The application of semiconductors as oxidants in synthetic organic chemistry

By

Vineet Jeena

A thesis submitted in fulfillment of the requirements for the degree of

Doctor of Philosophy

Department of Chemistry

University of KwaZulu-Natal

Pietermaritzburg

January 2012

Thesis Declaration

The experimental work described in this thesis was carried out in the School of Chemistry, University of KwaZulu-Natal in Pietermaritzburg, South Africa under the supervision of Professor Ross S. Robinson. The studies represent original work by the author and have not been submitted in candidature for any other degree.

Signed……. V. Jeena (Candidate)

I hereby certify that the above statement is correct.

Signed…… Professor Ross S. Robinson (Supervisor)

School of Chemistry

University of KwaZulu-Natal

Pietermaritzburg

South Africa

January 2012

Publication Declaration

The experimental work discussed in the publications as well as the writing of the publications was performed by myself and was carried out within the School of Chemistry, University of KwaZulu-Natal, Pietermaritzburg, under the supervision of Professor Ross S. Robinson. I was the primary author for the publications 1 to 3 and minor grammatical changes were performed at a later stage under the suggestion of my research supervisor. Titles and full literature references for these publications are as follows.

1. *Convenient photooxidation of alcohols using dye sensitised zinc oxide in combination with silver nitrate and TEMPO,* Jeena, V.; Robinson, R. S. *Chem. Commun.* **2012,** *48,* 299–301.
2. *Convenient photooxidation of alcohols using dye sensitised zinc oxide in combination with silver nitrate and TEMPO – an electron paramagnetic resonance study,* Jeena, V.; Robinson, R. S. Dalton Trans., DOI:10.1039/C2DT12030E.
3. *The use of diamondoids in the photocatalysed tandem synthesis of quinoxalines,* Jeena, V.; Robinson, R. S. article in preparation.

Signed……. V. Jeena (Candidate)

I hereby certify that the above statement is correct.

Signed…… Professor Ross S. Robinson (Supervisor)

School of Chemistry

University of KwaZulu-Natal

Pietermaritzburg

South Africa

January 2012

This thesis is dedicated to two very special people…my parents

Contents

Chapter 1: Introduction

Chapter 2: Discussion

Chapter 3: Electron paramagnetic resonance study

Chapter 4: The use of diamondoids in tandem coupling reactions

Chapter 5: Experimental

Acknowledgements

First and foremost, I wish to express my sincere gratitude to my supervisor Professor Ross S. Robinson for all his encouragement and guidance during the course of this project. I would also like to sincerely thank the following people:

- Dr Colin Southway for all his advice and help regarding GC analysis.
- Mr. Craig Grimmer for his expert advice on NMR spectroscopy, friendly words of support as well as taking the time to proofread this thesis.
- Mr. Shawn Ball for assisting with ordering of chemicals.
- Messrs Raj Somaru and Fayzel Shaik for technical assistance.
- Mrs. Caryl Janse van Rensburg for her advice on the GC/MS analysis and for proofreading this thesis.
- Messrs Paul Forder and Clarence Mortlock for providing, repairing and designing all the necessary glassware.
- Professor Rudolph Erasmus (University of the Witwatersrand, School of Physics) for the diffuse reflectance analysis.
- My colleagues in the Warren Research Laboratory for all their useful scientific discussions.

The National Research Foundation (NRF) of South Africa is gratefully acknowledged for providing a postgraduate bursary.

My deepest thanks go my mother and sister for all their support and patience during the course of this research project.

Finally, I'd like to thank god for giving me the strength to attempt and complete my doctoral degree.

Abbreviations

CH_3CN	acetonitrile
AR	alizarin red
Al_2O_3	aluminium oxide
CdS	cadmium sulfide
CdSe	cadmium selenide
CeO_2	cerium oxide
$ClSO_3H$	chlorosulfonic acid
iPr_2NEt	diisopropylethylamine
Me_2SO	dimethyl sulfoxide
$Ph_3P{=}CHCO_2Et$	(ethoxycarbonylmethylene)-triphenylphosphorane
Fe_2O_3	ferric oxide
$HCONH_2$	formamide
HCO_2H	formic acid
GaAs	gallium arsenide
GaP	gallium phosphide
HeLa S_3	human epithelial carcinoma cell line
H_2O_2	hydrogen peroxide
LDA	lithium diisopropylamide
$Ph_3P{=}CHCO_2Me$	methyl (triphenylphosphoranylidene)acetate
NHE	normal hydrogen electrode
$(COCl)_2$	oxalyl chloride
PivCl	pivaloyl chloride
PEG 400	polyethylene glycol 400
NaOAc	sodium acetate
NaHMDS	sodium hexamethyldisilazide
$Sn(OTf)_2$	stannous trifluoromethanesulfonate
H_2SO_4	sulfuric acid
TBDMS	*tert*-butyldimethylsilyl
TBSCl	*tert*-butyldimethylsilyl chloride
H_2TMP	tetramesityl porphyrin
TESCl	triethylsilyl chloride
TEA	triethylamine

TMSCl	trimethylsilyl chloride
Tr	trityl
WO_3	tungsten trioxide
ZnS	zinc sulfide

Abstract

Oxidation of alcohols is a vital transformation in synthetic organic chemistry as evidenced by their numerous applications in natural product synthesis. However, the traditional oxidants employ hazardous, toxic and malodorous reagents. A welcome addition to the field of alcohol oxidation is the emergence of tandem coupling reactions in which the oxidized alcohol is immediately trapped by an appropriate nucleophile.

In previous research within the group, the synthesis of quinoxalines using a photocatalyzed tandem coupling approach was demonstrated. However, an extension of this research to other tandem coupling reactions was unsuccessful due to the high redox potential of the active oxidizing species. Thus, the immediate goal of this project was to develop a photocatalyzed oxidative system that was selective and high yielding. The assembling of this photooxidative system began with the choice of TiO_2 and ZnO as the photocatalysts, Alizarin Red S as the dye, silver (I) ions as the electron acceptor and 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) as the active oxidizing species. A test reaction was conducted using the dye sensitized TiO_2/silver/TEMPO and dye sensitized ZnO/silver/TEMPO systems. While the dye sensitized ZnO system afforded a good yield the dye sensitized TiO_2 system produced only a trace amount of product. Thus, a full study was conducted on a range of alcohols using the developed dye sensitized ZnO system. In addition, the oxidation of alcohols using the dye sensitized ZnO system could also be scaled-up with notable success. The developed system was applied to a one-pot tandem Wittig reaction which unfortunately was unsuccessful. The dye sensitized ZnO/silver/TEMPO system was however successful when applied to a pseudo-tandem Wittig reaction.

Subsequently, an electron paramagnetic resonance (EPR) study was conducted using the dye sensitized TiO_2/silver/TEMPO and the dye sensitized ZnO/silver/TEMPO system. The results of the EPR study supported the proposed mechanism for the dye sensitized ZnO system and revealed a 'break' in the photooxidative chain for the dye sensitized TiO_2 system which accounted for the low yields obtained.

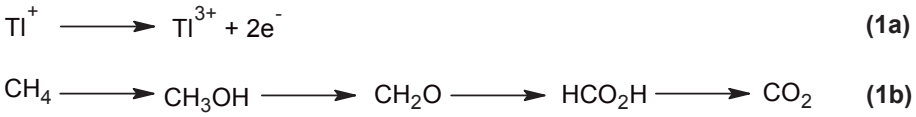
As part of our interest in developing new photocatalyzed oxidative systems, attention was directed towards the application of impure diamondoid powder as a potential tandem coupling reagent. Using the diamondoid powder, the synthesis of highly conjugated quinoxalines was effected in moderate to excellent yields.

Chapter 1

Introduction

1.1 Introduction to oxidation

Oxidation reactions are one of the most fundamental reactions in chemistry and offer an important methodology for the introduction and modification of functional groups.[1] Within the realm of inorganic chemistry, oxidation refers to the loss of one or more electrons (**Scheme 1a**) whilst in the realm of organic chemistry; oxidation refers to the replacement of hydrogen with a more electronegative atom, usually oxygen (**Scheme 1b**).[2]



Scheme 1

The annual global production of carbonyl derivatives constitutes over 10 million tons with the majority of these compounds arising from the oxidation of alcohols and alkyl arenes.[3,4] The importance of alcohol oxidation reactions is evident when examining the role of this transformation in natural product synthesis.

1.2 Alcohol oxidation in natural product synthesis

Auripyrones A and B (**Figure 1**) were isolated from the sea hare, *Dolabella auricularia*, from the *aplysiidae* family of marine opisthobranchs in 1996 by Yamada and co-workers.[5] Auripyrones A and B were found to exhibit activity against HeLa S_3 cells with IC_{50} values of 0.26 and 0.48 μg/ml respectively. Over the past few years, auripyrones have generated much interest with a number of total syntheses being reported. The first total synthesis and absolute stereochemistry of auripyrone A **1** was reported by Perkins and co-workers in 2006 using a biomimetic cyclization of an acyclic triketone, producing the spiroketal moiety.[6] In 2009, Jung and co-workers reported the total synthesis of auripyrone A in high chemical yield using a highly convergent approach.[7] In 2010, Kigoshi and co-workers reported the synthesis of auripyrones A and B as well as elucidating the absolute configuration of auripyrone B using an aldol reaction as a key synthetic step.[8]

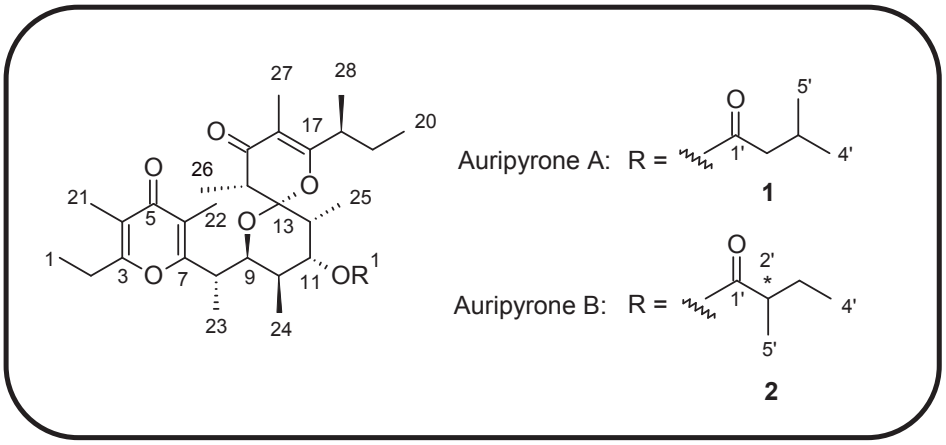
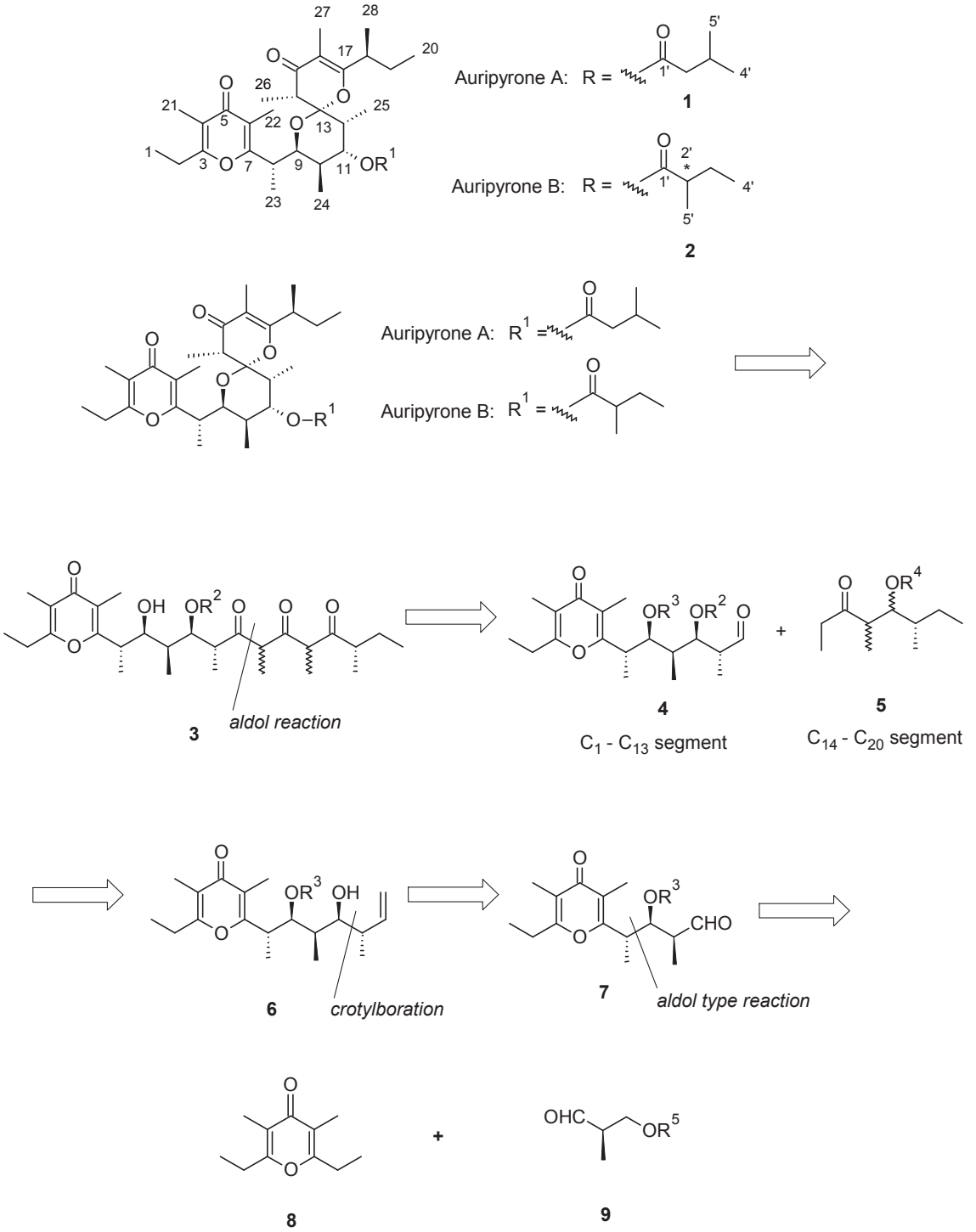


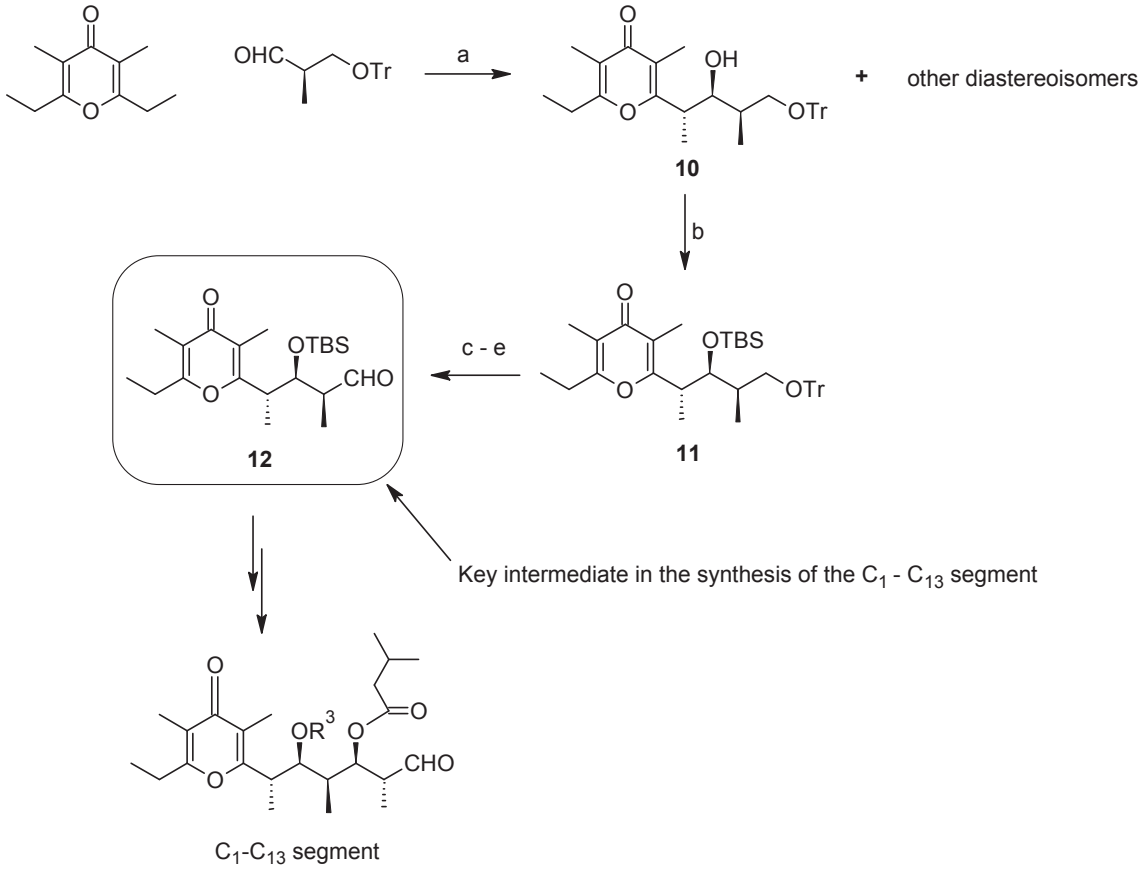
Figure 1

The retrosynthetic synthesis described by Kigoshi and co-workers is illustrated below (**Scheme 2**). Auripyrone A and B were envisaged to form *via* the triketone **3** which could in turn be formed by an aldol reaction between the C_1-C_{13} and C_{14}-C_{20} segments. The C_1-C_{13} segment **4** may be formed *via* crotylboration and diastereoselective aldol reaction between the pyrone **8** and the optically active aldehyde **9**.


Auripyrone A: R =
1
Auripyrone B: R =
2
Auripyrone A: R1 =
Auripyrone B: R1 =
3
aldol reaction
4
C1 - C13 segment
5
C14 - C20 segment
6
crotylboration
7
aldol type reaction
8
9

Scheme 2

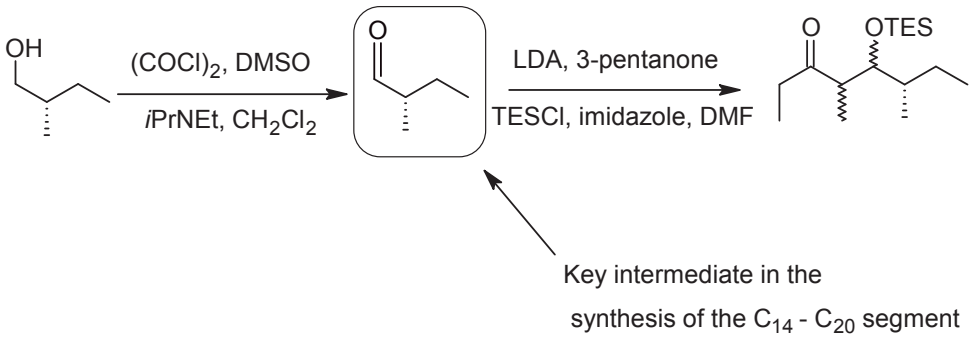
Thus, the synthesis of the C_1-C_{13} segment (**Scheme 3**) began with the diasteroselective aldol-type reaction between the pyrone and optically active aldehyde which produced the desired compound **10** in a yield of 47%. The secondary hydroxyl group was protected as a TBS ether to produce compound **11** and the trityl group was subsequently removed to produce the primary alcohol which was subjected to a Swern oxidation to produce the desired aldehyde **12**. Thus, the oxidation of an alcohol to an aldehyde is of vital importance in assembling a key precursor in the total synthesis of auripyrone A.



Scheme 3: Reagents and conditions: a) NaHMDS, THF, –78^{o}C; b) TBSCl, imidazole, DMF; c) HCO_2H, Et_2O, rt; d) 25% $NH_{3(aq)}$., MeOH, rt; e) $(COCl)_2$, DMSO, *i*Pr_2NEt, CH_2Cl_2, –78^{o}C then 0^{o}C (Swern oxidation).

The oxidation of alcohols also plays a vital role in the synthesis of the C_{14}-C_{20} segment (**Scheme 4**). The key aldehyde was synthesized from *(S)*-2-methyl butanol using the Swern

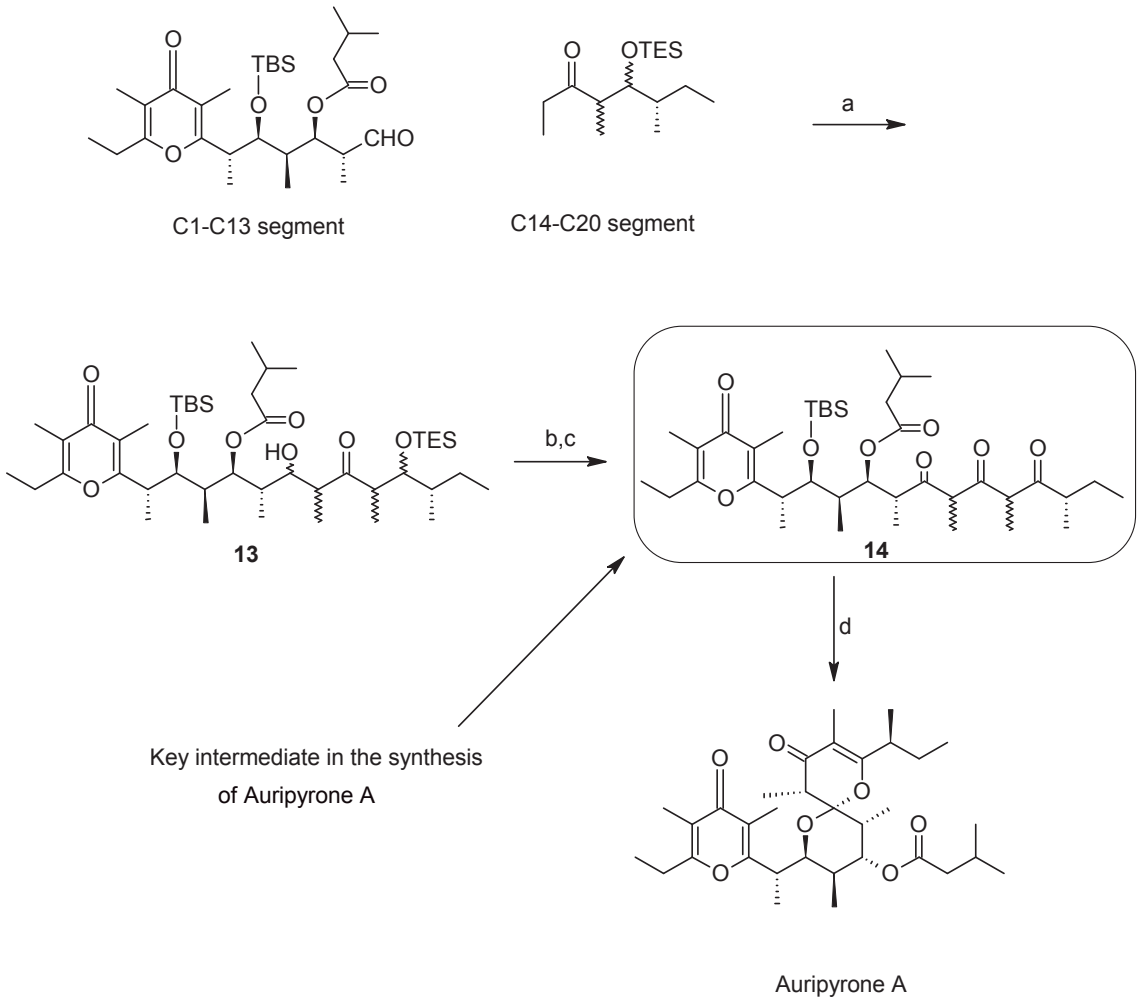
oxidation. An aldol reaction between the aldehyde and 3-pentanone and subsequent protection of the hydroxyl group affords the C_{14}-C_{20} fragment.



Scheme 4

With the two key fragments in hand, the next task was to couple these fragments to produce auripyrone A (**Scheme 5**). The coupling of the C_1-C_{13} fragment and C_{14}-C_{20} fragment using the aldol reaction afforded compound **13** as a diasteromeric mixture. Selective removal of the TES group followed by a Dess-Martin Periodinane mediated oxidation gave the triketone **14**. Cleavage of the TES group and spontaneous spiroacetalization produced auripyrone A.

The above synthesis is just one of many which highlight the important role played by alcohol oxidations. It is worth noting that many syntheses would be difficult, if not impossible, without this chemical transformation. Having evaluated the importance of alcohol oxidations in natural product synthesis, our discussion will now move on to methods available to effect this transformation. We will begin firstly with the traditional or 'classical' methods, followed by more recent advances in this field.



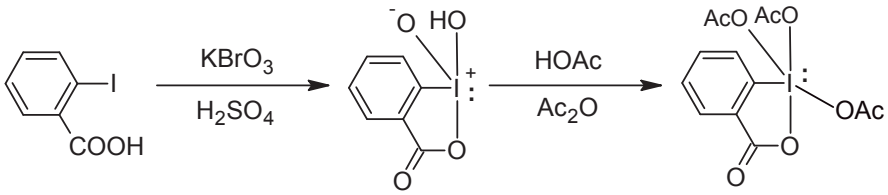
Scheme 5: Reagent and conditions: a) $Sn(OTf)_2$, NEt_3, CH_2Cl_2, –78°C, b) AcOH/THF/H_2O (4:1:4), rt; c) Dess-Martin Periodinane,† CH_2Cl_2, rt; d) HF•pyr/THF/pyr (5:7:3), 60°C.

† See scheme 6, pg. 7

1.3 Traditional alcohol oxidation procedures

1.3.1 The Dess-Martin Periodinane oxidation

The Dess-Martin Periodinane (DMP) oxidation is named after American chemists Daniel Benjamin Dess and James Cullen Martin who first reported this procedure in 1983.[9] The treatment of 2-iodoxybenzoic acid with potassium bromate and sulfuric acid leads to the cyclic tautomer of 2-iodoxybenzoic acid. The DMP reagent is generated by treatment of the cyclic tautomer with acetic anhydride and acetic acid (**Scheme 6**). The DMP reagent has been used for the successful oxidation of alcohols to aldehydes and ketones and has gained widespread popularity due to the high yields, simple work-up procedures and short reaction times to completion. A disadvantage of this procedure is the hazardous preparation of the cyclic tautomer and DMP reagent which are both heat and shock sensitive, exploding violently at temperatures > 130^{o}C.[10] Recently, Mocci and co-workers studied the DMP reagent to gain an understanding of the [1,3] sigmatropic shift of hypervalent iodine using a density functional theory (DFT) and ^{17}O NMR spectroscopic approach.[11] The results obtained revealed that the iodine undergoes a degenerate [1,3] sigmatropic shift between the two oxygen atoms of each of the three acetoxy groups in solution.



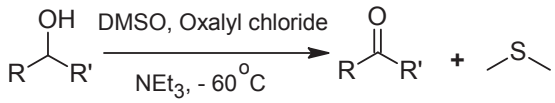
Dess-Martin Periodinane (DMP) reagent

Scheme 6

1.3.2 The Swern oxidation

The Swern Oxidation is named after American chemist Daniel Swern who first reported this oxidative procedure in 1977.[12] The oxidation is initiated by the low temperature reaction of dimethyl sulfoxide and oxalyl chloride in combination with triethylamine which leads to the

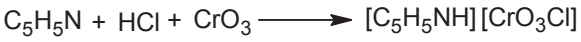
oxidation of alcohols to aldehydes and ketones (**Scheme 7**). This reaction is attractive due to the high yields obtained under mild reaction conditions and the simplicity of product isolation.[13] However, oxalyl chloride reacts violently with dimethyl sulfoxide at room temperature requiring the reaction conditions to be carefully controlled.[14] In addition, the formation of malodorous dimethyl sulfide deters from this procedure.



Scheme 7

1.3.3 Pyridinium chlorochromate (PCC) mediated alcohol oxidation

Pyridinium chlorochromate (PCC) mediated alcohol oxidations were first reported by American chemists Elias Corey and William Suggs in 1975.[15] PCC is easily prepared by the addition of pyridine to a solution of chromium trioxide in hydrochloric acid (**Scheme 8**).

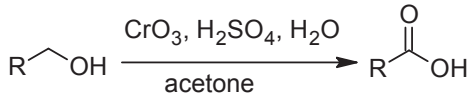


Scheme 8

PCC is a stable reagent that oxidizes a wide range of alcohols exclusively to the aldehyde without further oxidation with remarkable efficiency. However, purification of the oxidation products can often be tedious due to the formation of tar-like chromium by-products.[16] In addition, PCC is a known carcinogen[17] and therefore must be handled with care.

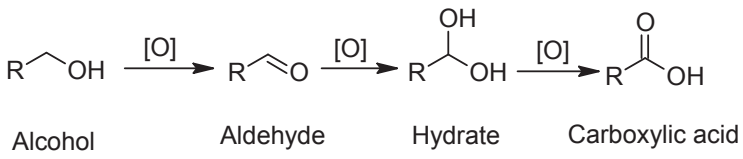
1.3.4 The Jones oxidation

The Jones oxidation is named after Welsh chemist Sir Ewart Jones who reported this oxidative procedure in 1946.[18] However, unlike the PCC mediated oxidations, the Jones oxidation results in the oxidation of primary alcohols to carboxylic acids (**Scheme 9**).



Scheme 9

The Jones oxidation begins with oxidation of the alcohol to the aldehyde which, in the presence of water, forms the hydrate. Hydrates are also subject to oxidation and, consequently form the carboxylic acid derivative (**Scheme 10**). However, allylic and benzylic alcohols do not result in stable hydrates and therefore selectively form the aldehyde in fair to good yields.[19]



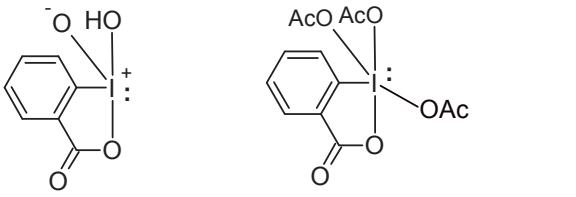
Scheme 10

Since these pioneering reports, a number of new and exciting oxidative processes have emerged. However, before we commence with a narrative of the latest developments in oxidative chemistry, attention must be given to the role of *o*-iodobenzoic acid (IBX) which over the past 20 years has generated much interest.

1.4 Recent alcohol oxidative procedures

1.4.1 2-Iodoxybenzoic acid

2-Iodoxybenzoic acid (IBX) was first reported in 1893[20] but was not widely used due to its limited solubility in organic solvents.[21] The solubility of IBX was increased by the attachment of acetate groups by Dess and Martin and thus, the DMP reagent was born (**Figure 2**).



IBX

Dess-Martin Periodinane (DMP) reagent

Figure 2

However, Frigerio and co-workers demonstrated that IBX is soluble in DMSO and smoothly oxidizes alcohols to aldehydes and ketones in good to excellent yields.[22] They also point out that IBX displays a number of advantages over the DMP reagent such as stability to moisture, which allows for the oxidation to be conducted in open vessels. DMSO however, is not an ideal solvent and displays a number of drawbacks. Thus, research groups have focused their efforts on the synthesis of solid phase analogues of IBX in an effort to broaden its application to other solvents. Giannis and co-workers reported the synthesis of polymer supported IBX which allowed for the oxidation to be conducted in THF at room temperature with excellent yields.[23] Since this report, many research groups have modified the IBX mediated oxidation with methods including the use of excess IBX at elevated temperatures,[24] solvent free conditions[25] and acid mediated protocols[26] to name but a few.

1.4.2 Silica supported gold nanoparticles

In early 2011, Rossi and co-workers reported the application of gold nanoparticles immobolized on silica.[27] The process involved firstly the synthesis of gold nanoparticles, followed by the silica coated magnetic component. However, attempts to adsorb the gold nanoparticles onto the silica coated magnetic component were futile. Yet, when the silica coated magnetic component was functionalized with amino groups the gold particles readily adsorbed to the surface. This result suggests that the amino functional groups interact more strongly with the gold nanoparticles than adsorbtion on the unfunctionalized surface. Using these particles in combination with potassium carbonate under an oxygen atmosphere, a range of alcohols were oxidized exclusively to their corresponding aldehyde. The oxidation method produced no aldehyde in the presence of the support alone, indicating that the adsorption of the gold nanoparticles onto the solid support is of vital importance. The most interesting aspect of this methodology is that due to magnetic properties of the synthesized catalyst, it can be easily recovered by applying an external magnetic source (**Figure 3**).

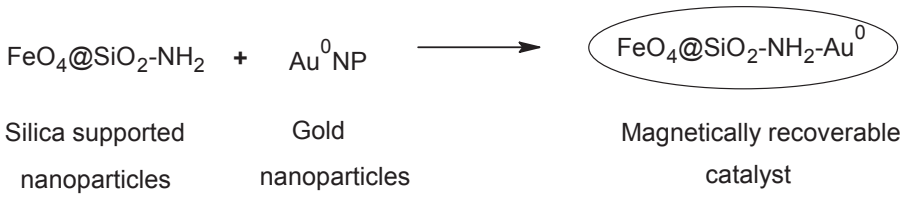
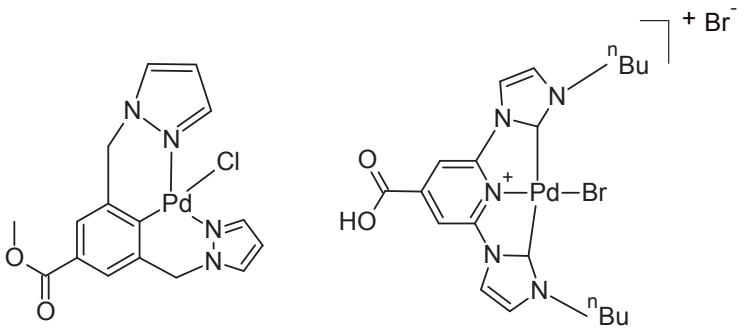


Figure 3

1.4.3 Palladium pincer complexes

Domínguez and co-workers reported the use of palladium pincer complexes for the oxidation of alcohols to aldehydes and ketones.[28] The authors describe a synthesis for the NCN and CNC type pincer ligands (**Figure 4**) and tested the performance of these complexes using 1-phenylethanol as a model substrate.

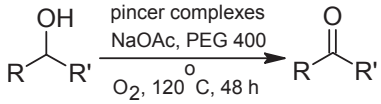


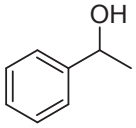
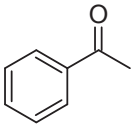
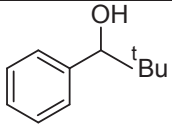
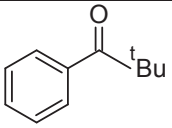
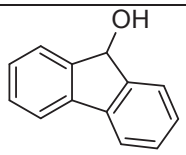
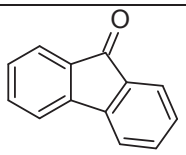
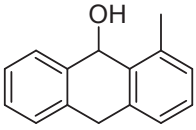
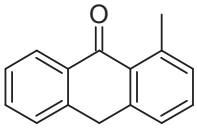
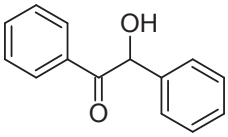
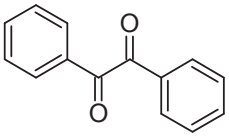
15a **15b**

Figure 4

Preliminary results revealed that the reaction was efficient under an oxygen atmosphere, using NaOAc as a base with polyethylene glycol as a solvent. The optimized oxidative procedure was applied to a number of secondary alcohols and in most cases almost quantitative yields were obtained regardless of the pincer complex used, except in the case of 2-methylbenzhydrol although the authors provide no explanation for this decrease in yield. A summary of the results obtained using these complexes have been described below (**Table 1**).

Table 1: Oxidation of secondary alcohols using pincer complexes



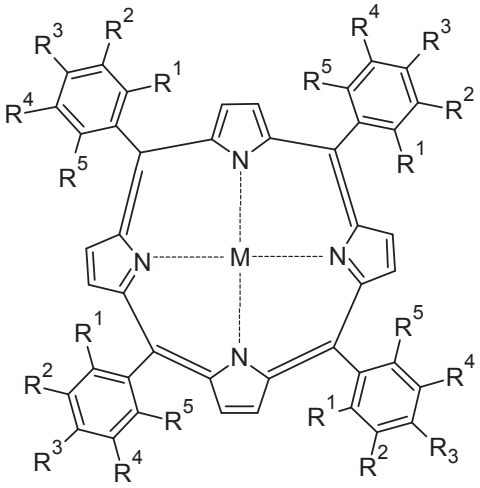
Entry	Substrate	Product	Pincer 15a (%)	Pincer 15b (%)
i			99	97
ii			98	94
iii			80	74
iv			50	55
v			97	98

Having briefly evaluated the most interesting recent developments in the oxidation of alcohols, attention will now shift to the application of a light-driven oxidative process. A light-activated oxidative procedure offers a number of advantages to a synthetic organic chemist, namely a certain amount of control in the reaction as the oxidation will not commence until the reaction vessel is irradiated with an appropriate light source and the oxidation will come to a halt when the light source is removed.

1.5 Light activated alcohol oxidation

1.5.1 Use of porphyrin sensitizers

Porphyrin has its origin from the word *porphura,* which means purple in ancient Greek and as the name implies, porphyrins are deeply colored red or purple crystalline pigments. In nature, porphyrins are involved in many light harvesting reactions such as photosynthesis and storage functions of cellular metabolism.[29] Consequently, porphyrins are ideal sensitizers for light activated oxidations of alcohols. Safari and co-workers have reported the use of a porphyrin mediated alcohol oxidation using sunlight or visible light as a source of irradiation and compared the performance of metallated and nonmetallated porphyrins (**Figure 5**).[30]



H_2TMP:R^1=R^3=R^5=CH_3, R^2=R^4=H, M: 2H

(Non metallated porphyrin)

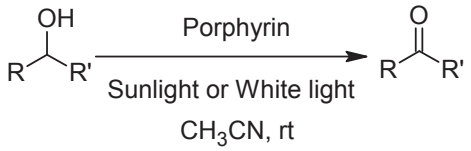
ClFeTMP: R^1=R^3=R^5=CH_3, R^2=R^4=H, M: FeCl

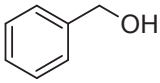
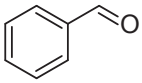
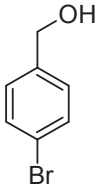
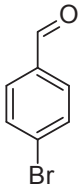
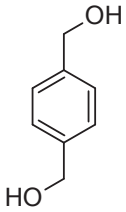
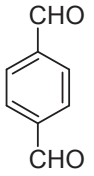
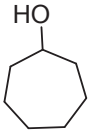
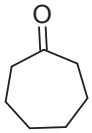
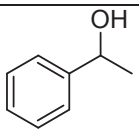
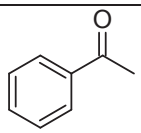
(Metallated porphyrin)

Figure 5

Firstly, monitoring the formation of 2-bromobenzaldehyde *vs.* time revealed that for the metallated porphyrin, regardless of time or concentration of porphyrin used, the aldehyde was formed exclusively. In the case of the non-metallated porphyrin, if an excess of porphyrin is present once all the alcohol has been converted to aldehyde, the oxidation of the aldehyde to the acid begins. Thus, in the case of free base porphyrins exact stoichiometry of the reactants is needed to prevent overoxidation to the acid. The efficiency of the porphyrin systems were determined by comparing their oxidizing ability on a variety of alcohols. The major results of these findings are summarized below (**Table 2**).

