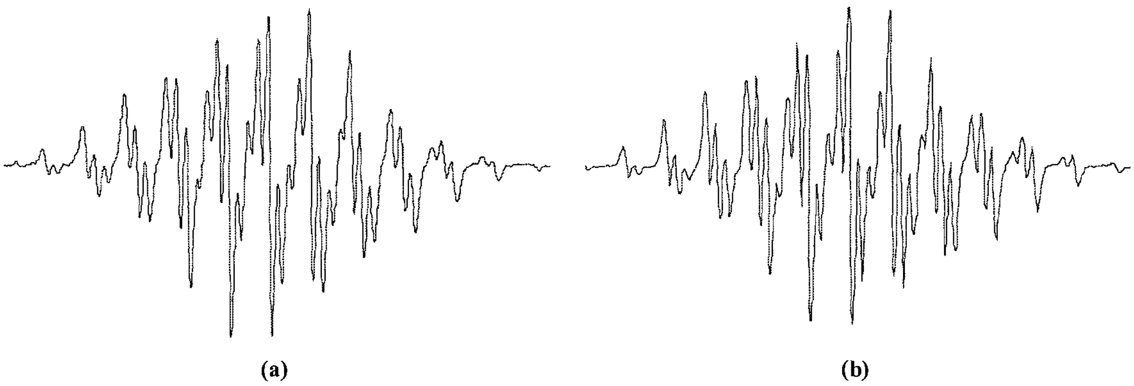


Figure 2.13 EPR spectrum of radical **2.32** at 298K in CH_2Cl_2 (a). Total spectral width 70 Gauss. Simulated EPR spectrum of **2.32** (b).

The EPR spectrum of radical **2.32** is shown in Figure 2.13 together with a simulated spectrum. EPR samples were generally prepared at concentrations of approximately 10^{-4} M and recorded at 298K in dry CH_2Cl_2. Samples were degassed using three cycles of the freeze-pump-thaw method. Hyperfine coupling constants (*a*) and electron g-factors were determined by simulation of the experimental spectrum and found to be consistent with other 1,5-dimethyl-6-oxoverdazyls.[36] Values were found to be the same for all of the verdazyls investigated; $a(N_{1,5})$ = 5.3 Gauss, $a(N_{2,4})$ = 6.5 Gauss, and $a(CH_3)$ = 5.3 Gauss with a g-factor of 2.0037.

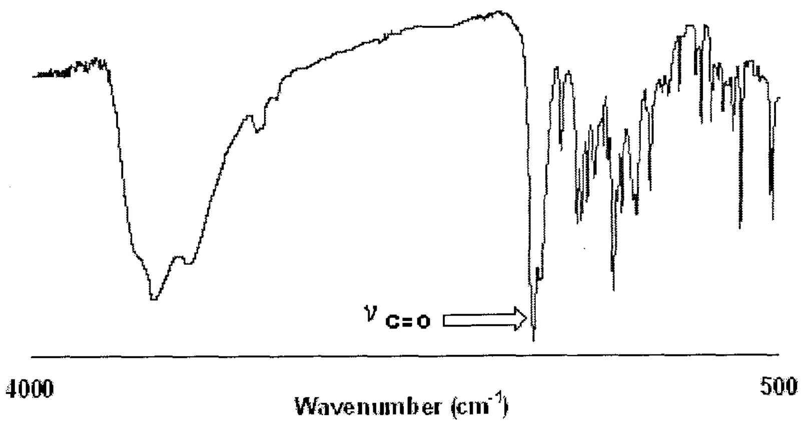


Figure 2.14 FTIR spectrum of radical **2.32** (KBr disc)

The FTIR spectrum of radical **2.32** (Figure 2.14) has features consistent with other 1,5-dimethyl-6-oxoverdazyls. This method is diagnostically useful to verify radical formation. The strong carbonyl stretching band, $\nu_{C=O}$, is at 1673 cm^{-1}, shifted to a higher frequency relative to the precursor tetrazane. Upon oxidation, the tetrazine ring becomes planar. The lone pairs of N1 and N5 participate more in the π framework and are less able to contribute to amide-type resonance. The result is an increase in the carbonyl stretching frequency. The loss of the sharp N-H stretching bands, relative to Figure 2.12, is also indicative of radical formation. This region is somewhat obscured by the O-H stretching bands from the phenol groups and is generally easier to see for other verdazyl derivatives.

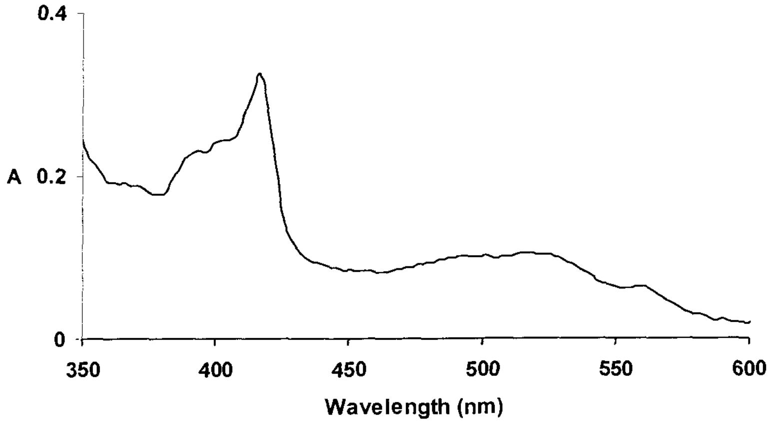
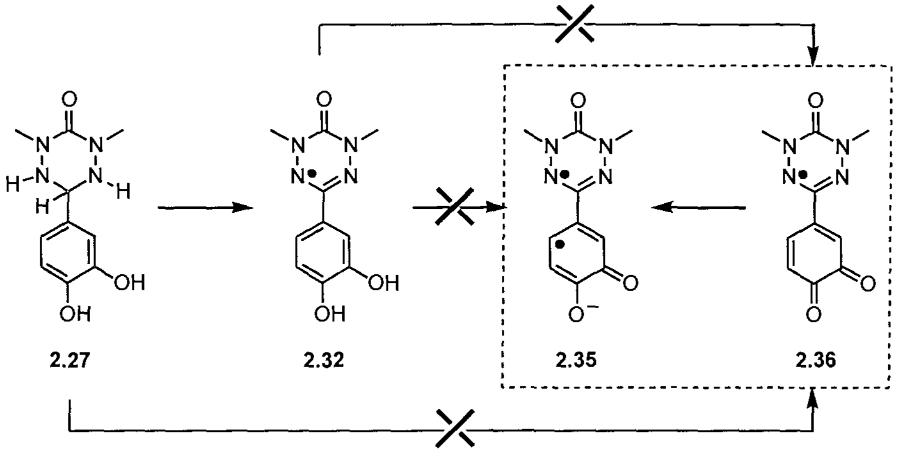


Figure 2.15 UV/visible spectrum of verdazyl **2.32** in CH_2Cl_2 (A = absorbance)

The UV/visible spectrum of radical **2.32** (Figure 2.15) shows a transition at 418 nm (ε = 800) and a second broad, lower intensity transition between 450 and 550 nm. The lowest energy absorption corresponds to the SOMO to LUMO transition. Both are indicative of a Type II verdazyl radical and responsible for its red colour.

2.5.3 Attempted Oxidation and Coordination Chemistry of Hydroquinone Containing Verdazyl Radicals

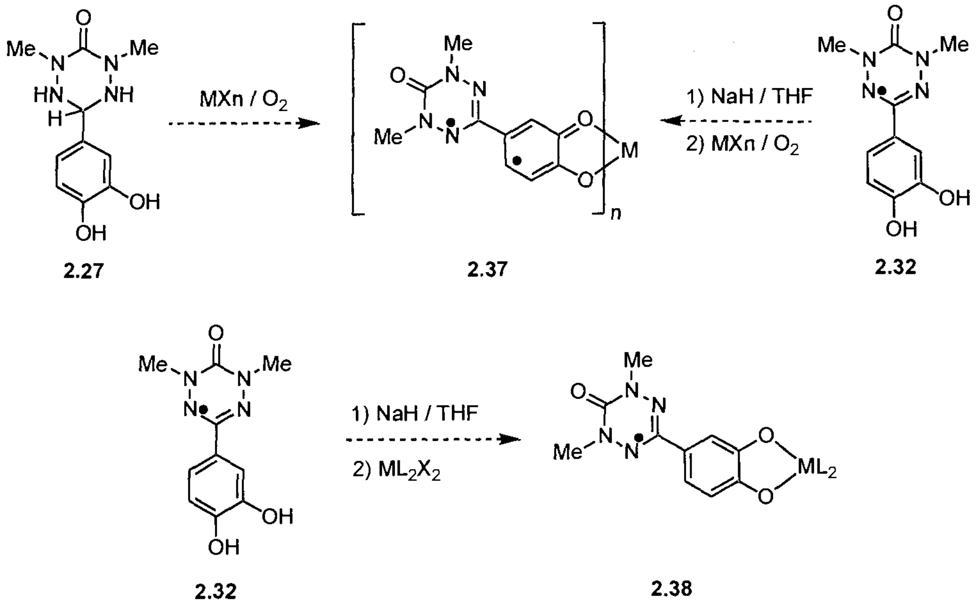
Oxidations to convert the hydroquinone to either semiquinones or quinones were attempted from both the verdazyl and directly from the tetrazane starting materials (Scheme 2.6). These followed a number of literature approaches with a variety of oxidants including: those mentioned for oxidation to the verdazyl (Section 2.5.2), chloronil, DDQ, MnO_2, PbO_2, and $Pb(OAc)_4$. The metal oxide reagents appeared too mild, stopping at the verdazyl radicals. Decomposition occurred with most other oxidants.



