## Synthesis and characterization of fluorous-stabilized metal nanoparticles for evaluation in fluorous biphasic catalysis

by

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## Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the authorship owner thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

April 2022

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## Dedication

Dedicated to

my beloved grandmother, Sheila Jakins

and to

the loving memory of Jan Fourie.

## Abstract

A fluorous biphasic approach as a green strategy for the facile recycling and re-use of expensive catalysts, has been probed. A series of fluorous-stabilized Au NPs were successfully synthesized using a micelle-template strategy. The strategy entailed modifying a hydrophilic G3-DAB PPI-NH<sub>2</sub> dendrimer to include peripheral palmitoyl groups yielding an amphiphilic unimolecular micelle (referred to as the modified dendrimer in this work). The modified dendrimer was characterized by FT-IR spectroscopy and <sup>1</sup>H NMR spectroscopy; and displayed complete solubility in CHCl<sub>3</sub>. Using the modified dendrimer as a template, organicsoluble Au DENs were prepared by the encapsulation of Au ions into the interior of the dendrimer, followed by reduction. These Au DENs were extracted from the organic phase into a fluorous phase (S1 or S2) with the use of fluorous ligands (L1 and L2). This extraction step was found to be the most challenging and much effort was placed on optimizing the extent of extraction into the fluorous phase. In instances incorporating high Au quantities, little or no extraction was observed and was ascribed to the larger size of the Au DENs making phase transfer more unlikely. It was identified that for the formation of small, uniform Au DENs, it was necessary that we identify the maximum quantity of Au ions which could be encapsulated by the dendrimer. Failure to determine this value could lead to overloading the dendrimer and subsequent reduction would form DSNs. For the purposes of this research, it was critical to prepare organic DENs and prevent the formation of DSNs, therefore an additional study was executed to identify the endpoints in a series of UV-Vis spectrophotometric titrations involving the dendrimer and metal salt being investigated. In the study, two dendrimers were investigated and included an unmodified, hydrophilic G3-DAB-PPI-NH<sub>2</sub> dendrimer and the aforementioned modified dendrimer. The metal loading capacities of these dendrimers were determined for a range of metal ions in triplicate, which include; Cu(II), Ni(II), Co(II), Zn(II), Cd(II), Pb(II), Ru(III), Rh(III), Pd(II), Pt(II) and Au(III). The results showed that the unmodified dendrimer, in most cases, housed fewer metal ions in comparison to the analogous modified dendrimer. This was attributed to the improved solubility of the modified dendrimer in organic solvents. This, in effect, causes the loading interaction to be driven by solubility differences between the hydrophilic interior of the modified dendrimer and the hydrophobic solvent as opposed to fixed stoichiometric ratios. Subsequently, eight unique, spherical, monodisperse and small fluorous-stabilized Au NPs were generated and characterized by UV-Vis spectroscopy, TEM and ICP-OES analysis. Systems incorporating both L1 and L2 as the fluorous stabilizer were produced. Moreover, the use of perfluoro-1,3dimethylperfluorocyclohexane (S2) provides smaller fluorous-stabilized Au NPs in comparison to the use of perfluoromethylcyclohexane (S1) in the extraction step. It was found that an

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increase in temperature during the extraction did not aid it but instead promoted the oxidation of the NPs or accelerated agglomeration in the organic phase. Thus it was discovered that the extraction of the organic soluble DENs into the fluorous phase was highly dependent on their size which in turn was dependent on the outcome of the reduction step. An alternative novel synthetic method (called the direct method) was designed and optimized for the preparation of fluorous-stabilized Au NPs stabilized by L1. Not only did this method offer a significantly reduced preparation time, but it also entailed a fluorous-aqueous biphasic reduction to yield the fluourous-stabilized Au NPs. Furthermore, it was shown by way of this method that it was possible to tailor different sizes of NPs by varying the Au: L1 ratio. It was found that increasing the quantity of ligand to gold resulted in smaller fluorous-stabilized Au NPs. The ratios of Au: L1; with Au = 1 eq. and L1 = 0.28 eq.; 0.56 eq.; 1.12 eq. and 2.24 eq. yielded Au NPs of sizes; 43.4 ± 22.2 nm, 17.8 ± 13.7 nm, 11.8 ± 15.8 nm and 2.0 ± 0.3 nm, respectively. From this work, it has been shown that a simple strategy exists to produce fluorous-stabilized Au NPs within 3 h at ambient temperatures using L1. Other attempts were made with the use of other fluorous ligands such as L2, L3 and L4. In these cases, no fluorous-stabilized Au NPs were attained. Ten fluorous-stabilized Au NP catalyst systems were prepared using both methods, using varying ratios of Au: L1 or L2, in S1 or S3, respectively. These systems were assessed as catalysts in the biphasic catalytic oxidation of 1-octene under the optimized catalytic reaction conditions. It was found that all the fluorous-stabilized Au NPs which were examined in these aforementioned experiments, were active in the fluorous biphasic catalytic oxidation of 1-octene. Not only this, but even after recycling up to five times, the catalyst continued to show steady activity and always performed better than the blank reaction (without catalyst) in terms of % conversion of substrate. There appeared to be a distinct relationship between the average particle diameter (nm) of the Au NPs in the system and the conversion of 1-octene. This was demonstrated for JHD12 and JHD16 which comprised the largest NPs and afforded the lowest conversions of 1-octene in relation to the other catalyst systems tested at this constant metal loading (C<sub>f (Au)</sub>) of 5  $\times$  10<sup>-7</sup> mol/mL and optimized experimental conditions. Although not tested at the same metal loading as the other catalyst systems, JHD15, was found to be the most active catalyst. This is because the catalyst was tested at a concentration ten times less than all the other catalysts and still provided a higher conversion of 1-octene. The high activity was attributed to the size of the Au NPs of **JHD15** which were  $2.0 \pm 0.3$  nm being much smaller than those associated with the other catalyst systems. GC-FID was employed to quantify the relevant chemical species after the catalysis runs. The recyclability and re-use of the catalysts was also investigated. In each case the epoxy product was the major product.

## Opsomming

'n Fluoor-bifasiese benadering as 'n groen strategie vir die maklike herwinning en hergebruik van duur katalisators, is ondersoek. 'n Reeks fluoor-gestabiliseerde Au NP's is suksesvol gesintetiseer met behulp van 'n misel-templaat strategie. Die strategie het behels dat 'n hidrofiele G3-DAB PPI-NH<sub>2</sub> dendrimeer gewysig moet word om perifere palmitoielgroepe in te sluit wat 'n amfifiliese unimolekulêre misel oplewer (in hierdie werk verder verwys as die gemodifiseerde dendrimeer). Die gemodifiseerde dendrimeer is gekenmerk deur FT-IR spektroskopie en <sup>1</sup>H KMR spektroskopie; en het volledige oplosbaarheid in CHCl<sub>3</sub> vertoon. Deur die gemodifiseerde dendrimeer as 'n templaat te gebruik, is organies-oplosbare Au DEN'e voorberei deur die inkapseling van Au-ione in die binnekant van die dendrimeer, gevolg deur reduksie. Hierdie Au DEN'e is uit die organiese fase in 'n fluoorfase (S1 of S2) onttrek met die gebruik van fluooragtige ligande (L1 en L2). Daar is gevind dat hierdie ekstraksiestap die mees uitdagendste was en baie moeite is gedoen om die mate van ekstraksie in die fluoorfase te optimaliseer. In gevalle waar hoë Au-hoeveelhede ingesluit is, is min of geen ekstraksie waargeneem en dit is toegeskryf aan die groter grootte van die Au DEN'e wat faseoordrag meer onwaarskynlik maak. Dit is geïdentifiseer dat vir die vorming van klein, eenvormige Au DEN'e dit nodig was dat ons die maksimum hoeveelheid Au-ione identifiseer wat deur die dendrimeer inkapsuleer kan word. Versuiming om hierdie waarde te bepaal kan lei tot oorlading van die dendrimeer en sal dan DSN'e vorm. Vir die doeleindes van hierdie navorsing was dit van kritieke belang om organiese DEN'e voor te berei en die vorming van DSN'e te voorkom, daarom is 'n addisionele studie uitgevoer om die eindpunte te identifiseer in 'n reeks UV-Vis spektrofotometriese titrasies wat die dendrimeer en metaalsout behels wat ondersoek word. In die studie is twee dendrimere ondersoek en het 'n ongemodifiseerde, hidrofiele G3-DAB-PPI-NH<sub>2</sub> dendrimeer en die voorgenoemde gemodifiseerde dendrimeer ingesluit. Die metaallaaivermoë van hierdie dendrimere is bepaal vir 'n reeks metaalione in drievoud, wat insluit; Cu(II), Ni(II), Co(II), Zn(II), Cd(II), Pb(II), Ru(III), Rh(III), Pd(II), Pt(II) en Au(III). Die resultate het getoon dat die ongemodifiseerde dendrimeer in die meeste gevalle minder metaalione gehuisves het in vergelyking met die gemodifiseerde dendrimeer analoog. Dit is toegeskryf aan die verbeterde oplosbaarheid van die gemodifiseerde dendrimeer in organiese oplosmiddels. Dit veroorsaak in werklikheid dat die laai-interaksie gedryf word deur oplosbaarheidsverskille tussen die hidrofiliese binnekant van die gemodifiseerde dendrimeer en die hidrofobiese oplosmiddel in teenstelling met vaste stoïgiometriese verhoudings. Vervolgens is agt unieke, sferiese, monodisperse en klein fluoor-gestabiliseerde Au NP's gegenereer en gekenmerk deur UV-Vis spektroskopie, TEM en ICP-OES analiese. Stelsels

wat beide L1 en L2 insluit as die fluoor stabilisator is vervaardig. Boonop verskaf die gebruik van perfluoro-1,3-dimetielperfluorosikloheksaan (S2) kleiner fluoor-gestabiliseerde Au NP's in vergelyking met die gebruik van perfluorometielsikloheksaan (S1) in die ekstraksiestap. Daar is gevind dat 'n toename in temperatuur tydens die ekstraksie dit nie aangehelp het nie, maar eerder die oksidasie van die NP's of versnelde agglomerasie in die organiese fase bevorder het. So is dit ontdek dat die ekstraksie van die organies oplosbare DEN'e in die fluoorfase hoogs afhanklik was van hul grootte, wat weer afhanklik was van die uitkoms van die reduksiestap. 'n Alternatiewe nuwe sintetiese metode (genoem die direkte metode) is ontwerp en geoptimaliseer vir die voorbereiding van fluoor-gestabiliseerde Au NP's wat deur L1 gestabiliseer is. Hierdie metode het nie net 'n aansienlik verminderde voorbereidingstyd gebied nie, maar dit het ook 'n fluoor-waterige bifasiese reduksie behels om die fluoorgestabiliseerde Au NPs te lewer. Verder is daar deur middel van hierdie metode getoon dat dit moontlik was om verskillende groottes NP's te verkry deur die Au:L1-verhouding te verander. Daar is gevind dat die verhoging van die hoeveelheid ligand na goud tot kleiner fluoor-gestabiliseerde Au NP's gelei het. Die verhoudings van Au: L1; met Au = 1 vgl. en L1 = 0,28 ekw.; 0,56 ekw.; 1,12 vgl. en 2,24 ekw. Au NP's van groottes opgelewer;  $43,4 \pm 22,2$  nm,  $17,8 \pm 13,7$  nm,  $11,8 \pm 15,8$  nm en 2,0  $\pm 0,3$  nm, onderskeidelik. Uit hierdie werk is dit getoon dat 'n eenvoudige strategie bestaan om fluoor-gestabiliseerde Au NP's binne drie uur te produseer by omgewingstemperature met behulp van L1. Ander pogings is aangewend met die gebruik van ander fluooragtige ligande soos L2, L3 en L4. In hierdie gevalle is geen fluoorgestabiliseerde Au NP's bereik nie. Tien fluoor-gestabiliseerde Au NP katalisatorstelsels is voorberei deur beide metodes te gebruik, met behulp van verskillende verhoudings van Au: L1 of L2, in S1 of S3, onderskeidelik. Hierdie sisteme is geassesseer as katalisators in die bifasiese katalitiese oksidasie van 1-okteen onder die geoptimaliseerde katalitiese reaksie toestande. Daar is gevind dat al die fluoor-gestabiliseerde Au NP's wat in hierdie voorgenoemde eksperimente ondersoek is, aktief was in die fluoor-bifasiese katalitiese oksidasie van 1-okteen. Nie net dit nie, maar selfs na herwinning tot vyf keer, het die katalisator aangehou om bestendige aktiwiteit te toon en het altyd beter presteer as die blanko reaksie (sonder katalisator) in terme van % omsetting van substraat. Daar was 'n duidelike verwantskap tussen die gemiddelde deeltjie deursnee (nm) van die Au NP's in die sisteem en die omskakeling van 1-okteen. Dit is gedemonstreer vir JHD12 en JHD16 wat die grootste NP's uitgemaak het en die laagste omsettings van 1-okteen verskaf het in verhouding tot die ander katalisatorstelsels wat getoets is by hierdie konstante metaallading (Cf (Au)) van 5 x 10<sup>-7</sup> mol/mL en geoptimaliseerde eksperimentele toestande. Alhoewel dit nie teen dieselfde metaallading as die ander katalisatorstelsels getoets is nie, is gevind dat JHD15 die mees aktiewe katalisator is. Dit is omdat die katalisator teen 'n konsentrasie tien keer minder as al die ander katalisators getoets is en steeds 'n hoër omsetting van 1-okteen verskaf het. Die

hoë aktiwiteit is toegeskryf aan die grootte van die Au NPs van **JHD15** wat  $2.0 \pm 0.3$  nm was wat baie kleiner was as dié wat met die ander katalisatorstelsels geassosieer word. GC-FID is aangewend om die relevante chemiese spesies na die kataliselopies te kwantifiseer. Die herwinbaarheid en hergebruik van die katalisators is ook ondersoek. In elke geval was die epoksieproduk, die hoofproduk.

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## **Conference Contributions**

• Joshua Hensberg and Rehana Malgas-Enus

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• Joshua Hensberg and Rehana Malgas-Enus

Oral Presentation: **Microwave-assisted preparation of metal nanoparticles.** Anton Paar Seminar, Durbanville, South Africa, 2019.

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# Symbols and Abbreviations

ATR	Attenuated Total Reflection
AU	Absorbance units
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
CuAAC	Copper-catalysed azide-alkyne cycloaddition
DAB	Diaminobutane
DEN	Dendrimer-encapsulated nanoparticle
DFT	Density functional theory
DSN	Dendrimer stabilised nanoparticle
EDX	Energy-dispersive X-ray spectroscopy
EOB	extent of binding
Eq.	Equivalents
FBC	Fluorous biphasic catalysis
FBS	Fluorous biphasic system
FT-IR	Fourier Transform – Infrared Spectroscopy
GC-MS	Gas Chromatography – Mass Spectrometry
Gn	Generation n
GNP	Gross National Product
h	hours
HPLC	High performance liquid Chromatography
HR	High resolution
ICP	Inductively-coupled plasma
L1	Ligand 1 (P donor atom)
L2	Ligand 2 (S donor atom)
LMCT	ligand-to-metal charge transfer
mbar	millibar
min	minutes

mL	milliliter
MNP	Magnetite nanoparticle
Nm	nanometer (nm)
NP	nanoparticle
OES	Optical Emission Spectroscopy
PAMAM	Poly(amidoamine)
PBE	Perdue Burke Ernzerhof
PFC	Perfluorinated compound
pm	picometer (1 x 10 <sup>-12</sup> m)
PPI	Poly(propylene)imine
ppm	parts per million
rbf	round bottom flask
RCM	Ring-closure metathesis
rpm	revolutions per minute
S	seconds
S1	solvent 1 (perfluoromethylcyclohexane)
S2	solvent 2 (perfluoro-1,3-dimethylcyclohexane)
SAM	Self-assembled monolayer
SEM	Scanning electron microscopy
SHOP	Shell high olefins process
SPR	surface plasmon resonance
ТЕМ	Transmission Electron Microscopy
ТОАВ	tetraoctyl ammonium bromide
TMS	tetramethylsilane
TPPTS	3,3',3"-Phosphanetriyltris(benzenesulfonic acid) trisodium salt
v/v	volume-to-volume ratio
λ	wavelength (nm)
	wavelength (http://wavelength.

# Synthesis and applications of gold nanoparticles, and their potential as green catalysts

#### 1.1. Materials at the nanoscale

#### 1.1.1. Definitions and classifications of nano-objects

Nanomaterials, nano-entities or nano-objects describe, in principle, things or entities of which a single unit, in its three-dimensional structure, is sized (in at least one dimension) between 1 and 100 nanometres (10<sup>-9</sup> m).<sup>1</sup> These nanomaterials are often categorized as to how many of their dimensions fall in the nanoscale or rather, do not fall into the nanoscale.



**Figure 1.1.** Examples of nanomaterials classed according to how many of their dimensions exceed 100 nm in size.<sup>2</sup>

Zero-dimensional nanomaterials include entities such as nanoparticles (NPs) or nanoclusters, and have all three dimensions (*length, breadth and height*) with measurements in the nanoscale range hence none (zero) of its dimensions exceeding 100 nm. One-dimensional nanomaterials have two of their dimensions with sizes in the nanoscale while one of its dimensions would exceed the nanoscale (i.e. only its *length* is not in the nano range). Examples include nanofibers, which can then be further divided into nanorods (or nanowires), which are solid internally, and nanotubes which are hollow. Finally, two-dimensional nanomaterials entail an entity which has only one of its dimensions in the nanoscale such as nanosheets, nanofilms or nanoribbons (i.e. the *height* of the object is in the nanoscale).

These nanomaterials represent a unique class of matter, and owing to their higher surface to volume ratio, and due to quantum confinement effects<sup>3</sup>, nanocrystalline materials show entirely different properties in comparison with bulk properties.<sup>3,4</sup>

Entities which have all three dimensions in the nanoscale have pronounced effects with regards to surface properties and the quantum confinement effect. Currently, many researchers have looked towards generating noble metal nanoparticles for their exceptionally unusual characteristics.<sup>5</sup>

#### 1.1.2. Behaviour compared to bulk materials

Two primary factors cause nanomaterials to behave significantly differently than bulk materials: surface effects, which cause pronounced surface properties and quantum effects, which are due to discontinuous behaviour because of quantum confinement effects in materials with delocalised electrons.<sup>5</sup> If we consider a sphere with radius *r*, its surface area to volume ratio can be written as follows:



**Figure 1.2.** *Left:* Schematic of a typical sphere, with radius r. *Right:* Equations for the volume (V) and surface area (SA) of a sphere, with the ratio SA/V showing an inverse relation to r.

The surface area to volume ratio ( ${}^{SA}/{}_{V}$ ) is inversely proportional to the radius (r) of the sphere, therefore as we transition from bulk materials to nanoparticles, this ratio becomes greater. This leads to the surface of the NP having a greater influence in defining its intrinsic chemical properties. For this reason, characterization methods are focusing more on the surface of these species because it governs the interesting and alluring properties responsible for their respective applications in nanotechnology.<sup>6</sup> One of the well-defined examples of specific properties of nanoparticles (NPs) is the ability to catalyse reactions by interacting with substrates and products.<sup>7</sup>

Nanocatalysis has gained popularity in the past decade. A simple search of *Scifinder* with the key word "nanocatalysis" lucidly demonstrates an exponential growth in scientific publications between the years 1994 and 2008 (Figure 1.3). In 2008 alone, for example, the number of publications was nearly 7000.



**Figure 1.3.** Graph illustrating the number of publications having the key word "nanocatalysis" in their respective titles for each year from 1994 - 2008.<sup>8</sup>

One of the main branches of nanocatalysis is nanoparticle (NP) catalysis in the liquid phase.<sup>8</sup> Metal nanoparticles are well known in the catalytic community owing to their abundant advantages over bulk materials. These unique properties of NPs derive from the large percentage of coordinatively unsaturated atoms present at the surface, edges and corners of the NPs compared to the total number of atoms. An additional benefit of this is that less expensive metal is used (as a lower quantity of catalyst is needed) in the system. Gold nanoparticles (Au NPs) are probably the most remarkable members of the metal NP groups and have attracted considerable interest.<sup>9</sup>

#### 1.2. Gold nanoparticles

Gold, in its bulk form, has captivated mankind since antiquity. Despite its magnificent appearance, a startling characteristic of this impressive element is its inertness, hence its resistance to corrosion via oxidation. These are not the only reasons for its popular use in jewellery fabrication, but also for its inactivity as a catalyst. Be that as it may, when transitioning from the bulk state to the nanoscale, it has been found that gold nanoparticles, in contrast to bulk gold, possess remarkable catalytic properties.
Au nanoparticles, in particular, are very attractive because of their size and shape-dependent properties, giving them numerous uncommon chemical and physical properties due to the effects of quantum size and large surface area, in comparison with other metal atoms or bulk metal.<sup>10</sup> With this said, nanogold has become a subject of heightened interest amongst researchers, finding an assortment of applications<sup>11</sup> in photonics, medicine, electronics, biochemical sensing, imaging and catalysis (as previously mentioned).

There are numerous strategies to produce Au NPs, all of which are categorized into two main approaches: "top down" or "bottom up" methods.<sup>12</sup> The "top down" approach entails the removal of matter from the bulk material to get the desired nanostructure and includes such processes as photolithography and electron beam lithography. Due to the extensive waste of material brought about by the "top down" approach, "bottom up" methods have received more attention and have become ubiquitous in the preparation of Au NPs. Conversely, in the "bottom up" strategy, Au NPs originate from the assembly of individual atoms, which are derived from a chemical or biological reduction. This chemical reduction method involves two steps: nucleation and successive growth. When the nucleation and successive growth are completed in the same process, it is called *in situ* synthesis; otherwise it is called the seed-growth method.<sup>13</sup>

## 1.2.1. Synthetic methods for producing Au NPs

Some of the more commonly used techniques involving "bottom up" methods for manufacturing Au NPs are explored below.

## 1.2.1.1. Turkevich method

The Turkevich method for generating Au NPs was pioneered by Turkevich et al.<sup>14</sup> (1951) and is one of the simplest and prevailing of the synthetic methods. The technique most commonly entails boiling an aqueous solution of HAuCl<sub>4</sub>, during which trisodium citrate dihydrate is added. In the preparative procedure, the citrate serves a dual purpose: it both reduces the Au ions and acts as a stabilizer for the emerging Au NPs which are approximately 20 nm in size. Later, in the 1970s, the method was improved by the work of Frens<sup>15</sup> (1973) in a paper titled "Controlled nucleation for the regulation of the particle size in monodisperse gold suspensions". In the paper, Frens and colleagues demonstrated that the particle size could be varied by adjusting the relative quantities of reactants to initiate changes in the relative rates of the two independent processes of nucleation and growth of the metal nanoparticles.

4

The group disclosed that by reducing the ratio of citrate/gold, the average diameter of the afforded nanoparticles increased. With these developments, modestly monodisperse and spherical Au NPs of sizes ranging from 16 to 147 nm, could be obtained. The observations unearthed by Frens<sup>15</sup> (1973) were explained by Kimling et al.<sup>16</sup> (2006) who investigated the mechanism for the formation of citrate-stabilized Au NPs. The group concluded that a high concentration of citrate more rapidly stabilizes Au NPs of smaller sizes, whereas a low concentration of citrate leads to large-size of Au NPs and even the aggregation of Au NPs. Ensuing this, Kumar's group<sup>17</sup> (2007) executed significant research on the mechanism of the Turkevich-Frens technique by way of an experiment involving multiple steps. The initial step of this multiple-step process, with reactions occurring in series and parallel, is the oxidation of citrate that yields dicarboxy acetone. Then, the auric salt is reduced to aurous salt and Au<sup>0</sup>, and the aurous salt is assembled on the Au<sup>0</sup> atoms to form the Au NPs (Figure 1.4).



Figure 1.4. Au nanoparticle synthesis using the Turkevich method.<sup>17</sup>

In addition, the presence of a citrate salt modifies the pH of the system and influences the size and size distribution of the formed Au NPs.<sup>18</sup> On these grounds, relatively monodispersed Au NPs with sizes spanning from 20-40 nm have been synthesized by varying the solution pH. This pH-dependent phenomenon was investigated by Ji et al.<sup>19</sup> (2007) The group suggested that the particle growth follows one of two pathways. Following the Turkevich-Frens method, experimentally they were able to vary the pH of the solution by controlling the concentration of the capping agent, trisodium citrate (Na<sub>3</sub>Ct). They discovered that for low pH values (3.7–6.5), the nanoparticles form via an intermediate, [AuCl<sub>3</sub>(OH)]<sup>-</sup>. The intermediate subsequently undergoes a LaMer burst nucleation, whereby nucleation occurs within 10 s. This is followed by fast random attachment and lastly, intraparticle ripening. Conversely, the group found that for higher pH values (~6.5–7.7), the particles undergo reduction through

 $[AuCl_2(OH)]_2^-$  and  $[AuCl(OH)]_3^-$ . By way of this route, there is a much longer nucleation of about 60 s which is superseded by a stage involving slow growth, as exemplified in Figure 1.5.



**Figure. 1.5.** Schematic illustration of two reaction pathways for the formation of gold nanoparticles by citrate reduction. Na<sub>3</sub>C

The effect of temperature on the size of Au NPs prepared by the Turkevich method, was also evaluated by Link et al.<sup>20</sup> (2002) and Rohiman et al.<sup>21</sup> (2011). They found that with increasing temperature, smaller size Au NPs were attained. The group postulated that the higher temperatures shortened the time required to achieve activation energy for the reduction step. The resulting Au NPs were characterized by SEM, showing the size of Au NPs with average diameters between 20 and 27 nm.<sup>20</sup>

Recently, the evolution of the spherical Au NPs in the Turkevich reaction has been elucidated by Pong et al.<sup>22</sup> (2007). Interestingly, and in stark contrast to the widely accepted LaMer nucleation-growth model, the initially formed nanoclusters of about 5 nm in diameter self-assemble to form an extensive network of nanowires (which are responsible for the dark appearance of the reaction solution before it turns ruby-red). The "so-called" nanowires are in fact chains of Au nanoparticles and were visualised using TEM and UV-Vis spectroscopy (Figure 1.6). The diameter of the nanowires progressively increases in size, and at the same time the connected network is fragmented into small segments. Subsequent Ostwald ripening leads to the formation of the final spherical particles. Pong et al.<sup>22</sup> were also able to observe these chains when using HAuCl<sub>4</sub> and sodium borohydride, NaBH<sub>4</sub>. However, with the strong reducing agent, NaBH<sub>4</sub>, the transient state appears to be too short-lived to isolate from the reaction solution.



**Figure. 1.6.** Left and middle: TEM images of the dark intermediate showing an extensive network of gold nanowires (adapted from ref 22). Right: UV-Vis spectra and visual colours of the colloids; (a) colourless, (b) dark blue, (c) dark purple, (d) purple and (e) ruby-red (adapted from reference 22).

Other techniques which do not require thermal activation have also been investigated, these systems employ UV radiation to produce chemically stable Au NPs with narrow-size distributions and size ranges between 5 and 20 nm. Some notable instances include the introduction of fluorescent light irradiation<sup>23</sup> and the use of high-power ultrasound.<sup>24</sup>

Citrate-stabilized Au NPs are commonly larger than 10 nm, due to the very meek reducing ability of trisodium citrate dihydrate. A fascinating result from Puntes' group<sup>25</sup> (2010) with reference to citrate-stabilized Au NPs, is the use of D<sub>2</sub>O as the solvent instead of H<sub>2</sub>O during the synthetic procedure. The size of the Au NPs were tailored to 5 nm and it was concluded that D<sub>2</sub>O increased the reducing strength of citrate.

In general, we are still far from fully understanding the influences of synthesis parameters on the growth process and thus the final size of the nanoparticle obtained. Only the combination of the chemical reduction process and the physicochemical particle growth can deliver a full and comprehensive picture of the Turkevich synthesis.<sup>26</sup>

# 1.2.1.2. Brust-Schiffrin method

The stabilization of Au NPs with alkanethiols was first reported by Giersig and Mulvaney<sup>27</sup> (1993), who showed the possibility of using thiols of different chain lengths and their analysis.<sup>28</sup> One year later, Brust and Schiffrin<sup>29</sup> (1994), inspired by Faraday's<sup>30</sup> (1857) two-phase system for the synthesis of colloidal gold, published their method to produce Au NPs with alkanethiols self-assembled monolayers (SAMs) in organic solvents. Their technique has had a considerable impact on the overall field in less than a decade because it allowed the facile

synthesis of thermally stable NPs and controlled size for the first-time providing sizes between 1.5 and 5.2 nm.

The tactic involves a biphasic system of aqueous HAuCl<sub>4</sub> in contact with a toluene solution comprising of tetraoctyl ammonium bromide (TOAB) which acts as the phase-transfer agent.<sup>29</sup> Thereafter, sodium borohydride is employed as the reducing agent in the presence of excess alkanethiol (more specifically, dodecanethiol). The simplistic synthetic procedure is depicted in Figure 1.7.





The alkanethiols stabilize the Au NPs<sup>27</sup> resulting in a colour change in which the reaction transitions from orange to brown.<sup>29,30</sup> The Brust-Schiffrin method is also called the two phase-transfer method.<sup>29,32</sup> The technique uses thiol ligands and is carried out in a two-phase system because the thiol group can strongly bind to gold. The gold salt, dispersed in the aqueous phase, is transferred to an organic phase using tetraoctylammonium bromide as the phase transfer agent and then is reduced by sodium borohydride in the presence of an alkanethiol. The gold nanoparticles are formed and stabilized in the organic phase by the alkanethiol ligands.<sup>32</sup> The process can be described as:

$$AuCl_{4}(aq) + TOAB_{(org)} \rightarrow AuCl_{4}(TOAB_{(org)})$$
(1)  

$$AuCl_{4}(aq) + RSH_{(org)} \rightarrow (-Au^{1}SR)(polymer)_{(org)}$$
(2)  

$$(-Au^{1}SR)(polymer)_{(org)} + BH_{4}(aq) \rightarrow Au_{x}(SR)_{y}(org)$$
(3)

The second major advance with regards to this method came after the discovery of the place exchange reaction<sup>33</sup> by Murray and co-workers<sup>34</sup> (1997) that enabled the introduction of a rich variety of functional thiolates in the monolayer of pre-formed nanoparticles. Virtually any functional group can be introduced in the monolayer of gold nanoparticles by this method. This is particularly useful when functional thiols cannot be used in the Brust-Schiffrin procedure; either because of limited stability under reducing conditions or because synthetic limitations hamper the use of the excess thiol needed in the direct synthesis.

## 1.2.1.3. Martin method

Slightly more than a decade ago, a creative method for the preparation of Au NPs, was revealed by the efforts of Martin et al.<sup>35</sup> (2010). The technique formulates "naked" gold nanoparticles in water by the reduction of HAuCl<sub>4</sub> with NaBH<sub>4</sub>. The gold nanoparticles formed, are stably dispersed even without any other stabilizer such as citrate with their size distribution being nearly monodisperse. In addition, the diameter of the formed NPs can be precisely and reproducibly tuned from 3.2 to 5.2 nm (Figure 1.8). The principal feature of this system is the stabilization of HAuCl<sub>4</sub> and NaBH<sub>4</sub> in the aqueous stock solutions with HCl and NaOH for at least 3 months and 3 hours, respectively. Moreover, it is required that the proportion of NaBH<sub>4</sub>-NaOH ions to HAuCl<sub>4</sub>-HCl ions be strictly regulated within an optimal region.



**Figure 1.8.** Left: UV-Vis extinction spectra of five aqueous solutions of gold nanoparticles of 3.2, 4.0, 4.8, 4.2 and 5.2 nm. The numbers of total gold ions are the same without data normalization. Right: TEM images of the Au NPs where A = 3.2 nm, B = 4.0 nm, C = 4.8 nm, D = 4.2 nm, and E = 5.2 nm.

In the experimental procedure, "bare" gold nanoparticles are coated with 1-dodecanethiol, assembling a monolayer. The derived organic-soluble gold nanoparticles are then effortlessly

phase-transferred to hexane by shaking the mixture consisting of water, acetone, and hexane for precisely 30 seconds. This method is rather straight-forward since all the unwanted reaction by-products display solubility in the water-acetone phase, thus there is no need for post-synthesis purification required for the hexane-soluble Au NPs. What's more is that only 0.1 equivalents of 1-dodecanethiol are required for every one equivalent of gold atom in the system.<sup>35,36</sup>

In conclusion, this novel synthesis strategy is uncomplicated, inexpensive, easy to appropriate, greener and rapid in that the preparation takes no longer than 10 minutes. Although the final step in the preparation appears to be short, it must be noted that there is a lengthy reagent preparation step of over 3 months. The other limitation is the narrow range of solvents which can be used in this synthesis method. Nevertheless, the Martin method remains critical for a variety of practical applications by uniting the simplistic Turkevich method with the monolayer-protection of the Brust method.

# 1.2.1.4. Dendrimer-templated method

Another method to harvest relatively monodisperse gold nanoparticles is by virtue of the dendrimer-template approach. This technique involves the use of dendrimers, which are hyper-branched, highly symmetrical and spherical macrocyclic compounds with a distinctive molecular structure and a monodisperse, controllable size. Dendrimers have garnered much attention due to their well-defined structures and chemical versatility. Notably, the structure and chemical properties of dendrimers can be systematically controlled by modification of the core, the type and number of repetitive branch units and the terminal functional groups (Figure 1.9).<sup>38</sup>



Figure 1.9. Simplistic and general structure of a dendrimer.<sup>38</sup>

Specifically, at higher generations, dendrimers possess hollow cavities that can function as ideal nano-scale reactors with very dense exteriors. Zhao et al.<sup>39</sup> (1998) pioneered a method which uses dendrimers as templates for producing NPs. They serve to stabilize and control growth during the synthesis of metal nanoparticles. The first step of the synthetic method entails complexation of metal ions with interior tertiary amine groups of the dendrimer. Once this reaction is complete, a reducing agent, often excess NaBH<sub>4</sub> is added to the solution with vigorous stirring. In the case of dendrimers, it has been revealed that metal ions tend to coordinate to the functional groups within the dendrimer interior according to a fixed stoichiometric ratio and because each dendrimer contains a specific number of ions, the resulting metal nanoparticles are, in many cases, of nearly monodisperse size.

Dendrimer-based metal nanoparticles can be prepared either by encapsulating the metal ion inside the void cavities of dendrimers [intra-dendrimer encapsulated nanoparticles (DENs)], or by trapping the metal in between dendrimers [inter-dendrimer stabilised nanoparticles (DSNs)]. In the former instance, dendrimers act as templates; in the latter, they act as stabilising agents (Figure 1.10).



**Figure 1.10.** *Left*: Dendrimer-encapsulated nanoparticle (DEN). *Right*: Dendrimer-stabilized nanoparticle (DSN).

Many new classes of dendrimers have been reported since the original synthesis of poly(propyleneimine) dendrimers imparted by Vogtle et al.<sup>40</sup> (1978). Examples include starburst poly(amidoamine) dendrimers by Tomalia et al.<sup>41</sup> (1985) and the arborols by Newkome et al.<sup>42</sup> (1985). With this said, an assortment of studies has been conducted with the two of the most popular groups of dendrimers, namely, poly(amidoamine) PAMAM and diaminobutane poly(propyleneimine) DAB-PPI dendrimers, both of which are commercially available. Particularly concerning the synthesis of Au NPs, dendrimers have been applied as molecular templates for the preparation of stable Au DENs as reported by Gröhn et al.<sup>43</sup>

(2000), where they used PAMAM-NH<sub>2</sub> (G2-G4) dendrimers. They found that stable Au DENs could be formed if the concentration of the dendrimer is low (dendrimer mass fraction < 1%). However, the resulting Au DENs show a wide size distribution. When a dendrimer mass fraction of 0.12% or lower is used, Au DENs with a narrow size distribution were observed. The formation of these uniform Au DENs is also dependent on the rate of the addition of NaBH<sub>4</sub>.

Esumi et al.<sup>44</sup> (2000) also prepared Au DENs stabilized by different generations (G3-G5) of PAMAM-NH<sub>2</sub> dendrimers. The synthesis of Au DENs was monitored by UV-Vis spectroscopy, where the group deduced that for all the generations used, the average nanoparticle diameter decreased as the [dendrimer]/[Au<sup>3+</sup>] ratio increases. The average diameter of the NPs formed with G3 dendrimers was greater than those for G4 and G5 at the same [dendrimer]/[Au<sup>3+</sup>] ratio but are still smaller than the diameter of the dendrimer used.