Table 2: Oxidation of alcohols using metallated and non-metallated porphyrins[30]



Entry	Substrate	Product	Porphyrin[a]	Conversion (%)
i			M (120 h) NM (72 h)	65 70
ii			M (73 h) M (75 h)[b] NM (16 h) NM (16 h)[b]	73 75 95 95
iii			M (80 h) NM (72 h)	43 75
iv			M (140 h) NM (140 h)	45 53
v			M (32 h) NM (20 h)	74 95

[a] M = Metallated porphyrin, NM = Non-metallated porphyrin. Numbers in parentheses refer to the reaction time.
[b] Sunlight as an irradiation source.

1.5.2 Use of semiconductors

1.5.2.1 History of semiconductors

Photocatalysis, by semiconductor metal oxides, has been identified as a promising route for organic chemistry in the 21st century.[31] The unique application of semiconductors is best explained by the band theory[32] which compares the differences between an insulator, semiconductor and conductor. When individual atoms are brought together and form a solid, electrons from neighbouring atoms are forced to have different energy levels which results in a band gap. In the case of a conductor, the energy levels are so close together that an overlap occurs and they merge into one band. Therefore they have a high conductivity as in the case of copper or gold. If the band gap is too large for the electrons to overcome, these materials are termed insulators. An example of an insulator is diamond which displays a band gap of 5.5 eV. In the case of a semiconductor, the band gap from the filled valence band to the empty conduction band is not as large as in the case of an insulator and consequently, a semiconductor can be converted into a conductor by applying an external energy source. These differences are schematically illustrated in **Figure 6**.

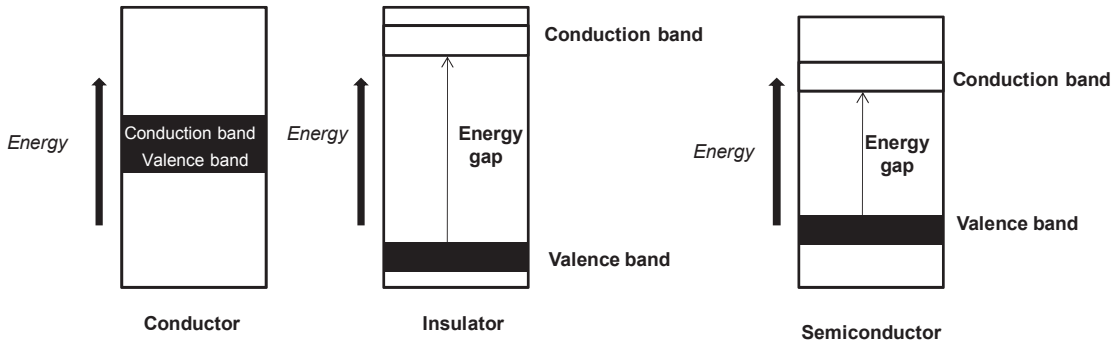


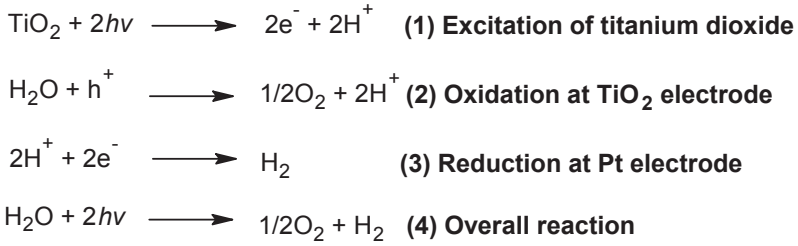
Figure 6

There are a number of semiconductors available that have band gaps ranging from 1.4 to 3.8 eV (**Table 3**). However, a literature review revealed that the ideal semiconductor was not dependent on band gap alone. Pelizzetti and co-workers reported that the ideal semiconductor should be stable under irradiation, have a relatively low cost and be environmentally friendly.[33] They suggested that titanium dioxide and zinc oxide fulfill these requirements and are ideal semiconductors.

Table 3: Comparison of the band gap of various semiconductors[34]

Semiconductors	Valence Band (v NHE)	Conduction Band (v NHE)	Band Gap (eV)	Band Gap (nm)
SnO_2	+4.1	+0.3	+3.8	318
ZnS	+1.4	–2.3	+3.7	335
TiO_2	+3.1	–0.1	+3.2	387
ZnO	+3.0	–0.2	+3.2	387
WO_3	+3.0	+0.2	+2.8	443
CdS	+2.1	–0.4	+2.5	496
GaP	+1.3	–1.0	+2.3	539
CdSe	+1.6	–0.1	+1.7	729
GaAs	+1.0	–0.4	+1.4	886

Thus, the discussion turns to the properties of these two fascinating materials and their broad range of applications. Titanium dioxide exists in three crystalline forms namely, anatase, rutile and brookite. Rutile is the stable form while anatase and brookite are metastable and readily turned into rutile upon heating.[35] However, it is known that of the three polymorphs of titania, anatase is the most active as a photocatalyst,[36] probably due to the extent and nature of the hydroxyl groups present in the anatase structure.[37] Titanium dioxide embodies all the attributes of an ideal photocatalyst and, in its anatase form, is considered the benchmark against which other emerging photocatalysts are measured.[38] Titanium dioxide first rose to prominence in the late 1960s through its application on photoelectrochemical solar cells.[39] When a titanium dioxide electrode was irradiated with ultraviolet light, Fujishima and co-workers noticed that the photocurrent flowed from the platinum electrode to the titanium dioxide electrode.[40] The direction of current revealed that oxidation was taking place at the titanium dioxide electrode (O_2 evolution) while reduction was taking place at the platinum black electrode (H_2 evolution). This landmark discovery showed that water could be split into hydrogen and oxygen without applying a current through the cell as highlighted in **Scheme 11**[41]:-



Scheme 11

Recently the Park research group, based at Harvard University, reported a novel addition to the photolysis of water using TiO_2.[42] They reported a procedure for the preparation of TiO_2 nanowires which were deposited on a Ti electrode and coated with gold or silver. This newly synthesized electrode was able to effect the photolysis of water under visible light due to the high surface architecture afforded by the nanowires.

The photolysis of water marked an exciting time in photochemistry with both the industrial and research application of titanium dioxide being touted. The strength of this argument emerged from titanium dioxide's ability to produce strongly oxidizing hydroxyl radicals under ultraviolet irradiation.[‡] The use of the strong oxidizing power of TiO_2 has formed the basis of many studies, some of which will be highlighted below.

1.5.2.2 Use of TiO_2 as a sterilizing agent

Titanium dioxide has been used as a sterilizing agent against infectious causing bacteria. Fujishima and co-workers described how the strong oxidizing ability of TiO_2 can be used to degrade *E. coli* suspensions.[43] This procedure involved placing the *E. coli* suspension on a glass plate coated with TiO_2 which was then irradiated with ultraviolet light. After 1 hour of irradiation, no surviving *E. coli* cells were detected. Under identical conditions but in the absence of TiO_2 only 50% of cells were degraded after 4 hours of irradiation. The strong oxidizing ability of the hydroxyl radicals generated by titanium dioxide has also found

[‡] A full explanation of the formation of hydroxyl radicals will be given later in the discussion.

applications in the purification of water. The World Health Organization (WHO) estimates that 884 million people lack access to proper water supplies and many are forced to rely on microbiologically unsafe water which results in cholera and typhoid infections.[44,45] One possible solution is the use of Solar Disinfection of Water (SODIS), which involves placing water in a clear bottle and exposing it to sunlight for at least 6 hours, and has been shown to be effective against a wide range of diarrheal illnesses.[46-48] However, due to the emergence of drug-resistant microorganisms, the SODIS procedure requires modification. A possible solution would be to use SODIS in combination with titanium dioxide whose strongly oxidizing hydroxyl radicals would destroy the resistant bacteria.[49]

1.5.2.3 Use of TiO_2 in cancer therapy

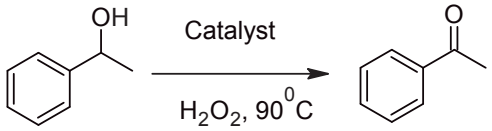
A new and exciting application of titanium dioxide mediated photocatalysis is its use in cancer therapy. Falaras and co-workers recently reported the effect of titanium dioxide irradiated particles on breast epithelial cancer cells.[50] It was found that the irradiated titanium dioxide particles can induce apoptosis of the cancer cells, although the large band gap of titanium dioxide, requiring ultraviolet light for activation is a serious drawback of this research. However, the authors state that modification of the titanium dioxide surface is possible which may allow titanium dioxide to be activated by visible light. The most invigorating aspect of this research is the future plan proposed by the authors. They recommend that this research may be used to treat cancerous tumors by injection of titanium dioxide particles near the tumor region, followed by irradiation of these particles *via* a fibre optic cable. While still a work in progress, this proposal, if successful, will mark a new dawn in the fight against cancer.

1.5.2.4 Use of TiO_2 in synthetic chemistry

Another interesting application of titanium dioxide is that as a solid support, as demonstrated by Cao and co-workers, in the oxidation of secondary alcohols to their carboxylic acid or ketone derivatives.[51] The authors' evaluated a series of solid supported gold catalysts in combination with hydrogen peroxide using 1-phenylethanol as a model substrate. The results revealed that gold supported carbon leads to a low conversion, while Au/Fe_2O_3 donated from the World Gold Council (WGC) and Au/Al_2O_3 gave moderate conversions. Au/TiO_2 (WGC)

and Au/CeO_2 also gave satisfactory yields. The highest yield was however obtained using Au/TiO_2 obtained from Mintek with the desired ketone formed in a 99% conversion (**Table 4**).

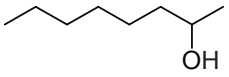
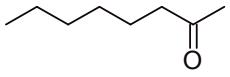
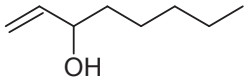
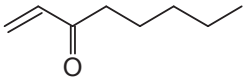
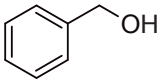
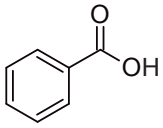
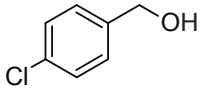
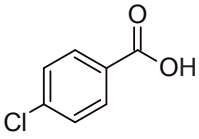
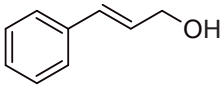
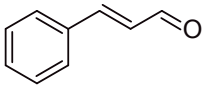
Table 4: Oxidation of 1-phenylethanol using various catalysts[51]



Entry	Catalyst	Conversion (%)
i	0.8% Au/C (WGC)	12
ii	4.5% Au/Fe_2O_3 (WGC)	34
iii	1.5% Au/TiO_2 (WGC)	62
iv	0.9% Au/Al_2O_3 (Mintek)	37
v	1% Au/CeO_2	58
vi	1% Au/TiO_2 (Mintek)	99

A brief study of the relationship between alcohol oxidation and a series of Mintek catalysts calcined at different temperatures revealed that due to the smaller gold particles, superior yields were obtained. A study was conducted on a range of primary and secondary alcohols with a series of carboxylic acids and ketones synthesized in good to excellent yields. A summary of the results obtained is described below (**Table 5**).

Table 5: Oxidation of alcohols using a Au/TiO_2 system[51]

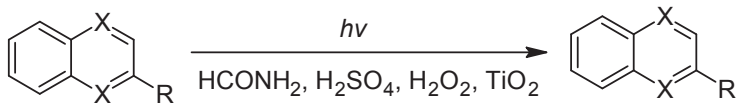
Entry	Substrate	Product	Conversion (%)	Selectivity (%)
i			87	100
ii			>99	100
iii			>99	85[a]
iv			>99	37[a]
v			>99	100

[a] Aldehyde formed as by-product.

The $Au/TiO_2/H_2O_2$ system is remarkable as it is able to oxidize unactivated substrates in high yields and high selectivity. The system is however less prolific on benzylic alcohols with the corresponding aldehyde formed as a by-product. In the case of cinnamyl alcohol (**Table 5, entry v**), no corresponding acid was formed with the aldehyde obtained exclusively. Since gold nanoparticles can substantially facilitate the decomposition of H_2O_2, the results obtained suggest that the high dispersion of gold nanoparticles in combination with a synergetic interaction with TiO_2 is key in achieving the high activity for $Au/TiO_2/H_2O_2$ mediated alcohol oxidation.

The photoinduced behaviour of titanium dioxide has also been extended to synthetic organic chemistry. Caronna and co-workers reported the use titanium dioxide in the functionalization of heterocyclic bases (**Scheme 12**).[52] It is known that heterocyclic bases are attacked by radicals which are created by reaction of hydroxyl radicals with amides, ethers and so forth.[53]

The authors report that in the presence of titanium dioxide, using sunlight as a source of irradiation, the functionalization proceeds in higher yields.



X = CH, R = H
X = CH, R = CH_3
X = C-CH_3, R = H
X = N, R = H

X = CH, R = $CONH_2$, 90%
X = C-$CONH_2$, R = CH_3, 100%
X = C-CH_3, R = $CONH_2$, 69%
X = N, R = $CONH_2$, 42%

Scheme 12

The applications of titanium dioxide highlighted above are but a brief introduction. As outlined by Carp and co-workers,[54] there are a number of applications for photoactivated titanium dioxide (**Figure 7**).

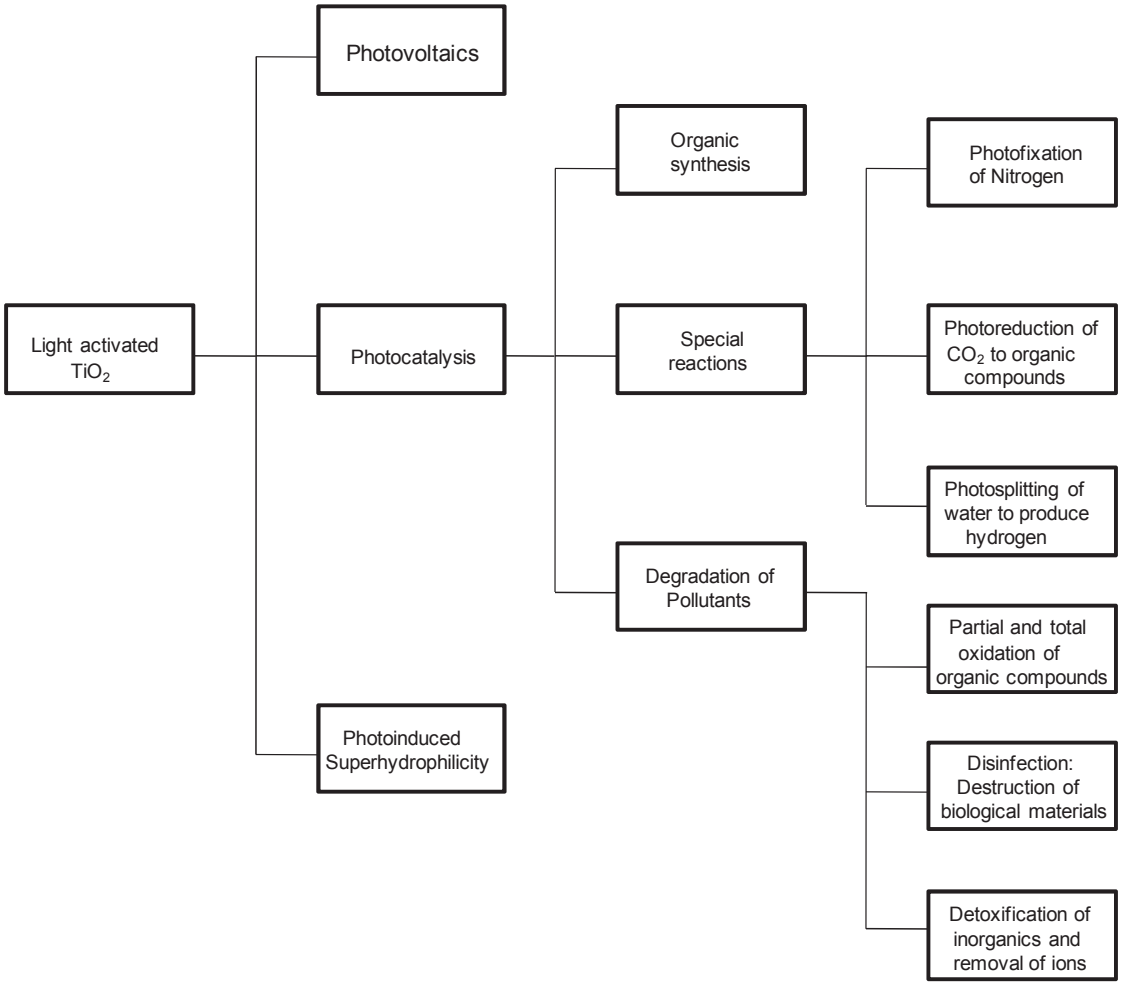


Figure 7

Having evaluated the benchmark photocatalyst, our discussion now moves on to the use of the lesser studied but equally important semiconductor namely, zinc oxide.

1.5.2.5 Use of ZnO in the cosmetic industry

Zinc oxide is expected to display similar behaviour to titanium dioxide[55] but has gained supremacy over titanium dioxide in the cosmetics industry. The exposure to ultraviolet irradiation has been shown to be one of the leading causes of skin cancer.[56] Sunscreen lotions provide an effective method of protection with a number of active ingredients able to filter

UV light. **Figure 8** compares the UV blocking ability of common ingredients in sunblock lotions.

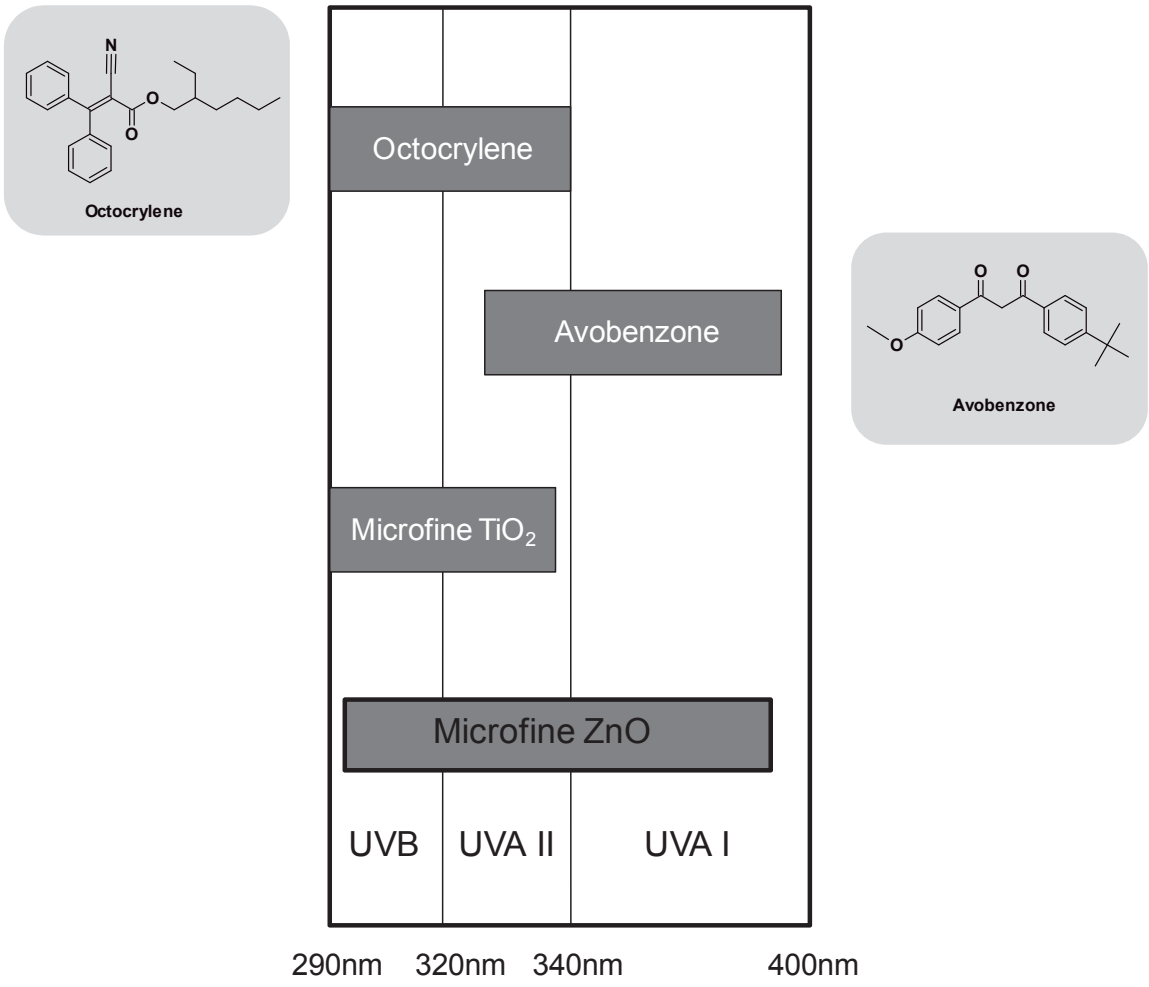


Figure 8

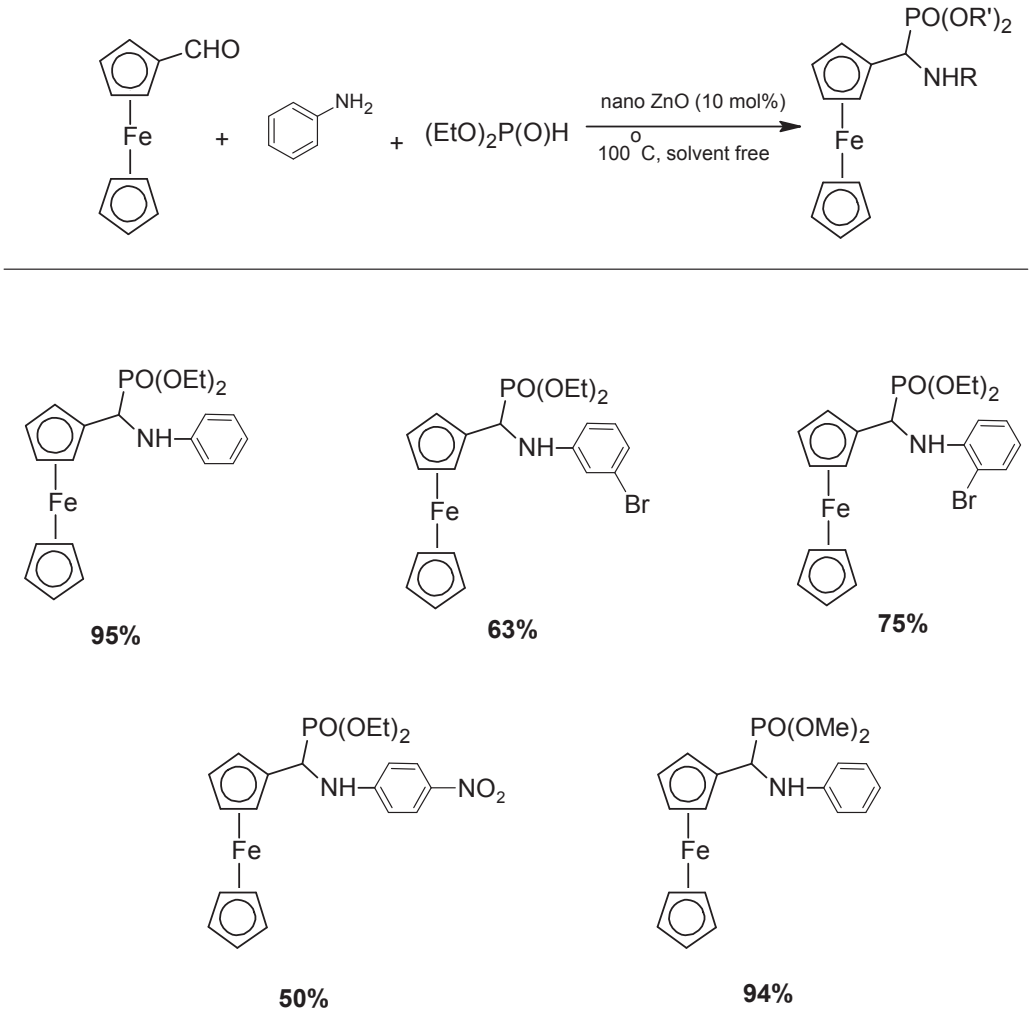
Octocrylene only filters UVA II and UVB light while avobenzone only filters a portion of UVA I and UVA II light. Interestingly, microfine TiO_2 only covers portion of the UVA II and UVB region. Zinc oxide has gained widespread prominence for being the active ingredient in many sunscreen lotions. Microfine ZnO covers the widest range of spectrum and provides the most protection against skin cancer. In 2000, Sheldon and co-workers compared the performance of microfine TiO_2 and microfine ZnO as active sunscreen ingredients.[57] Using diffuse reflectance spectroscopy, it was shown that microfine ZnO absorbs more in the 340-380 nm range compared to microfine TiO_2. They also compared the whiteness of 6%

microfine TiO_2 and 6% microfine ZnO on Fitzpatrick type IV human skin.[§] The results suggest that microfine TiO_2 is appreciably whiter than microfine ZnO which is undesirable from a cosmetics point of view. An ideal sunscreen protection cream should blend in with the natural colour of the skin unlike microfine TiO_2 which results in clearly visible white patches on the skin surface. The authors thus concluded that microfine ZnO is far superior to microfine TiO_2 as an active sunscreen ingredient as it offers wider protection and is invisible on skin. While microfine TiO_2 and microfine ZnO have been commonly used in cosmetic sunscreen, concerns have been raised about the safety of these powders. In 1997, Nakagawa and co-workers tested the photogenotoxicity of irradiated titanium dioxide particles against mouse and hamster cells.[58] It was reported that irradiated titanium dioxide can induced DNA damage and structural chromosomal aberrations in mammalian cells. However, this data must be placed in context as the penetration into rat skin is greater than human skin.[59] In a recent review by Schellauf and co-workers they have concluded that the risks from titanium dioxide and zinc oxide in sunscreens are negligible as long as they do not penetrate the skin.[60] A further complication arises from the fact that sunscreen lotions are often applied to sunburned skin which may be susceptible to further damage by the irradiated titanium dioxide or zinc oxide particles. However, Gunther and co-workers have reported that sun damaged skin produces a thickened epidermis layer that enhances the protection of the skin.[61] However, more studies are required to determine if this applies to sun damaged skin coated with TiO_2 or ZnO based sunscreen lotions.

1.5.2.6 Use of zinc oxide in synthetic chemistry

Recently, Sarvari reported the three component one-pot synthesis of ferrocenyl aminophosphonic esters using nanocrystalline zinc oxide[**] as a catalyst.[62] Using the conditions highlighted below, a series of derivatives was formed in yields ranging from 50-95%. A selection of the results obtained is illustrated in **Scheme 13**.

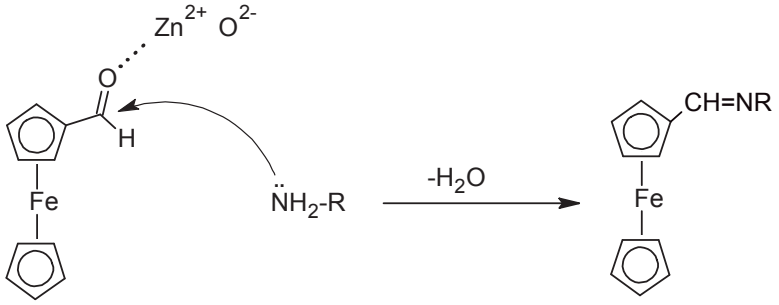
[§] Numerical classification for the colour of skin
[**] Particle size: 20-30 nm



Scheme 13

The following mechanism for this reaction was proposed in which the essential role of zinc oxide was highlighted (**Figure 9**):

Step (i)



Step (ii)

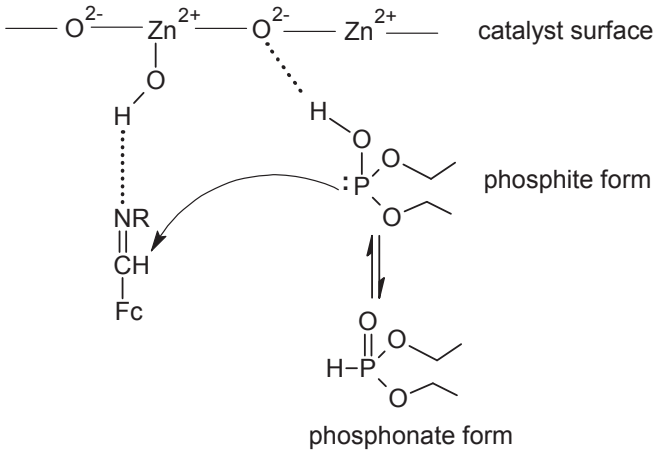
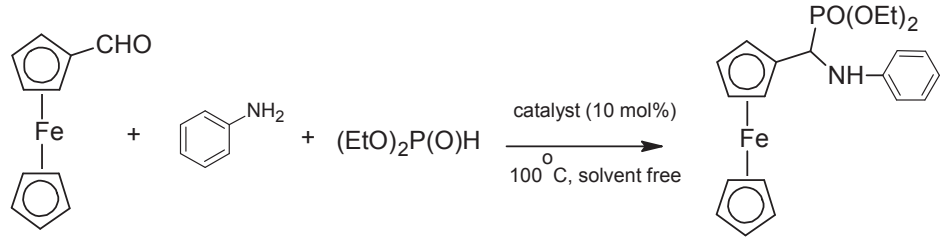


Figure 9

The proposed mechanism can be separated into two steps: (i) the first step involves the coordination of Lewis acid sites (Zn^{2+}) of zinc oxide to the substrate oxygen atom, which increases the reactivity of the ferrocene carbaldehyde, resulting in the formation of a Schiff base. (ii) The second step is initiated by hydrogen bonding of the catalyst surface and the Schiff base. Since it is known that the phosphite form is the nucleophile and not the phosphonate form,[63] coordination of the Lewis basic sites to the phosphite form occurs, followed by attack of the electrophillic azomethine carbon.

To further emphasize the role of zinc oxide, the author carried out a model reaction using a variety of other catalysts. A selection of the catalysts used and the yields obtained are highlighted below (**Table 6**).

Table 6: Synthesis of ferrocenyl aminophosphonic esters using a range of catalysts [62]



Entry	Catalyst	Time (h)	Yield (%)
i	bulky basic-Al_2O_3	12	45
ii	bulky TiO_2	12	50
iii	nano TiO_2	12	50
iv	bulky ZnO	12	84
v	nano ZnO	2	95

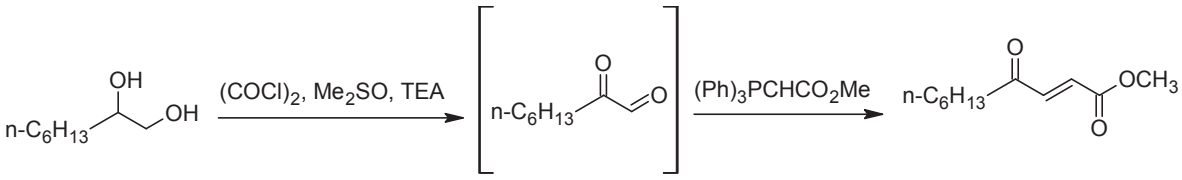
The use of bulky basic Al_2O_3 as a catalyst resulted in formation of the desired product in an isolated yield of 45% after 12 hours. Interestingly, the use of titanium dioxide in either its bulky form or nano form resulted in the formation of the product in a 50% isolated yield. Superior results were obtained when zinc oxide was used as a catalyst as its bulky form resulting in the formation of product in an 84% isolated yield after 12 hours. The use of zinc oxide in its nano form resulting in the formation of the product in a 95% isolated yield after only 2 hours. All other catalysts used such as CuO, MgO and CaO resulted in either trace or no product formation. Thus, the superiority of ZnO was attributed to its superior coordination in steps (i) and (ii) of the proposed mechanism while nano ZnO outperformed bulky ZnO as it has more surface atoms participating in the reaction.

On successful evaluation of these fascinating materials, it is worth mentioning that they are able to effect another important chemical transformation – the oxidation of alcohols to their carbonyl derivatives with hydroxyl radicals as the active oxidizing species. The procedure is however characterized by low yields and the formation of unidentifiable side-products. A full discussion of semiconductor mediated photooxidations will be given later in the discussion.

As the most relevant and recent methods to oxidize alcohols to their carbonyl derivatives have been discussed, our discussion now moves to techniques available to elaborate these carbonyl derivatives further. This branch of research originates from the instability of the synthesized carbonyl derivative which can often be volatile, noxious and highly lachrymatory. This problem can be circumvented by applying either the pseudo tandem reaction (Ireland procedure) or the tandem oxidation process (TOP).

1.6 Pseudo tandem coupling reactions

In late 1984, Robert Ireland and co-workers were developing synthetic routes towards polyether ionophore antibiotics and, *en route* encountered several aldehydes that were unstable. To traverse this problem, Ireland and co-workers devised a method based on the Swern oxidation.[64] This procedure involved carrying out the alcohol oxidation under general Swern oxidation conditions, followed by the addition of the Wittig reagent to the crude mixture *without* isolating the problematic intermediate aldehyde. The utility of this procedure was demonstrated on aliphatic keto-aldehydes, which due to their propensity towards hydration, polymerization and air oxidation,[65] have been seen to have little use in organic synthesis.[66] However, using the procedure described above the desired product was isolated in an excellent yield of 90% (**Scheme 14**).



90%

Scheme 14

This one-pot Swern oxidation mediated protocol has also found application in natural product synthesis. The obscure mealybug, *Pseudococcus viburni*, is an important agricultural pest that damages important tropical crops and ornamental plants.[67] The flightless adult female releases a potent sex pheromone to attract the short-lived, winged male for reproduction. This sex pheromone was isolated by Millar and co-workers and the structure was deduced, from NMR and mass spectra, to have a monoterpenoid skeleton (**Figure 10**).[68]

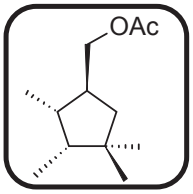
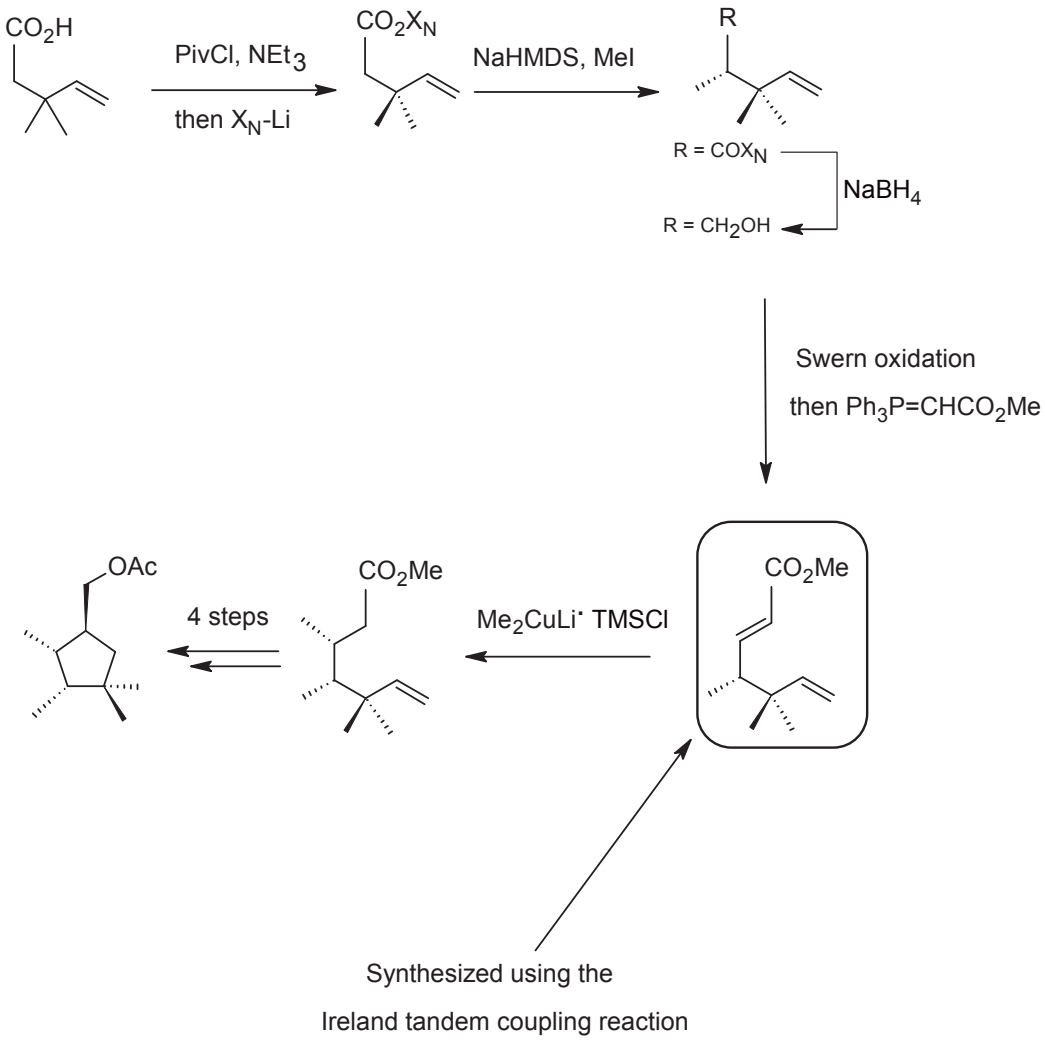


Figure 10

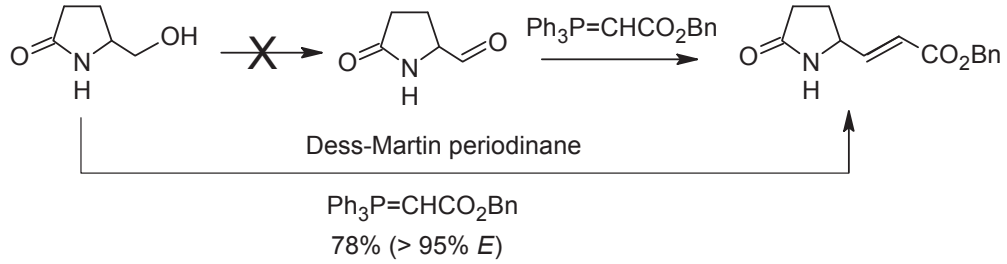
Kuwahara and co-workers then set about the first enantioselective synthesis of this sex pheromone (**Scheme 15**).[69] The procedure began with the treatment of the known carboxylic acid with pivaloyl chloride and NEt_3, followed by installation of the (*S)*-phenylalaninol-derived auxiliary (X_N). This was followed by asymmetric methylation at the α-position to produce a single stereoisomer which was subsequently reduced with $NaBH_4$ to furnish the desired alcohol. The resulting alcohol was subjected to a Swern oxidation but, due to its volatility, the isolated yield of the aldehyde was disappointing. The volatility of the aldehyde was overcome by employing the Swern oxidation and adding the Wittig reagent to the mixture containing the crude aldehyde. Using these conditions, the desired *E*-olefinic ester was isolated in a satisfactory yield of 83%. This was followed by methylation of the enoate and the implementation of four more synthetic steps to produce the desired sex pheromone in an overall yield of 13% from the known carboxylic acid.