Scheme 2.6 Attempted synthesis of verdazyl / semiquinone diradical **2.35**

Coordination chemistry was also investigated with radicals **2.31**, **2.32**, and **2.33**, which bear *ortho*-hydroquinone groups. The *ortho*-hydroxy groups form a chelating environment, which can bond to a metal through two oxygen atoms. Coordination has been shown to stabilize the semiquinone radical anion.[72] This would allow for the addition of a paramagnetic metal ion as a third spin carrier as in structure **2.37**. As structure **2.37** also shows, a metal ion may also serve to bridge two radicals.

Two methods were used towards forming coordination complexes of some first row transition metals, one starting from the tetrazane, the other from the radical. The first method involved combining the tetrazane and a metal salt, MX_2 or MX_3 (M = Mn, Fe, Co, Ni, or Cu and X = Cl, Br, OAc, ClO_4 or OH) in methanol and letting the solution sit for several days. All resulted in either no reaction or a small amount of the radical forming from aerial oxidation. The second route involved deprotonation of the hydroxyl groups of the radical with NaH. This was followed by addition of a metal source which included: MX_2, $M(bipy)X_2$, and $M(CTH)X_2$ (M = Mn, Co, Fe, or Cu, and X = Cl or ClO_4 (Scheme 2.7). In all of these reactions, only starting materials were recovered.



Scheme 2.7 Attempted coordination chemistry of radicals **2.31**, **2.32**, and **2.33**. (Radical **2.32** shown)

2.6 Conclusions

This chapter presented the synthesis and characterization of a new class of verdazyl radicals that bears a hydroquinone group. The verdazyl precursor tetrazanes were synthesized using standard procedures for 1,5-dimethyl-1,2,4,5-tetrazane 6-oxides. Oxidation of the tetrazanes with pBQ, IO_4^-, Ag_2CO_3 / celite and Ag_2O was successful in forming the corresponding verdazyl monoradicals. All attempts to further oxidize these compounds to form verdazyl / quinone monoradicals, verdazyl / semiquinone diradical anions or verdazyl / phenoxyl diradicals were unsuccessful. The reasons behind this are not fully understood. It may be that these forms are inherently unstable and decompose rapidly upon formation. Orthoquinones, in particular, are known to be prone to attack at the ring if not protected by bulky substituents. Coordination chemistry of the verdazyls bearing *ortho*-hydroquinones was also unsuccessful. These radicals are likely poor ligands for the metal precursors used possibly due to the withdrawing effects of the verdazyl moiety.

This project still warrants some future exploration. The verdazyl radicals may require bulky substituents on the phenyl ring to provide both steric protection and to alter their oxidation potentials. This may also change the electronic properties of the system to make coordination chemistry viable.

2.7 Experimental

General procedures

All reactions, unless stated otherwise, were carried out under argon using standard Schlenk techniques. All glassware was either flame dried or stored overnight in an oven at 150°C before use. Solvents, with the exception of methanol, ethanol and DMF, were distilled before using: THF and diethyl ether from Na/benzophenone, toluene and benzene from Na, and hexanes and dichloromethane from CaH_2. All reagents were purchased from Aldrich or Lancaster and used as received. $^{1}H/^{13}C$NMR spectra were recorded on a Bruker AC300 (300 MHz) instrument. FT-IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer as pressed KBr discs. EPR spectra were recorded on a Bruker EMX instrument (9.51 GHz) and the spectra obtained were simulated using WinEPR SimFonia. Elemental analyses were performed by Canadian Microanalytical Services Ltd., New Westminister, BC, Canada. UV-visible spectra were recorded on a Varian Cary 50 Scan spectrometer. Mass spectra were recorded on a Kratos Concept spectrometer using electron impact (EI) or secondary ion (+LSIMS) sources. Melting points (uncorrected) were taken on Gallenkamp melting point apparatus.

1,5-dimethyl-3-(2,5-dihydroxyphenyl)-1,2,4,5-tetrazane-6-oxide (2.25). A solution of 2,5-dihydroxybenzaldehyde **2.20** (1.17 g, 8.5 mmol) in MeOH (200 mL) was added dropwise to a warm solution of carbonic acid bis(1-methylhydrazine) **2.6** (1.0 g, 8.5 mmol) in MeOH (10 mL). After addition was complete (3 h), the solution was refluxed for 18 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed under reduced pressure to yield an off-white solid. The crude product was dissolved in warm EtOH and filtered to remove an insoluble byproduct. Solvent was again removed and the crude product recrystallized from MeOH/EtOAc (approximately 1:10) to give tan crystals of **2.25**, yield 0.7 g (34.5 %). ^{1}H NMR (DMSO-d_6): δ 9.13 (s, 1H, O$\underline{H}$), 8.75 (s, 1H, O$\underline{H}$), 6.72 (d, 1H, J = 3 Hz, aryl), 6.63 – 6.54 (m, 3H, aryl), 5.69 (d, 2H, J = 10 Hz, N$\underline{H}$), 4.91 (t, 1H, J = 10 Hz, C$\underline{H}$), 2.94 ppm (s, 6H, C$\underline{H}_3$). ^{13}C NMR (DMSO-d_6): δ (154.2, $\underline{C}$=O), (149.8, 147.5, 122.0, 116.3, 115.8, 114.3, aryl), (66.3, $\underline{C}$H), (37.4, N$\underline{C}$H$_3$) ppm. FT-IR (KBr): 3329 (m, br), 3276 (w, sh), 3203 (m, br), 2976 (vw), 2937 (vw), 1579 (s, νC=O), 1524 (m), 1483 (s), 1433 (vw), 1394 (m), 1333 (m), 1285 (w), 1236 (m, sh), 1224 (m), 1165 (w), 1114 (vw), 1075 (vw), 977 (vw), 933 (vw), 858 (vw), 824 (vw), 815 (vw), 785 (m), 736 (m), 651 (vw, br), 567 (vw), 531 (w) cm^{-1}. Anal. Calcd. for $C_{10}H_{14}N_4O_3$: C, 50.41; H, 5.92; N, 23.52. Found: C, 50.08; H, 5.64; N, 23.33. MS (EI): *m/z* 238 {M$^+$, 100 %}. Mp: 164 °C.

1,5-dimethyl-3-(2,3-dihydroxyphenyl)-1,2,4,5-tetrazane-6-oxide (2.26). A solution of 2,3-dihydroxybenzaldehyde **2.21** (1.17 g, 8.5 mmol) in MeOH (200 mL) was added dropwise to a warm solution of carbonic acid bis(1-methylhydrazine) **2.6** (1.0 g, 8.5 mmol) in MeOH (10 mL). After addition was complete (3 h), the solution was refluxed for 18 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed under reduced pressure to yield an off-white solid. The crude product was recrystallized from MeOH/EtOAc to give **2.26** as transparent blocks, yield 1.7 g (80 %). ^{1}H NMR (DMSO-d$_6$): δ 9.21 (s, 1H, O$\underline{H}$), 9.04 (s, 1H, O$\underline{H}$), 6.78 – 6.58 (m, 3H, aryl), 5.69 (d, 2H, *J* = 10 Hz, N$\underline{H}$), 5.00 (t, 1H, *J* = 10 Hz, C$\underline{H}$), 2.94 ppm (s, 6H, C$\underline{H}_3$). ^{13}C NMR (DMSO-d$_6$): δ (154.2, $\underline{C}$=O), (145.3, 143.3, 122.3, 118.9, 117.5, 115.4, aryl), (66.0, $\underline{C}$H) (37.4, N$\underline{C}H_3$) ppm. FT-IR (KBr): 3274 (s), 3196 (s), 2946 (m), 1604 (s, νC=O), 1592 (m), 1476 (s), 1430 (m), 1390 (s), 1354 (m, sh), 1270 (s), 1230 (w), 1188 (m), 1113 (w), 1067 (w), 981 (m), 939 (w), 855 (w), 831 (w), 785 (w), 736 (m), 727 (w), 703 (w), 684 (w), 607 (vw), 531 (m) cm^{-1}. Anal. Calcd. for $C_{10}H_{14}N_4O_3$: C, 50.41; H, 5.92; N, 23.52. Found: C, 50.29; H, 5.61; N, 23.56. MS (EI) *m/z* 238 {M$^+$, 100 %}. Mp 147 °C.

