Core-shell silica nanostructures for greener catalysis

A thesis submitted to McGill University in partial fulfillment of the requirements

of the degree of Doctor of Philosophy

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December 2022

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To my little brother, João Paulo.

"Cada um sabe a dor e a delícia e ser o que é"

Caetano Veloso, Dom de Iludir

Acknowledgements

I have lived in Montreal now for more than five years and I have only amazing things to say about this city that received me, taught me a new culture and language, and gave me countless opportunities for professional and personal growth (of course there were a few winters, but nothing is ever perfect). I humbly acknowledge having lived and received my Ph.D. training in the traditional land of the Huron, Abenaki, and Anishinaabeg peoples.

I thank the funding agencies who supported my research projects and travel to conferences, especially the Fonds de Recherche du Québec - Nature et Technologies, which funded me for most of my graduate studies. I also thank the SELF-Clark program for funding the Mini-MBA program I took at McGill's business school.

I have been extremely lucky to have been guided throughout my scientific career by amazing women. First, I thank my Ph.D. supervisor Dr. Audrey Moores, who has supported me since the very first moment I applied to join the group as a master's exchange student back in 2016. You have always believed in me and given me confidence when I needed it. Merci beaucoup, je serai toujours reconnaissant! Second, I also want to thank my M.Sc. supervisor, Dr. Flavia Moura, who supported me unconditionally on my application to McGill (and many following endeavors) and whose counsel I have been privileged to enjoy throughout all these years. Sou muito feliz de te ter como referência e poder contar com você, muito obrigado! Third, a very special thanks to Dr. Iara Guimarães and Dr. Aline Tireli, who first inspired me to be a researcher, were my first professional role models, and gave me confidence to be myself, trust my potential, and follow my career and ambitions. Vocês são muito importantes para esta conquista, muito obrigado mesmo!

I also want to thank the people who have collaborated with me throughout these years, your partnership and insights were crucial for the fruition of this thesis: Dr. Zacharias Amara, Ariane Desgranges, Dr. Cyrille Monnereau, Elena Sanchez, Dr. Jose Angel De Toro, Amanda Martins, Dr. Cameron Weber, Dr. Jesus Angel Valdez, and Jackson DeWolfe. I also thank Dr. Chao-Jun Li and Dr. Amy Blum for being on my committee throughout these years and giving me valuable feedback.

To the fantastic Chantal Marotte, the person who helped me navigate safely and with stability throughout the graduate program: thank you for being so amazing and efficient! I probably come

to you much more than the average student and you are always timely and precise, I appreciate it enormously.

I joined the Moores group as a master's exchange student and then as a Ph.D. student, so I have spent a fair amount of time in this group and seen different generations of people. Throughout the years I have had the pleasure to overlap with Madhu, Alain, Thomas, Luis, Blaine, Alex, Aude, Tony, Austin, Galen, Sara, Faezeh, Mike, Ju, Jasmine, Ruby and Ana. You have all been amazing and I want to thank you for the partnership, the conversations, the coffee breaks, the parties, and of course the mandatory group lunch breaks due to my insatiable starvation every day precisely at noon! Alain, the one who has helped me since day zero, my favorite "Uptown Funk" guitar player, thank you for the friendship and the countless teachings in the lab! Você é trilegal, muito obrigado por tudo! Alex (#1), the brightest rockstar I (h)ave ever known who is forever seventeen! Mamma Mia, I (h)ave no words to express (h)ow important you are to me! You are one of the most beautiful gifts McGill (h)as given me and I am grateful to (h)ave you in my life! I (h)ave learned (and still learn) so much from your determination and practicality, and I can't thank you enough for all your support and love throughout all these years! Aude, my cohort, review-day, EELS-course, mini-MBA, and Summer-School buddy! (phew!) We have been through so much together! It would have been a way less interesting and fun journey without your friendship and support! Your good mood, calm, tranquility, and down-to-Earth attitude have inspired me enormously all these years, I could not have asked for a more "awesome!" graduate school colleague and friend! Merciiii! Blaine, can I ask you a question? Ooooooh boy, I have asked so many! And you are always patient and kind. Thank you for being such an amazing friend! I miss our deep conversations about our futures, careers, frustrations, and dreams. I am extremely lucky to have shared all of those years with you! Tony, isn't D.C. crazy? Or is Barcelona crazier? Or is it just us together? Anyway, it has been an amazing (and sometimes crazy) few years! You always bring this positive energy which makes everything light and fun! Thank you for being such an awesome friend! Cheers to many more trips together to come (com ar condicionado)! Mike, we did not spend that much time together, but it definitely feels like it! Thank you for all of the conversations, sometimes deep and sometimes not so deep, always fun, and interesting! I loved sharing with you glories and frustrations, always over a nice coffee or diet-threatening treats (yum)! I really hope our paths will cross again! Jas, you have this amazing energy around you that just makes me feel happy! I love spending time with you, it is fantastic to have you as a friend. I do hope our paths cross again.

Maybe we'll work together "*for the government*"? Wearing safety red? Last but not least: Juju, você veio pra trazer felicidade, brasilidade, e mineridade na minha vida no lab! É muita sorte a gente ter se encontrado e quero te guardar pra sempre na minha vida! Brigado por tudim, viu?

Not only of Moores Group a Ph.D. is built, so I also want to thank Hathem Titi, mon ami, for all the great moments together. I also want to thank my fellow lover of Brazilian music, the great songwriter Sosthène, who also helped me from day zero here in Montreal. Muito obrigado!

I am only able to submit this thesis because I have had an incredible support network outside of the university as well. And Alex, my handsome life partner, is the most important part of it. While I have been working on my science degree, Alex has earned a degree in kindness, patience, and generosity, with a minor in Brazilian culture. I have never met a more loving and understanding person and I have no words to describe how grateful I am to you and to the universe for having put you in my life. Merci, mon cœur.

O núcleo brasileiro também não pode faltar nesses agradecimentos, e não posso deixar de começar pelo Lucas, mais conhecido como: a Bill! Billzinha, a gente ter vindo juntos para o Canadá em 2012 e depois de novo em 2018 foi uma coincidência generosa do destino, mas você ter vindo pra Montreal foi o maior presente que você poderia me dar! Você é uma parte fundamental da minha vida desde Toronto, mas ainda mais nesse período de doutorado. Você é minha família fora de casa! Você ilumina minha vida sua energia solar, me alegra com seus olhos de gato, e me faz me sentir amado e acolhido sempre que estou Triste! Obrigado por tudo! Estendo esse agradecimento à rede de amigos brasileiros em Montreal que são e foram todos essenciais pra eu chegar até aqui. Menção especial com muito amor pra Zé, Victor, Hudson, João Batista, Amanda e Naíla.

Um agradecimento mais que especial para minha família no Brasil. Tenho a sorte imensa de ter nascido nessa família maravilhosa que é unida, me aceita como sou e me ama incondicionalmente. Agraço à minha mãe Sueli por ser o meu maior exemplo de amor e cuidado, por ter me ensinado a sonhar muito alto a não ter medo dos obstáculos. Talvez a senhora se arrependa de ter me ensinado a sonhar tão alto, né? Mas eu nunca vou conseguir te agradecer o suficiente por isso. Estendo esse agradecimento de amor maternal para a minha Vovó e pra Dindinha. Minha vó é o meu exemplo de força, fé, bondade, bom humor, inteligência, sabedoria e humildade. Ela estudou pouco, mas tem um entendimento que nenhum doutorado ensina. Eu sonho em um dia aprender um pouquinho de cada uma dessas habilidades que ela tem. À Dindinha eu agradeço pelo exemplo

de força, determinação e, sobretudo, empatia. Assim como falei da vó, um pouquinho da sua empatia já valeria mais do todo meu doutorado, um dia eu aprendo. Obrigado por ser esse exemplo na minha vida. Agradeço ao meu pai pelo amor e apoio em todos os momentos. Agradeço ao meu irmão Joãozinho por alegrar a minha vida e as dos meus pais e só dar orgulho pra gente! Um agradecimento especial para a Tia Rozi por me inspirar a ser determinado e ter me ensiando a ver alegria em tudo. E claro, também agradeço os meus primos mais que primos, que são tão importantes na minha vida. Mi, com seu coração enorme, alma livre e uma energia leve! Cacá, que me ensinou a habilidade que mais amo: a adaptabilidade! Um dia serei camaleoa igual você! Lalishe, tão novinha e com tanta bondade e sabedoria! Melissandra, a lacradora! Obrigado por fazerem parte da minha vida e me inspirarem, cada um do seu jeito! Também agradeço às minhas tias Terra: Tia Doda, Tia Kika e Tinês, pelo amor e carinho de sempre. Um agradecimento também mais que especial pra Dielle, essa flor que chamo de prima e que me inspira a apreciar as coisas simples da vida.

Agradeço também ao meu Brasil, meu povo e minha cultura brasileira, que são a essência de quem eu sou. Direciono esse agradecimento a Gal Costa, a musa da música brasileira que nos deixou este ano. Gal, sua voz trouxe o Brasil pra mim quando eu mais precisei, e ainda traz. Você é a voz brasileira que me alegra além dos oceanos, e além das nações. Obrigado por tanto!

Thank you to all of you for supporting me and believing in me!

Muito obrigado!

Abstract

Catalysis is present in most chemical transformations, and the improvement of catalytic processes is key to the movement toward more sustainable chemistry. Silica is the basis of many catalytic systems, it is made from abundant elements, and its synthesis is highly controllable at the nanoscale; therefore, silica nanomaterials are a convenient tool that can be used to make catalytic systems greener. In this thesis, we explore the construction of hierarchical silica nanostructures by using silica shells that play specific roles in two different contexts: magnetic photocatalysis and confined catalysis.

In the first part, we cover the synthesis and main applications of silica nanoparticles, basic concepts in magnetic photocatalysis, and extensively review the field of confined catalysis for greener chemical transformations. Then, we developed silica-coated magnetic nanoparticles to perform the photo-oxidation of β -citronellol using ruthenium (II) tris(bipyridine) as a photosensitizer and were able to develop a system that combined photocatalytic activity and magnetic properties; in addition, we systematically demonstrated the role of light absorption by the support in the photocatalytic activity of the system by tuning the silica nanoshells. Following, we utilized the same silica-coated supports to immobilize rose bengal, a metal-free photosensitizer, and observed the same effect of absorption of light by the support in photocatalytic activity; we also studied the stability of the photocatalytic system and demonstrated that the immobilization method had an impact on the photostability of the photosensitizer. Additionally, we applied the silica nanodesign tools to prepare hollow core-shell materials composed of ruthenium hydroxide supported on alumina as the core and mesoporous silica as the shell; we applied this system to the alcohol amination reaction, a hydrogen borrowing process, and found that confining the reaction inside the nanoshells provided a 3-fold improvement in the selectivity to the fully reduced product; we also systematically demonstrated the central role of tuning the yolk-shell gap in the nanostructures by controllably etching the silica shells.

In summary, we were able to apply the principles of green chemistry to catalytic systems in different contexts by exploring the design possibilities of core-shell silica nanostructures.

Résumé

La catalyse est présente dans la plupart des transformations chimiques, et l'amélioration des processus catalytiques est cruciale pour le mouvement vers une chimie plus durable. La silice est à la base de nombreux systèmes catalytiques, elle est fabriquée à partir d'éléments abondants, et sa synthèse est hautement contrôlable à l'échelle nanométrique ; par conséquent, les nanomatériaux de silice sont un outil pratique qui peut être utilisé pour rendre les systèmes catalytiques plus verts. Dans cette thèse, nous explorons la construction de nanostructures de silice hiérarchiques en utilisant des coquilles de silice qui jouent des rôles spécifiques dans deux contextes différents : la photocatalyse magnétique et la catalyse confinée.

Dans la première partie, nous couvrons la synthèse et les principales applications des nanoparticules de silice, des concepts de base dans la photocatalyse magnétique, et ensuite nous faisons une revue détaillée sur le domaine de la catalyse confinée pour des transformations chimiques plus vertes. Ensuite, nous avons développé des nanoparticules magnétiques enrobées de silice pour effectuer la photooxydation du β -citronellol en utilisant le ruthénium (II) tris(bipyridine) comme photosensibilisateur, et nous avons obtenu un système qui combine l'activité photocatalytique avec les propriétés magnétiques ; en autre, nous avons systématiquement mis en évidence le rôle de l'absorption de la lumière par le support dans l'activité photocatalytique du système en contrôlant l'épaisseur des nanocouches de silice. Par la suite, nous avons utilisé les mêmes supports revêtus de silice pour immobiliser le rose Bengale, un photosensibilisateur organique, et avons observé le même effet d'absorption de la lumière par le support dans l'activité photocatalytique ; nous avons également étudié la stabilité du système photocatalytique et démontré que la méthode d'immobilisation du photosensibilisateur avait un impact sur sa photostabilité. De plus, nous avons appliqué les outils de conception de nanosilice pour préparer des matériaux avec une architecture cœur-coquille creuse composés d'hydroxyde de ruthénium supporté sur de l'alumine comme cœur et de la silice mésoporeuse comme coquille ; nous avons appliqué ce système à la réaction d'amination d'alcool, un processus d'emprunt d'hydrogène, et avons constaté que le confinement de la réaction à l'intérieur des nanocoquilles permettait de multiplier par 3 la sélectivité vis-à-vis du produit entièrement réduit ; nous avons également systématiquement démontré le rôle central du réglage de l'écart entre le cœur et la coquille par la dissolution des coquilles de silice de manière contrôlée.

En résumé, nous avons réussi à appliquer les principes de la chimie verte à des systèmes catalytiques dans différents contextes en explorant les possibilités de conception de nanostructures cœur-coquille de silice.

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List of abbreviations

¹ O ₂	singlet oxygen	
ADPA	anthracene-9,10-dipropionic acid	
Al ₂ O ₃ /Ru(OH) _x	alumina-supported ruthenium hydroxide	
Al ₂ O ₃ /Ru(OH) _x @pSiO ₂	alumina-supported ruthenium hydroxide yolk in porous silica shell	
APTES	(3-aminopropyl)tetraethyoxysilane	
APTMS	(3-aminopropyl)tetramethyoxysilane	
BEP	Brönsted-Evans-Polanyi	
BET	Brunauer-Emmett-Teller	
BET	Brunauer, Emmett, and Teller	
C _{min}	minimal nucleation concentration	
CNT	carbon nanotube	
Ср	cyclopentadienyl	
CTAB	cetylmethylammonium bromide	
DFT	density-functional theory	
DI	deionized	
DLS	dynamic light scattering	
DRIFTS	diffuse reflectance infrared Fourier-transform spectroscopy	
EDAX	energy-dispersive X-ray analysis	
EDC	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide	
EDS	energy-dispersive X-ray spectroscopy	
ET	triplet state energy	
EX (X = 0, 2, 3, 4, 5, 6)	Al ₂ O ₃ /Ru(OH) _x @pSiO ₂ etched for X hours in NaOH	
EXP (X = 0, 2, 3, 4, 5, 6)	EX pyrolyzed	
FC	field cooling	
Fe@SiO ₂	silica-coated Fe (0) nanoparticles	
Fe@SiO ₂ ^{TX}	silica-coated Fe (0) nanoparticles, being X the number of TEOS	
	additions necessary for the coating	

Fe@SiO ₂ ^{TX}	silica-coated Fe (0) nanoparticles made with X (3-12) TEOS
	additions of 25 µL
Fe@SiO ₂ ^{TX} @Ru	$Ru(bpy)_3^{2+}$ immobilized on silica-coated Fe (0) nanoparticles,
	being X the number of TEOS additions necessary for the coating
GC-FID	gas chromatography with a flame ionization detector
GC-MS	gas chromatography coupled with mass spectrometry detection
GC-TCD	gas chromatography with a thermal conductivity detector
HAADF	high-angular annular dark-field
H _E	exchange bias effect
HMF	5-(hydroxymethyl)-2-furfural
ICP-OES	inductive coupled plasma optical transmission spectroscopy
IR	infrared
KHMDS	potassium hexamethyldisilazide
LCT	liquid crystal template
LDH	layered double hydroxide
LED	light-emitting diode
LED	light-emitting diode
LSPR	localized surface plasmon resonance
LT-ESR	low-temperature ethanol steam reforming
МСМ	Mobil composite material
MES	2-(N-morpholino)ethanesulfonic acid
MLCT	metal-to-ligand charge transfer
MNP	magnetic nanoparticle
MOF	metal-organic framework
MRI	magnetic resonance imaging
NMR	nuclear magnetic resonance
NP	nanoparticle
ORR	oxygen reduction reaction
PANI	polyaniline structure
PDI	polydispersity index
PEO	polyethylene oxide

phen	1,10-phenanthroline	
PPh ₃	triphenylphosphine	
РРО	polypropylene oxide	
PS	photosensitizer	
PS*	excited-state photosensitizer	
PVP	polyvinyl pyrrolidone	
QY	quantum yield	
RB	rose bengal	
RB/ Fe@SiO ₂	rose bengal immobilized on silica-coated Fe (0) nanoparticles	
RBF	round-bottomed flask	
ROS	reactive oxygen species	
RT	room temperature	
$\operatorname{Ru}(\operatorname{bpy})_3^{2^+}$	ruthenium (II) tris(bipyridine)	
Ru(bpy) ₃ / Fe@SiO ₂	ruthenium (II) tris(bipyridine) immobilized on silica-coated Fe (0)	
	nanoparticles	
SAPO	silicoaluminophosphate	
SAXS	small angle X-ray scattering	
SBA	Santa Barbara amorphous	
SET	single electron transfer	
SiO ₂ @Ru	Ru(bpy) ₃ ²⁺ immobilized on silica nanoparticles	
TEM	transmission electron microscopy	
TEOS	tetraethyl orthosilicate	
TGA	thermogravimetric analysis	
TOF	turn-over frequency	
TON	turnover number	
UV	ultraviolet	
UV-Vis	ultraviolet and visible	
vis-light	visible light	
WGS	water-gas shift reaction	
XPS	X-ray photoelectron spectroscopy	
XRD	X-ray diffraction	

ZFC	zero-field cooling
$ au_{\mathrm{T}}$	triplet state lifetime
$\Phi_{ m ISC}$	intersystem crossing quantum yield

Contributions of authors

All original sections of this thesis were written by Julio Terra (JT) and edited by Professor Audrey Moores (AM). Professor Moores provided funding and guidance for all projects described in this thesis. Co-authors' contributions are found in the following chapters:

Chapter 2: This chapter was originally written for this thesis, except for Section 2.6 which is an excerpt from a review article. Sub-sections 2.6.1, 2.6.2, and 2.6.4 were written by JT and edited by Flavia Moura (FM), Cameron Weber (CW), and AM. Sub-section 2.6.3 was written by Amanda Martins and edited by JT, FM, CW, and AM.