Scheme 15

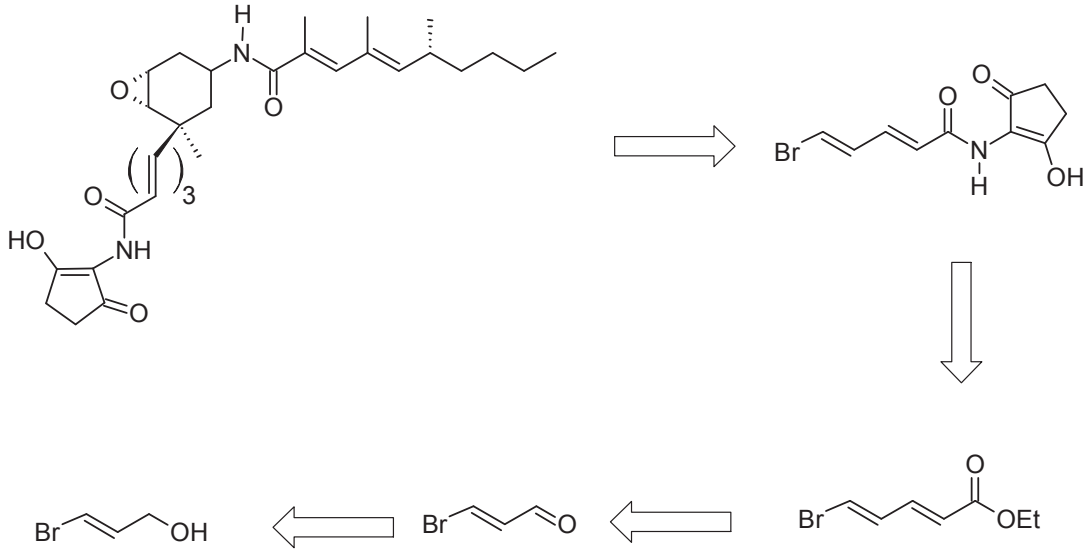
1.7 The tandem oxidation process (TOP)

An alternative take on the tandem coupling reaction was reported by Huang and co-workers while attempting to synthesize carbon-14-labelled CI-933.[70] An important step of this protocol involved the oxidation of the alcohol to the aldehyde followed by a Wittig reaction. However, several attempts at oxidizing the alcohol proved unsuccessful until Huang mixed the alcohol, Wittig reagent and the Dess-Martin periodinane reagent in one pot. The desired unsaturated ester was isolated in a yield of 78% (**Scheme 16**).



Scheme 16

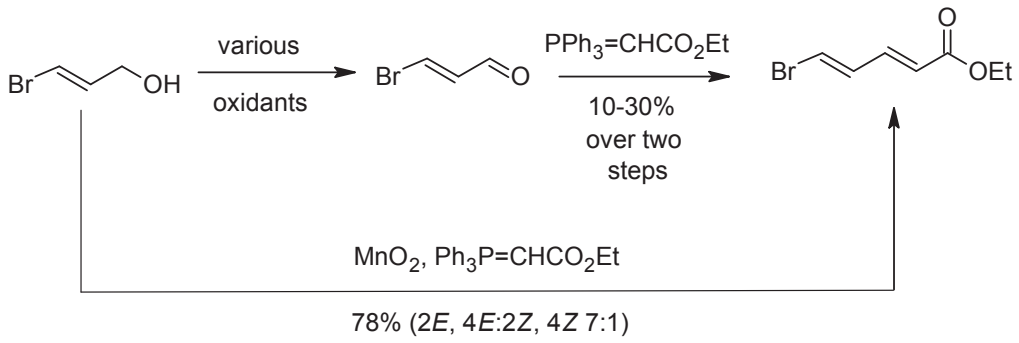
In 1998, the Taylor research group was investigating synthetic routes towards the manumycin family of antibiotics.[71-74] A key step involved the oxidation of the 3-bromopropen-1-ol to its aldehyde derivative followed, once again, by a Wittig reaction. A retrosynthetic analysis is described below (**Scheme 17**).



Scheme 17

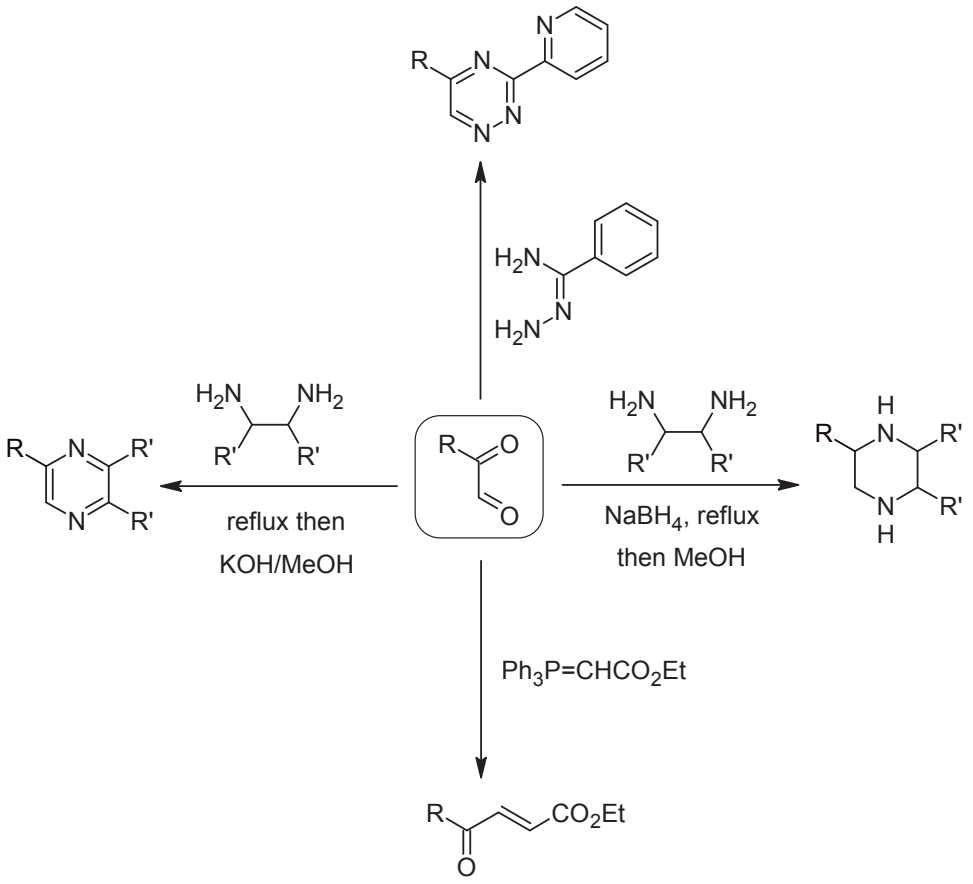
Despite their best efforts, the desired dienoate was isolated in a yield of 10-30% over the two steps. The low yields emanated from the propensity of the aldehyde to

polymerize/oligomerize[75] while its highly lachrymatory nature further compounded the issue. Attempts were made using the Ireland procedure as previously described but no success was obtained, highlighting the labile nature of the aldehyde. Finally, Xudong Wei (a member of the Taylor research group) mixed the alcohol, Wittig reagent and manganese dioxide in one pot. It was reasoned that manganese dioxide would oxidize the alcohol to the aldehyde which would immediately be trapped by the Wittig reagent. Using this methodology, the desired dienoate was isolated in a yield of 78% (**Scheme 18**) and was dubbed, by the Taylor group, the 'tandem oxidation process' (TOP) in order to differentiate it from the procedure used by Ireland.



Scheme 18

This landmark discovery resulted in the emergence of a new branch of research, with the Taylor group pioneering the development of MnO_2-based tandem coupling reactions. The use of manganese dioxide as an oxidant was preferred due to its low cost, low toxicity and ease of handling. In addition, due to its heterogenous nature, work-up often involves simple filtration and evaporation of the solvent. Using this methodology, a plethora of synthetically useful compounds can be prepared in high yields and short reaction times.[76] A brief summary of the compounds synthesized using this methodology applied to keto-alcohols is provided below (**Scheme 19**) although the tandem oxidation process is applicable to a wide range of allylic, benzylic and even non-activated alcohols.

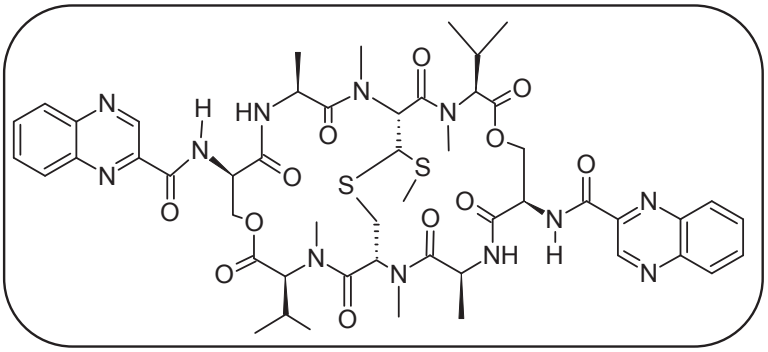


Scheme 19

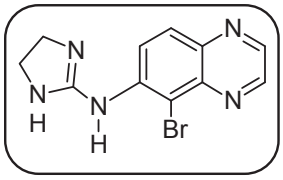
While the opportunities for tandem coupled reactions are endless, attention now moves specifically to the synthesis of quinoxalines using this innovative methodology.

1.8 Synthesis of quinoxalines

Quinoxaline derivatives display a wide range of biological properties (**Figure 11**) ranging from DNA cleaving drugs[77] to antibiotic[78] and antitumor activity.[79] Hence, techniques available to access this important moiety are of vital importance.

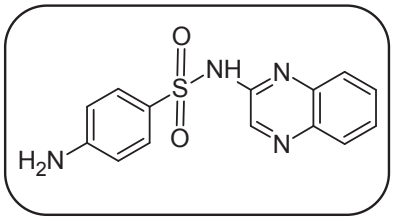


Echinomycin (antitumor activity)



Alphagan

(treatment of ocular hypertension)



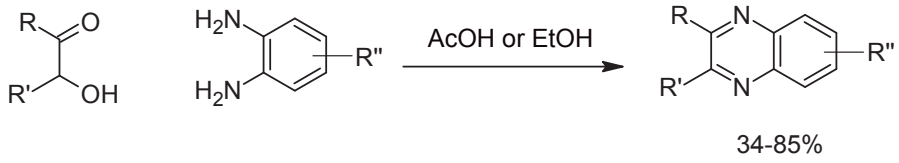
Sulfaquinoxaline

(treatment of coccidiosis)

Figure 11

1.8.1 General procedure for the synthesis of quinoxalines

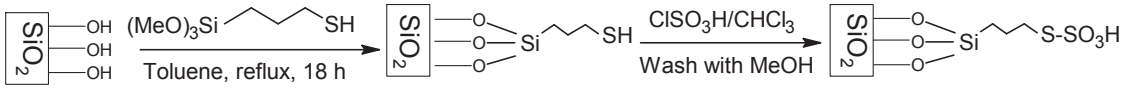
There are a number of procedures available to synthesize quinoxalines,[80,81] but the traditional method involves the condensation of a 1,2-dicarbonyl or an α-hydroxyketone and a 1,2-diamine in refluxing acetic acid or ethanol for 2-12 hours with yields ranging from 34-85% (**Scheme 20**).[82]



Scheme 20

1.8.1.1 Silica bonded *s*-sulfonic acid

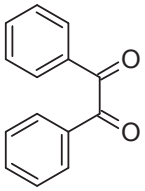
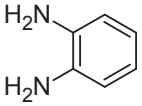
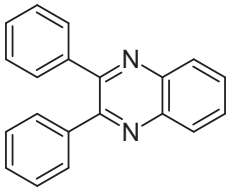
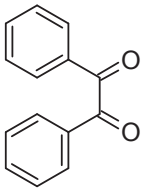
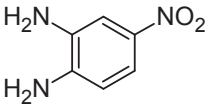
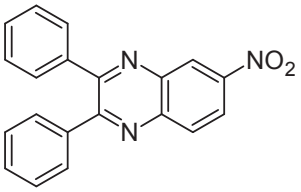
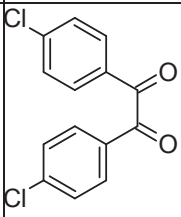
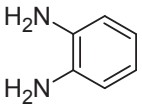
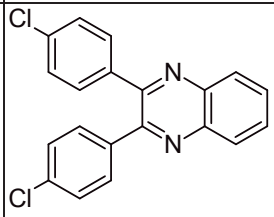
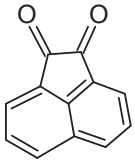
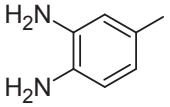
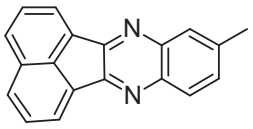
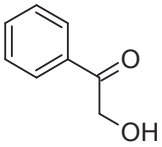
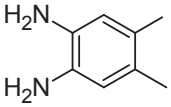
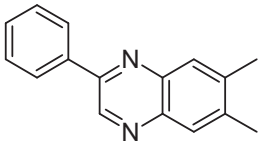
An interesting variation of the traditional quinoxaline reaction was reported by Niknam and co-workers in which they used a solid recyclable catalyst to promote quinoxaline synthesis.[83] The solid catalyst was prepared by refluxing silica gel with (3-mercaptopropyl)trimethoxysilane in toluene for 18 hours to produce 3-mercaptopropylsilica, to which chlorosulfonic acid was added producing the silica bonded functionalized sulfonic acid as a cream powder (**Scheme 21**).



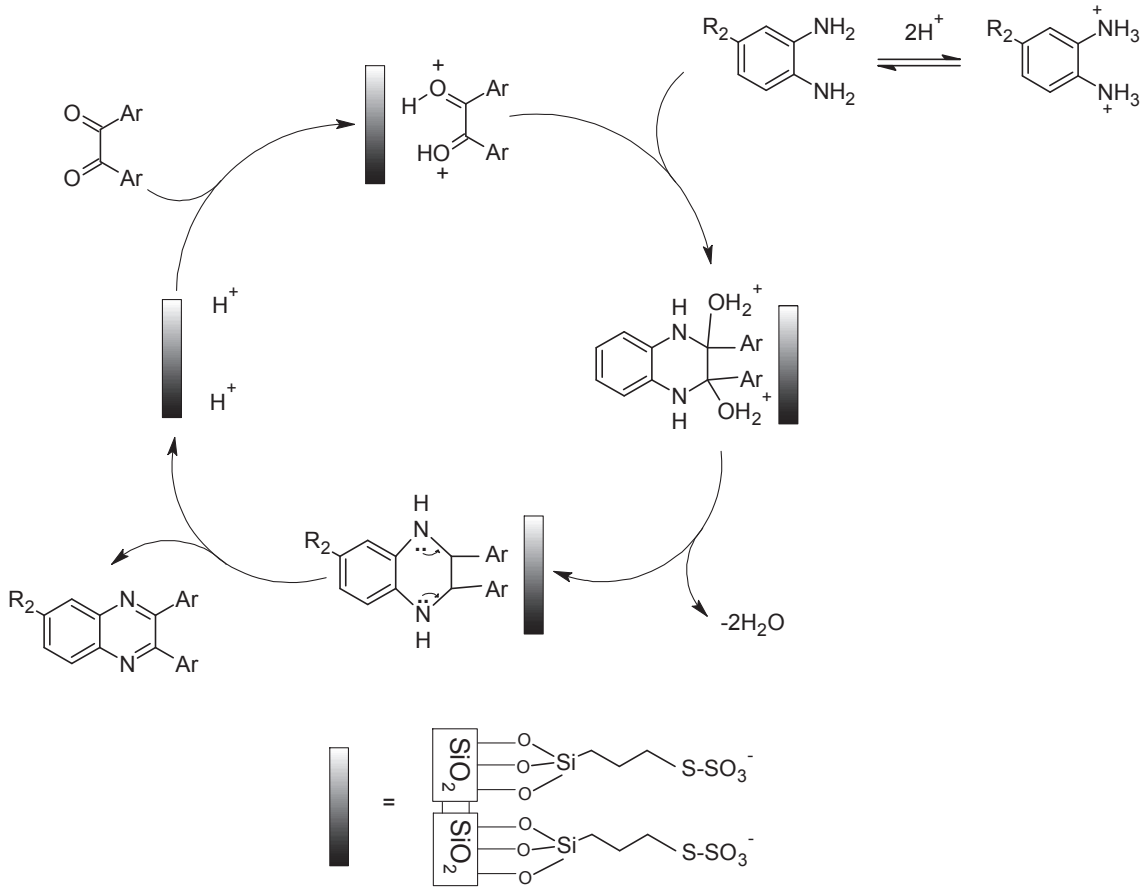
Scheme 21

A brief optimization study revealed that using a biphasic solvent of ethanol and water with 3 mol% of the solid acid catalyst can catalyze the coupling of benzoin and *o*-phenylenediamine in an isolated yield of 96% in 5 minutes. A full study was then conducted in which the scope of the catalyst on a range of diketones and diamines was investigated. A summary of the results obtained is given below (**Table 7**).

Table 7: Sulfonic acid catalyzed synthesis of quinoxalines[83]

Entry	Dicarbonyl	Diamine	Product	Time (min)	Yield (%)
i				5	96
ii				200	90
iii				220	93
iv				8	92
v				15	91

The mechanism is assumed to follow a regular acid catalyzed condensation reaction, with the sulfonic acid protonating the diketone, as well as promoting the dehydration step to produce the carbocationic intermediate (**Scheme 22**).



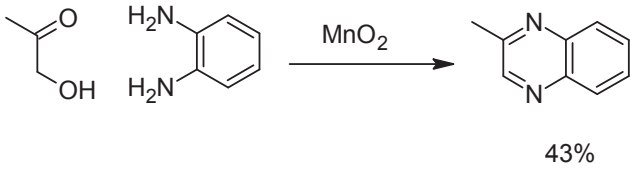
Scheme 22

1.9 Tandem oxidation process mediated quinoxaline synthesis

1.9.1 MnO_2-mediated quinoxaline synthesis

While the general method for the synthesis of quinoxaline has gained widespread prominence, the synthesis of this valuable moiety can also be achieved using the tandem coupling reaction. Taylor and co-workers reported the synthesis of quinoxalines' using

manganese dioxide as an oxidant.[84] A test reaction was conducted with α-hydroxyacetone, *o*-phenylenediamine and a portion of manganese dioxide in refluxing dichloromethane. The desired quinoxaline was formed, however in a disappointing yield of 43% (**Scheme 23**).



Scheme 23

The addition of acid or base, change of solvents and increasing the amount of manganese dioxide did not improve the yield. The major by-product of the reaction was isolated and identified as the known diazobenzene[85] arising from the oxidative coupling of *o*-phenylenediamine (**Figure 12**). Due to this, two equivalents of *o*-phenylenediamine were added and the reaction proceeded smoothly producing the desired quinoxaline in an isolated yield of 78%. The oxidant can be removed by simple filtration but purification is required to remove the desired quinoxaline from its polymeric by-product.

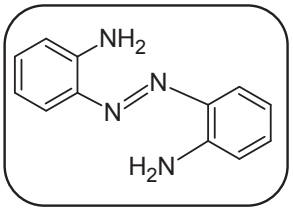
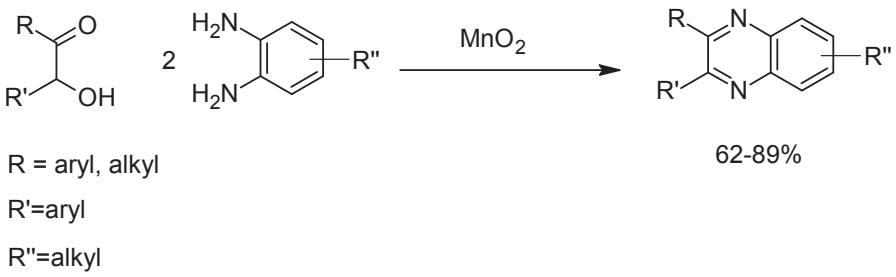


Figure 12

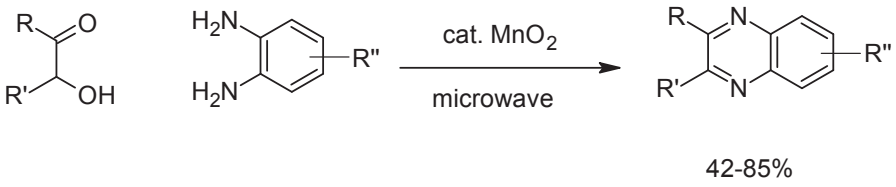
With this optimized procedure in hand, Taylor and co-workers set about exploring the scope and limitations of a manganese dioxide mediated tandem coupling of quinoxalines using a

range of diverse alcohols and 1,2-diamines. Using this methodology, assorted arrays of quinoxalines were isolated in yields ranging from 62-89% (**Scheme 24**).



Scheme 24

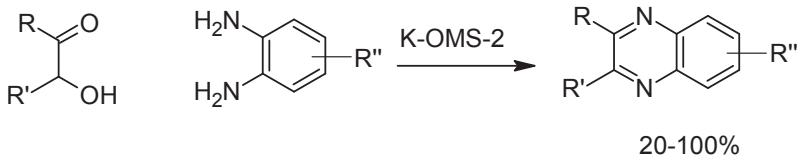
In continuation of a manganese dioxide mediated tandem quinoxaline synthesis, Chung and co-workers reported the use of a microwave assisted tandem coupling reaction.[86] With the implementation of microwave energy, the desired quinoxaline can be synthesized in good yields using a catalytic amount of manganese dioxide. It was reported that under pressurized microwave reaction conditions, 1 mol% of manganese dioxide can catalyze the synthesis of a range of quinoxalines in 42-85% yields (**Scheme 25**).



Scheme 25

While the manganese dioxide mediated oxidation displays a number of advantages such as high yields, short reaction times and simple purification methods; one disadvantage is the use of a 10 fold excess of manganese dioxide. In 2008, Suib and co-workers reported an interesting procedure to circumvent this problem through the use of manganese oxide octahedral molecular sieves (K-OMS-2).[87] Octahedral molecular sieves is a cryptomelane

type manganese oxide with the composition $KMn_8O_{16}{\cdot}nH_2O$ and consists of MnO_6 octahedral units.[88,89] The use of K-OMS-2 in the tandem oxidation process resulted in the formation of quinoxaline derivatives in yields ranging from 20-100% (**Scheme 26**). The advantage of this procedure is that K-OMS-2 is required only in catalytic amounts and can be regenerated and reused without any loss in activity.



Scheme 26

While we focused our attention exclusively on a MnO_2-mediated synthesis of quinoxalines, this procedure can also be conducted using other oxidants.[90-92] The importance of this ever expanding research can be summed up by the fact that the original MnO_2-mediated quinoxaline synthesis, reported by the Taylor group, has been cited over 80 times since it was first reported in 2004.

Aims of the Project

The aim of this project was a broad one, most importantly to highlight and advance the application of semiconductors as an oxidant in synthetic organic chemistry. It is well established that photocatalyzed semiconductor mediated oxidations are unselective due to the presence of strong oxidizing species. Hence, the first task was to develop a light activated photooxidative system that is selective and high yielding with the overall aim of applying this system to a synthetic reaction. This is expected to occur via:

- the choice of appropriate visible light absorbing dyes
- the selection of an electron acceptor to drive the photooxidative system
- determination of an active oxidizing species to effect the alcohol oxidation

In addition, an optimization of yields and reaction conditions as well as mechanistic elucidations will be evaluated. The designed photooxidative system will then be subsequently assessed on a tandem coupling reaction.

References

1. Shaabani, A.; Behnam, M.; Rezayan, A. H. *Catalysis Communications* **2009,** *10*, 1074-1078.
2. Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*; Acdemic Press: New York, 1981.
3. Satterfield, C. N.; Backvall, J. E. *Modern Oxidation Methods*; Wiley-VCH: Germany, 2004.
4. Trost, B. M.; Fleming, I.; Ley, S. V. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 7.
5. Suenaga, K.; Kigoshi, H.; Yamada, K. *Tetrahedron Lett.* **1996,** *37*, 5151-5154.
6. Perkins, M. V.; Lister, T. *Angew. Chem. Int. Ed.* **2006,** *45*, 2560-2564.
7. Jung, M. E.; Salehi-Rad, R. *Angew. Chem. Int. Ed.* **2009,** *48*, 8766-8769.
8. Hayakawa, I.; Takemura, T.; Fukasawa, E.; Ebihara, Y.; Sato, N.; Nakamura, T.; Suenaga, K.; Kigoshi, H. *Angew. Chem. Int. Ed.* **2010,** *122*, 2451-2455.
9. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983,** *48*, 4156-4158.
10. Boeckman, R. K.; Shao, P.; Mullins, J. J. *Org. Synth.* **2000,** *77*, 141-152.
11. Fusaro, L.; Luhmer, M.; Cerioni, G.; Mocci, F. *J. Org. Chem.* **2009,** *74*, 8818-8821.
12. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978,** *43*, 2480-2482.
13. Tidwell, T. T. *Synthesis* **1990**, 857-870.
14. Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.* **1979,** *44*, 4148-4150.
15. Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975,** *31*, 2647-2650.
16. Luzzio, F. A.; Fitch, R. W.; Moore, W. J.; Mudd, K. J. *J. Chem. Educ.* **1999,** *76*, 974-975.
17. Andrade, L. N.; Bizaia, N.; Caetano, B. L.; Silva, M. L. A.; Cunha, W. R.; da Silva Filho, A. A.; Calefi, P. S.; Nassar, E. J.; Bastos, J. K.; Ciuffi, K. J. *Catalysis Communications* **2009,** *10*, 669-672.
18. Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39-45.
19. Harding, K. E.; May, L. M.; Dick, K. F. *J. Org. Chem.* **1975,** *40*, 1664-1665.
20. Hartmann, C.; Meyer, V. *Chem. Ber.* **1893,** *26*, 1727-1732.
21. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991,** *113*, 7277-7278.
22. Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994,** *35*, 8019-8022.
23. Mulbaier, M.; Giannis, A. *Angew. Chem. Int. Ed.* **2001,** *40*, 4393-4394.
24. More, J. D.; Finney, N. S. *Org. Lett.* **2002,** *4*, 3001-3003.
25. Moorthy, J. N.; Singhal, N.; Venkatakrishnan, P. *Tetrahedron Lett.* **2004,** *45*, 5419-5424.
26. Lin, C.-K.; Lu, T.-J. *Tetrahedron* **2010,** *66*, 9688-9693.
27. Oliveira, R. L.; Zanchet, D.; Kiyohara, P. K.; Rossi, L. M. *Chem. Eur. J.* **2011,** *17*, 4626-4631.
28. Urgoitia, G.; SanMartin, R.; Herrero, M. T.; Dominguez, E. *Green Chem.* **2011,** *13*, 2161-2166.
29. Milgrom, L. R. *The Colours of Life: An Introduction to the Chemistry of Porphyrins and Related Compounds*; Oxford University Press: Oxford, 1997.
30. Hajimohammadi, M.; Safari, N.; Mofakham, H.; Deyhimi, F. *Green Chem.* **2011,** *13*, 991-997.
31. Palmisano, G.; Augugliaro, V.; Pagliaro, M.; Palmisano, L. *Chem. Commun.* **2007**, 3425-3437.
32. Morgan, D. V.; Howes, M. J. *Solid State Electronic Devices*; Wykeham Publication Ltd: London, 1972.

33. Bahnemann, D.; Cunningham, J.; Fox, M.; Pelizzetti, E.; Pichat, P.; Serpone, N. *Aquatic and Surface Photochemistry*; Lewis Publishers: USA, 1994.
34. Para, S., 2001.
35. Di Paola, A.; Cufalo, G.; Addamo, M.; Bellardita, M.; Campostrini, R.; Ischia, M.; Ceccato, R.; Palmisano, L. *Colloids and Surfaces A: Physiochem. Eng. Aspects* **2008,** *317*, 366-376.
36. Ovenstone, J. *J. Mat. Sci.* **2001,** *36*, 1325-1329.
37. Wold, A. *Chem. Mater.* **1993,** *5*, 280-283.
38. Rajeshwar, K.; Chenthamarakshan, C. R.; Goeringer, S.; Djukic, M. *Pure Appl. Chem.* **2001,** *73*, 1849-1860.
39. Fujishima, A.; Honda, K.; Kikuchi, S. *Kogyo Kagaku Zasshi* **1969,** *72*, 108-113.
40. Fujishima, A.; Honda, K. *Nature* **1972,** *238*, 37-38.
41. Fujishima, A.; Rao, T. N.; Tryk, D. A. *J. Photochem. Photobiol C: Photochem. Rev.* **2000,** *1*, 1-21.
42. Liu, M.; de Leon Snapp, N.; Park, H. *Chem. Sci.* **2011,** *2*, 80-87.
43. Kikuchi, Y.; Sunada, K.; Iyoda, T.; Hashimoto, K.; Fujishima, A. *J. Photochem. Photobiol. A: Chem.* **1997,** *106*, 51-56.
44. Clasen, T.; Edmondson, P. *Int. J. Hyg. Environ. Health.* **2006,** *209*, 173-181.
45. Burch, J. D.; Thomas, K. E. *Solar Energy* **1998,** *64*, 87-97.
46. Kehoe, S. C.; Barer, M. R.; Devlin, L. O.; McGuigan, K. G. *Lett. Appl. Microbiol.* **2004,** *38*, 410-414.
47. Lonnen, J.; Kilvington, S.; Kehoe, S. C.; Al-Touati, F.; McGuigan, K. G. *Water Res.* **2005,** *39*, 877-883.
48. Boyle, M.; Sichel, C.; Fernandez-Ibanez, P.; Arias-Quiroz, G. B.; Iriarte-Puna, M.; Mercado, A.; Ubomba-Jaswa, E.; McGuigan, K. G. *Appl. Environ. Microbiol.* **2008,** *74*, 2997-3001.
49. Byrne, J. A.; Fernandez-Ibanez, P. A.; Dunlop, P. S. M.; Alrousan, D. M. A.; Hamilton, J. W. J. *Int. J. Photoenergy* **2011**.
50. Lagopati, N.; Kitsiou, P. V.; Kontos, A. I.; Venieratos, P.; Kotsopoulou, E.; Kontos, A. G.; Dionysiou, D. D.; Pispas, S.; Tsilibary, E. C.; Falaras, P. *J. Photochem. Photobiol A: Chem.* **2010,** *214*, 215-223.
51. Ni, J.; Yu, W.-J.; He, L.; Sun, H.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Green Chem.* **2009,** *11*, 756-759.
52. Caronna, T.; Gambarotti, C.; Palmisano, L.; Punta, C.; Recupero, F. *Chem. Commun.* **2003**, 2350-2351.
53. Citterio, A.; Gentile, A.; Minisci, F.; Serravalle, M.; Ventura, S. *J. Org. Chem.* **1984,** *48*, 3364-3367.
54. Carp, O.; Huisman, C. L.; Reller, A. *Prog. Solid State Chem.* **2004,** *32*, 33-177.
55. Dindar, B.; Icli, S. *J. Photochem. Photobiol A: Chem.* **2001,** *140*, 263-268.
56. Rigel, D. S. *J. Am. Acad. Dermatol.* **2008,** *58*, S129-S132.
57. Pinnell, S. R.; Fairhurst, D.; Gillies, R.; Mitchnick, M. A.; Kollias, N. *Dermatol Surg.* **2000,** *26*, 309-314.
58. Nakagawa, Y.; Wakuri, S.; Sakamoto, K.; Tanaka, N. *Mutation Research* **1997,** *394*, 125-132.
59. Nohynek, G. J.; Lademann, J.; Ribaud, C.; Roberts, M. S. *Crit. Rev. Toxicol.* **2007,** *37*, 251-277.
60. Schilling, K.; Bradford, B.; Castelli, D.; Dufour, E.; Nash, J. F.; Pape, W.; Schulte, S.; Tooley, I.; van den Bosch, J.; Schellauf, F. *Photochem. Photobiol. Sci.* **2010,** *9*, 495-509.

61. Gunther, C.; Kecskes, A.; Staks, T.; Tauber, U. *Skin Pharmacol. Appl. Skin Physiol.* **1998,** *11*, 35-42.
62. Hosseini-Sarvari, M. *Catal. Lett.* **2011,** *141*, 347-355.
63. Wiemer, D. F. *Tetrahedron* **1997,** *53*, 16609-16644.
64. Ireland, R. E.; Norbeck, D. W. *J. Org. Chem.* **1985,** *50*, 2198-2200.
65. Verhe, R.; Courtheyn, D.; De Kimpe, N.; De Buyck, L.; Schamp, N. *Synthesis* **1982**, 667-670.
66. Lipshutz, B. H.; Morey, M. C. *J. Org. Chem.* **1983,** *48*, 3745-3750.
67. Blumberg, G.; Van Driesche, R. G. *Biol. Control* **2001,** *22*, 191-199.
68. Millar, J. G.; Midland, S. L.; McElfresh, J. S.; Daane, K. M. *J. Chem. Ecol.* **2005,** *31*, 2999-3005.
69. Hashimoto, K.; Morita, A.; Kuwahara, S. *J. Org. Chem.* **2008,** *73*, 6913-6915.
70. Huang, C. C. *J. Labelled Compd. Radiopharm.* **1987,** *24*, 676-681.
71. Taylor, R. J. K.; Alcaraz, L.; Kapfer-Eyer, I.; Macdonald, G.; Wei, X.; Lewis, N. J. *Synthesis* **1998**, 775-790.
72. Macdonald, G.; Alcaraz, L.; Wei, X.; Lewis, N. J.; Taylor, R. J. K. *Tetrahedron* **1998,** *54*, 9823-9836.
73. Alcaraz, L.; Macdonald, G.; Ragot, J.; Lewis, N. J.; Taylor, R. J. K. *J. Org. Chem.* **1998,** *63*, 3526-3527.
74. Alcaraz, L.; Macdonald, G.; Ragot, J.; Lewis, N. J.; Taylor, R. J. K. *Tetrahedron* **1999,** *55*, 3707-3716.
75. Meyers, A. I.; Babiak, K. A.; Campbell, A. L.; Comins, D. L.; Fleming, M. P.; Henning, R.; Heuschmann, M.; Hudspeth, J. P.; Kane, J. M.; Reider, P. J.; Roland, D. M.; Shimizu, K.; Tomioka, K.; Walkup, R. D. *J. Am. Chem. Soc.* **1983,** *105*, 5015-5024.
76. Taylor, R. J. K.; Reid, M.; Foot, J.; Raw, S. A. *Acc. Chem. Res.* **2005,** *38*, 851-869.
77. Toshima, K.; Kimura, T.; Takano, R.; Ozawa, T.; Ariga, A.; Shima, Y.; Umezawa, K.; Matsumura, S. *Tetrahedron* **2003,** *59*, 7057-7066.
78. Kim, Y. B.; Kim, Y. H.; Park, J. Y.; Kim, S. K. *Bioorg. Med. Chem. Lett.* **2004,** *14*, 541-544.
79. Hazeldine, S. T.; Polin, L.; Kushner, J.; White, K.; Corbett, T. H.; Horwitz, J. P. *Bioorg. Med. Chem.* **2005,** *13*, 3910-3920.
80. Porter, A. E. A. *Comprehensive Heterocyclic Chemistry*; Pergamon: Oxford, 1984.
81. Woo, G. H. C.; Snyder, J. K.; Wan, Z.-K. *Prog. Heterocycl. Chem.* **2002,** *14*, 279-309.
82. Brown, D. J. *The Chemistry of Heterocyclic Compounds*; John Wiley & Sons: New Jersey, 2004.
83. Niknam, K.; Saberi, D.; Mohagheghnejad, M. *Molecules* **2009,** *14*, 1915-1926.
84. Raw, S. A.; Wilfred, C. D.; Taylor, R. J. K. *Org. Biomol. Chem.* **2004,** *2*, 788-796.
85. Bhatnagar, I.; George, M. V. *J. Org. Chem.* **1968,** *33*, 2407-2411.
86. Kim, S. Y.; Park, K. H.; Chung, Y. K. *Chem. Commun.* **2005**, 1321-1323.
87. Sithambaram, S.; Ding, Y.; Li, W.; Shen, X.; Gaenzaler, F.; Suib, S. L. *Green Chem.* **2008,** *10*, 1029-1032.
88. Shen, Y. F.; Zerger, R. P.; DeGuzman, R. N.; Suib, S. L.; McCurdy, L.; Potter, D. I.; O'Young, C. L. *Science* **1993,** *260*, 511-515.
89. DeGuzman, R. N.; Shen, Y. F.; Neth, E. J.; Suib, S. L.; O'Young, C. L.; Levine, S.; Newsam, J. M. *Chem. Mater.* **1994,** *6*, 815-821.
90. Crich, D.; Mo, X.-S. *Synlett* **1999,** *1*, 67-68.
91. Barrett, A. G. M.; Hamprecht, D.; Ohkubo, M. *J. Org. Chem.* **1997,** *62*, 9376-9378.
92. Shuto, S.; Niizuma, S.; Matsuda, A. *J. Org. Chem.* **1998,** *63*, 4489-4493.

Chapter 2

Discussion

2.1 Preface

The focus of this project was to extend the application of semiconductors to tandem coupling reactions. In the discussion which follows, attention will be focused on the evaluation of the semiconductors available with the overall aim of developing a photooxidative system applicable to a multitude of tandem coupling reactions. This discussion will begin with an evaluation of literature as we seek to develop the most productive photooxidative system. In the subsequent pages, attention will be focused on the thought process developed in assembling such a photooxidative system.

2.2 Titanium dioxide and zinc oxide as photocatalysts

It is generally accepted that titanium dioxide and zinc oxide are ideal photocatalysts as they embody all the attributes of an ideal semiconductor such as low cost, stability under irradiation and environmental friendliness. These semiconductors display band gaps of approximately +3.2 eV (corresponding to a wavelength of 387 nm), implying that ultraviolet irradiation is required for their activation. It is generally accepted that the following steps occur when these semiconductors are subjected to ultraviolet irradiation, which can be divided into the 'direct' and 'indirect' methods.[1]

2.2.1 The 'indirect' method (Figure 13)

- Upon ultraviolet irradiation, an electron is promoted from the valence band to the conduction band.
- The electron is quenched by oxygen, which is reduced to superoxide.

- The ejected electron leaves behind a 'positive hole' in the valence band which is a strong oxidant that is able to oxidize water to a hydroxyl radical.

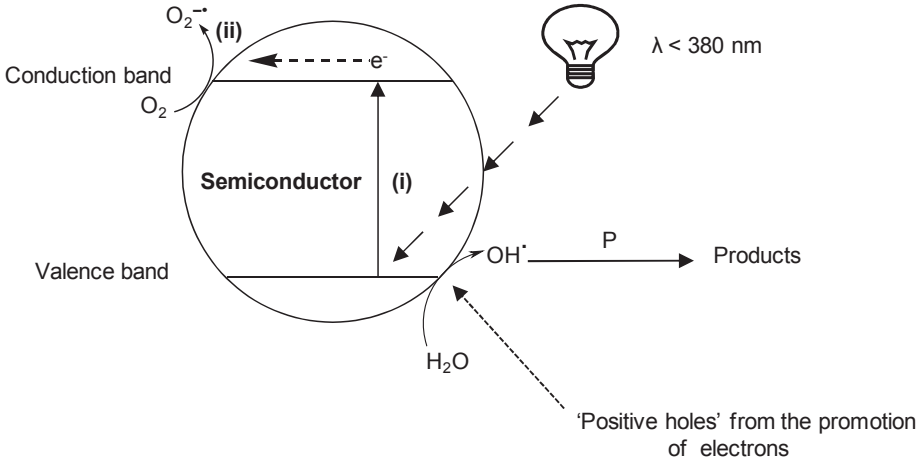


Figure 13

Hydroxyl radicals are one of the strongest known oxidants and, as previously highlighted, have found widespread applications. A list of common, strong oxidizing agents and their oxidizing potential is given below in **Table 8**. Hydroxyl radicals are a stronger oxidizing agent than ozone, one of the strongest oxidizing agents and a well known water purification agent. However, the operating costs for ozone mediated water purification are high since ozone is generated by converting a stream of oxygen into ozone using electricity.[2] Thus, the production of hydroxyl radicals is advantageous as a stronger oxidizing agent is produced using cheap, environmentally friendly semiconductors.