Contrary to this and other reports,<sup>44,45</sup> Garcia-Martinez and Crooks<sup>46</sup> (2004) showed that the size of Au NPs does not depend on the generation of the dendrimer but rather on the [dendrimer]/[Au<sup>3+</sup>] ratio. In this study, Crooks and co-workers used G4 and G6 PAMAM-NH<sub>2</sub> dendrimers to synthesize narrowly distributed Au DENs of 1-2 nm. These dendrimers were first partially functionalized on their periphery by quaternary ammonium groups. This method has two main advantages: firstly, the unfunctionalized primary amine groups of the partially guaternized dendrimer can be used as a handle to covalently attach Au DENs to surfaces of other molecules, and secondly, the quaternized amines provide a large positive charge on the dendrimer periphery, which in turn, reduces the possibility of dendrimer agglomeration.<sup>43</sup> To illustrate the effect of partially quaternized dendrimers on the preparation of Au DENs, Au DENs synthesized with PAMAM-NH<sub>2</sub> dendrimers were also prepared for comparative purposes. A [dendrimer]/[Au<sup>3+</sup>] ratio of 1:55 was used in both cases and the HRTEM images revealed that the particle size and size distribution were essentially very similar. The Au NPs derived from the unmodified dendrimer were shown to have sizes corresponding to  $1.3 \pm 0.5$ nm and the partially quaternized dendrimer showed sizes of 1.3 ± 0.3 nm. It was also found that, the use of magic numbers for the [dendrimer]/[Au<sup>3+</sup>] ratios (1:13, 1:55 and 1:147) led to the formation of NPs having narrow size distributions while the other ratios (e.g. 1:100) resulted in the formation of polydisperse Au DENs.

## 1.2.2. Magic-Number Gold Nanoclusters

It is known that clusters with certain special numbers of atoms are much more abundant than others when generated in typical cluster experiments, and these numbers are called geometric "magic numbers".<sup>47</sup> For nanoclusters of close-packed metals, the geometric magic numbers

normally are 13, 55, 147, 309, 561, and 923 corresponding to highly symmetric structures such as icosahedral, ino-decahedral, and cuboctahedral, with  $I_h$ ,  $D_{5h}$ , and  $O_h$  symmetries, respectively (see Figure 1.11).<sup>48</sup>



**Figure 1.11.** Optimized structures using PBE functional within DFT method of (a) icosahedral ( $I_h$ ), (b) ino-decahedral ( $D_{5h}$ ) and (c) cuboctahedral ( $O_h$ ).

The magic numbers coincide with the closure of successive shells, respectively. The best explanation for this is that when interatom bonding does not have strong directional preferences, it is common for atoms to gravitate toward a kissing number of 12 nearest neighbours. In small clusters, perhaps because of their slightly higher surface area, icosahedral arrangements may be preferred. These icosahedral numbers were seen first in a cluster beam experiment on Xe clusters.<sup>48</sup> The favoured icosahedral numbers are 13, 55, 147, 309 where atoms successively grow through the addition of shells as exemplified in Table 1.1. Interestingly, magic-number gold nanoclusters can exhibit special properties. For example, it has been suggested that the Au(55) cluster is a superior oxidation catalyst due to large oxidation resistance.<sup>50,51</sup>

Table 1.1. Illustration of the first five successive closed-packed magic number clusters.

	\$				
Number of shells	1	2	3	4	5
Number of atoms in cluster	13	55	147	309	561
Percentage of surface atoms	92	76	63	52	45

## 1.2.3. Application of gold nanoparticles in catalysis

Gold nanoparticle catalysts are unique in their activity under mild conditions, even at ambient temperature or less. When Au nanoparticles less than ~ 5 nm in size are supported on base metal oxides or carbon, very active catalysts are produced.<sup>52</sup> At the end of the 1980s, Haruta et al.<sup>53</sup> (1987) established that Au on oxide can be used to oxidize CO at less than 0 °C, while Hutchings<sup>54</sup> (1996) proved that Au on carbon is the catalyst of choice for the hydrochlorination of ethyne. These important advances followed earlier work by Bond et al.<sup>55</sup> (1973) who had shown that Au on boehmite is selective for the hydrogenation of alkynes in the presence of alkenes and highlighted the unexpected activity of Au on oxide catalysts for unsaturated hydrocarbon hydrogenation.<sup>56</sup>

Numerous studies since then have explored various Au NPs in catalyzing reactions that include CO oxidation,<sup>57</sup> propylene epoxidation,<sup>58</sup> low temperature water gas shift reactions,<sup>59,60</sup> alcohol oxidation,<sup>61</sup> nitroarene reduction<sup>62</sup> and carbon-carbon cross coupling<sup>63</sup> to name a few.

It must be highlighted, however, that colloidal gold nanoparticles dispersed in the liquid phase have been theorized to be more catalytically active, have greater selectivity, and have greater opportunity in chiral catalysis in contrast to supported NPs. However, due to the countless issues arising in connection to their separation from the reaction mixture, much less research has been executed in this direction. For the industrial production of fine chemicals, Au NPs and other colloidal nanoparticle catalysts are consequently immobilized on different supports, primarily due to the advantage of catalyst recovery by expending facile mechanical methods like centrifugation, filtration or sedimentation.<sup>64</sup> Supported catalysts are also effectively implemented in continuous reactor systems with a stationary support for large-scale chemical reactions.<sup>64,65</sup> In this regard, a considerable amount of effort has been placed on understanding the catalytic activity in gas phase, in particular, gold nanoparticles supported on different oxides. Different parameters, such as size and shape of Au clusters, the nature of the support or preparation method, play a crucial role in influencing the catalytic activity.<sup>66-70</sup>

## 1.3. Catalysis

Catalysts are widely used in the large-scale manufacture of chemicals and in the production of fine chemicals and pharmaceuticals. Fuel processing is a good example: the gasoline that we use in our cars requires at least ten different catalysts during its transformation from crude oil.<sup>71</sup> Environmental technologies also rely heavily on catalysts; the best-known example is the

catalytic converter in the exhaust of every car. It is estimated that more than 20% of the gross national product (GNP) of industrial companies relies in one way or another on catalysis.<sup>72</sup> In general, the most effective and active catalysts involve transition metal complexes owing to their low energy d orbitals which facilitate catalytic pathways. Unfortunately, the cost of metals is a perturbing factor which must be addressed. Thus, finding a suitable method for recovering and re-using these metals is paramount, and in alignment with the green chemistry notion.

# 1.3.1. Homogeneous vs heterogeneous catalysis

Homogeneous catalysts have many attractive properties and offer a number of important advantages over their heterogeneous counterparts. For example, all catalytic sites are accessible because the catalyst is usually a dissolved metal complex. Furthermore, it is often possible to tune the chemoselectivity, regioselectivity, and/or enantioselectivity of the catalyst. Despite these advantages, many homogeneous catalytic systems have not been commercialized because of one major disadvantage compared with heterogeneous catalysts: the difficulty encountered when trying to separate the reaction product from the catalyst and from any reaction solvent. This is because in homogeneous catalysis, at the end of the chemical reaction, the catalysts and the products are in most instances, in the same phase. The most straight-forward remedy would be to isolate the catalyst via distillation, which is the easiest and most commonly employed separation procedure on an industrial scale.<sup>73,74</sup> Unfortunately, this strategy is ineffective due to the relative thermal instability of many homogeneous catalysts, which are typically unstable above ~150 °C.

This is a major problem as it inhibits the effective recovery and recyclability of the catalyst. So far, a comprehensive solution has not been achieved which represents a major hurdle to their large-scale application.

# 1.3.2. Heterogenizing homogeneous catalysts

This limitation of homogeneous catalysts has led to a growing volition to heterogenize homogenous catalysts.<sup>74</sup> These catalytic systems draw upon the principal advantages of both homogeneous and heterogeneous catalysts. One way to do this, is through the immobilization of catalysts, by anchoring them to an insoluble support or on soluble supports such as dendrimers and polymers, where the separation is commonly carried out by a filtration technique. This, however, generally leads to loss in activity of the catalyst when recycled. Also, due to breaking of bonds during the catalytic process, the catalyst may leach from the support.

However, robust systems have been developed in flow chemistry. Leeuwen and co-workers<sup>75</sup> (2001) successfully immobilized a Ru catalyst, employed in transfer hydrogenation reactions, by covalently attaching the ligand to silica gel which was packed in a glass column. Their catalytic system accomplished a high conversion (95%) and enantioselectivity (90%). Moreover, they could continuously use it for a week without significant catalyst deactivation. Lamb et al.<sup>76</sup> (2010) succeeded in immobilizing Ru catalysts on a phosphine-bound polymer in continuous flow N-alkylation of morpholine with benzyl alcohol. The conversion to the desired tertiary amine was 98% but decreased at higher flow rates. The reactor could be operated continuously for 72 h without drastically affecting the activity of the catalyst.

With regards to performing cross-coupling reactions in continuous flow, Cantillo et al.<sup>77</sup> (2015) showed that using heterogeneous (immobilized) catalysts was not feasible. This is explained with the reaction mechanism of the cross-coupling reaction. As an example, for the palladium transition metal catalyst, the Pd<sup>0</sup> species is transformed into Pd<sup>2+</sup>, which becomes soluble in the mobile phase. Ultimately, in continuous flow, this leads to major leaching of metal from the support, causing reduced activity and contamination of the reaction product. In an earlier report by Kappe et al.<sup>77</sup> (2015) they observed leaching of copper from the charcoal support in their experiment in which they employed the Cu/C catalyst for the copper-catalyzed azide–alkyne cycloaddition (CuAAC) reaction in continuous flow. Their investigation confirmed a homogeneous mechanism with the charcoal acting as the reservoir for Cu.

Therefore, the use of homogeneous catalysts has been found to be more fitting together with a suitable catalyst recycling technique.<sup>73</sup> This statement renders it even more imperative to cultivate creative strategies for homogeneous catalyst recovery and perhaps also recyclability in continuous flow operations.

## 1.3.3. Recycling strategies in homogenous catalysis

The green chemistry definition proposed by Anastas and Warner<sup>78</sup> as "the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products" has encouraged the scientific community to look for efficient ways to separate homogenous catalysts from the reaction media and their subsequent recycling. A few of the creative approaches under investigation are reviewed in more detail below.

# 1.3.3.1. Magnetic separation

Superparamagnetic materials are intrinsically non-magnetic but can be readily magnetized in the presence of an external magnetic field. As a result of this unique property, superparamagnetic materials have been widely used in biomedical applications, such as protein purification, cell sorting, MRI contrast enhancement, and drug targeting.<sup>79</sup> Recent advances in the synthesis of superparamagnetic nanoparticles facilitate their exploitation in many technological and biomedical applications. In this regard, the use of magnetite nanoparticles (MNPs) as efficient supports for catalysts has become a subject of intense investigation. The MNPs offer advantages in the development of clean and sustainable green processes as they are non-toxic, easy-accessible, retrievable and reusable.

Gawande et al.<sup>80</sup> (2014) synthesized iron oxide NPs and decorated them with nickel nanocatalysts directly on the magnetic NPs by the chemical reduction of nickel chloride. The designed magnetic catalysts reportedly provided high regio- and chemo-selectivity for the reduction of nitro compounds under the environmentally-friendly solvent, glycerol, as a hydrogen source, along with a high level of reusability.<sup>81</sup> In another effort, Gawande and colleagues introduced a sustainable protocol for the reduction of aromatic nitro compounds under magnetic supporting gold nanocatalyst under mild reaction conditions.<sup>81,82</sup> Over the last years, two seminal manuscripts describing the immobilization of ruthenium catalysts onto MNPs have been reported.<sup>83</sup> In these works, descriptions of magnetically-modified Noyori (Figure 1.12) and Hoveyda-Grubbs (Figure 1.13) catalysts are expounded.

Ryoji Noyori shared the Nobel Prize in Chemistry in 2001 for the study of asymmetric hydrogenation. One reaction in particular, the Noyori asymmetric hydrogenation of ketones, is a chemical reaction involving the enantioselective hydrogenation of ketones, aldehydes, and imines. The reaction exploits chiral ruthenium catalysts introduced by Noyori. Mindful of the aforementioned, Hu et al.<sup>79</sup> (2005) modified a Noyori-type ruthenium catalyst immobilized on MNPs using a phosphoric acid-substituted BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl). The MNPs-Ru-BINAP chiral material catalyzed the asymmetric hydrogenation of aromatic ketones in quantitative yields and excellent enantioselectivities. The system could be recycled by magnetic decantation and reused for up to 14 times without loss of activity and enantioselectivity.<sup>80</sup>

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Figure 1.12. Noyori catalyst immobilized onto Fe<sub>3</sub>O<sub>4</sub> for separation by magnetism.<sup>80</sup>

The Grubbs-type and Hoveyda-Grubbs-type catalysts are the most widely expended catalysts in ring-closure metathesis (RCM). They are extremely useful in the way they tolerate a variety of functional groups in alkene substrates and are compatible with an inclusive array of solvents. Despite these advantages, the separation of the soluble catalyst from the product and any reaction solvent remains difficult. Considering this, Che et al.<sup>83</sup> (2009) immobilized a second generation Hoveyda-Grubbs catalyst onto surface-modified magnetite nanoparticles by a divergent synthetic approach. The catalytic system is exceedingly effective for self- and cross-metathesis reactions of methyl oleate, and the catalyst offered easy separation by magnetic attraction.



**Figure 1.13.** Illustration of the separation of magnetic nanoparticle catalysts from the reaction system in the RCM reaction.

In summary, the use of these magnetic NP catalysts can address the isolation and recycling problem encountered in many catalytic reactions. Most importantly, the magnetic NP-supported catalysts show not only high catalytic activity, but also a high chemical stability. This is because MNPs can be well dispersed in reaction mixtures without a magnetic field, providing a large surface area that is readily accessible to substrate molecules. Moreover, after completing the reactions, the MNP-supported catalysts can be isolated efficiently from

the product solution through simple magnetic separation, eliminating the need for catalyst filtration and centrifugation. Furthermore, they can be reused up to several runs almost without loss of catalytic activity. Some issues with this technique have been pointed out, which include the dissolution of iron oxide NPs in acidic media which leads to loss of magnetic recovery.<sup>84</sup> Another issue was raised by Alibegovic et al.<sup>85</sup> (2017) whereby iron oxide was found to catalyze side reactions resulting in undesired products, as was shown in their work involving the hydrogenation of furfuryl to furfuryl-alcohol with magnetically recoverable catalysts containing Pd and Pt NPs.

# 1.3.3.2. Aqueous-organic biphasic catalytic systems

Another tactic involves designing the catalyst so that it is solubilized in a solvent that, under specific reaction conditions, is immiscible with the reaction product. This is usually conducted using a water-soluble catalyst dissolved in an aqueous phase. The substrate may be introduced neat or dissolved in an organic solvent thus yielding a biphasic system.<sup>86</sup> Because most organic compounds do not mix with water, the reaction can be carried out in two phases with rapid mixing to ensure maximum contact between the catalyst and the substrate (thus, not achieving true homogeneity). After the reaction, the mixture is allowed to settle, and the product is decanted, leaving the catalyst in the aqueous phase (Figure 1.14).



**Figure 1.14.** Simplistic diagram denoting the aqueous-organic biphasic system. Top phase = organic phase containing the reactants or substrate. Bottom phase = aqueous phase containing the water-soluble catalyst. (i) initial biphasic system before mixing; (ii) during mixing (organic and aqueous phase become dispersed in one another i.e., true homogeneity is not achieved); (iii) after mixing is complete the two phases begin to separate; (iv) visibility of the liquid-liquid interface indicating complete separation of phases.

One such biphasic system that has been commercialized for the hydroformylation of propene uses the ligand, TPPTS, to produce a water-soluble rhodium-based catalyst<sup>86,87</sup> depicted in Figure 1.15. The system, however, has drawbacks. For example, the system does not achieve true homogeneity when heated and mixed and because of the very low solubility of long-chain alkenes in water, the rates of reaction are too low for commercialization of this process to produce longer-chain aldehydes.<sup>87</sup>



**Figure 1.15.** Chemical structure of the water-soluble Rhodium catalyst commercialized for the hydroformylation of propene.

Organometallic catalysis in aqueous systems sometimes leads to high selectivity and activity, as has been well shown by the success of the processes ``Shell high olefins process" (SHOP) and ``Ruhrchemie/Rhone-Poulenc oxo process" for the hydroformylation of propylene.<sup>86,88</sup> Unfortunately, two-phase aqueous-organic systems also have their limits, e.g., they cannot be used in the presence of water sensitive substances; in addition reactions involving organic compounds that are not fully soluble in water proceed at a very slow rate, a condition that is not compatible with practical use.

## 1.3.3.3. Fluorous/organic biphasic catalysis

The fluorous biphasic system (FBS) was first proposed by Vogt<sup>89</sup> in his in 1991 Ph.D. dissertation and later, popularized by Horváth and Rábai in their 1994 *Science* paper.<sup>90</sup> It presents a unique solution to the problem of industrial catalyst recycling by modifying the catalyst to include fluorinated-ligands which affords the catalyst solubility in perfluorocarbons (Figure 1.16).

Perfluorocarbons (PFCs) are chemically inert, have high densities, low refraction indexes, low surface tensions, and low dielectric constants. Their miscibility with common organic solvents, such as toluene, acetone, and alcohols, is negligible at room temperature. However, according to a long-standing article by Grosse and Cady<sup>91</sup> (1947), the phase diagrams of mixtures of PFCs and non-fluorinated solvents are characterized by strong deviations from the Raoult's law and typically a prompt increase in miscibility is observed as the temperature is raised. Overall, the solvent power of PFCs towards functionalized organic molecules is exceptionally low due to their unusual properties that include extremely hydrophobic and lipophobic parameters, which renders them relatively insoluble in water, and in most organic solvents at room temperature. At the same time, they can dissolve various gases, such as  $O_2$ ,  $H_2$  and  $CO.^{92}$ 



Figure 1.16. Examples of fluorinated solvents with applications in FBC.

In fluorous biphasic catalysis (FBC), the catalyst is preferentially soluble in the fluorous solvent within a biphasic system. The other phase is the organic phase, containing an organic solvent and/or substrate. The two phases are immiscible at room temperature, however, when the temperature is raised the system becomes a homogeneous mixture. This is an advantage because the catalyst and the substrate are allowed to interact with each other. Through subsequent cooling, the system returns to its biphasic state allowing for facile separation of the catalyst and desired products into separate immiscible solvents. The desired solubility properties of the catalyst are attained through the incorporation of fluorous 'ponytails' onto,

most commonly, trialkyl and triaryl phosphine ligands. The overwhelming majority of ponytails in current use have the formula  $(CH_2)_m R_{fn}$  where the  $R_{fn}$  segment should consist of at least six carbons ( $R_{f6}$ ).

In his dissertation, Vogt<sup>89</sup> (1991) endeavoured to accomplish the oxidation of cyclohexene with  $O_2$  in the presence of fluorous-modified cobalt or manganese complexes. The reactions, carried out in a perfuoroether/alkene two-phase system, furnished only small quantities of cyclohexenone and cyclohexene oxide and there was severe catalyst decomposition during the reaction process. As the reaction proceeded, the catalyst was progressively extracted into the organic phase and could not be recovered. The electron-deficiency of the binding sites was recognized as one of the causes of the partial failure of these catalysts and elaborated in the initial report by Horváth and Rábai<sup>90</sup> (1994). The two verified that the electron-withdrawing character of the fluorine atoms present in the R<sub>f</sub> moiety led to a weakened coordination ability of the ligand donor atom, ultimately upsetting the catalytic activity and stability. For this reason, it is required that a "spacer" moiety be incorporated between the donor heteroatom and the perfluoroalkyl segment (R<sub>fn</sub>). The "spacer" consists of the entire sequence of atoms between the R<sub>fn</sub> moiety and the chemically active site of the reagent or catalyst.

In the same paper, Horváth and Rábai<sup>90</sup> (1994) presented an influential study which employs  $HRh(CO){P[(CH_2)_2(CF_2)_5CF_3]_3}$  as a hydroformylation catalyst in a fluorous biphasic system (See Figure 1.17). They demonstrated the hydroformylation of primary alkenes to aldehydes accompanied by effective separation of the catalytically active fluorous phase and the hydrocarbon phase upon restoring the reaction mixture to ambient conditions. The catalyst contained in the fluorous phase was then effortlessly isolated from the hydrocarbon phase, constituting the organic products, and recycled. In an ensuing investigation, Horváth et al.<sup>93</sup> (1998) extended the hydroformylation to include smaller alkenes such as ethylene, as well as higher alkenes like 1-octene and 1-decene. The fluorous biphasic catalyst recovery concept semi-continuous hydroformylation of 1-decene was tested in а with the  $HRh(CO){P[(CH_2)_2(CF_2)_5CF_3]_3}$  catalyst. During nine consecutive reaction/separation cycles, a total turnover of more than 35 000 was achieved with a loss of 1.18 ppm of Rh/mol of undecanals. The same catalyst was also tested for the continuous hydroformylation of ethylene using the high-boiling fluorous solvent FC-70, which allows continuous removal of propanal at the reaction temperature of 110 °C. The long-term stability of the fluorous-modified Rh catalyst is better than that of the Rh/PPh<sub>3</sub> catalyst. Thus, the Rh/P[CH<sub>2</sub>CH<sub>2</sub>(CF<sub>2</sub>)<sub>5</sub>CF<sub>3</sub>]<sub>3</sub> catalyst is the first catalyst system which can be used for the hydroformylation of both low and high molecular weight olefins and provides facile catalyst separation for both low and high molecular weight aldehydes.





Figure 1.17. Fluorous biphasic catalysis operating procedure carried out by Horvath et al.93

Since the advent of the FBC approach, the catalytic activities, and prospective recoveries of an array of fluorous-modified catalysts have been probed. In summary of these efforts, Curran et al.<sup>94</sup> (1999) demonstrated high levels of recovery of fluorous tin hydrides employed in a variety of catalytic transformations. Klement et al.<sup>95</sup> (1997) reported a fluorous ruthenium catalyst for olefin oxidation that can be recovered in 95% yield after several cycles. Richter et al.<sup>96</sup> (2000) synthesized two fluorous analogues of Wilkinson's catalyst, namely, RhCl{P[C<sub>6</sub>H<sub>4</sub>p-SiMe<sub>2</sub>-(CH<sub>2</sub>)<sub>2</sub>C<sub>n</sub>F<sub>2n+1</sub>}<sub>3</sub>]<sub>3</sub> with n=6 and n=8, respectively. The catalytic activities of these species, as measured in C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, were shown to be alarmingly similar to that of the Wilkinson's catalyst for the hydrogenation of 1-alkenes. The experimental success was considered a result of incorporating the -SiCH<sub>2</sub>CH<sub>2</sub>- spacer. Moreover, the group identified that the catalyst recovery was highly dependent on the magnitude of fluorous character constituting the ligand. Chechik et al.<sup>97</sup> (2000) illustrated the feasibility of utilizing dendrimerencapsulated Pd nanoparticles for catalysis in a fluorous biphasic system. The dendrimerencapsulated nanoparticles (DENs) are rendered soluble in perfluoro-2-butyltetrahydrofuran (Fluoroinert FC-75) by reacting the peripheral primary amine group of the dendrimer with the carboxylic end group of a perfluoropolyether. The new catalysts exhibited high activity and selectivity for the biphasic hydrogenation of alkenes and conjugated dienes. Moreover, the catalysts could be easily recovered and used for multiple reactions.

With regards to the chemical inertness of PFCs and their capacity to solubilize  $O_2$  in higher concentrations compared to organic solvents and water, the FBC concept has rapidly emerged as a highly appealing protocol for catalytic oxidation reactions. Two notable examples demonstrating the efficacy of the FBC approach is the work carried out by Bernini et al.<sup>98</sup> (2009) and Wang et al.<sup>99</sup> (2010). They investigated the catalytic activities of gold nanoparticles stabilized by the fluorous thiol ligand seen in Figure 1.17, which was in turn, adsorbed on fluorous silica gel. The nanocatalysts were then assessed in alcohol-to-carbonyl oxidation reactions. Bernini et al. (2009) used toluene as the solvent and regulated at 100 °C with  $O_2$  as

the oxidant while, on the other hand, Wang et al. (2010) employed water at 25 °C with H<sub>2</sub>O<sub>2</sub> as the oxidant. Both research groups typically employed low catalyst loadings (0.05–0.5 mol %) which provided turnover frequencies values of > 1000 h<sup>-1</sup> for some of the most reactive benzyl alcohol substrates. Conversely, the oxidation of aliphatic alcohols was revealed to be much slower, delivering turnover frequencies values of < 50 h<sup>-1</sup>. The heterogeneous catalyst was recovered by straightforward centrifugation and could be re-used up to seven times. This was shown by Bernini et. al. (2009) in the oxidation of phenyl ethanol with O<sub>2</sub> and by Wang et. al. (2010) in the oxidation of benzyl alcohol with H<sub>2</sub>O<sub>2</sub>, with a 20% decrease in the yield being observed on the eighth trial.<sup>98,99</sup>



**Figure 1.18.** Fluorous ponytailed thiol ligand used in the work of Bernini et. al. and Wang et. al. Adapted from references 98 and 99.

Fluorous biphasic catalysis has been validated for many other catalytic reactions. Some other examples include, but are not limited to, hydroboration<sup>100</sup>, hydrosilylation<sup>101</sup> and Stille coupling<sup>102</sup> However, this inventory is likely to continue to grow as interest intensifies in this area. Extended research must be conducted in order to optimize current systems and diminish costs in an effort to bring forth promising systems to commercial practice.

## 1.4. Project aims and objectives

The science and technology of catalysis is particularly important currently due to the energy and environmental challenges facing society. While homogeneous catalysis offers numerous advantages over heterogeneous catalysis, the significant problem of separating and recycling the catalyst remains. In this regard, the concept of fluorous biphasic catalysis (FBC) has become an area of considerable interest within green chemistry due to its focus on catalystrecycling. Since this potential was revealed by Horvath and Rabai in 1994, an enormous variety of catalytic reactions have been investigated. Numerous researchers have shown that the fluorous biphasic system offers facile separation of the catalyst and desired products into separate immiscible solvents. With this precedent in mind, combining the fluorous biphasic system with the advantages of nanoparticles, particularly gold nanoparticle catalysts, may

provide some exciting potential for commercial application. Nanoparticles, due to their high surface area to volume ratio, are well suited for catalytic purposes, however stabilization of these nanoparticles and preventing agglomeration remains an important obstacle. Nevertheless, some degree of stabilization may be achieved by preparing fluorous-stabilized metal nanoparticles.

The main purpose of this project was to develop a 'proof of concept' for the fluorous biphasic system combined with the notion of catalytically active Au NPs soluble in fluorous media. This combination, if successful, could offer a feasible strategy for the recovery and recycling of expensive metals comprising many catalyst systems. Furthermore, the combination of FBC and Au NP catalyst systems simply warrants further exploration due to few reports incorporating metal nanoparticles in FBC and no literature, to our knowledge, of fluorous-stabilized Au NP catalysts participating in FBC. With this precedent in mind, the aims and objectives of the project were four-fold.

Firstly, the project entails: (i) the synthesis and characterization of a G3-DAB-PPI-( $NH_2$ )<sub>16</sub> dendrimer modified to include peripheral aliphatic palmitoyl (C15) groups. This will be done to produce two comparable templates (the modified and unmodified dendrimer) to produce DENs.

(ii) UV-Vis spectrophotometric titrations involving several metal ions with the unmodified and modified-dendrimer, respectively. The metal ions investigated in this study include Cu(II), Ni(II), Co(II), Cr(III), Au(III), Rh(III), Ru(III), Pt(II) and Cd(II). This will be executed to determine the maximum amount of a metal ion which can be encapsulated within the dendrimers. The importnce, and reason for this investigation will be revealed in Chapter 3. Moreover, the comparative study concerning the two unique dendrimers could serve as a platform for future studies relating to their templating abilities in the preparation of metal DENs. The results of the study for the titration of Au(III) and the modified dendrimer will be necessary for the next section of the project.

Secondly, the project involves (i) the development of a reproducible synthetic procedure to produce fluorous-stabilized Au NPs by generating organic-soluble Au DENs followed by their subsequent extraction into a fluorous phase.

(ii) Optimization of the synthetic procedure which includes adjusting variables such as temperature, permitted reduction time and/or extraction time, Au: dendrimer ratio, Au: NaBH<sub>4</sub> ratio and the use of different ligands possessing fluorous segments. During the optimization

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process, UV-Vis spectroscopy is employed to monitor the synthesis by paying careful attention to the LMCT band and the surface plasmon resonance corresponding to Au NPs.

(iii) The synthesis and characterization of several fluorous-stabilized Au NP catalyst systems generated using this synthetic approach under optimized conditions. Each system is characterized by UV-Vis spectroscopy, TEM and ICP-OES.

(iv) Reproducibility studies which involve duplicating a successfully prepared system to identify the degree of reproducibility the synthesis can achieve in terms of replicating particle sizes, morphology, dispersity, and other important characteristics.

(v) Stability studies involving the successfully prepared fluorous-stabilized Au NPs. Time studies will be conducted, which entail analysing the systems over time increments to identify the extent of agglomeration over time, hence the stability of the systems if they were to be stored prior to use. These studies will be conducted using UV-Vis spectroscopy in most instances and additional characterization by TEM, in some instances.

Thirdly, the research entails (i) the development of an improved, unique, more green and reproducible synthetic procedure to produce fluorous-stabilized Au NPs without the requirement of the modified-dendrimer template and organic solvent. This synthetic strategy entails a biphasic reduction step and will be explained in more detail in Chapter 4.

(ii) Optimization of this synthetic approach with the selected fluorous ligands and solvents. This entails adjusting experimental parameters in an effort to determine the optimal experimental conditions to provide small, monodisperse and spherical fluorous-stabilized Au NPs which are also reproducible.

(iii) Synthesis and characterization of successfully generated fluorous-stabilized Au NPs employing this unique synthetic strategy. Each successful system is characterized by UV-Vis spectroscopy, TEM and ICP-OES.

(iv) Reproducibility studies which entails using a successful system and employing the exact experimental conditions to reproduce it. The visual appearance of the Au NP system, UV-Vis spectroscopy and TEM analysis would be used to compare the duplicate experiments to identify the degree of reproducibility.

(v) Stability studies involving the successfully prepared fluorous-stabilized Au NPs. Some systems are analysed at discrete time intervals to identify changes to the NP system over

time. These studies will be conducted using UV-Vis spectroscopy in most instances and additional characterization by TEM, in some instances.

Lastly, the final part of the project will include: (i) the assessment of the prepared fluorousstabilized Au NP catalyst systems in the fluorous biphasic catalytic oxidation of an alpha linear olefin, 1-octene, as the model substrate.

(ii) Optimization of the catalytic parameters by adjusting different variables during the experimental procedure. In this regard, the effect of; metal loading, oxidants ( $O_2$ ,  $H_2O_2$  and TBHP), varying the oxidant to metal ratio and employing different solvents (**S1** vs **S3**) was investigated.

(iii) Comparison of characterized catalytic systems by exposing them to the optimized reaction conditions. The fluorous catalysts differed in terms of their respective sizes and size distributions, stabilizing ligands (L1 or L2) and their method of preparation (micelle-template strategy or the direct method). In addition, fluorous-stabilized Au NP systems were purposely prepared with varying quantities of ligand to metal to intentionally produce systems with different sizes to comparatively study them. GC analysis was employed to quantify 1-octene conversions, identifying major and minor products and to gauge the process of catalysis to gain insight into the possible catalytic mechanism of the oxidation process using these catalytic systems.

(iv) Recyclability and reusability of the fluorous catalysts to identify how many times the catalysts could be recycled and the effect of re-use on the activity and selectivity of the oxidation of 1-octene. In addition to this, the effect of adding oxidant, namely, TBHP, between successive recycling trials was also investigated.

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# Chapter 2

# Elucidating the metal ion-loading capacities of a modified and unmodified G3-DAB PPI dendrimer via UV-Vis spectrophotometric titrations

# 2.1. Introduction

Innovations in macromolecular chemistry such as the fabrication of dendritic polymers are offering unprecedented opportunities to develop high-capacity nanoscale chelating agents with well-defined molecular composition, size, and shape.<sup>1</sup> Unlike linear polymers, dendrimers branch out of a core leading to a tree-like, star-shaped molecule having diameters between 2 and 10 nm. The terminal groups present on the periphery of the dendrimer controls its solubility properties. What's more, is that these properties can be further tuned by functionalisation of the terminal surface groups of the dendrimer. All these characteristics make them highly appealing as templates for the synthesis of metal NPs. Two of the most explored classes of dendrimers as templates for metal NPs are the PPI and PAMAM dendrimers. Poly(propyleneimine) (PPI) dendrimers (the focus of this research) possess functional nitrogen and amide groups arranged in regular "branched upon branched" patterns which are displayed in geometrically progressive numbers as a function of generation level. This high density of nitrogen ligands and the possibility of attaching various functional groups such as carboxyl, hydroxyl, and so forth to PPI dendrimers make them particularly attractive as high-capacity chelating agents for metal ions.<sup>2</sup>

Dendrimer-based metal nanoparticles can be prepared either by encapsulating the metal ion inside the void cavities of dendrimers [intra-dendrimer encapsulated nanoparticles (DENs)], or by trapping the metal in between dendrimers [inter-dendrimer stabilised nanoparticles (DSNs)] as exemplified in Scheme 2.1. In the former instance, dendrimers act as templates; in the latter, they act as stabilising agents. Since we intend to use the dendrimers as templates (Chapter 3), the formation of DSNs is unfavourable and therefore our efforts targeted the production of DENs to be later extracted by fluorous ligands into a fluorous solvent.

In the case of hydrophilic dendrimers, it has been shown that metal ions tend to coordinate to the functional groups within the dendrimer interior according to a fixed stoichiometric ratio. Failure to determine the loading capacity of individual generations could result in agglomeration or the formation of DSNs. One of the major reasons DSNs form and not the desired DENs is a consequence of the interaction of certain metal ions with the terminal functional groups present on the peripheries of these dendrimers.

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**Scheme 2.1.** Schematic diagram illustrating the formation of DENs and undesirable DSNs, respectively.

Both Crook's<sup>3</sup> and Tomalia's<sup>4,5</sup> groups found that metal ions such as Cu(II), Co(II), Pd(II) and Pt(II) can complex with both internal electron donor groups (like tertiary amines), and exterior functional groups (such as amine or carboxylic acid groups). This resulted in the formation of both intra-dendrimer DENs and inter-dendrimer (DSNs) nanoparticles. Since having a narrow-size distribution and small nanoparticle sizes is a pre-requisite for the synthesis of well-defined metal nanoparticles, the aggregation of the dendrimer terminal groups via intermolecular collisions is undesirable.<sup>6</sup> Therefore, coordination of metal ions to terminal groups should be prevented to produce DENs. There are two methods of achieving this. The first entails lowering the pH to ensure protonation of the terminal amine or carboxylic acid groups and the second involves modifying the terminal group with non-coordinating functional groups. An example of this is the modified G3-DAB PPI dendrimer, obtained by appending palmitoyl groups onto the amine terminated G3-DAB-PPI dendrimer (shown in Figure 2.1).



**Scheme 2.2.** Method involving protonation of the dendrimer periphery to prevent the aggregation of the dendrimer terminal groups via intermolecular collisions.

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**Scheme 2.3.** Method involving modifications of the peripheries to include non-coordinating functional groups. R = non-coordinating alkyl or acyl groups.



**Figure 2.1.** Left: G3-DAB PPI ( $NH_2$ )<sub>16</sub> dendrimer (unmodified dendrimer). Right: G3-DAB PPI ( $NH_2$ )<sub>16</sub> dendrimer modified to include palmitoyl groups on the peripheries (modified dendrimer).

It is sensible to concede that hydrophobically-modified dendrimers are superior templates for the synthesis of nanoparticles displaying a narrow-size distribution, with the additional benefit of displaying solubility in organic solvents. With these inverse unimolecular micelles, the driving force for the encapsulation of metal ions appears to be the result of the difference in solubility between the exterior organic solvent and the hydrophilic interior or the micelle. This has been demonstrated by Crook's<sup>7</sup> group, using modified PPI dendrimers, and titrating with Cu(II). They found that the end points, of Cu(II) titrated against PPI-16-palmitoyl, PPI-32-palmitoyl and PPI-64-palmitoyl modified dendrimers, were  $20 \pm 2$ ,  $40 \pm 3$  and  $75 \pm 3$ , respectively. These values were inexplicably larger than the number of tertiary amine functionalities found in the end points of the titration of Cu(II) with unmodified PPI dendrimers. These end points were 14, 20 and 62, respectively.