Chapter 3: the project was conceptualized by AM and Zacharias Amara (ZA). JT designed and optimized the synthetic procedures, Ariane Desgranges (AD) and JT performed synthetic procedures and TEM imaging. Helena Sanchez (HS) and Jose De Toro (JDT) performed SQUID measurements. Cyrille Monnereau (CM) and JT performed photospectroscopic measurements. JT performed all other characterizations and catalytic tests, and wrote the manuscript which was edited by HS, JDT, CM, ZA, and AM.

Chapter 4: the project was conceptualized by AM. AD contributed to the development of the immobilization strategy and initial catalytic tests. JT performed, designed, and optimized most synthesis, catalytic tests, and characterization procedures. JT wrote the manuscript, which was edited by AM and ZA.

Chapter 5: the project was conceptualized by JT and AM. JT designed and optimized all experimental procedures and performed most of them. Jackson DeWolfe reproduced synthetic procedures and performed TGA analysis. Jesus Valdez performed EDAX and tomography experiments. JT wrote the manuscript, which was edited by AM.

1

Introduction

1.1. Contribution to knowledge

The chemical industry is currently not sustainable, and this issue needs to be addressed if we want to continue delivering chemical products to fulfill the needs of society. Catalysis is at the heart of most chemical transformations and can deliver effective changes in the industry toward greener and more sustainable practices. In this thesis, we utilize existing knowledge in nanoscience to synthesize silica-based nanostructures and demonstrate how intricate design in the nanoscale can be used to improve catalytic processes in different contexts, namely magnetic photocatalytic systems, and confined catalysis.

Photocatalytic systems have great potential for making fine chemicals with low energy input and milder reaction conditions but are still limited for large-scale applications. The first specific contribution of this thesis is the development of magnetically recoverable supports that are compatible with visible-light photosensitizers, this system opens the possibility of the development of photocatalytic systems in flow which can benefit from the high light penetration in capillary tube reactors and in-flow magnetic separation and recirculation of the heterogenized catalysts. At the fundamental level, in Chapter 3 we have systematically studied the photophysical properties of our supports and their influence on the absorption of photons by the photosensitizer, which directly influences photocatalytic activity. It is the first systematic study of this type, which was

made possible by the precision of the silica nanodesign strategy developed to create $Fe@SiO_2$ dense core-shell systems with varying iron-to-silica ratios. These supports were used as a platform for the immobilization of two different photosensitizers, and Chapter 4 follows up exploring the effect of immobilization on the stability of the different systems.

The second concept explored in this thesis is the use of nanodesign strategies to construct systems that induce enhanced reactivity under nanoconfined spaces. We have demonstrated the use of such effects in green chemistry by writing a review article which is partly reproduced in section 2.6 in the background chapter of this thesis. With the review, we highlighted selected and creative examples of nanoconfined systems in the scientific literature that made catalytic processes greener and more sustainable in different ways, with the aim of introducing confinement effects as a tool to be used and investigated by green chemists. We then used silica nanodesign strategies to confine a catalytic system based on alumina nanoparticles inside mesoporous silica shells in a hollow yolk-shell model, which is reported in Chapter 5. We demonstrated the importance of the mesoporous structure and the effect of tuning the space in the void between the nucleus and the shell of this design, and how this parameter directly affects catalytic performance. We applied for the first time the concept of confined catalysis to a hydrogen borrowing reaction, providing a concept for the development of a library of confined cascade reaction systems.

In summary, this thesis contributes to knowledge by applying silica nanodesign strategies to improve catalytic systems. It provides fundamental knowledge about the investigated systems while envisaging the development of initial concepts with relevant large-scale applications.

1.2. Thesis organization

This thesis is organized into six chapters which describe a journey to exploring the use of silica core-shell structures to improve different catalytic systems. This chapter introduces the organization of the thesis, while Chapter 2 provides the theoretical background. Chapter 2 begins by describing silica nanoparticles, nanoarchitectures, synthetic strategies, and their role in green chemistry and catalysis (sections 2.1, 2.3, and 2.4). It then moves on to a brief overview of photocatalysis and magnetic recovery in section 2.5, followed by a more extensive overview of the use of confinement effects for sustainable catalysis in section 2.6. This last section was extracted from a review article¹ written by the author of this thesis and collaborators for the journal

Green Chemistry of the Royal Society of Chemistry and published in 2022, entitled "Making less with more: confinement effects for more sustainable chemical transformations."

The concept of magnetic photocatalysis is explored in Chapters 3 and 4. The former describes the development of magnetically recoverable core-shell Fe@SiO₂ nanostructures with varying amounts of silica coverage; the composites were used for the immobilization of the photosensitizer ruthenium (II) tris(bipyridine) and the effect of light absorption by the support was systematically studied. The text and images presented in Chapter 3 were published as an article² in 2020 in the journal ACS Applied Materials & Interfaces. Chapter 4 is a follow-up of the previous chapter, in which the same magnetic supports were used to immobilize the metal-free photosensitizer rose bengal to show the versatility of the magnetic platform with a different photosensitizer and a distinct immobilization protocol; we also studied the stability of the system and compared it with the previous Ru-based one. Text and images presented in Chapter 4 were published in 2022 as an original publication³ in the journal Catalysis Today by Elsevier.

Chapter 5 describes the use of a yolk-shell catalytic system based on ruthenium species immobilized on alumina and encapsulated in mesoporous silica shells to develop a confined catalytic system for the alcohol amination reaction. It is a result of the inspiration obtained from writing the review that makes section 2.6 and from a collaboration project⁴ that is previous to this thesis. Text and images presented in Chapter 5 have been published in ChemRxiv in 2022.⁵

Finally, Chapter 6 contains general conclusions of these combined pieces of work and directions for future development.

2

Background

2.1 Preamble

This chapter contains the theoretical background and state of the art to the concepts that will be presented throughout the thesis, starting from general synthesis and applications of silica coreshell nanoarchitectures, and narrowing down to the applications of interest to this thesis which are magnetic photocatalysis and confined catalysis.

Section 2.6 (confined catalysis) is adapted from a published review article. The Royal Society of Chemistry and all co-authors gave permission to reprint.

Terra, J. C. S.; Martins, A. R.; Moura, F. C. C.; Weber, C. C.; Moores, A., Making more with less: confinement effects for more sustainable chemical transformations. *Green Chem.* **2022**, *24* (4), 1404-1438.

2.2 Silica in the nanoscale

2.2.1 Nanomaterials

The prefix "nano" comes from the Greek word for dwarf⁶ and it is used in metrology to define a billionth, hence the nanometer is a billionth of a meter. It is ironic how a term carrying such a "small" meaning has had gigantic impacts on science and technology in the last decades.

Nanomaterials are traditionally defined as those with at least one dimension in the 1-100 nm range, although health and environment agencies tend to favor a larger range of up to 300 nm.⁷ The most exciting feature of a nanomaterial is however not its size, but the consequences of it, and the 100 nm threshold is not always precise. More complete definitions focus on the fact that, be it inside or outside of the 100 nm boundary, nanomaterials have unique properties that emerge from their dimensions, behaving neither like their macroscopic (bulk) analogs, nor single atoms or molecules.⁸ The distinctive properties of nanomaterials happen mainly because of two reasons: 1) high surface-to-volume ratio and 2) intrinsic size-related electronic effects. Atoms on surfaces have fewer neighbours, higher free energy, and increased mobility when compared to inner atoms in a given material. Materials in the nanoscale have a much larger fraction of surface atoms, hence a larger contribution from surface chemistry. They may for instance form stable colloidal systems, as well as experience increased reactivity, elasticity, and plasticity when compared to macroscale materials. Intrinsic electronic effects can also arise from the nano size, like the classical example of gold nanoparticles (NPs) which have plasmonic resonance properties in the visible region. Although bulk gold is known for its golden color, gold NP suspensions have bright colors that span across the visible spectrum depending on the size of the nanostructures.⁹

Nanomaterials are not a novelty for Nature. DNA for instance has a diameter of around 2 nm,¹⁰ viruses diameters are mostly under 100 nm,^{11, 12} some bacteria can have diameters in the range of 100-150 nm.¹³ Volcanic eruptions are also known for releasing NPs on the surface of the planet, and naturally occurring colloids such as milk and blood derive their colors from the scattering of light of their constituent NPs.⁷ Ancient civilizations already harvested the power of nanoscience. Ancient Romans built a cup describing the death of King Lycurgus which, thanks to the presence of nanostructured gold and silver, changes color from green to red when a light source is placed inside the cup.¹⁴ In the new world, the Maya blue paint, a nanostructured clay-based pigment,

provided lively blue tones to Mayan art.¹⁵ Scientists began to understand the nanometric world when Richard Zsigmondy (Nobel Prize in Chemistry 1925) introduced the concept of the nanometer and measured the size of colloidal gold NPs using a microscope in the early 1900s.¹⁶ The revival of nanoscience is however considered to be at the iconic lecture given by Richard Feynman at the American Physical Society annual meeting of 1959, titled "There's plenty of room at the bottom: An invitation to enter a new field of physics",¹⁷ which gave him the title of father of nanotechnology. Among his many topics, he highlighted the availability of potent microscopes and invited fellow scientists to prepare new nanostructures by exploring for instance electron beam lithography, stamping on small scale, and evaporation mechanisms.

Following Feynman's call, it was not until 1985 that the discovery of fullerene by the Smalley's group¹⁸ effectively marked the beginning of the modern era of nanoscience. A plethora of nanomaterials has been developed in the last decades, comprising the most varied shapes, architectures, and compositions. Given the variety of existing nanostructures, Tomalia proposed a nano-periodic classification system, inspired by the periodic table of elements.¹⁹ It this approach, NPs were split into two categories: well-defined and undefined materials, based on the uniformity of the nanostructures. Within the well-defined materials, the authors proposed 12 nano-elements, which were grouped into hard and soft NPs. The hard nano-elements are the inorganic materials: metal nanoclusters (H-1), metal-chalcogenide nanocrystals (H-2), metal oxide nanocrystals (H-3), silica NPs (H-4), fullerenes (H-5), and carbon nanotubes (H-6). The soft nano-elements are the organic materials: dendrimers and dendrons (S-1), nano-latexes (S-2), polymeric micelles (S-3), proteins (S-4), viruses (S-5), and DNA/RNA (S-6). The combination of the different nanoelements will form tables of possible nano-compounds (hard-hard, soft-hard, and soft-soft for 2component systems), forming families and periods of organized nano-compounds from which properties can be extracted and even predicted, much like in the work of Dmitri Mendeleev (Figure 1). Although this system will lead to high complexity organization on more than 2-component systems, it is an interesting approach to nano-classification. It is worthy noting that, although most nano-elements comprise categories of nanomaterials, silica NPs form a category by themselves. Silica NPs are of true paramount importance in the nanoscience community and will be the central subject of this thesis.

Nanomaterials Classification Roadmap



Figure 1. Roadmap for the classification of nanomaterials as proposed by Tomalia. Reproduced from reference 19.

2.2.2 Silica nanostructures

Silicon is an abundant element in the Earth's crust, second only to oxygen; silicon-oxygen compounds make up 75% of the foundation of our planet. Silica, which is a term to denote silicon dioxide (SiO₂), is formed by an infinite three-dimensional network of oxygen atoms arranged tetrahedrally around atoms of silicon. The majority of naturally occurring silicas are in the macroscale and crystalline forms, such as quartz, cristobalite, and tridymite.²⁰

Silica possesses excellent thermal and mechanical stabilities, melting at about 1700 °C and with a tensile strength of about 44 MPa.²¹ Moreover, silica nanomaterials are known for their biocompatibility²² and rich surface chemistry due to the presence of silanol groups, which are susceptible to functionalization.²³ They have been used for many different applications including food and cosmetics, biomedicine, agriculture, bioimaging, environmental remediation, and catalysis.

Silica NPs are food additives used as anticaking and antifoaming agents in powdered food; and as clarifying agents in the juice, oil, and brewery sections. In the cosmetics sector, silica NPs are added to hair, skin, lips, face, and nail products to enhance properties like UV protection, and skin penetration.²⁴ Mesoporous silicas are highly used as carriers for controlled drug delivery; their large and functionalizable internal surfaces can be used to carry drugs, which are protected inside the pores from enzyme degradation in the blood stream and then released in the target cells upon stimuli such as pH changes.²⁵ Using the same concept, pesticides can also be loaded on mesoporous silica NPs as carriers for efficient and controlled release in plants; this strategy can avoid the overuse of pesticides and reduce environmental impacts.^{26, 27} Functionalized silica NPs can be used to immobilize cell membrane staining agents, showing potential applications for biosensing and biomarking.²⁸ Silica-coated NPs also find extensive application as magnetic resonance imaging (MRI); in addition to biocompatibility and opportunities for surface modification, the interaction of silica shells with water molecules makes them good contrast enhancement agents.²⁹ The large surfaces of mesoporous silica NPs can also be functionalized for environmental remediation, such as the addition of hydrophobic groups for oil adsorption³⁰ or the modification with amines and thiols for heavy metal adsorption.³¹

Moreover, silica is omnipresent in the catalysis literature, being one of the most popular catalytic supports. Supports are used to disperse and dilute the catalytically active species and maintain the

mechanical strength of the catalyst. Silica is an oxide that is hard to reduce, tending to be chemically inert when used as a support in contrast to reducible oxides such as TiO₂ and CeO₂, which migrate around the metals in a reducing atmosphere.^{32, 33} Mesoporous silica NPs have been extensively used as supports for example for metal NPs,^{34, 35} heterogenization of metal complexes^{36, 37} and organocatalysts,^{36, 38} as well as biocatalysts.^{39, 40}

2.2.3 Synthesis of nanosilica: sol-gel chemistry and the Stöber method

Nature produces silica through silification processes that occur in organisms such as bacteria, protists, and plants. The main source of silicon for biogenic silica production is monosilicic acid, Si(OH)₄, which has low solubility and is easily deprotonated to form mono- or divalent anions in basic media. Silicic acid concentrations of about 100 ppm trigger condensation reactions, forming Si-O-Si siloxane bonds with the elimination of water. The oligomers grow to form spherical particles that are then branched to form various structures.⁴¹ Some exceptional biogenic silica structures are produced by unicellular photosynthetic algae called diatoms. Also known as "jewels of sea", this phytoplankton is the originator of the food chain in marine ecosystems, but there are over 10,000 species of diatoms inhabiting all sorts of aquatic environments. Their cell walls are protected by amorphous silica shells called frustules, which are arranged in magnificently complex three-dimensional nano- and micro-structured porous patterns (Figure 2).^{42, 43} The biogenic



Figure 2. SEM images of biosilica from a single cell of diatom T. pseudonana; side view (a), top view (b), and details (c and d). Scale bars: $1 \mu m$ (a-c) and 200 nm (d). Reproduced from reference 42.

formation of silica from monosilicic acid as described follows the general solution-gelation mechanism, mostly known as sol-gel.⁴¹ Sol-gel is an extremely versatile inorganic polymerization process used to produce solid materials from molecular precursors. This bottom-up approach "traps the randomness of the solution state", ensuring an atomic-level mixing which is carried up to the final solid network that is formed.^{44, 45}

As suggested by the nomenclature, the sol-gel process has two phases: the sol and the gel. The term sol refers to a colloidal dispersion in a liquid, with solid particles with diameters of 1-100 nm. Gels are interconnected three-dimensional non-fluid networks which extend through a fluid phase.⁴⁶ Danks *et. al.*⁴⁴ have postulated the 5 key steps of a sol-gel process:

- 1) Hydrolysis and partial condensation of precursors to form the sol;
- 2) Formation of the metal-oxo-metal system through polycondensation to give the gel;
- 3) Aging for further condensation and elimination of solvent from the gel structure;
- Drying to either collapse the pores to form a xerogel or to keep the porous structure in the case of an aerogel;
- 5) Optional calcination to remove surface hydroxyl groups.