Table 8: Oxidation potential of common oxidizing agents[3]

Oxidant	Oxidizing potential (V)
Hydroxyl radicals	2.80
'Positive holes'	2.70
Ozone	2.07
Hydrogen peroxide	1.77
Hypochlorous acid	1.49
Chlorine	1.36

2.2.2 The 'direct' method (Figure 14)

The 'direct' method for semiconductor mediated photocatalysis follows an identical pathway as highlighted for the 'indirect' method. However, in this case, special care is taken to exclude water which prevents the formation of hydroxyl radicals. In a typical procedure, the semiconductor powder is dried overnight in an oven to remove adsorbed water, before the photoreaction is conducted in a dry reaction vessel with an anhydrous solvent. In this case, the photooxidation is executed exclusively by the strongly oxidizing positive holes.[4]

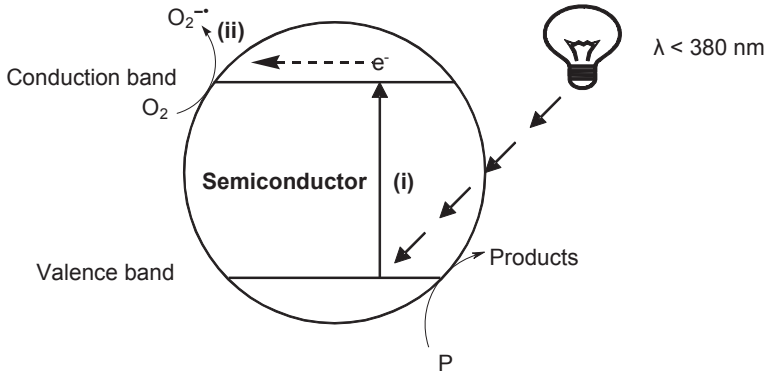
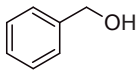
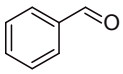
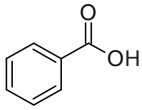
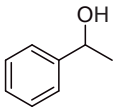
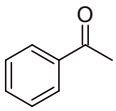
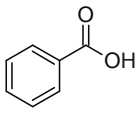
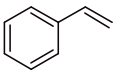
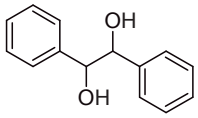
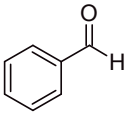
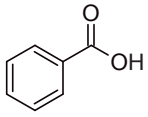
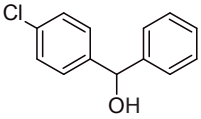
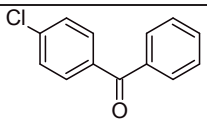
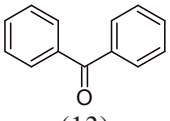
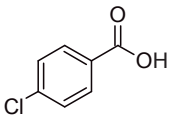
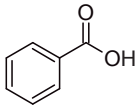


Figure 14

Whether the reaction proceeds *via* the 'direct' or 'indirect' route the overall result is the formation of a strongly oxidizing species. Abdel-Wahab and co-workers have reported the

photocatalyzed oxidation of alcohols using titanium dioxide using the 'direct method'.[5] The photooxidative procedure was found to be extremely efficient with the alcohols converted in > 90% yield. However, a serious drawback was the variety of products formed with the aldehyde, acid as well as additional unidentifiable side products also present (**Table 9**). This observation is unsurprising considering the active oxidizing agent is the strongly oxidizing 'positive hole'.

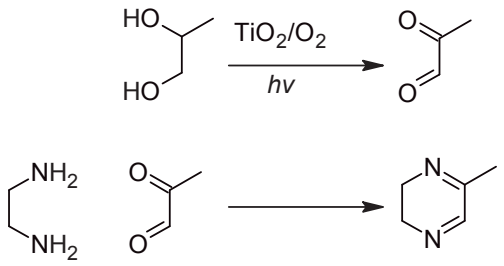
Table 9: Photooxidation of alcohols using titanium dioxide

Entry	Time (h)	Conversion (%)	Substrate	Product 1 (%)	Product 2 (%)	Other minor products (%)
i	6	92		 (48)	 (29)	Unknowns (7), (8)
ii	6	95		 (93)	 (2)	 (4) Unknown (1)
iii	8	90		 (31)	 (39)	 (4) Unknowns (3, 11, 12)
iv	6	92		 (51)  (13)	 (16)  (5)	Unknown (7)

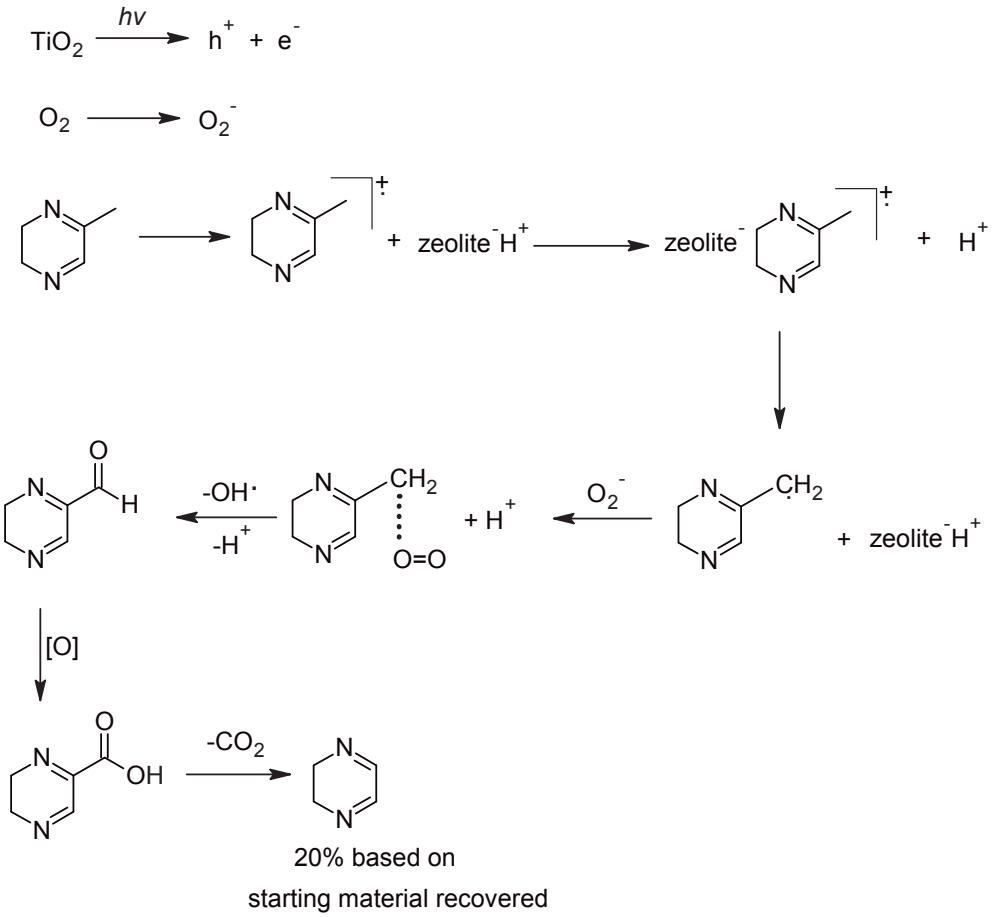
A photocatalyzed tandem coupling reaction was also reported by Subrahmanyam and co-workers in which dihydropyrazine was synthesized from ethylene glycol and ethylenediamine.[6] TiO_2 and ZnO in combination with various polymorphs of zeolite were tested, in which the desired dihydropyrazine was formed in yields ranging from 8-20%. A highly elaborate mechanism for the formation of dihydropyrazine was proposed with the desired product formed in a disappointing yield of 20% based on the starting material recovered using the TiO_2/zeolite system (**Scheme 27**).

These results were a cause for concern as the photooxidation of alcohols was non-selective, with a variety of products formed. Since the yield of the desired aldehyde was low, the tandem coupling reaction would also be inefficient as evidenced by the tandem coupling synthesis of dihydropyrazine. Thus, the high oxidizing strength of the hydroxyl radicals leads to uncontrollable reactions with limited selectivity. These predictions had come to fruition within our research group whilst attempting a one-pot photocatalyzed tandem Wittig reaction. In this case, an attempt was made to oxidize an alcohol using titanium dioxide and couple the generated aldehyde with a Wittig reagent in a one-pot synthesis.[7] However, subsequent analysis by NMR spectroscopy revealed the presence of a number of unidentifiable signals, none of which were attributable to the product. Thus, before we could embark on a series of photocatalyzed tandem coupling reactions, the photooxidative procedure needed to be refined so that the aldehyde could be formed in high yield without the formation of side-products.

Step 1



Step 2



Scheme 27

2.3 Designing a photooxidative system

2.3.1 Shifting the absorbance of the semiconductor

While there are a variety of applications for semiconductor mediated photocatalysis, the procedure suffers from one major drawback. Due to the large band gaps of these semiconductors, ultraviolet light is required for their activation. Since natural sunlight can only supply 2-3% ultraviolet light, the industrial application of these materials is limited.[8] Consequently, many research groups have developed methods to modify the band gap of titanium dioxide in an effort to shift its absorbance from the ultraviolet region into the visible region. This can be accomplished in two main routes, either by doping or surface sensitization.

2.3.1.1 Doping of semiconductor

The method commonly used to shift the absorbance of semiconductors involves the purposeful addition of impurities to the semiconductor in an effort to alter its band gap. This procedure commonly referred to as doping, results in an impurity band which decreases the band gap, resulting in a shift in absorbance into the visible region (**Figure 15**).

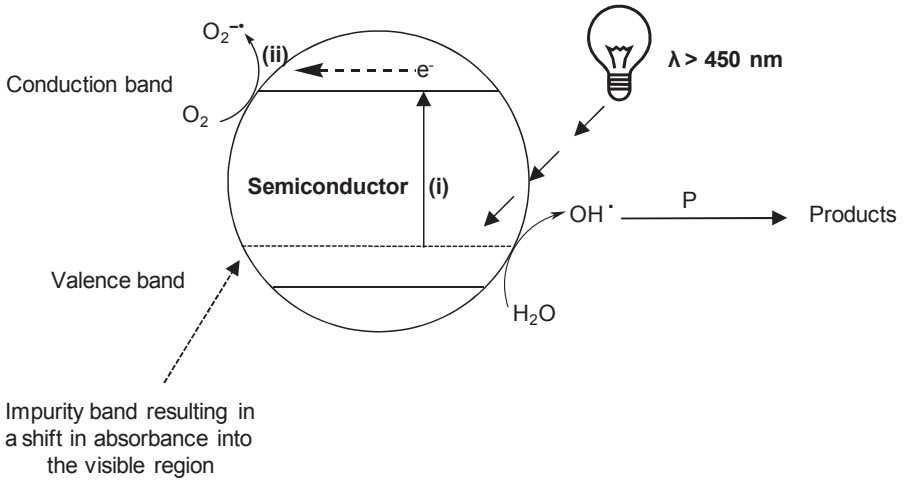


Figure 15

A classic example of doping was reported by the Wu research group in which various quantities of vanadium were incorporated into the titania photocatalyst enabling visible light absorbtion.[9] This procedure involved the addition of titanium butoxide and vanadium chloride in ethanol to an aqueous solution of hydrochloric acid. The resultant powdered product was subsequently dried, pulverized and calcined at 400 ^{o}C to produce the vanadium doped titanium dioxide powder. Analysis of the synthesized powder by diffuse reflectance spectroscopy revealed a shift in absorbance into the visible region while the absorbance of pure titanium dioxide remained in the ultraviolet region. This shift in absorbance into the visible region was attributed to the incorporation of a vanadium(IV) state into the titania photocatalyst. The photocatalytic activity of these powders was evaluated by monitoring the decomposition of methylene blue under visible light irradiation. The results revealed that the degradation of methylene blue was higher on V-doped TiO_2 when compared to pure, undoped TiO_2.

Whilst the doping of semiconductors results in a decrease in band gap, the overall result is the formation of hydroxyl radicals as an electron is promoted from the impurity band to the conduction band. The difference lies in the fact that the promoted electron originates from the impurity band and not the valence band of the semiconductor under visible light irradiation. Thus, in our case the doping of the semiconductors would be futile as the strongly oxidizing hydroxyl radicals (or 'positive holes') would still be formed resulting in a decrease in selectivity.

2.3.1.2 Dye sensitization of the semiconductor

The adsorbtion of visible light absorbing dyes is another method that can improve the photocatalytic response of these semiconductors. This strategy employs the attachment of a visible light absorbing dye to the surface of the semiconductor. Upon visible light irradiation, the activated dye injects an electron into the conduction band of the semiconductor.[10] Most importantly under these conditions, the dye and *not* the semiconductor is activated preventing the formation of a strongly oxidizing species (**Figure 16**).

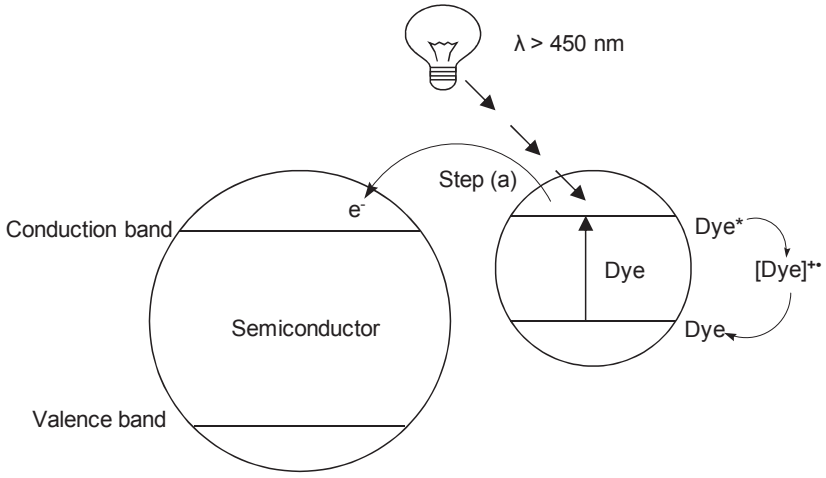


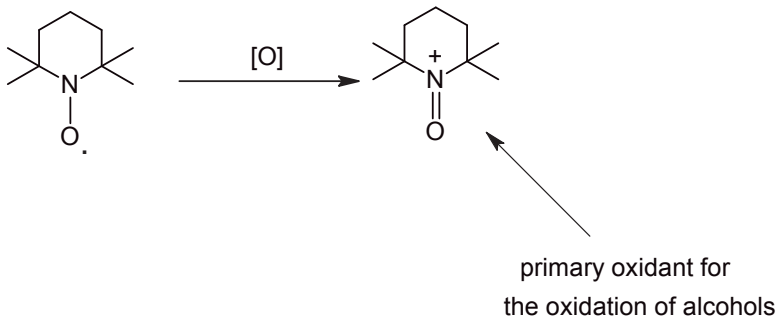
Figure 16

Thus, the first piece of the photooxidative system had been established which allowed for the accomplishment of two major goals. Firstly by using a dye sensitized semiconductor, the formation of a strongly oxidizing species (such as the hydroxyl radicals or positive holes) would be prevented, allowing for more selectivity in the photooxidative system. Secondly, the use of readily available visible light irradiation, rather than harsh ultraviolet irradiation, further increases the attractiveness of this procedure.

2.3.2 Determination of an active oxidizing species

2.3.2.1 Use of 2,2,6,6-tetramethylpiperidine-1-oxyl-radical (TEMPO)

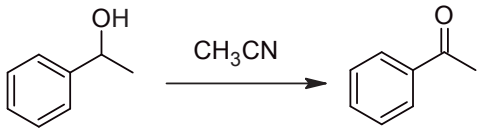
Since the formation of strongly oxidizing hydroxyl radicals will not occur under visible light irradiation, a new oxidant needs to be generated to effect the oxidation of the alcohol to the carbonyl derivative. In 1984, Semmelhack and co-workers reported the use of *N*-oxoammonium salt for the selective oxidation of alcohols to aldehydes.[11] The *N*-oxoammonium salt must however, be generated from the commercially available 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) *via in situ* oxidation by a terminal oxidant (**Scheme 28**).



Scheme 28

The valuable application of TEMPO in the oxidation of alcohols was elegantly depicted by Kim and co-workers using a ceric ammonium nitrate CAN/TEMPO/O_2 system.[12] The system was evaluated using 1-phenylethanol as a model substrate and the results are shown below (**Table10**).

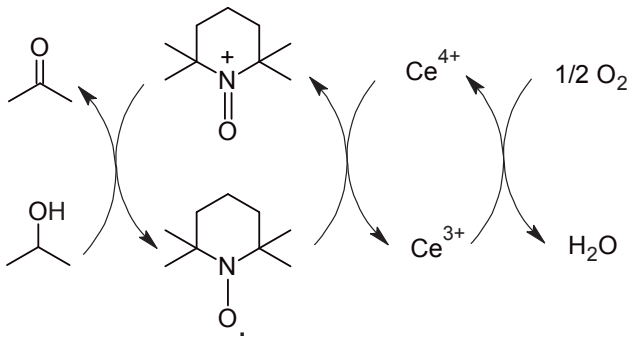
Table 10: Evaluation of the CAN/TEMPO/O_2 system using 2-phenylethanol as a model substrate



Entry	CAN (mol%)	TEMPO (mol%)	O_2	Time (h)	Yield (%)
i	–	10	O_2	1	NR[a]
ii	20	–	O_2	1.5	5
iii	20	10	–	1.5	40
iv[b]	10	10	O_2	1	11
v[c]	10	10	O_2	1	99

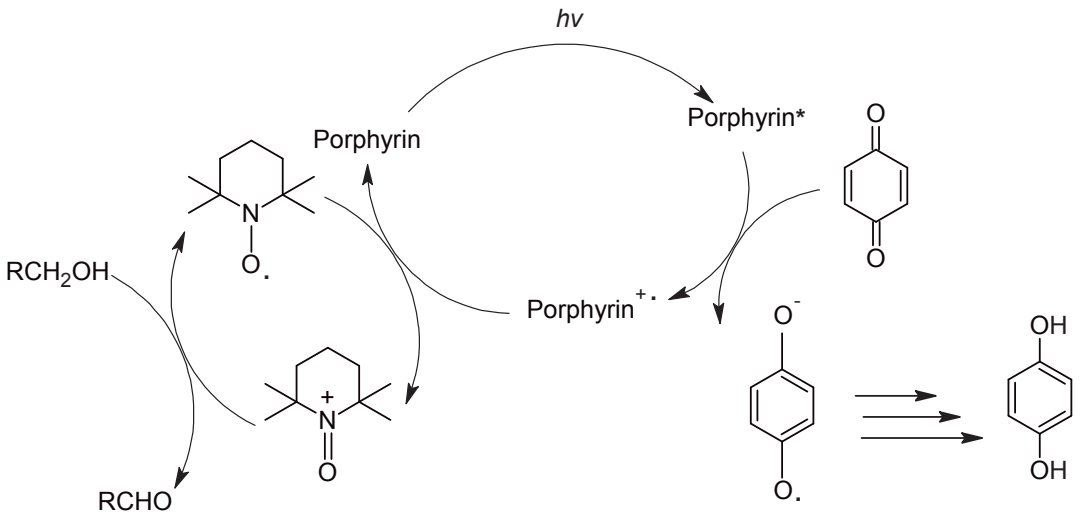
[a] No reaction. [b] Room temperature. [c] Refluxing CH_3CN.

The contribution of each of the additives can be summarized as follows: In the absence of CAN, no reaction takes place as the actual oxidant is the *N*-oxoammonium salt and not the TEMPO radical (**entry i**). Ceric ammonium nitrate is a weak oxidant and can only oxidize the alcohol in trace quantities (**entry ii**). Entries **iii** and **iv** highlight the importance of oxygen and temperature on the yield of the reaction. The results obtained indicate that CAN is a weak oxidant and singlehandedly is unable to effectively oxidize the alcohol to the ketone. TEMPO in its radical form is unable to oxidize the alcohol to the ketone. However, CAN is sufficiently strong a oxidant to convert TEMPO from its radical form to the *N*-oxoammonium salt which efficiently carries out the oxidation. Based on these results, the following mechanism was proposed (**Scheme 29**). In the proposed mechanism, dioxygen is oxidized to water by oxidation of Ce^{3+} to Ce^{4+} which in turn oxidizes TEMPO from its radical form to the *N*-oxoammonium salt which selectively oxidizes alcohols to their carbonyl derivatives.



Scheme 29

Thus, the use of TEMPO in the photooxidative reaction emerged as a valuable proposition for the oxidation of alcohols to their carbonyl derivatives. The proposal was further strengthened by an interesting report by Nagata and co-workers in which they described the photooxidation of alcohols using a porphyrin/quinone/TEMPO system (**Scheme 30**).[13] This procedure involved the visible light mediated activation of the porphyrin which, in its activated state transfers an electron to the quinone resulting in the formation of a porphyrin cation radical. This radical is a sufficiently strong oxidant to convert TEMPO to the *N*-oxoammonium salt which selectively oxidizes alcohols to aldehydes. While this report was a valuable addition to our knowledge, it was noted that the reaction was conducted on a minute scale with long reaction times. Using the porphyrin/quinone/TEMPO system, 300 μmol of alcohol was oxidized to the aldehyde in 37-84% yields under 24 hours of irradiation.



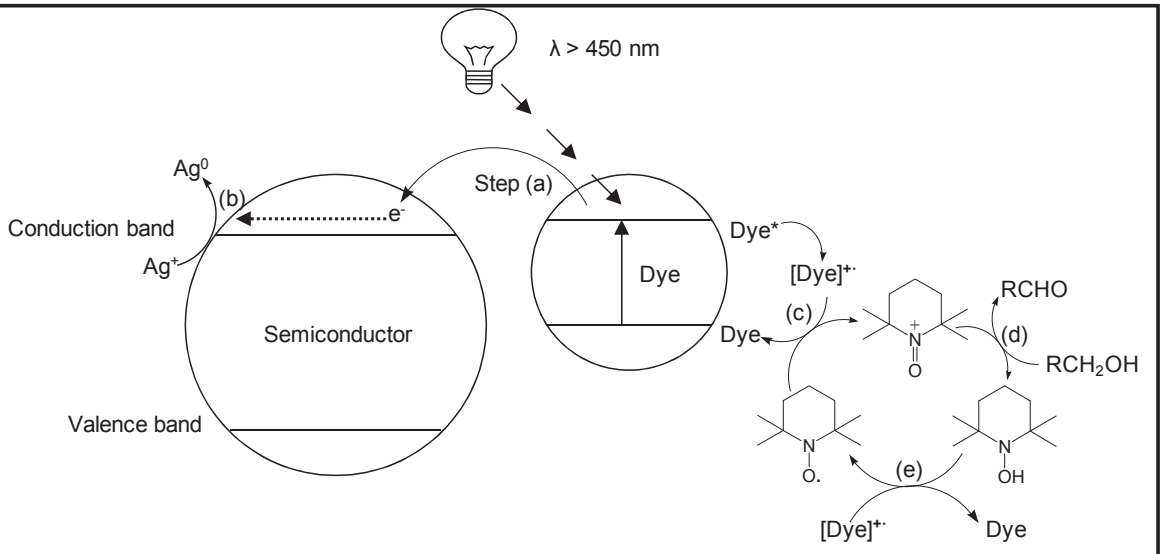
Scheme 30

Thus, the second component of the photooxidative system had been developed with TEMPO chosen as the active oxidizing species. Using TEMPO as the active oxidant was advantageous as the conversion of TEMPO to the *N*-oxoammonium salt will selectively effect the conversion of alcohols to aldehydes. Having identified the use of a visible light absorbing dye and TEMPO as vital components of the photooxidative system, attention was turned to the last component, the choice of the electron acceptor.

2.3.3 Choice of electron acceptor

The final step of the system was to choose an efficient reagent to trap the electrons injected into the conducted band by the activated dye. Traditionally molecular oxygen is most commonly employed as an electron acceptor in the semiconductor and it has been suggested that the transfer of electrons to oxygen is the rate determining step in semiconductor mediated photocatalysis.[14] Consequently, it was understood that the choice of electron acceptor was fundamental for a productive photooxidative system. During the course of a literature search, attention was drawn to the use of silver (I) as a potential electron acceptor. The Rol research

group has advocated the use of silver (I) as an electron acceptor in semiconductor mediated photocatalysis. They have argued that since silver (I) is a superior electron acceptor to dioxygen, the photooxidative system would be more efficient, resulting in higher yields in shorter reaction times. They demonstrated the application of silver (I) by conducting a series of photocatalyzed oxidations on benzylic alcohols.[15] As expected, due to the presence of the positive holes, the corresponding aldehyde, acid and undetermined products were formed. However, the most interesting result was that in the presence of silver (I) the yield of the aldehyde was almost double that in the presence of oxygen as an electron acceptor. Hence, it was envisaged that silver (I) had a crucial role to play in the photooxidative system by trapping the ejected electron. Thus, on completion of this literature survey the following photooxidative system was conceptualized in which each additive made a unique contribution to its success (**Figure 17**).



Step a: Upon visible light irradiation, the activated dye injects an electron into the conduction band of the semiconductor.
Step b: The ejected electron is rapidly quenched by silver (I) which is converted to silver (0).
Step c: The generated dye radical oxidizes TEMPO to the *N*-oxoammonium salt.
Step d: The *N*-oxoammonium salt oxidizes the alcohol to the aldehyde resulting in the formation of the hydroxylamine.
Step e: The hydroxylamine regenerates TEMPO *via* oxidation by the dye radical.

Figure 17

Based on the literature review, it was decided that a dye sensitized semiconductor/silver/TEMPO system would be most efficient. However, a few issues still needed to be evaluated which included the choice of dye and solvent.

2.3.4 Choice of dye

The choice of dye for the photooxidative system was one of the most important components in the photooxidative system. Semiconductors have been sensitized with a wide range of dyes that are all able to absorb visible light, but in this case the oxidizing strength of the dye radical was of crucial importance. The generated dye radical needs to be a strong enough oxidant to oxidize TEMPO from its radical form to the *N*-oxoammonium salt. Zhao and co-workers have also reported a selective photooxidative system using dye sensitized titanium dioxide in combination with TEMPO and oxygen.[16] In this system, developed by Zhao and co-workers, Alizarin Red S (**Figure 18**) was chosen as a dye as its cation radical was able to convert TEMPO into the active oxidizing species.

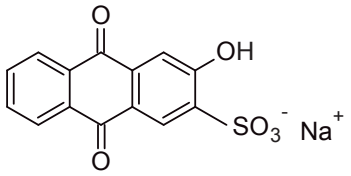


Figure 18

The oxidation of benzylic alcohols, conducted on a 0.1 mmol scale, produced the desired aldehydes in varying yields ranging from 49-100% over 18-24 hours of irradiation. Based on the above reported results, Alizarin red S was chosen to sensitize titanium dioxide and zinc oxide as its dye radical would convert TEMPO into the active oxidizing species.

A literature search revealed that thermodynamically, the proposed mechanism was viable as evidenced by the following table of standard redox potentials (**Table 11**).

Table 11 Redox potentials of various components of oxidative cycle

Compound	E^0 vs. SHE (V)
E_{cb} (ZnO)	– 0.42[17]
TEMPO/$TEMPO^+$	0.64[18]
Ag^+/Ag^0	0.80[19]
$AR^{+\cdot}/AR$	0.79[20]
E_{cb} (TiO_2)	– 0.50[21]
$AR^*/AR^{+\cdot}$	–1.57[21]

- The standard redox potential for the excited state of Alizarin red ($AR^*/AR^{+\bullet}$) is lower than E_{cb}[†] of ZnO and E_{cb} of TiO_2 indicating that the excited state of the dye is capable of injecting electrons into the conduction band of the semiconductors.
- The standard redox potential of silver (I) (Ag^+/Ag^0) is higher than E_{cb} for the semiconductors indicating that the injected electrons can be trapped by silver (I).
- The standard redox potential of ($AR^{+\bullet}/AR$) is higher than the standard redox potential of TEMPO/$TEMPO^+$ indicating that the dye radical is capable of oxidizing TEMPO.

2.4 Assembling the photooxidative system

2.4.1 Diffuse reflectance analysis

Thus, the scene was set to test the proposed system experimentally by carrying out the oxidation of a series of alcohols. Initial studies commenced with the sensitizing of the semiconductors in which a portion of Alizarin red S was mixed with the semiconductor in a minimum amount of water. The mixture was stirred overnight to produce a colored, dye sensitized powder. To confirm the adsorbtion of the dye to the semiconductor, the synthesized powders were subjected to analysis by diffuse reflectance spectroscopy in an effort to probe the absorbance of these newly synthesized powders. Both the synthesized powders showed absorbtion in the ultraviolet region characteristic of these semiconductors (**Figure 19**). However, most importantly, these powders also showed absorbtion in the visible

[†] cb = conduction band

region (> 430 nm) with the dye sensitized ZnO showing a marginally higher absorbtion than the dye sensitized TiO_2 powder. These results are in excellent agreement with literature as the diffuse reflectance spectra obtained was identical to those reported by Zhao and co-workers.[16] Thus, it was concluded that Alizarin red S had successfully adsorbed onto titanium dioxide and zinc oxide and that both these powders displayed absorbance in the visible region.

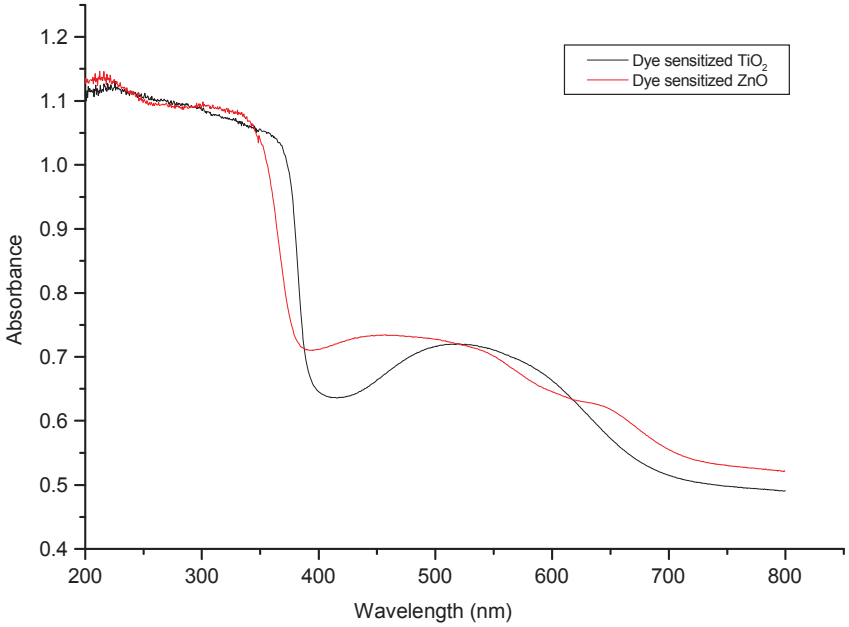


Figure 19

2.4.2 Stability of dye sensitized semiconductor

Having successfully adsorbed Alizarin Red S onto the surface of the semiconductor, attention was now directed towards another crucial factor namely, the choice of solvent. The most important dynamic was that for a successful photocatalyzed system, the electron acceptor should be highly soluble in the solvent. Since silver (I) was chosen as the electron acceptor, the most obvious choice of solvent was water. However, dye sensitized semiconductors are known to be unstable in water with the dye readily detaching from the semiconductor.[22] In the late 1970's the Hada research group reported the photoreduction of silver (I) using dye

sensitized titanium dioxide[23] and dye sensitized zinc oxide in aqueous solutions.[24] This early piece of research into dye sensitized semiconductors would prove invaluable as it postulated that in a concentrated silver solution the dye sensitized semiconductor would be stable. The above hypothesis was tested by placing the dye sensitized powders in concentrated silver solutions and pure water and comparing its behaviour.

2.4.3 UV/Vis analysis of dye sensitized semiconductors

To validate the proposal, the above mixtures were subjected to analysis by UV/Vis spectroscopy. Firstly, a concentrated solution of silver nitrate was prepared and a UV/Vis spectrum obtained. Next, the dye sensitized metal oxides were placed in solutions containing pure water and silver nitrate solutions and subjected to analysis by UV/Vis spectroscopy (**Figure 20**). Both the dye sensitized metal oxides (ZnO and TiO_2) were found to be stable in concentrated silver nitrate solutions with identical spectra to pure silver nitrate solutions obtained. As expected, the dye sensitized metal oxides were found to be unstable in pure water and the dye readily detached from the metal oxide as evidenced by UV/Vis spectra. From these results, it was concluded that both the dye sensitized metal oxides were stable in concentrated silver solutions and unstable in a pure aqueous solution in agreement with previous literature.

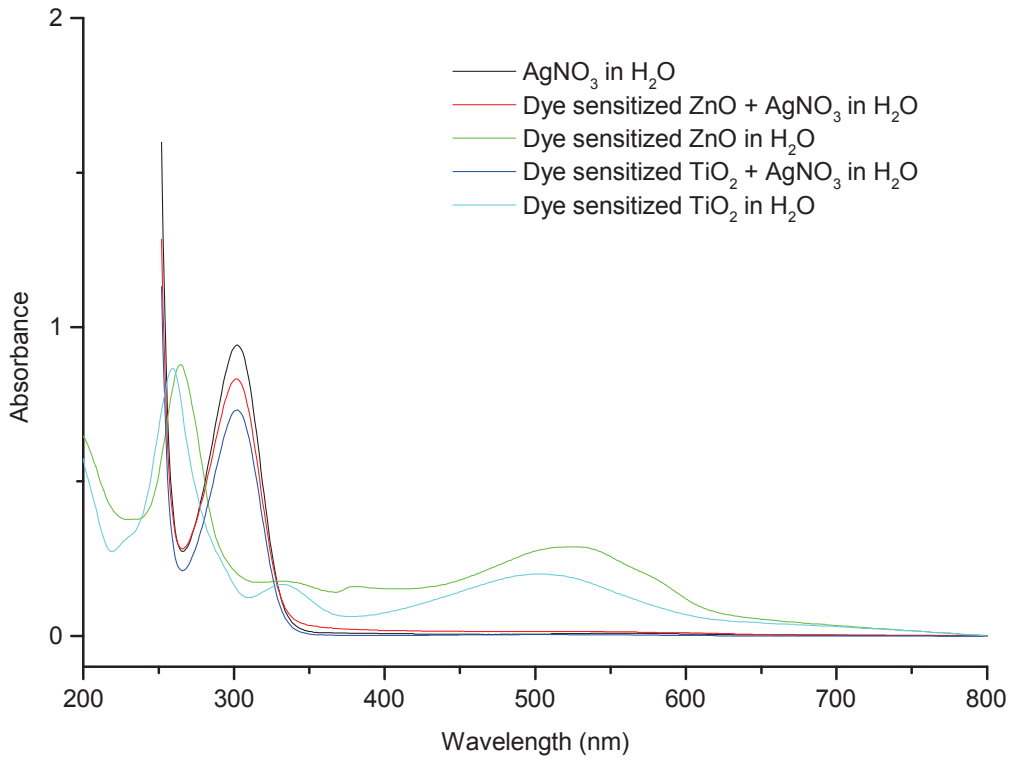


Figure 20

2.4.4 Effect of silver nitrate

With the complete photooxidative system in hand, a test reaction was carried out in which a portion of dye sensitized semiconductor, TEMPO, silver nitrate and benzyl alcohol in an aqueous solution was stirred under visible light irradiation for 2 hours. In the case of the dye sensitized ZnO, benzaldehyde was formed in a 27% yield while no product formation was evident in the case of dye sensitized TiO_2. While the reasons for the failure of the reaction in the dye sensitized TiO_2/silver/TEMPO was at this point unclear to us, the results obtained with the dye sensitized ZnO/silver/TEMPO system was most encouraging and a full study was required to fully explore this system. Although the yield of 27% was disappointing, it did indicate that the system was viable and an optimization of the reaction conditions was necessary in order to maximize product formation. Since many photooxidative systems that

use silver (I) as an electron acceptor require the silver salt in excess,[25,26] the quantity of silver nitrate added and its effect on the yield of benzaldehyde was monitored. This study involved mixing a portion of dye sensitized ZnO, TEMPO, benzyl alcohol and various quantities of silver nitrate in an aqueous environment under visible light irradiation for 2 hours. An increase in silver nitrate concentration brought about a corresponding increase in the conversion of benzaldehyde until an optimum of 18 equivalents of silver nitrate produced the desired aldehyde in an excellent yield of 82% (**Figure 21**).

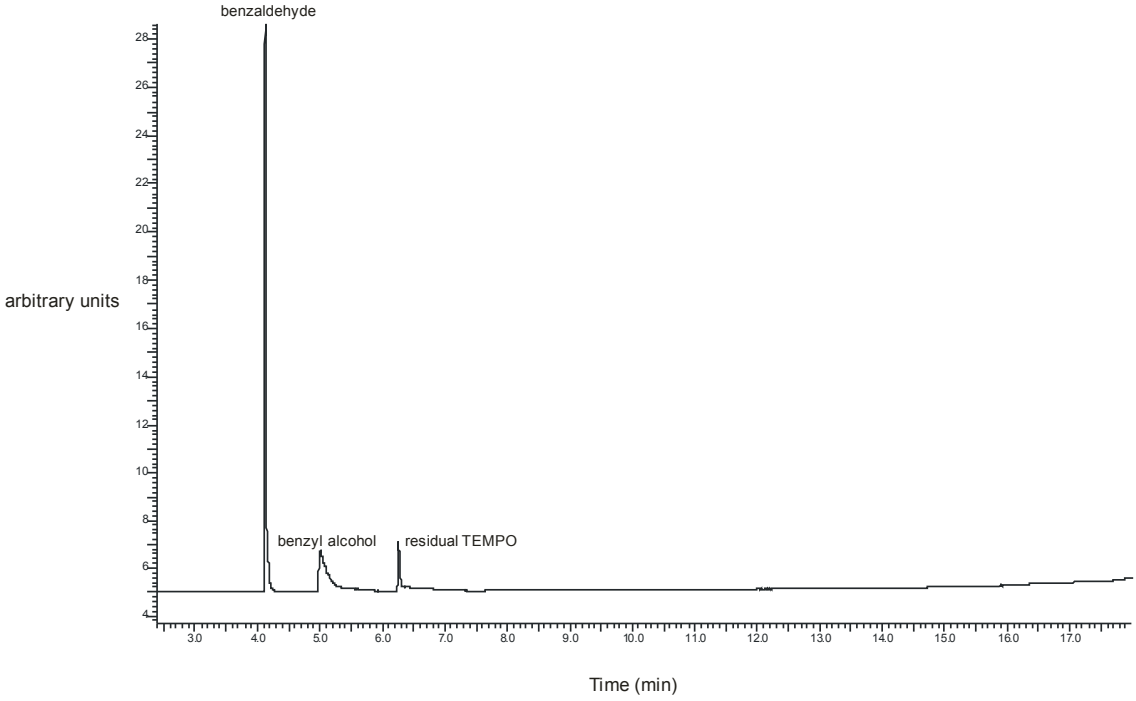


Figure 21

The results of the effect of silver nitrate on the yield of the aldehyde can be elegantly represented by the following graph (**Figure 22**).