Mindful of the above, no further investigation has been conducted, to our knowledge, with respect to the binding nature of these metal ions within the interior of hydrophobically-modified dendrimers. A deeper understanding of this binding phenomenon is paramount if we strive to produce well-defined sizes and narrow size distributions of metal nanoparticles using the micelle-template strategy. Having explored the modified G3 DAB PPI (NH<sub>2</sub>) dendrimer in much detail in our research group (in NP synthesis), its templating abilities were examined herein. In this study, we investigate and report the maximum number of metal ions which can be encapsulated into the interiors of two dendrimers, namely, an unmodified G3 polypropyleneimine (PPI-NH<sub>2</sub>) dendrimer and a hydrophobically-modified analogue (Figure 2.1). The loading capacities were determined through UV-Vis spectrophotometric titrations and the method followed, involved adapting a procedure offered by Niu et al.<sup>8</sup> (2003). The endpoints of the titrations (representing maximum loading) were realised by a change in gradient of the graph of absorbance at lambda max as a function of equivalents of M/dendrimer. This change in the slope of this graph as portions of metal are added to the dendrimer, signifies a change in the molar absorptivity and occurs once the dendrimers are completely loaded.

The unmodified dendrimers, which are water-soluble, were assessed with the metal ions (deriving from chloride salts) which were also completely soluble in H<sub>2</sub>O. These metal ions included Cu(II), Ni(II), Co(II), Zn(II), Cd(II), Cr(III), Au(III), Rh(III), Ru(III), Pt(II) and Pd(II). The modified dendrimers, on the other hand, were limited by the fact that a solvent or solvent system which could both dissolve the modified dendrimer and the metal chloride of interest was required. The solvent system which provided the most promising results was CHCl<sub>3</sub>/MeOH (v/v 4:1), in which the modified dendrimer showed complete solubility. The metal chloride salts which also shared solubility in this solvent system and were therefore included in these titrations were Cu(II), Ni(II), Co(II), Zn(II), Rh(III), Pd(II) and Au(III). In some cases, where the metal chloride showed poor or partial solubility in this solvent system (Rh and Pd), the salt was refluxed in acetonitrile to afford bis(acetonitrile) complexes which improved the solubility of the metal complex in the organic solvent system.

## 2.2. Results and discussion

## 2.2.1. Synthesis and characterization of modified dendrimer

The modification of the G3-DAB PPI dendrimer to include palmitoyl groups was carried out in a similar way to that reported by Stevelmans et al.<sup>9</sup> (1996). In the synthesis, the terminal NH<sub>2</sub>
groups are reacted with excess palmitoyl chloride to produce amide functionalities as shown in Scheme 2.4. The modified dendrimer was characterized by FT-IR spectroscopy and <sup>1</sup>H NMR spectroscopy and showed complete solubility in dry CHCl<sub>3</sub> and was completely insoluble in  $H_2O$ .



**Scheme 2.4.** Synthetic modification of a commercially-obtained G3 DAB PPI dendrimer to include peripheral palmitoyl groups.

The FT-IR (ATR) spectrum of the modified G3-DAB PPI dendrimer (Figure 2.2) exemplifies a more distinguished N-H stretch corresponding to the amide functionality, with a much less pronounced band in the region 3200-3500 cm<sup>-1</sup>, indicative of the absorption band corresponding to that of water. Furthermore, the carbonyl absorption peak is observed at 1634.78 cm<sup>-1</sup> which is associated with the newly-formed secondary amide moiety. The relevant bends and stretches of the functional groups of the modified dendrimer correspond well to the characterization reported in the literature, as obtained by Stevelmans et al.<sup>9</sup> (1996).



Figure 2.2. FT-IR (ATR) spectrum of the modified G3-DAB PPI dendrimer.

The <sup>1</sup>H NMR spectrum (Figure 2.3) of the modified dendrimer reveals a triplet at 0.88 ppm which corresponds to the methyl protons present on the peripheries of the modified dendrimer. It seems that there may be a slight break in symmetry for the respective alkyl arms attached to the dendrimer which is indicated by the broader signals of the multiplets associated with the methylene protons present on the palmitoyl groups of the product. In conclusion, all resonances are accounted for in the <sup>1</sup>H NMR spectrum, however, due to the extensive quantities of protons present on the molecule, defined peaks are not obtained but instead more rounded multiplets. Furthermore, there are no signals emanating for either of the reagents used in the modified dendrimer preparation indicating that purification was successful.





2.2.2. Unmodified dendrimer UV-Vis spectrophotometric titrations

# 2.2.2.1. Cu(II), Ni(II) and Co(II)

Zhao et al.<sup>10</sup> (1998) reported that in the absence of dendrimer,  $Cu^{2+}$  exists primarily as  $[Cu(H_2O)_6]^{2+}$ , which results in a broad weak absorption band centred at 810 nm. This corresponds to the well-known d-d transition for  $Cu^{2+}$  in a tetragonally distorted octahedral or square planar ligand field. The same group of researchers identified that the binding between  $Cu^{2+}$  and dendrimer is pH-dependent. Moreover, it was shown that, depending on solution conditions, the sorption is irreversible: the d-d transition band at 605 nm does not decrease significantly even after 36 h of dialysis against pure water. However, Ottaviani et al.<sup>11</sup> (1999) proved that H<sup>+</sup> effectively competes with  $Cu^{2+}$  for the tertiary amine sites, and so it is possible to release  $Cu^{2+}$  from the G4-OH interior in a pH 1.3 HCl solution.

Several investigators have used Cu(II) as a probe to typify metal ion complexation in aqueous solutions of PAMAM dendrimers. Diallo et al.<sup>12</sup> (1999) combined ultrafiltration with atomic absorption spectrophotometry to measure the extent of binding (EOB) of Cu(II) ions in aqueous solutions of generations G3-G8 PAMAM dendrimers with ethylenediamine (EDA) core and terminal NH<sub>2</sub> groups. For the G3-NH<sub>2</sub>, G4-NH<sub>2</sub>, and G5-NH<sub>2</sub> PAMAM dendrimers, they reported maximum EOB of  $8 \pm 1$ ;  $13 \pm 1$ , and  $29 \pm 3$  Cu(II) ions per dendrimer molecule at metal ion-dendrimer loadings of 11, 18, and 41 Cu(II) ions per dendrimer molecule, respectively. For the G6-NH<sub>2</sub>, G7-NH<sub>2</sub>, and G8- NH<sub>2</sub> PAMAM dendrimers, the same group found maximum EOB of  $46 \pm 9$ ,  $83 \pm 9$ , and  $153 \pm 20$  Cu(II) ions per dendrimer molecule at metal ion-dendrimer loadings of 91, 114, and 306 Cu(II) ions per dendrimer molecule, respectively.<sup>12</sup> Earlier spectrophotometric titrations described by Zhao et al.<sup>10</sup> (1998), indicated that for increasing generations of G2-G4 and G6-PAMAM-OH, a loading of Cu(II) (derived from CuSO<sub>4</sub>) of 4, 8, 16 and 64, respectively, were attained. In addition, the Cu(II) loading onto a G4-PAMAM-NH<sub>2</sub> was also reported and found to be approximately 36 Cu(II) ions. Binding studies between Cu<sup>2+</sup> and the PPI dendrimers were first reported by Bosman et al.<sup>13</sup> (1997). Subsequently, Vassilev and Ford<sup>14</sup> (1999) reported that a maximum of 32 Cu<sup>2+</sup> ions could be coordinated into PPI 64-NH<sub>2</sub>.

In the hopes of further understanding the binding nature of CuCl<sub>2</sub> within the void cavity of the G3-DAB PPI (NH<sub>2</sub>)<sub>16</sub> dendrimer, a UV-Vis spectrophotometric titration was exercised. With this said, the UV-Vis experiment reported herein was executed with deionised H<sub>2</sub>O contained in the reference cuvette. This, however, resulted in a maximum absorption being reached early in the titration (before the attainment of enough absorbance values to plot a reliable linear graph for "after the endpoint"). To remedy this obstacle, the dendrimer solution was placed in the reference cuvette to subtract the absorbance values arising from the free dendrimer. This assisted in de-convoluting the spectral range 190 - 300 nm. The graph of absorbance vs wavelength (Figure 2.4 - left) for one of the triplicate runs (denoted run 1) is provided as a representation of similar spectra obtained for the other two runs. The graph of absorbance at lambda max vs equivalents of Cu(II)/dendrimer (Figure 2.4 - right) indicates the change in gradient associated with the endpoint. The endpoints were realised from this plot for each titration run by identifying the intersect of the two linear equations associated with the metal equivalents before and after the endpoint, respectively (Figure 2.5). Extrapolating we identify the equivalents of Cu(II)/dendrimer which is indicative of the endpoint and loading capacity. In this study, the values for the loading of Cu(II)/unmodified dendrimer, derived from the triplicate titration runs, were determined to be  $x_1 = 6,754$ ,  $x_2 = 6,795$  and  $x_3 = 7,001$ , with  $x_{ave} \sim 7$  Cu(II) ions. The  $\lambda_{max}$  values assessed were in the range of 266 - 271 nm, this is indicative of the

strong ligand-to-metal-charge-transfer (LMCT) transition band, which appears once Cu<sup>2+</sup> ions become bound to the tertiary amine groups (observed for PAMAM-OH in literature<sup>10</sup>).



**Figure 2.4.** Left: Graph of absorbance vs wavelength (nm) with respect to equivalents of Cu(II)/unmodified dendrimer - run 1. Right: Graph of absorbance at  $\lambda_{max}$  (266 - 271 nm) vs equivalents of Cu(II)/unmodified dendrimer (run 1-3). Cu(II) from CuCl<sub>2</sub>·2.5H<sub>2</sub>O.



**Figure 2.5.** Extrapolation of endpoint for the Cu(II)/unmodified dendrimer titration. The graph of absorbance at  $\Lambda_{max}$  vs eq. of Cu(II)/unmodified dendrimer with *Run 1* used as a typical representation of other runs.

Previous literature studies reveal very little with regards to Ni(II) uptake by hydrophilic dendrimers. However, Ni(II) ions are expected to behave similarly to Pd(II) ions due to their analogous electron configurations with both being d<sup>8</sup> transition metal ions. Plotting the graph of absorbance at  $\lambda_{max}$  vs equivalents of Ni(II)/unmodified dendrimer (run 1 - 3), we lucidly observe a change in gradient appearing around 5 eq. of Ni(II)/dendrimer (Figure 2.6 – left). In this investigation, the values for the loading of Ni(II)/unmodified dendrimer, attained from the

triplicate titration runs were ascertained to be  $x_1 = 5.54$ ,  $x_2 = 5.45$  and  $x_3 = 5.65$ , therefore  $x_{ave} \sim 6$  Ni(II) ions.



**Figure 2.6.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). Left: M = NiCl<sub>2</sub>·6H<sub>2</sub>O;  $\lambda_{max}$  = 219 - 220 nm. Right: M = CoCl<sub>2</sub>·6H<sub>2</sub>O;  $\lambda_{max}$  = 217 - 226 nm.

In an account by Khaled Al-Rabe<sup>15</sup> (2004) of California Institute of Technology, it was reported that by pH 8, all primary nitrogens are protonated for the G4-NH<sub>2</sub> PAMAM dendrimer. The study deduced that at this pH value, Co(II) is not bound to the primary nitrogens, but instead Co(II) must bind to the tertiary inner nitrogen atoms. The maximum EOB (extent of binding) for pH 7 and 9 was reported to be  $\pm$  17, meaning there are approximately 17 Co(II) ions bound to each dendrimer. As there are 62 tertiary amines, it was inferred that it takes approximately 4 tertiary nitrogen atoms to bind one Co(II). In this study, the value of  $\lambda_{max}$  which was scrutinised in the spectrophotometric titration corresponds well with the value reported by Murcia et al.<sup>16</sup> (2018). The graph of absorbance at  $\lambda_{max}$  vs equivalents of Co(II)/unmodified dendrimer (run 1 - 3) is shown in Figure 2.6 (right). Accordingly, the values for the endpoint of the Co(II)/unmodified dendrimer titration were found to be around 7 to 8 Co(II) ions ( $x_{ave} =$ 7.545) for every dendrimer molecule ( $x_1 = 7.786$ ;  $x_2 = 7.543$ ;  $x_3 = 7.305$ ). For the G3-DAB-PPI-(NH<sub>2</sub>)<sub>16</sub> dendrimer, there are precisely 14 tertiary amine groups within the interior of the dendrimer. Considering that in the pH range of 7-9, the primary amine functionalities on the peripheries of the dendrimer are protonated, and are therefore not involved in the coordination of the Co(II) ions, then two tertiary amine groups are involved in the binding to each Co(II) ion.

2.2.2.2. Zn(II) and Cd(II)

The UV-Vis spectrum derived from the titration showed the presence of the Zn(II) ion at  $\lambda_{max}$  = 197 nm. This corresponds to the value reported by Trivedi and co-workers<sup>17</sup> (2017), they report

for Zn(II), ZnCl<sub>2</sub>, that  $\lambda_{max} = 197$  nm. In addition, due to Zn(II) having a d<sup>10</sup> electron configuration, the solution appears colourless due to very weak d-d transitions. In this investigation, the values for the endpoint of the Zn(II)/unmodified dendrimer titration were found to be approximately 7 Zn(II) ions for every dendrimer molecule (x<sub>1</sub> = 6.49; x<sub>2</sub> = 6.75; x<sub>3</sub> = 6.47). Cd(II) has an analogous electron configuration to Zn(II), having a completely filled valence d subshell (d<sup>10</sup> electron configuration) hence, it is also colourless. With this said, the coordination chemistry of Cd(II) demonstrates that it behaves as a soft Lewis acid.<sup>22</sup> The spectrophotometric titrations with respect to Cd(II) revealed that approximately 10 - 11 Cd(II) ions could be encapsulated into the unmodified dendrimer.



**Figure 2.7.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). Left: M = ZnCl<sub>2</sub>;  $\Lambda_{max}$  = 197 nm. Right: M = CdCl<sub>2</sub>;  $\Lambda_{max}$  = 191 – 193 nm.

### 2.2.2.3. Cr(III) and Fe(III)

Cr(III), having the smallest ionic radius<sup>18</sup> of all the metal ions investigated in this study, delivered an endpoint of approximately 7 mol of Cr(III) ions per mol of dendrimer. This makes sense as it is higher than the endpoints of M/dendrimer, where M = Cu(II), Ni(II), Co(II), Zn(II) (the ions possessing valence 3d orbitals). Given its higher oxidation state of 3+, it is believed to be smaller than these ions and therefore, presumably more of these ions can be loaded onto the dendrimer. Furthermore, because it is a d<sup>3</sup> transition metal, it is high spin. According to the hard-soft acid base principle<sup>19</sup>, Cr(III) would be classed as the 'hardest' of all the metal ions investigated so it should have the highest affinity for the hard nitrogen donor atoms of the tertiary amine groups within the interior of the dendrimer. The titration, which was performed in quadruplicate, afforded endpoint values of  $x_1 = 10.024$ ;  $x_2 = 5.573$ ;  $x_3 = 4.878$  and  $x_4 = 6.597$ . The average endpoint value was determined to be approximately 6.768 ( $x_{ave}$ ) with only three of the four runs being represented in the graph below.





**Figure 2.8.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). Left: M = CrCl<sub>3</sub>·6H<sub>2</sub>O with  $\lambda_{max}$  = 195 - 200 nm. Right: M = FeCl<sub>3</sub> with  $\lambda_{max}$  = 302 nm.

A titration employing Fe(III) was also conducted, however, the endpoint could not be realised as no change in the gradient of the graph (Figure 2.8 – right) was seen up to 30 eq. of Fe(III) for the 3 runs. Although it is possible that the endpoint has not been reached in the titration, according to Mankbadi et al.<sup>20</sup> (2011), Fe<sup>3+</sup> and Fe<sup>2+</sup> species exhibit very slow kinetics in the coordination to the interior tertiary amines found in the dendrimer void spaces. For this reason, a UV-Vis titration study becomes more difficult, as the five minutes of incubation time is not nearly sufficient for the successful encapsulation of the Fe-species. Therefore, an alternative approach to the titration study is necessary in which aliquots possessing varying ratios of Fe(III) ions-to-unmodified dendrimer are given more than 24 h to interact before each of these aliquots are analysed by UV-Vis spectroscopy.

2.2.2.4. Pt(II) and Pd(II)

The  $\lambda_{\text{max}}$  value which was scrutinised for the determination of the endpoint of the titration was 210 - 220 nm. This corresponded to a value very similar to that demonstrated by Esumi et al.<sup>21</sup> (2004) using H<sub>2</sub>PtCl<sub>4</sub> with G4-PPI-NH<sub>2</sub>. In their article, the group was investigating reduction of the Pt(II) ion using UV-Vis spectroscopy, the graph from the paper correlates well to the spectrum reported herein. The final endpoints for the triplicate runs correspond to;  $x_1 = 9.29$ ,  $x_2 = 9.00$  and  $x_3 = 8.77$ , therefore  $x_{ave} \sim 9$  Pt(II) ions. The endpoint of the Pd(II)/unmodified dendrimer delivered an endpoint ( $x_{ave} = 9.83$ ) which corresponded to about 9-10 Pd(II) ions which could be encapsulated.

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**Figure 2.9.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). Left: M = K<sub>2</sub>PtCl<sub>4</sub> with  $\lambda_{max}$  = 210 - 220 nm. Right: M = PdCl<sub>2</sub> with  $\lambda_{max}$  = 212 - 230 nm.

2.2.2.5. Rh(III) and Ru(III)

The  $\lambda_{max}$  value which was scrutinised for the determination of the endpoint of the Rh(III) titration was 400 nm. The average endpoint values ( $x_{ave}$ ) for triplicate runs were found to be 9 - 11 Rh(III) ions for every unmodified dendrimer.



**Figure 2.10.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). Left: M = RhCl<sub>3</sub>·*x*H<sub>2</sub>O with  $\Lambda_{max}$  = 400 nm. Right: M = RuCl<sub>3</sub>·*x*H<sub>2</sub>O with  $\Lambda_{max}$  = 320 nm.

Ru(III) has a d<sup>5</sup> high spin electron configuration, thus all d-orbitals are occupied with one electron in each. None of the possible d-d transitions is spin allowed, since for any transition the spin of the electron must be reversed (both higher energy  $e_g$  orbitals already contain one electron, according to the Pauli principle the spin of the second electron must be reversed).

For this reason, all possible transitions are very weak, and  $Ru(H_2O)_6^{3+}$  is very pale in colour. The endpoint for Ru(III) could not be achieved due to the constant gradient of the graph which indicates no interaction with the unmodified dendrimer. This observation warrants further investigation, as currently the experimental obstacle is the solubility of this complex in the solvent under investigation.

#### 2.2.2.6. Au(III)

Au(III) being the largest of all the metal ions investigated in this study would be expected to show the lowest endpoint for the M/dendrimer titration. This was shown with only 3 Au(III) ions being loaded onto the dendrimers. In addition, since Au(III) is also the most susceptible to reduction of all the metal ions investigated in this study, it was thought that Au(III) could be reduced in the prepared aqueous solution. This was tested, however no absorption bands corresponding to the formation of Au nanoparticles were observed during a 3-hour UV study of the stability of the Au(III) ion in water.



**Figure 2.11.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/unmodified dendrimer (run 1-3). M = HAuCl<sub>4</sub>·*x*H<sub>2</sub>O with  $\lambda_{max}$  = 217 - 226 nm.

#### 2.2.3. Summary of unmodified dendrimer titrations

The individual metal ion-loading capacities of a water-soluble, unmodified G3-DAB-PPI- $(NH_2)_{16}$  dendrimer, were determined for a range of metal ions. These include Cu(II), Ni(II), Co(II), Cn(II), Cd(II), Cr(III), Pb(II), Ru(III), Rh(III), Pd(II), Pt(II) and Au(III). The metal ion-loading capacities were ascertained by means of UV-Vis spectrophotometric titrations. The results showed that the loading capacity is not only dependent on the size of the metal ion,

but its oxidation state, as well as the valence electronic configuration of the metal ion in question.

Metal Ion	Calculated loading	Metal Ion	Calculated loading
Cu(II)	7	Pt(II)	8-9
Ni(II)	6	Pd(II)	9-10
Co(II)	8	Ru(III)	Undetermined <sup>a</sup>
Zn(II)	7	Rh(III)	10-11
Cd(II)	10-11	Au(III)	3
Cr(III)	6-8	Fe(III)	Undetermined <sup>b</sup>

Table 2.1. Summary of the endpoints attained for M/unmodified dendrimer titrations.

<sup>*a, b*</sup> No change in gradient seen (endpoint not visualised under the employed experimental conditions).

#### 2.2.4. Modified dendrimer UV-Vis spectrophotometric titrations

### 2.2.4.1. Cu(II), Ni(II) and Co(II)

It has been reported by Crooks and co-worker's<sup>7</sup> that for modified PPI dendrimers, having appended palmitoyl groups, the maximum number of Cu(II) ions which could be loaded was not completely dependent on the number of tertiary amine functionalities found in the unmodified dendrimers. Their results indicated that the end-points of Cu(II) titrated against PPI 16-palmitoyl, PPI 32-palmitoyl and PPI 64-palmitoyl were  $20 \pm 2$ ,  $40 \pm 3$  and  $75 \pm 3$ , respectively.



**Figure 2.12.** Left: Graph of absorbance vs wavelength (nm) with respect to equivalents of Cu(II)/modified dendrimer - run 1. Right: Graph of absorbance at  $\lambda_{max}$  (835 nm) vs equivalents of Cu(II)/modified dendrimer (run 1-3).

It is evident from the graph, that the  $\lambda_{max}$  (free metal ion) has a contrasting shift in the UV-Vis spectrum in relation to the analogous unmodified dendrimer titrations. This difference is entirely attributed to the solvent used in the respective experiments. According to an MSc dissertation, compiled by E. Slazus<sup>22</sup> (2015) at Stellenbosch University, the results she obtains for the same titration also does not correlate well with the value obtained by Crooks and colleagues. In the dissertation, a maximum Cu(II) loading of ~ 37 is obtained. In our results a maximum loading of around 41 Cu(II) ions into the interior of the modified dendrimer is reported.

NiCl<sub>2</sub>·6H<sub>2</sub>O exhibited complete solubility in CHCl<sub>3</sub>:MeOH 4:1 v/v and thus the endpoint could be attained through the employed spectrophotometric method. The results of the titration showed that approximately 38 Ni(II) ions were encapsulated within the interior of the modified G3-DAB PPI dendrimer. The results of the triplicate runs are exemplified in Figure 2.13.



**Figure 2.13.** Graph of absorbance at  $\lambda_{max}$  vs equivalents of M/modified dendrimer (run 1-3). Left: M = NiCl<sub>2</sub>·6H<sub>2</sub>O;  $\lambda_{max}$  = 291 nm. Right: M = CoCl<sub>2</sub>·6H<sub>2</sub>O;  $\lambda_{max}$  = 650 nm.

Vogtle et al.<sup>23</sup> (2000) investigated the coordination of Co(II) ions in the interior of poly(propylene amine) dendrimers containing fluorescent dansyl units in the periphery. Their research demonstrated these molecules can reversibly coordinate Co(II) ions. The final Co(II) loading capacity for the modified G3 DAB PPI dendrimer was around 18 Co(II) ions for each modified dendrimer. This result further supplements the notion that the modified dendrimer shows a higher loading capacity in comparison to its unmodified counterpart.

### 2.2.4.2. Zn(II)

The titration endpoint was found to be around 10 eq. of Zn(II)/modified dendrimer. In other words, approximately 10 Zn(II) ions could be encapsulated in the hydrophilic interior of the modified dendrimer. No reports were found in literature to collate our findings. Nevertheless, this result indicates that more Zn(II) ions may be encapsulated by the modified dendrimer in comparison to the unmodified dendrimer.





### 2.2.4.3. Rh(III)

The final endpoints for the triplicate runs correspond to;  $x_1 = 17.91$ ,  $x_2 = 18.18$  and  $x_3 = 18.08$ , therefore  $x_{ave} \sim 18$  Rh(III) ions. These values are greater than those attained for the Rh(III)/modified dendrimer titration.





### 2.2.4.4. Au(III)/modified dendrimer titration

It is imperative to identify the number of Au(III) ions which can be encapsulated within the dendrimer micelle to attain a narrow-size distribution of Au DENs. If too few Au(III) ions are introduced into the micelle solution, there would be a range in the number of Au(III) ions per micelle. On the other hand, supplying an excess of Au(III) ions would lead, upon reduction, to the formation of Au nanoparticles outside the micelle. This, in turn, would promote the formation of dendrimer-stabilized Au nanoparticles (DSNs), which would be disadvantageous for the purposes of this project.

### 2.2.4.4.1. Experimental obstacles

Previous attempts at attaining the endpoint resulted in no change in the gradient upon addition of incremental portions of Au(III)/micelle. In doing this, there were issues brought about by the concentration requirements of the metal solution to titrate against the micelle solution. During the titrations, the absorbance value associated with  $\lambda_{max}$  for Au(III) rapidly reached the maximum value of 4.0 absorbance units. In addition, flattening of the scrutinised absorbance bands was observed. This further confirmed that the concentration of Au(III), introduced into the micelle solution, was too high, making it impossible to attain accurate data points to realise the endpoint. In an attempt to circumnavigate this obstacle, both the Au(III) and micelle solutions were diluted 2 times. Even after these dilutions were made, no promising results were acquired.

### 2.2.4.4.2. Additional experiments

A study was executed where, in the end, it was found that the absorbance at approximately 321 nm was solely the result of free Au(III) ions in CHCl<sub>3</sub>. Understanding that the absorption band associated with free Au(III) ions in solution (Figure 2.16), appears to decrease in the UV spectrum as seen in this experiment. In the investigation, the modified dendrimer was introduced into the solution of Au(III) in the sample cuvette. A time-dependent study (Figure 2.17) revealed that the absorption lowers over time after the modified dendrimer is added. It was postulated that this may be the result of an electronic shielding effect that provides a lower absorption to this peak over time. Two stock solutions were prepared for Au(III) and the modified dendrimer, respectively, in CHCl<sub>3</sub>. The modified dendrimer solution was prepared as follows; precisely 0.0275 g of G3-DAB-PPI dendrimer micelle was transferred to a 100 mL volumetric flask which was made up to the mark with dried CHCl<sub>3</sub>. The Au(III) solution was

prepared by carefully transferring exactly 0,05097 g of HAuCl<sub>4</sub>·xH<sub>2</sub>O to a 10 mL (20 mL for a 2× dilution) volumetric flask, which was accurately made up to the mark with dried CHCl<sub>3</sub>. A UV-Vis spectrum was obtained for the dilute solution of the modified dendrimer (blue in Figure 2.16). Thereafter, a notable excess of HAuCl<sub>4</sub> was added to this solution and another UV spectrum run (red in Figure 2.16).



**Figure 2.16.** Graph of absorbance vs wavelength (nm) after addition of excess Au(III) to the dilute modified dendrimer solution.



**Figure 2.17.** Graph of time-dependent study showing the decrease in absorbance ( $\lambda$  = 321 nm) with respect to time (min) due to an interaction with the modified dendrimer.

### 2.2.4.4.3. Suggested strategy for endpoint attainment

In the hopes of attaining an endpoint for the HAuCl<sub>4</sub>/micelle titration in pure CHCl<sub>3</sub>, a different UV-Vis study could be conducted. Firstly, the study entails attaining a standard concentration vs absorbance graph from which the molar absorptivity of the Au(III) species (at 320 nm) in CHCl<sub>3</sub> can be derived. Secondly, using this molar absorptivity value, the concentration of Au(III) could be determined given a particular absorption value. With this knowledge, it would be possible to determine the number of moles "swallowed" by the modified dendrimer.



**Figure 2.18.** Magnified region of the time-dependent study, illustrating the net change in absorbance with respect to time (min).

This would inadvertently provide the number of Au(III) ions encapsulated by this G3-DAB PPI dendrimer micelle which would further supplement the understanding of the current Au NP manufacturing process. The hypothetical standard graph of absorbance (at 321 nm) vs concentration of Au(III) in CHCl<sub>3</sub> is offered in Figure 2.19, the molar absorptivity coefficient of Au(III) in CHCl<sub>3</sub> can be deduced from the gradient of the graph. This can be done using the Beer-Lambert Law (Eq. 2.1):

 $A = \varepsilon lc \qquad (Eq. 2.1)$ 

Acknowledging that the Beer-Lambert Law is constrained to chemical species existing at a concentration of < 10 mM. Specific concentration values (5 data points) were chosen for Au(III), based on a finite volume ( $v_i$ ) of the stock solution to add to the sample cuvette, fixing the final volume ( $v_f$ ) of the sample solution to 3.5 mL in all cases.

$$n_i = n_f$$
.....(Eq. 2.2)

$$n_i = c_i v_i$$
.....(Eq. 2.3)  $n_f = c_f v_f$ .....(Eq. 2.4)

$$c_i v_i = c_f v_f$$
.....(Eq. 2.5)

The initial volumes ( $v_i$ ) were chosen to be 50, 75, 100, 125 and 150 µL, respectively which ultimately afforded the concentration values (*x* coordinates of the data points) plotted on the graph in Figure 2.19 This is plotted with arbitrary hypothetical values which would provide a positive gradient (this graph is a hypothetical plot).



**Figure 2.19.** Hypothetical graph of absorbance ( $\lambda$  = 321 nm) vs concentration of Au(III) in CHCl<sub>3</sub>.

Since the value of c = 0 provides no absorption without the presence of Au(III), the line passes through the origin and has the form y = mx. The gradient (*m*), following the Beer-Lambert Law, is derived according to the following equations.

$$A_i = \varepsilon_i l_i c_i$$
 (Eq. 2.6)  $A_f = \varepsilon_f l_f c_f$  (Eq. 2.7)

So the change in the absorbance because of a change in concentration can be written as:

$$A_i - A_f = \varepsilon_i l_i c_i - \varepsilon_f l_f c_f$$
(Eq. 2.8)

Because we know that the path length does not change because the same cuvette is being used:

$$l_i = l_f$$

Eq. 2.8 can now be re-arranged to afford Eq. 2.9.

 $A_i - A_f = l(\varepsilon_i c_i - \varepsilon_f c_f)$ (Eq. 2.9)

Because the path length (I) = 1 cm, this term can be extracted from the equation to give Eq. 2.10:

$$A_i - A_f = \varepsilon_i c_i - \varepsilon_f c_f$$
(Eq. 2.10)

Finally, the molar absorptivity  $(\mathcal{E}_{Au})$  remains constant for the same oxidation state so then:

$$A_i - A_f = \mathcal{E}(c_i - c_f)$$
 (Eq. 2.11)

Using the above equation, we can calculate the change in concentration  $(c_i - c_f)$  which is ultimately equal to the "swallowed" concentration. This value can then be used to work out the moles of Au(III) encapsulated  $(n_i - n_f)$  within the modified dendrimer.

$$c_i - c_f = \frac{(n_i - n_f)}{v}$$
....(Eq. 2.12)

Where v = 3.5 mL (volume of sample cuvette) and  $c_i$  and  $c_f$  can be calculated using the equation of the graph in Figure 2.19.

 $n_{"swallowed"} = c_{"swallowed"} \cdot (0.0035 L)$  (Eq. 2.13)

$$n_{"swallowed"} / n_{micelle} = no. of Au(III) ions per micelle_____(Eq. 2.14)$$

Using these derived equations, the number of Au(III) ions encapsulated within the modified dendrimer can be theoretically elucidated. However, with our current system, this was not achieved due to the concentration requirement of Au(III) in the experiment. For this experiment to be successful, the system must be diluted even further. Thus the incubation time between the additions of metal portions must be extended.

### 2.2.4.4.4. Theoretical Calculation of Maximum Au loading

It was particularly challenging to pinpoint the endpoint of the Au(III)/modified dendrimer titration. For this reason, the theoretical maximum Au loading was estimated using the volume of a sphere and determining the maximum volume occupied by the modified dendrimer. This value represents the maximum space or volume (nm<sup>3</sup>) which can contain the Au(III) ions in the modified dendrimer by way of the encapsulation process. Determining the volume of an individual Au atom, we can divide the entire volume of the system using the maximum radius which includes the peripheral alkyl arms as seen in Figure 2.20 below and represented by r<sub>1</sub>. It should be noted that the volume determined by using the value of r<sub>1</sub> would give the absolute maximum volume representing the interior of the modified dendrimer. It is more likely that the void space would be represent by  $r_2$  as a sizeable portion of the alkyl chains are predicted to be solvated by the organic solvent (CHCl<sub>3</sub>). Although one should not make speculative assumptions, only the value of  $r_2$  could be found in literature where it featured in a Ph.D. dissertation compiled by Niu<sup>24</sup> (2003) titled "Dendrimer-encapsulated metal nanoparticles and their applications to catalysis". In the thesis, the diameter of the unmodified dendrimer (as employed in this work) was reported to be 2.4 nm, as was determined by small-angle neutron scattering (SANs). This value allowed for the calculation of the volume of the void space. Based on the calculation, the void space included the interior atoms and therefore the accumulative volumes of interior atoms, were subtracted to calculate the available void space for encapsulation. This result, in combination with the known volume of an Au atom was applied in the calculation of the likely Au loading capacity of the modified dendrimer. The interior atoms removed from the void space in the calculation (Figure 2.20) included all atoms of the unmodified dendrimer (C<sub>88</sub>H<sub>288</sub>N<sub>30</sub>). The interior atoms exclude the carbonyl moieties of the palmitoyl groups brought forth by the alkylation, because they are not included in the radius, r<sub>2</sub>, found in literature. As a result of some of the assumptions which have been made, it is acknowledged that the entire calculation carried out and typified in Figure 2.20, simply serves as a means of approximating the possible quantity of Au atoms which can be contained in the dendrimer's void.





**Figure 2.20.** Diagram showing the modified dendrimer and its maximum void space into which the Au NPs will reside upon DEN formation.

# 2.2.5. Evaporation studies

2.2.5.1. Unmodified dendrimer titrations

In this experiment,  $CoCI_2 \cdot 6H_2O$  was dried under vacuum and then weighed in preparation of an aqueous solution of the metal salt with a concentration of 0,225 mM. De-ionized H<sub>2</sub>O was transferred to the reference cuvette while the Co(II) solution was introduced into the analyte cuvette. Absorbance readings corresponding to the ligand-to-metal charge transfer (LMCT) band of Co(II)-Cl/H<sub>2</sub>O at exactly 226 nm, were captured over a period of 300 min (5 h – the anticipated time frame of the entire titration experiment) in intervals of 15 min to track the overall change to the concentration of the analyte in the analyte cuvette. This was executed to inevitably monitor the evaporation occurring during the course of these titration experiments. It was assumed that the extent of evaporation could be adequately gauged since the Beer-Lambert Law shows that the absorbance is directly proportional to the concentration of the analyte.

Therefore, over time, the absorbance should remain the same if the concentration of analyte over time does not change, unless evaporation was occurring, which would increase the concentration of the analyte, leading to an increased absorbance value for the analyte. The results of this experiment are provided in Figure 2.21. It can be deduced from the graph that the absorbance gradually increases over time ( $\Delta A_t > 0$  with t = time elapsed (0 – 300 min) from the first data reading taken at the initial start of the spectrophotometric titration ( $A_{t=0}$ ). This observed difference between the absorbance values at the specific time increments was therefore acknowledged in the processing of the spectrophotometric titrations to account for the effect of evaporation occurring over the course of the titration experiment. Overall, it can be seen that evaporation is taking place at a low rate provided by the steady gradient of the graph.



**Figure 2.21.** Graph of absorbance at  $\lambda_{max}$  (226 nm) of Co(II) in H<sub>2</sub>O as a function of time (min).

#### 2.2.5.2. Modified dendrimer titrations

Due to the volatile nature and low boiling points of methanol and chloroform (solvent system used in the modified dendrimer titrations), a UV-Vis time study was conducted in which the reference cell and a sample cell was made up of CHCl<sub>3</sub>/MeOH 4:1 v/v. Approximately 15 eq. of Co(II) was added to the sample cell and the spectrum was recorded over 10 min intervals for 6 h (projected analysis period for the modified dendrimer titrations). The study was conducted to determine whether evaporation during the titration experiments should be accounted for to prevent inaccurate endpoints being deduced.

Since for both the unmodified and modified dendrimer titrations,  $\lambda_{max}$  was established for Co(II) in H<sub>2</sub>O as well as CHCl<sub>3</sub>/MeOH 4:1 v/v, hence it was used as a reference in the respective time-dependent studies. With this said, a fixed concentration of Co(II) was prepared in CHCl<sub>3</sub>/MeOH 4:1 v/v and 3.5 mL of this solution was transferred to the sample vial referenced to the aforementioned solvent system. Absorbance values were collected over incremental time intervals where the absorbance at 663 nm for Co(II) was scrutinised to monitor the evaporation process.



**Figure 2.22.** Graph of absorbance at  $\lambda_{max}$  of Co(II) in CHCl<sub>3</sub>/MeOH 4:1 v/v as a function of time (min).

Looking at Figure 2.22, the net evaporation over the allotted time interval is illustrated by the change in absorbance denoted "B". Interestingly, there seems to be condensation taking place presumably on the lid of the cuvette. This finding is drawn from an additional change in absorbance beginning at t = 30 min and is annotated with the symbol "A" in the figure. This change in absorbance eventually returns to zero as time progresses to 300 min.