The precursors of sol-gel processes are alkoxides, most commonly alkoxides of early transition metals like Ti and Zr, or early p-block elements such as Al and Si. The formation of the sol and the gel rely on an intricate balance between the rates of the alkoxide hydrolysis and condensation reactions, and several factors influence the final solid material. For silica, the process is feasible through either acid or base catalysis. The hydrolysis step (Scheme 1a and b) happens through an $S_N 2$ mechanism that is governed by: 1) the nature of the R-group, which determines the nucleophilicity of the Si center; 2) the Si/H₂O ratio, which influences the number of alkoxy groups that will be hydrolyzed; and 3) the relative electron withdrawing or donating power of -OH *versus* -OR groups, which determines the stability of the transition state. The condensation step (Scheme 1c and d) follows a similar mechanism, and it is responsible for the formation of the siloxane bonds, which are the basis of the silica networks.
Chapter 2



Scheme 1. Sol-gel reactions of a silicon alkoxide: a) acid-catalyzed hydrolysis, b) base-catalyzed hydrolysis, c) acid-catalyzed condensation, and d) base-catalyzed condensation.

The rate of hydrolysis is central to the progression of the condensation step since it will determine the number of sites available for condensation. This parameter has enormous consequences on the morphology and structure of the final gel (

Figure 3). A fully hydrolyzed silicon alkoxide will still have 6 sites available for condensation upon the formation of the first dimer $(OH)_3Si-O-Si(OH)_3$, which will favour highly branched structures. This is the case when there is a high H₂O/Si ratio and upon basic catalysis. As hydrolysis happens and -OR groups are replaced by -OH groups, the silicon atoms get more electrophilic and less hindered, making hydrolysis progressively faster and favouring the formation of the fully hydrolyzed alkoxide. On the other hand, slow hydrolysis will result in the formation of long chains in the sol. This is the case when there is a low H₂O/Si ratio and under acid catalysis. In this case, hydrolysis gets progressively slower, so condensation begins before the alkoxide is fully hydrolyzed.^{44, 47}



Figure 3. Effect of acid or base catalysis in the growth and structure of a gel. Reproduced from reference 47.

The sol-gel process is a general mechanism that operates for many alkoxides, but it is specially studied and developed for the chemistry of silicon alkoxides. A major contribution in the field was reported by Stöber, Fink, and Bohn in 1968.⁴⁸ The authors looked at the different parameters of silica chemistry and developed a method for the synthesis of colloidal silica particles. It consists of an ammonia-catalyzed sol-gel reaction based on the hydrolysis and condensation of tetraorthosilicate (TEOS, Figure 4) in the presence of water and low molecular weight alcohols like ethanol. Ethanol and water are by-products of the TEOS hydrolysis and condensation reactions respectively (Scheme 1), so controlling the water : ethanol : TEOS ratios is key to tuning the intricate balance between the hydrolysis and condensation processes. The adaptation of these parameters allows control of particle sizes and the formation of colloidal suspensions by not feeding the process to go past the gel stage.⁴⁹



Figure 4. Tetraehtylorthosilicate (TEOS), the silicon alkoxide used in Stöber method.

2.2.4 Nucleation and growth

When a sol is formed, particles are generated from a homogeneous solution. The process of nucleation and growth of nanoparticles in solution is classically described by the LaMer mechanism.^{50,51} LaMer postulates that the formation of nanoparticles is separated into three stages, as depicted in Figure 5, which shows the evolution of solute concentration over time.⁵² In the case of a Stöber silica synthesis, for instance, the solute is hydrolyzed TEOS. Phase I is the hydrolysis stage when the concentration of hydrolyzed TEOS is building up. At this stage, there is not enough hydrolyzed TEOS to trigger condensation reactions. Phase II begins when the minimum nucleation concentration (C_{min}) is reached, it is the bursting nucleation stage. At this stage, condensation reactions are operating to form silica nuclei. This is when the sol is initially formed, and the solution loses its colorless and translucid appearance. At phase III, most of the free hydrolyzed TEOS species have been consumed. Since its concentration will not reach C_{min} again, no further nucleation will take place. This is the growing stage, when all remaining hydrolyzed TEOS will eventually condensate on the pre-formed nuclei.⁵³ An extra addition of TEOS in phase III can have two different effects, depending on the amount of solute added. If the concentration surpasses C_{min} , then a new nucleation event will happen and particles of two distinct size domains will co-exist. On the other hand, if the concentration does not exceed C_{min}, the pre-existing nuclei will grow, and size uniformity will be maintained. ⁵⁴ This leads to the fractionated addition strategy which is useful in the coating mechanisms which will be discussed in the following section.

Naturally, several studies have put the LaMer mechanism to the test. The Stöber process was investigated with *in-situ* SAXS by the Rennie group, and the authors found that particles most likely nucleate first, but then the nuclei combine to form larger particles.⁵⁵ In another study, the



Figure 5. Concentration of solute plotted against reaction time, following the the LaMer nucleation mechanism. Reproduced from reference 52.

Harris group used a combination ²⁹Si NMR spectroscopy, SAXS, and DLS to find that nucleation is continuous throughout the growing process of nanoparticles in the Stöber synthesis.⁵⁶ The Thill group also used SAXS to study the same process and found that the LaMer theoretical predictions agreed with experiments to describe particle size and concentration, but it failed to predict the size distribution.⁵⁷

Several other particle growth mechanisms have been described, and Thanh *et. al.* made a succinct compilation of some of the main ones.⁵³ Ostwald ripening is a growth mechanism that draws from the premise that smaller particles are more soluble than larger ones, so the former are gradually dissolved to feed the growth of the latter. The inverse of Ostwald ripening is digestive ripening, in which context the larger particles redissolve due to their large surface energy, providing monomers to grow the smaller ones. The Finke-Watzy mechanism, on the other hand, describes a slow and continuous nucleation process that happens simultaneously with autocatalytic surface growth; this mechanism is a good fit for platinum group metal systems. Another compelling mechanism is

interparticle growth, which happens when different facets of a nanoparticle have different surface energies; in this situation, monomers will move from higher energy to lower energy facets, causing a change in the particle shape over time.

2.3 Silica nanoarchitectures

The previous section described the sol-gel mechanism and how solid particles form from liquid solutions. Although the different mechanisms diverge in how particles grow and whether nucleation is punctual or continuous, they all converge in the fact that particle formation begins with nucleation. Nucleation can be either homogeneous or heterogeneous. The discussion in this text has so far been restricted to homogeneous nucleation, *i.e.* when there are no foreign bodies in the medium so the probability of nucleation is the same throughout the whole system. On the other hand, when the starting medium is not a clear, homogeneous solution, heterogeneous nucleation takes place preferentially. This happens because the activation barrier of nucleation is lower when it happens on the surface of a pre-existing seed, so in these cases, the probability of nucleation is higher on those surfaces than on the bulk of the solution.⁵⁸ This thermodynamic condition governs for instance the formation of clouds and rain droplets, which nucleate heterogeneously on the surface of aerosols rather than homogeneously in the atmosphere.⁵⁹ The thermodynamic advantage of heterogeneous nucleation is also a tool for adding complexity to the synthesis of silica nanostructures. Instead of only creating plain silica nanospheres, the nanosynthetic chemist can use this strategy to grow silica on top of nuclei of various sizes, shapes, compositions, and hierarchical structures. These nuclei act as templates for the formation of silica shells in the sense that their shape is generally propagated by the silica coverage. Templates can be either soft or hard. Soft templates are organic structures that can be easily removed with calcination or solvent extraction once the silica skeleton is made, leading to imprinted cavities and porosity in the silica structures. This strategy is for instance extremely popular for the formation of mesoporous silica, as it will be described later in this section. Templates can also be hard, such as metal networks or nanoparticles. Those can also be removed to yield hollow structures through harsher methods like treatment with acid solutions, but this strategy is less common for silica structures. Instead, hard templates in silica structures are usually maintained in the final material. Some may not consider this latter case templating since the template is not removed after silica formation, but it will be considered templating throughout this text on the basis that, removed or not, they provide the

physical structure and shape upon which the silica network is built. When the template is maintained, one does not obtain a hollow structure, but instead, a multicomponent hierarchical structure based on the shape of the chosen nucleus, as is the case for classical core-shell structures (Figure 6a). Everything is possible for the creative minds of nanosynthetic scientists, so of course, hard and soft templates have been combined to create more complex architectures. A typical example is when a soft template is sandwiched between a hard nucleus and a silica shell. Soft template removal gives a hollow silica structure, containing a mobile nucleus inside. The structure resembles an egg yolk inside its shell, hence the so-called yolk-shell model (Figure 6b).



Figure 6. Intersected three-dimensional model of a) a dense core-shell structure, and b) a hollow core-shell (yolk-shell) structure.

This section on silica nanoarchitectures will start with an overview of both soft and hard templating strategies, which are the synthetic strategies used to make core-shell silica structures. The final subsection will expand on the types and uses of the core-shell architectures that are the basis of the next chapters of this thesis: dense (or continuous) core-shell structures, and hollow (or yolk-shell) core-shell structures.

2.3.1 Soft templating techniques

Mann *et al.* published a very insightful review in 1997 on the sol-gel synthesis of organized matter in which the authors systematically categorize soft-templating mechanisms.⁶⁰ Their proposed three

basic mechanisms will guide the discussion in this subsection: 1) *transcriptive synthesis*, 2) *synergistic synthesis*, and 3) *morphosynthesis*.

2.3.1.1 Transcriptive templating

The first and simplest category, *transcriptive synthesis*, describes the process in which pre-formed self-assembled structures are used to obtain inorganic replicas of their shapes. The steps in this methodology are: self-assembly \rightarrow transcription \rightarrow replication. The organic templates in this case must be formed before the inorganic synthesis begins. For example, Vollmer and co-workers obtained hollow silica nanospheres by coating polystyrene nanospheres with silica and then calcinating the nanocomposite; the void in the resulting hollow structure was a replica of the spheric templates (Figure 7a and b).⁶¹ An analogous strategy was adopted by the Konishi group but using *Escherichia coli* bacterial cells as templates; again the resulting hollow rods imprinted the shape of the bacteria in their interiors (Figure 7c and d).⁶²



Figure 7. Templated hollow silica structures. SEM (a) and TEM (b) micrographs of structures templated with polystyrene nanospheres, reproduced from reference 61; and SEM micrographs of bacteria-templated structures (c and d), reproduced from reference 62.

2.3.1.2 Synergistic templating

The second category proposed by Mann *et al.* is *synergistic synthesis*. As the name suggests, in this case, there are cooperative interactions between the template and the inorganic precursors. This is the case in which the templates are not pre-formed, but rather self-assembled in the reaction mixture and are hence in equilibrium with the whole sol-gel system. These systems are more complex than transcriptive ones and require more control over all the components, but they also allow for more elaborated architectures. Synergistic synthesis follows the steps: coadaptation \rightarrow coassembly \rightarrow replication. The textbook examples in this category are the templated mesoporous silicas; MCM-41 and SBA-15 are the most illustrious representatives of the category.

The original strategy for soft-templated mesoporous silica synthesis dates back to 1992, in the context of the search for the expansion of the applicability of zeolites in the petrochemical industry. Zeolites are naturally occurring microporous aluminosilicate materials used as catalysts in oil refineries, but their small pore size (1-10 Å) is incompatible with the large molecules common in that field. In this context, scientists at the Mobil Oil Company developed a method to create silica structures containing mesopores in the 2-10 nm range.⁶³ Such porosity was achieved using the Liquid Crystal Template (LCT) mechanism, which takes advantage of the supramolecular selfassembly of surfactants in solution. The original method of Kresge⁶⁴ and Beck⁶⁵ reports the synthesis of MCM-41, where MCM stands for Mobil Composition of Matter. There is a family of MCM structures, from which MCM-41 is the most stable and popular member. MCM-41 is templated with cetyltrimethylammonium bromide (CTAB), a surfactant that forms micelles that can be induced to arrange themselves in rod-shaped structures of about 3 nm in diameter; under optimized conditions of temperature, concentration and pH, those structures self-assemble hexagonally into a liquid-crystalline phase. Sol-gel chemistry is then used to condense walls of amorphous silica around the micellar structures, forming the skeleton of MCM-41. Removal of the surfactant through calcination or solvent extraction reveals a porous structure that mimics the shape and size of the template liquid crystals (Figure 8).⁶⁶ Six years later, Zhao et al. at the University of California in Santa Barbara, developed the synthesis of another important mesoporous silica structure, the SBA-15 (Santa Barbara Amorphous 15). The synthesis follows the same LCT mechanism but with larger templates. Using triblock copolymers PEO-PPO-PEO made with different ratios of ethylene oxide (EO) and propylene oxide (PO), SBA-15 can be

obtained with porous sizes ranging from 5 to 30 nm.⁶⁷ Together, MCM-41 and SBA-15 cover the whole range of mesopores (2-50 nm). Although high control over pore size was obtained in the 1990s, control over the size of the mesoporous particles themselves was only mastered in the 2000s. The groups of Cui,⁶⁸ Mann,⁶⁹ and Ostafin⁷⁰ obtained size-controlled mesoporous silica nanoparticles by adjusting reaction conditions such as pH, characteristics of surfactants and copolymers used, and concentration of the sources of silicon.⁷¹



Figure 8. Schematic for the preparation of MCM-41 and SBA-15 using the LCT mechanism, adapted from reference 66.

2.3.1.3 Morphosynthetic templating

The third basic mechanism described by Mann *et al.* is morphosynthesis, which refers to the process in which organized and delineated environments shape the external contour of the inorganic materials. This synthesis happens hence inside the template, in opposition to the other mechanisms which take place outside of the soft templating structures. Morphosynthesis generally happens with emulsions as templates, and the main requirement is that the structure of the template is not affected by sol-gel conditions (solvent, temperature, pH). The general steps in this approach are: reaction assembly \rightarrow replication \rightarrow metamorphism.

A prime example of morphosynthesis is the microemulsion approach. Microemulsions are mixtures of water, organic solvent (oil), and surfactants that look homogeneous to the naked eye, but are in reality formed by nanodomains of water droplets surrounded by interfacial surfactant layers.⁷² These emulsions have for instance been used to perform organic reactions in water.⁷³ In the nanosynthesis world, these domains can template the formation of nanoparticles. Lin *et al.* used an emulsion system consisting of water and cyclohexane with surfactant Trition X-100 to make hollow silica NPs. The silicon source was a mixture of TEOS and aminopropyltrimethoxy silane (APTMS),⁷⁴ which is analogous to TEOS but with methyl groups instead of ethyl and one

non-hydrolyzable aminopropyl group substituting one of the alkoxys. Since sol-gel chemistry happens in water, the formation of silica happens in the interior of the micelles, but the presence of APTMS favoured interactions with the micelle surface, so silica condensation followed the shape of the interface. The authors obtained particles that replicated the shape of the micelles to form hollow silica spheres with no internal template, hence no need for template removal.

Microemulsions have also been used extensively for coating hydrophobic nanoparticles with silica. Those procedures are incompatible with the standard sol-gel processes because hydrophobic nanoparticles aggregate in water, hence no individual coating can be achieved. The microemulsion silica coating process was well described by Rossi et al. for the coating of magnetite particles stabilized with oleic acid (Figure 9),⁷⁵ and will be central to the next chapter of this thesis. The first step to the procedure is to add oleic-acid-capped particles to a mixture of surfactant IGEPAL-520 in cyclohexane. The surfactant molecules arrange themselves in micelles and the hydrophobic particles suspend in the solvent. Following, ligand exchange processes take place (Figure 9, step 2) and oleic acid on the surface of the particles is replaced by surfactant molecules. Ammonia solution is then added to the mixture (Figure 9, step 3). The aqueous droplets then complete the microemulsion by occupying the interior of the remaining IGEPAL-520 micelles, forming those aqueous domains which will be nanoreactors where sol-gel chemistry can take place. When TEOS is added (Figure 9, step 4), it is hydrolyzed inside the aqueous domains these hydrolyzed molecules then replace IGEPAL-520 capping the magnetite surfaces. This will cause the once-hydrophobic particles to migrate to the aqueous phase (Figure 9, step 5), where sol-gel chemistry can operate and generate the silica shells (Figure 9, step 6). This process is a mixture of hard templating, which will be discussed in the next subsection, and morphosynthesis, which operates in delimiting the sol-gel domain to guarantee individual coating of the nanoparticles. Microemulsions are however difficult to scale, and their precision depends on a fine one-to-one match of the number of micelles and the number of individual particles to be coated; an excess of micelles results in core-free silica particles, while an excess of particles results in multi-core systems.⁷⁶



Figure 9. Proposed mechanism for silica-coating of magnetite particles coated with oleic acid using the reverse microemulsion method. Adapted from reference 75.

2.3.2 Hard templating techniques

Hard templates are inorganic structures also used to imprint shapes, cavities, and customized architectures, much like soft templates. These hard templates are most useful when the synthesis of the nanomaterial of interest requires high temperatures that soft templates do not withstand, such as the synthesis of carbon materials. However, such higher robustness naturally comes with harsher removal methods. He and co-workers reviewed the use of hard templates to make three-dimensional interconnected carbon materials and produced an informative compilation of the most common templates and removal methods,⁷⁷ which are presented here in Table 1.

Table 1	. Hard templates	used in the synthesis	of three-dimension	al carbon materia	ls and removal method	 Adapted from reference
72.						