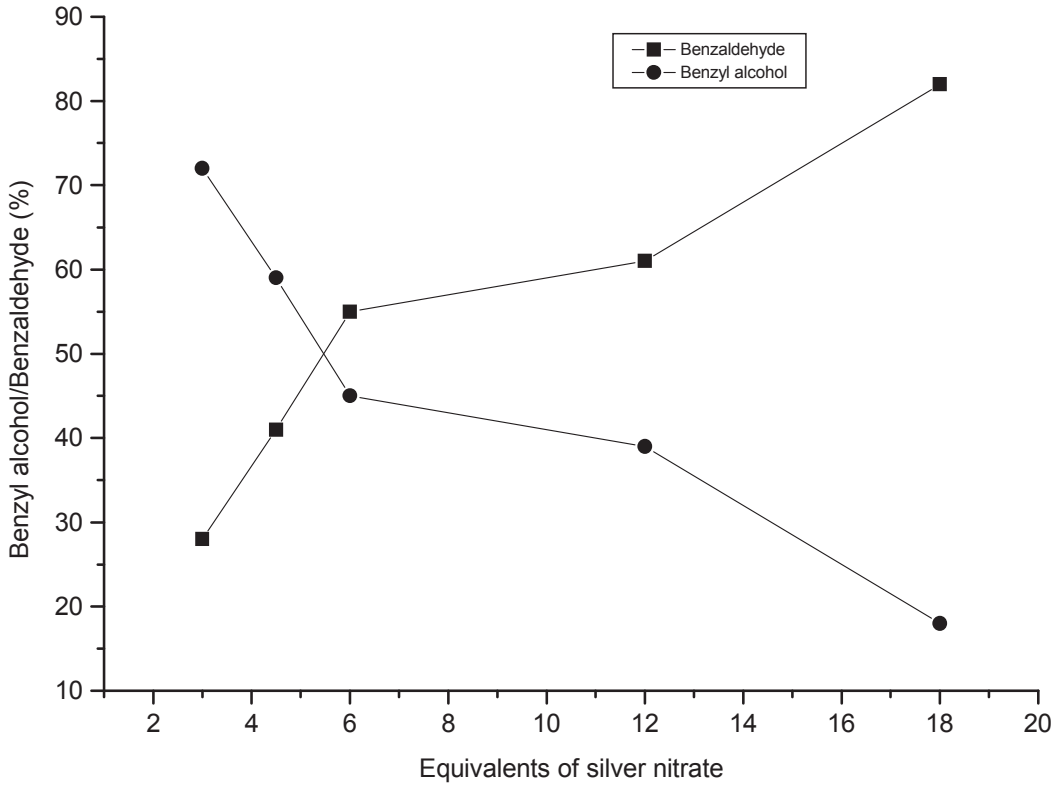


Figure 22

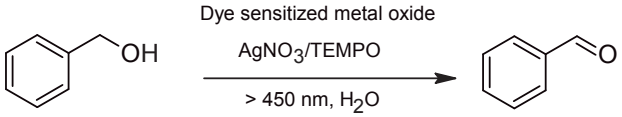
While the quantity of silver nitrate may be deemed to be excessive, the yield of benzaldehyde was far superior to the other photocatalyzed TEMPO mediated oxidative systems. The oxidation of benzyl alcohol to benzaldehyde using the dye sensitized TiO_2/O_2/TEMPO system reported by Zhao and co-workers[16] resulted in formation of benzaldehyde in a comparable yield of 80% (*vs.* 82% for the dye sensitized ZnO/silver/TEMPO system) however the reaction was much faster in the dye sensitized ZnO/silver/TEMPO system as the reaction required only 2 hours of irradiation as opposed to the 18 hours required for dye sensitized TiO_2/O_2/TEMPO system. The porphyrin/quinone/TEMPO system[13] produced the desired aldehyde in yield of 84% after 24 hours of irradiation on a smaller scale. The advantage of our methodology is that procedures are available for the recovery of the precipitated silver which will allow for the reuse of the photocatalyst.[27,28] Accordingly, the

preliminary investigation had been most fruitful as the designed system produced the desired aldehyde in high yield and short reaction times and was more productive than other reported photooxidative systems.

2.4.5 Contribution of each of the additives to the photooxidative system

The optimized reaction conditions were then reevaluated on the dye sensitized TiO_2/silver/TEMPO system with disappointing results. Attention was then shifted exclusively to the dye sensitized ZnO/silver/TEMPO system to probe the contribution of each of the additives to the photooxidative system. Firstly, the reaction was conducted under identical conditions but in the absence of dye sensitized ZnO. Under these conditions, a dramatic decrease in yield was observed with the aldehyde formed in only 16%. This result was most significant as it suggested that the dye sensitized ZnO played a decisive role in the success of this photooxidative system. In the absence of TEMPO, the yield of the aldehyde also plummeted with the desired compound formed in only 12% yield. As expected, when the reaction was conducted in the absence of silver nitrate the dye readily detached from the semiconductor. Similar results were obtained when water was replaced with acetonitrile as a solvent further highlighting the importance of water in the photooxidative system. The results of this study are represented below in **Table 12**.

Table 12: Oxidation of benzyl alcohol using a dye sensitised metal oxide/$AgNO_3$/TEMPO system



Entry	Metal Oxide	Time/h	Yield[a] (%)
i	TiO_2	1	3
ii	ZnO	1	54
iii	TiO_2	2	8
iv	ZnO	2	82
v[b]	–	2	16
vi[c]	ZnO	2	12
vii[d]	ZnO	–	nd[f]
vii[e]	ZnO	–	nd[f]

[a] GC yield. [b] Absence of zinc oxide. [c] Absence of TEMPO. [d] Absence of silver nitrate. [e] CH_3CN as solvent. [f] Not determined as the dye sensitized ZnO was unstable under these conditions.

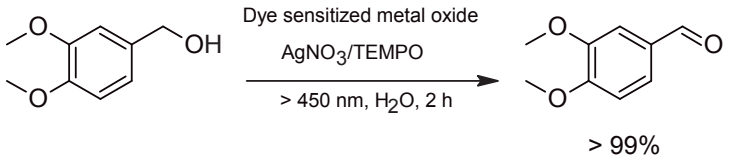
2.5 Expansion of the dye sensitized ZnO/silver/TEMPO system to a series of alcohols

With this optimized procedure in hand, the scope of the dye sensitized ZnO/silver/TEMPO system was explored on a series of alcohols. All reactions were conducted on a 0.1 mmol scale to aid comparison with the previously reported dye sensitized TiO_2/O_2/TEMPO[16] and porphyrin/quinone/TEMPO[13] photocatalyzed systems.

2.5.1 Synthesis of 3,4-dimethoxybenzaldehyde

The next substrate was 3,4-dimethoxybenzyl alcohol which was subjected to photooxidation using the dye sensitized ZnO/silver/TEMPO system. Subsequent analysis by gas chromatography revealed the presence of the aldehyde peak indicating that 3,4-dimethoxybenzyl alcohol was completely converted to the aldehyde (**Figure 23**). Thus, the effect of substitution had a positive effect on the yield of the aldehyde with the dimethoxy derivative formed in a higher yield than benzyl alcohol. This compound was not synthesized

using the dye sensitized TiO_2/O_2/TEMPO[16] or porphyrin/quinone/TEMPO systems[13] so no direct comparison of the yields or efficacy of the method is possible. Nevertheless, the developed photooxidative system was shown to be highly effective on this substrate with quantitative conversion from the alcohol to the aldehyde (**Scheme 31**).



Scheme 31

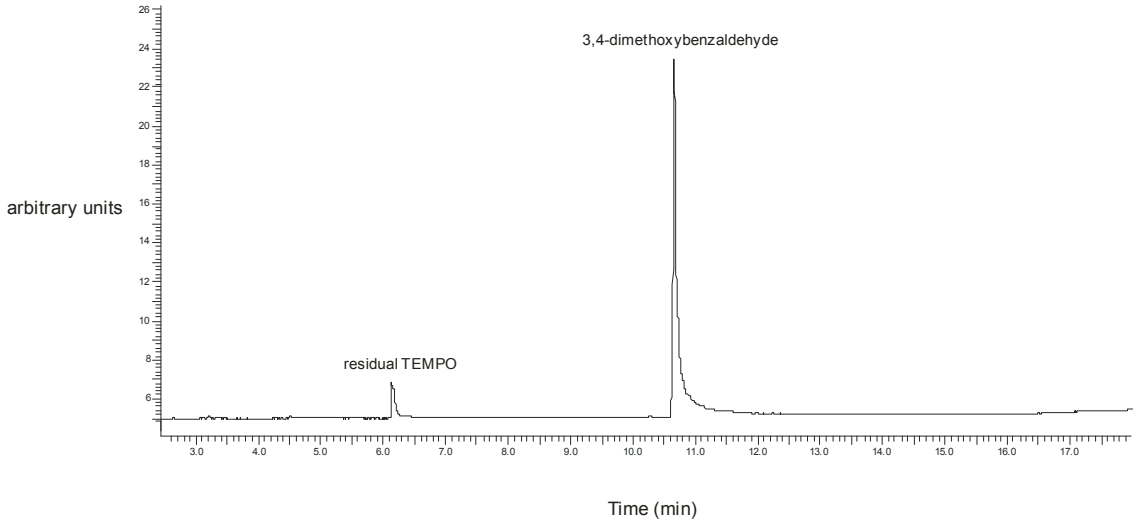
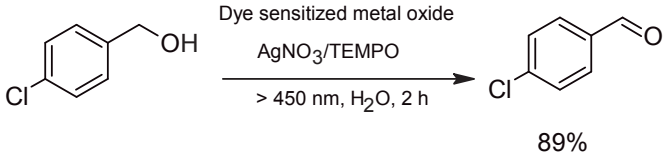


Figure 23

2.5.2 Synthesis of 4-chlorobenzaldehyde

The next alcohol that was evaluated was 4-chlorobenzyl alcohol which was subjected to photooxidation using the dye sensitized ZnO/silver/TEMPO system. Under these conditions, the desired aldehyde was formed in a yield of 89% as determined by gas chromatography after 2 hours of irradiation (**Scheme 32**). The obtained yield was superior to that of dye

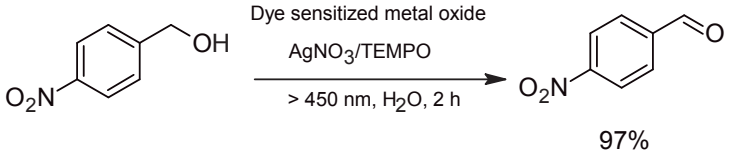
sensitized TiO_2/O_2/TEMPO system[16] which produced the desired compound in 59% yield after 15 hours of irradiation. The yield obtained using the dye sensitized ZnO/silver/TEMPO system was also superior to the porphyrin/quinone/TEMPO system[13] which produced the aldehyde in 82% yield after 24 hours of irradiation. While the yields using the porphyrin and ZnO systems are comparable, the immense decrease in time using the ZnO system is certainly noteworthy. It is also worth mentioning that the porphyrin mediated oxidation was conducted on a much smaller scale (300μmol) compared to the ZnO system (0.1mmol).



Scheme 32

2.5.3 Synthesis of 4-nitrobenzaldehyde

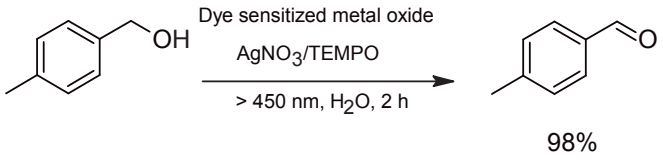
The next alcohol that was evaluated was 4-nitrobenzyl alcohol which was subjected to oxidation *via* the dye sensitized ZnO/silver/TEMPO system. Using this photooxidative system the desired aldehyde was formed in a yield of 97% as determined by gas chromatography after 2 hours irradiation (**Scheme 33**). Once again the yield obtained was far superior to the other photocatalyzed systems in terms of reaction yield and time. Using the dye sensitized TiO_2/O_2/TEMPO system[16] the desired aldehyde was formed in a yield of 49% after 20 hours of irradiation while the porphyrin/quinone/TEMPO system[13] produced the desired aldehyde in a yield of 50% after 24 hours of irradiation.



Scheme 33

2.5.4 Synthesis of 4-methylbenzaldehyde

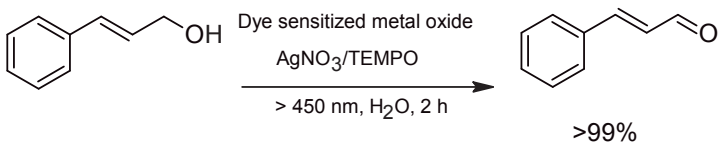
The dye sensitized ZnO/silver/TEMPO photooxidative system was applied to 4-methylbenzyl alcohol to produce the aldehyde in a 98% yield by GC analysis (**Scheme 34**). The dye sensitized TiO_2/O_2/TEMPO system[16] produced the desired aldehyde in a yield of 87% while the porphyrin/quinone/TEMPO system[13] previously afforded the aldehyde in a yield of 70%. The product yields obtained using all three systems were satisfactory however, the reaction was much faster using the dye sensitized ZnO/silver/TEMPO system. The reaction was complete after 2 hours while the dye sensitized TiO_2/O_2/TEMPO and porphyrin/quinone/TEMPO systems required 15 and 24 hours of irradiation, respectively. This massive decrease in reaction time is envisaged to be due to the superior electron accepting ability of silver(I), compared to dioxygen,[29] which rapidly quenches the electron injected into the conduction band of the semiconductor.



Scheme 34

2.5.5 Synthesis of cinnamaldehyde

Cinnamyl alcohol was also subjected to photooxidation using the dye sensitized ZnO/silver/TEMPO system. Analysis of the reaction mixture by gas chromatography (**Figure 24**) after 2 hours revealed the presence of the aldehyde peak only (**Scheme 35**). The observed yield (> 99%) obtained using the dye sensitized ZnO/silver/TEMPO system was once again superior to the dye sensitized TiO_2/O_2/TEMPO system[16] which produced the aldehyde in a yield of 66% after 13 hours of irradiation.



Scheme 35

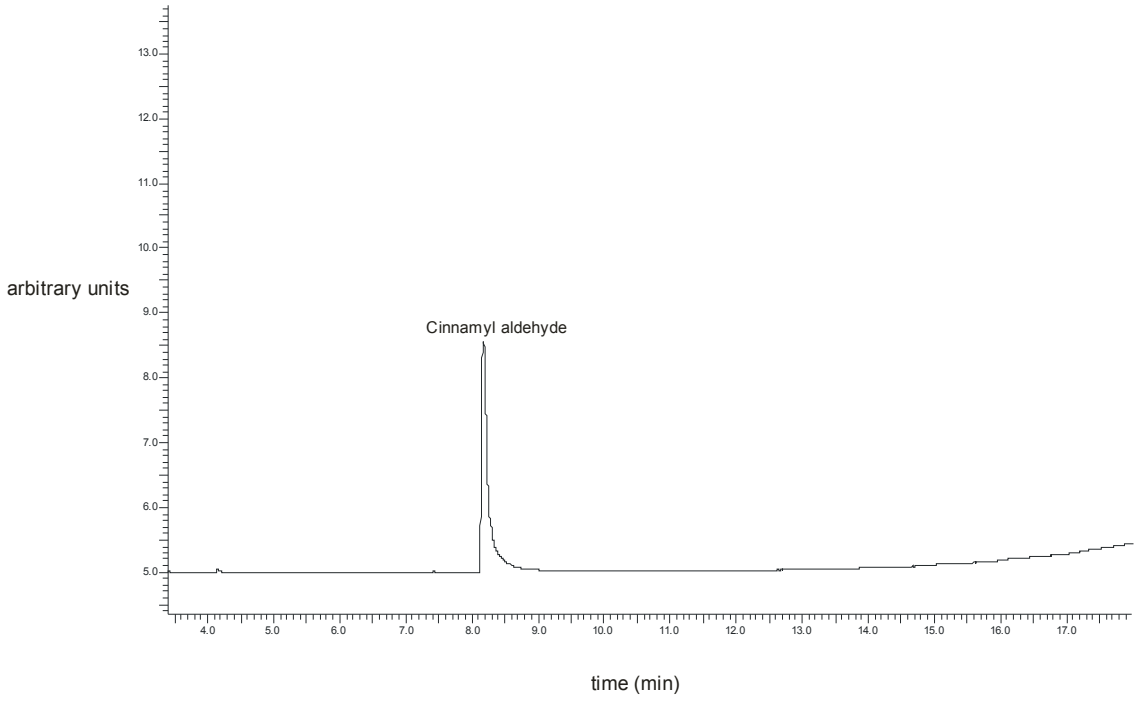
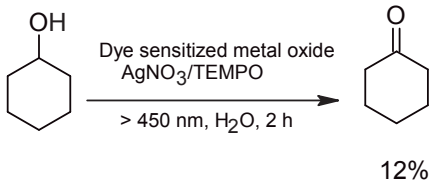


Figure 24

Thus far, the performance of the dye sensitized ZnO/silver/TEMPO system was evaluated on benzylic alcohols; attention was now focused on an unactivated alcohol.

2.5.6 Synthesis of cyclohexanone

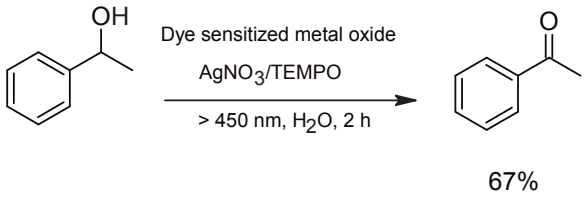
Cyclohexanol was subjected to photooxidation using the dye sensitized ZnO/silver/TEMPO system but in this case the desired ketone was formed in a very low yield (12%) as determined by gas chromatography (**Scheme 36**). The synthesis of cyclohexanone was also reported using the dye sensitized TiO_2/O_2/TEMPO system.[16] The desired ketone formed was in a yield of 7% after 16 hours of irradiation. This observation can be linked to the limitations of the *N*-oxoammonium salt as an oxidant which is unable to oxidize unactivated alcohols.[12]



Scheme 36

2.5.7 Synthesis of acetophenone

The final substrate that was analyzed was 1-phenylethanol as we sought to probe the effect of the dye sensitized ZnO/silver/TEMPO system on the photooxidation of a secondary benzylic alcohol. When 1-phenylethanol was subjected to our general photooxidative conditions the desired ketone was formed in a satisfactory yield of 67% based on gas chromatography (**Scheme 37**). This was a significant observation as it showed that the *N*-oxoammonium salt was capable of oxidizing secondary benzylic alcohols. No comparison with the previously reported photooxidative systems was possible such derivatives were not tested using these systems.

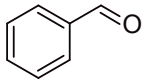
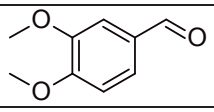
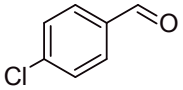
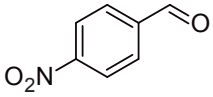
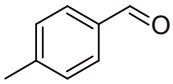
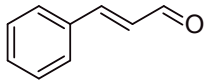
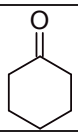
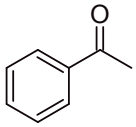


Scheme 37

Thus, the initial investigations into the scope of a dye sensitized ZnO/silver/TEMPO system were completed and can be summarized below (**Table 13**). The photooxidative system was found be most efficient on benzylic alcohols with good to excellent yields obtained (82 to >99%). The system was, however, found to be less effective on unactivated alcohols with the desired compound formed in a disappointing yield of 12%. More encouraging was the performance of the photooxidative system on secondary benzylic alcohol which produced

the desired ketone in a satisfactory yield of 67%. In all cases, the yields are superior to other photooxidative systems in terms of yield and reaction times.

Table 13: Summary of the results obtained using the dye sensitized ZnO/silver/TEMPO photooxidative system

Entry	Product	Time (h)	Yield (%)
i		2	82
ii		2	>99
iii		2	89
iv		2	97
v		2	98
vii		2	>99
vii		2	12
viii		2	67

Having evaluated the scope of the dye sensitized ZnO/silver/TEMPO photooxidative system on a series of alcohols, attention was shifted to their possible application in tandem coupling reactions. At present, the system is extremely efficient on benzylic alcohols with the desired aldehydes or ketone formed in good to excellent yields. However, these reactions were conducted on a 0.1 mmol scale and if they were to find application in tandem coupling reactions, they should be conducted on a larger scale. Thus, attempts were made to scale up

certain reactions to demonstrate their potential application in tandem coupling reactions. The dye sensitized TiO_2/O_2/TEMPO[16] and porphyrin/quinone/TEMPO[13] required long reaction times to oxidize minute quantities of alcohols and, consequently, are unlikely to find application in routine organic synthesis. In contrast, the dye sensitized ZnO/silver/TEMPO system, due to the superior electron accepting ability of silver(I), was able to effect the oxidation of alcohols in only 2 hours and accordingly, this system has the potential to be scaled up. To demonstrate this point, 3,4-dimethoxybenzyl alcohol was chosen as a model substrate as the reaction on a small scale gave approximately quantitative yields.

2.6 Scale-up reactions of selected alcohols

2.6.1 Synthesis of 3,4-dimethoxybenzaldehyde

To demonstrate the scale-up application of the dye sensitized ZnO/silver/TEMPO 3,4-dimethoxybenzyl alcohol (0.5 mmol), dye sensitized ZnO, TEMPO and 18 equivalents of silver nitrate were mixed in water and subjected to visible light irradiation for 10 hours. The mixture was extracted with dichloromethane and concentrated *in vacuo* to produce the crude product. Thin layer chromatography revealed the presence of only one spot and this single compound was isolated, subjected to analysis by NMR spectroscopy and found to be 3,4-dimethoxybenzaldehyde with the characteristic aldehyde peak clearly evident at δ 9.85 ppm (**Figure 25**). Analysis of the synthesized compound by infrared spectroscopy showed a strong absorbtion at ν_{max} 1677 cm^{-1} due to the carbonyl group (**Figure 26**). Thus, it was concluded that the alcohol oxidation *via* the dye sensitized ZnO/silver/TEMPO system could also be scaled up with comparable success as the desired compound was isolated in a yield of 87%. To place this achievement in context, the dye sensitized TiO_2/O_2/TEMPO system[16] required 13-22 hours to oxidize alcohols on a 0.1 mmol scale while the dye sensitized ZnO/silver/TEMPO system was able to oxidize an alcohol on a 5 fold larger scale in just 10 hours (!)

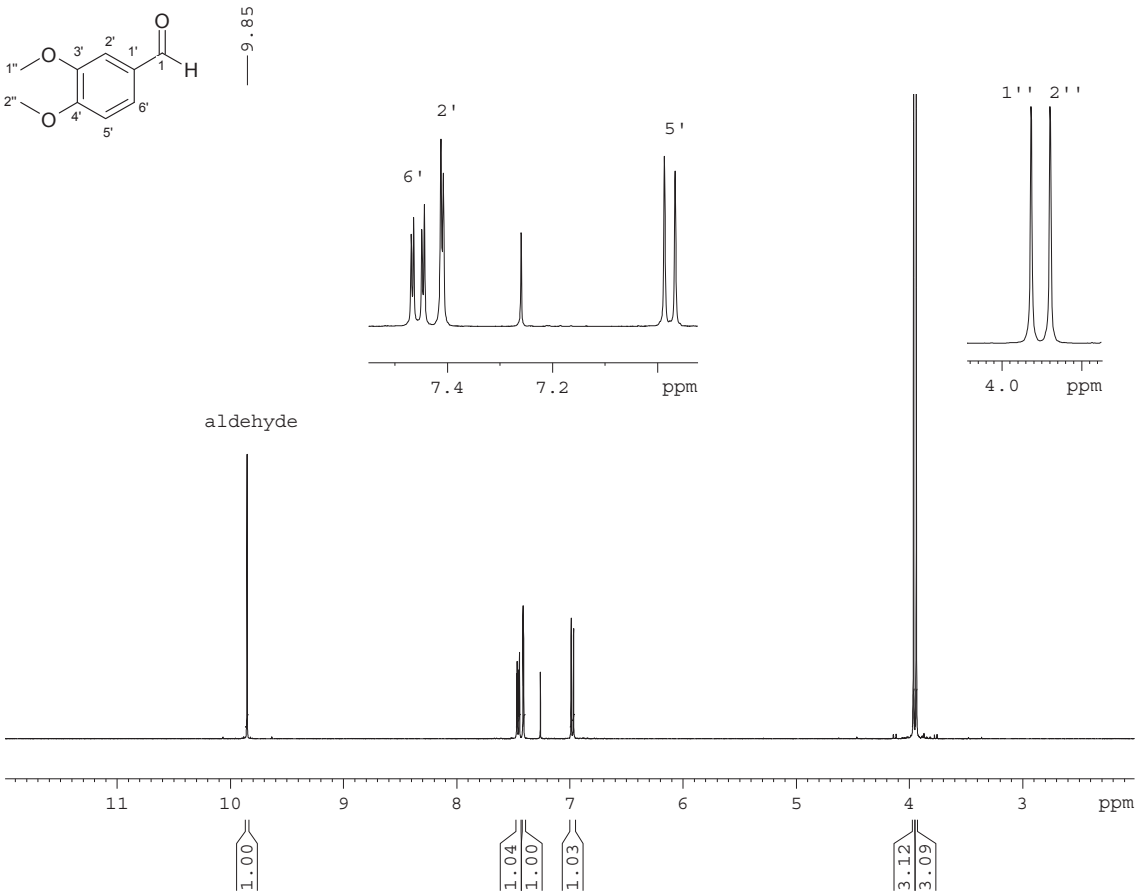

9.85
aldehyde
2'
6'
5'
7.4
7.2
ppm
1'' 2''
4.0
ppm
11
10
9
8
7
6
5
4
3
ppm
1.00
1.04
1.00
1.03
3.12
3.09

Figure 25

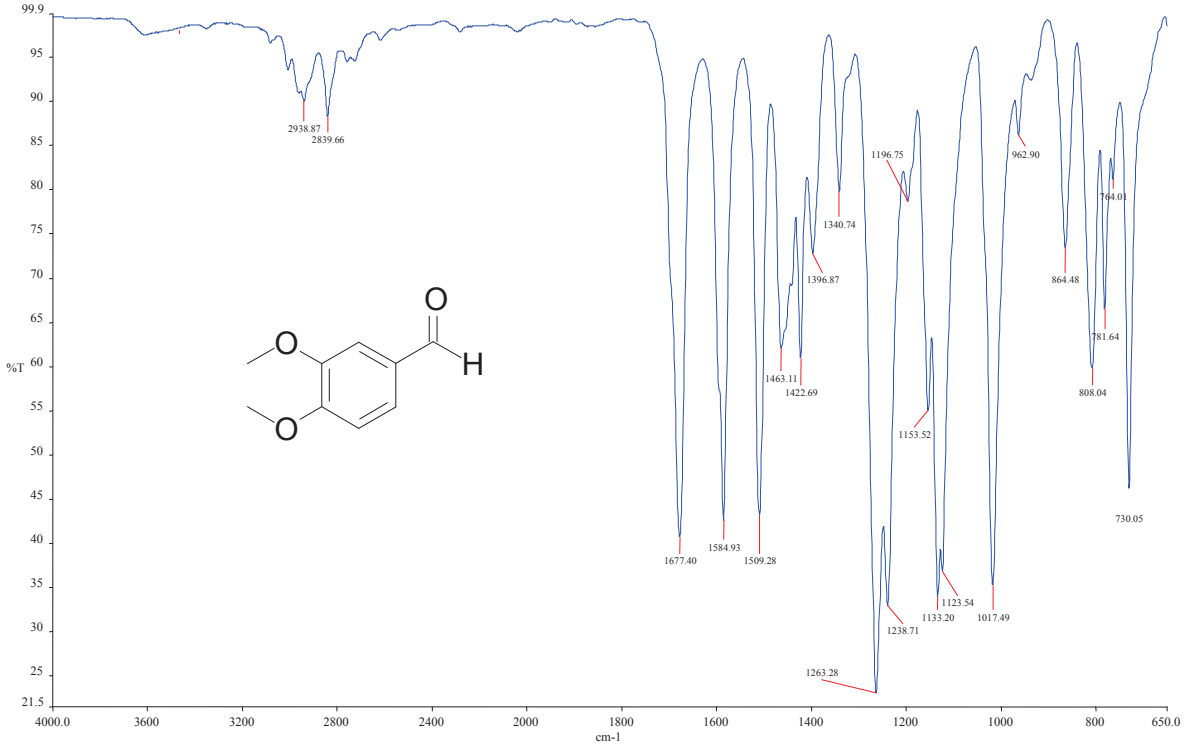


Figure 26

2.6.2 Synthesis of benzil

Encouraged by the above results, one final scale up reaction was attempted on benzoin using the dye sensitized ZnO/silver/TEMPO system. The oxidation of benzoin to benzil and subsequent attack of the diketone by an appropriate nucleophile is an important transformation in tandem coupling reactions.[30] Thus, it would be interesting to examine the performance of the secondary hindered alcohol benzoin using the developed photooxidative system. Benzoin was subjected to oxidation using the dye sensitized ZnO/silver/TEMPO system under visible light irradiation for 10 hours and subsequently purified using radial chromatography. The yield of the isolated product was 78% and its ^{1}H NMR spectral data (**Figure 27**) was in excellent agreement with literature data.[31] Also shown below is the mass spectrum of the purified product with the observed peaks corresponding to the desired compound indicating that the reaction had proceeded efficiently (**Figure 28**).

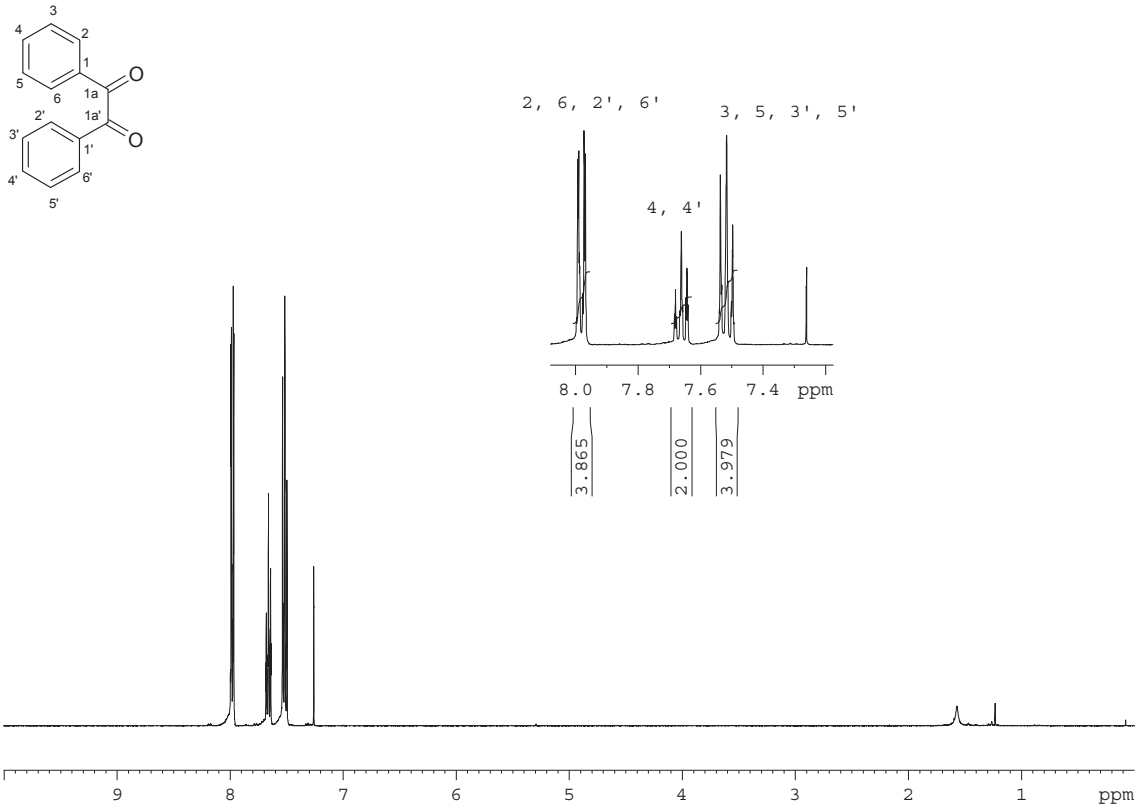

3
4
2
1
5
6
1a
O
2'
1a'
3'
1'
O
4'
6'
5'
2, 6, 2', 6'
3, 5, 3', 5'
4, 4'
8.0
7.8
7.6
7.4
ppm
3.865
2.000
3.979
9
8
7
6
5
4
3
2
1
ppm

Figure 27

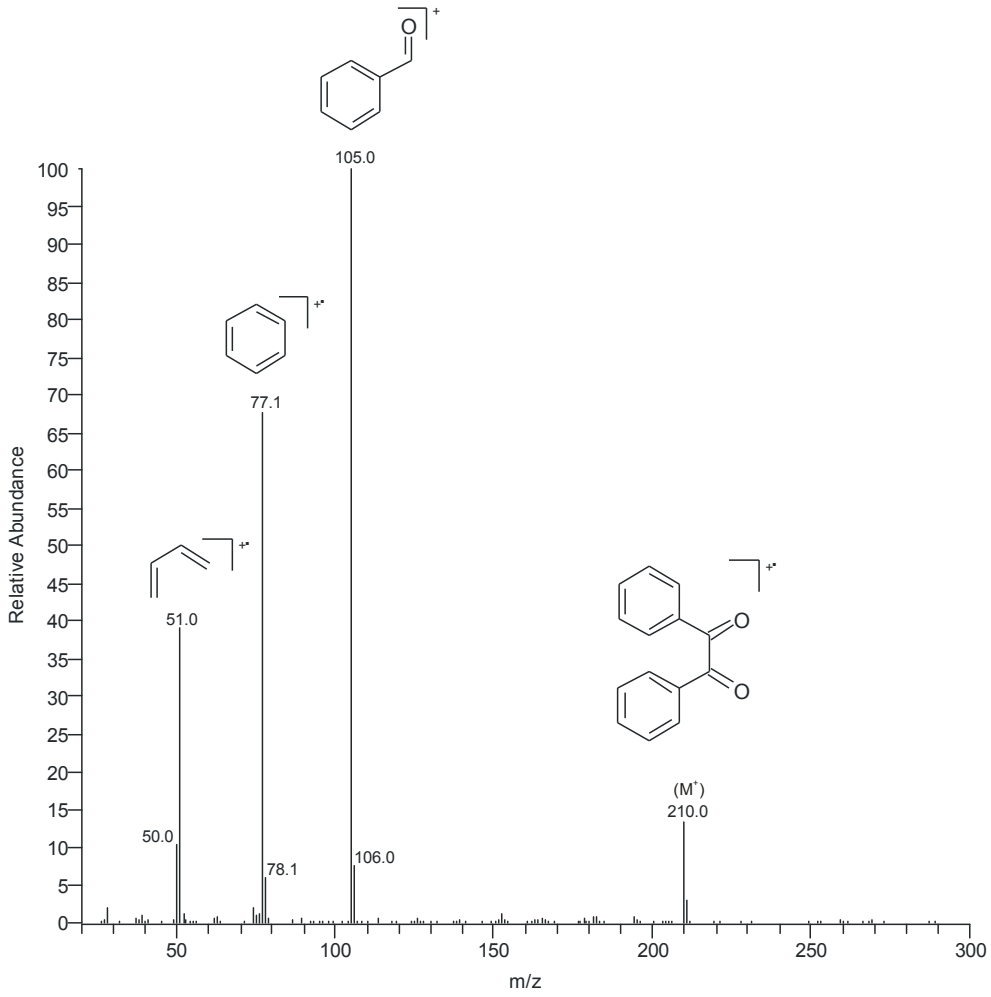


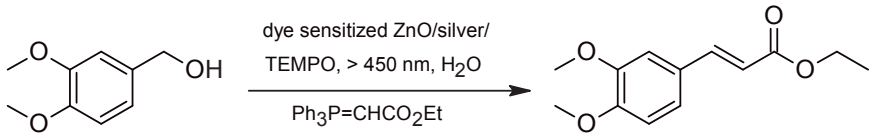
Figure 28

2.7 Application of photooxidative system to a Wittig reaction

Having successfully demonstrated the scale up potential of the dye sensitized ZnO/silver/TEMPO system, attention was now focused on a tandem coupling reaction. Since the tandem coupling reaction was initiated with the Wittig reaction, it was deemed appropriate to apply the newly developed system to a tandem Wittig reaction.

2.7.1 Synthesis of Ethyl 3-(3,4-dimethoxyphenyl)acrylate

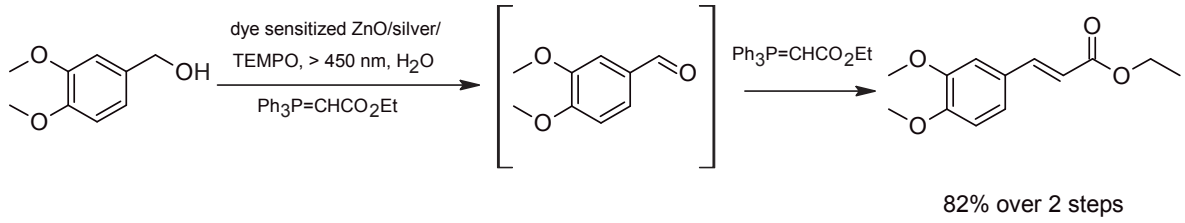
This reaction involved the mixing of 3,4-dimethoxybenzyl alcohol, dye sensitized ZnO, TEMPO, silver nitrate and (ethoxycarbonylmethylene)-triphenylphosphorane in water under visible light irradiation for 10 hours (**Scheme 38**).



Scheme 38

However, under these conditions no product was observed with the starting alcohol recovered. While the reasons for the failure of this reaction are relatively unclear, some points may be highlighted. It was firstly envisaged that the limited solubility of the Wittig reagent in water may have contributed to the failure of this reaction. However, the Bergdahl research group has demonstrated that water is in fact an excellent solvent for the Wittig reaction and produces higher yields than common organic solvents.[32,33] The superior performance of water as a solvent was attributed to its ability to stabilize the polar transition state of the Wittig reaction as well as being able to participate in the reaction due to its polar nature. A more likely scenario was reported by Vincente and co-workers[34] and more recently by the Sabouchei research group[35] in which various metal complexes were synthesized by mixing silver nitrate and phosphorus ylides. Thus, it is proposed that the failure of the Wittig reaction was due to the formation of a silver phosphorane complex.

The failure of the tandem coupling reaction led us to turn our attention to a *pseudo* tandem coupling reaction. Under these reaction circumstances, we aimed to conduct the photooxidation under our general photooxidative conditions, extract the mixture and to the filtrate (which contains the crude aldehyde) add the Wittig reagent (**Scheme 39**).



Scheme 39

Using the above modified conditions, the desired acrylate was isolated in an excellent yield of 82% over the 2 steps. The formation of the desired acrylate was confirmed by ^{1}H NMR spectroscopy which showed the presence of all of the expected peaks (**Figure 29**). Since the coupling constant (*J*) are greater than 12 Hz, it was concluded that the desired acrylate was isolated in the *E* configuration.[36] Thus, the extraction of the crude aldehyde, followed by the addition of the Wittig reagent can drastically improve the yield of the acrylate.