1,5-dimethyl-3-(3,4-dihydroxyphenyl)-1,2,4,5-tetrazane-6-oxide (2.27). A solution of 3,4-dihydroxybenzaldehyde **2.22** (1.17 g, 8.5 mmol) in MeOH (200 mL) was added dropwise to a warm solution of carbonic acid bis(1-methylhydrazine) **2.6** (1.0 g, 8.5 mmol) in MeOH (10 mL). After addition was complete (3 h), the solution was refluxed for 18 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed under reduced pressure to yield an off-white solid. The crude residue was recrystallized from MeOH / EtOAc to give pale golden needles of **2.27**, yield 1.9 g (95 %). ^{1}H NMR (DMSO-d_6): δ 8.89 (s, 2H, O$\underline{H}$), 6.92 (d, 1H, J = 1.47 Hz, aryl), 6.78 – 6.68 (m, 2H, aryl), 5.48 (d, 2H, J = 9 Hz, N$\underline{H}$), 4.71 (t, 1H, J = 9 Hz, C$\underline{H}$), 2.94 ppm (s, 6H, C$\underline{H}_3$). ^{13}C NMR (DMSO-d_6): δ (154.6, $\underline{C}$=O), (144.9, 127.4, 117.7, 115.2, 114.6, 103.8, aryl), (68.5, $\underline{C}$H), (37.7, N$\underline{C}$H$_3$) ppm. FT-IR (KBr): 3428 (m, br), 3264 (s), 3242 (s), 3116 (s, br), 2972 (w, sh), 2729 (w, sh), 1607 (vw, sh), 1571 (s, νC=O), 1524 (s), 1467 (m), 1437 (m), 1396 (s), 1330 (w), 1308 (vw), 1284 (s), 1218 (m), 1196 (w), 1163 (w), 1121 (m), 1077 (w), 1036 (vw), 975 (w), 948 (w), 926 (vw), 890 (vw), 867 (w), 804 (w), 789 (w), 750(w), 727 (vw), 721 (vw, sh), 693 (vw), 623 (w), 602 (vw), 563 (vw), 542 (vw), 525 (vw) cm^{-1}. Anal. Calcd. for $C_{10}H_{14}N_4O_3$: C, 50.41; H, 5.92; N, 23.52. Found: C, 50.13; H, 5.70; N, 22.88. MS (EI) *m/z* 238 {M$^+$, 100 %}. Mp 142 °C.

1,5-dimethyl-3-(3,4-dihydroxy-5-methoxyphenyl)-1,2,4,5-tetrazane-6-oxide (2.28). A solution of 3,4-dihydroxy-5-methoxybenzaldehyde **2.23** (860 mg, 3 mmol) in MeOH (150 mL) was added dropwise to a warm solution of carbonic acid bis(1-methylhydrazine) **2.6** (600 mg, 3.0 mmol) in MeOH (10 mL). After addition was complete (3 h), the solution was refluxed for 18 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed under reduced pressure to give a yellow powder. Purification by trituration with EtOAc gave **2.28** as a white solid, yield 925 mg (67 %). ^{1}HNMR (DMSO-d$_6$): δ 8.87 (s, 1H, O$\underline{H}$), 8.25 (s, 1H, O$\underline{H}$), 6.61 (s, 2H, aryl), 5.53 (d, 2H, *J* = 9 Hz, N$\underline{H}$), 4.71 (t, 1H, *J* = 9 Hz, C$\underline{H}$), 3.73 (s, 3H, OC$\underline{H}_3$), 2.94 ppm (s, 6H, C$\underline{H}_3$). ^{13}C NMR (DMSO-d$_6$): δ (154.6, $\underline{C}$=O), (148.1, 145.5, 133.7, 126.6, 108.0, 102.3, aryl), (68.6, $\underline{C}$H), (55.8, O$\underline{C}$H$_3$), (37.7, N$\underline{C}$H$_3$) ppm. FT-IR (KBr): 3401 (m, br), 3277 (s), 3010 (m), 2961 (vw, sh), 2940 (m), 2796 (vw), 2719 (w), 2598 (w, sh), 1616 (vw, sh), 1594 (s, *ν*C=O), 1528 (s), 1505 (vw, sh), 1455 (s), 1393 (m), 1348 (m), 1326 (m), 1234 (s), 1155 (w), 1124 (vw), 1092 (m), 1060 (m), 975 (m), 953 (vw, sh), 930 (vw), 889 (w), 874 (w), 847 (vw), 833 (vw), 786 (vw), 723 (w), 702 (w), 665 (vw), 650 (w), 603 (vw, br), 557 (w), 536 (w), 498 (vw) cm^{-1}. Anal. Calcd. for $C_{11}H_{16}N_4O_4$: C, 49.25; H, 6.01; N, 20.88. Found: C, 48.96; H, 5.67; N, 20.80. MS (EI) *m/z* 268 {M$^+$, 100 %}. Mp 151 °C.

1,5-dimethyl-3-(3,5-di-*tertiary*-butyl-4-hydroxyphenyl)-1,2,4,5-tetrazane-6-oxide (2.29). A solution of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde **2.24** (2.0 g, 8.5 mmol) in MeOH (200 mL) was added dropwise to a warm solution of carbonic acid bis(1-methylhydrazine) **2.6** (1.0 g, 8.5 mmol) in MeOH (10 mL). After addition was complete (3 h), the solution was refluxed for 18 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed under reduced pressure to yield an off-white solid. The crude product was recrystallized from MeOH/EtOAc to give **2.29** as a white microcrystalline solid, yield 2.28 g (81 %). ^{1}H NMR (DMSO-d$_6$): δ 7.29 (s, 2H, aryl), 6.94 (s, 1H, O$\underline{H}$), 5.60 (d, 2H, *J* = 8 Hz, N$\underline{H}$), 4.75 (t, 1H, *J* = 8 Hz, C$\underline{H}$), 2.93 (s, 6H, NC$\underline{H}_3$), 1.37 ppm (s, 18H, C$\underline{H}_3$). ^{13}C NMR (DMSO-d$_6$): δ (154.5, C=O), (153.5, 138.8, 127.4, 123.4, aryl) (68.9, $\underline{C}$H), (37.8, N$\underline{C}$H$_3$), (34.6, $\underline{C}$), (30.4, $\underline{C}$H$_3$) ppm. FT-IR

(KBr): 3553 (m), 3267 (m), 2957 (m), 2912 (m), 2874 (m, sh), 1737 (vw), 1597 (s, *v*C=O), 1483 (m), 1433 (s), 1400 (w, sh), 1388 (m), 1365 (m), 1337 (vw), 1292 (w), 1230 (m), 1198 (w), 1098 (s), 1065 (vw, sh), 968 (m), 893 (w), 865 (m), 813 (vw), 777 (vw), 734 (m), 694 (vw), 636 (m), 565 (vw), 548 (vw), 521 (w) cm^{-1}. Anal. Calcd. for $C_{18}H_{30}N_4O_2$: C, 64.64; H, 9.04; N, 16.75. Found: C, 64.45; H, 8.96; N, 16.55. MS (EI) *m/z* 334 {M^+, 100 %}. Mp 187 °C.

1,5-dimethyl-3-(2,5-dihydroxyphenyl)-6-oxoverdazyl (2.30). To a stirred solution of **2.25** (210 mg, 0.88 mmol) in methanol (20 mL) was added $NaIO_4$ (285 mg, 1.26 mmol). The mixture was vigorously stirred for 15 min during which time the solution became a deep violet. The solution was then filtered to give **2.30** as a fluffy copper solid, yield 130 mg (63 %). The product can be further purified by recrystallization from EtOAc / diethylether to give a deep purple microcrystalline solid. EPR (CH_2Cl_2, 298K): $a(N_{1,5})$ = 5.3, $a(N_{2,4})$ = 6.5, and $a(CH_3)$ = 5.3 Gauss. FT-IR (KBr): 3323 (m, br), 2946 (vw), 1694 (m, sh), 1668 (s, *v*C=O), 1626 (w, sh), 1592 (w), 1488 (m), 1424 (w), 1406 (w), 1380 (vw), 1337 (w), 1299 (w), 1232 (m, sh), 1220 (m), 1132 (vw), 1031 (vw), 974 (vw), 957 (vw), 896 (vw), 880 (vw), 824 (vw), 789 (w), 762 (vw), 735 (vw), 711 (w), 674 (w), 640 (vw, br), 567 (vw), 545 (w), 512 (vw), 476 (vw) cm^{-1}. Anal. Calcd. for $C_{10}H_{11}N_4O_3$: C, 51.06; H, 4.71; N, 23.82. Found: C, 50.83; H, 5.11; N, 23.49. λ_{max} (CH_2Cl_2) ($\varepsilon(M^{-1}cm^{-1})$): 418 nm (800). MS (LSIMS) *m/z* 236 {MH^+, 99%}, 235 {M^+, 100 %}. Mp 133-135 °C.

1,5-dimethyl-3-(2,3-dihydroxyphenyl)-6-oxoverdazyl (2.31). To a stirred solution of **2.26** (100 mg, 0.42 mmol) in methanol (20 mL) was added Ag_2O (146 mg, 0.63 mmol). The mixture was vigorously stirred in the dark for 4h during which time the solution became deep violet. The solution was then filtered to remove the silver metal before the solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2, EtOAc) gave **2.31** as a bright violet powder, yield 68 mg (68 %). EPR (CH_2Cl_2, 298K): $a(N_{1,5})$ = 5.3, $a(N_{2,4})$ = 6.5, and $a(CH_3)$ = 5.3 Gauss. FT-IR (KBr): 3381 (m), 3150 (w, br), 2940 (vw), 1673 (s, νC=O), 1587 (w), 1500 (vw), 1475 (vw), 1405 (w), 1370 (w), 1299 (vw), 1238 (m), 1174 (vw), 1047 (vw), 993 (vw), 954 (vw), 889 (vw), 832 (vw), 790 (vw), 735 (w), 710 (vw), 685 (vw), 615 (vw), 539 (w) cm^{-1}. Anal. Calcd. for $C_{10}H_{11}N_4O_3$: C, 51.06; H, 4.71; N, 23.82. Found: C, 51.10; H, 4.98; N, 23.64. λ_{max} (CH_2Cl_2) ($\varepsilon(M^{-1}cm^{-1})$): 419 nm (900). MS (EI) *m/z* 235 {M^+, 90 %}, 43 {$NNCH_3^+$, 100%}. Mp 118 °C.