Template	Example	Removal method
Metal foam	Ni foam	Acid solution
Porous metal	Porous Cu	Acid solution
Metal powder	Ni/Cu powders	Acid solution
Salt	Water	NaCl, Na ₂ CO ₃
Silica	Silica sphere	NaOH, HF
MOF	MOF-5, ZIF-8	Acid solution
Zeolite	Zeolite X/Y	HF

Given the diversity of template removal techniques, one must bear in mind the compatibility of the removal procedure in order to not affect the non-sacrificial component of the composite. One very illustrative example is the work of the Gooding group on the synthesis of nanostructures to mimic enzyme cavities (nanozymes).⁷⁸ The authors made bimetallic nanoparticles of platinum and nickel and took advantage of the greater stability of platinum towards nitric acid to selectively corrode nickel in the structures (Scheme 2). This strategy led to the formation of platinum nanospheres containing cavities, and the variation of the Ni/Pt ratio gave either isolated cavities (lower Ni contents) or connected ones (higher Ni contents).



Scheme 2. Use of Ni as a template to create porosity in a PtNi nanoparticle. Adapted from reference 78.

Since sol-gel chemistry does not require high temperatures, it is perfectly compatible with soft templating. Hence soft templating is a preferred method for the synthesis of silica hollow structures. That does not mean hard templating is not used for silica, but it is used rather to create composites than hollow structures. Those are the cases in which the templates are not removed but maintained to give a final core-shell structure. Although those templates do serve the function of providing the shape of the particle, their primary role is mostly to provide additional properties to the composite such as magnetism or catalytic activity.

2.3.3 Core-shell silica nanostructures

The core-shell terminology dates back to the early 1990s when layered semiconductor materials were first reported.⁷⁹ These were concentric spherical single-shell CdSe-ZnSe nanostructures in which the core and the shell are physically connected. That is the simplest and most common coreshell architecture, but the versatile templating methods discussed in sections 2.3.1 and 2.3.2 have provided the foundation for the development of several different architectures. Ghosh Chaudhuri *et al.* published a review on core-shell nanoparticles and grouped them into 5 categories⁸⁰ as shown in Figure 10: a) spherical core with a single shell, the most common example (also shown in Figure

6a); b) hexagonal core-shell nanoparticles; c) multi-core systems with a single shell; d) multi-shell systems with a single core, also known as nanomatryushka nanoparticles; and e) movable core with a hollow shell (also known as yolk-shell, shown in Figure 6b).⁸¹ Despite the variety of core-shell architectures, this discussion will focus the dense core-shell (Figure 6a, Figure 10a) and hollow core-shell (Figure 6b, Figure 10e) nanostructures, as mentioned in the beginning of the section.



Figure 10. Classes of core-shell nanoparticles as described by Ghosh *et al.*: a) spherical core-shell, b) hexagonal core-shell, c) multi-core, d) multi-shell, e) movable core in hollow shell. Adapted from reference 80.

Core-shell nanostructures are organized nanocomposites containing at least two phases, in which one phase completely involves the other (or others). Core-shell materials are highly functional and versatile, and sometimes the combination gives properties that are different from the core and the shell materials separated. The properties of core-shell materials can be tuned both by exploring the numerous possibilities of composition combinations as well as the core-to-shell ratios.

Silica is a convenient shell material for three main reasons. First, the versatile sol-gel chemistry and compatibility with templating mechanisms, as explored in the previous sections, make silica ideal for the development of elaborated nanoarchitectures. Second, the composition with a metal or metal oxide core, the most explored combinations in the literature, brings advantageous properties including reduced bulk conductivity, and increased suspension stability; also, the limited interference in the metal's redox chemistry is desirable in certain catalytic systems, and the low visible light absorption of silica also makes it an ideal coating for optical applications.⁸⁰ Third, silica shells can be made porous, so one can induce communication between the outer (bulk) and the inner (core) environments through the shells; this diffusion can be controlled by tuning the porous silica networks.⁸²

Some of the main applications of core-shell nanoparticles are in the biomedical fields, namely bioimaging and drug delivery. The high surface-to-volume ratio and ease of surface silica

modification open possibilities for improving their pharmacokinetic properties, vascular circulation lifetime, and bioavailability. Silica coating is a favorite choice mainly for its high biocompatibility, dispersibility in biological systems (aqueous), and surface chemistry modification possibilities for the conjugation of different molecules.^{83, 84} The use of core-shell nanoparticles for biomedical applications has been presented in several reviews, including the ones the by the Paria⁸³ and the Nie⁸⁴ groups. Bioimaging techniques such as MRI are relevant tools for medical diagnosis and early detection of diseases. MRI produces detailed digital pictures of internal body structures through a combination of magnetic resonance and radio frequency pulses; the images are generated by photons liberated by the excitation-relaxation of water molecules. Abnormal cells are selectively highlighted by contrast agents, which are paramagnetic compounds.⁸³ Pinho et al. for instance, coated superparamagnetic maghemite nanoparticles with mesoporous silica shells, which gave them biocompatibility and dispersibility.⁸⁵ The authors also loaded Gd and Eu complexes on the pores of the silica shells, making them also luminescence probes. The high versatility of the silica shells can be illustrated as well by the work of Fang *et al.*, who used zinc-doped iron oxide nanoparticles coated with mesoporous silica shells to load DOX, an anti-cancer drug. The DOX molecules were engineered to be released under acidic conditions, so the system combined both imaging and targeted drug delivery properties.⁸⁶

In addition to biomedicine, silica shells have found numerous applications in catalysis. Those applications will differ depending on the specific architecture. Dense core-shell silica nanosystems (Figure 6a) are used in applications in which the core does not contain the catalytically active species. In those cases, the core provides an additional feature to the system, and the silica shells are decorated with accessible catalytically active sites which benefit from the properties of the core. These core properties can be for instance plasmonic enhancement or magnetic properties. In hollow core-shell nanoparticles, on the other hand, the core will most often be or support the catalytically active phase.

One example of dense core-shell silica systems used in catalysis is the work of our group in harvesting the plasmonic properties of silver nanoparticles to increase the activity of photocatalysts. Electron clouds of coinage metal nanoparticles such as silver and gold interact with visible light through the localized surface plasmon resonance (LSPR) effect. It causes oscillation of the electron clouds with the electric field of light, generating charge displacement in the

nanoparticles; the polarization then creates a restoring force that brings the system to resonance. This collective oscillation enhances the electromagnetic field in the vicinity of the nanoparticles, in other words concentrating light in their surroundings.⁸⁷ The effect of LSPR in catalysis is however dependent on the distance between the plasmonic core and the photocatalyst, and Gellé *et al.* used silica shells to study this dependence.⁸⁸ The authors used silver nanoparticle cores coated with silica shells of various thicknesses, and the silica surface was used to immobilize the photocatalyst ruthenium (II) tris(bipyridine). The authors studied the singlet oxygen oxidation of β -citronellol and found photocatalytic activity to be the lowest when the photocatalyst was the closest to the plasmonic core (8 nm distance), reaching a maximum at the intermediate distance of 28 nm, and then decreasing at longer distances. This is a prime example of the use of a dense coreshell system for catalysis: the catalytic site is not the core of the design, but a decoration added on the silica surface; nevertheless, both the core, the shell, and the hierarchical placement are essential for the desired catalytic activity.

Another example of dense core-shell architecture in catalysis is the extensive literature on silicacoated iron oxide. Iron oxide cores give magnetic properties to the materials, a valuable asset in heterogeneous catalysis, while the silica coating gives the versatility of surface functionalization and decoration. In those cases, again, the core does not contain the catalytically active phase but instead, it provides an additional feature to the catalytic system.⁸⁹ This concept will be explored in depth in chapters 3 and 4 of this thesis.

Contrastingly, hollow core-shell nanoparticles (Figure 6b) have the catalytically active phase inside the shell. Hollow-shell structures with mobile cores (yolk-shell) are particularly important in catalysis since the silica shells can protect the core containing active catalytic species while also allowing access to it though porous systems. Such hollow structures often stabilize metals against sintering. Yolk-shell architectures can also promote light reflection and scattering, which is even more maximized on particles with multi-level systems. This architecture is versatile because it allows modulation of the core and the shell as well as the core-to-shell ratio, as discussed for dense core-shell systems, but there is also modulation of the void, which is where the desired chemistry will likely happen. The voids provide confined environments for catalytic reactions and multi-shell or multi-core systems allow the compartmentalization of incompatible catalytic functions in the same system. This confinement of reactions in the voids may favour cascade reactions that happen in the interior of the shells, and porous shells and small yolk-shell gaps can create diffusion gradients to improve selectivities. Concentrations of free species can also be enriched in the interior of the shells, directly affecting reactivity,^{90, 91} which is a phenomenon that will be explored in chapter 5 of this thesis.

In summary, this section summarized the types of core-shell nanostructures, some main applications, and the synthetic methodologies available to access these intriguing materials. Catalysis is one of the main applications of core-shell nanostructures, and it can be used to achieve more sustainable chemical processes through green chemistry.

2.4 Green Chemistry and catalysis

Chemistry has enabled scientists to invent products that are today essential and beneficial for society. Although the function of products has historically been the drive for discovery, their consequences can not be neglected. The chemical sector nowadays is mostly linear, and most of the feedstock is non-renewable. There is also high reliability on reactants that are designed to be highly reactive, but as a consequence are also toxic, persistent, and at increased risk of accidents.⁹² Many of those processes produce waste at much higher rates than desired products (1-5 times the amount of waste per product for bulk chemicals, 5-50 times for fine chemicals, and 25-100 times for pharmaceuticals).⁹³ Despite this scenario, society depends and will continue to depend on the functions provided by those products, so the question lies in how to continue delivering those functions but with better products and processes. Chemistry is the heart of this solution, and this is where Green Chemistry steps in.

Green Chemistry can be defined as "the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances";⁹⁴ it is an approach to addressing sustainability and pollution prevention at the molecular level. It is not a field of Chemistry itself but rather an interdisciplinary concept that goes across all fields and calls for the elimination of hazard and waste generation at the chemical design stage rather than remediation. As well highlighted by Kirchoff,⁹⁵ Green Chemistry envisages a more sustainable society through a collaborative effort with synergy between the academic, industrial, and governmental sectors. The concepts of Green Chemistry are also closely related to the United Nations' Sustainable Development Goals.⁹⁶

Green Chemistry is guided by 12 principles that were proposed by Anastas and Warner in 1998.⁹⁷ They expand the definition of Green Chemistry and provide a range of concepts and actions that are aligned with Green Chemistry approaches. The 12 principles were originally stated as:

- 1. **Waste prevention**: "It is better to prevent waste than to treat or clean up waste after it is formed."
- 2. Atom economy: "Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product."
- 3. Less hazardous chemical syntheses: "Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment."
- 4. **Designing safer chemicals**: "Chemical products should be designed to preserve efficacy of function while reducing toxicity."
- 5. **Safer solvents and auxiliaries**: "The use of auxiliary substances (*e.g.* solvent, separation agents, etc.) should be made unnecessary whenever possible and innocuous when used."
- 6. **Design for energy efficiency**: "Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure."
- 7. **Use of renewable feedstocks**: "A raw material feedstock should be renewable rather than depleting whenever technically and economically feasible."
- 8. **Reduce derivatives**: "Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible."
- 9. **Catalysis**: "Catalytic reagents (as selective as possible) are superior to stoichiometric reagents."
- 10. **Design for degradation**: "Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products."
- 11. **Real-time analysis for pollution prevention**: "Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances."

12. **Inherently safer chemistry for accident prevention**: "Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires."

Catalysis is principle number nine of Green Chemistry, and an undisputable major player in the field. Catalysts are an essential part of almost all chemical processes which intrinsically makes them less energy-consuming and more selective. Green chemists often find inspiration in Nature, and how good of a catalyst maker Nature is! Enzymes are highly selective catalysts that operate at mild conditions and carry out complex transformations with Earth-abundant, low-toxicity metals.⁹⁸

Industrial chemistry also relies heavily on catalysis; for example, the three chemical products produced in the largest volume every year, namely sulfuric acid, ethylene, and ammonia, all come from catalyzed processes. Sulfuric acid was produced at the 260 million ton scale in 2021; its synthesis involves the oxidation of SO₂ to SO₃, which happens over a catalyst composed of vanadium, potassium, sodium, and cesium all molten as a film on porous silica.⁹⁹ Ethylene is the highest volume organic compound produced globally, with 200 million tons in 2021; it comes from steam cracking over zeolite catalysis.¹⁰⁰ The third one on the podium, ammonia, was produced on the 150 million ton scale in 2021 and comes from the Harber-Bosch synthesis catalyzed mostly by fused-iron catalysts with various promoters.¹⁰¹

Catalysts have the power to change reaction pathways and if used correctly, reach out to many of the other principles of Green Chemistry. A catalyst that improves the selectivity of a given process will contribute to waste prevention. A catalytic cascade process will likely avoid auxiliaries and hazardous activating or protecting agents. A catalyzed process that operates under mild temperature and pressure conditions will make the process safer and less prone to accidents.¹⁰² Catalysts have also allowed more and more the conversion of renewable feedstock into chemical building blocks,¹⁰³ as well as the use of alternative energy sources such as light¹⁰⁴ or mechanical energy.¹⁰⁵

Catalysis is generally classified as either homogeneous catalysis, *i.e.* when the catalyst and reactants are in the same phase; or heterogeneous, *i.e.* when the catalyst and reactants are in different phases. Homogeneous catalysts have all reaction sites accessible to the substrate since they are most usually soluble metal complexes operating in a liquid phase. Their structure is well designed and controlled down to the atomic level, allowing precise tuning of chemo-, regio-, and

enantioselectivity through the infinite possibilities of combinations of the metal center and ligands. Although homogeneous catalysts are employed in industrial processes, remarkedly polymerization processes, their intrinsic miscibility with reaction media makes recovery and reuse difficult. At the end of the reaction, the catalysts necessarily become contamination in the product, and the purification effort is a problem, especially for applications with highly controlled amounts of metals such as pharmaceuticals. Heterogeneous catalysts, on the other hand, are popular in industrial settings due to their robustness, relative stability to harsh reaction conditions, ease of recovery, product purification, and recycling. The drawbacks of heterogeneous catalysts are however many, including limited mass transfer in solution, limited access to catalyst (surface only), and poor level of control of the catalytic sites and mechanisms, making catalyst optimization and tuning an arduous task.¹⁰⁶ Catalysts in the nano-dimensions, also referred to as nanocatalysts, are a concept that can bridge this gap. The high surface-to-volume ratio allows high access to the catalysts and increased mass transfer, while nanodesign techniques allow high control of placement and electronic of atoms on the surfaces. At the same time, nanocatalysts are not soluble, so they can be easily separated for instance by centrifugation or magnetic recovery in certain cases. Nanocatalysts can therefore bring together the best of both words and deliver greener chemistry through catalysis.¹⁰⁷

In this thesis, with the aim of progressing toward the principles of Green Chemistry, the concepts laid out in section 2.1 will be applied to design core-shell silica nanostructures. We will demonstrate the central of the silica shells in two contexts: magnetically recoverable photocatalysis (chapters 3 and 4), and confined catalysis (chapter 5).

2.5 Photocatalysis and magnetic recovery

Photocatalysis speaks directly to the Green Chemistry principles of catalysis (principle 9) and energy efficiency (principle 6), especially when it happens under low energy wavelengths such as visible light; but it also has the potential to reach other concepts in Green Chemistry. Chemical reactions catalyzed by visible light are often quite selective, hence making fewer by-products and preventing waste generation (principle 1). Visible-light activated reactivity happens mostly close to ambient temperature and pressure conditions, therefore being inherently safer and posing less risk of accidents (principle 12) than traditional thermally activated and high-pressure chemistry. Visible light can also trigger the formation of singlet oxygen, a powerful reactant that can replace hazardous oxidants (principle 3) and provide highly atom economical transformations (principle 2). These relationships are illustrated in Figure 11.



Figure 11. Examples of ways in which photocatalysis is used to apply the principles of Green Chemistry.

Visible light is however often sensitized by either organometallic compounds containing rare metals, which are scarce and toxic, or halogenated organic compounds, also toxic. Product purification and recovery of valuable catalysts is made easier when those compounds are immobilized on heterogeneous supports. There are several strategies for the recovery of solid catalysts including filtration, centrifugation, and magnetic recovery. The latter is highly advantageous because it involves low product manipulation, which makes it compatible with flow systems, for instance.¹⁰⁸ The main requirement is of course that the support has magnetic properties, which may be troublesome in the case of certain photocatalytic applications.

Magnetic nanoparticles (MNPs) such as iron, cobalt, nickel, and their oxides are well-known for feasible synthesis in the nanoscale and magnetic tractability, but their intense dark color means high absorption of visible light. Since photocatalysis relies on light absorption by the catalytically active species, the presence of high light absorbing component inside the reactor means competition, so fewer photons are available for photocatalyst activation. Silica coating can be used to circumvent this issue, which will be discussed in Chapters 3 and 4. This section will briefly review the concepts of photocatalysis, singlet oxygen sensitization, and magnetically recoverable photocatalysts.

2.5.1 Photocatalysis

Light is an abundant, clean, and inexhaustible form of energy. The sun provides the Earth with photons that are used directly by plants for photosynthesis for instance, but sunlight is indirectly the source of most energy on the planet. Fossil fuels, in the words of Giacomo Ciamician, "offer to mankind solar energy in its most concentrated form", but the direct utilization of solar energy is a much more sustainable alternative.¹⁰⁹ In an iconic article published in 1912, Ciamician called fellow chemists to utilize light as a direct source of energy and predicted a future in which forests of glass tubes would rise in the deserts to carry out photochemical reactions of all sorts. His vision was so revolutionary at the time that Ciamician's article is considered by some as the birth of Green Chemistry itself;⁹⁶ so one could say photochemistry and Green Chemistry are closely related to each other since their birth.