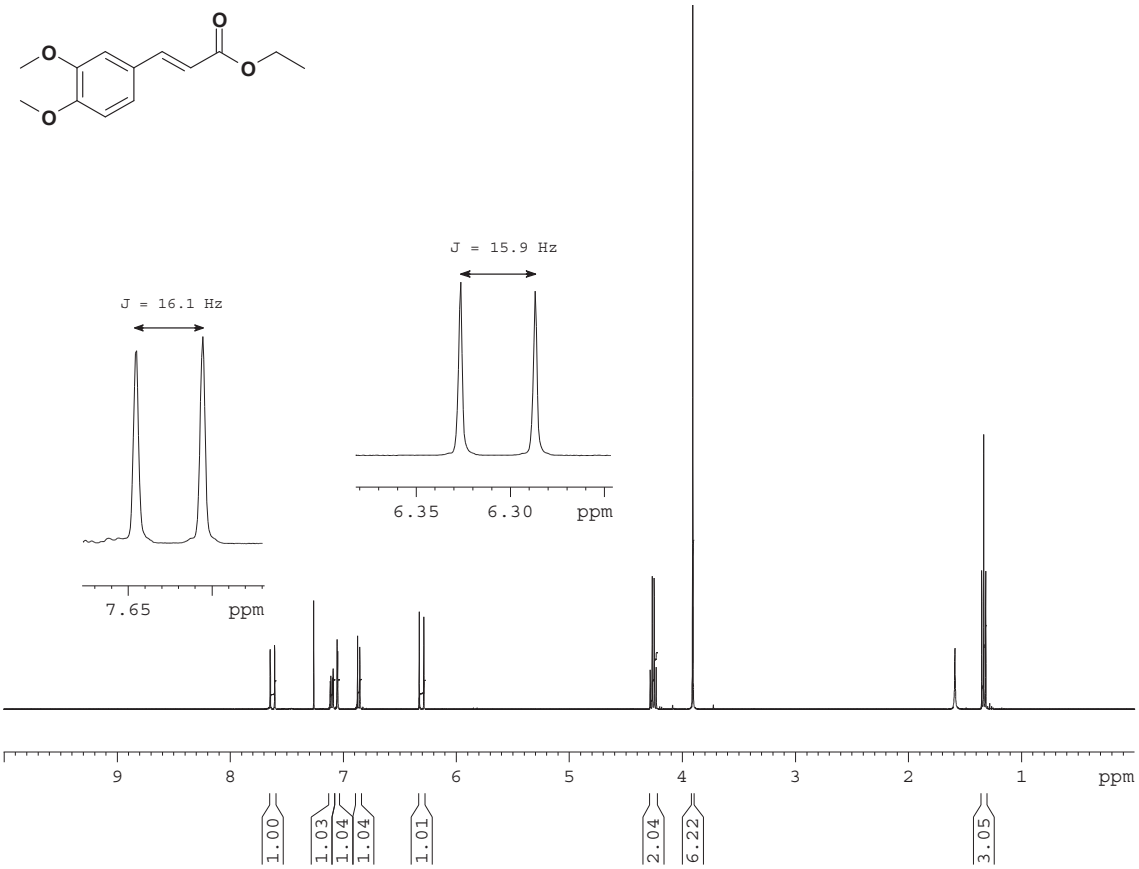


Figure 29

In summary, a novel dye sensitized ZnO/silver/TEMPO system for the oxidation of alcohols was developed. This system was found to be efficient on benzylic alcohols with good to excellent yields obtained. The system was, however, less prolific on unactivated alcohols. More encouraging was the fact that the above photooxidative system could be scaled up with notable success. The photooxidative system was applied to the tandem oxidation process but was unfortunately unsuccessful probably due to complexation between the Wittig reagent and silver (I) ions. The photooxidative system was successfully applied to the pseudo tandem coupling reaction and the desired acrylate isolated in an excellent yield.

The results obtained from this study was drawn up for publication and subsequently accepted by Chemical Communications. A copy of this paper follows.[‡] Jeena, V.; Robinson, R. S. *Chem. Commun.,* **2012,** *48,* 299-301.

[‡] Copy of the paper included in the body of the text as per faculty guidelines.

ChemComm

View Online / Journal Homepage / Table of Contents for this issue
Dynamic Article Links

Cite this: *Chem. Commun.*, 2012, **48**, 299–301

www.rsc.org/chemcomm

COMMUNICATION

Convenient photooxidation of alcohols using dye sensitised zinc oxide in combination with silver nitrate and TEMPO†

Vineet Jeena and Ross S. Robinson*

Received 19th September 2011, Accepted 31st October 2011
DOI: 10.1039/c1cc15790f

A novel photooxidative system using dye sensitised zinc oxide in combination with silver nitrate and 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) in an aqueous solution is described. Under visible light irradiation the selective oxidation of alcohols to their corresponding aldehydes and ketones was effected in good to excellent yields.

Photocatalysis, by semiconductor metal oxides, has been identified as a promising route for organic chemistry in the 21st century.[1] Of the semiconductors available, TiO_2 (the most studied semiconductor) and ZnO have emerged as the semiconductors of choice due to their low cost, stability under irradiation and environmental friendliness.[2] From a synthetic chemistry point of view, the most appealing aspect of semiconductor mediated photocatalysis is their ability to oxidise alcohols to their carbonyl derivatives.[3]

As part of our interest in tandem coupling reactions,[4] we aimed to carry out a photocatalysed tandem oxidation coupling reaction which involves the oxidation of an alcohol to its aldehyde, followed by a trapping of the generated aldehyde by an appropriate nucleophile without the isolation of the intermediate aldehyde. While the TiO_2 mediated alcohol oxidation has been well documented the photocatalytic procedure is unselective, due to the high oxidative potential of the holes created in the valence band,[5] resulting in a variety of products in addition to the desired carbonyl compound.[6] Thus, before embarking on a photocatalysed tandem coupling reaction, the photooxidative procedure needed to be refined. Recently, Zhao *et al.*[7a] and Nagata *et al.*[7b] have demonstrated the light activated oxidation of 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) to the oxoammonium salt ($TEMPO^+$) which selectively oxidises alcohols to their carbonyl compounds. However, due to the small scale (300 μmol–0.1 mmol) and long reaction times (18–24 h) these procedures are unlikely to find application in traditional organic synthesis.

Herein, we report an improved strategy for the oxidation of alcohols to aldehydes using a dye sensitised metal oxide/silver/TEMPO system in an aqueous solution. The semiconductor was sensitised with alizarin red to allow the system to be activated by visible light irradiation. Under the above conditions, the dye and not the semiconductor will be activated preventing the formation of strongly oxidising hydroxyl radicals.

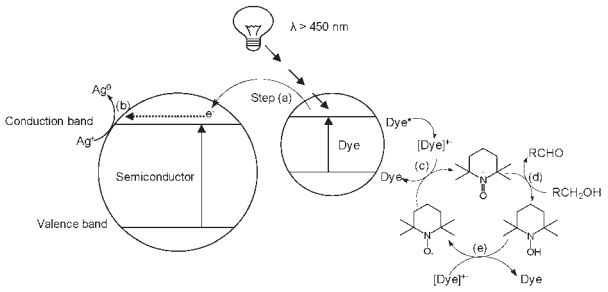


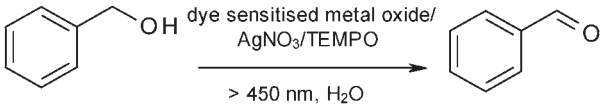
Fig. 1

Upon visible light irradiation, the activated dye transfers an electron into the conduction band of the semiconductor (see Fig. 1, step a). The injected electron is readily consumed by silver(I) which is reduced to metallic silver (Fig. 1, step b). The activated dye returns to its ground state oxidising TEMPO from its radical form into the oxoammonium salt (the active oxidising species of TEMPO) (Fig. 1, step c). The oxoammonium salt oxidises the alcohol to its carbonyl derivative (Fig. 1, step d), forming the hydroxylamine which can regenerate the TEMPO radical *via* oxidation by the dye radical (Fig. 1, step e) (see ESI† for table of standard redox potentials).

In an effort to validate the proposed mechanism, we attempted a test reaction which involved mixing a portion of dye sensitised TiO_2 or ZnO, silver nitrate, TEMPO and benzyl alcohol in water under visible light irradiation. The reactions were conducted on the 0.1 mmol scale to aid comparison with the previously mentioned photooxidative systems.[7] Preliminary investigations revealed that the quantity of silver nitrate was vital for the photooxidative system to proceed (see ESI† for details) with 18 equivalents shown to be optimum. While the quantity of silver nitrate may be deemed to be excessive, there are a number of beneficial effects relating to the use of silver(I) as a sacrificial electron acceptor. Firstly, dye sensitised photocatalysts are unstable in aqueous solution as the dye can easily detach from the photocatalyst.[8] Concentrated silver solutions are known to stabilise dye sensitised photocatalysts preventing the detachment of the dye.[9] Secondly, the superior electron accepting ability of silver(I) would drive the photooxidative

Department of Chemistry, University of KwaZulu-Natal, Scottsville, Pietermaritzburg, 3209, South Africa. E-mail: robinsonr@ukzn.ac.za
† Electronic supplementary information (ESI) available: Analytical data, experimental procedures and NMR data. See DOI: 10.1039/c1cc15790f

Table 1 Oxidation of benzyl alcohol using a dye sensitised metal oxide/$AgNO_3$/TEMPO system



1 2

Entry	Metal oxide	Time/h	Yield[a] (%)
1	TiO_2	1	3
2	ZnO	1	54
3	TiO_2	2	8
4	ZnO	2	82
5[b]	—	2	16
6[c]	ZnO	2	12
7[d]	ZnO	—	nd[f]
8[e]	ZnO	—	nd[f]

[a] GC yield. [b] Absence of Zinc oxide. [c] Absence of TEMPO. [d] Absence of $AgNO_3$. [e] CH_3CN as solvent. [f] Not determined as the dye sensitised ZnO was unstable under these conditions, see ESI.

system resulting in shorter reaction times and higher yields (*vide infra*). Additionally, methods are available to recover the precipitated silver[10] which would allow for the reuse of the photocatalyst.

Using the conditions as highlighted above, we aimed to probe the contribution of each of the additives to the photo-oxidative procedure (Table 1). As can be seen, pleasing yields were produced in the presence of dye sensitised ZnO while the reaction using dye sensitised TiO_2 produced only trace amounts of the product. This result is somewhat surprising as TiO_2 is expected to display similar behaviour to ZnO.[11]

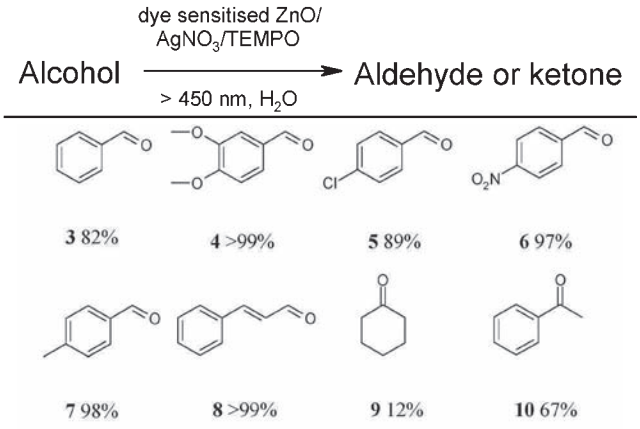
On analysis of the reaction vessel at the completion of the reaction, the ZnO system shows a high degree of metallic silver while the TiO_2 system shows only minute quantities of silver (see ESI†). This implies that electrons are not being efficiently injected into the conduction band of TiO_2. One possible explanation is the strong back electron transfer (BET) on the TiO_2/Alizarin system[12] which decreases the quantity of electrons injected into the conduction band. Further detailed studies are underway to probe the mechanism of these systems.

In the absence of dye sensitised ZnO or TEMPO a dramatic decrease in yield was observed (Table 1, entries 5 and 6). The formation of benzaldehyde in the absence of dye sensitised ZnO suggests that other mechanisms may be occurring but the highest yield of 82% is only obtained in the presence of all the additives indicating that the proposed mechanism is the major route for product formation. This observation is in agreement with other research in the development of complex oxidative systems.[7a] The results of this study highlight the importance and distinct contribution of each of the additives to the oxidative system. The turnover number (TON) was calculated and found to be less than 100, indicating that this is a photoreaction rather than a photocatalytic reaction. In the absence of silver nitrate, the dye sensitised ZnO was unstable and as expected the dye readily detached from ZnO (Table 1, entry 7) (see ESI†). Similar results were observed when water was replaced with acetonitrile as a solvent (Table 1, entry 8). With this optimised procedure in hand, we attempted to explore the scope of the oxidation system on a series of alcohols (Table 2).

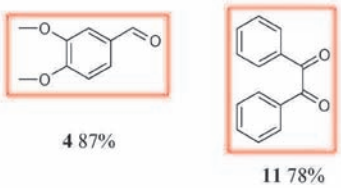
The present oxidative system was particularly effective on benzylic alcohols with good to excellent yields being obtained (Table 2, entries 3–8). This point is even more impressive considering certain alcohols are solids at room temperature and display limited solubility in water (Table 2, entries 5–7). The effect of substitution resulted in an increase in yield with the lowest increase observed for the 4-chloro derivative (82% for benzyl alcohol *vs.* 89% for 4-chlorobenzyl alcohol). The dimethoxy, 4-nitro, 4-methyl derivatives as well as cinnamyl alcohol showed almost quantitative conversion to the aldehyde. In all cases, the obtained yields are superior to those previously reported. Hence, the high yields obtained make the tandem coupling reaction on benzylic alcohols a highly attractive and viable procedure. The dye sensitised ZnO/$AgNO_3$/TEMPO system was, however, less prolific on an unactivated alcohol (Table 2, entry 9) due to oxoammonium salt's limitation on these substrates.[13] More encouraging was the performance of the system on a secondary benzylic alcohol (Table 2, entry 10) which produced the desired ketone in a satisfactory yield of 67% after 2 hours of irradiation. To the best of our knowledge, this is the first report of a photocatalysed oxoammonium salt oxidation on a secondary benzylic alcohol.

To illustrate the potential utility of this system, we attempted two scale-up reactions. Firstly, we chose to oxidise 3,4-dimethoxybenzyl alcohol as the reaction on the smaller scale gave quantitative yields. Secondly, we chose to attempt the oxidation of benzoin to benzil as benzoin is an important starting material for tandem

Table 2 Oxidation of alcohols using a ZnO/$AgNO_3$/TEMPO system[a]



[a]Reaction conditions: alcohol (0.1 mmol), dye sensitised Zinc oxide (20 mg), TEMPO (1.5 mg) and $AgNO_3$ (18 equiv.) in 1.5 ml H_2O under visible light irradiation for 2 hours. [b] GC yield.



[a]Reaction conditions: alcohol (0.5 mmol), dye sensitised Zinc oxide (100 mg), TEMPO (10 mg) and $AgNO_3$ (18 equiv.) in 10 ml H_2O under visible light irradiation for 10 hours. [b] Isolated yield.

coupling reactions.[14] The oxidation of 3,4-dimethoxybenzyl alcohol resulted in the formation of the desired aldehyde in an isolated yield of 87%, highlighting the 'scale up' applicability of this procedure. The oxidation of benzoin to benzil also proceeded smoothly with the desired ketone isolated in a yield of 78% despite the hindered nature of the alcohol.

In conclusion, we have shown that the combination of dye sensitised ZnO in combination with $AgNO_3$ and TEMPO in water under visible light irradiation leads to selective oxidation of alcohols to aldehydes and ketones in good to excellent yields. The system is appealing due to the high yields, short reaction times together with mild reaction conditions. The photooxidative system was also scaled up with great success further highlighting its efficacy. Further studies are underway to expand the scope of the methodology and extend the application of the oxidative system to tandem coupling reactions.

Notes and references

1 G. Palmisano, V. Augugliaro, M. Pagliaro and L. Palmisano, *Chem. Commun*., 2007, 3425.
2 (*a*) D. Chatterjee and S. Dasgupta, *J. Photochem. Photobiol., C*, 2005, **6**, 186; (*b*) W. J. E. Beek, M. M. Wienk and R. A. J. Janssen, *Adv. Mater*., 2004, **16**, 1009.
3 (*a*) F. A.-Z. G. Gassim, A. N. Alkhateeb and F. H. Hussein, *Desalination*, 2007, **209**, 342; (*b*) S. Yurdakal, G. Palmisano, V. Loddo, V. Augugliaro and L. Palmisano, *J. Am. Chem. Soc*., 2008, **130**, 1568.
4 (*a*) R. S. Robinson and R. J. K. Taylor, *Synlett*, 2005, 1003; (*b*) V. Jeena and R. S. Robinson, *Beilstein J. Org. Chem*., 2009, **5**, no. 24.
5 A. Fujishima, T. N. Rao and D. A. Tryk, *J. Photochem. Photobiol., C*, 2000, **1**, 1.
6 O. S. Mohamed, A. E.-A. M. Gaber and A. A. Abdel-Wahab, *J. Photochem. Photobiol., A*, 2002, **148**, 205.
7 (*a*) M. Zhang, C. Chen, W. Ma and J. Zhao, *Angew. Chem., Int. Ed*., 2008, **47**, 9730; (*b*) T. Nagasawa, S. I. Allakhverdiev, Y. Kimura and T. Nagata, *Photochem. Photobiol. Sci*., 2009, **8**, 174.
8 T. Lindgren, J. M. Mwabora, E. Avendaño, J. Jonsson, A. Hoel, C.-G. Granqvist and S.-E. Lindquist, *J. Phys. Chem. B*, 2003, **107**, 5709.
9 (*a*) H. Hada, H. Tanemura and Y. Yonezawa, *Bull. Chem. Soc. Jpn*., 1978, **51**, 3154; (*b*) H. Hada, Y. Yonezawa and M. Saikawa, *Bull. Chem. Soc. Jpn*., 1982, **55**, 2010.
10 (*a*) M. Huang, E. Tso, A. K. Datye, M. R. Prairie and B. M. Stange, *Environ. Sci. Technol*., 1996, **30**, 3084; (*b*) M.-J. López-Muñoz, J. Aguado, R. van Grieken and J. Marugán, *Appl. Catal., B*, 2009, **86**, 53.
11 B. Dindar and S. Içli, *J. Photochem. Photobiol., A*, 2001, **140**, 263.
12 G. Ramakrishna, A. K. Singh, D. K. Palit and H. N. Ghosh, *J. Phys. Chem. B*, 2004, **108**, 1701.
13 S. S. Kim and H. C. Jung, *Synthesis*, 2003, 2135.
14 S. V. More, M. N. V. Sastry and C.-F. Yao, *Green Chem*., 2006, **8**, 91.

Having developed the dye sensitized ZnO/silver/TEMPO system and demonstrated its application on a series of alcohols, attention was then focused on an evaluation of the reaction mechanism. Since the dye radical and TEMPO radical were conceptualized to play vital roles in the reaction, an electron paramagnetic resonance (EPR) study was conducted. The purpose of this study was firstly to detect the dye radical and consequently determine the effect of the dye radical on the TEMPO radical. It was also envisioned that EPR spectroscopy would provide insight into the failure of the dye sensitized TiO_2/silver/TEMPO system.

References

1. Fox, M. A.; Dulay, M. T. *Chem. Rev.* **1993,** *93*, 341-357.
2. Summerfelt, S. T.; Hochheimer, J. N. *Prog. Fish-Cult.* **1997,** *59*, 94-105.
3. Amemiya, S.: Tokyo, 2004.
4. Yoon, S.-H.; Lee, J. H. *Environ. Sci. Technol.* **2005,** *39*, 9695-9701.
5. Mohamed, O. S.; Gaber, A. E.-A. M.; Abdel-Wahab, A. A. *J. Photochem. Photobiol. A: Chem* **2002,** *148*, 205-210.
6. Subba Rao, K. V.; Srinivas, B.; Prasad, A. R.; Subrahmanyam, M. *Chem. Commun.* **2000**, 1533-1534.
7. Jeena, V., M. Sc. Dissertation, University of KwaZulu-Natal (PMB), 2009.
8. Sakthivel, S.; Kisch, H. *Angew. Chem. Int. Ed.* **2003,** *42*, 4908-4911.
9. Wu, J. C.-S.; Chen, C.-H. *J. Photochem. Photobiol. A: Chem* **2004,** *163*, 509-515.
10. Moser, J.; Gratzel, M. *J. Am. Chem. Soc.* **1984,** *106*, 6557-6564.
11. Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984,** *106*, 3374-3376.
12. Kim, S. S.; Jung, H. C. *Synthesis* **2003**, 2135-2137.
13. Nagasawa, T.; Allakhverdiev, S. I.; Kimura, Y.; Nagata, T. *Photochem. Photobiol. Sci.* **2009,** *8*, 174-180.
14. Gerischer, H.; Heller, A. *J. Phys. Chem.* **1991,** *95*, 5261-5267.
15. Amori, L.; Giacco, T. D.; Rol, C.; Sebastiani, G. V. *J. Chem. Res. (S)* **1998**, 644-645.
16. Zhang, M.; Chen, C.; Ma, W.; Zhao, J. *Angew. Chem. Int. Ed.* **2008,** *120*, 9730-9733.
17. Kryukov, A. I.; Ya. Kuchmii, S.; Pokhodenko, V. D. *Theor. Exp. Chem.* **2000,** *36*, 69-89.
18. Rychnosky, S. D.; Vaidyanathan, R.; Beauchamp, T.; Lin, R.; Farmer, P. J. *J. Org. Chem.* **1999,** *64*, 6745-6749.
19. Zhu, A.; Tian, Y.; Liu, H.; Luo, Y. *Biomaterials* **2009,** *30*, 3183-3188.
20. Dai, H. P.; Shiu, K. K. *Electrochimica Acta.* **1998,** *43*, 2709-2715.
21. Liu, G.; Li, X.; Zhao, J.; Horikoshi, S.; Hidaka, H. *J. Mol. Catal. A: Chem.* **2000,** *153*, 221-229.
22. Lindgren, T.; Mwabora, J. M.; Avendano, E.; Jonsson, J.; Hoel, A.; Granqvist, C.-G.; Lindquist, S.-E. *J. Phys. Chem. B* **2003,** *107*, 5709-5716.
23. Hada, H.; Yonezawa, Y.; Saikawa, M. *Bull. Chem. Soc. Jpn.* **1982,** *55*, 2010-2014.
24. Hada, H.; Tanemura, H.; Yonezawa, Y. *Bull. Chem. Soc. Jpn.* **1978,** *51*, 3154-3160.
25. Baciocchi, E.; Rol, C.; Rosato, G. C.; Sebastiani, G. V. *J. Chem. Soc., Chem. Commun.* **1992**, 59-60.
26. Baciocchi, E.; Rosato, G. C.; Rol, C.; Sebastiani, G. V. *Tetrahedron Lett.* **1992,** *33*, 5437-5440.
27. Huang, M.; Tso, E.; Datye, A. K.; Prairie, M. R.; Stange, B. M. *Environ. Sci. Technol.* **1996,** *30*, 3084-3088.
28. Lopez-Munoz, M.-J.; Aguado, J.; van Grieken, R.; Marugan, J. *Appl. Catal. B: Environ.* **2009,** *86*, 53-62.
29. Baciocchi, E.; Rol, C.; Rosato, G. C.; Sebastiani, G. V. *J. Chem. Soc., Chem. Commun.* **1992,** *1*, 59-60.
30. More, S. V.; Sastry, M. N. V.; Yao, C.-F. *Green Chem.* **2006,** *8*, 91-95.
31. Lee, S. W.; Lee, K.; Seomoon, D.; Kim, S. K.; Kim, H.; Kim, H.; Shim, E.; Lee, M.; Lee, S.; Kim, M.; Lee, P. H. *J. Org. Chem.* **2004,** *69*, 4852-4855.

32. Dambacher, J.; Zhao, W.; El-Batta, A.; Anness, R.; Jiang, C.; Bergdahl, M. *Tetrahedron Lett.* **2005,** *46*, 4473-4477.
33. El-Batta, A.; Jiang, C.; Zhao, W.; Anness, R.; Cooksy, A. L.; Bergdahl, M. *J. Org. Chem.* **2007,** *72*, 5244-5259.
34. Vincente, J.; Chicote, M. T.; Fernandez-Baeza, J.; Martin, J.; Saura-Llamas, I.; Turpin, J.; Jones, P. G. *J. Organomet. Chem.* **1987,** *331*, 409-421.
35. Sabounchei, S. J.; Jordaian, V.; Nemattalab, H. *S. Afr. J. Chem.* **2009,** *62*, 9-13.
36. Bible, R. H. *Intrepetation of NMR Spectra - An Empirical Approach*; Plenum Press: New York, 1965.

Chapter 3

Electron Paramagnetic Study

3.1 Preface

Having successfully applied the dye sensitized ZnO photooxidative system to a series of alcohols, the mechanism of this system was investigated by conducting an electron paramagnetic resonance* (EPR) study. Since EPR spectroscopy is not commonly applied by organic chemists, a basic explanation of this unique technique is required.

3.2 Principles of EPR

A comprehensive explanation of the intricacies of electron paramagnetic spectroscopy is beyond the scope of this project, however, a few comments relating to this technique is necessary. EPR spectroscopy is commonly used to study paramagnetic species in both solid and liquid states. The method is related to NMR spectroscopy as both make use of magnetic properties, one in the form of nuclei and the other in the form of unpaired electrons.[1] The substances are characterized by the *g* factor at the centre of the spectrum. The g factor is used to characterize the resonance point position and this parameter is used to characterize where the unpaired electron is located.

3.3 Introduction to basic electron paramagnetic spectroscopy

3.3.1 Transition metal ions

EPR is a procedure commonly used to analyze paramagnetic species that contain unpaired electrons such as transition metals in their paramagnetic valence states. A brief representative table highlighting these paramagnetic species is given below:

* Also called electron spin resonance (ESR)

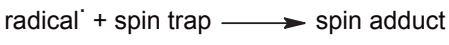
Table 14: Common paramagnetic states of transition metal ions

d^1	d^2	d^3	d^4	d^5	d^6	d^7	d^8	d^9
V^{4+}	V^{3+}	Mn^{4+}	Mn^{3+}	Mn^{2+}		Ni^{3+}	Ni^{2+}	Ni^{+}
Mo^{5+}	Mo^{4+}	Mo^{3+}	Cr^{2+}	Fe^{3+}	Fe^{2+}	Rh^{2+}	Rh^{+}	Rh^{0}
Cr^{5+}		Cr^{3+}		Ru^{3+}	Ru^{2+}		Pt^{2+}	Pt^{+}
Ti^{3+}				Os^{3+}	Os^{2+}	Pd^{3+}	Pd^{2+}	Pd^{+}
Zr^{3+}				Ir^{4+}	Co^{3+}	Co^{2+}	Co^{+}	Ag^{2+}

The use of EPR spectroscopy was elegantly used by Thirumavalavan and co-workers to probe the ligand environment of a macrocyclic VO^{2+} complex.[2] The attractiveness of the vanadyl ion is that one coordination site is always occupied by the vanadyl oxygen and therefore, the metal binding sites are altered in ligand geometry which consistently produces sharp EPR signals.

3.3.2 Hydroxyl radicals and superoxide ions

Other species commonly monitored by EPR spectroscopy are radicals which has widespread application in the study of semiconductor mediated photocatalysis. As previously outlined, the general accepted mechanism involves the promotion of an electron from the valence band to the conduction band. Subsequent trapping of the ejected electron by molecular oxygen gives rise to the superoxide anion radical ($O_2^{\bullet -}$) while the oxidation of water by the positive holes produces hydroxyl radicals. This oxidation of water gives rise to hydroxyl radicals which are too short lived to be detected by EPR spectroscopy. In such situations, a spin trap reagent is added to lead to the formation of a spin adduct which is detectable by EPR spectroscopy (**Scheme 40**).



Scheme 40

There are a number of spin trapping reagents available such as 1,1-diphenyl-2-picrylhydrazyl (DPPH), α-phenyl-*N*-*tert*-butyl nitrone (PBN) and 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) (**Figure 30**).

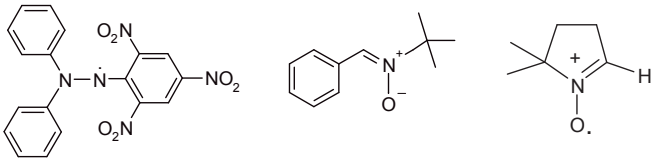
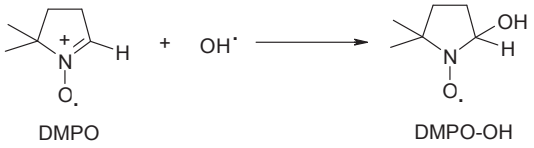


Figure 30

The most popular spin trap is DMPO, due to the β proton which is very sensitive to the nature of the trapped radical and adds to hydroxyl radicals by the following equation (**Scheme 41**):



Scheme 41

This technique was developed by Janzen[3] and first applied to titanium dioxide mediated photocatalysis by Bard and co-workers using titanium dioxide and platinized titanium dioxide powders.[4] Since this pioneering report, a number of research groups have used this method to detect the presence of hydroxyl radicals.

While the positive holes give rise to the hydroxyl radicals, the ejected electron in the conduction band is quenched by dioxygen giving rise to the superoxide anion ($O_2^{\bullet -}$). This radical, like the hydroxyl radical, is also short lived and must be trapped by DMPO to produce an EPR detectable spin adduct. Early interest in this species was reported by the Harbour research group by the irradiation of CdS and metal free phthalocyanines.[5] Thus, the

use of EPR spectroscopy is particularly useful in semiconductor mediated photocatalysis as it allows for the detection of the active oxidizing species (**Figure 31**).

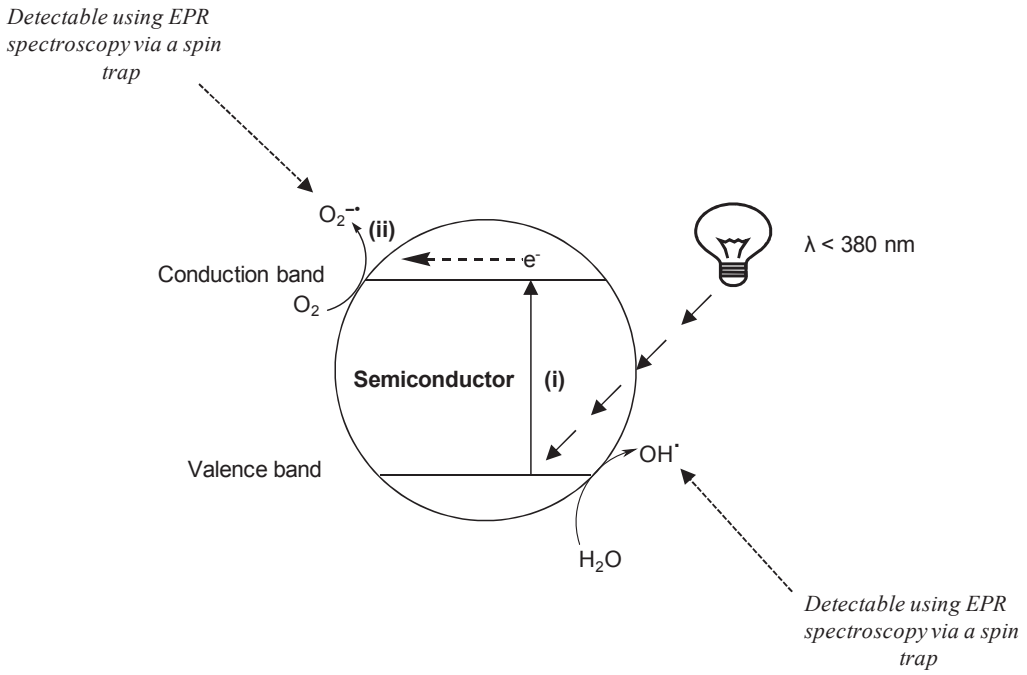


Figure 31

An extension of this methodology on semiconductors has been applied to dye sensitized semiconductors. Under visible light irradiation, hydroxyl radicals will not form and consequently, only $O_2^{\bullet-}$ radicals will be detected. However, the activation of the dye under visible light irradiation gives rise to another connotation as the dye injects an electron into the conduction band of the semiconductor, giving rise to a dye radical by the following scheme:

$$\text{Dye} + h\nu \longrightarrow \text{Dye}^* \qquad (1)$$

$$\text{Dye}^* + \text{semicondcutor} \longrightarrow \text{Dye}^{+\bullet} + \text{semicondcutor}\,(e_{cb}^-) \qquad (2)$$

Scheme 42

An example of this methodology is best illustrated by a classic example reported by Zhao and co-workers who monitored the EPR characteristics of a dye sensitized TiO_2 system.[6] This procedure involved firstly the adsorbtion of the ethyl ester of fluoroscein (FLEt, **Figure 32**) to the surface of titanium dioxide.

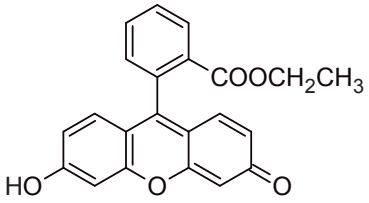
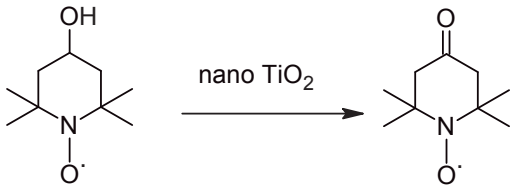


Figure 32

The authors then proceeded to monitor the EPR spectra of fluoroscein sensitized TiO_2 using oxygen as an electron acceptor. The excitation of fluorescein sensitized TiO_2 gave rise to a signal at g = 2.0047 which was assigned to the $FlEt^{+\bullet}$ radical. The addition of the spin trap DMPO gave rise to the spin adduct O_2–DMPO of the superoxide $O_2^{\bullet-}$ radical. Thus, the visible light irradiation of dye sensitized TiO_2 generates the EPR detectable dye radical and the $O_2^{\bullet-}$ spin adduct.

3.3.3 Stable nitroxyl radicals

The final class of radicals to be evaluated are the nitroxyl radicals, based on 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), which are highly stable, isolable species. In early 2011, the Blanksby research group reported the oxidation of TEMPO derivatives using nano-TiO_2 and EPR spectroscopy was used to monitor the oxidation of TEMPOL to TEMPONE (**Scheme 43**).[7]

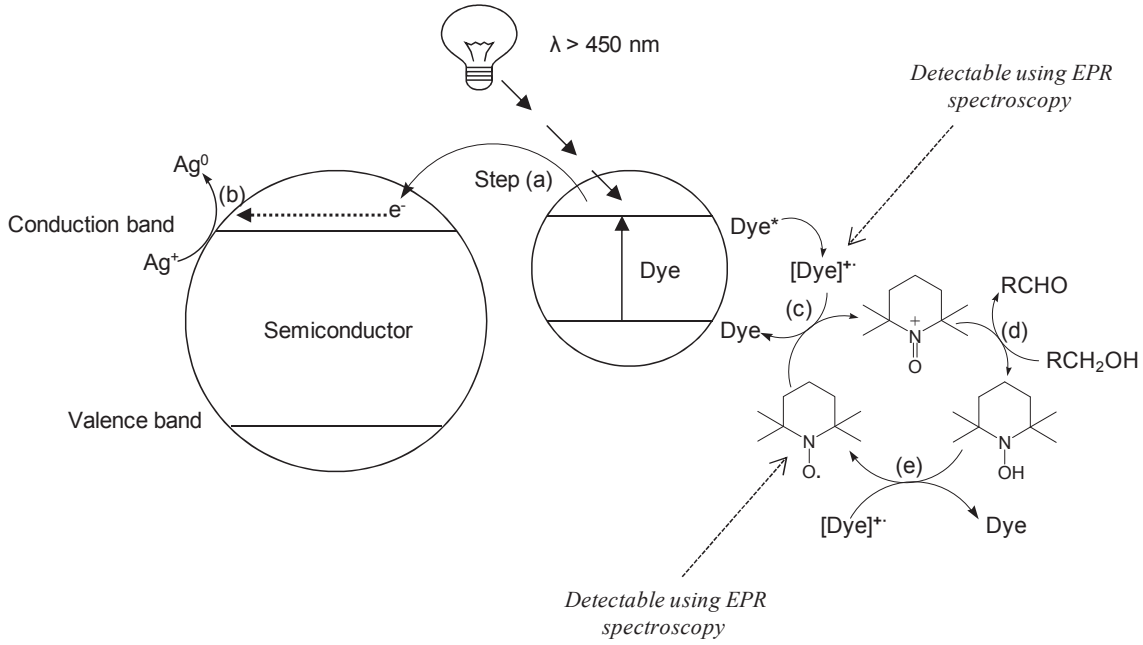


Scheme 43

The EPR spectra of TEMPOL in a TiO_2 solution with no irradiation revealed a characteristic triplet peak due to the TEMPOL radical. Subsequent irradiation for 150 min with *in situ* scanning revealed the emergence of a new radical and after 360 min, the original peaks assigned to the TEMPOL radical had completely disappeared and only the new radical peaks were present. These peaks were assigned to TEMPONE by comparison of the measured spectra with the spectra of an authentic sample of TEMPONE.

3.4 Application of EPR spectroscopy to the dye sensitized ZnO/silver/TEMPO system

Having provided a basic explanation of EPR spectroscopy, attention will now shift to the developed dye sensitized ZnO/silver/TEMPO system and to the information envisaged to be gained from the EPR spectra. Upon visible light irradiation, the activated dye injects an electron into the conduction band of ZnO resulting in a dye radical. Thus, the first goal of the EPR study was to detect the dye radical, followed by determining the effect of the dye radical on the TEMPO radical. The redox potential of $E^0_{AR*/AR+\bullet}$ (0.79 V *vs.* standard hydrogen electrode) is higher than the redox potential of $E^0_{(TEMPO/TEMPO+)}$ (0.64 V *vs.* standard hydrogen electrode) indicating that the dye radical is capable of oxidizing TEMPO to the *N*-oxoammonium salt which is able to oxidize alcohols to their carbonyl derivatives (**Scheme 44**). In addition, EPR spectroscopy was also used to provide insight into the failure of the dye sensitized TiO_2/silver/TEMPO system.



Scheme 44

The results obtained from these findings have been consolidated that has been accepted for publication by Dalton Transactions. A copy of this paper follows.[†] Jeena, V.; Robinson, R. S. Dalton Trans., DOI:10.1039/C2DT12030E. As such, the results for this section of the thesis have been presented in this format.

[†] Copy of the paper included in the body of the text as per faculty guidelines.

Journal Name

Dynamic Article Links ►

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Convenient photooxidation of alcohols using dye sensitised semiconductors in combination with silver nitrate and TEMPO – an electron paramagnetic resonance study†

Vineet Jeena and Ross S. Robinson*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A mechanistic investigation into the photooxidation of alcohols using dye sensitised titanium dioxide and dye sensitised zinc oxide is described. The varying yields using the two photocatalysts have been explained using electron paramagnetic resonance (EPR) spectroscopy, which indicated that electron injection occurs in the dye sensitised ZnO system but is sluggish in the dye sensitised TiO_2 system. Due to the failure of the electron injection step, a 'break' in the photooxidative system occurs resulting in a decrease in the conversion of benzyl alcohol to benzaldehyde for the dye sensitised TiO_2 system.

Photocatalysis, by semiconductor metal oxides has developed into an innovative and exciting tool for chemistry over the past 40 years.[1] Titanium dioxide and zinc oxide have emerged as ideal photocatalysts due to their low cost, environmental friendliness and stability under irradiation.[2] From a synthetic chemistry point of view, the most valuable application of metal oxide mediated photocatalysis is the oxidation of alcohols to their carbonyl derivatives.[3]

While the oxidation of alcohols using metal oxide mediated photocatalysis has been well documented, the oxidative procedure is unselective resulting in a variety of products in addition to the desired carbonyl compound.[4] Our interest in metal oxide mediated photocatalysis has focussed primarily on tandem oxidation coupling reactions in which the oxidised alcohol is trapped *in situ* by a nucleophile in a one-pot procedure.[5] Due to the high oxidising potential of the hydroxyl radicals, many attempts within our group at photocatalysed one-pot tandem coupling reactions have been futile with the starting materials being oxidised indiscriminately. For a tandem coupling reaction, a photooxidative system is needed that is selective and high yielding. We have recently reported the development of a dye sensitised ZnO/silver/TEMPO system for the selective oxidation of alcohols to their carbonyl derivatives.[6] This procedure, which involves the sensitising of the photocatalyst with a visible light absorbing dye (Alizarin red)(AR), holds two distinct advantages; firstly the system can be activated using readily available visible light rather than harsh ultraviolet irradiation. Secondly, under visible light irradiation the dye and not the photocatalyst is activated, preventing the formation of strongly oxidising hydroxyl radicals.