1,5-dimethyl-3-(3,4-dihydroxyphenyl)-6-oxoverdazyl (2.32). To a stirred solution of **2.27** (200 mg, 0.84 mmol) in methanol (20 mL) was added Ag_2O (292 mg, 1.26 mmol). The mixture was vigorously stirred in the dark for 4h during which time the solution became a deep violet. The solution was then filtered to remove the silver metal, diluted into diethylether (100 mL) and washed with distilled water (3 x 30 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give **2.32** as a violet powder, yield 134 mg (68 %). Further purification by flash chromatography (SiO_2, EtOAc) gave an analytically pure sample of **2.32**. EPR (CH_2Cl_2, 298K): $a(N_{1,5})$ = 5.3, $a(N_{2,4})$ = 6.5, and $a(CH_3)$ = 5.3 Gauss. FT-IR (KBr): 3421 (s, br), 3258 (m, br), 2950 (vw), 2923 (vw), 2850 (vw, sh), 1650 (s, νC=O), 1615 (m), 1529 (w), 1447 (w), 1427 (w), 1402 (w), 1372 (w), 1328 (vw), 1302 (vw), 1275 (m), 1257 (vw), 1239 (w), 1188 (vw), 1173 (w), 1124 (vw), 1105 (w), 1053 (vw), 1028 (vw), 970 (vw), 895 (vw), 870 (vw), 825 (vw), 795 (vw), 764 (vw), 742 (vw), 719 (vw), 684 (w), 617 (vw), 592 (vw), 544 (w), 534 (w) cm^{-1}. Anal. Calcd. for $C_{10}H_{11}N_4O_3$: C, 51.06; H, 4.71; N, 23.82. Found: C, 51.37; H, 4.96; N, 23.84. λ_{max} (CH_2Cl_2) (ε($M^{-1}cm^{-1}$)): 419 nm (1000). MS (LSIMS) *m/z* 235 {M$^+$, 100 %}. Mp 122 °C.

1,5-dimethyl-3-(3,4-dihydroxy-5-methoxyphenyl)-6-oxoverdazyl (2.33). To a stirred solution of **2.28** (100 mg, 0.37 mmol) in methanol (15 mL) was added Ag_2O (130 mg, 0.56 mmol). The mixture was vigorously stirred in the dark for 4h during which time the solution became deep violet. The solution was then filtered to remove the silver metal, diluted into diethylether (50 mL) and washed with distilled water (3 x 20 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give **2.33** as a violet powder, yield 60 mg (61 %). EPR (CH_2Cl_2, 298K): $a(N_{1,5})$ = 5.3, $a(N_{2,4})$ = 6.5, and $a(CH_3)$ = 5.3 Gauss. FT-IR (KBr): 3480 (m), 3293 (m, br), 3000 (vw), 2962 (w), 2926 (w), 2853 (vw), 1667 (s, νC=O), 1612 (m), 1536 (w), 1518 (w), 1462 (m), 1419 (m), 1403 (vw), 1376 (m), 1352 (vw, sh), 1326 (m), 1261 (m), 1231 (m), 1207 (m), 1080 (s), 982 (w), 947 (vw), 852 (vw), 839 (vw, sh), 802 (w), 717 (vw), 693 (w), 660 (vw), 642 (vw), 609 (vw), 552 (w), 536 (vw), 510 (vw, sh) cm^{-1}. λ_{max} (CH_2Cl_2) (ε($M^{-1}cm^{-1}$)): 416 nm (1000). High-res MS (EI) *m/z* 265.0937 {M$^+$, 56 %}, Calcd. for $C_{11}H_{16}N_4O_4$ 265.0937. Mp 129 °C.

1,5-dimethyl-3-(3,5-di-*tertiary*-butyl-4-hydroxyphenyl)-6-oxoverdazyl (2.34). To a stirred solution of **2.29** (200 mg, 0.6 mmol) in methanol (20 mL) was added $NaIO_4$ (192 mg, 0.9 mmol) as a solid. The mixture was vigorously stirred for 0.5 h during which time the solution became deep purple. The solution was then filtered to remove any insoluble materials before the solvent was removed under reduced pressure. Purification by column chromatography (SiO_2, EtOAc) gave **2.34** as a dark purple powder, yield 151 mg (76 %). EPR (CH_2Cl_2, 298K): $a(N_{1,5}) = 5.3$, $a(N_{2,4}) = 6.5$, and $a(CH_3) = 5.3$ Gauss. FT-IR (KBr): 3565 (m), 2957 (m), 2949 (vw, sh), 2874 (vw, sh), 1677 (s, νC=O), 1601 (vw), 1440 (w, br), 1397 (m), 1343 (w), 1299 (w), 1242 (w, sh), 1238 (m), 1201 (vw), 1158 (vw), 1112 (m), 1043 (vw), 1023 (vw), 972 (vw), 931 (vw), 902 (vw), 888 (vw), 810 (vw), 774 (vw), 756 (vw), 717 (vw), 693 (w), 652 (vw), 532 (w) cm^{-1}. Anal. Calcd. for $C_{18}H_{27}N_4O_2$: C, 65.23; H, 8.21; N, 16.90. Found: C, 65.39; H, 8.50; N, 16.76. λ_{max} (CH_2Cl_2) ($\varepsilon(M^{-1}cm^{-1})$): 422 nm (600). MS (LSIMS) *m/z* 331 {M^+, 100 %}. Mp 150-151 °C.

Attempted synthesis of M^{II}bis(4-(1,5-dimethyl-3-(3,4-semiquinonate)-6-oxoverdazyl) complexes (M = Mn, Fe, Co, Ni, or Cu) (2.37) To a stirred solution of **2.32** (60 mg, 0.26 mmol) in dry THF (10 mL) under Ar was added excess NaH. After the effervescence subsided, the solution was filter under Ar, and to the filtrate MX_2 (0.10 mmol, X = Cl or ClO_4) was added in one portion. The mixture was brought to reflux for up to 3 h. No colour changes were observed at any stage of the reaction. The mixture was allowed to cool and solvent was removed under vacuum to give what appeared to be a mixture of starting materials, which was supported by FTIR.

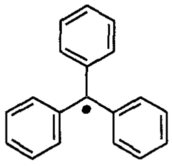
Attempted synthesis of bis(2,2'-dipyridyl)M^{II}(4-(1,5-dimethyl-3-(3,4-catacholate)-6-oxoverdazyl) complexes (M = Mn, Fe, Co, or Cu) (2.38) To a stirred solution of **2.32** (60 mg, 0.26 mmol) in dry THF (10 mL) under Ar was added excess NaH. After the effervescence subsided, the solution was filter under Ar, and to the filtrate $M(bipy)_2X_2$ or $M(CTH)X_2$ (0.25 mmol, X = Cl or ClO_4) was added in one portion as a solid or as a CH_2Cl_2 or acetonitrile solution. The mixture was brought to reflux for up to 3 h. No colour changes were observed at any stage of the reaction. The mixture was allowed to cool and solvent was removed under vacuum to give what appeared to be a mixture of starting materials, which was supported by FTIR.

Chapter 3

Synthetic Efforts Towards Tris(4-pyridyl)methyl Radicals

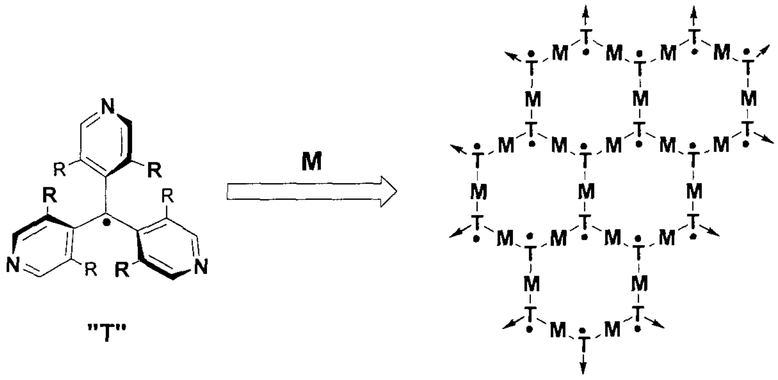
3.1 Introduction

The triphenylmethyl, or trityl, radical (**3.1**) was first reported in 1900 and has the distinction of being the first organic free radical to be discovered. This radical consists of a trivalent carbon bound to three phenyl rings. The phenyl rings act to stabilize the unpaired electron through a combination of resonance delocalization and steric bulk. Yet, this first trityl radical is better considered persistent than stable.



3.1

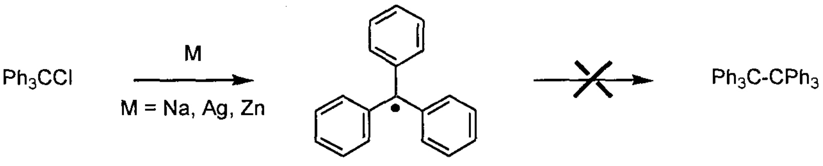
Since their initial discovery, much work has been dedicated to placing different substituents onto the aromatic rings. Inadvertently, this has led to the discovery of many new trityl derivatives that are truly stable. Other groups have synthesized and studied a host of trityl-based polyradicals. Beyond this, little work has been dedicated to expanding the available chemistry of the trityl radical towards facilitating strong interactions of its unpaired electron with other substrates. This chapter describes the efforts towards the synthesis of tripyridylmethyl radicals with the intention of utilizing the pyridyl nitrogen as a way of making interactions possible between the unpaired electron of the trityl radical and another spin carrier. As shown below, this also may act as a building block towards extended, multi dimensional structures.