Figure 12. Ciamician and Silber performing photochemical experiments with sunlight. Source: online archive of the University of Bologna. Accessible from https://chemistry.unibo.it/en/department/presentation/history-of-the-department, on 2022 Nov 7.

Most organic molecules however only absorb light in the ultra-violet (UV) region, which is an impediment for large-scale applications for many reasons. The generation of UV radiation, which is not abundant in the solar spectrum, involves a relatively high energy input; additionally, the

manipulation of UV radiation requires dedicated reactors and equipment, and safety is of concern when dealing with UV.¹¹⁰ Moreover, the high energy of UV radiation, comparable to that of C-C bonds, can cause undesirable decompositions of weaker bonds in substrates with structural complexity. Visible light photons, on the other hand, are much milder and safer to handle than UV, they are compatible with structurally complex substrates and are also the most abundant fraction of the solar spectrum.¹¹¹ Visible light can also be generated at low energy expense using LED lights.¹¹²

Since most of the substrates of interest for photochemical transformations do not absorb visible light, compounds that do absorb visible light are required to carry out such transformations. Those agents are called photosensitizers; they absorb photon energy to reach an excited state, which can be utilized either by directly transferring this energy to another substrate or by going through a redox cycle.¹¹¹ Photocatalysis is the branch of photochemistry that studies the catalytic processes triggered by the absorption of ultraviolet, visible, or infrared radiation,¹¹³ hence the definition of photosensitizers and photocatalysts have a certain overlap and these two terms are used interchangeably in many contexts, as will happen throughout this text.¹¹⁴

When a photosensitizer absorbs light at appropriate energy, it is elevated to an excited state and can be quenched back to its ground state through several different spontaneous pathways, as illustrated in the Jablonski diagram in Figure 13. From the excited singlet state S_1 , energy loss can occur either through fluorescence (Figure 13b) when a photon is emitted, or though non-radiative decays (Figure 13c) which typically involve vibrational energy. Intersystem crossing is another



Figure 13. Jablonski diagram showing light absorption and decay pathways: a) excitation, b) fluorescence, c) singlet-state non-radiative decay, d) intersystem crossing, e) phosphorescence, and f) triplet-state non-radiative decay. Reproduced from reference 115.

pathway of energy dissipation, which brings the excited species from S_1 to a lower energy excited triplet state T_1 (Figure 13d). From T_1 , the species can return to the ground state either through the emission of a photon by phosphorescence (Figure 13e) or though a non-radiative pathway (Figure 13e).¹¹⁵

If the photosensitizer is long lived enough in S_1 or T_1 , external agents can act to quench it back to S_0 and acquire this energy difference. There are three quenching pathways that trigger photocatalytic processes, they are presented in Figure 14 using ruthenium (II) tris(bipyridine), $Ru(bpy)_3^{2+}$ as an example. $Ru(bpy)_3^{2+}$ is highly studied photosensitizer that can efficiently undergo all three pathways: the reductive cycle (path a), the oxidative cycle (path b), and energy transfer (path c).¹¹¹



Figure 14. Photoexcitation of $Ru(bpy)_{3^{2+}}$ and photocatalytic pathways that quench the excited $Ru(bpy)_{3^{2+}}$ species. Adapted from reference 111.

The photoexcited species $\text{Ru}^*(\text{bpy})_3^{2+}$ is both a stronger oxidant and a stronger reductant than ground state $\text{Ru}(\text{bpy})_3^{2+}$, hence it can either initiate single electron transfers (SET) to electron-deficient substrates or receive a SET from electron-rich substrates (Figure 14, paths a and b). The full potential of photoredox chemistry was really unlocked in 2008 by the combined efforts of the

MacMillan group, which coupled the Ru(bpy)₃²⁺ photoredox cycle with an imidazolidinone organocatalyst for the α -alkylation of aldehydes;¹¹⁶ and the Yoon group, which coupled the redox cycle of Ru(bpy)₃²⁺ with diisopropylethylamine to trigger SET to perform [2+2] enone cycloadditions.¹¹⁷ In the following year, the Stephenson group reported a reductive dehalogenation reaction carried out with photoredox chemistry using Ru(bpy)₃²⁺, diisopropylethylamine, and formic acid,¹¹⁸ confirming the powerful versatility of the approach. These combined efforts brought photoredox chemistry to the spotlight and the field has ever since blossomed; the general strategy of using photosensitizers to trigger SET under visible-light has now been employed for all sorts of organic processes, and it has been extensively reviewed in the literature.^{119, 120}

An alternative pathway for quenching the excited photosensitizer is through energy transfer (Figure 14, path a). This happens when the excited photosensitizer has enough energy and compatible spin state to bring a reactant placed in its vicinity to an excited state, in which case the photosensitizer returns to its ground state and the species that received the energy is responsible for carrying out the desired photocatalytic process. A major example of this type of sensitization is the formation of singlet oxygen.

2.5.2 Singlet oxygen

When Joseph Priestly discovered "dephlogisticated air" in 1774, he announced that he had "discovered an air five or six times as good as common air." Few years later, Lavoisier called this new air oxygen, and by the late 1780s the phlogiston theory had fallen; oxygen has ever since sparked new discoveries and exploded to occupy its central role chemistry and biology. The paramagnetism of the dioxygen molecule was discovered by Faraday in the 1840s and interpreted by Mulliken as a consequence of the unpaired parallel spins in its electronic structure (Scheme 3). Ground state oxygen (spectroscopic term ${}^{2}\Sigma_{g}$, simplified notation ${}^{3}O_{2}$) has a triplet spin state as shown in Scheme 3, and can be excited to singlet states (${}^{1}O_{2}$) either by pairing the two electrons (${}^{1}\Delta_{g}$) or by having unpaired inverted spins (${}^{1}\Sigma_{g}^{+}$). The lower energy singlet state ${}^{1}\Delta_{g}$ has a much longer lifetime than ${}^{1}\Sigma_{g}^{+}$, being for instance able to withstand 10⁸ collisions with methanol molecules in the gas phase, while the higher energy one only lasts 10 collisions.¹²¹ Due to its lower energy and longer lifetime, the singlet state ${}^{1}\Delta_{g}$ is present in several chemical and biological processes and is therefore the most relevant singlet state of molecular dioxygen; in fact ${}^{1}\Sigma_{g}^{+}$ rapidly decays in solution to form ${}^{1}\Delta_{g}{}^{122}$ Unless specified, the terms singlet oxygen or ${}^{1}O_{2}$ throughout this text (and most literature) refer to the most stable and relevant ${}^{1}\Delta_{g}$ form.



Scheme 3. Simplified diagram of molecular oxygen electronic configuration. Adapted from reference 121.

The empty π^* orbital in singlet oxygen gives it extremely high and specific reactivity, making it a powerful tool in organic synthesis. As represented in Scheme 4, singlet oxygen can act as a dienophile in a Diels-Alder type [2+4] addition, as well a [2+2] additions; it can also add across π bonds to make hydroperoxides from alkenes ('ene' reaction), and oxidize heteroatoms such as sulfur and phosphorus.¹²³



Scheme 4. Synthetic pathways in which singlet oxygen can be used to generate oxygenated hydrocarbons. Adapted from reference 123.

Singlet oxygen is formed when ground state oxygen is excited with enough energy to reach one of the excited states, and this energy can be transferred from a photosensitizer, as discussed in section 2.5.1. Such a process is represented in the diagram in Figure 15, which is an expanded version of the one in Figure 13. Although the energy transfer to trigger ${}^{3}O_{2} \rightarrow {}^{1}O_{2}$ can happen from the internal conversion $S_{1} \rightarrow S_{0}$,¹²⁴ the most efficient pathway starts from T_{1} since the spin-forbiddance of the $T_{1} \rightarrow S_{0}$ transition makes the T_{1} state much longer-lived than S_{1} .¹²⁵ Hence, photosensitizers with high rates of intersystem crossing $S_{1} \rightarrow T_{1}$ are a wise choice for ${}^{1}O_{2}$ sensitization. In addition to the high quantum yield of intersystem crossing ($\Phi_{T} > 0.4$), DeRosa *et al.* highlighted that the ideal singlet oxygen photosensitizer would also have a high absorption coefficient at the transition wavelength, appropriate triplet state energy ($E_{T} \ge 95$ kJ mol⁻¹), long triplet lifetimes ($\tau_{T} > 1\mu$ s), and high photostability.¹²⁶



Figure 15. Diagram showing the triple stated sensitized production of singlet oxygen. S represents singlet states, T represents triple states, IC stands for internal conversion and ISC, for intersystem crossing. Adapted from reference 125.

An important advantage of singlet oxygen photogeneration is that the photoexcitation happens at the sensitizer, not at the substrate, so the process itself is wavelength selective. In other words, the photosensitizer only requires a narrow wavelength range, making it compatible with dedicated narrow light sources and broad solar light alike. In fact, Nature produces singlet oxygen in the photosystem II center using photons from the sun, oxygen from the atmosphere, and chlorophyll; Schilling *et al.* took advantage of this fact and used chlorophyll under direct sunlight to obtain α -amino carbonyl products through singlet oxygen reactivity.¹²⁷ Quoting Ciamician again, "Nature is not in a hurry and making is",¹⁰⁹ hence scientists have now found a handful of synthetic photosensitizers that can produce singlet oxygen more efficiently than chlorophyll; those include organic dyes and transition metal complexes.

Highly conjugated organic molecules such as rose bengal, eosin blue, and methylene blue (Figure 16) are excellent singlet oxygen photosensitizers as they are high visible-light absorbers and possess triplet states with enough energy to excite the dioxygen molecule. The presence of heavy atoms such as the halogens in eosin and rose bengal increases the yield of intersystem crossing, making them more efficient singlet oxygen photosensitizers than their less halogenated derivatives.¹²⁶



Figure 16. Structures of typical organic dyes used for singlet oxygen sensitization.

Rose bengal (RB), for instance, is the photocatalyst of one of the few photochemical process used the chemical synthesis industry, which is the production of rose oxide following a patent of the Symrise Group (Scheme 5). Rose oxide is a mixture of the four diastereomers illustrated in Scheme 5, it has an intense floral aroma that comes mostly from the (-)-*cis* isomer. This isomer is extracted from bulgarian rose or geranium bourbon for the making of high value perfumes, but the isomeric mixture is produced synthetically from the oxidation of β -citronellol for use in the large scale production of cosmetics and scents.¹²⁸



Scheme 5. Production of rose oxide from β -citronellol using rose bengal photocatalysis, as patented by Dragoco. The leftmost isomer in the rose oxide mixture, (-)-cis, has the most olfactive properties.

Transition metal complexes can also be used to generate singlet oxygen, and ruthenium (II) compounds such as the ones shown in Figure 17 are common in the literature. They have relatively high blue light absorption coming from a transfer from the d orbital centered on the metal to the π orbital of the ligand, *i.e.* a metal-to-ligand charge transfer (MLCT), and these transitions have enough energy to promote the excitation of the dioxygen molecule. Although these dyes do not absorb as much light as their organic counterparts, the MLCT makes up for it by bringing the S₁ and T₁ states very close to each other in energy, so the rate of intersystem crossing S₁ \rightarrow T₁ for Ru(bpy)₃²⁺, for instance, is 100% efficient. The triplet state formed is also long-lived, so Ru(bpy)₃²⁺ checks many boxes for efficient singlet oxygen photosensitization. Ru(bpy)₃²⁺ has also been used to produce singlet oxygen for the oxidation of β -citronellol to give rose oxide,¹²⁹ as well as for the semi-synthesis of antimalarial drug artemisinin.^{129, 130}



Figure 17. Structures of typical Ru (II) dyes used for singlet oxygen sensitization. From left to right: ruthenium (II) tris(bipyridine), ruthenium (II) tris(1,10-phenanthroline), and ruthenium (II) tris(diphenyl-1,10-phenanthroline).

2.5.3 Magnetically recoverable nanocatalysts

Magnetic tractability is a highly desirable feature of nanocatalysts to improve product purification and catalyst reusability, especially given the difficulty in filtrating such small entities.¹³¹ Magnetic separation is preferred over filtration and centrifugation for offering higher efficiency and specificity. It is used in many sectors, and it can be either positive or negative. Positive selection (Scheme 6a) is for the separation of a non-magnetic component, in which a magnetic carrier is introduced and either binds or adsorbs the species to be separated, and the resulting composite is magnetically decantated. Negative selection Scheme 6b), on the other hand, is used when the magnetic component is to be removed to purify a product.⁷⁵



Scheme 6. Positive (a) and negative (b) magnetic separation strategies. Reproduced from reference 75.

Well-known magnetic nanomaterials such as the ones containing Fe, Co, and Ni have been largely used due to their magnetic tractability and accessible nanoparticles. Since those metals are also known for catalytic activity, both properties have been simultaneously explored in different systems including their pure and mixed oxides being used as catalysts as well as active supports for reduced metal nanoparticles.¹³²

Magnetic separations are also promising for applications in reaction systems in flow, which suffer from clogging and pressure limitation issues when operating with packed heterogeneous catalysts. Their applicability was demonstrated by the Kim group in a capillary microtube reactor. The concept is to flow the nanocatalyst in the system with the reactants and add a magnetic separation station before the product collection end, as shown in Figure 18a. In this separation chamber, the product stream carrying the catalyst flows in the same direction as the fresh stream that is introduced. Following a laminar flow model, the catalyst flows on the top half of the channel while the fresh stream flows on the bottom half. The introduction of a magnet directs the catalyst to the bottom part and gets it recirculated in the reactor while clean product is continuously collected (Figure 18b). It is a literal separation system in flow. The authors performed alkene deoxygenation reactions using Pd on magnetic supports using 10% of the amount of catalyst required for the analogous reaction in batch.¹³³ Photocatalytic systems also highly benefit from flow setups because light penetration is much more efficient through thin tubes than through large batch reactors.¹³⁴ In this context, there is considerable interest in the development of magnetic photocatalysts.



Figure 18. a) Microreaction system consisting of a microseparator chip and a capillary microtube reactor, and b) magnetic particles in the product stream in the laminar flow regime move toward the magnet and join the feed stream. Reproduced from reference 133.

2.5.4 The combination of photocatalysis and magnetic properties

Magnetically recoverable photocatalytic systems have been reported in the literature, but mostly in systems designed for the degradation of pollutants in aqueous media. The most common magnetic components found in the literature are iron oxides and Co, Cu, and Zn ferrites. Iron oxides are particularly known for their photoactivity under UV light in advanced oxidative processes,¹³⁵⁻¹³⁷ but their role in photocatalysis has been expanded by the combination with a variety of semiconductor materials like carbon nitrides, graphene oxide, and titania. Light-responsive metal-organic frameworks have also been combined with magnetic components in the context of pollution degradation, and recently highlighted in a review by Ma and co-workers.¹³⁸

Wang and co-workers¹³⁹ coated CuFe₂O₄ NPs with carbon nitride to make hybrid catalysts to induce the visible-light photolysis of H₂O₂ for orange II degradation in a Fenton-like process. The authors observed that the hybrid composite performed better than both parts alone, likely due to the synergic match of lattice and energy level between graphitic carbon nitride and the copper ferrite; such compatibility facilitated the transfer of electron-hole pairs at the interfaces. Similar synergies have also been observed for systems based on graphene oxide. Fu et al.¹⁴⁰ decorated reduced graphene oxide sheets with CoFe₂O₄ NPs and observed enhanced photodegradation of methylene blue (MB) with the composite when compared to the ferrite or graphene oxide alone. Like in the carbon nitride case, graphene oxide enhances charge separation in the magnetic NPs by accepting electrons from the electron-hole pairs; the MB molecules, which π - π stack on the supports, are oxidized either by superoxide anions formed when the negatively charged support reacts with dissolved oxygen or by hydroxyl radicals generated when the holes (from the electronhole pairs) scavenge water molecules. The Guo group¹⁴¹ also worked with reduced graphene oxide, but on a ternary system with CoFe₂O₄ and Ag₃PO₄; this catalytic system had enhanced activity for the degradation of levofloxacin. An interesting point in Guo's system is that the combination Ag₃PO₄/CoFe₂O₄ performed worse than Ag₃PO₄ alone, while better performance was observed when graphene oxide was introduced, which the authors attributed to the adsorption of the substrate on graphene oxide by π - π stacking interactions.

Titanium dioxide, or titania, is perhaps the most studied semiconductor photocatalyst; it is highly available, non-toxic, and compatible with several different systems. Titania needs high-energy UV light ($\lambda < 387$ nm) to be activated, but its band gap can be narrowed through doping or photosensitizing.¹⁴² Xu *et al.*,¹⁴³ for instance, coated magnetite NPs with TiO₂ and decorated the composite with AgPO₄; the system generated superoxide species under visible light irradiation, which were used to inactivate bacteria. In another study, the Gu group¹⁴⁴ prepared yolk-shell magnetite-TiO₂ nanoparticles that were used to degrade MB under UV irradiation; the authors

noticed a reduction in the photoactivity of TiO_2 upon the combination with the magnetic nanoparticle, which was attributed to the electron-hole recombination promoted by the contact of titania with the magnetic core. In fact, Yao *et al.*¹⁴⁵ published a review on the utilisation of magnetic titania-based materials for the photodegradation of pollutants in which they mention that composites of titania and MNPs often have lower catalytic activity than titania itself; the authors attribute this inhibition by the screening effect of magnetic supports.