These studies provided an insight into the accuracy of the obtained data values obtained in the unmodified and modified dendrimer titrations respectively. It was therefore shown that due to the long period of the titration experiments and the necessary incubation times, the effect of evaporation becomes noticeable and should be considered when using more volatile solvents, especially when conducting a UV-Vis experiment over an extended period of time.

### 2.2.6. Summary of modified dendrimer titrations

The metal ion-loading capacities of a hydrophobically-modified G3-DAB dendrimer was determined for Cu(II), Ni(II), Co(II), Zn(II), Rh(III), Pd(II) and investigated for Au(III). The other metal ions, which were titrated against the unmodified dendrimer (but not the modified dendrimer), displayed partial solubility or were insoluble in the titration solvent required for the complete solubility of the modified dendrimer, hence were not included in this work. In successful cases, the metal ion-loading capacities were ascertained by means of UV-Vis spectrophotometric titrations. The results showed an increase in the quantity of metal ions which could be accommodated within the modified dendrimer interior in comparison to the analogous unmodified dendrimer. The endpoints for the successful spectrophotometric titrations are reported in Table 2.2.

Metal Ion	Calculated loading	Metal Ion	Calculated loading
Cu(II)	41	Fe(III)	12-16
Ni(II)	38	Pd(II)	24
Co(II)	18	Rh(III)	18
Zn(II)	10		

# 2.3. Conclusions

The individual metal ion-loading capacities of a water-soluble unmodified G3-DAB-PPI dendrimer as well as an analogous hydrophobic modified dendrimer possessing palmitoyl groups, was determined for a range of metal ions. These include Cu(II), Ni(II), Co(II), Zn(II), Cd(II), Pb(II), Ru(III), Rh(III), Pd(II), Pt(II) and Au(II). The metal ion-loading capacities were determined by means of UV-Vis spectroscopy via spectrophotometric titrations. The results showed that the loading capacity is not only dependent on the size of the metal ion, but its oxidation state, as well as the valence electronic configuration of the metal ion in question. Moreover, it was found that the unmodified dendrimer, in most cases, housed fewer metal ions in comparison to the analogous modified dendrimer. This was attributed to the improved solubility of the modified dendrimer in organic solvents. This, in effect, causes the loading

interaction to be driven by solubility differences between the hydrophilic interior of the modified dendrimer and the hydrophobic solvent as opposed to fixed stoichiometric ratios.

According to Pearson's principle of the Hard-Soft Acid-Base theory,<sup>19</sup> Cr(III) is a hard acid and is expected to coordinate strongly with the primary amines present on the periphery of the G3 DAB PPI (NH<sub>2</sub>) dendrimer. Metal ions considered to be of intermediate hard and soft acid character include Co(II), Ni(II), Cu(II) and Zn(II). The other metal ions investigated such as Ru(III), Rh(III), Pd(II), Pd(II), Pt(II) and Au(III), on the other hand, resemble more "soft" acids given their larger size and polarizability. In addition, it is known that Pt(II) and Au(III) are isoelectronic and therefore are expected to behave quite similarly. With all this said, the exact nature and mechanism of encapsulation of the metals to the interior of the modified dendrimer remains speculative.

One of the main reasons for executing these titrations was to determine the endpoint of the Au(III)/modified dendrimer titration. This was particularly important because in the work to follow, Au is the metal of choice in the fabrication of the fluorous stabilized NP catalysts to be tested in FBC. More extensive work using Au and the modified dendrimer in the production of fluorous stabilized Au NPs is provided in Chapter 3.

# 2.4. Experimental section

# 2.4.1. Chemicals and materials

G3-NH<sub>2</sub> PPI dendrimer having a diaminobutane (DAB) core was obtained from Dendritech, Inc. (Midland, MI). All metal chloride salts were purchased from Sigma Aldrich and were further dried using a vacuum pump operating at reduced pressure prior to employment. HPLC grade methanol and chloroform were purchased from EMD Chemicals Inc., and further dried using molecular sieves of the appropriate size. Prior to analyses, all metal chloride salts were dried under vacuum to ensure the correct masses were used in the preparation of their respective solutions. A sonicator was used to ensure that the metal ion solution was completely homogeneous, in instances where 'impartial solubility' was perceived. Finally, a heat gun was also used to warm up the dendrimer solution to room temperature before the required volumes were transferred to the cuvettes for analysis.

### 2.4.2. Instrumentation

All <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance spectra were obtained using a 300 MHz Varian VNMRS, 400 MHz Varian Unity Inova or 600 MHz Varian Unity Inova NMR instrument using deuterated solvents. Chemical shifts ( $\delta$ ) were recorded using the residual solvent peak or external reference (TMS). All chemical shifts are reported in parts per million and all spectra were obtained at 25 °C. Data was processed using Mestrenova file version 10.0.2. Infrared spectra were readily obtained using a Nicolet Avatar 330 FT-IR instrument as neat samples (ATR), in some spectral collection cases, where necessary, the instrument was flushed with N<sub>2</sub> (g) to eliminate the manifestation of CO<sub>2</sub>. UV-Vis absorbance spectra were obtained at 25  $\pm$  0.1 °C using quartz cells and the various dendrimer-metal ion solutions were obtained on a Shimadzu UV-1800 UV-Vis spectrophotometer in the wavelength range of 190-850 nm, unless stated otherwise. ICP-OES analysis was further employed to ascertain the intended concentrations of the solutions employed in the spectrophotometric titrations.

### 2.4.3. Synthesis of modified G3-DAB-PPI dendrimer

Palmitoyl chloride (0.880 g, 3.20 mmol, 18 eq.) in THF (5 mL) and triethylamine (3 mL) was added to a solution of G3 DAB-dendr-(NH<sub>2</sub>)<sub>16</sub> (0.299 g, 0.177 mmol) in THF (15 mL). The resulting mixture was stirred at room temperature (controlled at 25 °C) for 72 h. After the reaction, the solvent was removed in vacuo to afford a pale orange oil which was dissolved in diethyl ether (30 mL) and refluxed for approximately 30 min. Thereafter, the solution was filtered, and the pale orange residue was isolated and dissolved in a 50 mL solution of Na<sub>2</sub>CO<sub>3</sub> (0.09 M) which was then refluxed for approximately 16 h. The solution was then filtered affording a yellow-orange residue which was dried under vacuum yielding the product as a light orange-yellow powder (0.554 g, 74.2 %). The powder was further dried overnight in an oven operating at 50 °C to ensure that the product had no or very little entrapped water prior to weighing for solution preparation. FT-IR (ATR):  $v_{C=0}$  (secondary. amide) 1635.1 cm<sup>-1</sup>;  $v_{C-H}$  (saturated) 2915.2 cm<sup>-1</sup>;  $v_{N-H}$  (amide-stretch) 3292,3 cm<sup>-1</sup>;  $v_{N-H}$  (bend) 1550.5 cm<sup>-1</sup>. <sup>1</sup>H NMR (600 MHz, CDCl3)  $\delta$  3.41–3.08 (m, CH<sub>2</sub>NHCO), 2.76–2.35 (m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>C, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCO), 2.19 (t, NHCOCH<sub>2</sub>), 1.76-1.50 (m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHCO), 0.88 (t, CH<sub>3</sub>).

### 2.4.4. Synthesis of bis(acetonitrile)PdCl<sub>2</sub>



Scheme 2.5. Preparation of bis(acetonitrile) PdCl<sub>2</sub>.

Due to the poor solubility of PdCl<sub>2</sub> in the solvent systems required for the modified dendrimer spectrophotometric titrations, a reaction was executed to convert the palladium(II) chloride to a palladium(II) complex exhibiting improved and complete solubility in CHCl<sub>3</sub>. This was accomplished by reaction of PdCl<sub>2</sub> with acetonitrile at reflux temperatures for approximately 4 h. Due to the colossal excess of acetonitrile in the system, the reaction is able to achieve a 100 percent yield, whereby confirmation of the final complex is identified by colour change and exhibiting complete solubility in pure CHCl<sub>3</sub>.

# 2.4.5. Unmodified dendrimer UV-Vis spectrophotometric titrations

The spectrophotometric titrations with respect to metal ions loaded onto the unmodified G3-DAB-PPI-NH<sub>2</sub> dendrimer were performed using a Shimadzu UV-1800 Spectrophotometer which was temperature-regulated at 25 °C  $\pm$  0.1 during all analyses. The method followed, involved adapting a procedure for these titrations proposed by Niu et. al.<sup>7</sup> A dendrimer solution containing the unmodified dendrimer having a concentration of exactly 0,015 mM was prepared with deionised water as the solvent. Precisely 20 µL (serving as 2 eq. additions of the metal ion to 1 eq. of the unmodified dendrimer) of the metal chloride solution was pipetted into each cuvette between triplicate runs. After each portion of the metal solution was added, the cuvettes were stirred and mixed thoroughly using a Pasteur pipette. After about 10+ minutes, the UV spectra of the samples were recorded. In the primitive stages of the investigation, the reference cell housed the solvent of the unmodified dendrimer solution and was thus made up to 4 mL with deionized H<sub>2</sub>O. Prior to adding portions of the metal ions solution, each of the sample cuvettes contained 3 mL of the unmodified dendrimer solution (Figure 2.23). This strategy resulted in issues pertaining to the addition of the metal ion

solutions because, in instances, the unmodified dendrimer absorption (without subtraction) overlapped/interfered with the absorption at  $\lambda_{max}$  for the metal ion being analysed.



**Figure 2.23.** Arrangement of cuvettes (prior to addition of the investigated metal ion) used in the titrations, where the reference cuvette = R and sample cuvettes = S. Final titrations, where R = unmodified dendrimer solution (4 mL) and S = dendrimer solution (3 mL).

This obstacle prompted an adjustment to the experimental setup, which entailed changing the composition of the reference cell to that of the unmodified dendrimer solution so as to subtract absorptions delivered by the free unmodified dendrimer. It must be pointed out that, in some cases, there were not enough data points acquired for the absorption values at  $\lambda_{max}$  associated with the metal ion. This was due to such a high concentration of the metal ion being detected which ultimately delivered absorption values of 4, which was the maximum allowed for the instrument. In these cases, the unmodified dendrimer and metal solutions were diluted two times. This was executed for the Au(III)/unmodified dendrimer titration and is required for the Ru(III)/unmodified dendrimer titration. For the unmodified dendrimer titrations, each trial was performed in triplicate. Precisely 3 mL of an aqueous solution of the G3-NH<sub>2</sub> PPI dendrimer (5 × 10<sup>-5</sup> M) was transferred to a sample cuvette. The reference cuvette comprised the same solution so that the absorbance associated with the metal ion could be easily distinguished. In addition, this prevented convolution of the absorbance resulting from the free dendrimer with that of the metal ion. The absorbance values associated with the wavelengths 190 – 850 nm were scrutinised or scanned in most instances.

# 2.4.6. Modified dendrimer UV-Vis spectrophotometric titrations

The experimental procedure closely shadowed the method proposed by Niu and co-workers<sup>7</sup> (2003). Firstly, a solution of the modified dendrimer is prepared in a CHCl<sub>3</sub>/MeOH (4:1 v/v) solvent system and secondly, a solution of the appropriate metal chloride salt is prepared in a CHCl<sub>3</sub>/MeOH (4:1 v/v) solvent system. Precisely 20  $\mu$ L (serving as 2 eq. additions of the metal

ion to 1 eq. of the modified dendrimer) of the metal chloride solution was pipetted into each cuvette between triplicate runs. Subsequently, the cuvettes were stirred and mixed using a Pasteur pipette. After an incubation period of about 10 minutes, the UV spectra of the samples were recorded.

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# **Chapter 3**

Synthesis & characterization of fluorous-stabilized Au NPs via a modified dendrimer-template approach

## 3.1. Introduction

Dendrimers are particularly suitable for accommodating metal nanoparticles for the following reasons: Firstly, the dendrimer templates themselves are of uniform composition and structure and therefore they afford well-defined nanoparticle reproductions.<sup>1</sup> Secondly, the nanoparticles are stabilized by encapsulation within the dendrimer and therefore they should not agglomerate.<sup>1,2</sup> Lastly, the terminal groups present on the dendrimer periphery may be modified to control the solubility of the hybrid nanocomposite.

The template synthesis strategy for preparing metal nanoclusters within dendrimer "nanoreactors" was first described by Crooks and colleagues<sup>2</sup> (1998). The group successfully prepared Cu clusters in the interior of a poly(amidoamine) (PAMAM) Starburst dendrimer. In their work, they show that the nanoclusters are generated by sequestering metal ions within dendrimers, followed by subsequent chemical reduction to yield the corresponding zerovalent metal nanoparticle. At around the same time, Esumi et al.<sup>3</sup> (2000) independently investigated the preparation of Au NPs in toluene and chloroform using an organic-soluble, modified G4 PAMAM dendrimer having an ethylenediamine core. The dendrimer was hydrophobically modified by reacting the peripheral functional groups with 1,2-epoxydodecane in MeOH. Using the dendrimer as a template, the group was able to produce Au DENs. This was confirmed by UV-Vis spectroscopy and TEM. During their study they noted that the Au NPs were not very stable in toluene or chloroform as the particles began to precipitate just one day after their respective preparation. Later, a separate account on making Au NPs in organic solvents was described by Niu et al.<sup>4</sup> (2003). In their investigation, they demonstrated that instead of relying on specific interactions between metal ions and intra-dendrimer functional groups for metalion encapsulation, a dendrimer micelle could act as a superior template for the control of NP growth, size and shape. With this said, it has been observed in this research that the solubility of HAuCl<sub>4</sub>·xH<sub>2</sub>O is significantly enhanced in chloroform upon addition of G3 DAB-PPI dendrimer, possessing peripheral alkyl chains or (palmitoyl)<sub>16</sub> groups. This brings forth the notion that Au(III) ions are being encapsulated within the hydrophilic interior of the amphiphilic dendrimer micelle (Figure 3.1) and thereby facilitating its solubility in chloroform.

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**Figure 3.1.** Chemical structure of the amphiphilic dendrimer micelle (also referred to as the modified dendrimer) in this work.

The very first preparation of fluorocarbon-stabilized Au NPs was circulated by Kimizuka and colleagues<sup>5</sup> (2001). The group produced fluorous nanoparticles in ethanol by reduction of AuCl<sub>4</sub><sup>-</sup> with NaBH<sub>4</sub> in the presence of fluorinated alkane thiols as stabilizers. The two stabilizers employed were 1H,1H,2H,2H-perfluorodecanethiol and 1H,1H,2H,2H-perfluorooctanethiol. The material obtained precipitated from the solution, because of the poor solvating properties of ethanol for these systems. The Au NPs had a mean diameter of around 2.5 nm and these systems were essentially insoluble in several organic solvents while they were readily soluble in fluorocarbons.<sup>6</sup> This makes them ideal candidates for fluorous biphasic catalysis reactions. Other reports in literature make use of modified Brust methods for producing fluorinated Au NPs, but none of these reports describe the preparation of Au DENs and their successive extraction from an organic phase into a fluorous solvent.

The desire to produce fluorous-stabilized Au NPs which are dispersed in a fluorous solvent is due to their intended application in fluorous biphasic catalysis. The principle behind this catalyst recovery strategy is based on the properties of the fluorous solvent and the organic substrate or solvent (if not executed neat). In order to exploit the monophasic nature of the biphasic system at elevated temperature, it is necessary for the catalyst to be dissolved in this fluorous solvent so that after the catalytic reaction, cooling of the system will permit it to become biphasic again. This allows for the fluorous catalyst will exhibit exclusive solubility in the fluorous solvent.

For the endeavoured preparation of fluorous-stabilized Au NPs, it would be convenient to first prepare dendrimer-encapsulated Au NPs in chloroform before subsequent extraction into the fluorous phase facilitated by fluorous-soluble ligand coordination and stabilization of the Au NPs. In this way, it was hoped that the size of nanoparticles formed could be controlled by the modified dendrimer due to its uniform chemical formula and defined cavity size. Thereafter, the fluorous-soluble ligand may coordinate to the nanoparticle surface making it soluble in the respective fluorous solvents and hence be extracted.



**Scheme 3.1.** Extraction step (**A**) Upon contact of the organic phase and fluorous phase at the beginning of the extraction step. (**B**) During stirring of the two phases over the permitted extraction time. (**C**) After the permitted extraction time with the two layers being separated.

The objectives of this research were to arrive at a reproducible strategy to tailor Au nanoparticles in organic solvents and then subsequently extract them using fluorous-soluble ligands into one of two fluorous solvents, perfluoromethylcyclohexane (**S1**) and perfluoro-1,3-dimethylperfluorocyclohexane (**S2**), respectively. The reasons for the choice of **S1** were due to its popularity in literature, known miscibility data<sup>7</sup> with CHCl<sub>3</sub>, acceptable boiling point and lower cost compared to other commercially available solvents. Similarly, perfluoro-1,3-dimethylperfluorocyclohexane was chosen as a result of its similarity to **S1** and its slight dissimilarity with the inclusion of an additional perfluoro-methyl (CF<sub>3</sub>) group. Therefore, with this slight structural discrepancy, a rational comparison could be made between the two solvents and their performance in the synthesis and application of the endeavoured fluorous-stabilized Au NPs. The ligands investigated possessed fluorous-soluble ponytails which usually facilitated solubility in **S1** or **S2**.

In this chapter, we describe (i) the development and optimization of a synthetic strategy to afford fluorous-stabilized Au NPs. This strategy first entails the synthesis of organic-soluble DENs (by a reduction step) and then subsequent extraction of these DENs from the organic phase into the chosen fluorous solvent (facilitated by an appropriate fluorous ligand). In this work, two ligands (L1 and L2) provided success in the extraction step as described by our experimental conditions, while other attempts using L3 and L4 were made but to no avail. Even so, the creative attempts to produce Au NPs stabilized by these other ligands are reported in the hopes of serving some sort of platform for future experiments. Moreover, other strategies which were attempted to afford fluorous-stabilized Au NPs by way of this method are also offered and explained. The chapter will also (ii) discuss the synthesis and characterization of fluorous-stabilized Au NPs successfully generated using this strategy. The characterization techniques employed in this regard and used to arrive at some of the optimal experimental conditions, included UV-Vis spectroscopy, TEM and ICP-OES. Finally, we (iii) discuss the reproducibility of this strategy and (iv) some storage considerations learned by way of stability studies which entailed monitoring these fluorous-stabilized Au NPs over time.

### 3.2. Results and discussion

### 3.2.1. General synthetic approach

The preparation of the fluorous-stabilized Au NPs was executed by (i) preparing the organicsoluble Au DENs (Scheme 3.2) and (ii) subsequent extraction of the Au DENs from the organic phase into the fluorous phase to afford fluorous-stabilized Au NPs (Scheme 3.3). The general method adopted to initially produce organic-soluble Au DENs prior to the extraction step shadowed the methods of Niu et al.<sup>4</sup> (2003) with slight adjustments to the experimental procedures, which will be discussed herein. Initial attempts at the reduction step made use of an NaBH<sub>4</sub> solution consisting of MeOH (200  $\mu$ L). This, however, delivered issues with the subsequent extraction. Since the MeOH is miscible with CHCl<sub>3</sub> at room temperature, the NaBH<sub>4</sub> molecules are in the same phase as the Au DENs during this method of reduction. This allows for quicker reduction using the MeOH system, however, after the reduction step, components remain in one phase and it is often laborious to separate the components from the solvent system. In addition, the extraction step becomes more complicated due to several other ions or chemical species hindering coordination of the perfluoro ligand to active sites on the surface of the Au nanoparticle, making it more difficult to extract.

With this said, the optimized synthetic procedure arrived at, entails the use of an aqueous solution of NaBH<sub>4</sub> which may contact the organic phase to yield a biphasic system. This allows

for the facile removal of unwanted components by use of a separating funnel, to separate the two independent phases, after the reduction step. The optimized method of reduction employed in this investigation is shown by a typical representative trial experiment.



Scheme 3.2. Illustration of the general reduction step with modified dendrimer/Au = 13 eq.

It is important to note that in this investigation, the desire to achieve complete reduction was paramount in order to sequester as many Au NPs into the fluorous phase as part of the optimization of the synthetic process. Furthermore, complete reduction was crucial to providing a reliable ICP-OES measurement to determine the quantity of Au in its nanoparticle NP form. In other words, if there were unreduced Au(III) species in the sample, the ICP-OES value would not be reliable for the purpose of this work. The extent of reduction could, to some degree, be monitored visually through a perceived colour transition from yellow to dark purpleviolet as shown in Figure 3.2. Routine analysis by UV-Vis spectroscopy was carried out on the organic phase immediately before reduction as well as on the successively reduced organic phase (in contact with the aqueous phase directly after the reduction). The wavelengths analysed in this step were, in most instances, between the spectral window 190 and 900 nm, with special scrutiny of the band at 330 nm corresponding to the Ligand-Metal Charge Transfer (LMCT) band of Au(III) in CHCl<sub>3</sub> in the presence of modified-dendrimer. The presence of organic-soluble Au NPs was visualised by monitoring the surface plasmon resonance (SPR) at around 550 nm (after the permitted reduction time). Two samples which showed complete and incomplete reduction are illustrated in Figure 3.3 to visualise the extent of reduction. In some instances where leaching into the aqueous phase was suspected due to a colour change, the aqueous phase was also analysed by UV-Vis spectroscopy to gain insight into the reduction process.



**Figure 3.2.** Reduction step for **JHM01**: 1:4 (Au/NaBH<sub>4</sub>), 250 rpm, 10 min, 25 °C. Image 1-24: Successive images captured within the first 27 seconds of the reduction step. Image 25-30: captured successively every 10 seconds thereafter. Image 31-44: captured every 30 seconds until the end of the reduction period (image 44 indicates the final image at the end of stirring).



**Figure 3.3.** UV-Vis analysis before and after reduction with **JHM02** showing complete reduction and **JHM03** showing incomplete reduction. Sampling of UV-Vis was done by extracting 20 µL of the organic phase and diluting to 3.5 mL with CHCl<sub>3</sub> and referenced to CHCl<sub>3</sub>. \***JHM02**: Au:NaBH<sub>4</sub> 1:8 stirring speed of 250 rpm for 30 min.\*\***JHM03**: 1 Au: 4 NaBH<sub>4</sub>, stirring speed of 250 rpm for 15 min.



Directly after the reduction, the reduced organic phase and the aqueous phase are separated using a separating funnel and the reduced organic phase is contacted with a fluorous solution containing the appropriate ligand (L1 or L2) in either S1 or S2 (Figure 3.4). The organic phase and fluorous phase are stirred at 650 rpm with the temperature controlled usually at 25 °C for a period between 24 and 48 h.



Figure 3.4. Chemical structures of the perfluoro-ligands, L1 and L2, and fluorous solvents, S1 and S2.

Due to the price of the commercially-available fluorous solvents, it was obligatory to use as little of the solvent as possible, and for this reason it was decided that the fluorous phase for each extraction trial would have a total volume of 2 mL. The corresponding organic phase was thus chosen to have the same total volume of 2 mL. It is important to note that these scaled-down volumes are much smaller than the total volumes used by others in literature to prepare organic-soluble Au DENs such as with the work of Crooks<sup>4</sup> et al. (2003), Garcia-Martinez<sup>8</sup> et al. (2004), and Cloete<sup>9</sup> et al. (2017). As a result, specialised and smaller experimental glassware was employed.




Directly after the extraction step, the two layers are separated into three vials so that there is no portion of the fluorous phase in the organic phase sample, and vice versa. This strategy was prompted by an EDX analysis of the organic phase (after the extraction step in a trial experiment) which showed the presence of fluorine atoms.

The extent of the extraction of the organic-soluble Au DENs from the chloroform layer into the fluorous phase was monitored by UV-Vis spectroscopy. Specialised cuvettes (having a minimum required volume of 700 µL) were employed to use solvent sparingly during analysis by UV-Vis spectroscopy. The presence of fluorous-stabilized Au NPs was evidenced by the surface plasmon resonance (SPR) at ~ 550 nm. A representative experiment (Scheme 3.3) taken from this work, illustrates the ideal extraction of organic-soluble Au DENs from the modified dendrimer in the CHCl<sub>3</sub> (top layer/phase in Scheme 3.3) into the fluorous phase (bottom phase/layer in Scheme 3.3). In this regard, special attention was paid to the fluorous phase for a colour change from clear to dark red/ brown (as demonstrated in Scheme 3.3). This colour change, in combination with UV-Vis spectroscopy, was routinely employed for trial experiments. Additional characterization by TEM and ICP-OES was usually limited to successful systems having improved extraction results such as for JHM01, JHM04, JHM05 and JHM06, which were prepared but not tested in catalysis and JHM13, JHM14, JHM15 and JHM16 which were assessed in the biphasic catalytic oxidation of 1-octene shown in Chapter 5. Details relating to these samples are reported in Table 3.1.

**Table 3.1.** Sample information pertaining to the fluorous-stabilized Au NPs produced by the micelle-template strategy.

Catalyst system	Ligand	Solvent	Au: L	Particle diameter
JHM01	L1	S1	1 : 0.56	9.5 ± 1.1
JHM04	L1	S2	1 : 0.56	6.8 ± 1.5
JHM05	L2	S1	1:1	11.8 ± 3.8
JHM06	L2	S1	1:1	12.7 ± 3.5
JHM13	L2	S1	1 : 0.28	4.1 ± 3.8
JHM14	L2	S1	1 : 0.56	3.6 ± 2.7
JHM15	L2	S1	1 : 1.12	$3.8 \pm 2.8$
JHM16	L2	S1	1 : 2.24	3.2 ± 2.8

\*JHM05 and JHM06 differ as JHM05 was executed under inert conditions. \*JHM01 and JHM04 also differ by their Au: NaBH<sub>4</sub> ratio which was employed during the 10 min reduction where JHM01 = 1:4 and JHM04 = 1:8 (Au: NaBH<sub>4</sub>).

### 3.2.2. Optimization of synthetic variables

### 3.2.2.1. Reductive formation of Au DENs towards enhanced extraction

In the chloroform solution (2 mL) which is comprised of the modified dendrimer (0.01 g), we add a weighed quantity of HAuCl<sub>4</sub> xH<sub>2</sub>O (as yellow-orange crystals) into the solution in its solid form. It has been found that in the absence of micelle, the gold is impartially soluble in the chloroform, however in the presence of micelle, the gold gradually dissolves. The organic solution is permitted to stir for about 45 min before the initiation of the reduction step. This additional stirring time allows for the Au(III) ions to be encapsulated by the modified dendrimer as a result of solubility differences between the organic solvent and hydrophilic interior cavity. Following this encapsulation period, NaBH<sub>4</sub> is weighed into a sample vial using an analytical balance and then 2 mL of H<sub>2</sub>O is added to it, to afford a NaBH<sub>4</sub> aqueous solution. The concentration of this solution is dependent on the desired ratio of Au: NaBH<sub>4</sub> required for the experiment. The rapid dissolution and reaction of NaBH<sub>4</sub> with water is accounted for by immediately transferring this solution by means of a micropipette onto the organic phase. The biphasic mixture is stirred for a particular time interval (permitted extraction time) whereby the phases are immediately isolated using a separating funnel. The temperature of the extraction process is controlled using a temperature probe connected to a hot plate, while additional monitoring of the temperature is achieved by means of a thermometer submerged in the oil bath.

### 3.2.2.1.1. Au: modified dendrimer ratio

Increasing the Au: modified-dendrimer ratio to 55 eq. did not appear to be successful in the collective experiments executed using this ratio. Numerous issues arose, one of which included solubility problems in the organic phase, which becomes more pronounced with the quantity of Au required in the system. The concentration of micelle is already low, as it is barely detected by UV-Vis spectroscopy, any further dilution of the system will make analysis by UV-Vis spectroscopy more difficult.

It was not possible to compare with Au<sub>101</sub> because the quantity of Au required in the system would not make it homogeneous due to the high concentration of gold required to meet the ratio of 1 mol of micelle to 101 mol of Au. Subsequently with an increased Au amount, the required quantity of NaBH<sub>4</sub> becomes inexplicitly higher and thus the reduction becomes too

vigorous (uncontrolled growth), resulting in agglomeration. Consequently, no extraction is observed into the fluorous phase due to less passivated sites on the Au nanoparticle. This makes it more challenging for the ligand to successfully coordinate to and stabilize the Au nanoparticle which usually promotes phase transfer.

It was found that by increasing the equivalents of Au: modified dendrimer, the subsequent quantity of NaBH<sub>4</sub> which was required for the experiment was too high for the small glass vessel used in the system because of the build up of pressure in the small head space. The reduction was found to become increasingly stringent with increasing quantities of NaBH<sub>4</sub>. Furthermore, the poor extraction established from the experiment can be attributed to the outcome of the reduction step. It has been commonly seen that there is significant leaching into the aqueous phase during the reduction step (A in Figure 3.5), and this was most notable when 1: 4 Au:NaBH<sub>4</sub> was used (JHM07). In addition, during the extraction step, substantial agglomeration occurred on the sides of the reaction vessel and some reduced Au NPs precipitated. When Au:NaBH<sub>4</sub> 1: 16 was used, complete reduction was observed yet no extraction was seen because of substantial agglomeration. Finally, with a ratio of Au:NaBH<sub>4</sub> of 1: 8, the reduction step still appeared quite stringent, and the system appeared too concentrated for controlled growth of Au<sub>55</sub> NPs.



**Figure 3.5**. (**A**) Issues with leaching into the aqueous phase when increasing the ratio of Au: micelle from 13 eq. to 55 eq. (**A**) UV-Vis spectrum and image of the aqueous phase shown for **JHM07** 1: 4 (Au: NaBH<sub>4</sub>). (**B**) Solubility issues due to the higher amount of Au required. (**C**) Vigorous reduction conditions causing agglomeration and precipitation.

# 3.2.2.1.2. Au: NaBH<sub>4</sub> ratio, reduction time and stirring speed

At first, it was thought that for every Au(III) ion, three equivalents of NaBH<sub>4</sub> would be necessary to achieve complete reduction of Au ions in the chloroform solution. This notion arose from stoichiometric reasoning, however, the ratio which was initially chosen was 1: 4 Au:NaBH<sub>4</sub> so that NaBH<sub>4</sub> would be in excess, and this would account for some loss of NaBH<sub>4</sub> upon reaction with H<sub>2</sub>O. The results of the extraction shown for a 10 min reduction time are illustrated in Figure 3.6, with the image on the left corresponding to the use of **S1** and the image on the right, **S2**, respectively. This ratio, although not sufficiently high to result in complete reduction according to UV-Vis spectroscopy, afforded the best subsequent extraction results where it can be seen in the Figure 3.6 that there are exceptional levels of extraction with both solvents.





**Figure 3.6.** Left: Before and after extraction incorporating L1 in S1, with reduction parameters: Au:NaBH<sub>4</sub> = 1:4; t = 10 min; T = 25°C stirring rate = 250 rpm. Right: Before and after extraction incorporating L1 in S2, with reduction parameters: Au:NaBH<sub>4</sub> = 1:4; t = 10 min; ; T = 25°C; stirring rate = 250 rpm. S1 = perfluoromethylcyclohexane; S2 = perfluoro-1,3-dimethylcyclohexane.

To assess whether a longer reduction time was necessary given the same ratio, additional experiments were executed with the only variable change being an extension of the reduction time from 10 min to 15 min. An additional experiment employed 30 min (JHM02) while another experiment (JHM08) was only allowed a 90 s reduction time. The UV-Vis results from this experiment, are typified in the graph depicted in Figure 3.7.

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**Figure 3.7**. UV-Vis spectra afforded after reduction of 90 s (**JHM08**) - green; 10 min (**JHM09**) - orange; 15 min (**JHM10**) - blue and 30 min (**JHM11**) - red.

It can be observed from the UV-Vis spectra above, that as expected a 90 s reduction is far too short to allow for complete reduction of Au ions with the currently employed Au: NaBH<sub>4</sub> ratio. It could be said that this ratio is too small to allow for complete reduction of Au ions to Au NPs, irrespective of the time employed. Looking at JHM09 it is clear that the system has the smallest, and broadest, SPR band which may insinuate that the Au NPs are smaller but with a wide size distribution. Strangely, the reduction time of 30 min leaves more Au ions than for 90 seconds of reduction and it can thus be acknowledged that the time permitted for the reduction plays an important role in the size of the Au NPs formed and the quantity of Au ions reduced. There are many factors which would influence the final sizes of NPs achieved after the 10 min reduction step. Some of these include the stirring speed, slight changes in temperature, the use of different stir bars, the number of nucleation sites available for agglomeration and so forth. The colour of the solution over the course of reduction can provide a much better idea of the state of the NPs prior to the reduction. This is because the wavelength of light responsible for the perceived colour is related to the shape and sizes of the Au NPs generated. If one could distinguish the optimal colour of the reduced organic phase signifying small NPs, it would allow one to end the reduction when the NPs are small enough to be extracted and not after they are too big.

The subsequent extraction results using L1 in a 1:1 eq. of Au: L showed that 1: 4 (Au:NaBH<sub>4</sub>) equivalents was optimal given that JHM09 showed the presence of an SPR band in the fluorous phase. The other experiments such as JHM02 and JHM12 having Au:NaBH<sub>4</sub> 1: 8 and 1: 16, respectively both showed poor extraction results with JHM02 showing a smaller SPR band in the fluorous phase while for JHM12, no SPR band was seen. It must be noted that in the system, a ratio higher than 1: 4 showed signs of increased agglomeration in and on the walls of the reaction vessel due to the more "violent" reduction step which makes the nanoparticles too big resulting in low or no extraction.



**Figure 3.8**. UV-Vis spectra of the reduction of 10 min with varying ratios of Au:NaBH<sub>4</sub> with 1:4 (**JHM09** – yellow); 1:8 (**JHM02** – blue); 1:16 (**JHM12** – red). Spectra recorded as solid lines represent the spectra recorded before reduction. Spectra recorded as dashed lines indicate the spectra after the 10 min reduction time.

# 3.2.2.2. Extraction into fluorous phase

It has been shown in other accounts<sup>10</sup> and additionally proven herein, that the subsequent extraction of metal nanoparticles is highly dependent on the outcome of the reduction step. The ligand's ability to pull the nanoparticle into the fluorous phase, depends on the characteristics of the Au nanoparticle obtained after reduction. For example, a larger nanoparticle will have fewer sites for coordination by the ligand while the reverse is true for smaller nanoparticles. Additionally, the presence of other components such as anions or weakly coordinating ligands or solvent molecules surrounding the nanoparticle may to some degree hinder the coordination of the selected ligand to the NP surface. Within the extraction

step, there are a number of parameters which may be tweaked to provide higher levels of extraction. For example; extraction time, stirring speed, extraction temperature and ligand concentration. Furthermore, it has been reported by Van den Broeke<sup>7</sup> (2002) and co-workers that the combination of CHCl<sub>3</sub> and perfluoromethylcyclohexane (**S1**) is immiscible at room temperature, but the solvent system becomes completely miscible and monophasic at approximately 50 °C. For this reason, it was postulated that the extraction process could be enhanced by elevating the temperature to this monophasic point and could thus allow for efficient mixing of the two phases and hence increased interaction allowing successful coordination of the perfluoro ligands to the Au DENs. The notion of this monophasic phenomenon can be visualised in Figure 3.9 adapted from this work.



**Figure 3.9**. Left: Biphasic mixture with top layer = reduced organic phase and bottom layer = fluorous phase. Middle: Initiation of stirring at 650 rpm and heating to 50 °C. Right: Monophasic solution develops at the elevated temperature.

This increase in temperature did not assist the extraction but instead increased the likelihood of either going backwards (oxidation of Au NPs) if there was not complete reduction, or alternatively, increase the likelihood of agglomeration due to increased kinetic energy of the components in the system. From these findings, it was established that for the remainder of the investigation, 25 °C would be employed as the controlled temperature during the extraction duration. Hence, the true benefits of fluorous solvents and their monophasic properties would unravel in the catalysis section (Chapter 5) of this dissertation. Through a study of the extraction step, it was found that temperature played a significant role in the preparation of Au NPs. A result which was not anticipated, showed that an increase in the extraction temperature actually led to the 'reverse NP synthesis" ie: oxidation of the Au NPs to their corresponding Au ions. In an experiment, a synthesis reactor (Monowave 50) obtained from the chemical company, *Anton Paar*, was used to identify whether we could optimize the extraction time by exploiting Rauolt's Law tailored to solvent extraction, where an increase in temperature would lead to an exponential decrease in the necessary reaction time. The experiment was executed immediately after isolating the organic phase after the reduction step. This was achieved by

transferring exactly 2 mL of perfluoromethylcyclohexane (**S1**) to tris[4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl) phenyl]phosphine (**L1**) (0.01674 g, 0.02363 mmol, 0.56 eq. to Au). The method of extraction involved a stirring rate of 650 rpm (to mimic the other systems which have been endeavoured) and a 5 min ramp time from 25 °C to 80 °C. At this regulated temperature, the extraction was carried out for 40 min, thereafter, the system experienced a cooling period of 5 min to ambient temperature. The pressure-temperature vs time plot for the extraction process, as provided by the instrument, is illustrated in Figure 3.11.