3.2 Triarylmethyl Radicals

3.2.1 Synthesis

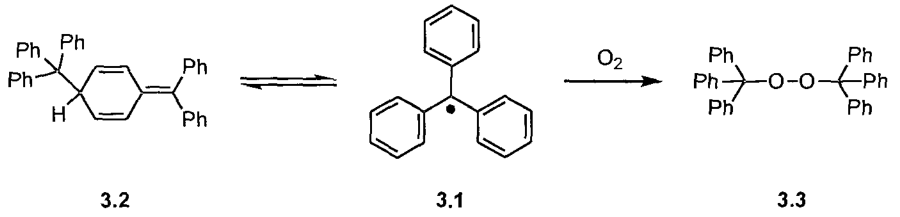
In his 1900 paper, Moses Gomberg described the formation of what he thought was a trivalent carbon species from failed attempts to synthesize hexaphenylethane by reacting triphenylmethyl halides with certain reducing metals (Scheme 3.1).[73]



3.1

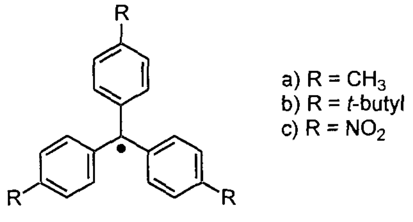
Scheme 3.1 Synthesis of triphenylmethyl radical **3.1**

Though persistent, the first trityl radicals were far from being considered stable. In concentrated solutions, they form unsymmetric *para*-methyl dimers (**3.2**) as was finally proven through NMR studies seventy-four years after their initial discovery.[74] Upon exposure to oxygen, they are prone to forming symmetric peroxide dimers (**3.3**) (Scheme 3.2).



Scheme 3.2 Decomposition products formed from trityl radical **3.1**

Dimerization to form *para*-methyl dimer **3.2** can be prevented by using blocking groups in the *para* positions (Figure 3.1). However, these derivatives (**3.4**) are still prone to attack from small molecules and, as a result, still form peroxide dimers analogous to structure **3.3** upon exposure to air.

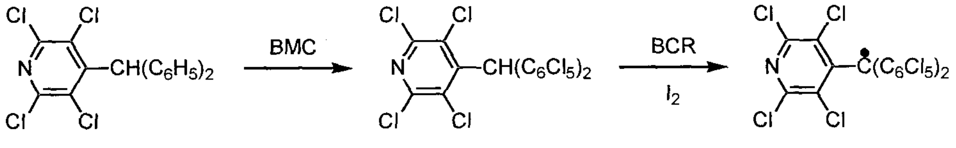


3.4

Figure 3.1 Trityl radicals **3.4** with blocking groups in *para* positions

Another modification to the trityl structure that greatly enhanced stability compared to the parent system was the addition of *ortho* substituents. This has been achieved with perchloro[75], polychloro[76] and polymethoxy[77] derivatives. The degree of coplanarity between the phenyl rings is further reduced. This gives the molecule a more pronounced propeller shape with each ring twisted 50 – 60° out of the plane compared to the 35° twist angle observed in the unsubstituted parent system. The degree to which the unpaired electron can reside on the *para* positions is reduced and therefore *para*-methyl dimerization is prevented. This negates the requirement of having blocking groups on the *para* positions. The reduction in resonance stabilization is countered by the six *ortho* substituents that effectively form a protective cage around the central methyl carbon, shrouding it from attack by small molecules like oxygen.[75,77]

The sterically crowded triarylmethyl radicals are typically made by one of three general synthetic routes. The first utilizes unsubstituted triarylmethyl as a starting material followed by rigorous chlorination with BMC reagent (SO_2Cl_2, $AlCl_3$, and S_2Cl_2).[78] This yields perchlorinated triarylmethanes that can be converted to the respective triarylmethyl radicals as mentioned previously for other polychlorinated derivatives. This is a useful method for making sterically crowded radicals, or polyradicals, which may not be easy to make directly. Julia and Ballester have used this approach to synthesize perchlorinated triarylmethyl radicals that contain a 4-pyridyl ring (Scheme 3.3).[79] The stability of these radicals is comparable to the non-heteroaromatic ring containing radicals.

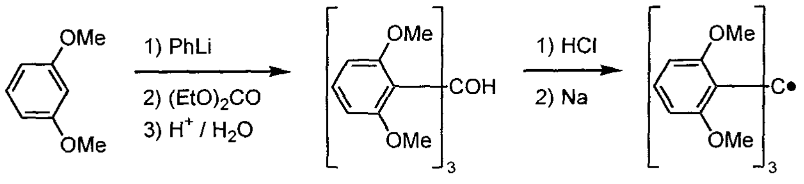


3.5 **3.6** **3.7**

Scheme 3.3 Synthesis of perchlorodiphenyl(4-pyridyl)methyl radical **3.7**

The second route utilizes organolithium or organomagnesium chemistry, which allows for the use of a wide range of substituted aromatics. In 1964, Martin and Smith reported the first synthesis of triarylmethanol **3.8,** prepared from 2,6-

dimethoxyphenyllithium and diethyl carbonate (Scheme 3.4).[80] Because the synthesis starts from a bulky aryl substrate, forcing conditions are required to insert all three rings. This requires a three-day reflux in benzene / Et_2O (3:1) to reach completion. Many derivatives have since been prepared based on this general route.

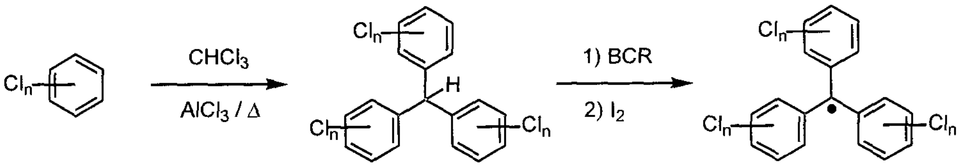


3.8 **3.9**

Scheme 3.4 Synthesis of triarylmethyl radical **3.9**

Conversion of the triarylmethanol **3.8** to the corresponding radical **3.9** was achieved through formation of a triarylmethyl cation followed by a one-electron reduction. Triarylmethanol **3.8** is treated with concentrated HCl to give a triarylmethyl chloride, which can be reduced with an alkali metal (Scheme 3.4). This is also possible with other Lewis acid / reducing agent combinations such as BF_3•Et_2O with $SnCl_2$.[81]

In 1986, Ballester *et al.*, synthesized highly crowded polychlorinated triarylmethanes via a Friedel-Crafts alkylation (Scheme 3.5).[82] This reaction requires high temperatures and a sealed pressure vessel to drive the reaction to completion. The reaction of a chlorinated benzene with chloroform in $AlCl_3$ gives either mono, di, or tri(polychlorophenyl) methane depending on the relative proportions of the aryl group to chloroform. Thus, methane **3.10** can be symmetric or made with three differently chlorinated rings. The advantages to this approach over previously mentioned routes are: short reaction times (< 4 h), high yields (65 – 95 %), and ease of purification.



3.10 **3.11**

Scheme 3.5 Friedel-Crafts synthesis of tris(polychlorophenyl) methane **3.10** and oxidation to radical **3.11**

Perchlorinated triarylmethane **3.10** is oxidized to radicals **3.11** through a conventional two-step process.[83] **3.10** is first treated with BCR reagent (NaOH, DMSO and diethylether) to give a carbanion, which is then oxidized with I_2 to give radical **3.11**. Yields are typically 60 – 80 %. A modified method has more recently been developed by Veciana *et al.* for oxidation of both perchlorinated and polychlorinated triarylmethanes.[76] Aqueous tetrabutylammonium hydroxide in THF is used to form the carbanion, which is oxidized with *p*-chloronil to the radical.

3.2.2 Properties of Triphenylmethyl Radicals

The EPR spectra of triphenylmethyl radicals are typically quite complex and depend on the substituents present on the phenyl rings. The SOMOs of both the parent radical and an *ortho*-substituted radical are shown in Figure 3.2. Relative spin densities were determined from EPR spectra and have been supported with molecular orbital calculations.[76,84] In the unsubstituted parent radical **3.1**, hyperfine coupling constants are $a(\mathrm{H}_{\mathrm{para}}) = 2.75$, $a(\mathrm{H}_{\mathrm{ortho}}) = 2.53$, and $a(\mathrm{H}_{\mathrm{meta}}) = 1.11$ Gauss.[84] This approximate values for the coupling constants and the trend, where $a(\mathrm{H}_{\mathrm{para}}) > a(\mathrm{H}_{\mathrm{ortho}}) >> a(\mathrm{H}_{\mathrm{meta}})$, follows for most radicals of this type. The central methyl carbon bears most of the spin density with $a(^{13}C) = 23.5$ Gauss.