Although various magnetically recoverable photocatalytic systems have been developed for pollutant degradation, reports of magnetic photocatalysts producing fine chemicals are scarce in the literature. One rare example is the work of Huang *et al.* who used a layered double hydroxide (LDH) as a matrix for a composite with magnetite NPs and the photosensitizer rose bengal (RB). The authors successfully used the catalyst in the cross-dehydrogenative coupling reaction of amine and nitroalkanes, aerobic oxidation of sulfides, and radical additions reactions of thiols and alkenes.¹⁴⁶ Several substrates were used in each case, giving moderate to excellent yields, as depicted in Scheme 7.

The interaction of photosensitizers with supports is not trivial, yet it is highly under-investigated. Supports that absorb visible light, which is the case of magnetic nanoparticles, compete with the photosensitizers for photon adsorption, and this competition can potentially compromise photocatalytic activity. The Simard group studied the use of magnetic iron oxide nanoparticles to immobilize dyes for biomedical applications and found that direct attachment of the dye pyrene on the surface of the magnetic nanoparticles led to complete quenching of pyrene's photoluminescence. When a silica shell was added between the magnetic core and the dye, the authors observed emission from pyrene but it was broader, less intense, and red-shifted. The authors also observed a decrease in the magnetic enough for the desired applications.¹⁴⁷ Also, although magnetic properties are often assets in a catalytic system, the chemical properties of magnetic metals are not always desirable. This is another situation when silica shells in dense coreshell architectures are very useful, as they can be designed to maintain the magnetic properties of the core while providing a surface prone to chemical functionalization.

As showcased by many of the above examples, light absorption by the magnetic core is also an effect that actively affects photocatalysis, and it is possibly one reason why magnetically



recoverable visible-light fine chemistry catalysts are highly unexplored. A systematic study of this issue for photocatalytic applications is the topic of Chapter 3 of this thesis.

Scheme 7. Visible-light photocatalytic transformations accomplished by the Huang *et al.* using a magnetic composite made of magnetite NPs and rose bengal embedded in a layered double hydroxide matrix: a) cross-dehydrogenative coupling of amine and nitroalkanes, b) aerobic oxidation of sulfides, and c) radical additions reactions of thiols and alkenes. Reproduced from reference 146.

2.6 Confined catalysis

Conventionally, chemical solutions are viewed as continuous, homogenous, and isotropic systems with a random distribution of solutes in the solution. Yet, many important chemical phenomena occur outside of this idealized view. For instance, in liquid crystals, colloidal suspensions, and supramolecular arrangements, anisotropy is central to understanding effects from the molecular to macroscopic scales.¹⁴⁸⁻¹⁵⁰ The ability to influence the distribution and conformation of molecules and ions at the nanoscale through their confinement within certain spaces provides the opportunity to impart greater control over chemical reactions and their outcomes. Such control has the potential to markedly improve chemical selectivity, reduce waste, increase reaction rates, and reduce energy requirements, highlighting the great potential of this approach from a Green Chemistry perspective. Herein, we refer to confinement as the spatial restriction of reactants, intermediates, and catalysts within structures of nanoscale and sub-nanoscale dimensions. Such restrictions result in unique adsorption and diffusion properties, which cause the confined species to behave differently from what they would do in a homogeneous, isotropic environment. Confinement effects can allow for a local increase in the concentration of reactants as well as influence their interaction with catalytic sites. Combined, these effects can be used by chemists to improve processes and move towards meeting the principles of Green Chemistry.¹⁵¹ As will be exemplified in this section, confined systems can enable, for instance, higher selectivities (waste prevention, principle 1), less excess of reactants (atom economy, principle 2), lower use of highly reactive species (less hazardous synthesis, principle 3), milder reaction conditions (energy efficiency, principle 6), improved catalytic properties (catalysis, principle 9) and, overall, safer chemical processes (safer chemistry, principle 12). These relationships are illustrated in Figure 19. Hence, by introducing physical spatial constraints, chemists can make more with less, and effectively deliver on the promise of greener chemical processes.



Figure 19. Various ways confinement effects can be used to apply Green Chemistry principles. This scheme is a simplification of the main principles related to each improvement observed throughout the examples that will be highlighted in this review, but each improvement might be related to more than one principle and vice-versa. Reproduced from reference 1.

Confinement effects have played an essential role in chemical reactivity since the beginning of life itself. Nature, a renowned inspiration to green chemists, relies on confinement effects to carry out numerous chemical processes inside enzymatic cavities, which would likely not happen otherwise. However, the concept of confinement was only introduced in catalysis in the 1980s with the seminal work of Eric Derouane *et coll*.¹⁵²⁻¹⁵⁵ They established that molecules inside zeolite pores tend to optimize their van der Waals interactions with the walls and experience magnified physisorption energetics because of the atomic-range curvature inside the pores. Such effects reflect in the diffusion properties of reactants and intermediates inside the pores and directly influence reaction rates. The work of Derouane on zeolites is ubiquitous when studying confinement effects, and it has already been excellently reviewed.^{156, 157}

The concept of confinement has now expanded beyond zeolites, and it has also been observed inside the porous channels of mesoporous silica^{4, 158, 159} and carbon nanotubes,¹⁶⁰⁻¹⁶² for instance. Such materials feature pores that are connected to the bulk reaction medium, generating gradients of diffusion rates that play important roles in the reactivity of substrates.^{163, 164} In addition, different encapsulation strategies have also emerged to confine chemical reactions. In this review, encapsulated reactions will differ from the ones inside porous structures in the sense that they will refer to closed, discrete nanoreactors rather than pores contained in continuous solid networks. The encapsulation of reactions includes strategies with rich organic and inorganic chemical

compositions and architectures ranging from hollow to multi-shelled particles.⁸¹ Apart from solid cages, supramolecular chemists have been able to create self-assembled structures which take advantage of the organization of molecules in solution to also carry out spatially confined reactions.¹⁶⁵⁻¹⁶⁷

The effects of confinement have already been reviewed in different contexts, including an enlightening review by Goettmann & Sanchez in 2006¹⁶⁸ and more recent ones that highlighted synergic effects,¹⁶⁹ supramolecular arrangements,^{170, 171} and a broad and comprehensive book edited by Poli and published in 2017.¹⁷² Here we do not intend to exhaustively review the literature on confinement effects, but we will rather explore it from a green chemistry perspective. We will be highlighting recent creative studies with the aim of introducing spatial confinement into the green chemistry toolbox as an approach for chemists to make more products from fewer resources. We also focused our attention on examples where confinement was employed as a means to deliver better processes in strategic sustainable areas such as energy, biomass, or pollution remediation.

We will begin by reviewing recent theoretical and mechanistic studies that provide evidence for the role of spatial confinement. Following, we will present selected works from the literature, which are organized in two major sections according to the nature of the confining medium in each specific case: confinement in pores or confinement by encapsulation.

2.6.1 Theoretical studies of confinement

While it has been experimentally observed for over three decades that chemical reactivity can be influenced by the introduction of spatial constraints, it is intrinsically challenging to experimentally isolate the various factors that can account for it. By using the reactive Monte Carlo simulation method and transition state theory, the Gubbins group studied confinement in several reactions, which they have compiled in a series of review articles.¹⁷³⁻¹⁷⁵ The group pioneered computational studies on confinement effects, showing that both the equilibrium position and dynamics of chemical reactions can be affected by spatial restrictions. Equilibria can be shifted by two main mechanisms: firstly, an increase in the density of molecules inside of the confined space can favour reactions that decrease the number of molecules of the system; secondly, equilibria can also change as a result of selective adsorption to the walls, which will change the effective concentration of the adsorbed component in the reaction media. Much of the recent literature,
however, has been dedicated to the study of what the Gubbins group referred to as dynamic effects, which stem from either geometrical constraints or host-guest interactions, that alter energy barriers by impacting the formation of activated complexes. As a consequence of the combination of those dynamic effects, species inside nanopores were shown to, for instance, experience pressures up to 5 orders of magnitude higher than those in the bulk.¹⁷⁶⁻¹⁷⁸ The Gubbins group has recently applied these concepts in a study of the dimerization of nitric oxide inside carbon nanopores¹⁷⁹ and found excellent agreement with experimental results. Inspired by this body of work, many other researchers have taken advantage of molecular simulations to study confined environments. This section will highlight recent examples of studies that systematically decoupled the two main factors that contribute to such modified reactivity: host-guest interactions (*i.e.* electronic effects) and geometric constraints. We will compare selected studies and attempt to draw general conclusions about the interplay between mechanisms in spatially confined systems.

A range of selected simple reactions confined within two metal surfaces was studied by Balbuena and co-workers through the use of DFT calculations.¹⁸⁰ The dissociation of O₂ was simulated both on a free Pt surface and between two surfaces that were 4.9 Å apart. The authors found that the confined system provided more efficient charge transfer from the metal to the substrate, which decreased the energy gap between the bonding and antibonding orbitals of O₂. The larger population on the π^* orbital weakened the O-O bond, which was observed to be longer in the adsorbed molecule. This effect decreased the activation energy of the O_2 dissociation reaction by 35% when compared to the reaction on a single metal surface. BEP (Brönsted-Evans-Polanyi) relationships were also calculated for the dissociation of O_2 , CO, and NO on different metal surfaces, and revealed a good correlation between adsorption and activation energies for all systems, with a negative relationship between the strength of adsorption and activation energy. The effect of confinement on activation energy decreased in the order $CO > NO > O_2$. The confinement effect on the activation energy of dissociation was found to be relatively independent of the metal, but highly dependent on the arrangement of the substrate molecules inside the confined space (Figure 20). Molecules adsorbed in a conformation that optimized the interactions with both metal layers benefited from more charge transfer, which resulted in more effective bond weakening and, consequently, a larger decrease in activation energy. In other words, geometrical constraints that led to stronger host-guest interactions were key for the enhancement of reactivity in this study.



Figure 20. Electronic density maps for molecules adsorbed between two Pt (111) surfaces at a surface-surface separation distance H = 4.9 Å. (a) CO, (b) NO, and (c) O₂. Reproduced from reference 180.

Another compelling study was carried out by the Huang and Fang groups, who used superlocalization-based imaging techniques to observe single molecules and study nanoconfined dynamic processes.¹⁶³ The catalytic system consisted of Pt nanoparticles sandwiched between a dense silica core and a mesoporous silica shell. The pores were cylindrical (100 nm in length and 2.3 nm in diameter) and perpendicular to the core, having the top open to the bulk reaction medium and the bottom blocked by Pt nanoparticles. The oxidation of amplex red to resofurin (a fluorogenic reaction) was studied as a probe, and the authors found enhanced reaction rates in the confined reaction. The molecules had their rate of diffusion reduced by 5 orders of magnitude when confined inside the pores of the catalyst compared to the diffusion rate in the bulk, which came from the comparable hydrodynamic size of the product (0.51 nm) to the pore, the increased viscosity of the confined solution (4 times larger than in the bulk), and the interaction of the molecules with the polar siloxane groups on the silica walls. Such slow diffusion caused extremely high concentrations of molecules inside the pores, explaining the higher reaction rates. The same study was carried out using shorter channels (80 nm) and provided unchanged diffusion coefficients and adsorption-desorption constants, but a reduced rate constant. The diffusion coefficients and adsorption-desorption constants resulted in high effective concentrations inside both longer and shorter pores, but the longer ones were able to trap more reactants in the vicinity of Pt atoms, creating a larger reservoir of molecules ready to react, which translated into boosted rate constants. The Huang and Fang groups also published a follow-up study in the following year,¹⁸¹ in which they studied the effect of the pore diameter by comparing smaller 2.2 nm and

wider 3.3 nm pores. In addition to finding slower diffusion in the smaller ones, the authors demonstrated through fluorescence polarisation microscopy that substrate molecules inside the nanopores were prevented from π -stacking on the surface due to spatial restrictions, so the interaction with the reactant happened in an upright position, in which the long axis of the substrate was parallel to the length of the porous channels (Figure 21). This created a favourable geometry for electron transfer, which reduced the activation energy of the reaction. Since the geometric constraints were more pronounced in smaller pores, the system with 2.2 nm pores provided higher catalytic activity. The work of the Huang and Fang groups presents host-guest interactions and geometrical restrictions that were both beneficial for the reaction rate. The former contributed to the slower diffusion rate inside the pores, which led to higher concentrations in the vicinity of the catalyst; while the latter was responsible for a lower activation energy by locking the substrate in a position that facilitated more effective interactions with the catalyst.



Figure 21. On the right, amplex red oxidation to resofurin in silica pores catalyzed by Pt NPs. On the left, the view of a single pore and the geometrical constraints when the substrate approaches the catalyst. Adapted from reference 163.

Host-guest interactions were studied using an interesting approach by the Peruchena group, which used quantum mechanical electron density distribution studies to investigate the methylation of benzene with methanol inside two different zeolite structures: H-ZSM-5 and H-Beta.¹⁸² H-ZSM-5

has its porous structure formed by 10 rings that can fit a sphere of maximum diameter 6.36 Å, while H-Beta has slightly larger pores, formed by 12 rings and that can fit a sphere of maximum diameter 6.68 Å. The authors approached the analysis by splitting the interactions between the zeolite host and molecular guests into two types: primary and secondary. Primary interactions were the strong ones and related to the reaction itself such as adsorption, co-adsorption, bond breaking, and bond formation. Secondary interactions, on the other hand, were the weaker interactions that happened between the substrate and the atoms on the zeolite walls not directly involved in the catalytic process. Such secondary interactions are consequences of spatial confinement, which the authors systematically demonstrated by quantifying their contribution to the stabilization of the system for each individual reaction step. The zeolite with smaller pores consistently proved to provide stronger confinement contributions with, for instance, a maximum of about 40% of stabilization due to secondary interactions, hence confinement, in the benzene adsorption step, against 26% of confinement stabilization in the larger pore for the same process. Confinement also had a higher contribution to the stabilization of the transition state in the smaller cavity, but the larger cavity had a lower energy barrier for this step because it had more space to allow the optimal transition state geometry. The authors found that, from an electronic standpoint, tighter-fitting pores improve host-guest interactions and therefore the stabilization by confinement, but such small spaces might compromise the formation of optimal geometric arrangements that are required in reaction pathways. This demonstrated that a high level of geometric restriction is not always beneficial in confined catalysis, since the confined geometry might not be the preferred one for reactivity.

Another illuminating example is the work of Chattaraj and co-workers,¹⁸³ who studied the [4+2] cycloaddition of 1,3-butadiene and ethylene not inside porous structures, but when encapsulated within two different molecular cages. The first one, ExBox⁴⁺, was a semi-rigid cyclophane with a box-like shape, 9.42 Å wide and 14.86 Å long. The second cage, CB[7] (cucurbit[7]uril), was a macropolycyclic compound formed from the condensation of seven glycoluril units, with a circular interior cavity of diameter 7.3 Å (Figure 22). The authors found that the rate decreased in ExBox⁴⁺ by 4 orders of magnitude relative to the unconfined reaction while the reaction in CB[7] increased by 2 orders of magnitude. Electron-density analysis showed that confinement inside ExBox⁴⁺ caused the reactants to be parallel to the pyridinium rings of the cage, preventing the optimal positioning of the molecules to form the transition state. On the other hand, the reactants inside

CB[7] did not interact with the cage but were instead held closer together, which facilitated the desired orbital overlap. This behaviour was seen as a consequence of a more favorable reactant-ExBox4+ than reactant-reactant interaction, while CB[7] had the opposite effect. Even though CB[7] increased reactivity in this specific system, it had previously been shown to hinder reactivity when used to encapsulate proteases in an earlier study. This example is the opposite of what was observed in Peruchena's work:¹⁸² here, too effective host-guest interactions took place at the expense of the formation of the transition state, while spatial constraints favored reactants interactions and thus reactivity.



Figure 22. Non-covalent interaction (NCI) surfaces. On top, left to right: reactant@ExBox⁴⁺, TS@ ExBox⁴⁺, product@ExBox⁴⁺. On the bottom, left to right: reactant@CB[7], TS@CB[7], product@CB[7]. Reproduced from reference 183.

Carbon nanotubes (CNTs) are also a very useful confinement platform. An illustrative example is the DFT study of the dissociation of O_2 and N_2 on Pt NPs inside CNTs carried out by Bao and co-workers.¹⁶⁴ The authors aimed to test whether reaction rates were affected by the nanotube

diameter because of changes in curvature and distortion of the sp² hybridization on the carbon walls. It was found that, because of the strong interaction between metal clusters and carbon walls, the bonding energy between reactants and catalysts was weakened inside the nanotubes. For example, up to 40% reduction of the Pt-O₂ bonding energy was observed for Pt inside 0.95 nm tubes compared to an unconfined $Pt-O_2$ complex. Such weakened bonding energy favored the dissociation of activated species from the Pt surface, which increased the reaction rate for this reaction. However, while bonding energy was continuously reduced for smaller tubes, catalytic activity formed a volcano plot, with maximum activity in pores of around 1 nm in diameter. This occurred due to a change in the rate-limiting step as the substrate-catalyst bonding energy is progressively weakened. In tubes larger than 1 nm, where $Pt-O_2$ bonding energy was only slightly weakened, the rate of the final desorption step improved but remained limiting, and the reaction rate was enhanced. In tubes smaller than 1 nm, where Pt-O₂ bonding energy was too weak, the initial step of substrate adsorption to the catalyst was compromised and there was a steep drop in the reaction rate. This work, although not considering the effects of geometrical constraints explicitly, is unique in demonstrating the fine line between favourable and unfavourable effects of host-guest interactions on the rates of confined reactions.