Reduction

Monowave 50

**Figure 3.10**. Left: Captured images of the organic solution before and after the reduction. Right: Before and after the attempted extraction of the Au DENs (top phase) into the fluorous phase (bottom phase).



**Figure 3.11**. Left: Temperature (°C) and pressure (mbar) vs time plot for the attempted extraction of Au<sub>13</sub> using the *Monowave 50* synthesis reactor. Right: UV-Vis spectrum after the heating process.

Further work is required to explore the mechanism of this phenomenon. At this stage, a simple hypothesis has been offered which entails the Au DENs being oxidised by each other, given that they are potential oxidation catalysts (Scheme 3.4). A similar observation by Goulet et al.<sup>10</sup> (2012) reported the rapid, stoichiometric oxidation of gold nanoparticles by tetraalkylammonium and tetraalkylphosphonium Au(III) complexes. These results suggest that the unreduced Au(III) ions in association with the modified dendrimer may promote the oxidation of Au NPs.



Scheme 3.4. Mechanistic hypothesis as a plausible explanation for the observed phenomena.

To identify the oxidant, it was thought that the fluorous ligand/solvent system in question may be responsible for playing a role as an oxidant. For this reason, an experiment was conducted which entailed heating only the reduced organic solution under the same extraction conditions and heating parameters.



**Figure 3.12**. Left: Captured images of the organic solution before the heating procedure (left) and after the heating procedure (right) in the *Monowave 50* synthesis reactor. Right: UV-Vis spectra associated with the Au<sub>13</sub> DENs experiment.

The results showed that the fluorous ligand and solvent play no role in the observed phenomena and they can be dismissed as being necessary for the oxidation to occur. It is therefore concluded that for these results, a small quantity of molecular oxygen in the air and

the elevated temperature may just be necessary for the oxidation of the Au DENs to their corresponding Au ions.

Other experiments involving an increase in temperature during the extraction process were usually problematic given the small volumes used in the experiments. In the experiments which involved the extraction of systems with Au: modified dendrimer = 55:1, a number of experimental issues ensued. Firstly, due to the larger size of the Au DENs formed in the organic phase (Figure 3.13), coordination of fluorous ligands and hence extraction becomes more futile. Comparing the extraction of Au(13) to Au(55), more agglomeration is seen in the system with the higher ratio. No SPR band has been found in the fluorous phase for Au NPs with ratios of 55 eq.



**Figure 3.13**. TEM images of the organic phase after extraction at a scale of 50 nm. Left: Au DENs produced using 1:13 (modified dendrimer/Au). Right: Au DENs produced using 1:55 (modified dendrimer/Au).

An initially implemented stirring speed of 250 rpm was found to be too low to cause any significant extraction of the Au DENs into the fluorous phase, since at this rate the two phases simply do not interact sufficiently, and for this reason, the stirring rate was elevated to 650 rpm, where a much better mixing of the two phases was observed. The stirring rate of 650 rpm was thus used for all subsequent extractions. The extraction time was found to be a crucial parameter in ensuring optimal extraction into the fluorous phase. Too short a time leads to no extraction and too long may lead to increased agglomeration of the Au DENs in the organic phase, which also leads to minimal extraction. For this reason, after a number of different extraction times, it was found that 24 h was suitable for the current system. This observation is shown in the effect of a 24 h vs a 48 h extraction period, by monitoring the fluorous phase at the respective time intervals via UV-Vis spectroscopy. It can be seen that there is little to no

change in the UV-Vis spectra, specifically for the fluorous phases (green lines in Figure 3.14) suggesting no further extraction is transpiring between 24 h and 48 h.



**Figure 3.14**. UV-Vis spectra associated with the time intervals of 24 and 48 h over the course of extraction step.

It was also seen that there is a relationship between the quantity of ligand used and the average particle diameter obtained in the fluorous phase. This relationship held for the series however, **JHM14** (0.56 eq.) and **JHM15** (1.12 eq.) showed very similar sizes and size distributions, suggesting that between these two ratios there is almost no change to the particle diameter. **JHM13** providing the largest Au NP and largest associated size distributions is the result of using less ligand which compromises the stability of the NP. This leads to less stabilization and therefore heightened agglomeration. Lastly, it was seen that increasing the quantity of **L2** to 2.24 eq. in relation to Au results in a slight decrease in the average particle diameter, although the size distribution remains similar, if not the same. This suggests that for the purposes of producing smaller and therefore more active NP catalysts, a ratio of 1: 2.24 Au: **L2** is most viable.





**Scheme 3.5**. The relationship between the quantity of ligand **L2** used in the NP preparation versus particle diameter (nm).

Mindful of the aforementioned, it was observed that employing less ligand in relation to Au results in more staining of the glass reaction vessel (indicative of an unstable colloid). This observation has been recognised in literature by a few groups, however, the precise explanation of this phenomenon is debatable. It may also be possible that any solvent residue on the glass walls of the reaction vessel may act as nucleation sites resulting in the purple staining of the glass walls. Even so, the staining of glass was found to be more severe when decreasing the quantity of **L2** in relation to Au. This may mean that less stabilization of the Au NPs results in more staining and therefore the staining of glass is indicative of unstable sols.



**Figure 3.15**. Image depicting the staining of the glassware which becomes more pronounced when decreasing the quantity of stabilizing agent.

#### 3.2.3. Synthesis & characterization of fluorous-stabilized Au NPs

Once we had established the optimal reaction conditions, a small library of fluorous-stabilized Au<sub>13</sub> NPs were successfully prepared with varying fluorous ligands (L1 or L2) in varying fluorous solvents, S1 or S2 by way of this modified dendrimer-template strategy. The general synthesis of these systems is exemplified in Scheme 3.6. The fluorous-stabilized Au NPs corresponding to the experiments JHM01, JHM04, JHM05 and JHM06 were successfully produced with the colour of the fluorous phase in each case suggesting the presence of fluorous-soluble Au NPs. These systems were additionally characterized by UV-Vis spectroscopy, TEM and ICP-OES analysis before their individual assessment as catalysts in the biphasic oxidative transformation of 1-octene (Chapter 5).



Scheme 3.6. Overall synthesis of fluorous-stabilized Au NPs using the micelle-template strategy for the formation of Au DENs and subsequent extraction into the fluorous phase. (i) HAuCl<sub>4</sub> (13 eq. to modified dendrimer), stirring at 200 rpm for ~ 1 h. (ii) JHM01; JHM04; JHM13 – JHM16: 1:4 (Au/NaBH<sub>4</sub>), 250 rpm, 10 min, 25 °C; JHM05; JHM06: 1:8 (Au/NaBH<sub>4</sub>), 250 rpm, 10 min, 25 °C. (iii) JHM01: L1 in S1 (1:1 Au/L), 650 rpm, 48 h, 25 °C. JHM04: L1 in S2 (1:1 Au/L), 650 rpm, 48 h, 25 °C. JHM05: L2 in S1 (1:1 Au/L), N<sub>2</sub>, 650 rpm, 48 h, 25 °C. JHM06: L2 in S1 (1:1 Au/L), 650 rpm, 24 h, 45 °C. JHM16: L2 in S1 (0.28 eq. – 2.24 eq.), 650 rpm, 24 h, 25 °C.

#### 3.2.3.1. Characterization via UV-Vis spectroscopy

The extraction of the Au DENs from the organic phase into the fluorous phase was confirmed by UV-Vis spectroscopy (Figure 3.16). In this regard, the fluorous phase was monitored for the presence of the surface plasmon resonance (SPR) band occurring between 500 and 600 nm, which is confirmation of Au NPs, or more specifically, indicative of fluorous-stabilized Au NPs within the fluorous solvent.



Figure 3.16. Left: UV-Vis spectra of the fluorous phases of JHM01, JHM04, JHM05 and JHM06. Right: UV-Vis spectra of the fluorous phases of JHM13-JHM16.

All samples showed the SPR band between 500 and 600 nm, proving the presence of fluorousstabilized Au NPs. JHM06 showed the most pronounced and broad SPR band of the four samples and this was attributed to its corresponding size and size distribution obtained from TEM analysis, 12.7 nm, the biggest of the fluorous-stabilized Au NPs. The tall absorbances in the range of 270 - 290 nm with respect to JHM01 and JHM04 arise from the conjugation in the perfluoro phosphine ligand (L1). The lower absorbance values in the same range for JHM05 and JHM06 correspond to presence of the perfluoro-thiol ligand (L2). The low absorbance values corresponding to JHM05 are most-likely due to dilution errors in the sample cuvette solution. This leads to the SPR band almost being undetectable in the UV-Vis spectrum. It can also be seen that with L1 and S1, the SPR band appears at a lower wavelength with increasing particle size. The same phenomenon can be reported for JHM05 and JHM06 which were prepared using L2 in S1. For the samples, JHM13- JHM16 involving different ratios of Au: L2, the SPR band is smallest for JHM16 which is the smallest of these NP systems and is consistent with using more ligand and forming small Au NPs. On the other hand, JHM13 using 0.28 eq. of L2 provides the largest and broadest SPR band indicative of the larger particle diameter and size distributions associated with this sample in comparison to others in this series. It is also possible that less ligand will allow more of the surface of the Au NPs to be exposed which gives rise to a more pronounced SPR band.

# 3.2.3.2. Characterization by TEM

The fluorous samples which showed an SPR and clear colour change in the fluorous phase were analyzed by TEM. The particle diameters and size distributions are reported in Table 3.2 with the associate histograms and TEM images of the samples shown in the figures below.

Table 3.2.	Particle sizes and size distributions of the samples determined by TEM.

Sample	Particle sizes (nm)	Sample	Particle sizes (nm)
JHM01	9.5 ± 1.1	JHM13	3.8 ± 2.8
JHM04	6.8 ± 1.5	JHM14	4.1 ± 3.8
JHM05	11.8 ± 3.8	JHM15	3.6 ± 2.7
JHM06	12.7 ± 3.5	JHM16	3.2 ± 2.8





**Figure 3.17**. Left: Histogram for sample **JHM01** depicting the size and size distribution. Right: TEM images of **JHM01** (**L1** and **S1**) at varying magnification. Right:



**Figure 3.18**. Left: Histogram for sample **JHM04** depicting the size and size distribution. Right: TEM images of **JHM04** (**L1** and **S2**) at varying magnification.

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**Figure 3.19**. Left: Histogram for sample **JHM05** depicting the size and size distribution. Right: TEM images of **JHM05** (**L2** and **S1**) at varying magnification.



**Figure 3.20**. Left: Histogram for sample **JHM06** depicting the size and size distribution. Right: TEM images of **JHM06** (**L2** and **S1**) at varying magnification.



**Figure 3.21**. Left: Histogram for sample **JHM13** depicting the size and size distribution. Histogram illustrating the sizes and size distributions of NPs measured from the TEM images of **JHM15**. \*Total count = 300. \*\*80:20 small (diameter ~ 2 nm):big (greater than 2 nm). Right TEM images of **JHM13** (**L2** and **S1**) at varying magnification.



**Figure 3.22**. Left: Histogram for sample **JHM14** depicting the size and size distribution. Right: TEM images of **JHM14** (L2 and S1) at varying magnification.



**Figure 3.23**. Left: Histogram for sample **JHM15** depicting the size and size distribution. Histogram illustrating the sizes and size distributions of NPs measured from the TEM images of **JHM15**. \*Total count = 300. \*\*80:20 small (diameter ~ 2 nm):big (greater than 2 nm). Right: TEM images of **JHM15** (**L2** and **S1**) at varying magnification.



**Figure 3.24**. Left: Histogram for sample **JHM16** depicting the size and size distribution. Right: TEM images of **JHM16** (**L2** and **S1**) at varying magnification.

## 3.2.3.3. Characterization by ICP-OES

JHM01, JHM04, JHM05 and JHM06 were characterized using ICP-OES with the experimental concentrations reported in Table 3.3. These four samples showed lower concentration values for Au in comparison to JHM13 – JHM16. These values should not be compared, as the former four samples were diluted by different amounts. The samples JHM13 – JHM16 showed a higher quantity of Au in the samples compared to the other systems. It was found for this series of samples, that although the quantity of Au was kept the same for each experiment, the quantity of ligand L2 was adjusted to give the different ratios of Au: L2. Sample JHM13 (employing 0.28 eq. of L2) showed the lowest concentration of Au in the fluorous phase since less ligand was available to stabilize the Au, facilitating phase transfer. Similar concentrations of Au were obtained when using 0.56 eq. of L2 (JHM14) and 1.12 eq. of L2 (JHM15) as reported in Table 3.3. Finally, the main reason for analysis with ICP-OES was to determine the Au concentration (Ci) in each sample so that the same metal loading (C<sub>i</sub>) could be employed in the catalyst evaluation and therefore the catalysts could be effectively compared.

Sample	Concentration (mol/mL)	Sample	Concentration (mol/mL)
JHM01	1.505 × 10 <sup>-7</sup>	JHM13	2.568 × 10 <sup>-6</sup>
JHM04	1.808 × 10 <sup>-7</sup>	JHM14	4.542 × 10 <sup>-6</sup>
JHM05	1.552 × 10 <sup>-7</sup>	JHM15	4.498 × 10⁻ <sup>6</sup>
JHM06	1.326 × 10 <sup>-7</sup>	JHM16	2.745 × 10 <sup>-6</sup>

**Table 3.3**. Concentrations (mol/mL) of the respective samples derived from the micelle-template method, derived from ICP-OES.

# 3.2.4. Reproducibility studies

The reproducibility of the fluorous-stabilized Au NPs produced by this DEN-MPC method was assessed by executing the same experiments over different time intervals. Of course, in order to be successful in terms of synthetic reproducibility; their sizes, shapes, dispersity and various surface characteristics must be reproduced. Using the available instruments at our disposal, the reproducibility of a catalyst system employing **L1** was assessed. It was found that when using Au:NaBH<sub>4</sub> of 1:4 and using **L1**, the synthesis of fluorous-stabilized Au NPs was basically guaranteed. This is demonstrated for the repeat experiments of **JHM17** (Figure 3.25 top) which

included **JHM18** and **JHM01** (Figure 3.25 bottom) (all of which were carried out using exactly the same experimental conditions). It is clear from these experiments that all were successful and show a colour change to the fluorous phase after the extraction and an SPR band in the UV-Vis spectra for the fluorous phase.



**Figure 3.25**. UV-Vis spectra of the fluorous and organic phases after extraction shown for attempted reproducibility of **JHM17** and images of the fluorous phases. Top: **JHM17**. Bottom left: **JHM18**. Bottom right: **JHM01**.

Unfortunately, only the TEM results of **JHM01** were attained. Therefore we were unable to assess the actual extent of reproducibility of these NPs, however, what can be said is that fluorous-stabilized Au NPs incorporating **L1** and dispersed in the appropriate fluorous solvent, can be successfully produced each time the experimental conditions of these experiments (**JHM17**, **JHM18** and **JHM01**) are used.

## 3.3. Conclusions

A micelle-template strategy was employed to generate fluorous-stabilized Au NPs by first loading Au ions onto a G3-DAB PPI dendrimer micelle modified with palmitoyl groups on the periphery. Subsequent reduction of the solution afforded organic-soluble Au DENs which was confirmed both by UV-Vis spectroscopy and TEM in some instances. These Au DENs were extracted into a fluorous phase (S1 or S2) with the use of fluorous ligands (L1- L4). This extraction step was found to be the most challenging step and much effort was placed on optimizing the extent of extraction into the fluorous phase. In instances incorporating high Au quantities, little or no extraction was observed, which was attributed to the larger size of the Au DENs making phase transfer more unlikely.

Over the course of this investigation, many synthetic parameters were optimized, and these adjustments were then exploited to produce other Au NP systems. In the end, eight unique, spherical, monodisperse and small fluorous-stabilized Au NPs were generated and characterized by UV-Vis spectroscopy, TEM and ICP-OES analysis. It was found that the position of the SPR band in the UV-Vis spectrum correlated with particle size, and for the respective ligand systems; the higher the wavelength of the SPR, the smaller the Au NP size. It was also found that the position of the SPR band is related to the ligand as well as the fluorous solvent used. Moreover, the use of perfluoro-1,3-dimethylperfluorocyclohexane (S2) smaller fluorous-stabilized Au NPs in comparison to the provides use of perfluoromethylcyclohexane (S1) in the extraction step. It appears that the use of L1 provides smaller Au NPs in comparison to the use of L2 which may be the result of solubility differences of the fluorous solvent, ligand size and shape and the different heteroatom involved in coordination to the Au NP.

Due to the large number of steps involved and the associated parameters which must be strictly controlled, these systems tend to be to somewhat reproducible as demonstrated for the repeat experiments, **JHM17**, **JHM18**, and **JHM01**, respectively, all of which show a colour change to the fluorous phase after the extraction and an SPR band in the UV-Vis spectra for the fluorous phase. In terms of reproducing the sizes of the fluorous-stabilized Au NPs, this would require more sophisticated instruments and reactors to control as many parameters as possible during each step of the preparation. In addition, it may be useful to identify a routine method of gauging the sizes of the organic soluble DENs before extraction to ensure the sizes of the Au DENs in the organic phase are consistent among duplicate experiments. This would further eliminate discrepancies between repeat experiments (in terms of the sizes of organic DENs afforded after reduction), and thereby remove additional steps which would add to

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experimental error between duplicate runs and make the reproducibility of such systems more achievable. This may aid in terms of replicating characteristics particularly important to their catalytic performance, such as their particle sizes, shapes, dispersity and so forth.

# 3.4. Experimental section

# 3.4.1. Chemicals and materials

All chemicals were used as received from various chemical-producing companies and used without further purification. Perfluoromethylcyclohexane (**S1**); Perfluoro-1,3-dimethyl cyclohexane (**S2**); Tris[4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl) phenyl]phosphine (**L1**) and 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-decanethiol (**L2**) were attained from Sigma-Aldrich, with **L2** being stored under nitrogen conditions in a glove box. HAuCl<sub>4</sub>·*x*H<sub>2</sub>O was acquired in its anhydrous form from Sigma-Aldrich and Merck. NaBH<sub>4</sub> pellets were obtained from Sigma-Aldrich. De-ionised H<sub>2</sub>O was attained in a laboratory in our building through distillation. MeOH and chloroform was obtained from Sigma-Aldrich.

# 3.4.2. Instrumentation

UV-Vis absorbance spectra were obtained using a GBC 920 UV-VIS spectrometer and quartz cuvettes having a path length of 1.00 cm. The spectrum of either chloroform or water was used as the background depending on the solution being analyzed. TEM images were obtained using a FEI/Tecnai T20 TEM operating at 200 kV at UWC. Samples were prepared by dropwise addition of the sample onto a carbon coated copper grid. Average nanoparticle sizes and size distributions were determined from the TEM images using ImageJ image processing software and plotted using Origin 2019 Software. Au concentrations were measured on a Spectro Acros ICP-OES spectrometer at Stellenbosch University. DLS analysis was executed using the LightsizerTM 500 Particle Analyzer equipped with Kalliope™ software. A Monowave 50 conventional microwave oven was used in some experimental instances in the synthesis optimization. Microwave reactions made use of the Monowave 450: Automated Microwave-assisted Extraction instrument operating at 850 W unpulsed microwave output power with setting and parameter adjustments were executed on the interface screen of the instrument.

#### 3.4.3. Preparation of samples for UV-Vis analysis

Analysis of the organic phase was routinely executed with the reference cuvette being made up to 3.5 mL with CHCl<sub>3</sub> while the sample cuvette most commonly housed 3.48 mL of CHCl<sub>3</sub> before the addition of 20  $\mu$ L of the organic phase sample to be analysed. Similarly, the analysis of the aqueous phase samples was executed using deionised H<sub>2</sub>O (3.5 mL) in the reference cuvette and in the sample cuvette. The concentration of the sample introduced into the sample cuvette was not a concern since the only necessity was for the analyte to be above the limit of quantification, therefore depending on the experiment, volumes ranging from 20 – 200 uL of the respective aqueous phases were added to the sample cuvette prior to analysis.

### 3.4.4. Preparation of JHM01

G3 DAB-PPI dendrimer micelle, (0.01 g, 0.00182 mmol, 1 eq.) was dissolved in CHCl<sub>3</sub> (2 mL) in a round-bottom flask. Once dissolved, HAuCl<sub>4</sub>·xH<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was introduced into the micelle solution in its solid form by rinsing it off the glass weighing boat using the micelle solution and an additional portion of  $CHCl_3$  (1 mL). This was meticulously performed using a Pasteur pipette. The solution was stirred at 200 rpm for approximately an hour at 25°C, the solution exhibited a very pale-yellow colour. Ensuing this, a separate solution of NaBH<sub>4</sub> (0.0036 g, 0.09452 mmol, 4 eq. to Au) in H<sub>2</sub>O (2 mL) was prepared. Directly after the NaBH<sub>4</sub> was weighed into a 50 mL beaker, H<sub>2</sub>O was added, and the solution was immediately transferred to the micelle/Au solution (after complete dissolution of the NaBH<sub>4</sub>  $\approx$ 45 s). The system was now comprised of two layers, where the bottom layer was the organic phase and the top layer was the aqueous NaBH<sub>4</sub> solution. Reduction was permitted to proceed for exactly 10 minutes at a stirring speed of 250 rpm at 25 °C. The reduction did not appear to be instantaneous, but instead the organic phase transitioned to a red-purple colour over the course of the reduction period. Thereafter, the two phases were separated, and the organic phase was isolated and implemented in the extraction procedure. The extraction of the Au nanoparticles commenced immediately after isolating the organic phase after the reduction step. This was achieved by transferring exactly 2 mL of perfluoromethylcyclohexane (S1) housing tris[4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl) phenyl]phosphine, L1 (0.01674 g, 0.02363 mmol, 1 eq. to Au). The extraction proceeded for exactly 48 h at a stirring speed of 650 rpm. The elevated stirring rate allowed for the efficient mixing of the two phases.

### 3.4.5. Preparation of JHM04

G3-DAB PPI dendrimer micelle (0.0101 g, 0.00182 mmol, 1 eq.) was weighed onto a glass weighing boat and transferred to a small round-bottom flask (rbf) equipped with a magnetic stirrer bar. Thereafter, HAuCl<sub>4</sub>·xH<sub>2</sub>O (0.0081 g, 0.02386 mmol, 13 eq.) was weighed onto a glass weighing boat and transferred into the same rbf while CHCl<sub>3</sub> (2 mL) was used to wash the reagent from the weighing boat into the rbf. The subsequent reaction mixture was sufficiently stirred to ensure everything was completely dissolved (about an hour). At the end of this period, the stirring speed was set to 250 rpm, and NaBH<sub>4</sub> (0.0072 g, 0.18904 mmol, 8 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly transferred in one portion to the rbf and the resulting biphasic solution was stirred for 10 min at 25 °C. Subsequently, the stirring was stopped, and the two phases were isolated, where the organic phase was contacted with a fluorous phase. The fluorous phase consisted of a homogeneous solution of tris[4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl) phenyl]phosphine L1 (0.0169 g, 0.02363 mmol, 1 eq. to Au) in perfluoro-1,3- dimethyl cyclohexane (S2) (2 mL) which was prepared prior to the reduction step. The organic and fluorous phase in the new rbf was stirred at 650 rpm at 25 °C for precisely 48 h.

### 3.4.6. Preparation of JHM05

G3-DAB PPI dendrimer micelle (0.0101 g, 0.00182 mmol, 1 eq.) was weighed onto a glass weighing boat and transferred to a small rbf equipped with a magnetic stirrer bar. Thereafter, HAuCl<sub>4</sub>·xH2O (0.0081 g, 0.02386 mmol, 13 eq.) was weighed onto a glass weighing boat and transferred into the same rbf while CHCl<sub>3</sub> (2 mL) was used to wash the reagent from the weighing boat into the rbf. The subsequent reaction mixture was sufficiently stirred to ensure everything was completely dissolved (about an hour). A 20 µL sample of this solution was analysed by UV-Vis spectroscopy. At the end of this period, the stirring speed was set to 250 rpm, and NaBH<sub>4</sub> (0.0072 g, 0.18904 mmol, 8 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly transferred in one portion to the rbf and the resulting biphasic solution was stirred for 15 min at 25 °C inside a fume hood. Subsequently, the stirring was stopped, and a 20 uL sample of this solution was analysed by UV-Vis spectroscopy to monitor the extent of reduction. The two phases were isolated using a separating funnel. The reduced organic solution was transferred directly from the separating funnel into a Schlenk tube equipped with a magnetic stir bar. This solution was then flushed with N2 gas. L2 (6.76 µL, 0.02386 mmol, 1 eq. to Au) was measured into a sample vial using a micropipette in the glovebox. A septum was then fitted onto the sample vial and further sealed using parafilm. The sample vial containing L2 was then taken

out of the glove box and placed in the fridge before use. At this time, N<sub>2</sub> was bubbled through perfluoromethylcyclohexane (**S1**) (2 mL) in a separate sample vial fitted with a septum. After about 20 min, a syringe was flushed with N<sub>2</sub> and then used to transfer the solvent to the sample vial containing **L2**, forming the fluorous solution, which was then transferred using the flushed syringe through the septum of the Schlenk tube, affording a biphasic solution of the reduced organic solution and fluorous solution. The resulting biphasic mixture was stirred at 25 °C for 48 h at 650 rpm within the fume hood.

### 3.4.7. Preparation of **JHM06**

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was weighed directly into a sample vial. G3-DAB PPI dendrimer micelle (0.0102 g, 0.00185 mmol, 1 eq.) was weighed onto a glass weighing-boat and transferred (by rinsing) into the same sample vial by means of a micropipette with CHCl<sub>3</sub> (2 mL). The resulting solution was stirred until the system appeared homogeneous, then the contents of the sample vial (including the magnetic stir bar) were transferred into a round-bottom flask, where stirring was continued for about 40 min. At this stage, a 50  $\mu$ L sample was taken for UV-Vis spectroscopy. Subsequently, NaBH<sub>4</sub> (0.0071 g, 0.1890 mmol, 8 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly pipetted into the solution. The biphasic reduction step was permitted to commence for exactly 10 min at 25 °C, at which point, stirring was stopped and the round-bottom flask was hoisted from the oil bath. The magnetic stir bar was removed from the biphasic mixture and then the mixture was decanted into a separating funnel. A 50  $\mu$ L sample of the reduced organic phase was isolated for UV-Vis spectroscopy. The reduced organic phase was then contacted with a fluorous phase containing L2 (1 eq. to Au) in perfluoromethylcyclohexane – S1 (2 mL) and the extraction proceeded at 45 °C for 24 h at 650 rpm.

### 3.4.8. Preparation of JHM13

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was weighed directly into a sample vial. G3-DAB PPI dendrimer micelle (0.0102 g, 0.00185 mmol, 1 eq.) was weighed onto a glass weighing-boat and transferred (by rinsing) into the same sample vial by means of a micropipette with CHCl<sub>3</sub> (3 mL). The resulting solution was stirred until the system appeared homogeneous, then the contents of the sample vial (including the magnetic stir bar) were transferred into a round-bottom flask, where stirring was continued for about an hour. At this stage, a 50 µL sample was taken for UV-Vis spectroscopy. Subsequently, NaBH<sub>4</sub> (0.0036 g,

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0.0945 mmol, 4 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly pipetted into the solution. The biphasic reduction step was permitted to commence for exactly 10 min at 25 °C. At the end of the reduction step, the stirring was stopped, and the round-bottom flask was hoisted from the oil bath. The magnetic stir bar was removed from the biphasic mixture and then the mixture was decanted into a separating funnel to isolate the two phases. The reduced organic phase was diluted with an additional 2 mL of CHCl<sub>3</sub> and then contacted with a fluorous phase containing L2 (0.28 eq. to Au – 1.5  $\mu$ L) in perfluoromethylcyclohexane – S1 (2 mL) and the extraction proceeded at 25 °C for 24 h at 650 rpm.

#### 3.4.9. Preparation of JHM14

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was weighed directly into a sample vial. G3-DAB PPI dendrimer micelle (0,0102 g, 0,00185 mmol, 1 eq.) was weighed onto a glass weighing-boat and transferred (by rinsing) into the same sample vial by means of a micropipette with CHCl<sub>3</sub> (3 mL). The resulting solution was stirred until the system appeared homogeneous, then the contents of the sample vial (including the magnetic stir bar) were transferred into a round-bottom flask, where stirring was continued for about an hour. At this stage, a 50  $\mu$ L sample was taken for UV-Vis spectroscopy. Subsequently, NaBH<sub>4</sub> (0.0036 g, 0.0945 mmol, 4 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly pipetted into the solution. The biphasic reduction step was permitted to commence for exactly 10 min at 25 °C. At the end of the reduction step, the stirring was stopped and the round-bottom flask was hoisted from the oil bath. The magnetic stir bar was removed from the biphasic mixture and then the mixture was decanted into a separating funnel to isolate the two phases. The reduced organic phase was diluted with an additional 2 mL of CHCl<sub>3</sub> and then contacted with a fluorous phase containing **L2** (0.56 eq. to Au – 3.2  $\mu$ L) in perfluoro methylcyclohexane – **S1** (2 mL) and the extraction proceeded at 25 °C for 24 h at 650 rpm.

### 3.4.10. Preparation of JHM15

HAuCl<sub>4</sub>·xH<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was weighed directly into a sample vial. G3-DAB PPI dendrimer micelle (0.0102 g, 0.00185 mmol, 1 eq.) was weighed onto a glass weighing-boat and transferred (by rinsing) into the same sample vial by means of a micropipette with CHCl<sub>3</sub> (3 mL). The resulting solution was stirred until the system appeared homogeneous, then the contents of the sample vial (including the magnetic stir bar) were transferred into a round-bottom flask, where stirring was continued for about an hour. At this

stage, a 50 µL sample was taken for UV-Vis spectroscopy. Subsequently, NaBH<sub>4</sub> (0.0036 g, 0.0945 mmol, 4 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly pipetted into the solution. The biphasic reduction step was permitted to commence for exactly 10 min at 25 °C. At the end of the reduction step, the stirring was stopped, and the round-bottom flask was hoisted from the oil bath. The magnetic stir bar was removed from the biphasic mixture and then the mixture was decanted into a separating funnel to isolate the two phases. The reduced organic phase was diluted with an additional 2 mL of CHCl<sub>3</sub> and then contacted with a fluorous phase containing **L2** (1.12 eq. to Au – 6.51 uL) in perfluoromethylcyclohexane – **S1** (2 mL) and the extraction proceeded at 25 °C for 24 h at 650 rpm.

# 3.4.11. Preparation of JHM16

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0.0080 g, 0.02363 mmol, 13 eq.) was weighed directly into a sample vial. G3-DAB PPI dendrimer micelle (0.0102 g, 0.00185 mmol, 1 eq.) was weighed onto a glass weighing-boat and transferred (by rinsing) into the same sample vial by means of a micropipette with CHCl<sub>3</sub> (3 mL). The resulting solution was stirred until the system appeared homogeneous, then the contents of the sample vial (including the magnetic stir bar) were transferred into a round-bottom flask, where stirring was continued for about an hour. At this stage, a 50  $\mu$ L sample was taken for UV-Vis spectroscopy. Subsequently, NaBH<sub>4</sub> (0.0036 g, 0.0945 mmol, 4 eq. to Au) in distilled H<sub>2</sub>O (2 mL) was swiftly pipetted into the solution. The biphasic reduction step was permitted to commence for exactly 10 min at 25 °C. At the end of the reduction step, the stirring was stopped, and the round-bottom flask was hoisted from the oil bath. The magnetic stir bar was removed from the biphasic mixture and then the mixture was decanted into a separating funnel to isolate the two phases. The reduced organic phase was diluted with an additional 2 mL of CHCl<sub>3</sub> and then contacted with a fluorous phase containing **L2** (1.12 eq. to Au – 13 uL) in perfluoro methylcyclohexane – **S1** (2 mL) and the extraction proceeded at 25 °C for 24 h at 650 rpm.

# 3.4.12. Preparation of ICP-OES samples

Sampling was executed by sonicating each sample and making the total volume of the fluorous solution 2 mL by pipetting the correct quantity of the fluorous solvent for the respective solution and then all systems were made up to 2 mL using perfluoromethylcyclohexane, except for **JHM04** which required perfluoro-1,3-dimethylcyclohexane. An O-ring was fitted onto a sample vial by first measuring 2 mL of distilled H<sub>2</sub>O into the seven respective sample vials and securing

the O-ring at the mark corresponding to exactly 2 mL of the distilled H<sub>2</sub>O. Once the O-ring was secure and the meniscus marked at 2 mL, the respective fluorous solutions were sonicated and then transferred to the respective sample vials (from their original sample vials) with the aid of a micro-pipette. Since each sample had been acquired over different periods of time, each sample initially possessed unique volumes. Each sample was then made up to the 2 mL mark using the appropriate solvent (S1 or S2). From each of the 2 mL solutions, exactly 200 µL of each solution was sampled into another sample vial. The solvent in each case was allowed to evaporate over time by making holes with the tip of a syringe in the lid of the sample vial. Once completely evaporated, a portion of concentrated HNO<sub>3</sub> was then added to each sample vial to digest the Au from the organic components (ligand). Due to the fragility of sample vials, especially under the corrosive effects of acid and heat, they were placed within Teflon beakers and heated to about 30 °C so that they could then be directly transferred to the Teflon beakers and the HNO<sub>3</sub> driven off with heat generated from the hot plate. Next, a fresh batch of agua regia was prepared and small portions were transferred to each sample vial to digest the residue remaining in the vials. The aqua regia in the sample vials was then decanted into the respective Teflon beaker and heated slowly to drive off the liquid, leaving behind solid residue which was dissolved in 0.1 M HNO<sub>3</sub> solution (10 mL) (using 1 M HNO<sub>3</sub> standard solution obtained from Science World) and transferred to the respective ICP tubes for analysis.

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# **Chapter 4**

# Preparation & characterization of fluorous-stabilized Au NPs using a biphasic reduction approach via the direct method

# 4.1. Introduction

The development and recognition of fluorinated nanoparticles is presently ascending across several fields of nanotechnology. The synthetic approaches evolved over time, from the use of perfluorinated alkanethiols and perfluorinated arylthiols to amphiphilic fluorinated thiols capable of ensuring solubility in conventional organic solvents and water. Zuckerman<sup>1</sup> et al. (1989) have reported on perfluorotributylamine-stabilized gold NPs formed by metal atom vapor deposition. Early attempts at synthesizing nanoparticles using heavily fluorinated alkanethiols, typically the commercially available 1H,1H,2H,2H-perfluoro alkanethiols (compounds **1** and **2** in Figure 4.1) and pentafluorobenzenethiol (compound **3** in Figure 4.1), led to materials of very low solubility that proved to be difficult to purify and characterize. Amongst these early attempts, the first preparation of perfluorinated silver nanoparticles was reported by Korgel<sup>2</sup> et al. (2000) by using **1** (Figure 4.1) in a modified Brust-Schiffrin procedure.

In the same year, Chechik<sup>3</sup> (2000) produced fluorous-soluble palladium nanoparticles using a dendrimer-template strategy. They fashioned fluorous-soluble dendrimers by reacting the terminal amine groups of the dendrimer, with perfluoropolyethers. Further work on palladium NPs was conducted by Moreno-Mañas<sup>4</sup> and colleagues (2001), they showed (using TEM) that 1,5-Bis(4,4'-bis(perfluorooctyl)phenyl)-1,4-pentadien-3-one stabilizes palladium(0) nanoparticles formed in the reduction of palladium dichloride with methanol. The palladium colloids exhibited solubility in perfluorinated solvents.

Around the same time, the first report on the synthesis of gold nanoparticles, which were dispersible in fluorocarbon media, was published by Kimizuka<sup>5</sup> et al. (2001). The synthetic procedure entailed using a single phase (ethanol) method in the presence of 1 or 2 (Figure 4.1). Fluorocarbon-stabilized gold nanoparticles were obtained by reduction of HAuCl<sub>4</sub> in ethanol (5.0 mM, 30 mL) in the presence of the stabilizer (1 eq.). Aqueous NaBH<sub>4</sub> was added dropwise to the above solution, and the single-phase mixture was vigorously stirred for 3 h. The yellow AuCl<sub>4</sub>- solution immediately turned brown by the addition of NaBH<sub>4</sub>, indicating the progress of reduction. After the stirring was stopped, a black precipitate separated from the collected filtration colourless supernatants and was by over а

poly(tetrafluoroethylene)membrane filter (pore size =  $0.2 \mu m$ ). The non-coordinating stabilizer molecules were completely removed by washing the filtrate several times with water, hot CHCl<sub>3</sub> and hot ethanol under ultrasonication. The absence of the unbound stabilizer molecules was established by repeated elemental analyses, which arrived at constant values after these ultrasonic purification steps. The nanoparticles had a mean diameter of 2.4 - 2.6 nm and these systems were essentially insoluble in several organic solvents while they were readily soluble in fluorocarbons including hexafluorobenzene, perfluorobutylalkyl ethers and in HCFC225® (a mixture of CF<sub>3</sub>CF<sub>2</sub>CCl<sub>2</sub>H and CF<sub>2</sub>CICF<sub>2</sub>CCIFH).