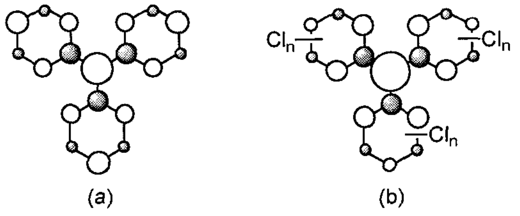


Figure 3.2 The SOMOs of (a) parent radical (**3.1**) and (b) *ortho*-substituted triarylmethyl radicals (**3.11**)

Heavily substituted triarylmethyl radicals are difficult to compare to their unsubstituted counterparts due to substituent effects and a lack of available hydrogens from which to determine hyperfine constants. EPR of ^{13}C labeled radicals have shown a slight reduction in spin density on the *para* position and an increase on the central methyl carbon with $a(^{13}C) \approx 30$ Gauss.[76,84] This is also the case for *ortho* substituted radicals and explains why *para*-methyl dimers are not as likely to form. In polychlorinated derivatives, $a(H_{para}) = 1.9$ Gauss with less drastic changes for the other ring protons: $a(H_{ortho}) = 2.2$, and $a(H_{meta}) = 1.2$ Gauss.[76]

3.3 Tripyridylmethyl Radicals

Until now, the majority of alterations to the trityl structure have enhanced its stability relative to the unsubstituted parent system (**3.1**) with the use of steric bulk. This prohibits magnetic or chemical interactions, limiting the properties and possible future applications of this radical. How can its structure be altered to expand available chemistry but, at the same time, maintain its properties as a stable free radical? Our choice was to replace the phenyl rings with pyridine rings. A nitrogen atom at the *para* position from the central methyl carbon may facilitate a range of intermolecular interactions from simple hydrogen bonding to metal ion coordination. This would open the door to new chemistry and many new properties that have not been explored with the trityl radical.

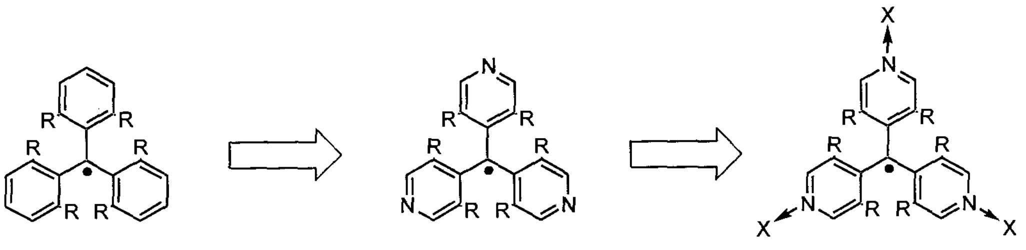
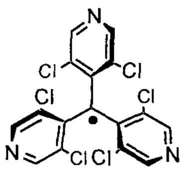


Figure 3.3 The use of pyridyl groups to expand the chemistry of the trityl radical

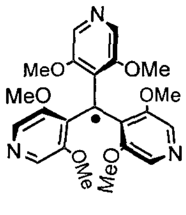
3.4 Results and Discussion

3.4.1 General Methodology

The most commonly used ring substituents in sterically crowded triarylmethyl derivatives have been chloro or methoxy groups. Therefore, we followed literature precedent in attempts to make tris(2,6-disubstituted-4-pyridyl)methyl radicals with either chloro (**3.12**) or methoxy substituents (**3.13**).



3.12



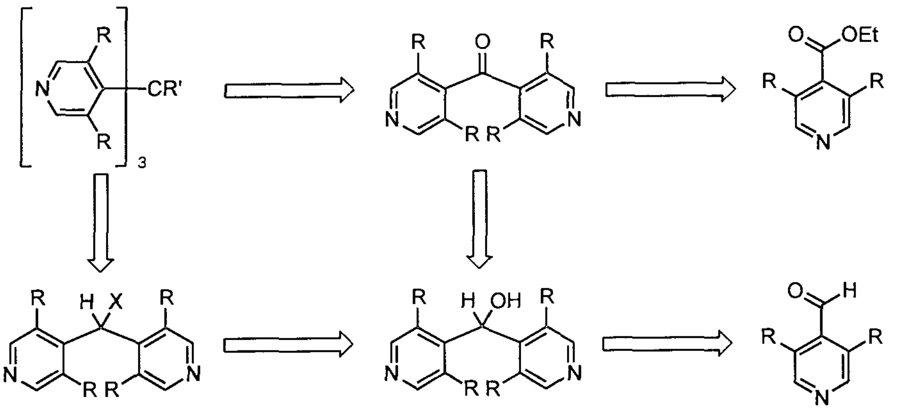
3.13

Figure 3.4 Target trityl radicals **3.12** and **3.13**

Other methods that have been used successfully for triphenylmethyl were not explored for several reasons. Pyridine is an electron-poor π-system so it does not undergo Friedel-Crafts chemistry. This is especially true when the ring is further deactivated by several chlorine substituents. Rigorous chlorination of an unsubstituted tripyridylmethane was also not investigated because it would likely also put chlorine groups in the positions *ortho* to the pyridyl nitrogens. This would effectively block the nitrogen and hinder any subsequent coordination chemistry.

Our initial synthetic approach towards sterically hindered tris(4-pyridyl)methanols was via a "one pot" method analogous to that used by Martin and Smith to make triarylmethanol **3.9** (Scheme 3.4). This entailed addition of an appropriate electrophile to three (or a slight excess) equivalents of 2,6-disubstituted-4-pyridyllithium. With 3,5-dichloropyridine as the aryl substrate, reactions resulted in full decomposition. In the case of 3,5-dimethoxypyridine, only starting material and a small amount of ethyl 3,5-dichloropyridine-4-carboxylate **3.16** were isolated.

Because previous attempts did not yield the desired triarylmethanols, we decided to add each ring as a separate step. This would enable a better understanding what the problems are and how to get past them. A "piece by piece" approach requires the synthesis and characterization of different precursors: the first ring from an aryl ester or arylaldehyde, insertion of a second ring to give a diarylketone or a diarylmethanol, and finally insertion of a third ring to give a triarylmethyl radical precursor (Scheme 3.6).

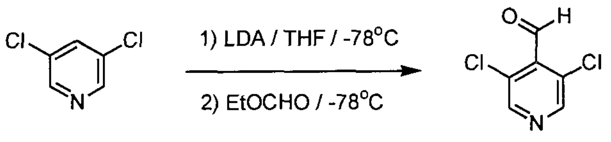


Scheme 3.6 Retrosynthetic analysis of the tris(2,6-disubstituted-4-pyridyl)methyl precursor

3.4.2 Aldehyde synthesis

Though aldehydes **3.14** and **3.15** had been reported previously in patent literature but no synthetic details were available. The synthesis of both compounds involved directed *ortho*-lithiation of a 3,5-disubstitutedpyridine substrate at low temperature followed by addition of ethyl formate as the electrophile.

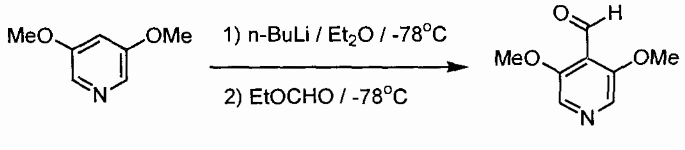
3,5-Dichloropyridine was lithiated according to a modified literature procedure.[85] The four position of the ring was lithiated with LDA generated *in situ* from n-BuLi and diisopropylamine at low temperature. Treatment of the cold lithium salt with ethyl formate gave the crude aldehyde **3.14** (Scheme 3.7). Purification by column chromatography gave **3.14** as an off-white crystalline solid in 71 % yield.



3.14

Scheme 3.7 Synthesis of 3,5-dichloropyridine-4-carboxaldehyde **3.14**

Aldehyde **3.15** was similarly prepared from 3,5-Dimethoxypyridine (Scheme 3.8). Lithiation in this case was with *n*-BuLi at low temperature. Treatment with ethyl formate gave crude **3.15** that was purified by column chromatography, yield 43 %.

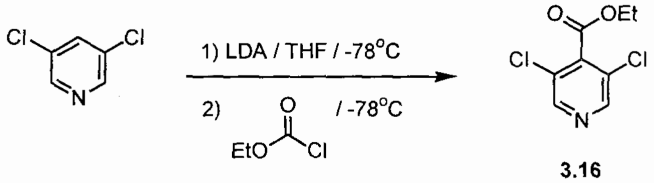


3.15

Scheme 3.8 Synthesis of 3,5-dimethoxypyridine-4-carboxaldehyde **3.15**

3.4.3 *Ester synthesis*

Ester **3.16** was synthesized in a manner similar to the aldehydes mentioned in the previous section. Low temperature lithiation at the four position of 3,5-dichloropyridine with LDA followed by addition of ethyl chloroformate gave the crude ester **3.16** (Scheme 3.9). **3.16** was purified by column chromatography, yield 80 %.



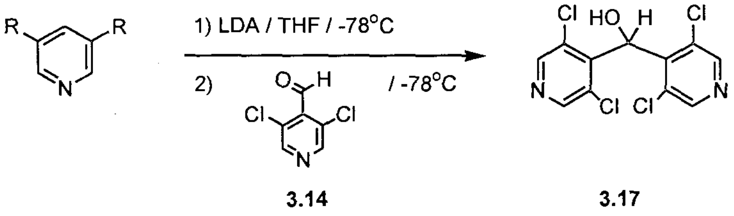
3.16

Scheme 3.9 Synthesis of ethyl 3,5-dichloropyridine-4-carboxylate **3.16**

3.4.4 *Alcohol synthesis*

Bis(2,6-dichloro-4-pyridyl)methanol **3.17** was synthesized as a possible precursor to both bis(2,6-dichloro-4-pyridyl)ketone **3.18** and tris(2,6-dichloro-4-pyridyl)methane.