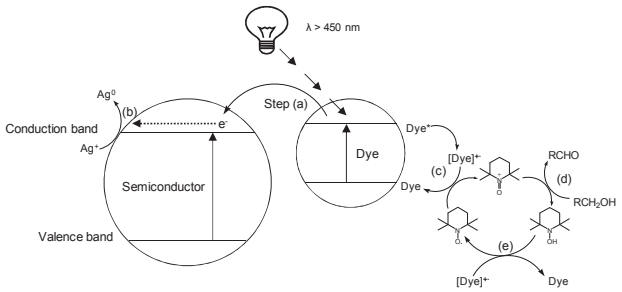


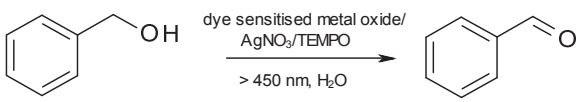
Fig. 1 Proposed mechanism for a selective photocatalysed alcohol oxidation

The following steps were proposed to occur in the photooxidative system:[7] (i) upon visible light irradiation, an electron would be injected from the dye into the conduction band of the photocatalyst (Fig. 1, step a). (ii) Since silver (I) is a superior electron acceptor to dioxygen,[8] the ejected electron would be readily quenched by silver (I) which is reduced to metallic silver (Fig. 1, step b). This step is of utmost importance as the use of silver (I) as an electron acceptor results in the efficient trapping of the electron which drives the photooxidative system, increasing its productivity. (iii) The activated dye would return to its ground state oxidising TEMPO from its radical form into the *N*-oxoammonium salt (the active oxidising species of TEMPO) (Fig. 1, step c). (iv) The *N*-oxoammonium salt would subsequently oxidise the alcohol to its carbonyl derivative (Fig. 1, step d), forming the hydroxylamine which can regenerate the TEMPO radical *via* oxidation by the dye radical (Fig. 1, step e).

Preliminary investigations involved sensitising the photocatalysts with a visible light absorbing dye and evaluating the photooxidative system *via* a test reaction. The test reaction involved mixing a portion of dye sensitised ZnO or dye sensitised

TiO_2, silver nitrate, TEMPO and benzyl alcohol in an aqueous solution under visible light irradiation for 1 hour. Benzaldehyde was formed in trace quantities for the dye sensitised TiO_2 system while the dye sensitised ZnO produced benzaldehyde in a 54% yield (Table 1, entries 1 − 2). Increasing the reaction time, had little effect on the dye sensitised TiO_2 system but a significant improvement in yield was observed for the dye sensitised ZnO system (Table 1, entries 3 − 4).

Table 1 Dye sensitised photocatalyst/silver/TEMPO mediated oxidation of benzyl alcohol in an aqueous solution.[a]



Entry	Metal oxide	Time (h)	Yield (%)[b]
1	TiO_2	1	3
2	ZnO	1	54
3	TiO_2	2	8
4	ZnO	2	82

[a] Reaction conditions: alcohol (0.1 mmol), dye sensitised metal oxide (20 mg), TEMPO (1.5 mg) and $AgNO_3$ (306 mg) in 1.5 ml H_2O. [b] GC yield.

A full study documenting the scope of the dye sensitised ZnO/silver/TEMPO system has been described elsewhere.[6] The system is attractive due to high yields in conjunction with short reaction times. Zhao[9a] and Nagata[9b] have also described complex photocatalysed alcohol oxidations but due to the small scale and long reaction times these systems are unlikely to find application in routine organic synthesis.[10] Next, we set our sights on evaluating the mechanism of our photooxidative system using dye sensitised TiO_2 and dye sensitised ZnO in an effort to explain the discrepancy in yields for the two systems. Initially, we attempted to explore the stability of the dye sensitised metal oxides by UV/Vis spectroscopy (see ESI† for details) as the dye can detach from the metal oxide in aqueous solutions.[11] The UV/Vis spectra revealed that both the dye sensitised metal oxides were stable in the concentrated silver solutions. This observation is in agreement with previously reported literature as dye sensitised TiO_2 and dye sensitised ZnO are known to be stable in concentrated silver solutions.[12] Thus, the discrepancy observed in conversion of benzyl alcohol to benzaldehyde can therefore not be attributed to the instability of dye sensitised TiO_2 in the silver solution.

Titanium dioxide and zinc oxide are known to display similar behaviour[13] so the failure of the dye sensitised titanium dioxide system is somewhat surprising (!). The reduction of Ag^+ to Ag^0 and the subsequent adsorbtion of metallic silver to the surface of semiconductor is known to be beneficial in the photooxidative system.[14] The adsorbed metals can act as electron traps and improve the efficiency of charge transfer, which would be beneficial to the photooxidative system.[15] However, analysis of the dye sensitised ZnO mixture at the end of the reaction showed a high degree of metallic silver (Fig. 2a) while only minute quantities of metallic silver was present in the dye sensitised TiO_2 system (Fig. 2b).

(a) (b)

Fig. 2 (a) Dye sensitised ZnO at end of reaction (b) Dye sensitised TiO_2 at the end of the reaction.

We thus postulated that electrons were not efficiently injected from the activated state of the dye into the conduction band of TiO_2. As a result, the electron was not readily consumed by silver (I) and therefore a decrease in precipitated metallic silver was observed (Fig. 3). Since the injection of electrons from the activated dye into the conduction band of titanium dioxide is vital for the photooxidative cycle to proceed,[9a] the failure of this step would result in a decrease in conversion of the alcohol to aldehyde. The oxidative system can be thought of having a domino effect with (i) electron injection into the conduction band, followed by (ii) quenching of the electron by silver (I) resulting in the dye radical which subsequently triggers the oxidation of the alcohol. The failure of the electron injection step would result in a 'break' in the oxidative system as the formation of the dye radical would be hindered and consequently the oxidation of the TEMPO radical to the *N*-oxoammonium salt. Since the *N*-oxoammonium salt is the active oxidising species, the oxidation of the alcohol would decrease. This is evident when comparing the yields for the dye sensitised TiO_2 (8%) *vs.* the dye sensitised ZnO (82%) systems. To validate our proposal, we aimed to monitor the dye sensitised TiO_2 and the dye sensitised ZnO oxidation using electron paramagentic resonance (EPR) spectroscopy (see ESI† for details).

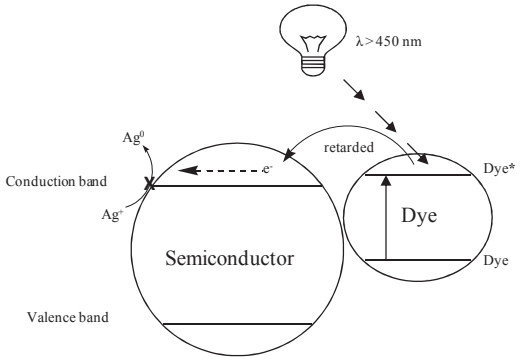


Fig. 3 Simplified diagram of the proposed 'break' in the oxidative system

Firstly, we sought to evaluate the behaviour of the dye sensitised zinc oxide system using EPR spectroscopy. Dye sensitised zinc oxide in a concentrated silver nitrate solution was stirred and put into a quartz tube. The mixture was analysed in the dark and no peaks were observed. Thereafter, the microwave cavity cover was removed and the quartz tube irradiated with a 532 nm green laser for 60 s with *in situ* scanning. To our delight, a single peak at g = 2.0034 was observed which was assigned to the dye radical (Figure 4).[16] Since the dye radical was detected by EPR spectroscopy, this indicates that electron injection from the activated state of dye into the conduction band of ZnO has occurred. The injected electron is readily quenched by silver (I) resulting in the formation of metallic silver which is clearly evident in Figure 2 (a). Next, we aimed to probe the effect of TEMPO on the oxidative system.

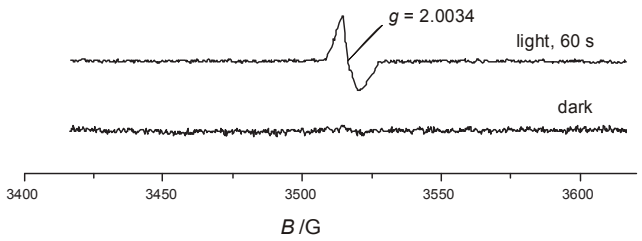


Fig. 4 EPR spectrum of dye radical using the dye sensitised ZnO system.

When TEMPO was added and the mixture analysed in the dark a triplet peak at g = 2.0030 with a splitting constant a_N = 17.6 G was observed which was assigned to the TEMPO radical. Upon irradiation with a 532 nm green laser for 120 s the singlet due to the dye radical reappeared and the intensity of the TEMPO radical diminished significantly. This indicates that the TEMPO radical underwent oxidation by the dye radical. After 240 s of irradiation, the intensity of the TEMPO triplet remained essentially constant indicating that TEMPO was part of a catalytic cycle (Fig. 5). These observations fully support the mechanism proposed in figure 1 as the dye radical oxidises TEMPO into the *N*-oxoammonium salt which carries out the oxidation of the alcohol. These results are in excellent agreement with those proposed by Zhao and co-workers.[9a]

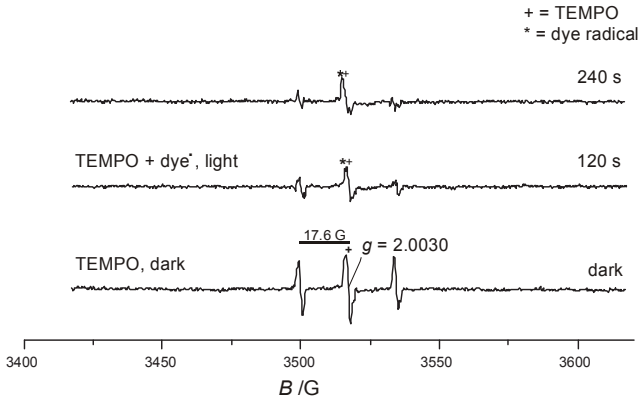


Fig. 5 EPR spectrum of dye radical and TEMPO using the dye sensitised ZnO system.

We turned our attention to the dye sensitised TiO_2 system in which dye sensitised TiO_2 in a concentrated silver nitrate solution was subjected to analysis by EPR spectroscopy (Figure 6). The mixture was analysed in the dark and no peaks were observed. Subsequent irradiation with a 532 nm green laser for 60 s produced no definite peak (corresponding to the dye radical) indicating that electron injection is sluggish in the dye sensitised TiO_2 system. This is in stark contrast to the dye sensitised ZnO system where a sharp single peak was observed immediately. The reasons for the failure of the electron injection step are relatively unclear at this stage but one possible explanation is that back electron transfer (BET) may be occurring in the dye sensitised TiO_2 system resulting in a decrease in quantity of electrons in the conduction band of TiO_2.[17] The BET reaction is known to occur in the TiO_2/AR system due to the strong interaction between Alizarin Red S and titanium dioxide.[18] It is worth mentioning that a TiO_2/AR/O_2/TEMPO in benzotrifluoride (BTF) system for selective oxidation of alcohols has been reported. Since the BET reaction is known to be dependent on experimental conditions,[18] the change in experimental conditions from BTF to a concentrated silver solution may favour the BET reaction, resulting in a decrease in yield. Further detailed studies are underway to fully understand this complex photooxidative system.

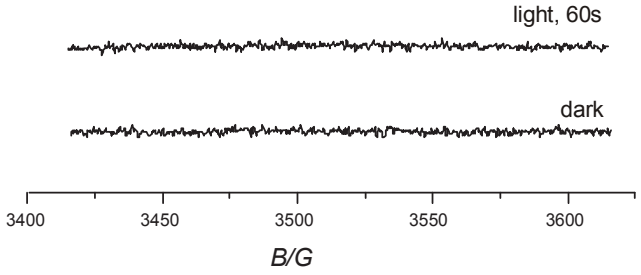


Fig. 6 EPR spectra of dye sensitised TiO_2 in the dark and under green laser (532 nm) irradiation for 60 s.

When TEMPO was added and the mixture analysed in the dark a the triplet peak at g = 2.0030 with a splitting constant of a_N = 17.6 G was observed which was assigned to the TEMPO radical. Upon laser irradiation for 120 s, the dye radical did not appear and the intensity of the TEMPO peaks remained relatively constant. Even after 240 s of irradiation, the dye radical peak did not appear and the triplet peak due to TEMPO was still clearly evident (Figure 7). This is in contrast with the dye sensitised ZnO system where after 240 s of irradiation, the intensity of the triplet peak had diminished significantly and was not clearly evident. Since the dye radical did not appear a break in the proposed oxidative system occurs as the TEMPO radical will not be converted into the *N*-oxoammnium salt in a significant amount. Thus, the conversion of the alcohol to the aldehyde will be minimal.

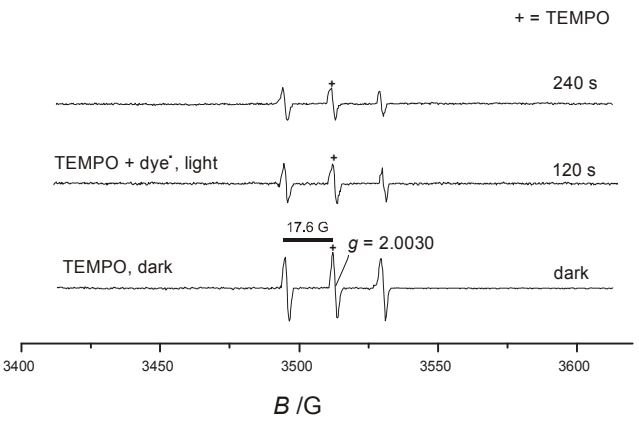


Fig. 7 EPR spectrum of dye radical and TEMPO using the dye sensitised TiO_2 system.

Conclusions

In conclusion, we have used EPR spectroscopy to provide insights into the mechanism of photocatalysed alcohol oxidations using dye sensitised TiO_2 and dye sensitised ZnO. The obtained electron paramagnetic resonance data fully supports the proposed mechanism for a dye sensitised ZnO system and indicates that electron injection may be sluggish in the dye sensitised TiO_2 system resulting in a decrease in yield for the oxidation of benzyl alcohol to benzaldehyde. Further studies are underway to fully understand the dye sensitised TiO_2 system and extend its application to tandem coupling reactions.

Acknowledgements

The National Research Foundation (NRF) of South Africa is gratefully acknowledged for providing a postgraduate bursary (VJ).

Notes and references

Department of Chemistry, University of KwaZulu-Natal, Scottsville, Pietermaritzburg, South Africa. E-mail: robinsonr@ukzn.ac.za

† Electronic Supplementary Information (ESI) available: Redox potential table, general information and experimental procedures. See DOI: 10.1039/b000000x/

1 *(a)* G. Palmisano, V. Augugliaro, M. Pagliaro and L. Palmisano, *Chem. Commun.,* 2007, 3425; *(b)* A. Fujishima, T. N. Rao and D. A. Tryk, *J. Photochem. Photobiol. C: Photochem. Rev.*, 2000, **1**, 1.

2 *(a)* D. Chatterjee and S. Dasgupta, *J. Photochem. Photobiol. C: Photochem. Rev.,* 2005, **6,** 186; *(b)* W. J. E. Beek, M. M. Wienk and R. A. J. Janssen, *Adv. Mater.,* 2004, **16,** 1009.

3 *(a)* F. A. –Z. G. Gassim, A. N. Alkhateeb and F. H. Hussein, *Desalination,* 2007, **209,** 342. *(b)* S. Yurdakal, G. Palmisano, V. Loddo, V. Augugliaro and L. Palmisano, *J. Am. Chem. Soc.,* 2008, **130,** 1568.

4 O. S. Mohamed, A. E. –A. M. Gaber and A. A. Abdel-Wahab, *J. Photochem. Photobiol. A: Chem.,* 2002, **148,** 205.

5 V. Jeena and R. S. Robinson, *Beilstein Journal of Organic Chemistry,* 2009, **5,** No. 24.

6 V. Jeena and R. S. Robinson, Chem. Commun., 2012 DOI:10.1039/c1cc15790f.

7 A redox potential table of various components of the photooxidative system has been included in the electronic supplementary information.

8 E. Baciocchi, C. Rol, G. C. Rosato and G. V. Sebastiani, *J. Chem. Soc., Chem. Commun.,* 1992, **1,** 59.

9 *(a)* M. Zhang, C. Chen, W. Ma and J. Zhao, *Angew. Chem. Int. Ed.*, 2008, **47**, 9730; *(b)* T. Nagasawa, S. I. Allakhverdiev, Y. Kimura and T. Nagata, *Photochem. Photobiol. Sci.*, 2009, **8**, 174.

10 The system reported by Zhao required 18 hours for the oxidation of 0.1 mmol alcohol while the system reported by Nagata required 24 hours to oxidise 300 µmol of alcohol. The dye sensitised ZnO/silver/TEMPO system produces the desired aldehydes in higher yields compared to these systems. In addition, the reactions can also be scaled up and the desired aldehydes isolated with notable success further enhancing their utility.

11 T. Lindgren, J. M. Mwabora, E. Avendaño, J. Jonsson, A. Hoel, C. –G. Granqvist and S. –E. Lindquist, *J. Phys. Chem. B,* 2003, **107,** 5709.

12 *(a)* H. Hada, H. Tanemura and Y. Yonezawa, *Bull. Chem. Soc. Jpn.,* 1978, **51,** 3154. *(b)* H. Hada, Y. Yonezawa and M. Saikawa, *Bull. Chem. Soc. Jpn.,* 1982, **55,** 2010.

13 B. Dindar and S. Icli, *J. Photochem. Photobiol. A: Chem.,* 2001, **140,** 263.

14 *(a)* Y. Liu, C. Liu, Q. Rong and Z. Zhang, *Appl. Surf. Sci.,* 2003, **220,** 7. *(b)* M. –W. Xu, S. –J. Bao and X. –G. Zhang, *Mat. Lett.,* 2005, **59,** 2194. *(c)* R. Wang, J. H. Xin, Y. Yang, H. Liu, L. Xu and J. Hu, *Appl. Surf. Sci.,* 2004, **227,** 312. *(d)* C. A. K. Gouvêa, F. Wypych, S. G. Moraes, N. Durán and P. Peralta-Zamora, *Chemosph.,* 2000, **40,** 427.

15 *(a)* N. Sobana, M. Muruganadham and M. Swaminathan, *J. Mol. Catal. A: Chem.,* 2006, **258,** 124. *(b)* V. Vamathevan, R. Amal, D. Beydoun, G. Low and S. McEvoy, *J. Photochem. Photobiol. A: Chem.,* 2002, **148,** 233 and references therein.

16 Z. Wang, W. Ma, C. Chen, H. Ji and J. Zhao, *Chemical Engineering Journal,* 2011, **170,** 353.

17 G. Ramakrishna, A. K. Singh, D. K. Palit and H. N. Ghosh, *J. Phys. Chem. B,* 2004, **108,** 1701.

18 S. Kaniyankandy, S. Verma, J. A. Mondal, D. K. Palit and H. N. Ghosh, *J. Phys. Chem. C,* 2009, **113,** 3593.

Concluding remarks

In summation, an electron paramagnetic study (EPR) study was conducted using dye sensitized TiO_2 and dye sensitized ZnO. The results of the EPR study support the mechanism proposed for the dye sensitized ZnO system as the Alizarin red (AR) dye radical was detected. The generated dye radical oxidized TEMPO from its radical form into the *N*-oxoammonium salt resulting in a decrease in intensity of the TEMPO radical signal. The intensity of the TEMPO radical signal remained at a certain level indicating that TEMPO was part of a catalytic cycle. In contrast, in the dye sensitized TiO_2 system the dye radical was not detected using EPR spectroscopy. The reasons for the failure of this reaction are relatively unclear at this stage but it is believed that this occurrence may be due to the strong back electron transfer (BET) between the TiO_2/AR system. As the dye radical was not formed, no oxidation of the TEMPO radical occurred and therefore the *N*-oxoammonium salt (the active oxidizing species) was not formed. Thus, the failure of the dye sensitized TiO_2/silver/TEMPO system to produce the *N*-oxoammonium salt would explain the low yields obtained using this system.

Having successfully completed a study on the dye sensitized ZnO/silver/TEMPO and the dye sensitized TiO_2/silver/TEMPO systems, attention was turned to an interesting report in literature concerning the activity of diamonds. This literary report demonstrated the remarkable activity of impure diamondoids under strong ultraviolet irradiation. Thus, in following chapter, attention will be directed towards preliminary studies in the use of impure diamondoids in tandem coupling reactions.

References

1. Lund, A.; Shiotani, M.; Shimada, S. *Principles and Applications of ESR Spectroscopy*: New York, 2011.
2. Thirumavalavan, M.; Martins, A. M. *Inorg. Chem. Commun.* **2006,** *9*, 497-499.
3. Janzen, E. G. *Acc. Chem. Res.* **1971,** *4*, 31-40.
4. Jaeger, C. D.; Bard, A. J. *J. Phys. Chem.* **1979,** *83*, 3146-3152.
5. Harbour, J. R.; Hair, M. L. *J. Phys. Chem.* **1978,** *82*, 1397-1399.
6. He, J.; Zhao, J.; Hidaka, H.; Serpone, N. *J. Chem. Soc., Faraday Trans.* **1998,** *94*, 2375-2378.
7. Marshall, D. L.; Christian, M. L.; Gryn'ova, G.; Coote, M. L.; Barker, P. J.; Blanksby, S. J. *Org. Biomol. Chem.* **2011,** *9*, 4936-4947.

Chapter 4

The use of diamondoids in tandem coupling reactions

4.1 Preface

Having successfully gained insight into the mechanism of dye sensitized ZnO and dye sensitized TiO_2 photooxidative systems, attention was now directed towards the use of impure diamondoids as a potential oxidant in tandem coupling reactions.

4.2 A brief history

Diamonds are one of the most valuable gemstones on earth and are produced in the earth's lithosphere when pressure conditions are appropriate for carbon to crystallize to diamond.[1] The first diamond was discovered in South Africa in 1866 and has been credited to Erasmus Jacobs, a 15 year old boy who found this valuable gem (which turned out to be a 22 carrat diamond) near Hopetown on the Orange (now Gariep) river. In 1869, a Griqua shepherd offered an 83.5 carrat diamond to Schalk van Niekerk who purchased it for a considerable amount of cattle. This diamond was termed "the Star of Africa" and sparked a large influx of European and American prospectors to Southern Africa, all in search of their fortune.[2]

Marilyn Monroe once sang "Diamonds are a girl's best friend" but in recent years, diamonds have been shown to be a chemists best friend.[3] Diamonds are known for their unusual properties such as hardness, high thermal conductivity, high carrier mobility and with a band gap of 5.5 eV, is considered the supreme insulator (**Figure 33**).[4]

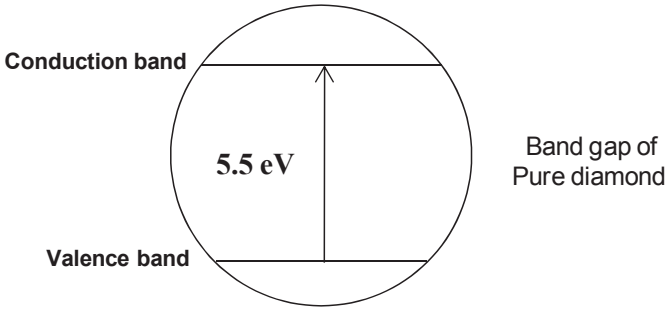


Figure 33

4.3 Doping of diamonds

Despite the number of positive attributes associated with diamond, its large band gap is a deterring factor. One possible solution to alleviate this problem would be to dope this material and thereby decrease its band gap. The doping of diamond would purposefully introduce appropriate impurities into the crystal lattice of diamond and convert it from an insulator into a semiconductor. Materials can exhibit either an *n* or *p*-type doping however, the intricacies of these doping mechanisms is beyond the scope of this project.[5] The most common dopant is boron, which inserts into the lattice of diamond resulting in a decrease in band gap.[6] The effect of doping is best explained in the following illustration using boron as an example (**Figure 34**).

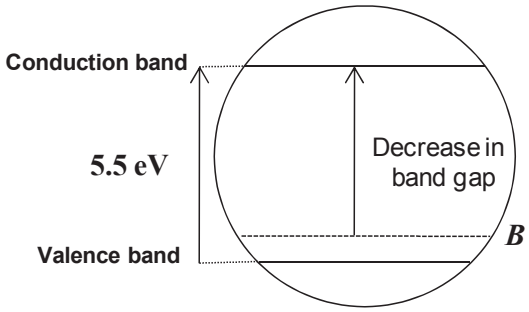


Figure 34

4.4 Application of doped diamond electrodes

4.4.1 Oxidation of phenol

The first report of the electrochemistry of boron-doped diamond electrodes was reported by the Pleskov research group in 1987.[7] When an appropriate potential is applied, an oxidation reaction can take place *via* the direct or indirect method, with direct transfer taking place when a potential (E < 2.3 V *vs.*SHE) while at potentials (E > 2.3 V *vs.* SHE) oxidation reactions are executed by the hydroxyl radicals that are generated by the decomposition of water. This point is neatly represented by the application of boron-doped diamond electrodes in the oxidation of phenol.[8] The results obtained revealed that in the potential region of water stability (E < 2.3 V *vs.* SHE) oxidation of phenol is executed directly by the boron doped diamond electrodes while in the potential region of water decomposition (E > 2.3 V), indirect oxidation takes place *via* the hydroxyl radicals which are generated by the decomposition of water by the following scheme:

Scheme 45

Thus, the electrochemical production of hydroxyl radicals using doped diamond electrodes has found widespread application, most notably in the purification of waste water.

4.4.2 Waste water purification

The application of boron doped diamond (BDD) electrodes has been extended to the degradation of impurities in waste water.[9] Azo dyes are commonly used in industrial processes such as cosmetic and pharmaceutical manufacturing and consequently, are commonly found in waste water effluent.[10] To avoid azo dye accumulation, different methods are being developed to remove these compounds from aqueous solutions. One of the recent advances in this field is the application of boron-doped diamond electrodes for the electrochemical removal of azo dyes from aqueous solutions.[11] The Chen research group reported the degradation of azo dyes using the Ti/BDD electrode and compared its performance to the Ti/Sb_2O_5-SnO_2 electrode. The Ti/BDD electrode was found to be superior

to the Ti/Sb_2O_5-SnO_2 electrode as it degraded 91% of a 2-naphthol orange (**Figure 35**) solution while under identical experimental conditions the Ti/Sb_2O_5-SnO_2 electrode was only able to degrade 26% of this solution.[12]

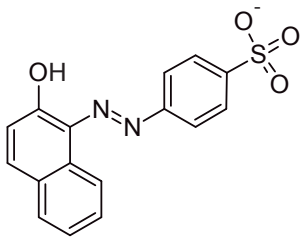


Figure 35

Thus, it was concluded that the Ti/BDD electrode is a superior electrode than Ti/Sb_2O_5-SnO_2 electrode as it was more efficient in the azo dye degradation process.

4.5 The use of diamond powders

Nanodiamonds, commonly referred to as diamondoids, have recently garnered much interest as they are now readily available from petroleum and crude oil.[3] This branch of research originated from a patent application from the Mobil Oil Coporation in 1990 to separate nano diamonds from oil and gas[13] and in 1999, the Dahl research group showed that diamondoids are present in petroleum sources by oil cracking (the breakdown heavy hydrocarbons into smaller ones). The authors proved that the unique thermal stability of diamondoids leads to their progressive concentration during cracking.[14]

4.5.1 Application of diamondoid powders as a solid support

4.5.1.1 Palladium loaded oxidized diamond catalysts

While much research has focused on the use of doped diamond electrodes, an alternate application is the use of these diamondoid powders. The Suzuki research group reported the use of palladium loaded oxidized diamond in the oxidation of alcohols.[15] This procedure involved the air oxidation of commercial diamond powder followed by impregnation of the oxidized diamond (O–Dia) surface with $Pd(OAc)_2$ to produce the Pd/O–Dia catalyst. The synthesized catalyst was shown to effectively oxidize alcohols in high conversion, however,

with moderate selectivity. A mechanism, using benzyl alcohol as a model substrate, is given below explaining the formation of the observed products (benzaldehyde and toluene) (**Figure 36**).

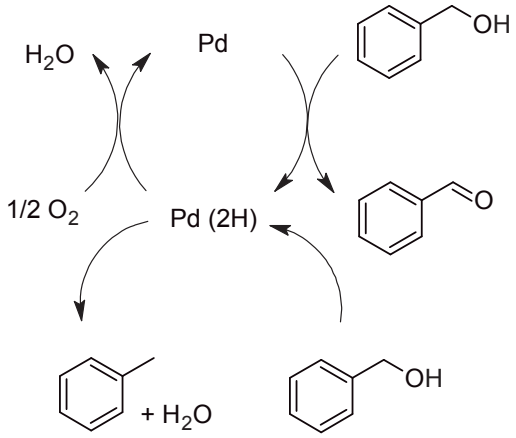


Figure 36

4.5.1.2 Fischer-Tropsch process

The Fischer-Tropsch process, named after German chemist Franz Fischer and Czech chemist Hans Tropsch, is a method used to convert carbon monoxide and hydrogen into liquid hydrocarbons (**Scheme 46**).[16]

$$nCO + (2n + 1)H_2 \longrightarrow C_nH_{2n+2} + nH_2O$$

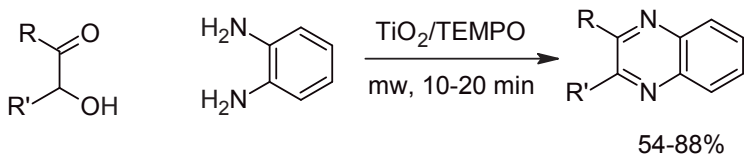
Scheme 46

This process requires the presence of a metal catalyst with only iron, cobalt and ruthenium. SASOL employing cobalt and iron catalysts at relatively high reaction temperatures.[17] Goodwin and co-workers have studied the effect of metal loaded solid supports as catalysts for the Fischer Tropsch process and found that Cobalt-loaded alumina and Cobalt-loaded SiO_2 exhibited similar activity.[18] Interestingly, Cobalt-loaded TiO_2 showed the lowest activity

due to the smaller surface area of the support resulting in large Cobalt particles. In late 2011, the Suzuki research group reported the application of a Cobalt-loaded oxidized diamond catalyst to the Fischer-Tropsch reaction. The authors found that Cobalt-loaded oxidized diamond was a superior catalyst than Cobalt-loaded SiO_2 as it demonstrated a higher carbon monoxide conversion. [19]

4.6 Proposed use of diamonds in tandem coupling reactions

Whereas the use of doped diamond electrodes has been well documented, the use of nano diamond powder is considerably less documented. This prompted us to apply this powder to a tandem coupling reaction. This need was initiated from earlier literature reports that diamond electrodes were shown to exhibit signifigant photocurrents even with *subband* gap illumination.[20] These electrodes were not expected to exhibit any activity as the band gap of diamond is too large under the above experimental conditions. The observed activity was attributed to minor impurities or surface states within the band gap allowing for the activation of these electrodes. Fujishima and co-workers showed that high quality (and expensive) diamond electrodes with little non carbon content showed no activity under subband gap illumination.[21] Thus, we were alerted to the possible application of diamondoid powder as an oxidant in tandem coupling reactions. The use of inexpensive diamond powder would contain minor impurities which would allow for the activation of the diamondoid powder under strong ultraviolet irradiation. We have previously shown that under microwave irradiation, titanium dioxide can be used to efficiently catalyze the synthesis of quinoxalines (**Scheme 47**).[22] It is postulated that due to the formation of a highly conjugated system, the quinoxalines were stable even in the presence of hydroxyl radicals.



Scheme 47

Therefore, the scene was set to test the hypothesis by attempting the synthesis of a series of quinoxalines using the commercially available inexpensive diamondoid powder. The results of this study are presented herein publication format which will be submitted for publication shortly.*

* Copy of the draft paper included in the body of text as per faculty guidelines.

((Catch Phrase))

DOI: 10.1002/anie.200((will be filled in by the editorial staff))

The use of diamondoids in the photocatalysed tandem synthesis of quinoxalines

*Vineet Jeena and Ross S. Robinson**

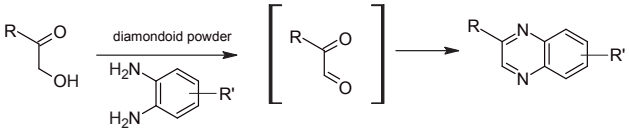
((Dedication----optional))

Diamonds are one of the most valuable gemstones on earth and are produced in the earth's lithosphere when pressure conditions are appropriate for carbon to crystallise to diamond.[1] The first diamond was discovered in 1866 and has been credited to Erasmus Jacobs, a 15 year old boy who found this valuable gem (which turned out to be a 22 carrat diamond) near Hopetown on the Gariep River in South Africa.[2]

Marilyn Monroe once said, 'diamonds are a girl's best friend' but in recent years, diamonds have been shown to be a chemists best friend.[3] Diamonds are known for their hardness, high thermal conductivity, high carrier mobility and with a band gap of 5.5 eV is considered the supreme insulator.[4] Despite these positive attributes, due to the large band gap of 5.5 eV, diamond is electrically insulating and cannot be used as an electrode material. One possible solution to alleviate this problem would be to dope this material and thereby, decrease its band gap with boron commonly used as a dopant.[5] When an appropriate potential is applied to these doped diamond electrodes an oxidation reaction can take place via the direct or indirect methods. When a potential (E < 2.3 V vs. SHE) is applied, the oxidation reaction is executed exclusively at the doped diamond electrode (direct method). However, when a potential (E > 2.3 V vs. SHE) is applied, the oxidation is executed by strongly oxidizing hydroxyl radicals ($OH^{\bullet}$), which are generated by the decomposition of water in aqueous solutions.[6]

While the application of doped diamond electrodes is well established, recent applications have focused on the use of nanodiamond powder, commonly referred to diamondoids.[7] These diamondoid powders have began to gain prominence in synthetic organic chemistry with the Suzuki research group reporting the oxidation of alcohols using a palladium loaded oxidized diamond catalyst.[8]

With the emergence of diamondoids in synthetic organic chemistry, our attention was directed towards the application of this material in the tandem coupling synthesis of quinoxalines (Scheme 1). The tandem oxidation reaction has gained widespread prominence as the oxidant oxidises the alcohol to the aldehyde which is effectively trapped by the nucleophile in a one pot synthesis.[9] Thus, the application of a diamondoid powder as an oxidant in the tandem coupling reaction was proposed in which, under strong ultraviolet irradiation, the diamondoid powder would oxidise the alcohol to the aldehyde resulting in the formation of the keto aldehyde which would be immediately trapped by the diamine to form the quinoxaline.



Scheme 1. Proposed synthesis of quinoxalines using the diamondoid powder

Due to its large band gap, the diamondoid powder should be doped in order to be effective however, our attention was drawn to a report in which diamond electrodes were shown to exhibit significant photocurrents even with *subband* gap illumination.[10] This unexpected occurrence was attributed to minor impurities or surface states within the band gap of diamond which allowed for the activation of these electrodes. Indeed, Fujishima and co-workers had shown that high quality (and expensive) diamond electrodes with little non carbon content showed no activity when subjected to subband gap illumination.[11] Thus, the use of commercially available impure and inexpensive diamondoids should, due to the presence of minor impurities, exhibit activity under strong ultraviolet irradiation. Thus, it was proposed that under strong ultraviolet light irradiation, an electron will be promoted form the impurity band to the conduction band, resulting in the formation of 'postive holes' (Figure 1).

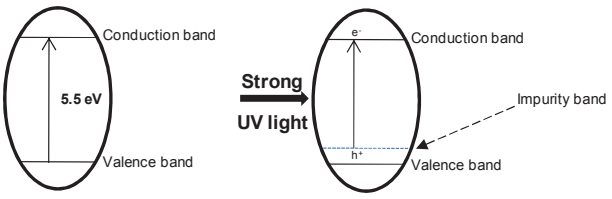


Figure 1. Illustrating the difference between pure and impure diamond

These 'positive holes' are strong oxidants ($E^0 = 2.70$ V) and are able oxidize alcohols (direct method) or will oxidize surface adsorbed

[*] V. Jeena, Prof. R. S. Robinson
Department of Chemistry
University of KwaZulu-Natal
Scottsville, Pietermaritzburg
Fax: (+)
E-mail: robinsonr@ukzn.ac.za
Homepage ((optional)):

[**] ((Acknowledgements))

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.((Please delete if not appropriate))

water to produce hydroxyl radicals which are equally strong oxidants ($E^0 = 2.80$ V). The keto alcohol will be oxidised to the keto aldehyde which will be immediately trapped by the diamine to produce the quinoxaline. The synthesized quinoxalines should be stable under the above conditions as these species are highly conjugated providing enhanced stability even under these harsh oxidising conditions.

Thus, it was proposed that under strong ultraviolet irradiation, an electron would be promoted from the impurity band to the conduction band where it would be rapidly quenched by dioxygen. The ejected electron would leave behind strongly oxidising positive holes in the conduction band. These positive holes would oxidise the keto alcohol to the keto aldehyde which would immediately be trapped by the diamine to produce the highly conjugated quinoxaline (Figure 2). Due to the extended conjugation throughout this system, quinoxalines will be stable even in the presence of the strongly oxidising positive holes.

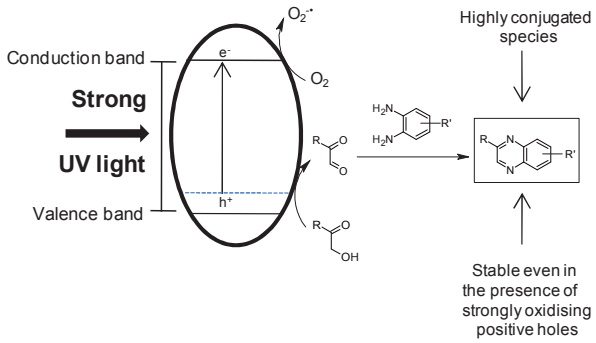
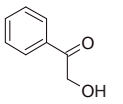
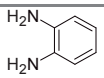
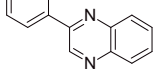
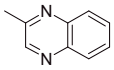
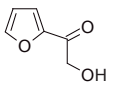
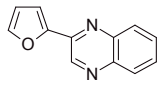
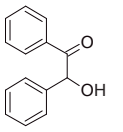
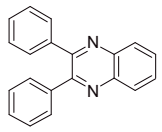
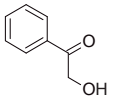
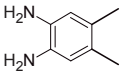
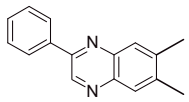
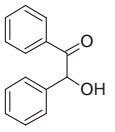
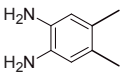
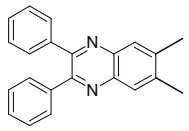


Figure 2. Schematic representation of the proposed diamond mediated photocatalysed quinoxaline synthesis

Thus, a 1µm diamond powder was purchased and used as an oxidant in the tandem coupling reaction between 2-hydroxyacetophenone and *o*-phenylenediamine. After 6 hours of irradiation, the resulting mixture was filtered and concentrated *in vacuo* to produce the crude product which was subsequently purified using radial chromatography to produce the desired quinoxaline in an isolated yield of 83%. Encouraged by this result, the diamondoid mediated system was extended to an α-keto alcohol (table 2, entry 2) whose corresponding aldehyde is difficult to isolate due to the 'hyper-reactivity' of the aldehyde function.[12] To our delight, under the above experimental conditions, the desired quinoxaline was isolated in a good yield of 81%. Similar results were obtained with a furyl system with the related quinoxaline isolated in a yield of 77%. The secondary hindered alcohol benzoin also responded well to a diamondoid mediated oxidation with the corresponding quinoxaline isolated in a yield of 73%. Next, the effect of varying the diamine component was investigated. Using, 6,7-dimethyl-*o*-phenylenediamine as a nucleophile, a decrease in yield was observed with the quinoxaline formed in a 58% yield using

Table 1. Diamondoid mediated tandem quinoxaline synthesis.