**Figure 4.1.** Structures of the (quasi) perfluorinated alkanethiols and aryl thiols used in the early synthesis of fluorinated gold nanoparticles (adapted from ref 5).

Lee et al.<sup>6</sup> (2002) reported on the uniform preparation of perfluorocarboxylate-stabilized silver nanoparticles via the thermal decomposition of layered silver perfluorocarboxylates  $(AgCO_2(CF_2)_nCF_3, n = 10, 12, 14 and 16)$ . A few years later, Voggu et al.<sup>7</sup> (2006) were able to prepare Au NPs soluble in fluorous medium (perfluorohexane) by two phase-transfer approaches. The first approach involved transferring gold nanoparticles from an aqueous solution to a fluorous phase, while the second entailed the phase transfer of Au NPs soluble in toluene, to a fluorous phase. In the first strategy, the group first prepared a hydrosol containing gold nanoparticles by the reduction of chloroaurate ions (0.55 mL of 25 mM aqueous solution) with partially hydrolysed tetrakis(hydroxymethyl)phosphonium chloride (THPC).8 Subsequently, a solution of 10 µL of heptadecafluoro-1-decanthiol (HDFD) in 25 mL of perfluorohexane was added at room temperature, followed by 30 mL of concentrated HCI under vigorous stirring. Within 5 min, gold nanoparticles transferred completely from the aqueous medium to the perfluorohexane medium, as was observed by the complete transfer of colour across the interface, as shown in Figure 4.2(a) - left. In Figure 4.2(b) - left, the TEM images of the Au NPs from perfluorohexane solution revealed the particles had an average diameter close to 3 nm. The associated UV-Vis spectrum (Figure 4.2(c) - left) in perfluorohexane showed the characteristic plasmon band at 520 nm.

The second approach demonstrated by the group entailed the phase transfer of Au NPs from toluene to the fluorous phase. In this synthetic strategy, gold nanoparticles were initially transferred from the aqueous medium to the toluene medium by following the literature procedure developed by Brust et al.<sup>8</sup> (1994), but with the use of the fluorous thiol as the phase transfer agent. 10  $\mu$ L of HDFD in 20 mL of perfluorohexane was contacted with 10 mL of the thiolated gold sol in toluene under vigorous stirring. Within 5 min, the thiolated gold nanoparticles were completely extracted into the perfluorohexane medium, as can be seen from Figure 4.2(a) - right. The UV-Vis absorption spectra of the gold nanoparticles in toluene and perfluorohexane are shown in Figure 4.2(b) - right, with the absorption maximum in the fluorous solvent being blue shifted compared to that in toluene, due to the lower refractive index of perfluorohexane.



**Figure 4.2.** Images adapted from the work of Voggu et al.<sup>7</sup> (2006). Left: (a) Photograph showing transfer of gold nanoparticles (colour) from an aqueous medium to the fluorous medium. (b) TEM image with a size distribution histogram as an inset of  $\sim$ 3 nm gold nanoparticles. (c) UV-vis absorption spectrum of  $\sim$ 3 nm gold nanoparticles in fluorous medium. Right: (a) Photograph showing the transfer of gold nanoparticles from toluene to the fluorous medium. (b) UV-Vis spectra of the gold nanoparticles in toluene and in perfluorohexane.

Other early examples of perfluorinated nanoparticles of smaller size, comprising of 44 - 75 gold atoms in their core, were reported by Dass et al.<sup>9</sup> (2008). These nanoparticles were much smaller than those reported by Kimizuka et al.<sup>5</sup> (2001) and were prepared by two different synthetic methods: (i) the reaction of compound **1** (Figure 4.1) with HAuCl<sub>4</sub> in a typical Brust–Schiffrin procedure and (ii) by reaction of the molecularly precise gold cluster Au<sub>55</sub>(PPh<sub>3</sub>)Cl<sub>6</sub> with pentafluorobenzenethiol **3** (Figure 4.1). MALDI-MS, thermogravimetric analysis and XPS results from the study, showed that the Brust synthesis product is a mixture of 8.5 kDa (Au<sub>44</sub>) and 14 kDa (Au<sub>75</sub>) species. Ligand replacement reaction of pentafluorobenzenethiol with Au<sub>55</sub>(PPh<sub>3</sub>)<sub>12</sub>Cl<sub>6</sub> gave a polydisperse mixture of MPCs as could be inferred from the UV–Vis analysis. The structural integrity of the cluster was therefore not retained, and the reaction

occurred with the formation of larger particles, including Au<sub>75</sub> clusters, identified by voltametric techniques and signalled by its characteristic 0.74 V electrochemical energy gap. Both varieties of fluorous nanoparticles exhibited solubilities typical of perfluorinated materials.

Gentilini et al.<sup>10</sup> (2008) demonstrated the first example of water-soluble gold nanoparticles protected by a monolayer of fluorinated amphiphilic thiolates (MPC-F8-PEG). In their investigation, the thiol ligand was designed to form a perfluorinated region close to the gold surface and to have a hydrophilic portion in contact with the bulk solvent to impart solubility in water. The monolayer protected clusters were prepared, in a homogeneous phase using sodium thiolates because of the low nucleophilicity of the alpha-perfluorinated thiols, and fully characterized with <sup>1</sup>H, <sup>19</sup>F NMR spectrometry, IR and UV-Vis absorption spectroscopies, transmission electron microscopy (TEM), thermogravimetric analysis (TGA), and X-ray photoelectron spectroscopy (XPS). Au NPs with core diameters ranging from 1.6 to 2.9 nm, depending on the reaction conditions, were obtained. Water-soluble NPs (MPC-F8-PEGs) were obtained with the thiol HS-F8-PEG ending with a short poly(ethylene glycol) unit, whereas thiols with shorter PEG chains gave rise to NPs insoluble in water. The MPC-F8-PEG was also soluble in methanol, ethanol, trifluoroethanol, N,N'-dimethylformamide, DMSO, ethyl acetate, acetonitrile, acetone, dichloromethane, and chloroform. The Au nanoparticles were insoluble in diethyl ether and hydrocarbon solvents. During their investigation, the group explored different reaction conditions for the synthesis of MPC-F8-PEG. When using a molar ratio of thiol/Au = 0.7 and performing the reduction at room temperature, gold nanoparticles with an average core diameter of 2.9 nm were formed. Increasing the molar ratio to thiol/Au = 2.5 gave rise to nanoparticles with a core diameter of 1.6 nm. In another experiment, the reduction was carried out at 0 °C with NaBH<sub>4</sub>, however, it was found that the nanoparticles precipitated from the reaction solution. This phenomenon was attributed to the low solubility of the thiolate-Au(I) complex at low temperature.

With this in mind, we propose a novel strategy of producing fluorous-stabilized Au NPs which exhibit solubility in a chosen fluorous solvent (S1, S2 or S3). The preparation method entails a biphasic reduction step which proceeds by dissolving Au in the fluorous solvent (S1-S3) with the desired phosphine ligand, to initially produce an Au-L complex displaying solubility in the fluorous solvent of choice. Thereafter, an aqueous NaBH<sub>4</sub> solution with a specific ratio to Au is contacted with the fluorous phase, producing a biphasic system. The reduction is permitted to commence for a certain time interval whereby at the end of the period, the two phases are separated and analysed by UV-Vis spectroscopy and TEM. The reduction was monitored by UV-Vis spectroscopy with special attention aimed at the LMCT band of the phosphine ligand

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(L1) and the emergence of the SPR band signalling the formation of the fluorous-stabilized Au NPs. Further confirmation of the existence of fluorous-stabilized Au NPs produced via this direct method was provided by TEM and quantification of Au in the systems was carried out using ICP-OES.

In light of this, the current chapter deals with the synthesis of a library of fluorous-stabilized Au NPs via a direct approach. The nanoparticle systems synthesized possessed varying ligands and varying solvents and were successfully characterized by UV-Vis spectroscopy, TEM and ICP-OES. Moreover, reproducibility experiments were performed and the stability of a few of these fluorous Au NPs were assessed by UV-Vis spectroscopy and in some instances, TEM.



Figure 4.3. Chemical structures of the ligands (L1-L5) and solvents (S1-S3) used to produce our fluorous-stabilized Au NP systems.

## 4.2. Synthesis & characterization of Au NPs generated via the direct method

4.2.1. Optimization of synthesis

4.2.1.1. Reduction time and Au: NaBH<sub>4</sub> ratio

In the early stages of the synthetic procedure, the reduction time required for complete reduction had not been elucidated. For this reason, the first experiment (JHD01) involved a trial Au: NaBH<sub>4</sub> ratio of 1: 4, stirring rate of 250 rpm and a reduction time of 40 min. It was identified (visually) upon addition of the NaBH<sub>4</sub> solution that the reduction is not spontaneous, as seen in the delayed colour change of the fluorous phase as a function of elapsed stirring time. The entire reduction step was monitored visually using a video-recording device, whereby the footage could be processed into discrete frames corresponding to an image at a particular incremental time value, recorded from the onset of contact of the aqueous phase with the fluorous phase. A particularly interesting observation in this regard, was the prolonged time it took for the fluorous phase to commence its colour transition. Upon addition of the NaBH<sub>4</sub> solution, the fluorous phase persisted as a yellow colour while the aqueous phase immediately transformed from a clear solution to a dark purple-black colour. This finding suggested that the Au NPs were reduced and sequestered in the aqueous phase for about 20 min before partitioning to the fluorous phase (demonstrated by a lucid colour change in both phases) with the fluorous phase transitioning from a yellow colour to a purple-brown colour and the aqueous phase from a dark purple-black to a clear solution. These observations are illustrated in the images provided in Figure 4.4.





For **JHD01**, it can be seen in the UV-Vis spectra after the reduction (Figure 4.14) that the SPR band for Au is present in the range 550 - 570 nm suggesting that Au NPs have successfully been produced. However, there is a band which does not disappear after reduction, which is present at around 330 nm and indicative of the LMCT band as a result of Au-P coordination. Moreover, the band arising for Au ions in **S1** can also be seen in the spectrum after the 40 min

reduction time. This signifies that both free Au ions and Au ions participating in complexation have to the potential be reduced by NaBH<sub>4</sub>. The increase in the number of Au species being reduced may explain the TEM results obtained for the afforded sample, **JHD01**. The TEM images captured of **JHD01** revealed fluorous-stabilized Au NPs having two distinct sizes or a bimodal size distribution. These results are depicted in the histograms and associated TEM images (Figure 4.15).

From these results, it can be inferred that Au(III) ions are still present in the sample and thus reduction was not completely carried out. It was obligatory to ensure complete reduction to achieve optimal formation of fluorous-stabilized Au NPs as well as to ascertain reliable ICP-OES results, which is necessary to assess as catalysts in the ensuing chapter. Increasing the stirring speed from 250 rpm to 500 rpm and increasing the reduction time from 40 min to 3 h, afforded the system, **JHD02**. The UV-Vis spectra (Figure 4.14) illustrates a notable decrease in the intensity of the LMCT absorption band corresponding to the Au(III) ions (~ 330 nm). However, the surface plasmon resonance of Au, which was anticipated, is obscure and thus it cannot be conclusively established by means of UV-Vis spectroscopy whether fluorous-stabilized Au NPs were successfully produced. These doubts vanished after analysis of the sample by TEM, which indicated that small, mono-disperse and spherical fluorous-stabilized Au NPs had formed with particle diameters of  $5.3 \pm 1.4$  nm.

Due to suspicions that complete reduction was still not achieved, given the presence of the LMCT band after the reduction period, the Au: NaBH<sub>4</sub> ratio was adjusted from 1: 4 to 1: 8. The increase in this ratio allowed the system to undergo complete reduction and it afforded smaller Au NPs with a narrower size distribution. This is confirmed by the TEM images and associated histogram plot showing the size and size distribution of the Au NP system (JHD03). The fluorous-stabilized Au NPs (afforded for JHD03) were well-dispersed, spherical and highly-monodisperse with particle diameters of  $3.0 \pm 1.0$  nm. The UV-Vis spectrum shows that the reduction almost achieved completion, however, the presence of the small band in the region of 260 nm suggests that free Au ions are remaining in the fluorous phase after the permitted reduction interval.

Increasing the Au: NaBH<sub>4</sub> to 1: 16 was executed to ensure that the reduction was completed. This condition would be carried out in the subsequent NP experiments in order to ascertain complete reduction. However, after **JHD11**, it was learned that the Au: NaBH<sub>4</sub> may be too high and causes larger particles to form due to the more stringent, bubbling conditions offering less control over this reduction period. For this reason, the Au: NaBH<sub>4</sub> ratio was adjusted to 1: 8 for the preparation of **JHD12** – **JHD17** (Table 4.1).

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Catalyst system	Ligand	Solvent	Au: L	Preparation method	Particle diameter
JHD12	L1	S1	1 : 0.28	Direct	43.4 ± 22.2
JHD16	L1	<b>S</b> 3	1 : 0.56	Direct	27.9 ± 25.6
JHD17	L1	S1	1 : 0.56	Direct	17.8 ± 13.7
JHD13	L1	S1	1 : 0.56	Direct	14.8 ± 15.1
JHD14	L1	S1	1 : 1.12	Direct	11.8 ± 15.8
JHD15	L1	S1	1 : 2.24	Direct	$2.0 \pm 0.3$

**Table 4.1.** Sample information regarding the fluorous-stabilized Au NP catalysts produced using the direct method.

# 4.2.1.2. Use of different perfluoro-ligands

One of the major foci in the development of catalysis under fluorous biphase conditions has been the electronic insulation of the ligand donor/metal centre from the powerful electron withdrawing influence of the perfluoroalkyl substituents. In Horvath and Rabai's seminal paper<sup>11</sup> this was attempted using  $C_2H_4$  units but, subsequently, theoretical calculations<sup>12</sup> and experimental studies on perfluoroalkyl-phosphines<sup>13</sup> and amines<sup>14</sup> have shown that complete electronic insulation is not achieved even with a pentyl,  $C_5H_{10}$ , spacer group. Bhattacharryya<sup>15</sup> et al. (1997) and others<sup>16,17</sup> have focused their attentions on aryl electronic insulating units. The direct attachment of one, two or three perfluoroalkyl groups in the ortho-, meta- or parapositions of triaryl-phosphine ligands, causes stepwise reductions in the  $\sigma$ -donor strength of these ligands indicating that the aryl groups are also not perfect electronic insulators.

Four different fluorous-soluble ligands were employed under the same conditions to identify whether they would be feasible to generate fluorous-stabilized Au NPs via the direct method. For the experiments, the scheme below illustrates the experimental conditions employed where the only adjustment was the use of either L1-L4 in each case.

The fluorous phosphine ligands are able to cap the Au NPs and thereby act as suitable ligand stabilizers imparting solubility of the Au NPs in fluorous solvents. Based on the chemical structure of the ligand, L1, the fluorous ponytail is further away from the phosphine donor atom and thus may not greatly affect its coordination ability in comparison to the other systems such as L4 which has only one  $CH_2$  spacer moiety between the oxygen donor atom and the perfluoroalkyl segment. The withdrawing effect in turn, results in weaker coordination to the metal ion centre. When considering L4, it is highly likely that the  $CH_2$  spacer moiety is too short to allow for proper electronic insulation from the highly electron-withdrawing fluorous ponytail,  $-(CF_2)_7CF_3$ .


\*Experimental ratios: Au: L = 1:1, Au: NaBH<sub>4</sub> = 1:16.

**Scheme 4.1.** Reaction scheme illustrating the general formation of fluorous-stabilized Au NPs with different ligands via the direct approach.

**L2**, which has the sulphur heteroatom, is expected to behave the best given the high affinity of sulphur atoms for gold. However, in this direct strategy, using **L2** did not produce any fluorous-stabilized Au NPs. This may be attributed to the short two  $CH_2$  spacer moieties ineffectively insulating the electronic withdrawing nature of the fluorous alkyl chain.

An experiment (**JHD05**) was executed for comparison purposes to identify the optimal ligand stabilizer to produce fluorous-stabilized Au NPs via this direct method approach. The experimental conditions for **JHD05** include Au: **L1** = 1:1, **S1**, Au: NaBH<sub>4</sub> = 1: 16, 3 h, 500 rpm, 30 °C (Figure 4.5). The UV-Vis spectrum (Figure 4.6 - left) of the fluorous phase after the





permitted reduction time lucidly indicates the SPR band at around 560 nm and the disappearance of the LMCT band at around 330 nm which proves that the reduction was driven to completion. Furthermore, the associated TEM images of the fluorous phase, show fluorous-stabilized Au NPs with particle diameters of  $5.7 \pm 1.3$  nm (Figure 4.6 – right).



**Figure 4.6.** Left: UV-Vis spectra of the fluorous phase of **JHD05** before and after reduction. Right: Representative TEM image of **JHD05**.

The same experimental conditions as above with the exception of using L2 instead of L1, provided JHD08 which provided a few issues. Upon addition of the NaBH<sub>4</sub> solution (2 mL), the aqueous phase immediately changed colour. This colour change to the aqueous phase persisted throughout the reduction step and the final appearance of this aqueous phase can be seen in Figure 4.7 (right). This suggests that Au ions are unable to form complexes and remain preferentially soluble in the fluorous phase and upon reduction the Au ions and NPs rapidly migrate to the aqueous phase. At the end of the experiment, no SPR band was visible in the UV-Vis spectrum and almost no change to the spectrum was seen in relation to the sample before reduction had taken place. The differences between JHD05 and JHD08 are pointed out in Figure 4.7. This strongly supports the claim that L2 fails to act as a suitable fluorous stabilizer via this approach. Similar issues were provided for JHD07, which employed the fluorous ligand, L3. No changes to the UV-Vis spectra were apparent subsequent to the reduction period.

Under the same experimental conditions employed as the above experiments, besides the use of **S2** instead of **S1**, the experiment **JHD09** was executed. It entailed the use of the alcohol reagent (**L4**) which possessed an adequate fluorous segment to afford solubility in the fluorous solvent. The experiment, however, was not fruitful and suggested that the choice of this ligand may be poor for its required function. In addition, it may be the result of the electron withdrawing fluorine chain which lowers the coordination ability of the oxygen donor atom. Lastly, the use of **L5** in the preparation of fluorous-stabilized Au NPs by way of the

aforementioned synthetic strategy, was attempted several times. The attempts were not successful and the main reason for this was the poor solubility of this ligand in the fluorous solvents S1 - S3. Comparing the structure of ligand (L5) with the analogous ligand (L1), it is palpable that L1 would exhibit greater solubility in fluorous media given it has two additional fluorous segments/ponytails in comparison to L5.



**Figure 4.7.** Images depicting the differences after the biphasic reduction when using the two different ligands. Left: Result of using L1 (JHD05). Right: Result of using L2 (JHD08).

The use of monophasic conditions for this biphasic reduction has been considered and assessed, however, it was found that the fluorous solvent and an aqueous phase may not bring forth true monophase conditions as in the case of organic-fluorous systems at elevated temperatures. Moreover, it has been observed numerous times in this work that an increase in temperature during the reduction step leads to uncontrolled growth and agglomeration.

# 4.2.1.3. Use of different solvents

With the employment of the stabilizer L1, the direct method was successful in preparing fluorous-stabilized Au NPs in the three solvents, S1 – S3. The use of the two solvents, S1 versus S2, were explored in the experiments JHD05 and JHD06 using L1 as the ligand of choice. From the UV spectra (Figure 4.8), the use of S1 provides a more pronounced SPR band and smaller Au NPs with a smaller size distribution in comparison to the use of S2. TEM indicates that larger Au NPs (JHD06) are present in S2 in comparison to S1 (JHD05). The mean NP diameters for JHD05 were 5.7  $\pm$  1.3 nm while for JHD06, they were 8.3  $\pm$  2.8 nm. The differences in these sizes could be the result of the solvent or it could be the error brought about by simple reproducibility. Nevertheless, it does not seem that the two solvents would

behave very differently, given that their structures are very similar affording them very similar chemical properties.



**Figure 4.8.** UV-Vis spectra of the fluorous phase after the 3 h of reduction for **JHD05** and **JHD06**, respectively. Experimental conditions: Au: L1 = 1:1, **S1** (JHD05) or **S2** (JHD06), Au: NaBH<sub>4</sub> = 1:16, 500 rpm, 3 h, 25 °C.

Continuing with the use of L1, the only ligand which offered success by way of this synthetic approach, S1 and S3 were investigated in experiments JHD17 and JHD16, respectively. In these experiments, the Au: NaBH<sub>4</sub> ratio was adjusted to 1: 8 from the ratio of 1: 16 used in the aforementioned experiments, JHD05 and JHD06. From the UV spectra (Figure 4.9), it is clear that under these conditions, the SPR band for JHD17 (employing S1) is not as distinct as for JHD16 (employing S3). The reason for this is the lower concentration of Au NPs present in the sample, JHD17, as found from ICP-OES.

The use of **S1** in **JHD17** yielded Au NPs having particle diameters of  $17.8 \pm 13.7$  nm while for **JHD16**, they were slightly bigger having mean particle diameters of  $27.9 \pm 25.6$  nm. The difference in these sizes is a result of the different chemical properties of these solvents. It is anticipated that the rate of reduction would be dependent to some degree on the diffusion coefficient of the fluorous matrix and should affect the kinetics of the reduction.

On the topic of employing a different solvent in the preparation of fluorous-stabilized Au NPs, an attempt was made using MeOH. It had been identified that HAuCl<sub>4</sub> and L2 showed solubility in MeOH. For this reason, the idea would be to initially produce an Au-L2 complex in MeOH,

followed by reduction. This would afford fluorous-stabilized Au NPs in MeOH. The MeOH would then be removed and the NPs redissolved in the fluorous solvent of choice.



**Figure 4.9.** UV-Vis spectra of the fluorous phase after the 3 h of reduction for **JHD16** and **JHD17**, respectively. Experimental conditions: Au: L1 = 1: 0.56, **S3** (JHD16) or **S1** (JHD17), Au: NaBH<sub>4</sub> = 1: 8, 500 rpm, 3 h, 25 °C.

Unfortunately, the experiments were abandoned due to substantial agglomeration upon the reduction step. Firstly, a solution of HAuCl<sub>4</sub> (1 eq.), **L2** (2 eq.) in MeOH was refluxed for about 12 hours whereby it was assumed the complex had formed. At this point, NaBH<sub>4</sub> (4 eq.) in MeOH (0.5 mL) was added dropwise to the solution (Figure 4.10). Surprisingly, the solution turned clear and a single mass of reduced metal was seen moving about the solution as it was stirred. The change in colour of the solution indicated the Au ions being reduced and falling out of solution, resulting in the observed individual precipitate.



**Figure 4.10.** Attempted use of MeOH to produce fluorous-stabilized Au NPs. Left: Refluxed solution containing **L2** and Au in MeOH. Right: After a few minutes upon reduction.

#### 4.2.1.4. Effect of Au: L ratio

Three experiments, **JHD06**, **JHD10** and **JHD11** were conducted to investigate the effect of changing the Au: L ratio. The UV-Vis spectra (Figure 4.11) illustrate these differences where the use of 0.5 eq. of **L1** (**JHD10**), resulted in a larger SPR band. This observation may be attributed to the fact that less coated gold NPs provide a more pronounced SPR band in comparison to more coated or stabilized Au NPs. Both systems employing 0.5 eq. and 1 eq. showed no sign of the SPR band. Although, it should be noted that for the system **JHD03**, the SPR band was absent, yet the TEM images revealed the presence of fluorous-stabilized Au NPs. It is also seen that the absorbance corresponding to the electronic conjugation of the phenyl rings corresponds to the quantity of ligand used in relation to Au.



**Figure 4.11.** UV-Vis spectra of the fluorous phases of **JHD06**, **JHD10** and **JHD11** prepared using varying ratios of Au:**L1** in **S2** with Au:NaBH<sub>4</sub> = 1: 16.

According to TEM analysis, it was seen that the use of less ligand (0.5 eq.) provided fluorousstabilized Au NPs with particle diameters of 5.0  $\pm$  2.6 nm while an increase to Au: L1 1:1 provides slightly larger fluorous-stabilized Au NPs with a similar size distribution. The use of 2 eq. of L1 which was thought to produce even smaller and more stabilized Au NPs could not be seen on TEM or UV-Vis spectroscopy. It was expected that they either had not formed or were too small to be seen on TEM and too small to deliver a visible SPR band in the UV-Vis spectrum. However, the same sample (JHD11) was analysed by TEM precisely six days later and a low concentration of spherical, dispersed Au NPs were apparent in the images having mean particle diameters of 6.7  $\pm$  1.4 nm. With evidence of small Au NPs having been synthesized in JHD11, the notion of a higher L: Au ratio affording smaller NPs is confirmed. Due to circumstances beyond our control (lockdown during the covid19 pandemic), the NP systems were stored for a period of four months which led to issues regarding agglomeration and/or oxidation. For this reason, another series of experiments were conducted which also investigated the effect of employing varying Au: L ratio in the synthesis of fluorous stabilized Au NP systems using this direct approach. With this said, systems **JHD12** – **JHD15** were prepared whereby Au: L ratios were 1: 0.28, 0.56, 1.12 and 2.24. The UV-Vis spectra of the fluorous phases of these samples is shown in Figure 4.12. The differences in sizes of these systems are apparent from the TEM histograms shown in Scheme 4.2.



**Figure 4.12.** UV-Vis spectra of the fluorous phase of **JHD12** – **JHD15**, prepared with varying ratios of Au: L1 with Au: NaBH<sub>4</sub> = 1: 8.



Increasing quantity of ligand – increased stabilization

Increasing average NP diameter (nm)



*Scheme 4.2.* Depiction of the inverse relationship between the quantity of ligand used in the NP preparation versus particle diameter (nm).

### 4.2.2. Characterization of fluorous-stabilized Au NP systems

### 4.2.2.1. Characterization by UV-Vis spectroscopy

The formation of the desired complex prior to the reduction step was discerned using UV-Vis spectroscopy. It has been recounted by Peck *et. al.* (1991) that in aqueous solutions at pH < 4, Au(III) chloride exists in the planar [AuCl<sub>4</sub>]<sup>-</sup> form.<sup>18</sup> The lowest-energy absorption of [AuCl<sub>4</sub>]<sup>-</sup> in the violet/near UV spectral region is reported at 311 nm and has been assigned previously to two unresolved ligand ( $\pi$ ) -to-metal ( $\sigma^*$ ) charge transfer transitions.<sup>19</sup> The coordination of the perfluoro phosphine ligand to Au(III) was identified by a Ligand-to-Metal Charge Transfer (LMCT) band which became visible at around 330 – 332 nm (Figure 4.13), after sufficient stirring and heating of the fluorous phase containing L1 and Au(III) in S1 or S2.



**Figure 4.13.** UV-Vis spectra of the bands corresponding to free Au(III) and free perfluorophosphine ligand in **S1** and the LMCT band corresponding to Au-P complexation.

The UV-Vis spectra (Figure 4.13) indicates the free absorption values of Au(III) ions and the ligand (L1), respectively, in S1. Upon complexation, the LMCT band appears which signifies the coordination of the phosphorous heteroatom of the perfluoro-phosphine ligand to Au(III). The above monitoring procedure was carried out in all synthetic instances (except JHD01 and JHD02), prior to the reduction of the fluorous phase affording the fluorous-stabilized Au NPs. The presence of fluorous-stabilized Au NPs using this synthetic method was evidenced by the

SPR band at around 550 nm whereby all the systems employing L1 via this biphasic reduction method afforded the UV-Vis spectra seen in Figure 4.14. The SPR bands corresponding to fluorous-stabilized Au NPs in these spectra are not completely distinct, although the presence of the NPs is evidenced by the TEM images of the fluorous phases. Moreover, the results from ICP-OES indicate a low concentration of Au in the fluorous phase which may be the reason for not being able to clearly detect the SPR band. Lastly, it was found that the L1: Au ratio also influences the visibility of the SPR band, and this may be due to electronic shielding by the ligand, since a greater quantity of ligand allows for better stabilization of the Au NPs in the fluorous phase. The more ligand surrounding the Au NP, the more the SPR band is shielded and its absorption at around 550 nm is reduced, similarly when less ligand is used it will allow for the SPR band to be more visible and pronounced, as a result of less shielding by the fluorous ligand, in this case, L1.



**Figure 4.14.** UV-Vis spectra of the fluorous-stabilized Au NPs produced from the direct approach. Left: Systems which were synthesized for optimization purposes. Right: Systems which were synthesized and promptly used for assessment in catalysis.

# 4.2.2.2. Characterization by Transmission Electron Microscopy (TEM)

Samples which showed an SPR band or adequate colour change in the fluorous phase, were analysed using TEM. The TEM samples were prepared by sonicating the sample and ejecting a portion of the sample onto a copper grid which was then analyzed. For the initial experiment, the incomplete reduction led to an assortment of peculiar observations being uncovered by TEM. Further magnification into these structures shows the existence of fluorous-stabilized Au NPs exhibiting bimodal size distributions (Figure 4.15).



**Figure 4.15**. TEM images and histograms of two different sets of nanoparticles in the fluorous phase of **JHD01** depicting the size and size distribution of the group of larger fluorous-stabilized Au NPs (right) and set of smaller fluorous-stabilized Au NPs (left).



**Figure 4.16.** Left: Histogram of **JHD02** depicting the size and size distribution of the fluorousstabilized Au NPs. Right: Representative TEM image of **JHD02**.

It was found through TEM analysis that an increase in the Au: NaBH<sub>4</sub> ratio to 1: 8 allowed the system to undergo complete reduction and it afforded smaller Au NPs with a narrower size distribution than **JHD02**. This is confirmed by the TEM images and associated histogram plot showing the size and size distribution of the Au NP system (**JHD03**). The fluorous-stabilized Au NPs (afforded for **JHD03**) were well-dispersed, spherical and highly-monodisperse with particle diameters of  $3.9 \pm 1.0$  nm.



**Figure 4.17.** Left: Histogram of **JHD03** depicting the size and size distribution of the fluorousstabilized Au NPs. Right: Representative TEM image of **JHD03**.

The analyzed systems appeared spherical and well-dispersed. Moreover, in all cases using this optimized method, small Au NPs having narrow-size distributions were acquired. The most promising system was found to be **JHD03** due to it being the smallest and most mono-disperse, making it an ideal model candidate in the catalytic evaluation to follow.





**Figure 4.18.** Left: Histogram of **JHD04** depicting the size and size distribution of the smaller fluorous-stabilized Au NPs. Right: Representative TEM image of **JHD04**.



**Figure 4.19.** Left: Histogram of **JHD05** depicting the size and size distribution of the smaller fluorous-stabilized Au NPs. Right: Representative TEM image of **JHD05**.



**Figure 4.20**. Left: Histogram of **JHD06** showing the mean size and size distribution of the fluorous-stabilized Au NPs. Right: Representative TEM image of **JHD06**.



**Figure 4.21.** Left: Histogram for **JHD10** displaying the size and size distribution of the fluorousstabilized Au NPs. Right: Representative TEM image of **JHD10**.





**Figure 4.22.** Left: Histogram of **JHD11** depicting the size and size distribution of the fluorousstabilized Au NPs. Right: Representative TEM image of **JHD11**.



**Figure 4.23.** Left: TEM histogram showing the average size and size distribution of **JHD13**. Right: TEM image of **JHD13**.









**Figure 4.25.** Left: TEM histogram showing the average size and size distribution of **JHD15**. Right: TEM image of **JHD15**.



**Figure 4.26.** Left: TEM histogram showing the average size and size distribution of **JHD16**. Right: TEM image of **JHD16**.

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**Figure 4.27.** Left: TEM histogram showing the average size and size distribution of **JHD12**. Right: TEM images of **JHD12**.





**Figure 4.28.** Left: TEM histogram showing the average size and size distribution of **JHD17**. Right: TEM images of **JHD17**.

Interestingly, during the analysis of some of the TEM images captured of **L1**-stabilized Au NPs produced by the biphasic reduction synthetic strategy referred herein as the direct approach, specific cluster shapes of Au crystalline nanoparticles were identified. Three of these shapes are presented in Figure 4.29.



**Figure 4.29.** Schematic illustration of three shapes of Au crystalline particles derived from the direct approach: (a) cuboctahedron, (b) icosahedron and (c) decahedron. Shape illustrations adapted from Guisbiers<sup>20</sup> and co-workers (2013).

# 4.2.2.3. Characterization by ICP-OES

All systems which were successfully characterized by UV-Vis spectroscopy and TEM were analysed by ICP-OES to establish the concentration of Au NPs in the volume of fluorous phase. This was necessary to elucidate the required volumes of the system in order to ultimately attain constant metal concentration values for each system in the anticipation of assessing them as catalysts. The concentrations of the samples determined by ICP-OES are reported in Table 4.2.

Sample	Concentration (mol/mL)	Sample	Concentration (mol/mL)
JHD01	2,93 × 10 <sup>-6</sup>	JHD13	5,11 × 10 <sup>-6</sup>
JHD02	8,83 × 10 <sup>-7</sup>	JHD14	5,73 × 10 <sup>-6</sup>
JHD03	3,85 × 10⁻ <sup>7</sup>	JHD15	1,33 × 10 <sup>-6</sup>
JHD04	1,65 × 10⁻ <sup>8</sup>	JHD16	2,06 × 10 <sup>-7</sup>
JHD05	7,43 × 10⁻ <sup>7</sup>	JHD12	7,53 × 10 <sup>-6</sup>
JHD10	5,70 × 10 <sup>-7</sup>	JHD17	1,17 × 10 <sup>-6</sup>

**Table 4.2.** ICP characterization data applicable to the successful fluorous systems.

# 4.2.3. Assessment of reproducibility

**JHD03** showed great potential as a NP system to be investigated due to the morphology, size, and size distributions of the fluorous-stabilized Au NPs gathered from the TEM images. For this reason, a simple study was conducted to assess whether it would be possible to reproduce the Au NP system, **JHD03**. The precise experimental conditions which were employed to produce **JHD03**, were mimicked for the new experiment, **JHD04**. The results of the study are illustrated in Figure 4.30 which shows the appearance of the end products for each experiment as well as the respective UV-Vis spectrum before and after the reduction step. Additionally, Figure 4.31 exemplifies the comparative TEM images as well as the calculated sizes and size distributions of each of the systems afforded in the reproducibility experiment.



**Figure 4.30.** Left image - *Top:* **JHD03**. *Bottom:* **JHD04**. *Left:* During separation of the fluorous and aqueous phases. *Right:* Isolated fluorous and aqueous phase after the respective experiment. Right image - UV-Vis spectra of the fluorous phase before and after the 3 h of reduction for the reproducible trial for **JHD03** and **JHD04**.



Figure 4.31. Mean particle diameters and associated TEM images of JHD03 and JHD04, respectively.

Therefore, it could be concluded that the synthetic procedure via the direct method is reproducible in terms of the morphology, dispersity, and narrow size distribution of  $\pm$  1.2 nm of the fluorous-stabilized Au NPs with a variation in size of 2.8 nm between the duplicate experiments. An additional and likely reason for the variation in nanoparticle size is the differences in the time between particle formation and the execution of TEM analysis. Up to this point in our research, it was quite common to have delays in performing TEM analysis due to the availability of facilities, so it was quite possible that a small degree of agglomeration was occurring during this time.

### 4.2.4. Stability assessment of fluorous-stabilized Au NP systems

It can be seen for **JHD01**, which had not undergone complete reduction, that the solution tends to be oxidized over time thus producing Au ions from the Au NPs. This observation has been noted by Goulet et al.<sup>21</sup> (2012) where they found that Au(III) complexes were responsible for the oxidation of Au NPs in toluene. The extent of oxidation of these samples could easily be monitored by UV-Vis spectroscopy paying attention to the absorption band at around 330 nm indicative of the formation of Au(III) ions. A similar observation was seen when handling **JHD05** as an optimization catalyst, oxidation was much more of an issue when consistently making use of the catalyst and exposing the catalyst to air. Unfortunately, the stability of systems JHD02 and JHD03 could not be thoroughly assessed by UV-Vis spectroscopy due to no S1 being available at the time to dilute the samples for qualitative analysis. Nevertheless, characterization was carried out by TEM on the same two samples four months apart (about 120 days between analyses). The samples were securely sealed and stored in a dark cupboard between the TEM analyses. It can be seen for **JHD02** that there is no change to the mean particle diameter after the 120 days and only the size distribution has changed by a fraction of a nanometre. The reason is clearly because the fluorous stabilized Au NPs produced by this method are relatively dilute in the fluorous phase (shown by the visual distribution in the TEM images of the NPs). This means that a longer storage period would be necessary for any significant agglomeration to take place with such dilute systems.