3,5-Dichloropyridine was lithiated as mentioned in Section 3.3.2 before addition of aldehyde **3.14**. The crude product was purified by trituration with dichloromethane before being used in the next step. The final yield was 89 %.

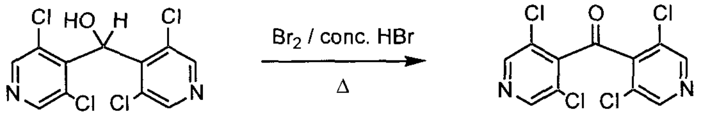


Scheme 3.10 Synthesis bis(2,6-dichloro-4-pyridyl)methanol **3.17**

3.4.5 Ketone synthesis

The synthesis of bis(2,6-dichloro-4-pyridyl)ketone **3.18** was initially attempted by two similar routes. The first involved combining two equivalents of the lithium salt of 3,5-dichloropyridine with an electrophile, such as diethyl carbonate, bis(trichloromethyl) carbonate, or ethyl chloroformate, at low temperature. The second route was the reaction of ester **3.16** with one equivalent of the lithium salt of 3,5-dichloropyridine at low temperature. Both of the aforementioned pathways gave the desired ketone but in very low yields (< 10 %). An explanation for this is that the 3,5-dichloropyridine anion decomposes when heated above approximately -10 °C. Because of the unfavourable steric bulk of both reactants, higher temperatures are required to drive the reaction.

In light of these problems, a third route was used that is more common for synthesis of ketones with bulky substituents and made use of the alcohol **3.17** discussed in the previous section. Alcohol **3.17** was oxidized with Br_2 in concentrated hydrobromic acid (Scheme 3.11). The conversion is very clean and gave ketone **3.18** in much higher overall yield. The yield of this reaction was 79 %.



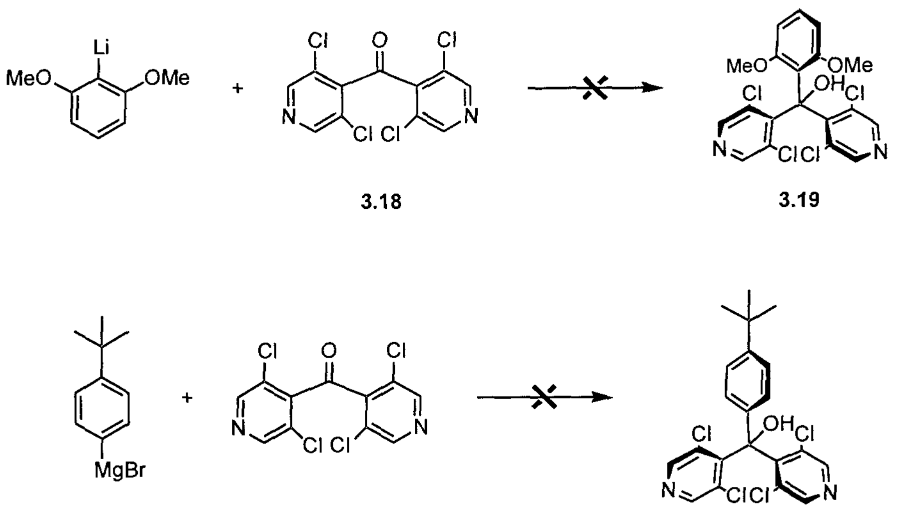
3.17

3.18

Scheme 3.11 Synthesis of bis(2,6-dichloro-4-pyridyl)ketone **3.18**

3.4.6 Attempted syntheses of tripyridylmethanols

Attempts to insert a third ring onto bis(2,6-dichloro-4-pyridyl)ketone **3.18** have so far been unsuccessful (Scheme3.12). These have included use of a bulky substrate, 2,6-dimethoxyphenyllithium, and a less sterically encumbered one, 4-*tert*-butylphenyl magnesium bromide. Reactions were carried out in refluxing toluene (or benzene) / Et$_2$O for several days. To increase the reactivity of the nucleophile, chelates, such as TMEDA and 12-crown-4, were used with no change to the reaction outcome. Upon work-up, most of the starting materials were recovered as verified by ^{1}H NMR.



3.18 3.19

3.18 3.20

Scheme 3.12 Attempted syntheses of methanols **3.19** and **3.20**

3.5 Conclusions

The goal of this project was the synthesis of a new class of 4-pyridyl containing triarylmethyl radicals. The one-pot approach, commonly used for similar molecules, did not yield the desired products. Attempts to make tris(2,6-dichloro-4-pyridyl)methanol likely failed due to the instability of the 2,6-dichloro-4-pyridyl anion used. High temperatures required to bring together three bulky substituents possibly resulted in decomposition through loss of LiCl and formation of a reactive benzyne-type intermediate.[86,87] In light of these discoveries, we decided to synthesize molecules that may be used to form the target one ring at a time. Using this more piecewise approach, 3,5-dichloropyridine-4-carboxaldehyde, ethyl 3,5-dichloropyridine-4-carboxylate and bis(2,6-dichloro-4-pyridyl)ketone were synthesized. Differences in the chemistry of pyridine compared to that of the parent triphenylmethyl chemistry is likely one of the major factors that has prevented both use a one-pot approach and insertion of a third ring onto dipyridylketone **3.18**.

The anion of 3,5-dimethoxypyridine has proven to be more stable though the one-pot approach has not yet worked in this case either. This has been due to difficulties in forming the 2,6-dimethoxy-4-pyridyl anion completely. Some preliminary work has been done towards complete lithiation and making the requisite building blocks.

There are still many options to be explored in the work towards tripyridylmethyl radicals. Because of the difficulties faced in adding a third ring onto dipyridylketone **3.18,** alternatives need to be considered. It is not known to what degree electronic factors have contributed to the low reactivity of **3.18**. Smaller nucleophiles may be more successfully inserted onto **3.18** and give insight into the problems faced so far. Other approaches may include increasing the reactivity of the carbonyl group of **3.18** using either, a Lewis acid catalyst or by using an N-oxide derivative of **3.18**. Synthesis of derivatives, such as a tosylate, of alcohol **3.17** would serve to readily form a diaryl carbocation that may increase the accessibility of the central methyl carbon to a neucleophile.

3.6 Experimental

3,5-dichloropyridine-4-carboxaldehyde (3.14). *n*-BuLi (20 mL of a 1.6M hexane solution, 32 mmol) was added dropwise to a stirred solution of diisopropylamine (4.5 mL, 32 mmol) and 3,5-dichloropyridine (4.7 g, 32 mmol) in THF (100 mL) at -78°C. The clear solution turned orange and turbid. Stirring was continued at low temperature for 2 h and then a solution of ethyl formate (2.6 mL, 32 mmol) in THF (20 mL) was added drop wise. The solution was allowed to reach room temperature, quenched with methanol, and diluted with distilled water (150 mL). The THF was evaporated under reduced pressure before the aqueous mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, CH_2Cl_2) to give **3.14** as a white crystalline solid, yield 3.998 g (71 %). ^1H NMR ($CDCl_3$): δ 10.29 (s, 1H, C$\underline{H}$O), 8.60 ppm (s, 2H, aryl). ^{13}C NMR ($CDCl_3$): δ (188.1, $\underline{C}$HO), (148.8, 141.8, 130.9, aryl) ppm. FT-IR (KBr): 3402 (vw), 3063 (vw), 3042 (vw), 2978 (vw), 2936 (vw), 2895 (vw), 2783 (vw), 2725 (vw), 1906 (vw), 1852 (vw), 1803 (vw), 1708 (s, *v*C=O), 1552 (vw), 1527(m), 1441 (vw), 1425 (vw), 1396 (s), 1247 (m), 1203 (w, sh), 1188 (s), 1137 (m), 1097 (s), 986 (vw), 952 (vw), 902 (m) 856 (m), 796 (m), 715 (w), 670 (m), 520 (w), 500 (w) cm^{-1}. Anal. Calcd. for $C_6H_3NOCl_2$: C, 40.95; H, 1.72; N, 7.96. Found: C, 40.76; H, 1.70; N, 7.63. MS (EI) *m/z* 176 {M^+, 100 %}. Mp 72 – 74 °C.

3,5-dimethoxypyridine-4-carboxaldehyde (3.15). *n*-BuLi (3.3 mL of a 1.6M hexane solution, 5.3 mmol) was added dropwise to a stirred solution of 3,5-dimethoxypyridine (440 mg, 3.2 mmol) and TMEDA (0.8 mL, 5.3 mmol) in diethylether (20 mL) at -78°C. The clear solution turned pale yellow and turbid. Stirring was continued as the solution was allowed to reach room temperature overnight. The temperature was returned to -78°C before a solution of ethyl formate (0.43 mL, 5.3 mmol) in diethylether (10 mL) was added drop wise. The solution was again allowed to reach room temperature before being quenched with methanol and diluted with distilled water (100 mL). The diethylether was removed and the aqueous mixture was further extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The residue was recrystallized from hot diethylether to give **3.15** as a fluffy white crystalline solid, yield 228 mg (43 %). ^1H NMR ($CDCl_3$): δ 10.50 (s, 1H, C$\underline{H}$O), 8.16 (s, 2H, aryl), 4.01 ppm (s, 6H, OC$\underline{H}_3$). ^{13}C NMR ($CDCl_3$): δ (189.4, $\underline{C}$HO), (155.9, 131.5, 108.9, aryl), (54.9, O$\underline{C}H_3$) ppm. FT-IR (KBr): 3081 (w), 3014 (w), 2963 (m), 2925 (m), 2878 (m), 2854 (m), 2784 (w), 1702 (s, *ν*C=O), 1577 (m), 1560 (m), 1475 (m), 1450 (m), 1432 (m), 1411 (m), 1305 (w), 1289 (s), 1235 (s), 1210 (w), 1176 (m), 1145 (w), 1124 (s), 1014 (w), 920 (w), 846 (w), 735 (vw), 706 (vw), 641 (vw), 562 (vw), 515 (w) cm^{-1}. Anal. Calcd. for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.12; H, 5.43; N, 8.14. MS (EI) *m/z* 167 {M^+, 35 %}, 138 {$(M\text{-}CHO)^+$, 100 %}. Mp 135 °C.