The studies presented in this section were chosen as an attempt to showcase the richness and complexity of confined mechanisms. We have highlighted the role of host-guest interactions and geometric constraints in spatially confined catalytic systems, which are summarized in Table 2. Both effects have proven to have the potential to be beneficial or detrimental to catalytic systems, depending on the specifics of each process. Geometric constraints, for instance, were shown to positively influence reaction rates by being able to bring reactants closer to catalysts and optimizing interactions, by forcing reactants closer together and facilitating orbital overlap, or even by promoting unlikely geometric arrangements that exposed reactive sites. Such geometric arrangements, however, can instead be destabilizing and lead to an increase in activation energy, as is the case of the methylation of benzene inside the pores of H-ZSM-5 zeolites. Host-guest interactions are no different and have also proven to be capable of significantly benefiting spatially confined systems by enhancing favourable charge transfer, contributing to slower diffusion and increased local concentrations of species in confinement, or by providing extra stabilization of transition states. Strong interactions might also compromise reactivity, for instance in the encapsulated [4+2] cycloaddition reaction, where stacking of the substrate to the host wall

prevented the optimal transition state geometry. All things considered, confinement effects depend on different factors, and theoretical work such as those presented in this section can deconvolute these and uncover individual contributions. The complexity and peculiarity of such effects are evident, therefore there is the need for a greater understanding of these effects in order to use these principles to design more efficient and potentially greener catalytic systems.

Table 2. Effects of host-guest interactions and geometric	al constraints in selected theory-based papers.
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Ref.	Catalyst	Reaction	Host-guest interactions	Geometrical constraints
180	Parallel Pt surfaces	O ₂ , CO, NO dissociation	Positive	Positive
163, 181	SiO ₂ @Pt@mSiO ₂	Amplex red oxidation	Positive	Positive
182	H-ZSM-5 and H-Beta	Benzene methylation	Positive	Negative
183	ExBox ⁴⁺ and CB[7]	[4+2] cycloaddition	Negative	Positive
164	Pt NPs in CNTs	O_2 and N_2 dissociation	Positive and	_
			negative	

2.6.2 Confinement in pores and cavities

Paolo Bettotti introduces his book on sub-micron porous materials by stating that "any material is porous if we consider that its crystallographic unit cells might act as cages for smaller molecular species".¹⁸⁴ In fact, all the unique properties of pores are consequences of their sizes or – more precisely – their relative dimensions when compared to entities positioned within their interiors. Pores are openings, usually on solid structures, that increase the material's surface area and can come in various sizes, shapes, and degrees of uniformity. Pores are also sometimes referred to as channels or cavities depending on their morphology.¹⁸⁵ Pores with diameters up to 100 nm, defined as nanopores,¹⁸⁶ have dimensions where the interactions of the walls of the pore with atoms and molecules become significant, making them strong candidates for hosting confined chemical reactions.

Zeolites are naturally occurring porous materials and represent the earliest and most widely studied cases of confinement.¹⁵⁷ However, other types of porous materials, mostly mesoporous silica and porous carbon, have also been reported to present confinement effects that improve catalytic

reactions. This section will review the role and activity of porous materials for catalytic applications that rely on confinement.

The use of confined catalysis has now crossed the whole spectrum of catalytic processes and shown the potential to improve chemical transformations across many facets of the chemical industry. We have here selected three main catalytic applications that significantly impact Green Chemistry: the sustainable production of high-energy-containing compounds for use as fuels, the greener manufacture of functionalized molecules to be used as building blocks or commodities, and the degradation of pollutants. Those three broad applications will be illustrated by selected examples of confined catalytic systems.

2.6.2.1 Confined catalysis for energy

Carbon dioxide conversion

Much of the energy consumed nowadays comes from fossil sources, which release CO_2 into the atmosphere and causes an unbalance of the natural carbon cycle. A solution that has been widely discussed is the capture of this carbon and its conversion to fuels, thus closing the anthropogenic carbon cycle.¹⁸⁷ Several carbon sequestration and conversion technologies are available in the literature,¹⁸⁸ and the use of confinement effect can greatly contribute to such catalytic transformations.

Copper has been historically used in the literature for CO₂ reduction because, in addition to being an abundant metal,¹⁸⁹ it can carry out both the CO₂ activation and *CO hydrogenation steps.¹⁹⁰ Nanoparticles of Cu₂O with cavities were used by Yang *et al.* to catalyze the electrochemical reduction of CO₂ into fuels.¹⁹¹ Several systems have already been used to transform CO₂ into reduced C₁ compounds, but the formation of C₂₊ products remains a challenge. The challenge comes from the fact that Cu⁺, the species responsible for catalyzing C-C bond formation, is readily reduced at the negative potentials necessary for the electrochemical process. The nano-cavities in Cu₂O nanoparticles were able to concentrate carbon species (Figure 23) and form a high carbon coverage on the catalyst's surface, which protected the Cu⁺ species from reduction and favored C-C coupling steps. A 9-fold enhancement of the C₂₊/C₁ product ratio was achieved when compared to the reaction on non-porous nanoparticles. Similar cavity-containing copper nanoparticles were used by Zhuang *et al.*, but to obtain C₃ alcohols from CO reduction.¹⁹² Higher-



Figure 23. Confinement of carbon intermediates in the nanocavities of Cu NPs, locally protecting the surface atoms from reduction. Reproduced from reference 191.

order alcohols are desirable molecules to be used as fuels due to their high volumetric energy density, hence the interest in renewable routes for obtaining n-propanol. CO₂-to-CO reduction is well-established, but CO-to-propanol conversions suffer from poor selectivity (around 10%). It was shown that a catalytic system with cavities could retain C₂ products in the vicinity of the catalyst surface and increase C-C coupling reactions, hence boosting C3 selectivity. Finite-element simulations based on the angle of the opening of the cavities corroborated with the C_3/C_2 selectivity observed experimentally: small opening angles ($< 30^{\circ}$) afforded low conversions, large opening angles (> 180°) gave high C_2 selectivity, and intermediate angles (45-90°) provided appreciable selectivity to C_3 products. While small angles limited the access of substrate to the catalytic surface and large angles favoured C₂ desorption, intermediate angles were able to both allow substrate adsorption and confine the C_2 intermediates close to the surfaces, leading to the formation of C_3 products. The formation of C_2 products on copper was also studied by the Tian & Liu groups, but using porous copper electrodes.¹⁹³ The authors found that methane is highly favoured in large 300 nm pores, while C₂ products were selectively produced in 30 nm pores. Comparing two electrodes with 30 nm-wide pores, but with different depths, high ethylene selectivity was found in short (40 nm deep) pores and high ethane selectivity in long (70 nm deep) ones. This difference was explained by the larger residence time of the substrate inside the longer pores, which allowed the formation of the fully saturated molecule. This fact was corroborated by the lower H₂ evolution observed in 70 nm-long pores. Copper electrodes for the reduction of CO2 into C2 products were

also used by Tang and co-workers but applying a novel halogen-assisted method to regenerate the electrode.¹⁹⁴ Iodide addition during the electrode reconstruction led to the formation of a hierarchical porous structure of copper nanowires, while bromide and chloride-assisted processes gave dense and quasi-cubic nanoparticles. All materials showed high electrochemical CO_2 reduction activity, but the porous structure afforded significantly higher selectivity to C_2 species. Such selectivity came from the accumulation of adsorbed CO* species on the surface of the porous electrode, which facilitated the *CO-*CO dimerization step and, consequently, increased the formation of multi-carbon species.

In addition to the direct reduction of CO_2 , the use of confinement to assist the photocatalytic reforming of CO_2 with CH_4 to produce syngas has been investigated.¹⁹⁵ Mao *et al.* prepared Pt NPs confined within mesoporous CeO_2 nanorods to be used as catalysts for this process. The reformation of CO_2 with CH_4 is a highly endothermic reaction, which only happens at temperatures around 700°C. In addition to the high energy consumption, such high temperatures lead to fast catalyst deactivation by the deposition of carbon on the active sites. It was found that confinement of the reactants and intermediates as the reaction unfolds created strong host-guest interactions, which activated oxygen atoms of CeO_2 that were at the interface with Pt NPs. These activated oxygen atoms facilitated all reaction steps, improving the catalytic activity of the system. The porous structure of the support also protected the active sites from carbon deposition and sintering, increasing the lifetime of the catalyst.

A significant outcome of CO_2 reduction technology is the sustainable production of methanol, a strong candidate as an energy vector¹⁹⁶ that can be used, for instance, in direct methanol fuel cells. Datta *et al.* developed an efficient methanol electro-oxidation system by confining Pd NPs inside mesoporous carbon supports.¹⁹⁷ The authors compared fully confined, partially confined, and non-confined Pd NPs. The fully confined NPs were obtained through a silica-template procedure which assured that the totality of the metal NPs was found inside the pores; the second system was obtained by a regular immobilization strategy that had NPs both inside the pores and on the outer surface; the third system was commercial Pd/C catalyst (no pores). The fully confined system contained only half the amount of Pd that was loaded on the other supports, yet it provided the highest anodic peak current density ever reported for a Pd catalyst. Confinement also enhanced the stability of the catalyst over 300 electrocatalytic cycles. This superior activity was attributed to the

protection of the Pd NPs against oxidation and leaching, as well as enhanced anodic potential due to greater electron density inside the pores.

Molecular hydrogen storage

Another important area of sustainable energy production is the use of molecular hydrogen as an energy carrier. H_2 has the highest energy density of a chemical energy vector and provides carbon-free combustion, but storage of H_2 is a significant challenge. Many research groups have investigated the storage of atomic hydrogen as chemical compounds that can release H_2 *in-situ* upon catalytic activation.^{198, 199} It has been found that this activation can be less energy-demanding upon confinement of the H_2 precursor in appropriately designed nanopores.

The Jongh group used confinement inside porous carbon structures to tackle the H_2 storage challenge.²⁰⁰ LiNH₂ is a strong H₂ carrier candidate, but it has the drawback of only releasing H₂ at temperatures above 300°C. Ammonia is another H₂ carrier option, but the current commercial catalyst for NH₃ conversion to H₂ is based on Ru, an expensive metal. The Jongh group approached the problem by confining $LiNH_2$ in porous carbon and converting it first to NH_3 . This conversion was favoured under confinement and carried out at 125°C. The in-situ generated NH₃ molecules were then converted to H_2 when the support was doped with Ni, with catalytic conversion rates comparable to the traditional Ru-catalysed process. Overall, confinement effects afforded a system that converted LiNH₂ to H₂ at reduced temperatures and using earth-abundant metal catalysis. The same group was also able to produce H₂ from ammonia using graphite nanoplatelets to embed nanoparticles of alkali metal amides (KNH2 and NaNH2) and transition metal catalysts (Ni and Ru).²⁰¹ Confinement increased the activity of the composites up to 4 times. The system with confined Ni at 8 wt% performed similarly to a 5 wt% state-of-art Ru/C catalyst (60-80% conversion) at 450°C. The confined Ru-doped catalyst had significantly high activity (95%) at 375°C, versus 475°C needed for commercial Pd/C catalysts. The confined systems had some of the lowest activation energies for ammonia decomposition reported in the literature, which were attributed to geometrical constraints that forced the close proximity of negatively charged intermediates inside the pores.

Looking at another H₂ carrier, Ding *et al.* investigated the decomposition of formic acid catalyzed by Pd NPs supported on carbon nanotubes.¹⁶⁰ The authors produced and compared the activity of two versions of the catalyst: with metal NPs placed inside or outside the pores. The reactions were

carried out at room temperature and, while metal-support interactions made both catalysts more active than pristine Pd NPs and Pd/C, the confined NPs afforded twice the TOF values of their unconfined counterparts. The confined system was also stable for 3 cycles, while the system with particles on the outside of the pores lost about 40% of their TOF upon recycling. Such deactivation was probably a result of CO poisoning, which was completely absent in the confined system.

2.6.2.2 Confined catalysis for commodity and specialty chemicals

Following the principles of green chemistry, important efforts have been geared towards the conversion of biomass into complex molecules to replace their sourcing from fossil resources. On the other end, the pursuit of more traditional petrochemical routes opens new avenues for chemical source diversification, for instance, via the gasification/Fisher Tropsch tandem reaction, now featured as a way for bio and urban waste recycling.^{202, 203} These approaches come with synthetic challenges associated with the ability for these processes to be selective, a problem which confinement can help solve.

Biomass conversion reactions

Biomass is a renewable and abundant source of raw materials that can be transformed into highvalue chemicals. These transformations proceed either by direct conversion, which takes advantage of the intrinsic oxygen content of bio-based compounds but requires the development of novel methods and infrastructure; or by full reduction to hydrocarbons or syngas followed by the reconstruction of functionality, which is redundant but utilizes the existing petrochemical infrastructure.²⁰⁴ Many research groups have provided interesting examples of direct biomass conversion with improved selectivity in confined systems.

Yokoyama *et al.*, for instance, used DFT calculations to study the dehydration of mannitol, a product of the conversion of woody biomass, to form isomannide, a precursor to plastics with superior properties.²⁰⁵ This acid-catalyzed reaction may take two pathways, one via a 1,4-dehydration to afford the desired isomannide and one, undesired, via the 2,5-dehydration (Scheme 8). It was found that the 2,5-dehydration pathway is energetically favoured over the 1,4-dehydration one, hence the low isomannide selectivity (35%) observed in the literature. The authors took a closer look into the transition states and observed a key difference in the reaction center of the two pathways. The 2,5-dehydration transition state features a nucleophilic

substitution step happening at a secondary carbon, requiring space for the elimination of water. Conversely, this step in the desired 1,4-dehydration pathway happens in a less hindered primary carbon, much less sensitive to spatial restrictions. In an effort to disfavor the bulkier pathway, the reaction was tested inside the micropores of zeolites. Not surprisingly, a maximum isomannide selectivity (63%) was found at the optimal pore size of 6.6 x 6.7 Å, slightly larger than mannitol's molecular diameter (6.3 Å). Super-caged zeolites (12 Å) afforded higher selectivity towards 2,5-dehydration products; and smaller pores (5.1 x 5.5 Å), which prevented the reactants from accessing the catalytic sites, led to low catalytic activity.



Scheme 8. Conversion of mannitol to either isomannide, though the 1,4-dehydration pathway; or to 2,5-sorbitan, through the 2,5-dehydration pathway. Adapted from reference 205.

Another example is the work of Gounder and co-workers, who studied the conversion of glucose to sorbose, the precursor to synthetic ascorbic acid.²⁰⁶ The process can be catalyzed by Lewis acids, so the authors screened Ti-modified zeolites, mesoporous silica, and non-porous silica as catalysts. The mechanism (Scheme 9) involves the adsorption of glucose to the Ti site at the O5 position, followed by ring-opening to the open-chain form followed by coordination of the carbonyl in the C1 position to the Ti site. At that point, the intermediate can undergo either a 1,2-hydride shift, which gives the desired product; or a 1,5-hydride shift, which yields fructose. No reaction happened on non-porous and mesoporous (>1.50 nm diameter pores) supports, while catalytic activity was observed in microporous zeolite materials, showcasing the fundamental role of van der Waals stabilization of the intermediates in narrow cavities. Zeolites with 12-membered ring pores (0.7 nm diameter) had fructose as their main product, while the ones with 8-membered ring

pores (0.55 nm diameter) yielded primarily sorbose, suggesting that 1,5-hydride shifts are unfavoured in the smaller pores. Pores formed with 8-membered rings (0.38 nm) were too small to fit the reactants and showed no activity.



Scheme 9. Glucose isomerization to fructose and sorbose over Ti sites and silicates. Adapted from reference 206.

In another study, the Borgna group¹⁶¹ contributed to the field with the conversion of cellobiose, a product of the hydrolysis of cellulose. The authors produced sugar alcohols (sorbitol and mannitol, Figure 24) over Ru nanoparticles immobilized on carbon nanotubes using closed-end and openend nanotubes to assure the presence of nanoparticles inside or outside the structures (Figure 25); the confined particles afforded higher catalytic activity. Three different tube diameters were studied (3-6 nm, 4-9 nm, and 6-15 nm) higher activities were consistently found in smaller tubes. This higher activity was attributed to the prevention of leaching and lower electron densities on carbon nanotube walls with higher curvature, corroborating with the strong electronic effects observed by Bao's molecular simulations.¹⁶⁴



Figure 24. Structures of sorbitol and mannitol, the sugar alcohols produced by the Borgna group¹⁶¹ from the hydrolysis of cellulose.



Figure 25. TEM of Ru NPs immobilized on CNTs, on their inner (a) or outer (b) surfaces. Adapted from reference 161.

A central platform molecule in the biorefinery scheme is 5-hydroxymethylfurfural (HMF), since it can be converted into a handful of useful products.²⁰⁷ The counterpart to this versatility is the need to develop effective and selective conversion pathways. Fang *et al.* looked at the aerobic conversion of HMF to 2,5-furandicarboxylic acid (Scheme 10), an important product in the pharmaceutical and polymer industries.64 The authors designed their catalyst by incorporating a Co-containing zeolitic imidazolate framework ZIF-67 inside the pores of a mesoporous silica support. The composite was then calcined to yield ultra-thin cobalt oxide NPs confined inside the pores. The system afforded quantitative conversion and selectivity to the desired product; a 10-fold yield enhancement compared to wet-impregnated (unconfined) cobalt oxide nanoparticles on the same silica support. The confined catalytic system provided TOFs that were up to a factor of 150 times higher than those in the literature that were based on precious metals and applying harsher reaction conditions.