**Figure 4.32.** Initial TEM results for **JHD02** (left) and TEM analysis executed on the same sample after 4 months (right).

Similarly, **JHD03**, showed decent stability with no precipitation of larger particles being seen on the bottom of the sample vial, a sign of a stable colloid. The mean particle diameter was found to decrease by almost 1 nm while the size distribution or standard deviation increased by 1 nm. This can be explained by larger particles coming out of solution over time leaving behind the smaller NPs which are seen on the TEM images. The increase in the standard deviation is a result of agglomeration over time giving rise to a slightly broader size distribution.



Figure 4.33. Left: Initial TEM results for JHD03. Right: TEM analysis executed on the same sample after 4 months.

Samples which were analysed by TEM were also assessed in terms of stability by analysing the fluorous phase a few days after their respective preparations. From the results below, it can be seen that the samples have remained more or less the same in terms of their visual appearance (colour) based on the images, which illustrates the appearance of the original sample and the same sample after a few days. The UV-Vis spectra, on the other hand, show that slight changes have taken place.



**Figure 4.34.** UV-Vis spectra of the original solution (solid line in each image) and solution after about a few days (dotted line in image).

### 4.3. Conclusions

The direct approach has been shown to successfully afford fluorous-stabilized Au NPs. From this work, it has been shown that a simple strategy exists to produce fluorous-stabilized Au NPs within 3 h at ambient temperatures. In all experiments making use of L1 (P ligand), small, spherical, and highly mono-dispersed fluorous-stabilized Au NPs were afforded. Other attempts were made with the use of other fluorous ligands having unique structural properties and in the cases of L2 and L4, atomically unique hetero-donor atoms. In these cases, no fluorous-stabilized Au NPs were attained. Instead, the aqueous phase and not the fluorous phase showed permanent colour change. This suggests that the afforded Au NPs from the reduction were preferentially soluble in water and were not stabilized by the ligand even though the ligand showed preferential solubility in the fluorous solvent. It was therefore postulated that the short -CH<sub>2</sub>- insulator moiety between the donor atom and fluorous moiety of L2 and L4, respectively, was not extended enough to insulate the electron-withdrawing effect from their fluorous ponytails. The use of L3, having the same donor atom as the successful L1, showed poor results. This was justified by the fluorine atoms directly attached to the phenyl rings of the ligand which may be too close to the P donor atom, hindering its coordinative ability due to pronounced electron withdrawing effects being experienced by the donor atom.

These fluorous-stabilized Au NP systems were successfully synthesized and characterized using UV-Vis spectroscopy, TEM and ICP-OES. In most cases, the SPR band was present in the fluorous phase which indicated fluorous-stabilized Au NPs above 2 nm. In other instances when the SPR band was absent, yet the system displayed some reduction colour, TEM confirmed the presence of fluorous Au NPs. From the TEM results, the analyzed systems appeared spherical and well-dispersed. Moreover, in all cases using this optimized method, small Au NPs having narrow-size distributions were acquired. With this said, these systems possessed the necessary characteristics for use as promising oxidation catalysts, making this synthetic method convenient in this regard. ICP-OES was employed to ascertain the initial concentrations of Au in the fluorous systems to achieve constant metal loading values for comparison as oxidation catalysts. Moreover, it was shown that by varying the Au: L1 ratio, a library of fluorous-stabilized Au NPs displaying different sizes could be attained.

Reproducibility of the direct approach was assessed by repeating the exact procedure for **JHD03**. The reproduction (**JHD04**) was also successful as confirmed by UV-Vis spectroscopy, TEM and ICP-OES. However, there were slight discrepancies in the particle sizes although the morphology of the systems were very similar in terms of shape, size distributions and

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dispersity. For **JHD03**, particles with mean diameters of  $3.9 \pm 1.0$  nm were attained, while for **JHD04**, particles having mean diameters of  $6.7 \pm 1.4$  nm were attained.

It was learned from stability tests that the fluorous-stabilized Au NPs show little or no agglomeration over a period of 4 months while the sample was sealed in a cupboard and stored at room temperature. For the incompletely reduced **JHD01**, after about 4 months, the solution had completely transitioned back to its original colour and the existing Au NPs had oxidized back to Au(III) ions. It was also found while handling **JHD05** as an optimization catalyst, the original sample showed signs of oxidation and thus the use of these systems as catalysts was not executed. A new series of fluorous Au NPs were prepared via the direct approach and characterized by UV-Vis spectroscopy, TEM and ICP-OES and the catalysts were then speedily employed in FBC before any significant changes to NP sizes by agglomeration and/or no oxidation had occurred prior to their evaluation in FBC.

#### 4.4. Experimental section

#### 4.4.1. Preparation of JHD01

HAuCl<sub>4</sub>·xH<sub>2</sub>O (0.0083 g, 0.02363 mmol, 1 eq.) was introduced to a solution of L1 (0,0168 g, 0,0237 mmol, 1 eq. to Au) in perfluoromethylcyclohexane (2 mL) by means of a glass weighing boat and using a Pasteur pipette to wash off the adhering Au reagent. The system was then stirred vigorously at 25 °C, however, this did little to dissolve the HAuCl<sub>4</sub>·xH<sub>2</sub>O and thus the system was sonicated for 3 min which greatly promoted the formation of a more homogenous system. The system was then heated to about 40 °C for 3 hours at a stirring speed of 500 rpm. At this stage, due to the visibility of some undissolved reagent, an additional 500 µL of perfluoromethylcyclohexane was added to the system to achieve complete solubility of the reagents and the system was then sonicated once more for 2 min. Subsequently, the resulting solution was transferred to a clean round bottom flask with the aid of a micropipette and a new stirrer bar. This reaction vessel, comprising the homogenous solution, was submerged in an oil bath positioned on a magnetic stirrer hot plate maintained at 25 °C with a stirring speed of 250 rpm. A sample of this solution was removed for analysis by UV-Vis spectroscopy to ensure the Au-P complex had formed prior to the reduction step. Subsequently, a solution of NaBH<sub>4</sub> (0,0036 g, 0,0945 mmol, 4 eq. to Au) in H<sub>2</sub>O (2 mL) was contacted with the fluorous solution and the resulting biphasic system was stirred at 300 rpm at 25 °C for precisely 40 min. Upon addition of the reducing agent solution to the fluorous phase, the aqueous phase immediately turned a very dark shade of purple, while the fluorous phase remained a yellowish colour. However, about 20 min into the reduction step, the fluorous phase began to show signs of a

colour change, thus the reduction was permitted to proceed for an additional 20 min. After the reduction, the stirring was halted, and the two phases isolated using a separating funnel.

### 4.4.2. Preparation of **JHD02**

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0081 g, 0,0238 mmol, 1 eq.) was transferred to a round bottom flask by means of a glass weighing boat. Perfluoromethylcyclohexane (2 mL) was pipetted through the neck of the glass weighing boat to rinse off residual gold adhering to its walls. Ensuing this, **L1** (0,0168 g, 0,0237 mmol, 0.56 eq.) was additionally transferred to the mixture which was stirred vigorously and then sonicated to ensure the complete dissolution of the gold species. The resulting solution was sequestered and transferred to a clean round-bottom flask, to which, NaBH<sub>4</sub> (0,0036 g, 0,0945 mmol, 4 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pouring it into the round-bottom flask. The resulting biphasic solution was stirred at 500 rpm for approximately 3 hours.

# 4.4.3. Preparation of JHD03

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0081 g, 0,0238 mmol, 1 eq.) was weighed directly into a round-bottom flask by means of a glass weighing boat. A solution of **L1** (0,0168 g, 0,0237 mmol, 0.56 eq.) in perfluoromethylcyclohexane (**S1**) (2 mL) was additionally transferred to the mixture which was sonicated for 5 min. Thereafter, an additional 500  $\mu$ L of perfluoromethylcyclohexane (**S1**) was included in the system to ensure complete solubility of all the chemical species within the rbf. The resulting solution was sonicated for 5 min and then allowed to stir for about an hour at 500 rpm. Following this, NaBH<sub>4</sub> (0,0072 g, 0,1890 mmol, 8 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours.

# 4.4.4. Preparation of JHD04

HAuCl<sub>4</sub>·xH<sub>2</sub>O (0,0044 g, 0,0119 mmol, 1 eq.) was weighed directly into a sample vial. L1 (0,0089 g, 0,0119 mmol, 0.56 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoromethylcyclohexane (S1) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred for about 45 min at 550 rpm. Following this, NaBH<sub>4</sub> (0,0036 g, 0,0950 mmol, 8 eq.) in distilled

 $H_2O$  (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The reduction temperature was maintained at 30 °C.

### 4.4.5. Preparation of JHD05

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0045 g, 0,0132 mmol, 1 eq.) was weighed directly into a sample vial. L1 (0,0095 g, 0,0134 mmol, 0.56 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoromethylcyclohexane (S1) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0080 g, 0,211 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 30 °C.

### 4.4.6. Preparation of JHD06

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0045 g, 0,0132 mmol, 1 eq.) was weighed directly into a sample vial. L1 (0,0095 g, 0,0134 mmol, 0.56 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoro-1,3-dimethylcyclohexane (S2) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0080 g, 0,211 mmol, 1 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 30 °C.

# 4.4.7. Preparation of JHD07

HAuCl<sub>4</sub>·xH<sub>2</sub>O (0,0044 g, 0,0129 mmol, 1 eq.) was weighed directly into a sample vial. L3 (0,0069 g, 0,0130 mmol, 1 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoromethylcyclohexane (S1) (2 mL) was additionally transferred to the sample vial, which was sonicated for around 5 min, however this time was extended to

attain complete dissolution. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0080 g, 0,211 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 30 °C.

### 4.4.8. Preparation of JHD08

HAuCl<sub>4</sub>·xH<sub>2</sub>O (0,0042 g, 0,0124 mmol, 1 eq.) was weighed directly into a sample vial. L2 (0,0124 mmol. 1 eq.) was weighed into the same sample vial. Next. perfluoromethylcyclohexane (S1) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0075 g, 0,211 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 30 °C.

### 4.4.9. Preparation of JHD09

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0042 g, 0,0124 mmol, 1 eq.) was weighed directly into a sample vial. L4 (0,0049 g, 0,0124 mmol, 1 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoro-1,3-dimethylcyclohexane (S2) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0075 g, 0,198 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 30 °C.

### 4.4.10. Preparation of JHD10

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0042 g, 0,0124 mmol, 1 eq.) was weighed directly into a sample vial. L1 (0,0043 g, 0,0061 mmol, 0.28 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoro1,3-dimethylcyclohexane (S2) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0077 g, 0,204 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 25 °C.

### 4.4.11. Preparation of JHD11

HAuCl<sub>4</sub>·*x*H<sub>2</sub>O (0,0043 g, 0,0127 mmol, 1 eq.) was weighed directly into a sample vial. L1 (0,0179 g, 0,0253 mmol, 1,12 eq.) was weighed onto a weighing boat and transferred into the same sample vial. Next, perfluoro1,3-dimethylcyclohexane (S2) (2 mL) was additionally transferred to the sample vial which was sonicated for 5 min. Thereafter, the contents of the sample vial were transferred to a small rbf equipped with a magnetic stir bar and the solution was stirred at 500 rpm until all components were dissolved in the system (and sufficient time for complexation was provided). Following this, NaBH<sub>4</sub> (0,0078 g, 0,206 mmol, 16 eq.) in distilled H<sub>2</sub>O (2 mL) was introduced instantaneously by pipetting it into the round-bottom flask using a Pasteur pipette. The resulting biphasic solution was stirred at 500 rpm for exactly 3 hours. The temperature of the 3 h reduction was controlled at 25 °C.

### 4.4.12. Preparation of JHD13

HAuCl<sub>4</sub>.xH<sub>2</sub>O (0,0083 g, 1 eq.) was weighed into a sample vial, together with **L1** (0,0168 g, 0.56 eq.) which was separately weighed onto a glass weighing boat and transferred to the sample vial by washing with **S1** (2.5 mL). Thereafter, the sample vial was sonicated for about 10 min and then the contents of the sample vial were transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 40 minutes, at which time, NaBH<sub>4</sub> (0,0073 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25

°C). At the end of the reaction time, the rbf was elevated from the oil bath and the magnetic stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials, while a bit of the middle fraction was decanted into its own vial.

### 4.4.13. Preparation of JHD14

HAuCl<sub>4</sub>xH<sub>2</sub>O (0,0041 g, 1 eq.) was weighed into a polytop, along with L1 (0,0169 g, 1.02 eq.) which was separately weighed onto a glass weighing boat and transferred to the sample vial with the aid of rinsing with S1 (2.5 mL). The contents of the polytop were sonicated for about 10 minutes and then transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 40 minutes, at which time, NaBH<sub>4</sub> (0,0037 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25 °C). At the end of the reaction time, the rbf was elevated from the oil bath and the magnetic stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials, while a bit of the middle fraction was tapped into its own vial.

# 4.4.14. Preparation of JHD15

HAuCl<sub>4</sub>xH<sub>2</sub>O (0,0021 g, 1 eq.) was weighed into a polytop, along with **L1** (0,0170 g, 2.03 eq.) which was separately weighed onto a glass weighing boat and transferred to the sample vial with the aid of rinsing with **S1** (2.5 mL). The contents of the polytop were sonicated for about 10 minutes and then transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 40 minutes, at which time, NaBH<sub>4</sub> (0,0018 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25 °C). At the end of the reaction time, the rbf was elevated from the oil bath and the magnetic stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials.

### 4.4.15. Preparation of JHD16

HAuCl<sub>4</sub>.xH<sub>2</sub>O (0,0079 g, 1 eq.) was weighed into a sample vial, together with **L1** (0,0171 g, 0.59 eq.) which was separately weighed onto a glass weighing boat and transferred to the sample vial by washing with **S3** (2 mL). Thereafter, the sample vial was sonicated for about 10 min and then the contents of the sample vial were transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 40 minutes, at which time, NaBH<sub>4</sub> (0,0073 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25 °C). At the end of the 3 h reduction period, the rbf was elevated from the oil bath and the magnetic stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials.

### 4.4.16. Preparation of JHD12

HAuCl<sub>4</sub>xH<sub>2</sub>O (0,0100 g, 1 eq.) and **L1** (0,009 g, 0.28 eq.) which was separately weighed onto a glass weighing boat and transferred to a sample vial with the aid of rinsing with **S1** (2.5 mL). The contents of the polytop were sonicated for about 10 minutes and then transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 2 hours, at which time, NaBH<sub>4</sub> (0,0087 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25 °C). At the end of the reaction time, the rbf was elevated from the oil bath and the magnetic stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials.

### 4.4.17. Preparation of JHD17

HAuCl<sub>4</sub>.xH<sub>2</sub>O (0,0083 g, 1 eq.) was weighed into a sample vial, together with **L1** (0,0168 g, 0.56 eq.) which was separately weighed onto a glass weighing boat and transferred to the sample vial by washing with **S1** (2.5 mL). Thereafter, the sample vial was sonicated for about 10 min and then the contents of the sample vial were transferred to a rbf equipped with a magnetic stirrer bar. The contents were stirred at 500 rpm at 25 °C for about 40 minutes, at which time, NaBH<sub>4</sub> (0,0073 g, 8 eq.) in distilled H<sub>2</sub>O was swiftly added to the stirring solution. The reaction was permitted to undergo reduction for 3 h at the same conditions (500 rpm, 25 °C). At the end of the reaction time, the rbf was elevated from the oil bath and the magnetic

stirrer bar removed and the contents were transferred to a separating funnel. The fluorous and aqueous phase after the reduction step were isolated into separate sample vials, while a bit of the middle fraction was decanted into its own vial.

# 4.4.18. ICP-OES sampling

Sampling for ICP-OES was achieved by extracting 10 percent of each sample vial and transferring it to a Teflon beaker. The solvent was evaporated from the Teflon beaker and a small portion of fresh aqua regia was added to each Teflon beaker for acid digestion. Again, the solvent (aqua regia) was boiled off in a fume hood leaving behind a residue at the bottom of the Teflon beaker. Thereafter, the residue was mixed with and made up to 10 mL with 0.1 M HNO<sub>3</sub>.

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# **Chapter 5**

# Fluorous biphasic catalytic oxidation of 1-octene

### 5.1. Introduction

"Green Chemistry" is an important topic, in both academia and industry, with regard to chemical synthesis in the 21st century.<sup>1</sup> Without this approach, industrial chemistry is not sustainable. The remarkable development of chemistry as a scientific discipline, has enabled humans to create highly valuable compounds from inexpensive raw materials. Our health and daily life rely on man-made substances such as pharmaceuticals, fine chemicals, synthetic fibres, and plastics which are produced by multi-step chemical conversions of petroleum- or biomass-based feedstocks. Still, the current standards of chemical synthesis need to be much improved. Many existing chemical processes, though beneficial, produce unwanted waste along with target products, and the inefficient recovery of solvents is an environmental problem.<sup>2</sup> Thus, the development of environmentally benign and clean synthetic technology is a goal of research and industry. Every reaction should proceed with a high atom-economy,<sup>3</sup> and the overall synthesis must be accomplished with a low E-factor (the ratio of the mass of waste per mass of product), thereby minimizing the cost of waste disposal.<sup>4,5</sup>

Oxidation reactions are a core technology for converting petroleum-based materials to various valuable oxygen-containing compounds. It finds wide application in different branches of industry and as a result the investigation of the oxidation process is very important. Be that as it may, oxidation is amongst the most problematic processes. Many textbook oxidation methods are unacceptable for practical synthesis; the heavy metal oxidants form toxic wastes, while known organic stoichiometric oxidants are usually very expensive. Nitric acid, the most conventional industrial oxidant,<sup>6</sup> is cheap but unavoidably forms various nitrogen oxides. Thus, there is a need for the invention of clean, safe oxidation procedures. Molecular oxygen is obviously an ideal oxidant, but aerobic oxidation is often difficult to control and sometimes results in combustion while the reaction is performed with a low conversion to avoid over-oxidation. Furthermore, although both oxygen atoms in  $O_2$  may be utilized for oxidation (100% atom efficiency),<sup>7.8</sup> only one oxygen atom has been used in most reactions (50% atom efficiency),<sup>9</sup> so the oxidation often requires certain reducing agents to capture the extra oxygen atom during the reaction.<sup>10,11</sup>

Hydrogen peroxide,  $H_2O_2$ , is a very attractive oxidant for liquid-phase reactions.<sup>12</sup>  $H_2O_2$  is an adduct of  $H_2$  and  $O_2$  that is also viewed as an adduct of an O atom and an  $H_2O$  molecule. It

can oxidize organic compounds with an atom efficiency of 47% and with the generation of water as the only theoretical by-product.<sup>13</sup> It should be noted that  $H_2O_2$  can be an ideal, waste-avoiding oxidant only when it is used in a controlled manner without organic solvents and other toxic compounds.<sup>14</sup> Thus, the discovery of an efficient catalyst and the choice of reaction conditions are the keys to realizing an ideal oxidation procedure. In light of this, the most reasonable and practical way of increasing the rate and selectivity of the oxidation reaction is via the application of various catalytic systems which influence definite stages of the oxidation process.<sup>15,16</sup>

Gold nanoparticle catalysts have been shown to be effective for several types of oxidation reactions, most notably for the oxidation of alcohols.<sup>17</sup> Specifically focussing on alpha olefin oxidation, Alshammari<sup>18</sup> et al. (2016) investigated the catalytic activity of gold nanoparticles on 1-octene oxidation under various reaction conditions using air as the oxygen source. They demonstrated that 1-octene can be oxidized by gold catalysts under solvent-free reaction conditions. The group also showed that increasing the temperature from 60 °C to 90 °C led to a significant increase in the conversion of 1-octene in the presence of TBHP and with Au/graphite as catalyst. It was clear that the selectivity for the epoxide increased with increasing temperature. In contrast, the selectivity to allylic products (1-octene-3-one, 1-octen-3-ol, 2-octenal, and 2-octen-1-ol) decreased with increasing temperature, which suggested that the catalyst may facilitate the reaction toward an epoxide, and this influence is enhanced at higher conversions facilitated by higher reaction temperatures.

The same group<sup>18</sup> investigated the effect of support, the preparation method, and the choice of metal. They showed that graphite provided the best support for these gold catalysts and the preparation methods that afforded the smallest particles were the most active. The effect of the gold: palladium ratio on the oxidation of 1-octene was investigated, and monometallic gold catalysts showed better activity when compared with bimetallic catalysts. Thus, it was concluded that the oxidation of 1-octene can be achieved using graphite-supported gold nanoparticles under solvent-free conditions in the presence of tert-butyl hydroperoxide as a radical initiator using oxygen from the air. Moreover, the epoxidation and the allylic oxidation route were the main reaction pathways under almost all conditions.

Aprile et al.<sup>19</sup> (2009) showed that the epoxidation reaction of 1-octene with molecular oxygen ( $P_{02}$  = 12 bars) at 90 °C, over AIBN–Au/CeO<sub>2</sub> + Ti-MCM-41-silylated catalytic system results in alkene conversions close to 9% (40% of the maximum conversion attainable) with epoxide selectivity around 90% when working with cumene as a sacrificial hydrocarbon.

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Hilal's group<sup>20</sup> (2001) investigated the kinetics of oxidation of 1-octene by 18-crown-6-ethersolubilized KMnO<sub>4</sub> in benzene and  $CH_2CI_2$ . In benzene, the oxidation of 1-octene was found to be first order with respect to the oxidant and zero order with respect to the substrate, whereas in  $CH_2CI_2$  the reaction was found to be first order with respect to both substrate and oxidant. The difference in the kinetic behaviour of the oxidation of 1-octene indicates that the solvent is, though not directly, involved in the reaction mechanism.

In his dissertation, Vogt<sup>21</sup> (1991) endeavoured to accomplish the oxidation of cyclohexene with  $O_2$  in the presence of fluorous-modified cobalt or manganese complexes. The reactions, carried out in a perfuoroether/alkene two-phase system, furnished only small quantities of cyclohexanone and cyclohexene oxide and there was severe catalyst decomposition during the reaction process. As the reaction proceeded, the catalyst was progressively extracted into the organic phase and could not be recovered. The electron-deficiency of the binding sites was recognized as one of the causes of the partial failure of these catalysts, mentioned in the initial report by Horváth and Rábai<sup>22</sup> (1994). The two verified that the electron-withdrawing character of the fluorine atoms present in the R<sub>f</sub> moiety led to a weakened coordination ability of the ligand donor atom, ultimately upsetting the catalytic activity and stability. For this reason, it is required that a "spacer" moiety be incorporated between the donor heteroatom and the perfluoroalkyl segment (R<sub>fn</sub>). The "spacer" consists of the entire sequence of atoms between the R<sub>fn</sub> moiety and the chemically active site of the reagent or catalyst.

In the same paper, Horváth and Rábai<sup>22</sup> (1994) presented an influential study which employs  $HRh(CO)\{P[(CH_2)_2(CF_2)_5CF_3]_3\}_3$  as a hydroformylation catalyst in a fluorous biphasic system. They demonstrated the hydroformylation of primary alkenes to aldehydes accompanied by effective separation of the catalytically active fluorous phase and the hydrocarbon phase upon restoring the reaction mixture to ambient conditions. The catalyst contained in the fluorous phase was then effortlessly isolated from the hydrocarbon phase (constituting the organic products) and recycled. In an ensuing investigation, Horváth et al.<sup>23</sup> (1998) extended the hydroformylation to include smaller alkenes such as ethylene as well as higher alkenes like 1-octene and 1-decene.

Fluorous biphasic catalysis (FBC) has been validated for many other catalytic reactions. Some other examples include, but are not limited to, hydroboration,<sup>30</sup> hydrosilylation<sup>31</sup> and Stille coupling.<sup>32</sup> However, this inventory is likely to continue to grow as interest intensifies in this area. Extended research must be conducted in order to optimize current systems and diminish costs in an effort to bring forth promising systems to commercial practice.

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Upholding the pursuit of "greener" chemical processes, the combination of Au NPs in the catalytic oxidation of 1-octene combined with the fluorous biphasic system (see Chapter 1) for catalyst recovery, is a novel, interesting and exciting research avenue worth exploring. Here we describe the fluorous biphasic catalytic oxidation of an alpha linear olefin, 1-octene, as the model substrate. The oxidants which were studied included O<sub>2</sub>, H<sub>2</sub>O<sub>2</sub> and TBHP, with the latter being probed more intensively. The oxidation process was facilitated by fluorous-stabilized Au NPs which were synthesized and fully characterized prior to their assessment as catalysts in this work. The fluorous catalysts differed in terms of their respective sizes and size distributions, stabilizing ligands (L1 or L2) and their method of preparation (micelle-template strategy or the direct method). In addition, fluorous-stabilized Au NP systems were purposely prepared with varying quantities of ligand: metal to intentionally produce systems with different sizes in order to comparatively study them. The different fluorous-stabilized Au NP systems which were studied are shown in Table 5.1.

With this said, initial catalysis runs were executed with a suitable catalyst which was specifically chosen and used to determine the optimized conditions before the other catalysts could be assessed. Considering this, the desired characteristics of this chosen catalyst included a relatively high concentration according to ICP-OES and a sizeable volume (enough to allow a number of duplicate reactions to be run). On this note, the initial catalyst chosen was **JHD16**. Thereafter, another system showing the most comparable qualities to the previous chosen catalyst was selected to continue the optimization process. Lastly, the recyclability and re-use of the fluorous catalysts were assessed to identify how many times the catalysts could be recycled and the effect of re-use on the activity and selectivity in the catalytic oxidation of 1-octene.

Catalyst system	Ligand	Solvent	Au: L	Preparation method	Particle diameter
JHD12	L1	S1	1 : 0.28	Direct	43.4 ± 22.2
JHD16	L1	<b>S</b> 3	1 : 0.56	Direct	27.9 ± 25.6
JHD17	L1	S1	1 : 0.56	Direct	17.8 ± 13.7
JHD13	L1	S1	1 : 0.56	Direct	14.8 ± 15.1
JHD14	L1	S1	1 : 1.12	Direct	11.8 ± 15.8
JHD15	L1	S1	1 : 2.24	Direct	$2.0 \pm 0.3$
JHM14	L2	S1	1 : 0.28	Micelle	4.1 ± 3.8
JHM15	L2	S1	1 : 0.56	Micelle	$3.6 \pm 2.7$
JHM13	L2	S1	1 : 1.12	Micelle	$3.8 \pm 2.8$
JHM16	L2	S1	1 : 2.24	Micelle	$3.2 \pm 2.8$

Table 5.1. Catalyst systems prepared for evaluation in FBC.

# 5.2. Catalytic oxidation of 1-octene

### 5.2.1. General reaction conditions and analysis of standards

The fluorous-stabilized Au nanoparticles were evaluated in the biphasic catalytic oxidation of 1-octene. According to a much earlier report by Hildebrand and Cochran<sup>33</sup> (1949), the biphasic mixture of toluene and perfluoromethylcyclohexane (**S1**) becomes monophasic at approximately  $\geq$  88.6 °C while for the biphasic mixture of chloroform and perfluoromethylcyclohexane (**S1**), the system becomes monophasic at  $\geq$  50.1 °C. Since solvent-free reactions are preferred in green chemistry,<sup>34</sup> the catalytic reactions were executed without organic solvents and instead with the substrate, 1-octene, neat. The preliminary catalytic reactions were carried out at 60 °C for 24 h (see Scheme 5.1), in the hopes that this temperature would be sufficiently high enough so that the biphasic system would be monophasic throughout the reaction period. The representative fluorous-stabilized Au NP system, **JHD16**, was used to optimize the catalytic reaction conditions and to assess the recyclability and re-use of the catalyst.



Scheme 5.1. General reaction scheme for the catalytic experiments executed.

In the catalytic runs, the fluorous phase containing the fluorous-stabilized Au NP system resided at the bottom of the Schlenk tube due to the high relative density of **S1**, perfluoromethylcyclohexane, in comparison to 1-octene, which formed the top layer. The oxidant in each case was introduced last in the experimental procedure and marked the initiation of the 24 h reaction period. It could be seen that a temperature of 60 °C was sufficiently high enough to result in a monophasic system as shown in Figure 5.1. Similar observations have been noted in the other biphasic catalytic runs employing the fluorous media; perfluoromethylcyclohexane (**S1**) or perfluorodecalin (**S3**).



**Figure 5.1.** Left: Monophasic conditions seen during the 24 h catalysis run at 60 °C. Right: Completion of the reaction and after the temperature has reached ambient.

Gas chromatography was used for quantification to determine the respective conversions. All relevant solutions of the standards were made up in toluene and prepared in GC vials to determine the relative response factors (Eq. 5.1) for the substrate and potential products, respectively.

$$RRF = \frac{C_{IS} \times A_{s/p}}{C_{s/p} \times A_{IS}}$$
(Eq. 5.1)

Where	C <sub>s/p</sub>	=	Concentration (g/ml) of substrate or product in sample
	CIS	=	Concentration (g/ml) of internal standard added to sample
	RRF	=	Relative Response Factor as calculated
	A <sub>s/p</sub>	=	Area of substrate or product in sample chromatogram
	A <sub>IS</sub>	=	Area of internal standard in sample chromatogram

The figure below (Figure 5.2) demonstrates a typical GC chromatogram showing good separation of some of the many standards which were assessed as potential and probable oxidation products. More information pertaining to the optimized GC method which was developed and used in this work for the catalytic oxidation of 1-octene, is offered in the Instrumentation section of this chapter.

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**Figure 5.2.** GC-FID chromatogram illustrating the elution of 1-octene and potential oxidation products from the GC column.

It should be noted that over the course of the catalysis optimization and GC method development, there were unknown peaks which could not be identified. Therefore, a number of standards were run as a means of possibly correlating the retention times and identifying compounds in the product mixture. For example, an unknown peak was seen in the GC-FID, however, it could only be established through GC-MS that it was unreacted TBHP because TBHP was not run as a standard. The more common C8 oxidation compounds are represented in Scheme 5.2 and most were available for use as standards. The compounds depicted in blue correspond to standards which were not at our disposal and thus could not be run on the GC-FID to determine their retention times. This is with the exception of octane-1,2-diol which is also depicted in blue (Scheme 5.2) but was analysed however it could not be seen on the chromatogram. Attempts to solve this issue included dramatically increasing the run time and/or increasing the column temperature and ensuring solubility of this standard in the toluene by thorough mixing. Other compounds which were analysed as standards included octane and heptaldehyde. The reason for choosing the latter was in case the TBHP was capable of oxidative cleavage of 1-octene under the employed conditions, leading to the production of heptaldehyde and formaldehyde. Even so, neither octane nor heptaldehyde was ever observed in the GC-FID or GC-MS analyses.




**Scheme 5.2.** General reaction scheme for the catalytic experiments showing possible oxidation products of the substrate, 1-octene. \*Compounds depicted in blue = standards not at our disposal and could not be run on the GC-FID to determine their retention times.

Table 5.2. Calculation of response factors of	of the substrate and potential oxidation produc	ts.
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	Ret. time (min)	IS (mg/mL)	Substr./prod. (mg/mL)	A(IS)	A(substr./prod.)	RRF
1-octene	4,81	44,0	41,9	37335,4	34085,5	0,958711
trans-2-octene	4,98	44,3	35,8	37632,2	23941,7	0,787256
trans-3-octene	4,85	42,7	34,8	36122,8	27888,4	0,947307
trans-4-octene	4,82	43,3	35,4	36533,2	26844,2	0,8987676
epoxy-1,2-octane	11,00	44,1	50,0	42617,4	36417,2	0,7536821
1-octenal	11,72	45,1	46,7	39080,3	27187,0	0,6718357
2-octenone	11,40	43,2	41,3	36525,8	25016,5	0,7164081
octanoic acid	22,79	43,8	45,8	36964,2	8472,2	0,2191914
toluene	5,23	-	-	-	-	-
para-xylene	6,98	-	-	-	-	-

### 5.3. Results and discussion

### 5.3.1. Effect of metal loading

The effect of increasing the quantity of fluorous catalyst in the system, is clearly demonstrated using  $H_2O_2$  and catalyst **JHD16** (Figure 5.3). Increasing the concentration of the fluorous phase affords a higher percentage conversion of 1-octene over the 24 h reaction period. This trend continues, in most part, as the fluorous phase is recycled up to five times. The increase in the percentage conversion of 1-octene upon recycling, however, is not substantial and indicates the catalysts capacity under these reaction conditions. This also proves the fluorous stabilized Au NP catalyst remains active after being re-used in the successive reactions.



**Figure 5.3.** Graph illustrating the percentage conversion of 1-octene as a function of the concentration of the fluorous catalyst **JHD16**. Oxidant = TBHP. **JHC23**:  $C_{cat.} = 3.0 \times 10^{-7}$  mol/mL and **JHC24**:  $C_{cat.} = 1.0 \times 10^{-6}$  mol/mL.

A similar pattern is observed with TBHP as the oxidant and the fluorous catalyst, **JHM15**, which showed a slight increase in percentage conversion of 1-octene with an increase in the

quantity of fluorous catalyst (Figure 5.4). It must be noted, however, that even with a doubling of the catalyst quantity, only a small increase in the percentage conversion is observed.



**Figure 5.4.** Graph illustrating the percentage conversion of 1-octene as a function of the concentration of the fluorous catalyst **JHM15**. Oxidant = TBHP. **JHC40**:  $C_{cat.} = 5.0 \times 10^{-7}$  mol/mL and **JHC32**:  $C_{cat.} = 1.0 \times 10^{-6}$  mol/mL.

#### 5.3.2. Effect of different oxidants

The use of green oxidants like  $O_2$ ,  $H_2O_2$  and tert-butyl hydroperoxide (TBHP) have bright prospects due to their attributes of mild, low cost and great sustainability in transition metal catalyzed oxidation reactions. Unlike O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>, TBHP is an organic peroxide making it soluble in organic solvents. In addition to its bulky structure, the use of TBHP as an oxidant can be advantageous or disadvantageous depending on the desired product selectivity from the oxidation of a particular substrate. For example, the bulky nature of TBHP can be viewed negatively as it contributes to a lower diffusion coefficient in comparison to H<sub>2</sub>O<sub>2</sub>. This leads to the oxidation by TBHP proceeding at a lower rate, in general. This was lucidly demonstrated by Valencia<sup>35</sup> et al where they showed the steric limitations of TBHP when using a large pore Ti Beta catalyst for the oxidation of linear, branched and cyclic olefins. The researchers highlighted the pronounced steric effects as a result of the bulkier Ti-OO-(CH<sub>3</sub>)<sub>3</sub> species which would form inside the zeolite pores. In contrast, the bulky nature of the oxidant may be advantageous in terms of improving selectivity. The efficacy of TBHP as a selective oxidant is notably demonstrated by its use in Sharpless epoxidation.<sup>36</sup> In view of the foregoing, a series of experiments were conducted to assess the effect of using different oxidants, namely,  $O_2$ , H<sub>2</sub>O<sub>2</sub> and TBHP in the catalytic oxidation of 1-octene through FBC.

In this regard, **JHM14** (5 × 10<sup>-7</sup> mol/mL) in **S1** (1 mL) constituted the fluorous phase for the three duplicate reactions. The same mol equivalents of  $H_2O_2$  and TBHP were used in each case such that 0.44 mL of  $H_2O_2$  was used while 0.50 mL of TBHP was used.



**Scheme 5.3.** Catalysis reaction scheme illustrating the use of different oxidants with **JHM14** (5 x  $10^{-7}$  mol/mL).

The fluorous solution (1 mL) containing **JHM14** (5 x  $10^{-7}$  mol/mL) in **S1** was transferred to reactor glass tubes by means of a micro-pipette together with 1-octene (1 mL). The duplicate reaction tubes for each experiment were then positioned in a parallel reactor already operating at 60 °C at a set stirring rate. The oxidant was introduced into the appropriate reaction vessel at which point, the stir bar was introduced and the 24 h reaction period was initiated. For **JHC44**, which investigated the use of oxygen as the oxidant, O<sub>2</sub> was bubbled through the mixture until the entire reactor tube was filled with O<sub>2</sub> (at which point the stir bar was added to the reactor tube). The respective reactions were stirred for 24 h. After the 24 h catalysis reaction, the magnetic stir bar was removed, and the contents of each reactor tube was permitted to cool to ambient before being transferred to a separating funnel. Thereafter, the octene layers were isolated into sample vials for GC analysis, while the fluorous phases were isolated into separate sample vials. The results from GC-FID are illustrated in the graph in Figure 5.5. It is clear from the graphs that TBHP is the more powerful oxidant giving the highest percentage conversion of 1-octene, while O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub> give similar conversions but with O<sub>2</sub> offering a 2% higher conversion in comparison to H<sub>2</sub>O<sub>2</sub>.