Ethyl 3,5-dichloropyridine-4-carboxylate (3.16). *n*-BuLi (16 mL of a 1.6M hexane solution, 25.6 mmol) was added dropwise to a stirred solution of diisopropylamine (3.6 mL, 25.6 mmol) and 3,5-dichloropyridine (3.8 g, 25.6 mmol) in THF (mL) at -78°C. The clear solution turned orange and turbid. The solution was stirred at low temperature for 2 h before being transferred by canula to a solution of ethyl chloroformate (2.5 mL, 2.6 mmol) in THF (mL) at -78°C over a period of 0.5 h. The solution was then allowed to reach room temperature, quenched with methanol, neutralized, and diluted with distilled water (100 mL). The THF was evaporated under reduced pressure before the aqueous mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure.

Purification by column chromatography (SiO_2, CH_2Cl_2) afforded **3.16** as a pale yellow oil, yield 4.5 g (80 %). ^1H NMR ($CDCl_3$): δ 8.53 (s, 2H, aryl), 4.48 (q, 2H, J = 7 Hz, $C\underline{H}_2$), 1.41 ppm (t, 3H, J = 7 Hz, $C\underline{H}_3$). ^{13}C NMR ($CDCl_3$): δ (162.7, $\underline{C}OOEt$), (147.8, 140.2, 128.8, aryl), (63.2, $\underline{C}H_2$), (14.3, $\underline{C}H_3$) ppm. FT-IR (neat film): 3470 (vw), 3050 (w), 2983 (m), 2937 (w), 2873 (w), 1869 (vw), 1813 (vw), 1747 (s, νC=O), 1587 (vw), 1560 (m), 1533 (m), 1466 (m), 1446 (m), 1415 (m), 1399 (w, sh), 1390 (m), 1367 (m), 1275 (s, br), 1231 (m), 1200 (w, sh), 1186 (s), 1120 (m), 1095 (m), 1080 (m), 1012 (m), 935 (vw), 884 (m), 826 (m), 811 (w, sh), 790 (vw), 759 (w), 738 (w), 691 (m), 654 (w), 593 (w) cm^{-1}. Anal. calcd. for $C_8H_7NO_2Cl_2$: C, 43.67; H, 3.21; N, 6.37. Found: C, 43.90; H, 3.01; N, 6.64. MS (EI) *m/z* 219 {M^+, 37 %}, 174 {$(M-OEt)^+$, 100%}.

Bis(2,6-dichloro-4-pyridyl)methanol (3.17). *n*-BuLi (20 mL of a 1.6M hexane solution, 32 mmol) was added dropwise to a stirred solution of diisopropylamine (4.6 mL, 32 mmol) and 3,5-dichloropyridine (4.74 g, 32 mmol) in THF (100 mL) at -78°C. The clear solution turned orange and turbid. Stirring was continued at low temperature for 2 h before the solution was transferred by canula to a solution of 3,5-dichloropyridine-4-carboxaldehyde **3.14** (5.64 g, 32 mmol) in THF (60 mL) at -78°C over a period of 0.5 h. The solution was then allowed to reach room temperature, quenched with methanol, neutralized, and diluted with distilled water (150 mL). The THF was evaporated under reduced pressure before the aqueous mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude white powder was washed with CH_2Cl_2 before being used in the preparation of **3.17**. Purity of the off-white powder was sufficient for elemental analysis, yield 9.27 g (89 %). ^{1}H NMR (DMSO-d_6): δ 8.60 (s, 4H, aryl), 6.86 (d, 1H, *J* = 6 Hz, O<u>H</u>), 6.55 ppm (d, 1H, *J* = 6 Hz, C<u>H</u>). ^{13}C NMR (DMSO-d_6): δ (148.9, 143.5, 131.5, aryl), (70.6, <u>C</u>HOH) ppm. FT-IR (KBr): 3130 (s, br, *ν*O-H), 2847 (m, sh), 2741 (w, sh), 2726 (m, sh), 2637 (vw, sh), 2516 (vw, sh), 2434 (vw, sh), 1869 (vw), 1822 (vw), 1775 (vw), 1705 (vw), 1626 (vw, br), 1563 (vw, sh), 1556 (w), 1520 (m), 1436 (w), 1396 (s), 1381 (s), 1348 (w), 1302 (w), 1235 (m), 1214 (s), 1149 (w), 1138 (w), 1103 (s), 1068 (w), 934 (w), 890 (m), 845 (m), 805 (m), 787 (m), 756 (w), 733 (w), 675 (w), 646 (s), 600 (w), 528 (w), 483 (vw) cm^{-1}. Anal. calcd. for $C_{11}H_6N_2OCl_4$: C, 40.78; H, 1.87; N, 8.65. Found: C, 40.71; H, 1.59; N, 8.77. MS (EI): *m/z* 324 {M$^+$, 83 %}, 176 {(M–H–Cl$_2$py)$^+$, 100 %}. Mp: >140 °C (decomp.).

Bis(2,6-dichloro-4-pyridyl)ketone (3.18). Bromine (1.0 g, 6.3 mmol) was added to a suspension of bis(2,6-dichloro-4-pyridyl)methanol **3.17** (2.0 g, 6.2 mmol) in concentrated aqueous hydrobromic acid (15 mL). The mixture was refluxed overnight, cooled to room temperature, and slowly neutralized with 3M NaOH. The crude product was isolated by vacuum filtration then purified by column chromatography (SiO_2, CH_2Cl_2) to give **3.18** as a fluffy white microcrystalline solid, yield 1.6 g (79 %). ^{1}H NMR ($CDCl_3$): δ 8.59 ppm (s, aryl). ^{13}C NMR ($CDCl_3$): δ (186.0, <u>C</u>=O), (149.0, 141.6, 129.9, aryl) ppm. FT-IR (KBr): 3243 (m, br), 3132 (m), 3050 (w), 2977 (m), 2724 (vw), 2428 (vw), 1888 (vw), 1832 (vw), 1770 (vw), 1743 (vw), 1705 (s, *ν*C=O), 1678 (m), 1642 (w), 1561 (vw), 1522 (m), 1505 (m), 1436 (vw), 1395 (s), 1336 (vw), 1327 (vw), 1296 (vw), 1255 (s), 1227 (s), 1211 (m), 1194 (s), 1162 (vw), 1101 (s), 1036 (s), 934 (w), 887 (m), 873 (w), 827 (s), 803 (w), 789 (w), 772 (vw), 757 (vw), 730 (w), 699 (vw), 663 (s), 614 (w), 588 (w), 524 (vw), 497 (w), 474 (w) cm^{-1}. Anal. calcd. for $C_{11}H_4N_2OCl_4$: C, 41.03; H, 1.25; N, 8.70. Found: C, 41.37; H, 1.09; N, 8.43. MS (EI) *m/z* 322 {M$^+$, 3 %}, 294 {(M–CO)$^+$, 100 %}. Mp 141 °C.

Attempted synthesis of Bis(2,6-dichloro-4-pyridyl)(2,6-dimethoxyphenyl)methanol (3.19). n-BuLi (0.97 mL of a 1.6M hexane solution, 1.6 mmol) was added dropwise to a stirred 3,5-dimethoxybenzene (0.2 g, 1.6 mmol) in diethylether (15 mL) at -78°C. The clear solution turned pale yellow and turbid. Stirring was continued at low temperature for 2 h to overnight before bis(2,6-dichloro-4-pyridyl)ketone **3.18** (0.5 g, 1.6 mmol) in toluene (60 mL) was added dropwise. The solution was then allowed to reach room temperature before being brought to reflux for several days. It was then allowed to cool, quenched with methanol, neutralized, and extracted with distilled water (150 mL). The organic layer was removed and the aqueous further extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The experiment was also repeated with TMEDA present. ^{1}H NMR revealed that in all cases only starting materials were present.

Attempted synthesis of Bis(2,6-dichloro-4-pyridyl)(4-*tertiary*-butylphenyl)methanol (3.20). 5 mL of a 4-bromo-*tertiary*-butylbenzene (0.34 g, 1.6 mmol) solution in diethylether (30 mL) was added to magnesium filings (45 mg, 1.9 mmol) along with a crystal of I_2. The solution was heated gently and, once the reaction was initiated, the remaining 4-bromo-*tertiary*-butylbenzene solution was added dropwise. The solution was stirred for 3 h and heated as required. bis(2,6-dichloro-4-pyridyl)ketone **3.18** (0.5 g, 1.6 mmol) in toluene (60 mL) was added dropwise. The solution was then allowed to reach room temperature before being brought to reflux for several days. It was then allowed to cool, quenched with methanol, neutralized, and extracted with distilled water (150 mL). The organic layer was removed and the aqueous further extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. ^1H NMR revealed that in all cases only starting materials were present.

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