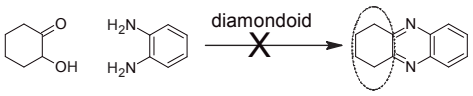
Entry	α-Hydroxy ketone	Amine	Product	Yield[b] (%)
1				83
2				81
3				77
4				73
5				58
6				38

[a] Reaction conditions: Alcohol (0.5 mmol), diamine (0.5 mmol), molecular sieves (0.5 g) and diamondoid powder (15 mg) in dry acetonitrile under strong UV irradiation for 6 hours. [b] Isolated yield

2-hydroxyacetophenone and 38% yield using benzoin as a substrate.

It is believed that due to the extended conjugation of the quinoxaline product, these species are stable even in the presence of the highly oxidising positive holes. To test our theory, the diamondoid mediated oxidation system was applied to 2-hydroxycyclohexanone which was an example of a non aromatic alcohol. Thus, a 2-hydroxycyclohexanone, *o*-phenylenediamine and the diamondoid powder was stirred in acetonitrile and subjected to strong ultraviolet irradiation for 6 hours. After this time, the obtained reaction mixture which had turned muddy brown was passed through a short silica plug and the residues washed well with dichloromethane. However, no compounds had eluted even with repeated washings with dichloromethane. Eventually, the silica plug was washed with methanol and the solvent removed *in vacuo* to produce a brown solid. Subsequent analysis by 1H NMR spectroscopy, revealed the presence of a number of peaks, none of which were attributable to

product. Hence, it was concluded that since the desired quinoxaline did not display the extended conjugation, this quinoxaline was unable to withstand the harsh oxidising conditions and was subsequently underwent degradation (Scheme 2).



Break in extended conjugation and subsequent degradadation by positive holes

Scheme 2: Showing the break in the extended conjugation

In conclusion, a novel method for the synthesis of quinoxalines has been developed. The use of diamondoids as a photocatalysed oxidant can effectively synthesise highly conjugated quinoxalines in fair to excellent yields in relatively short reaction times. The system was however unsuccessful in the synthesis of quinoxalines that did not display the extended conjugation as these compounds were unable to survive the strongly oxidising conditions. Further studies are underway to extend the methodology of diamondoid mediated oxidations with a view of incorporating them into other tandem coupling reactions.

Experimental Section

To a solution of alcohol (0.50 mmol) in dry acetonitrile was added *o*-phenylenediamine (0.50 mmol), molecular sieves (0.50 g) and the diamondoid powder (15 mg). The mixture was stirred under strong ultraviolet irradiation and after 6 hours, the resulting solution was filtered through a short silica pad and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce the crude product was subsequently purified using radial chromatography to afford the pure product.

Received: ((will be filled in by the editorial staff))
Published online on ((will be filled in by the editorial staff))

Keywords: diamondoid · oxidation · quinoxaline · tandem

[1] M. Field, J. Stiefenhofer, J. Robey, S. Kurszlaukis *Ore Geology Reviews.* **2008**, *34*, 33-75. b) A. Author, B. Coauthor, *ChemBioChem* **2006**, *7*, 1-10.))
[2] M. D. Lynn, P. E. Wipplinger, M. G. C. Wilson in *Mineral Resources of South Africa*, Pretoria, **1998**.
[3] H. Schwertfeger, A. A. Fokin, P. R. Schreiner *Angew. Chem. Int. Ed.* **2008**, *47,* 1022-1036.
[4] M. N. R. Ashfold, P. W. May, C. A. Rego, N. M. Everitt *Chem. Soc. Rev.* **1994**, *23*, 21-30.
[5] A. Kraft, *Int. J. Electrochem. Sci.* **2007**, *2*, 355-385.
[6] J. Iniesta, P. A. Michaud, M. Panizza, G. Cerisola, A. Aldaz, Ch. Comninellis *Electrochimica Acta.* **2001**, *46*, 3573-3578. b) A. Author, B. Coauthor, *ChemBioChem* **2006**, *7*, 1-10.))
[7] H. Schwertfeger, A. A. Fokin, P. R. Schreiner *Angew. Chem. Int. Ed.* **2008**, *47*, 1022-1036.
[8] T. Yasu-eda, R. Se-ike, N. Ikenaga, T. Miyake, T. Suzuki *J. Mol. Catal. A: Chem.* **2009**, *306*, 136-14.
[9] R. J. K. Taylor, M. Reid, J. Foot, S. A. Raw *Acc. Chem. Res.* **2005**, *38*, 851-869.
[10] A. Y. Sakharova, Y. V. Pleskov, F. Di Quarto, S. Piazza, C. Sunseri, I. G. Teremetskaya, V. P. Varnin *J. Electrochem. Soc.* **1995**, *142*, 2704-2709.
[11] L. Boonma , T. Yano, D. A. Tryk, K. Hashimoto, A. Fujishima *J. Electrochem. Soc.* **1997**, *144*, L142-L150; *Angew. Chem. Int. Ed.* **2006**, *45*, 1-5.
[12] R. E. Ireland, D. W. Norbeck *J. Org. Chem.* **1985,** *50,* 2198-2200.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

((Catch Phrase))

((Text for Table of Contents, max. 450 characters))

((Author(s), Corresponding Author(s)*))
_____ Page – Page

((Title Text))

((TOC Graphic))

Layout 2:

((Catch Phrase))

((Author(s), Corresponding Author(s)*))
_____ Page – Page

((TOC Graphic))

((Title Text))

((Text for Table of Contents, max. 450 characters))

Concluding remarks

In summation, diamondoid powder has been shown to be an excellent oxidant for the synthesis of quinoxalines. Using this methodology, a series of quinoxalines were synthesized in moderate to excellent yields in short reaction times. To the best of our knowledge, this is the first report of the application of diamondoid powder in a tandem coupling reaction. The above procedure is simple, innovative and uses an inexpensive oxidant. This first foray into the application of diamondoid powder as an oxidant in tandem coupling reaction will be a significant contribution to the exciting field of diamondoid chemistry.

References

1. Field, M.; Stiefenhofer, J.; Robey, J.; Kurszlaukis, S. *Ore Geology Reviews* **2008,** *34*, 33-75.
2. Lynn, M. D.; Wipplinger, P. E.; Wilson, M. G. C. *Mineral Resources of South Africa*: Pretoria, 1998.
3. Schwertfeger, H.; Fokin, A. A.; Schreiner, P. R. *Amgew. Chem. Int. Ed.* **2008,** *47*, 1022-1036.
4. Ashfold, M. N. R.; May, P. W.; Rego, C. A.; Everitt, N. M. *Chem. Soc. Rev.* **1994,** *23*, 21-30.
5. Zhang, S. B.; Wei, S.-H.; Zunger, A. *Phys. Rev. B*. **2001,** *63*, 075205-1 - 075205-7.
6. Kraft, A. *Int. J. Electrochem. Sci.* **2007,** *2*, 355-385.
7. Pleskov, Y. V.; Sakharova, A. Y.; Krotova, M. D.; Builov, L. L.; Spitsyn, B. V. *J. Electroanal. Chem.* **1987,** *228*, 19-27.
8. Iniesta, J.; Michaud, P. A.; Panizza, M.; Cerisola, G.; Aldaz, A.; Comninellis, C. *Electrochimica Acta.* **2001,** *46*, 3573-3578.
9. Alfaro, M. A. Q.; Ferro, S.; Martinez-Huitle, C. A.; Vong, Y. M. *J. Braz. Chem. Soc.* **2006,** *17*, 227-236.
10. Fernandez, C.; Larrechi, M. S.; Callao, M. P. In *Trends in Analytical Chemistry*, 2010; pp. 1202-1211.
11. Peralta-Hernandez, J. M.; Mendez-Tovar, M.; Guerra-Sanchez, R.; Martinez-Huitle, C. A.; Nava, J. L. *International Journal of Electrochemistry* **2011,** *2012*, 18 pages.
12. Chen, X.; Chen, G.; Yue, P. L. *Chem. Eng. Sci.* **2003,** *58*, 995-1001.
13. Alexander, R. A.; Knight, C. E.; Whitehurst, D. D.: USA, 1990.
14. Dahl, J. E.; Moldowan, J. M.; Peters, K. E.; Claypool, G. E.; Rooney, M. A.; Michael, G. E.; Mello, M. R.; Kohnen, M. L. *Nature* **1999,** *399*, 54-57.
15. Yasu-eda, T.; Se-ike, R.; Ikenaga, N.; Miyake, T.; Suzuki, T. *J. Mol. Catal. A: Chem.* **2009,** *306*, 136-142.
16. Khodakov, A. Y.; Chu, W.; Fongarland, P. *Chem. Rev.* **2007,** *107*, 1692-1744.
17. Bromfield, T. C.; Vosloo, A. C. *Macromol. Symp.* **2003,** *193*, 29-34.
18. Oukaci, R.; Singleton, A. H.; Goodwin Jr, J. G. *Appl. Catal. A: General* **1999,** *186*, 129-144.
19. Honsho, T.; Kitano, T.; Miyake, T.; Suzuki, T. *Fuel* **2011**.
20. Sakharova, A. Y.; Pleskov, Y. V.; Di Quarto, F.; Piazza, S.; Sunseri, C.; Teremetskaya, I. G.; Varnin, V. P. *J. Electrochem. Soc.* **1995,** *142*, 2704-2709.
21. Boonma, L.; Yano, T.; Tryk, D. A.; Hashimoto, K.; Fujishima, A. *J. Electrochem. Soc.* **1997,** *144*, L142-L150.
22. Jeena, V.; Robinson, R. S. *Beilstein Journal of Organic Chemistry* **2009,** *5*, No. 24.

Overall Conclusions

In an effort to advance the chemistry of photocatalyzed tandem coupling reactions, a new photooxidative system was developed. The use of a dye sensitized ZnO/silver/TEMPO system was optimized and evaluated for the photocatalyzed oxidation of alcohols. The developed system was shown to be highly efficient on aromatic alcohols with the desired alcohols formed in yields ranging from 82 to 99% in 2 hours. The system was however, less efficient on unactivated alcohols with the desired carbonyl formed in a disappointing yield of 12%. Nevertheless, the developed system is superior to other established photocatalyzed alcohol oxidations in terms of reaction times and yield. In addition, the dye sensitized ZnO/silver/TEMPO system can be scaled-up with corresponding success with the 3,4-dimethoxybenzaldehyde isolated in a yield of 87% and benzil isolated in a yield of 78%. The dye sensitized ZnO was applied to a one-pot tandem coupling reaction but was unfortunately unsuccessful, probably due to the complexation between the phosphoran and the silver ions. The dye sensitized ZnO/silver/TEMPO system was successfully applied to a pseudo-tandem reaction with the desired acrylate isolated in a yield of 82%.

While the dye sensitized ZnO/silver/TEMPO system was successful in the oxidation of alcohols, the reasons for the failure of the dye sensitized TiO_2/silver/TEMPO was not clear to us. Hence, an electron paramagnetic resonance (EPR) study was conducted in order to further understand the dye sensitized ZnO system as well as provide an explanation for the failure of the dye sensitized TiO_2 system. The EPR study for the dye sensitized ZnO system revealed the presence of a dye radical and a corresponding decrease in the intensity of the TEMPO radical signal. In contrast, when subjected to an EPR study, the dye sensitized TiO_2 system did not show the presence of the dye radical and consequently, no decrease in the intensity of the TEMPO radical was observed. Thus, the EPR study supported the proposed mechanism for the dye sensitized ZnO system as well as providing insight into the failure of the dye sensitized TiO_2 system.

The application of diamondoid powder as a potential tandem oxidant towards the synthesis of quinoxalines was evaluated. The diamondoid powder was shown to be highly efficient in the synthesis of high conjugated quinoxalines which were synthesized in moderate to excellent

yields under strong ultraviolet irradiation in 6 hours. The synthesis of a less conjugated quinoxaline was however unsuccessful, as the desired compound underwent degradation under the strongly oxidizing conditions. Nevertheless, this observation reinforces the notion of the presence of the strongly oxidizing 'positive holes' and hydroxyl radicals.

To the best of our knowledge, very few reports exist detailing the use of photocatalyzed tandem coupling reactions. The observed results form part of the knowledge buildup in the field of well known photocatalysts such as titanium dioxide and zinc oxide and present a new and exciting oxidant in the form of the impure diamondoid powder.

Future work

A dye sensitized ZnO/silver/TEMPO photooxidative system was found to be highly effective for the oxidation of alcohols. Preliminary investigations into one-pot tandem coupling reactions were unsuccessful probably due to complexation between the phosphorane and the silver ions. This hypothesis should be tested and future plans should encompass a study on the type of complex formed between the phosphorane and silver(I) ions which can be accomplished by the application of ^{31}P NMR spectroscopy.

The first foray into the application of diamondoids as a potential oxidant in tandem coupling reactions was successful with a series of quinoxalines which were isolated in moderate to excellent yields. Future studies should entail a determination of the active oxidizing species using EPR spectroscopy. The addition of a radical trapping agent such as DMPO will allow for the detection of hydroxyl radicals. The generation of these strong oxidizing species can also be applied to the degradation of dyes (such as methylene blue) as well as well as a sterilizing agent in the degradation of disease causing bacteria.

Chapter 5

Experimental

5.1 General Methods

Instrumentation:

NMR spectra were recorded using a Bruker Avance III 400 or a Bruker Avance III 500 spectrophotometer equipped with a 5 mm BBO-Z or 5 mm TBIZ probe at 30^{o}C.

^{1}H NMR spectra were recorded at 400 or 500 MHz, ^{13}C NMR spectra were recorded at 100 or 125 MHz respectively.

NMR spectra were referenced against the residual $CDCl_3$ present in δ_H 7.26 ppm or the δ_C77.0 ppm.

IR spectra were recorded on a Smiths IdentifyIR spectrometer or a Perkin Elmer Spectrum One.

Low resolution (Electron Impact) mass spectra were recorded using a ThermoFinnigan trace GC, coupled with PolarisQ mass spectra.

Gas Chromatography spectra were recorded using a Perkin Elmer precisely Clarus 500 Gas Chromatograph.

Melting points were determined using a Kofler hot-stage melting apparatus and are uncorrected.

UV/Vis spectra were recorded on a Shimadzu UV-1800 spectrophotometer.

Diffuse Reflectance spectra were obtained using a Cary 500 UV-Vis-NIR spectrophotometer (University of the Witwatersrand, School of Physics).

High resolution mass spectra were obtained using a Waters Acquity (LCT premier) ultra performance liquid chromatography-mass spectrometry instrument.

Reactions under visible light irradiation were conducted using an OSRAM VIALOX 70 W lamp.

EPR measurements were conducted using a Bruker EMX plus, with the following settings: centre field, 3516.87 G; microwave frequency, 9.86 GHz; and power, 2.00 mW. The same quartz tube was used in all experiments to minimize errors.

The tandem coupling synthesis using the diamondoid powder was conducted in a specially designed cylindrical glass vessel in a water bath using an OSRAM ULTRAMED® 2000 W lamp. The lamp was cooled by the circulation of water *via* a copper coil and a cooling fan placed at the entrance of the cylindrical vessel.

Chemicals:

Reagents were used as received from the supplier except for 1-(2-furanyl)-2-hydroxyethanone which was synthesized from the corresponding methyl ketone using the method described by Moriarty and co-workers.[1]

Chromatography:

Radial chromatography was performed on the Harrison Research Chromatatron (Model 7924T) with the solvent system delivered by gravity flow using a 1mm layer of Merck silica gel (7749). Thin layer chromatography was carried out using silica gel 60 PF_{254} aluminum backed plates. The plates were viewed under UV light and developed in anisaldehyde thereafter.

Explanation of NMR abbreviations:

s – singlet, d – doublet, dd – doublet of doublet, m – multiplet, q – quartet, t – triplet.

Spectra:

All spectra referred to in the discussion have been included within the text with supplementary spectra included in an electronic format. NMR, IR and GC/MS have been included as pdf documents with each folder designated its IUPAC name as it appears in the text. GC spectra have been allocated its own folder and contain four pdf documents, namely, (i) the determination of the response factor (which allowed for the determination of the yield from the peak area), (ii) optimization study using various quantities of silver nitrate, (iii) the effect of the additives and (iv) the chromatograms of various alcohols analyzed using the photooxidative systems.

5.2 Procedures and spectroscopic data

Synthesis of dye sensitized semiconductor powders

Dye sensitized TiO_2

To a stirred mixture of titanium dioxide (0.975 g, 12.2 mmol) and Alizarin Red S (0.025 g, 0.073 mmol) was added a minimum amount of water to generate a paste and the resulting mixture stirred overnight to produce the dye sensitized titanium dioxide powder.

Dye sensitized ZnO

To a stirred mixture of zinc oxide (0.975 g, 12.0 mmol) and Alizarin Red S (0.025 g, 0.073 mmol) was added a minimum amount of water to generate a paste and the resulting mixture stirred overnight to produce the dye sensitized zinc oxide powder.

Determination of response factors

Benzyl alcohol

Solutions of benzyl alcohol in methanol with varying concentration were prepared: (i) 5.04 x 10^{-3} M, (ii) 1 x 10^{-2} M, (iii) 2.52 x 10^{-2} M, (iv) 5.04 x 10^{-2} M and (v) 7.56 x 10^{-2} M. These solutions were analyzed using gas chromatography to determine the peak areas of these solutions.

Benzaldehyde

Solutions of benzaldehyde in methanol with varying concentration were prepared: (i) 5.04 x 10^{-3} M, (ii) 1 x 10^{-2} M, (iii) 2.52 x 10^{-2} M, (iv) 5.04 x 10^{-2} M and (v) 7.56 x 10^{-2}M. These solutions were analyzed using gas chromatography to determine the peak areas of these solutions.

A graph of peak area *vs.* concentration was plotted and from the slope the response factor determined. Since the slope for the alcohol and aldehyde were found to quite similar, it was found that the alcohol and aldehyde displayed a similar response and due to this fact, the yields for the alcohol oxidation could be determined by the integration of the peak areas.

Optimization study using various equivalents of silver nitrate

An optimization study using various equivalents of silver nitrate was carried out in order to determine the optimum amount of silver nitrate for a maximum yield of the carbonyl derivative.

3 equivalents of silver nitrate

To a solution of $AgNO_3$ (51 mg, 0.3 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 27%.

4.5 equivalents of silver nitrate

To a solution of $AgNO_3$ (77 mg, 0.45 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography.

The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 41%.

6 equivalents of silver nitrate

To a solution of $AgNO_3$ (102 mg, 0.60 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 53%.

12 equivalents of silver nitrate

To a solution of $AgNO_3$ (204 mg, 1.2 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 60%.

18 equivalents of silver nitrate

To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 82%.

Model study to probe the contribution of each of the additives to the photooxidative system

Dye sensitized TiO_2 under 1 hour of visible light irradiation

To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized TiO_2 (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 1 hour. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 3%.

Dye sensitized TiO_2 under 2 hours of visible light irradiation

To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized TiO_2 (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 8%.

Dye sensitized ZnO under 1 hour of irradiation

To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 1 hour. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 54%.

Dye sensitized ZnO under 2 hours of irradiation

To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl

acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 82%.

Absence of dye sensitized ZnO

To a solution of $AgNO_3$ (306 mg, 1.8 mmol) and TEMPO (1.5 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 16%.

Absence of TEMPO

To a solution of $AgNO_3$ (306 mg, 1.8 mmol) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the benzyl alcohol (0.0108 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 12%.

Absence of Silver nitrate

Dye sensitized ZnO (20 mg) was added to H_2O (1.5 ml). Under these conditions, the dye immediately detached from the semiconductor.

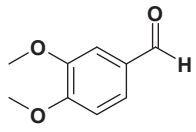
Acetonitrile as a solvent

To a solution of $AgNO_3$ (306 mg, 1.8 mmol) in CH_3CN (1.5 ml) was added the dye sensitized ZnO (20 mg). Under these conditions, the dye immediately detached from the semiconductor.

Exploring the scope of the photooxidative system on a series of alcohols

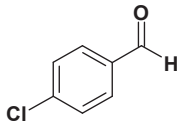
The scope of the dye sensitized ZnO/silver/TEMPO system was evaluated using a range of alcohols.

Synthesis of 3,4-dimethoxybenzaldehyde



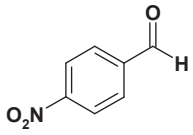
To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the 3,4-dimethoxybenzyl alcohol (0.0168 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be > 99% due to the presence of a singular product peak.

Synthesis of 4-chlorobenzaldehyde



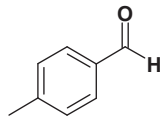
To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the 4-chlorobenzyl alcohol (0.0142 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 89%.

Synthesis of 4-nitrobenzaldehyde



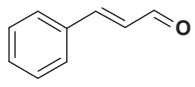
To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the 4-nitrobenzyl alcohol (0.0153 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 97%.

Synthesis of 4-methylbenzaldehyde



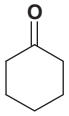
To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the 4-methylbenzyl alcohol (0.0122 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired aldehyde determined to be 98%.

Synthesis of cinnamaldehyde



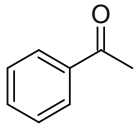
To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the cinnamyl alcohol (0.0134 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the aldehyde determined to be > 99% due to the presence of a singular product peak.

Synthesis of cyclohexanone



To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the cyclohexanol (0.0100 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired ketone determined to 12%.

Synthesis of acetophenone

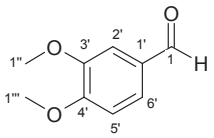


To a solution of $AgNO_3$ (306 mg, 1.8 mmol), TEMPO (1.5 mg) and dye sensitized ZnO (20 mg) in H_2O (1.5 ml) was added the 1-phenylethanol (0.0122 g, 0.1 mmol). The mixture was irradiated under visible light (> 450 nm) for 2 hours. The mixture was diluted with ethyl acetate to dissolve any insoluble organic compounds and the resulting mixture was passed through a membrane, with a pore diameter of 2 μm, and analyzed by gas chromatography. The structure was confirmed by comparison with an authentic sample and the yield of the desired ketone determined to be 67%.

Conducting the photooxidation on a large scale

The oxidation using the dye sensitized ZnO/silver/TEMPO system was scaled-up using 3,4-dimethoxybenzyl alcohol and benzoin as model substrates.

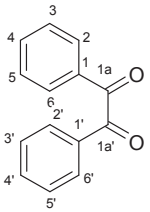
Synthesis of 3,4-dimethoxybenzaldehyde



To a solution of $AgNO_3$ (1.53 g, 9 mmol), TEMPO (10 mg) and dye sensitized ZnO (100 mg) in H_2O (10 ml) was added 3,4-dimethoxybenzyl alcohol (0.0841 g, 0.5 mmol). The mixture was irradiated under visible light (> 450 nm) for 10 hours. The resulting mixture was extracted with CH_2Cl_2 and the combined organic layers dried over anhydrous magnesium sulfate. The solution was filtered and subsequently concentrated under reduced pressure to produce a crude product which was purified using radial chromatography to afford the pure product as a colourless oil (0.0723 g, 87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.94 (3H, s, H- 1'''), 3.97 (3H, s, H- 1''), 6.98 (1H, d, J = 8.2 Hz, H- 5'), 7.41 (1H, d, J = 1.8 Hz, H- 2'), 7.46 (1H, dd, J_1 = 8.2 Hz, J_2 = 1.8 Hz, H- 6'), 9.85 (1H, s, H- 1).
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 56.0 (*C*- 1'''), 56.2 (*C*- 1''), 109.0 (*C*- 5'), 110.4 (*C*- 2'), 126.8 (*C*- 6'), 130.2 (*C*- 1'), 149.7 (*C*- 4'), 154.5 (*C*- 3'), 190.8 (*C*- 1).
MS (EIMS): *m*/*z* (%) = 166 [M^+] (100), 165 (94), 95 (16), 77 (31).
IR (neat) = 1678 cm^{-1}.

Synthesis of benzil



To a solution of $AgNO_3$ (1.53 g, 9 mmol), TEMPO (10 mg) and dye sensitized ZnO (100 mg) in H_2O (10 ml) was added benzoin (0.106 g, 0.5 mmol). The mixture was irradiated under visible light (> 450 nm) for 10 hours. The resulting mixture was extracted with CH_2Cl_2 and the combined organic layers dried over anhydrous magnesium sulfate. The solution was filtered and subsequently concentrated under reduced pressure to produce a crude product which was purified using radial chromatography to afford pure product as a yellow solid (m.p. 92-93^oC) (lit.[2] 95-97^oC), (0.0820g, 78%).

^1H NMR (400 MHz, $CDCl_3$) = 7.50-7.54 (4H, m, H -3, 5, 3', 5'), 7.64-7.68 (2H, m, H- 4, 4'), 7.97-7.99 (4H, m, H -2, 6, 2', 6').
^{13}C NMR (400 MHz, $CDCl_3$) = 129.0 (*C*- 3, 5, 3', 5'), 129.9 (*C*- 2, 6, 2', 6'), 133.0 (*C*- 4, 4'), 134.9 (*C*- 1, 1'), 194.5 (*C*- 1a, 1a').
MS (EIMS): *m/z* = 210 [M^+] (13), 105 (100), 77 (68), 51 (39).
IR (neat): 1655, 1591, 1446, 1207, 872, 794 cm^{-1}.

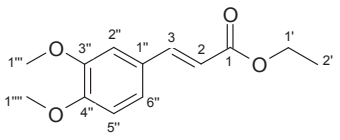
Application of the scaled-up alcohol oxidation to the Wittig reaction.

The scaled-up dye sensitized ZnO/silver/TEMPO system alcohol oxidation was extended to a tandem Wittig reaction.

Attempted synthesis of Ethyl 3-(3,4-dimethoxyphenyl)acrylate using the Tandem oxidation process (TOP)

To a solution of $AgNO_3$ (1.53 g, 9 mmol), TEMPO (10 mg) and dye sensitized ZnO (100 mg) in H_2O (10 ml) was added 3,4-dimethoxybenzyl alcohol (0.0840 g, 0.50 mmol) and (ethoxycarbonylmethylene)triphenylphosphorane (0.209 g, 0.6 mmol) was stirred under visible light irradiation (> 450 nm) for 15 hours. The resulting mixture was extracted using CH_2Cl_2 and the combined organic layers dried over anhydrous magnesium sulfate. The filtrate was concentrated *in vacuo* and subjected to NMR spectroscopic analysis which revealed the presence of the starting material only.

Synthesis of ethyl 3-(3,4-dimethoxyphenyl)acrylate using the pseudo-tandem oxidation process



To a solution of $AgNO_3$ (1.53 g, 9mmol), TEMPO (10 mg) and dye sensitized ZnO (100 mg) in H_2O (10 ml) was added 3,4-dimethoxybenzyl alcohol (0.0840 g, 0.50 mmol). The mixture was irradiated under visible light irradiation (> 450 nm) for 10 hours. The resulting mixture was extracted with CH_2Cl_2 and the combined organic layers dried over anhydrous magnesium sulfate. The combined organic layers were filtered and to the filtrate was added (ethoxycarbonylmethylene)triphenylphosphorane (0.209 g, 0.6 mmol). The mixture was stirred at room temperature for 4 hours, concentrated and subjected to radial chromatography to produce the desired acrylate as a viscous oil (0.0969 g, 82%).

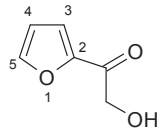
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, t, *J* = 7.1 Hz, H-2'), 3.91 (6H, s, 2 x OCH_3), 4.26 (2H, q, *J* = 7.1 Hz, H-1'), 6.31 (1H, d, *J* = 15.9 Hz, H- 2), 6.87 (1H, d, *J* = 8.3Hz, H- 5''), 7.06 - 7.10 (2H, m, H-2'', 6''), 7.63 (1H, d, *J* = 16.1 Hz, H- 3);
^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4 (*C*- 2'), 55.9 (*C*- 1''''), 56.0 (*C*- 1'''), 60.4 (*C*- 1'), 109.7 (*C*- 2'') , 111.1 (*C*- 5''), 116.0 (*C*- 2), 122.5 (*C*- 6''), 127.5 (*C*- 1''), 144.5 (*C*- 3), 149.3 (*C*- 4''), 151.1 (*C*- 3''), 167.2 (*C*- 1).
MS (EIMS): *m*/*z* = 237 [M+1] (14), 236 [M^+] (100), 191 (35), 164 (53).
IR (neat): 2936, 2983, 1690, 1626, 1597, 1582, 1509, 1466, 1422, 1364, 1220, 1159, 1142, 1023.

Procedure for the EPR measurements

A) EPR study for the dye radical: To a solution of silver nitrate (306 mg) dissolved in distilled water (0.5 ml) was added the dye sensitisedsemiconductor (10 mg). The mixture was stirred and put into a quartz tube.

B) EPR study for the addition of TEMPO: Dye sensitised semiconductor (10 mg), TEMPO (6 x 10-5 M) and benzyl alcohol (0.1 mmol) was added to a solution of silver nitrate (306 mg) in distilled water (0.5 ml). The mixture was stirred and put into a quartz tube.

Synthesis of 1-(2-furanyl)-2-hydroxyethanone[1]



2-Acetylfuran (0.550g, 5 mmol), was added to a stirred solution of trifluoroacetic acid (0.77 ml, 10 mmol), water (5 ml) and acetonitrile (25 ml). [Bis(trifluroacetoxy)] iodobenzene (4.30 g, 10 mmol) was added and the mixture heated to reflux for four hours. The reaction mixture was concentrated *in vacuo* to remove the acetonitrile. The residue was portioned between dichloromethane (125 ml) and water (50 ml). The aqueous phase was extracted with dichloromethane (3 x 25 ml), dried over magnesium sulfate and concentrate *in vacuo* to produce the crude product which was purified using radial chromatography to produce the title compound as brown solid (m.p. 76-78 ^{o}C) (lit.[3] 78 ^{o}C) (0.504 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 (2H, s, CH_2OH), 6.60 (1H, dd, J_1 = 3.50 Hz, J_2 = 1.49 Hz, H- 4), 7.30 (1H, d, H- 3), 7.63 (1H, d, H- 5).

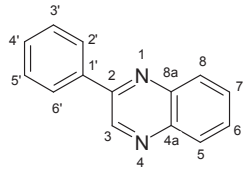
^{13}C NMR (400 MHz, $CDCl_3$) δ 65.1 (*C*H_2), 112.5 (*C*- 4), 117.8 (*C*- 3), 147.0 (*C*- 5), 150.2 (*C*- 2), 187.6 (*C* = O).

MS (EIMS): *m*/*z* = 126 [M^+] (11), 96 (19), 95 (100), 67 (7), 39 (38).

IR (neat): 3380, 3131, 1673, 1562, 1465, 1420, 1267, 1111, 1167, 1025, 977, 909, 880.

Synthesis of quinoxalines using diamondoid powder

2-Phenylquinoxaline

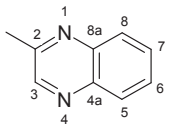


To a solution of 2-hydroxyacetophenone (0.068 g, 0.50 mmol) in dry acetonitrile was added *o*-phenylenediamine (0.054 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours.

Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange solid (m.p. 78-79 ^{o}C) (lit.[4] 79-80 ^{o}C); (0.086 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53-7.58 (3H, m, H- 3', 4', 5'), 7.77-7.78 (2H, m, H- 2', 6'), 8.14-8.20 (2H, m, H- 6,7), 8.22-8.24 (2H, m, H- 5,8), 9.34 (1H, s, H- 3).
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 127.6 (*C*- 2', 6'), 129.1 (*C*- 4'), 129.2 (*C*- 6, 7), 129.6 (*C*- 3'), 129.7 (*C*- 5'), 130.2 (*C*- 5), 130.3 (*C*- 8), 136.8 (*C*- 1'), 141.6 (*C*- 4a), 142.4 (*C*- 8a), 143.3 (*C*- 2), 151.9 (*C*- 3).
MS (EIMS): *m/z* (%) = 207 [M+1] (18), 206 [M^{+}] (100), 179 (30), 178 (16).
IR (neat): 1543, 1487, 1442, 1312 cm^{-1}.

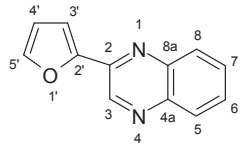
2-Methylquinoxaline



To a solution of α-hydroxyacetone (0.037 g, 0.50 mmol) in dry acetonitrile was added *o*-phenylenediamine (0.054 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours. Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange oil (0.057 g, 81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.79 (3H, s, CH_3), 7.69-7.77 (2H, m, H- 6, 7), 8.02-8.09 (2H, m, H- 5, 8), 8.75 (1H, s, H- 3).
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 22.5 (CH_3), 128.6 (*C*- 6), 128.9 (*C*- 7), 129.2 (*C*- 5), 130.1 (*C*- 8), 141.0 (*C*- 4a), 141.9 (*C*- 8a), 146.0 (*C*- 3), 153.7 (*C*- 2).
MS (EIMS): *m/z* (%) = 145 [M+1] (10), 144 [M+] (100), 117 (28), 77 (38).
IR (neat): 1562, 1491, 1442, 1409, 1368 cm^{-1}.

2-(2-Furanyl)quinoxaline



To a solution of 1-(2-furanyl)-2-hydroxyethanone (0.063 g, 0.50 mmol) in dry acetonitrile was added *o*-phenylenediamine (0.054 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours. Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange solid (m.p. 99-101^{o}C) (lit.[5] 101^{o}C) (0.035 g, 77%).

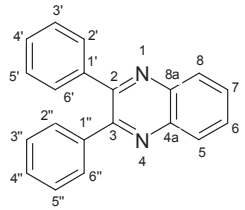
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 6.64 (1H, dd, J_1 = 3.2 Hz J_2 = 1.7 Hz, H- 4'), 7.33 (1H, d, J = 3.5 Hz, H- 3'), 7.69 (1H, d, H- 5'), 7.69-7.78 (2H, m, H- 6, 7), 8.07-8.12 (2H, m, H- 5, 8), 9.26 (1H, s, H- 3).

^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 111.8 (*C*- 4'), 112.5 (*C*- 3'), 129.3 (*C*- 6, 7), 129.3 (*C*- 5), 130.5 (*C*- 8), 141.4 (*C*- 4a, 8a), 142.10 (*C*- 3), 143.9 (*C*- 2), 145.1 (*C*- 5'), 151.7 (*C*- 2').

MS (EIMS): *m/z* (%) = 197 [M+1] (13), 196 [M^+] (100), 168 (32), 141 (17).

IR (neat): 1610, 1584, 1550, 1495, 1457 cm^{-1}.

2, 3 – Diphenylquinoxaline

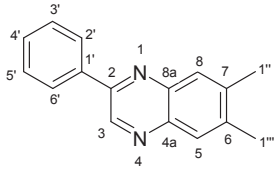


To a solution of benzoin (0.106 g, 0.50 mmol) in dry acetonitrile was added *o*-phenylenediamine (0.054 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours.

Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange solid (m.p. 121°C) (lit.[4] 124°C); (0.103g, 73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.34-7.37 (6H, m, H- 3', 4', 5', 3'', 4'', 5''), 7.51-7.53 (4H, m, H- 2', 6', 2'', 6''), 7.77-7.79 (2H, m, H- 6, 7), 8.18-8.20 (2H, m, H- 5, 8)
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 128.3 (*C*- 2', 6', 2'', 6''), 128.8 (*C*- 4', 4''), 129.2 (*C*- 6, 7), 129.9 (*C*- 3', 5', 3'', 5''), 129.9 (*C*- 5, 8), 139.1 (*C*- 1', 1''), 141.2 (*C*- 8a, 4a), 153.5 (*C*- 2, 3).
HRMS: found *m/z* (%) = 283.1236 (M + H), $C_{20}H_{14}N_2$ + H requires 283.1235
IR (neat) : 1681, 1599, 1495, 1476, 1442 cm^{-1}.

2-Phenyl-6,7-dimethylquinoxaline

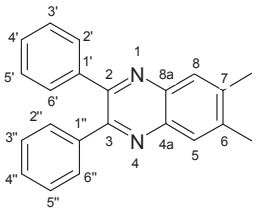


To a solution of 2-hydroxyacetophenone (0.068 g, 0.50 mmol) in dry acetonitrile was added 4,5-dimethyl-1,2-phenylenediamine (0.068 g, 0.50mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours. Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange solid (m.p. 119°C) (lit.[5] 120°C) (0.068 g, 58%).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.52 (6H, s, 2 x CH_3), 7.50-7.57 (3H, m, H- 3', 4', 5'), 7.87-7.92 (2H, m, H- 2', 6'), 8.16-8.18 (2H, m, H- 5, 8), 9.23 (1H, s, H- 3).
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 20.3 (*C*- 1'''), 20.4 (*C*- 1''), 127.4 (*C*- 2', 6'), 128.1 (*C*- 4'), 128.7 (*C*- 5), 129.1 (*C*- 3', 5'), 129.9 (*C*- 8), 137.1 (*C*- 1'), 140.2 (*C*- 6), 140.4 (*C*-7), 140.9 (*C*- 4a), 141.3 (*C*- 8a), 142.3 (*C*- 2), 151.1 (*C*-3).
MS (EIMS): *m/z* (%) = 235 [M+1] (19), 234 [M^+] (100), 219 (22), 207 (16).

IR (neat): 1536, 1483, 1446, 1312, 1211.

6,7-Dimethyl-2,3-diphenylquinoxaline



To a solution of benzoin (0.106 g, 0.50 mmol) in dry acetonitrile was added 4,5-dimethyl-1,2-phenylenediamine (0.068 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours. Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. The solvent was removed *in vacuo* to produce a crude product which was purified using radial chromatography to produce the desired compound as an orange solid (m.p. 172-174^{o}C) (lit.[6]172-174^{o}C) (0.059g, 38%) as a pale pink solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.52 (6H, s, 2 x CH_3), 7.30-7.34 (6H, m, H- 3', 4', 5', 3", 4", 5"), 7.48-7.51 (4H, m, H- 2', 6', 2", 6"), 7.93 (2H, s, H- 5, 8).
^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) = 20.4 (2 x CH_3), 128.2 (*C*- 2', 6', 2", 6"), 128.2 (*C*- 4', 4"), 128.5 (*C*- 5, 8), 129.8 (*C*- 3', 5', 3", 5"), 139.4 (*C*- 1', 1"), 140.2 (*C*- 6, 7), 140.5 (*C*- 4a, 8a), 152.5 (*C*- 2, 3).
MS (EIMS): *m/z* (%) = 311 [M+1] (24), 310 [M^{+}] (100), 309 (94), 207 (70).
IR (neat): 1666, 1621, 1595, 1517, 1476.

Attempted synthesis of 1,2,3,4-Tetrahydrophenazine

To a solution of 2-hydroxycyclohexanone (0.057 g, 0.50 mmol) in dry acetonitrile was added *o* - phenylenediamine (0.068 g, 0.50 mmol), molecular sieves (0.50 g) and the diamond powder (15 mg) and the mixture was stirred under ultraviolet irradiation for 6 hours. Thereafter, the reaction mixture was filtered through a short silica plug and the solid residues washed well with dichloromethane. TLC revealed that no spots were evident and the solid

residues washed well with methanol. Crude NMR spectroscopy showed a multitude of peaks, none of which were attributed to the product.

References

1. Moriarty, R. M.; Berglund, B. A.; Penmasta, R. *Tetrahedron Lett.* **1992,** *33*, 6065-6068.
2. Wang, X.; Zhang, Y. *Tetrahedron* **2003,** *59*, 4201-4207.
3. Boettcher, A.; Lichtenthaler, F. W. *Tetrahedron: Asymmetry* **2004,** *15*, 2693-2701.
4. Ihmels, H.; Maggini, M.; Prato, M.; Scorrano, G. *Tetrahedron Lett.* **1991,** *32*, 6215-6218.
5. Raw, S. A.; Wilfred, C. D.; Taylor, R. J. K. *Org. Biomol. Chem.* **2004,** *2*, 788-796.
6. Niknam, K.; Saberi, D.; Mohagheghnejad, M. *Molecules* **2009,** *14*, 1915-1926.