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**Figure 5.5.** Percentage conversion of 1-octene using **JHM14** ( $5 \times 10^{-7}$  mol/mL) with different oxidants; O<sub>2</sub> (excess), H<sub>2</sub>O<sub>2</sub> and TBHP. B<sub>oxidant</sub> = blank reactions (1-octene and fluorous solvent without catalyst) and the respective oxidant.

### 5.3.3. Effect of varying oxidant quantity

A series of experiments were executed to investigate the effect of increasing the quantity of oxidant, TBHP, to the catalytic system. With this said, 0.25 mL, 0.50 mL, and 1 mL of TBHP was used with **JHM15** as the catalyst ( $1 \times 10^{-6}$  mol/mL).



**Scheme 5.4.** Catalysis reaction scheme with **JHM15** ( $1 \times 10^{-6}$  mol/mL) with varying quantities of TBHP.

The results obtained from GC-FID are illustrated in the graph in Figure 5.6. It is clear from the graph that there is an increase in the conversion with an increase in quantity of oxidant. It appears that doubling the quantity of oxidant from 0.25 mL to 0.50 mL increases the conversion from 42.3% (JHC38) to 47.8% (JHC32). Doubling the quantity of oxidant from 0.50 mL to 1.00 mL leads to a conversion of 64.5%. An almost linear relationship was observed with regards to the quantity of TBHP added and the percentage conversion of 1-octene. Furthermore, the percentage error between the duplicate results was very small which suggests the data is reliable.



Catalysis runs with varying TBHP quantities

**Figure 5.6.** Percentage conversion of 1-octene using **JHM15** ( $5 \times 10^{-7}$  mol/mL) and varying quantities of TBHP. **JHC38** = 0.25 mL TBHP; **JHC32** = 0.50 mL TBHP and **JHC39** = 1.00 mL TBHP.

When looking at the products obtained, the selectivity for the epoxide appears to decrease with increasing quantity of TBHP in relation to the catalyst (Figure 5.7). It is also evident that the selectivity for the aldehyde is only seen for **JHC38** which employed the lower quantity of oxidant. An increase in this quantity of TBHP also results in a trend of increasing selectivity to octanoic acid. It is likely that the increased octanoic acid formation is a result of the extra oxidant which was included which leads to overoxidation in which the aldehyde species (1-octanal) is an intermediate. The aldehyde, or aldehydes, in general, are themselves, reducing agents and are readily oxidized further to form octanoic acid. Usually, the conversion of alkenes to aldehydes is carried out through hydroformylation with Rh catalysts whereby an additional carbon is added to the akene.<sup>37</sup> It can be seen through our process that oxidation

of alkenes can also yield the aldehyde, but in very low quantities. The selective oxidation of 1alkenes remains a daunting goal, specifically non functionalized alkenes which are even less reactive. There is very little literature reporting the oxidation of 1-octene by Au NPs, however, the literature shows many reports concerning the use of titanium-containing catalysts in the oxidation of terminal alkenes. One such example, which also uses 1-octene as the substrate in the presence of TBHP was the work of Palumbo et al.<sup>38</sup> (2015) who made use of a titanium silica catalyst as well as the uncommon solvent, trifluorotoluene. They were able to optimize their system by tuning the ratios of the catalyst, oxidant and solvent to afford alkene conversions of 73 % and very high selectivity of 98 % for the terminal 1,2-epoxide.<sup>38</sup>



**Figure 5.7.** Selectivities of catalyst experiments **JHC38**, **JHC32** and **JHC39**, employing increasing volumes of TBHP using **JHM15** ( $5 \times 10^{-7}$  mol/mL).

# 5.3.4. Effect of employing different solvents

A study was done to investigate the effect of changing the solvent employed in the fluorous catalyst solution from **S3** (JHC26) to **S1** (JHC27) while still making use of the catalyst JHD16. To a Schlenk tube, 1-octene (1 mL) was transferred by means of a micro-pipette followed by 0.5 mL TBHP. The duplicate reactions were stirred at 500 rpm at 60 °C for 24 h. Thereafter, the octene layers were isolated into sample vials for GC analysis, while the fluorous phases were recycled. After the 24 h catalysis reaction, the magnetic stir bar was removed and the contents of each Schlenk tube was permitted to cool to ambient before being transferred to a separating funnel. The fluorous phase (the bottom layer) in each case, was tapped off into a

clean Schlenk tube equipped with a clean stir bar. Exactly 1 mL of 1-octene was transferred to each of these Schlenk tubes, followed by 0.5 mL of TBHP. The duplicate recycled reactions were stirred at 500 rpm at 60°C for 24 h. This process was completed another four times so that in total the system had been recycled five times. The catalysis results realised from GC-FID are illustrated in the graph in Figure 5.8. This entire experimental series was done again but with **S1** being the fluorous catalyst medium. The procedure for this experiment was executed in otherwise the same manner as **JHC26** (see above procedure). One difference, however, has already been found which is that after the third recycle run, additional solvent (500  $\mu$ L of **S1**) was added to each of the Schlenk tubes because the quantity of the fluorous phase was too small to work with.



**Figure 5.8.** Percentage conversion of 1-octene using JHD16 ( $5 \times 10^{-7}$  mol/mL) in two different solvents and using TBHP as oxidant between successive runs. JHC27 = S1 and JHC26 = S3.

Based on the conversion of 1-octene, the fluorous solvent **S3** is the better choice between the two, but not by much. The reason for this is that **S3** has a higher boiling point than perfluoromethylcyclohexane, making it less likely to be lost during the catalysis runs and subsequent recycling of the fluorous phase.





Looking at the selectivity graphs in Figure 5.10 and Figure 5.11, it is clear that the change in solvent did not do much in terms of altering the selectivity ratios toward the oxidation products. If anything, the main difference can be seen on the first run before any subsequent recycling, however, the differences here are very slight and almost unnoticeable with a very small decrease in the epoxide selectivity and increase in aldehyde selectivity when employing **S3**. Therefore, the main reason perfluorodecalin (**S3**) would be the preferred solvent to employ within our study is almost solely predicated on the higher boiling point of this solvent.



Figure 5.10. Selectivity found for JHC26 (use of JHD16 in S3).



Figure 5.11. Selectivity found for JHC27 (use of JHD16 in S1).

It should be pointed out that according to Melero et al.<sup>39</sup> (2017), the polarity of the reaction solvent plays a role in the quantity of epoxide formed. The group investigated the epoxidation

of 1-octene with TBHP in the presence of a Mo catalyst in different organic solvents. The results clearly demonstrated that less polar solvents lead to higher 1,2-epoxyoctane yields. The explanation for this trend is that p-donor solvents are able to coordinate to the active sites of the molybdenum catalyst which actually hinders the coordination between these sites and the oxidant (TBHP), which is necessary for substrate epoxidation.

# 5.3.5. Comparison of catalysts

All fluorous-stabilized Au NP catalyst systems which were produced were assessed in comparison to each other, except for **JHD15**, which was too dilute according to ICP-OES to achieve the desired metal loading of  $5 \times 10^{-7}$  mol/mL.





The comparative experiment entailed using the optimized conditions for the catalytic oxidation of 1-octene using TBHP as oxidant and doing each reaction in duplicate.



**Figure 5.13.** The duplicate experiments executed for each catalyst with the images depicting the biphasic mixture of the fluorous-stabilized Au NP catalyst in contact with 1-octene prior to the addition of oxidant and initiation of the 24 h reactions.





**Figure 5.14.** Percentage conversion of 1-octene using the catalyst systems and employing the same metal loading ( $5 \times 10^{-7}$  mol/mL).

## 5.3.6. Effect of ligand and particle size

To discuss the results, the catalyst systems were divided up into those which were produced using **L1** and those which incorporate **L2**.

### 5.3.6.1. Systems with L1

Table 5.3. Catalyst systems incorporating L1 and their associated characteristics.

Catalyst system	Ligand	Solvent	Au: L	Preparation method	Particle diameter
JHD12	L1	S1	1 : 0.28	Direct	43.4 ± 22.2
JHD16	L1	<b>S</b> 3	1 : 0.56	Direct	27.9 ± 25.6
JHD17	L1	S1	1 : 0.56	Direct	17.8 ± 13.7
JHD13	L1	S1	1 : 0.56	Direct	14.8 ± 15.1
JHD14	L1	S1	1 : 1.12	Direct	11.8 ± 15.8
JHD15	L1	S1	1 : 2.24	Direct	$2.0 \pm 0.3$

It was found from the GC-FID results that all catalysts were in fact active in FBC providing conversions above the blank. In addition, **JHD12** shows one of the lowest conversions which was anticipated due to the large particles which were observed at the bottom of the sample vial prior to sonicating the solution.



**Figure 5.15.** Catalyst systems incorporating **L1** and their respective percentage conversion of 1-octene (excludes **JHD15**).

The next biggest system, **JHD16**, gives the second lowest conversion which is in accordance with this trend even though being prepared in **S3**. Among the catalysts which were tested, it was found that **JHD14** gave the highest conversion while being the smallest in terms of particle size. This is consistent with the notion of a higher surface area and the increased exposure of active sites offers a higher conversion of substrate over the reaction period (24 h).

Interestingly, JHD15, which was tested in another experiment (see JHC42 and JHC43 in recycling experiments) afforded percentage conversions rivalling that of JHD14 despite being executed at a 10 × lower catalyst loading. This can be justified by the extremely small sizes of JHD15 having particle diameters around 2 nm, which demonstrates the significant relationship between the size of these NP catalysts and their activity.





Figure 5.16. Selectivities of catalyst systems incorporating L1 in the conversion of 1-octene.

It appears that for the bigger NPs (JHD12 and JHD16) a higher selectivity for the aldehyde product becomes evident in comparison to 1-octanoic acid. However, this selectivity trend changes when the systems average particle diameter is smaller than 20 nm and the octanoic acid product becomes favoured over the aldehyde product, 1-octanal. It was found that the epoxy product is the favoured product in each of these systems. This selective epoxidation by Au NPs has been reported in a number of publications and is observed as a major oxidation product not only in the oxidative transformation of linear alkenes but for other substrates such as styrene and cyclooctadiene. It has also been shown that the use of  $H_2O_2$  and TBHP affords the epoxide selectively.<sup>39–41</sup>

### 5.3.6.2. Systems with L2

The systems in which **L2** was employed, exhibited bimodal size distributions according to TEM analysis. All have nanoparticles of sizes ranging from 2 - 3 nm and 8 - 11 nm. Depending on the system, each group of nanoparticle sizes contributed a different weighted percent of the overall count. For example, in **JHM14**, the two sizes of NPs in the sample were  $2.07 \pm 0.32$  nm and  $10.2 \pm 2.77$  nm, respectively. About 80 percent of the nanoparticle population (count) was made up of smaller NPs as can be seen in the TEM images. Using these weighted percentages and the two sets of NPs constituting the bimodal distribution in each case, it was possible to calculate a combined particle diameter for these fluorous systems.

Catalyst system	Ligand	Solvent	Au: L	Particle diameter (nm)	Combined (nm)
JHM13	L2	S1	1 : 1.12	2.56 ± 0.46; 8.91 ± 2.98	3.75 ± 2.82
JHM14	L2	S1	1 : 0.28	2.07 ± 0.32; 10.2 ± 2.77	4.09 ± 3.79
JHM15	L2	S1	1 : 0.56	2.57 ± 0.42; 9.64 ± 2.37	3.64 ± 2.72
JHM16	L2	S1	1 : 2.24	2.15 ± 0.27; 9.43 ± 2.28	3.24 ± 2.76

 Table 5.4.
 Catalyst systems incorporating L2 and their characteristics.



**Figure 5.17.** Catalyst systems incorporating **L2** and their respective conversions of 1-octene (%).

The lowest percentage conversion of 1-octene was attained by **JHM15** while the highest conversion in the series was accomplished with the catalyst system, **JHM14**. There is not much correlation with the size of the NPs in comparison to the percentage conversion of 1-octene. This is probably due to the sizes and size distributions which are rather similar.





Figure 5.18. Selectivities of catalyst systems incorporating L2 in the conversion of 1-octene.

Again, it is clear that the epoxide is the favoured product and has come to be expected in this work. Most of these systems share similar selectivity percentages with the exception of **JHM15** which does not afford the aldehyde product at the end of the 24 h catalysis run but instead a higher relative percentage of the product, octanoic acid.

# 5.3.7. Recycling tests

Two duplicate experiments were executed, **JHC40a**, **JHC40b**, **JHC41a** and **JHC41b**. All four of these experiments were identical in every regard. All employed 1 mL of **JHM15** (5 × 10<sup>-7</sup> mol/mL) in **S1** as the fluorous catalyst solution, together with 1 mL of 1-octene and TBHP (0.5 mL). Each was stirred for 24 h on the parallel reactor together at 60 °C. The differences in the experiments were initiated upon recycling of the fluorous phase after its first 24 h catalyst run. For **JHC40r** and **JHC41r**, the duplicate fluorous phases (from **JHC40** and **JHC41**) after the first 24 h run was isolated into clean reactor tubes and reused in a subsequent recycling of the fluorous phase, while for **JHC40r**, no additional TBHP was included in the recycling of the fluorous phase, while for **JHC41r**, the same quantity of TBHP was included in the subsequent recycling reaction as the first 24 h catalyst run.





**Scheme 5.5.** Catalysis reaction scheme with **JHM15** - with and without addition of TBHP between recycles



**Figure 5.19.** Percentage conversion of 1-octene with and without addition of oxidant upon catalyst recycling.



Figure 5.20. Selectivities of the catalyst experiments JHC40 and JHC41 and their respective recycle runs.

Two duplicate experiments were executed, JHC42a, JHC42b, JHC43a and JHC43b. All four of these experiments were identical in every regard. All employed 1 mL of JHD15 ( $5 \times 10^{-8}$  mol/mL) in **S1** as the fluorous catalyst solution, together with 1 mL of 1-octene and TBHP (0.5 mL). Together, each was stirred for 24 h on the parallel reactor together at 60 °C. The differences in the experiments were initiated upon recycling of the fluorous phase after its first 24 h catalyst run. For JHC42r<sup>1</sup> and JHC43r<sup>1</sup>, the duplicate fluorous phases (from JHC42 and JHC43) after the first 24 h run was isolated and transferred to clean reactor tubes and re-used in a subsequent recycling of the fluorous phase, while for JHC42r, no additional TBHP was included in the subsequent recycling reaction as the first 24 h catalyst run. This process of re-using the fluorous phase was executed up to 5 times without the addition of TBHP after subsequent recycles (JHC42r<sup>1</sup>-r<sup>5</sup>) and with the addition of TBHP after subsequent recycles (JHC43r<sup>1</sup>-r<sup>5</sup>).



Catalyst runs and subsequent recycles

**Figure 5.21.** Percentage conversion of 1-octene using **JHD15** ( $5 \times 10^{-8}$  mol/mL) without the addition of TBHP in subsequent recycles.

It is clear from the graph (Figure 5.21) that there is a drop in conversion when no oxidant is added between the recycling stages. Upon continued recycling, the conversion seems to be maintained at around 16 - 18 percent. This means that the fluorous-stabilized Au NP catalyst

(JHD15) may be associating with the oxidant from the first run, allowing it to still catalyse the transformation of 1-octene.



**Figure 5.22.** Selectivities of the catalyst experiment **JHC42** using **JHD15** ( $5 \times 10^{-8}$  mol/mL) without the addition of TBHP in subsequent recycles.

Looking at the graph for **JHC43** and its subsequent recycles, it is shown that the catalyst remains active, given that the blank duplicate TBHP run offered a conversion of  $28.6 \pm 2.30\%$ . Moreover, there is only a slight decrease in the conversion of 1-octene after each recycle. This decrease could then be attributed to degradation of catalyst over the course of the recycle period, but is probably a result of loss of some catalyst solution during repeated transferral between glassware upon separation of the phases between recycle runs.



Catalyst runs and subsequent recycling

**Figure 5.23.** Percentage conversion of 1-octene using **JHD15** ( $5 \times 10^{-8}$  mol/mL) with the addition of TBHP with each subsequent recycle.



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**Figure 5.24.** Selectivities of the catalyst experiment **JHC43** using **JHD15** ( $5 \times 10^{-8}$  mol/mL) with the addition of TBHP in subsequent recycles.

# 5.3.8. Catalytic pathways and proposed mechanism of oxidation

It has been postulated that there are likely two major chemical pathways to afford the oxidation products we have observed in this work.



**Scheme 5.6.** Proposed catalytic pathways to afford the observed oxidation products identified in this work.





**Scheme 5.7.** Proposed mechanism of catalytic oxidation of 1-octene using TBHP and affording the observed oxidation products.

A sample (JHC39b) was analysed using GC-MS to identify the products seen in the GC-FID spectrum of the same sample. The reason for using this sample was because its GC-FID chromatogram possessed the most unidentified peaks and many of these peaks appeared to be of sufficiently high concentration to allow qualitative analysis by way of GC-MS. JHC39b involved one of the duplicate reactions of an experiment in which 1-octene (1 mL) was stirred for 24 h with a larger than usual quantity of TBHP (1 mL) and fluorous catalyst system (JHM15). It was found from the GC-MS spectrum, the presence of trace amounts of the fluorous solvent, perfluoromethylcyclohexane (S1), suggesting minor leaching or that the phases were not permitted to cool sufficiently. Interestingly, there was a portion of unreacted TBHP seen in the spectrum and demonstrated in Figure 5.26. Moreover, the formation of tertbutanol as a by-product from the production of A (in Scheme 5.7) is confirmed in the GC-MS spectrum and illustrated by its fragmentation pattern (Figure 5.26). Other observations which must be noted were the presence of oxidation products resulting from the oxidation of toluene by TBHP. Some of these oxidation products included benzaldehyde and benzyl alcohol (Figure 5.27). Finally, the peaks corresponding to oxidation products of 1-octene which were not identified using GC-FID were found to be that of 1-octen-3-ol (E or Z isomers), 1-octen-3one, 2-octen-1-ol (E or Z isomers) and 2-octanoic acid (E or Z isomers). Unfortunately, peaks which could not be identified as seen in the range above 20 min were either too low in abundance or had overlapping peaks making identification too difficult since the column used was not chiral.



Figure 5.25. GC-MS chromatogram of sample JHC39b.

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**Figure 5.26.** GC-MS chromatogram of sample **JHC39b** with annotated MS fragmentation patterns corresponding to compounds which were too dilute to be identified using GC-FID or the appropriate standard was not run.





**Figure 5.27.** GC-MS chromatogram of sample **JHC39b** with annotated MS fragmentation patterns corresponding to compounds which were too dilute to identify using GC-FID since they were formed in very low quantities.

### 5.4. Conclusions

The "proof of concept" of the fluorous biphasic approach as a green strategy for the facile recycling and re-use of expensive catalysts, has been achieved. The catalysis work which has been described herein, employed fluorous-stabilized Au NPs as catalysts in the fluorous biphasic catalytic oxidation of an alpha olefin, more specifically, the model substrate, 1-octene. It was found that upon stirring the biphasic system and heating to 60 °C, it becomes monophasic (as for **S1** as the fluorous medium). Once the reaction is complete, the system is cooled to ambient and it becomes biphasic again. This allows the catalyst (which is soluble in the fluorous phase) and the substrate/product (organic phase) to be isolated (using a separating funnel) at the end of the catalytic reaction.

Ten fluorous-stabilized Au NP catalyst systems which were characterized by UV-Vis spectroscopy, TEM and ICP-OES, were assessed under the optimized catalytic reaction conditions. These systems were prepared using varying ratios of Au: L1 or L2, in S1 or S3, respectively. The catalysis experiments which were executed, have shown that all the fluorous-stabilized Au NPs which were examined in these aforementioned experiments, were active in the fluorous biphasic catalytic oxidation of 1-octene. Not only this, but even after recycling up to five times, the catalyst continued to show steady activity and always performed better than the blank reaction (without catalyst) in terms of % conversion of substrate. There appeared to be a distinct relationship between the average particle diameter (nm) of the Au NPs in the system and the conversion of 1-octene. This was demonstrated for JHD12 and JHD16 which comprised the largest NPs and afforded the lowest conversions of 1-octene in relation to the other catalyst systems tested at this constant metal loading ( $C_{f(Au)}$ ) of 5 x 10<sup>-7</sup> mol/mL and optimized experimental conditions. Although not tested at the same metal loading as the other catalyst systems, JHD15, was found to be the most active catalyst. This is because the catalyst was tested at a concentration ten times less than all the other catalysts and still provided a higher conversion of 1-octene. The main reason for this observation is the size of the Au NPs of JHD15 which were 2.0 ± 0.3 nm being much smaller than those associated with the other catalyst systems.

The use of two different fluorous solvents, **S1** and **S3**, were evaluated in the catalytic oxidation reaction. The same catalyst (**JHD16**) was dispersed in **S1** as well as in **S3** (same volumes and metal loading) and the oxidation carried out with TBHP while keeping all conditions the same besides the fluorous solvents. The results suggested that the adjusted solvent had very little effect on the catalysis process. In other words, the initial conversions of 1-octene were very similar, the subsequent conversions derived from recycling remained very similar and the product selectivities were all extremely similar. Although this was the case, the fluorous solvent

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**S3** was identified as the better choice between the two. The reasons for this are because **S3** has a higher boiling point than perfluoromethylcyclohexane, making it less likely to be lost during the catalysis runs and subsequent recycling of the fluorous phase. Moreover, during the course of the experiment the use of **S3** yielded slightly higher conversions of 1-octene in comparison to the use of **S1** as the fluorous medium.

It was shown that increasing the metal loading results in an increase in conversion of 1-octene. Increasing the volume of TBHP in relation to the Au catalyst affords higher conversion of 1-octene and can be understood as more oxidant would result in more oxidation over the 24 h catalysis run. With respect to selectivity, with increasing TBHP in relation to Au, the epoxide product becomes increasingly favoured (as the major oxidation product). This is entirely reasonable as the epoxy intermediate denoted "(**A**)" in Scheme 5.6 is the primary chemical intermediate produced upon interaction of TBHP, the catalyst and substrate (before undertaking *path 1* or *path 2* (Scheme 5.6) and being subsequently transformed to the final C8 oxidation products observed in the appropriate GC-FID chromatograms.

None of the expected oxidation standards/products are seen in the GC chromatograms in all cases when using the oxidants, O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>. Although, less powerful oxidants than TBHP, according to the chromatograms, a small percentage of substrate is being consumed and is evidenced by the reduced intensity of the substrate peak. The identity of the products, however, could not be determined using GC-FID due to the absence of peaks corresponding to a potential oxidation product. Solubility issues of the product in toluene may have prevented its identification using GC-FID. Other possibilities which have been thoroughly deliberated and actively practiced include increasing the column temperature to its maximum and increasing the analysis time to ensure all chemical components had eluted from the GC column during the analysis window. It has been considered that due to the diverse number of possible oxidation products formed in the oxidation of 1-octene and also due to their low levels of production, they may not be seen in the GC-FID but could still be accounted for by the consumption of 1-octene.

### 5.5. Experimental section

#### 5.5.1. Instrumentation

Analysis of samples by gas chromatography was executed using a VARIAN 3900 GC fitted with a polar Cyclosil-B column (30 m, 0.250 mm diameter and 0.25 um film) using helium as

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the carrier gas. GC-MS analysis was carried out by CAF at Stellenbosch University. In the later catalyst experiments, reactions were carried out in tandem using a parallel reactor thermoregulated at 60 °C. Additionally, the system was set up so that cold water would circulate into the condenser of the reactor. This was achieved by connecting the system to a source of ice water (by piping) and employing a water pump to circulate the cold water over the course of the catalysis reactions.

### 5.5.2. Sampling of standards

The appropriate standard (50  $\mu$ L), *p*-xylene (50  $\mu$ L) and anhydrous toluene (900  $\mu$ L) were added to a GC vial to afford a 1 mL solution which was analysed using GC-FID. In each case the masses of the 50  $\mu$ L quantities of the internal standard (*p*-xylene) and the standard analyte were logged for use in calculating the relative response factors for these standards.

# 5.5.3. Sampling of catalysis experiments

After the fluorous and organic (substrate/product layer) are separated after the catalysis run, the octene layer is isolated into a sample vial and a small portion (spatula tip) of MgSO<sub>4</sub> is added to the mixture. The solution is mixed by swirling the sample vial and then it is transferred to a separate sample vial by using a syringe filter for compliance with preparing the GC sample for injection onto the column. Precisely 200  $\mu$ L of the octene layer which has been dried is used in combination with 50  $\mu$ L *p*-xylene and toluene (750  $\mu$ L) to make up the respective GC sample. The masses of the 50  $\mu$ L quantities of internal standard (*p*-xylene) used in the GC vials were documented for use in calculating the results.

# 5.5.4. Blank catalyst reactions

# 5.5.4.1. Blank reaction – B<sub>O2</sub>

The fluorous solvent **S1** (1 mL) containing no catalyst was transferred by means of a micropipette together with 1-octene (1 mL) to glass reactor tubes. The duplicate reaction tubes for each experiment were then positioned in a parallel reactor already operating at 60 °C at a set stirring rate. whereby  $O_2$  was bubbled through the mixture until the entire reactor tube was filled with  $O_2$ . The respective reactions were stirred for 24 h. After the 24 h catalysis reaction, the magnetic stir bar was removed and the contents of each Schlenk tube was permitted to cool to ambient before being transferred to a separating funnel. Sampling for GC analysis follows the standard procedure above (5.5.3).

## 5.5.4.2. Blank reactions – BH2O2 and BTBHP

For the  $H_2O_2$  and TBHP assessments, the reactions were carried out using Schlenk tubes connected to condensers. The same mol equivalents of  $H_2O_2$  and TBHP were used in each case such that 0.44 mL of  $H_2O_2$  was used while 0.50 mL of TBHP was used. To a Schlenk tube, 1-octene (1 mL) was transferred by means of a micro-pipette followed by 1 mL of fluorous solvent **S1** containing no catalyst. The respective oxidant was included ( $H_2O_2$  or TBHP) and the duplicate reactions were stirred at 500 rpm at 60 °C for 24 h. Thereafter, the two layers were separated using a separating funnel. Sampling for GC analysis follows the standard procedure above (5.5.3).

# 5.5.5. Catalyst reactions

# 5.5.5.1. JHC32, JHC38 and JHC39

To a reactor tube, the fluorous solution (1 mL) containing JHM15 (1 ×  $10^{-6}$  mol/mL) in S1 was transferred by means of a micro-pipette together with 1-octene (1 mL). The duplicate reaction tubes for each experiment were then positioned in a parallel reactor already operating at 60 °C at a set stirring rate. Upon positioning the reactor tube on the parallel reactor, the appropriate amount of TBHP was included in the catalysis run by using a micro-pipette and incorporating the oxidant to the reaction through the inlet on the lid of the tube, which was resecured after the addition of the TBHP. The volume of TBHP added to each duplicate experiment, was as follows: JHC38a and JHC38b = 0.25 mL; JHC32a and JHC32b = 0.50 mL; JHC39a and JHC39b = 1.00 mL. The respective reactions were stirred for 24 h. After the 24 h catalysis reaction, the magnetic stir bar was removed and the contents of each Schlenk tube was permitted to cool to ambient before being transferred to a separating funnel. Thereafter, the octene layers were isolated into sample vials for GC analysis, while the fluorous phases were stored for future use.

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### Chapter summaries, concluding remarks & suggestions for future work

### 6.1. Chapter summaries & concluding remarks

*Chapter 1* provided an introduction to nanomaterials, with emphasis on the catalytic capabilities of metal nanoparticles in the liquid phase. On this topic, attention is paid to the application of gold nanoparticles as promising oxidation catalysts. In saying this, the different methods of producing Au NPs and the literature surrounding improvements to synthetic methods are reviewed. The chapter is then diverted to the general topic of catalysis. Here, the benefits of homogeneous catalysis over heterogeneous catalysis is deliberated, with the major issue of catalyst recovery (in the former instance) being highlighted. The innovative techniques showing potential in solving this issue are discussed such as magnetic separation, immobilization of dendrimers on supports, aqueous biphasic systems and more favourably, the fluorous biphasic system. On this note, the literature is combed and absorbed before it is announced that our intentions are to combine the benefits of using gold nanoparticles for oxidation reactions with the notion of the fluorous biphasic system for catalyst recovery. These intentions are made clear in the project aims and objectives which are then reported.

*Chapter 2* entailed UV-Vis spectrophotometric titrations with the aim of determining the maximum quantity of metal ions which could be encapsulated into two dendrimers. The dendrimers investigated included an unmodified G3-DAB PPI NH<sub>2</sub> dendrimer and a modified-version which included palmitoyl peripheral arms. The maximum loading capacities of both dendrimers were elucidated for Cu(II), Ni(II), Co(II), Zn(II), Rh(III) and Pd(II) with the unmodified dendrimer having suitable solubility properties to attain endpoint values for additional metal ions such as Au(III), Cr(III), Cd(II), and Pt(II) in H<sub>2</sub>O. Comparatively, the hydrophilic, unmodified dendrimer. This was justified by the additional driving force of the encapsulation process which was the result of the altered and enhanced solubility of the modified dendrimer in organic solvents. The encapsulation of the metal ion would, in addition to stoichiometric factors, be facilitated by the solubility difference between the hydrophobic exterior and hydrophilic interior of the modified dendrimer.

*Chapter 3* described the preparation and characterization of fluorous-stabilized Au NPs prepared by way of a micelle-template strategy (using the modified dendrimer). Firstly, organic-soluble Au DENs were prepared by the encapsulation of Au ions into the interior of

the dendrimer and this was followed by reduction with NaBH<sub>4</sub>. The reduction process was monitored by UV-Vis spectroscopy through scrutiny of the LMCT band at 330 nm and the SPR band at around 550 nm in CHCl<sub>3</sub>. These Au DENs were extracted from the organic phase into the chosen fluorous solvent, **S1** or **S2**, with the use of fluorous ligands. Finally, using the optimized conditions, eight unique, spherical and reasonably small fluorous-stabilized Au NPs were successfully prepared. It was found that NP systems featuring both **L1** or **L2** could be synthesized by way of this method. In each synthesis, the fluorous stabilized Au NP systems were characterized by UV-Vis spectroscopy, TEM and ICP-OES analysis. Four systems, **JHM13** – **JHM16**, were produced using varying ratios of Au: **L2** by way of this method. Contrary to expectation, this did not play a significant role in tailoring the sizes of fluorous-stabilized Au NPs which exhibited average particle sizes between 3.2 nm – 4.0 nm.

*Chapter* 4 presented a distinct and unique method of making fluorous-stabilized Au NPs by preparing an Au-L1 complex followed by a fluorous-aqueous biphasic reduction step to afford fluorous-stabilized Au NPs stabilized by L1. In this preparation, the preparation time is significantly reduced in comparison to the micelle template method and does not require a modified dendrimer or an organic solvent. Furthermore, it was shown that this method enabled the tailoring of different sizes of NPs by varying the Au: L1 ratio. In this regard, it was clearly shown that by increasing the quantity of L1 in relation to Au, smaller fluorous-stabilized Au NPs are obtained. This was shown for the sample series JHD12 – JHD15 incorporating of Au: L1 ratios of 1: 0.28, 0.56, 1.12 and 2.24, respectively, and yielding Au NP sizes of 43.4  $\pm$  22.2 nm, 17.8  $\pm$  13.7 nm, 11.8  $\pm$  15.8 nm and 2.0  $\pm$  0.3 nm, respectively. Other efforts were made using other fluorous ligands like L2, L3 and L4, despite these efforts, no fluorous-stabilized Au NPs could be isolated in the fluorous phase after reduction. Six catalyst systems produced by this method, namely, JHD12-JHD17 were studied in the subsequent catalysis experiments.

Chapter 5 involved the evaluation of ten different fluorous-stabilized Au NPs in the biphasic catalytic oxidation of 1-octene. Exploiting the monophasic properties of the fluorous-organic systems at elevated temperature, after employing a reaction temperature of 60 C and stirring for 24 h, the system appeared to become monophasic. At the end of each trial, the system was cooled to room temperature and the biphasic nature was restored, allowing for easy separation of the product layer and fluorous catalyst solution. Significantly, it was shown that every fluorous-stabilized catalyst which was tested was shown to be active in the fluorous biphasic catalytic oxidation of 1-octene. Furthermore, at the end of each catalysis reaction, the phases could be easily separated and the fluorous catalyst system could be re-used up to 5 times without significant loss in activity. The use of different green oxidants,  $O_2$ ,  $H_2O_2$  and TBHP, were assessed with the latter showing the most promise and therefore being explored more intensively. Using TBHP as the oxidant, there appeared to be a distinct inverse

relationship between the average particle diameter (nm) of the Au NP catalysts and the conversion of 1-octene. This was particularly noticeable for JHD12 and JHD16 which were two systems having the largest NPs offered the lowest conversions of 1-octene. The smallest system, JHD15 ( $2.0 \pm 0.3$  nm) was tested at a loading 10 × lower than the other catalysts and still gave the highest conversion of 1-octene. With this said, it was found that the major product seen in each instance when using TBHP was epoxy-1,2-octane with smaller quantities of octanal and octanoic acid being seen in the GC-FID. Additional characterization with GC-MS was helpful in proposing a mechanism which accounts for the products obtained. In conclusion, the work executed herein has shown the fluorous biphasic system to be an effective green tactic for catalyst recovery. With this said, much of this potential is yet to be realised and thus the FBC approach remains an interesting avenue of study definitely worthy of further exploration.

### 6.2. Suggestions for future work

Throughout this project, there have been numerous observations which simply warrant further investigation. The proposed future work is broken up into two larger topics and include the topic of the reduction step in preparing metal NPs and catalysis-related studies.

The reduction step

Looking at the micelle template strategy for producing fluorous-stabilized Au NPs, we have certainly grasped the significance of the reduction step on the extraction step, whereby the uptake of smaller and well-dispersed Au DENs by a suitable fluorous ligand is easier and more favoured. This is because the increased surface area- to-volume ratio of smaller particles provides the ligand with more accessible active sites to coordinate to and ultimately sequester the organic soluble DENs into the fluorous phase. Considering this size requirement, it would be insightful to determine a way to achieve complete reduction while also minimizing the reduction time. This is because as the reduction time is increased more time is provided for the NPs to grow leading to larger Au NPs.

It would be interesting to try other reducing agents other than NaBH<sub>4</sub> in the production of Au NPs. In our NP syntheses, an aqueous solution of NaBH<sub>4</sub> is prepared immediately prior to the reduction. This is done to minimize the extent of the reaction of NaBH<sub>4</sub> with water before making use of the reducing agent. The reaction of NaBH<sub>4</sub> and H<sub>2</sub>O produces H<sub>2</sub> gas as a by-product. Since we want to minimize the influence of synthetic variables which cannot be

controlled to be able to reproduce NP systems. A different strategy should be investigated as we cannot control the reaction of the reducing agent and water and the production of the  $H_2$  gas is expected to further complicate the reduction step. This is because both NaBH<sub>4</sub> and  $H_2$  gas are reducing agents and therefore the reduction step becomes more complicated and less controlled. It is also known that the reduction of  $Au^{3+}$  to  $Au^0$  by NaBH<sub>4</sub> is quite complicated and can involve a variety of different half reactions and side reactions. A suggested reducing agent to test would be  $H_2$  gas which could be bubbled through the metal ion solution. This appears uncomplicated and fewer side reactions are likely to occur.

Other studies could involve executing the reduction while the reaction vessel is submerged in an ice bath. This would slow the process of reduction and could prevent troublesome side reactions. However the study proceeds, it would be interesting to see the effect of reduced temperature on NP formation specifically using NaBH<sub>4</sub> and comparing with increased temperature intervals.

Another interesting test would be to reduce solutions of Au at different concentrations. The idea behind this is that lowering the concentration of Au ions while keeping the reducing agent quantity the same. It is expected that for the more dilute systems, the reduction will afford Au NPs which are more disperse and less inclined to undergo agglomeration as a result of the NPs being more spread out when diluted.

Catalysis-related studies

On the topic of fluorous biphasic catalysis, an exciting study would be to test different metal NPs stabilized by fluorous ligands in various catalytic reactions.

The substrate scope could be extended to include other alkenes such as styrene or cyclohexene in fluorous biphasic catalytic oxidation using fluorous-stabilized Au NPs, similar to the ones assessed herein. This would provide a better understanding of the oxidation mechanism depending on the oxidation products formed when employing different oxidants.

An additional investigation into the effect of using different fluorous ligands other than the ones used in this work as well as research into the effect of the fluorous solvent employed on the catalytic results. This would be investigated by assessing a range of other fluorous solvents while keeping the fluorous catalyst constant and making comparisons between the selectivity results as well as conversions of substrate (1-octene in this example).