Scheme 10. Conversion of 5-hydroxymethylfurfural (HMF) into 2,5-furandicarboxylic acid, as performed by Fang et al..²⁰⁷

A large fraction of the world's biomass conversion is dedicated to the production of ethanol.²⁰⁸ This compound, despite its wide utilization as a fuel, can also be converted into high-value products. Dai *et al.*, for instance, looked at the conversion of ethanol to butadiene, a monomer heavily used in the production of synthetic rubber.²⁰⁹ They introduced different metals in H-Beta zeolites and found that a mixture of zinc and yttrium was optimal to turn the multi-step conversion into a one-pot reaction. The process inside the zeolite pores afforded higher butadiene selectivity and lower reaction temperatures when compared to the state-of-art methodology, which was attributed to the confinement of the species inside the micropores of zeolites. Similar systems with different pore sizes were tested for comparison: micro (0.8 nm, H-Beta zeolite), meso (2.8 nm, MCM-41), and macropores (24 nm, porous silica). When compared to the macroporous support, mesopores and micropores had a 50% and a 400% increase in the productivity of butadiene, respectively. The results were explained by a super-concentration of ethanol around the catalytic sites in tighter pores.

In all the examples delineated above, researchers highlighted how confinement can be used as a means to improve yields or help selectivity, which are two important challenges to tackle in the effort to achieve an efficient biorefinery.

Hydrocarbons and syngas chemistry

Hydrocarbon and syngas conversions are central processes in petrochemistry and as such, account for a large amount of existing infrastructure. They also offer an important green chemistry opportunity, as these processes play a key role in the developing industry of bio and urban waste valorisation.^{210, 211} There are many contributions of confined catalysis to such conversions, some creative recent examples being highlighted below.

Arslan *et al.* gave one example of product selectivity in syngas conversion induced by confinement, in the context of the Fisher-Tropsch reaction.²¹² The Fischer-Tropsch synthesis typically affords a broad oligomerization product range. An unusually high selectivity of 70% in syngas conversion to tetramethyl benzene was observed using supported $ZnCr_2O_4$ on H-ZSM-5 zeolites. The metallic particles were responsible for the formation of C_1 oxygenated species, while the zeolite pores formed a "carbon pool" due to hindered rates of desorption and product diffusion. Aldol mechanisms then took place in the sub-nanoreactors allowing the chains to grow, but

overgrowth was prevented by geometrical restrictions induced by the small zeolitic pores, which led to the high selectivity to small aromatics (Scheme 11).



Scheme 11. Simplified schematic of the Fischer-Tropsch synthesis performed by Arslan *et al.* using ZnCr₂O₄ supported on H-ZSM-5 zeolites.²¹² ZnCr₂O₄ produced oxygen-containing intermediates, which grew thanks to the carbon pool created inside de pores. Hydrocarbons were formed through the aldol and aromatic cycles, but overgrowth was prevented by pore-size limitations. The system gave 60-70% selectivity to tetramethylbenzene in hydrocarbons.

Tan *et al.* also looked at syngas conversion but to prepare light olefins.²¹³ Like in the previous example, the authors utilized Zn-Cr metal oxide particles as catalysts to convert syngas to methanol, and the acidic sites of silicoaluminophosphate (SAPO) zeolites to catalyze the dehydration of methanol to olefins. It was found that, while a physical mixture of the two active phases provided low light olefin selectivity and a handful of side products, a hierarchical coreshell catalyst was able to boost selectivity to light olefins. The core-shell structure led to methanol production occurring exclusively inside the pores, which ensured the effectiveness of the hydrogenation steps. The zeolite walls were able to adsorb water and the light olefin products, suppressing CO_2 formation by the water-gas shift reaction and preventing further hydrogenation of the olefins.

Methanol can also be selectively converted into commodities.²¹⁴ The methanol-to-olefin process is an example of a methanol conversion that can be efficiently improved by confinement effects, as in the work of Liu and co-workers.²¹⁵ They designed a novel zeolite to enhance selectivity to propylene, a major building block molecule with several industrial applications. The conversion of methanol inside zeolites occurs through two mechanisms: the olefin cycle, which gives propylene and higher olefins; and the aromatic cycle, which goes through 5 or 6-membered ring intermediates to form ethylene. The latter is favored by a high concentration of acid sites, so the authors adjusted the Si/Al ratio in SAPO-14 to develop a zeolite with moderate acidity; such a strategy disfavored the latter cycle and prevented the formation of ethylene. The aromatic cycle

was also prevented by the ultra-small 8-ring cage on SAPO-14, which created a spatial restriction to the bulky intermediates. Within the olefin cycle itself, propylene was preferably formed over higher olefins because of the limited diffusion of C_{4+} molecules in the small openings. Propylene selectivity of 77.3% was achieved in the optimal system, the highest record of propylene selectivity in the methanol-to-olefin reaction. Another appealing outcome for methanol conversion is dimethyl carbonate, a platform chemical with extensive industrial applications. Zhao *et al.* used copper oxide nanoparticles supported on carbon nanotubes to accomplish such a transformation.¹⁶² The authors used nanotubes with three different diameters (2-5, 5-10, and 20-50 nm) and found that, although all of them gave high selectivity to dimethyl carbonate, catalytic activity increased with decreasing pore diameter. This activity was attributed not only to the better dispersion of nanoparticles in the smaller pores but to the higher stability of reduced copper species, which was confirmed by XRD and XPS. In fact, both Cu and Cu₂O were the active species in the reaction and higher curvatures on carbon nanotubes increased the electron density on the inner surfaces, which was beneficial to the reduction of the oxides observed in the study. Those findings also perfectly corroborate with the findings of the Bao group.¹⁶⁴

Confinement within pores has also played a key role in semi-hydrogenation reactions. Chai et al. constructed well-defined Ni centers coordinated to four framework oxygen atoms inside the micropores of chabatize.²¹⁶ In this unique design, the support worked as an inorganic ligand to the metal center. The catalyst was used in the semi-hydrogenation of acetylene, affording 100% conversion and 97% selectivity to the alkene and outperforming benchmark catalysts palladiumsilver and the Lindlar catalyst. It was demonstrated that the electrostatic field created by the nanoscale reactor inside the zeolite was responsible for inducing the heterolytic cleavage of H₂, which allowed the partial hydrogenation to happen so effectively. Another system was developed by the Gong group, who used SOD zeolites (pore size 0.36 nm) to confine Pd nanoparticles.²¹⁷ The authors performed acetylene hydrogenation and found 94.5% selectivity to ethylene, while Pd nanoparticles impregnated on the outer surfaces of the same zeolite afforded only 21.5% selectivity to the alkene under the same conditions. D_2 experiments with in-situ DRIFTS and DFT calculations demonstrated that, while exposed Pd NPs allowed the substrate to directly adsorb on the metal and be fully hydrogenated, spatial restrictions made the pore-confined nanoparticles accessible only to the tiny H_2 molecules (0.28 nm). H_2 could be split inside the pores and hydrogen spillover was responsible for the formation of active OH species on the outer surfaces of the

support. These OH groups were then approached by the larger acetylene molecules (0.38 nm), and a single hydrogenation step took place. Since the substrate did not strongly adsorb on the polar surface, it desorbed right after the first hydrogenation and led to high ethylene selectivity.

Selectivity in olefin metathesis is an important issue in the pharmaceutical industry that has also been addressed using confined catalysis. This reaction is very interesting for its high stereoselectivity, but it is difficult to selectively obtain macro(mono) cyclization products since this pathway competes with oligomerization. The Buchmeiser group performed olefin metathesis using the first-generation Grubbs-Hoveyda catalyst inside the pores of SBA-15 mesoporous silica.¹⁵⁹ The authors reacted mesitylimidazole with with an iodosilane, then the resulting salt was deprotonated with potassium hexamethyldisilazide (KHMDS) to give a free carbene. This free carbene was reacted with the first generation Grubbs-Hoveyda catalyst, giving it a silane functionality that was used as the site of attachment to the mesoporous silica surface (Scheme 12). First, the surface of the support was modified to become non-polar and reduce the residence time of the carbonyl-containing substrates near the catalytic sites in the pores. This prevented ringopening. Also, geometrical restrictions were used to limit the access of multiple substrate molecules to the catalyst at the same time, and limit oligomerization. Using surface-modified SBA-15 with 5.0 nm pores as a support, it was found that macro(mono)cyclization selectivity increased as the substrate hydrodynamic diameter increased from 0.75 to around 0.90 nm. However, larger than 0.90 nm substrates had a marked decrease in selectivity to the macro(mono)cyclic product. Such volcano plots are typical of confinement effects taking place with optimal selectivity for a specific type of substrate, resembling the confined mechanisms of enzymes.



Scheme 12. Functionalization of the 1st generation Grubbs-Hoveyda catalyst for immobilization on SBA-15 performed by the Buchmeiser group.¹⁵⁹

Hydrocarbons are highly inert molecules, so introducing functionality selectively to these molecules is essential for their manipulation but experimentally quite complex. In this context, Paunovic & Pérez-Ramírez performed a comprehensive study of methane halogenation in which several catalytic systems were evaluated.²¹⁸ The authors focused on chlorination and found that the reaction, which proceeds through a radical mechanism, was greatly affected by pore size when it occurred in the presence of zeolite catalysts. The catalytic activity also followed a volcano plot with maximum performance at a pore size of 0.5 nm, which is the sum of the kinetic diameters of methane and chlorine radicals. Such activity and selectivity were attributed to the stabilization of radical intermediates and transition states by the tightly confined space.

Oxidized hydrocarbons, such as diols, can often represent important commodities or precursors to commodity chemicals. Monoethylene glycol is one of the most important diols in the chemical industry, but its production from ethylene oxide requires high temperatures (423-493 K) and a large excess of water (H₂O/Ethylene oxide = 20-25) to prevent the self-condensation of the products and the formation of larger diols. Dai et al. approached this issue using Sn-zeolites.²¹⁹ The water-resistant Lewis acidic sites on the catalyst afforded high conversions, and supports with optimal pore sizes provided 99% conversion and 99% selectivity towards monoethylene glycol. It was found that the spatial restriction was responsible for limiting self-condensation, leading to highly increased selectivity to smaller molecules. The reaction temperature could be lowered to 313K and the water content reduced to almost stoichiometric amounts, which directly helps reduce the energy needed to distill the final product. The researchers estimated a 50% reduction in the overall energy consumption of the process and demonstrated its applicability to a large variety of substrates. Another example highlighting oxidized hydrocarbons is the work of Liu et al. on the oxidation of toluene to benzaldehyde using copper complexes immobilized on mesoporous silica.²²⁰ The authors found that the mesopores had the perfect geometry to hold the metals in a position to stabilize O_2 -bridged dicopper species (Figure 26), and the conversion was carried out at room temperature.



Figure 26. Reaction scheme for the toluene oxidation mediated by copper bis(4-imidazolyl methyl)-benzylamine complexes immobilized in mesoporous silica nanoparticles. Modified from reference 220.

These examples highlight the role that confinement can play in controlling the selectivity of complex, typically unselective processes by directly influencing either the speciation and diffusion of reactants or imposing geometrical constraints on the products formed.

Fine Chemicals

More complex and functional molecules are of special interest to the pharmaceutical and cosmetics industries and again call for the development of efficient and selective synthetic processes.²²¹ The focus is, in particular, on the reduction of precious metal loadings and improved selectivity and yields. Some fine chemical syntheses which have benefitted from the use of confined catalysis are discussed below.

Godino-Ojer *et al.* studied the synthesis of benzodiazepines, which are nitrogen-containing heterocyclic compounds of great importance as pharmaceuticals.²²² Specifically, the authors looked at the reaction of o-phenyldiamine with different ketones catalyzed by sulfated zirconia (Scheme 13). Carbon xerogels (mesoporous) and microporous carbon were tested as supports, and

the supported catalysts gave improved selectivity to the desired benzodiazepines. Catalysts supported on microporous carbon provided >90% conversions with 80% benzodiapene selectivities with low catalyst load, which was attributed to both chemical and morphological properties.



Scheme 13. Synthesis of a benzodiazepine from o-phenylendiamine and acetone, one of the reactions performed by Godino-Ojer *et al.*²²² catalyzed by sulfated zirconia supported on mesoporous and microporous carbon materials.

Our group has looked at the synthesis of propargylamines, another class of nitrogen heterocycles of relevance as medicine and chemical building blocks.⁴ These molecules were made from the A³-coupling reaction, a one-pot process that combines an aldehyde, an amine and an alkene (Scheme 14). We used amine-functionalized mesoporous silica to immobilize monovalent copper species, which partially leached inside the pores of the MCM-41 support, creating an in-situ catalyst delivery system. The limited diffusion inside the long channels caused a local increase in copper concentration, which led our system to outperform the homogeneous state-of-the-art copper iodide catalyst. The local concentration inside the pores also allowed for the use of ppm levels of the metal catalyst, providing excellent yields of products with extremely low metal contamination. We built a substrate scope combining aldehydes like cyclohexanecarboxaldehyde and benzaldehyde; amines like piperidine, pyrrolidine, and dimethylamine; and alkynes like phenylacetylene and 4-bromophenylacetylene.



Scheme 14. The A^3 -coupling reaction (one-pot coupling of amine, aldehyde and alkene functionalities to give propargylamines) was performed by our group⁴ with copper ions immobilized in the pores of functionalized mesoporous silica MCM-41.

Another interesting example is the work of the Tanaka group using Pd catalysts immobilized on a sophisticated multi-functionalized mesoporous silica support for C-C bond forming reactions that add allyl groups from allyl methyl carbonate and allyl alcohol to esthers and phenols (Scheme 15),¹⁵⁸ a C-C bond forming reaction that gives crucial synthetic intermediates. Using silane coupling reactions, the Pd complexes and tertiary amines were grafted on non-porous and mesoporous (1.6-5.3 nm) silica supports. A synergistic effect was observed, in which the nucleophile was activated by the tertiary amine via hydrogen abstraction, while Pd was responsible for activating the allylating agent. Non-porous structures showed little activity, while porous structures became more active at smaller pore sizes. TOF was improved from 220 on a non-porous support to 1240 when the reaction happened in 1.6 nm pores, even though the latter has only one-quarter of the Pd loading present in the former. The increase in activity at smaller pores was attributed to the spatial confinement of the active phases (Figure 27). The activation of allyl alcohol by silanol groups was a crucial improvement since allyl alcohols are simple and atom-economical but usually require activation by protic acid co-catalysts.



Scheme 15. Allylation reaction performed by the Tanaka group¹⁵⁸ using Pd catalysts supported on multifunctionalized mesoporous silica supports.



Figure 27. Design concept used by the Tanaka group for confined allylation reactions. Reproduced from reference 158.

These examples highlight that even for targeted selective transformations, catalytic confinement can yield improvements in activity resulting in the reduced use of metals, hazardous co-catalysts, and promoters.

2.6.2.3 Confined catalysis for pollution mitigation

Even though the concepts of benign by design and pollution prevention have been advocated for by Paul Anastas and John Warner since the 1990s,⁹⁷ we are still far from having achieved the full transition to benign chemicals and pollution-free processes. Examples provided in the previous sections highlight methods by which catalytic confinement can make chemical products in a greener way. Another key area is the use of catalysis for pollution remediation, which can be improved in terms of specificity and efficiency through the incorporation of principles of catalytic confinement, as highlighted below.

One work by the Delyianni group addressed the oxidative desulfurization of 4,6-dimethyldibenzothiophene (Scheme 16),²²³ a common sulfur contaminant found in fuels. The oxidative desulfurization process is proposed as a greener alternative to the high energy and hydrogendemanding hydrodesulfurization process currently used. Acid-treated porous carbon materials were used as metal-free catalysts and were able to fully oxidize sulfides into sulfoxides or sulfones under mild conditions with hydrogen peroxide. The supports with the largest proportion of micropores performed better, which was attributed to confinement effects.



Scheme 16. Oxidation of 4,6-dimethyl-dibenzothiophene, performed by the Delyianni group²²³ using acid-treated porous carbon materials.

Another important class of pollutants is phenolic compounds, which are toxic and considered priority pollutants by the European Commission.²²⁴ Bereckzi *et al.* approached the problem by anchoring cyclan and cyclen, which are tetraaza macrocyclic compounds, to the surface of silica aerogels, and coordinating Cu²⁺ ions to these ligands (Figure 28) as catalysts for the oxidation of

phenol in water.²²⁵ The goal was to obtain solid composites for easy recovery and low metal leaching. The immobilized catalysts had TOFs up to 15 times higher than the free Cu-cyclan and Cu-cyclen, and this unexpected high activity was attributed to the confinement of the reactants and catalysts inside the mesoporous support.



Figure 28. Structures of Cu-containing cylen and cyclam anchored on silica aerogels, the catalysts used by Bereckzi *et al.*²²⁵ for phenol degradation.

2.6.3 Confinement by encapsulation

Molecular confinement can also occur inside hollow materials. Those materials are defined as solid structures with space inside one or more distinct shells. Due to the void space within these materials, the shells can act as hosts and are capable of trapping guest molecules inside them, such as reactants and catalysts. Once the guest molecules are within the host, they are in a different nano environment and isolated from the bulk solution medium, being the truest examples of nanoreactors.²²⁶ Herein, we will define this approach as confinement by encapsulation.

Compared with porous hosts that are mostly restricted to silicon and carbon-based materials, encapsulation usually encompasses a wider range of hollow materials, allowing much richer chemistry. Different configurations can be used in the preparation of hollow materials for confinement by encapsulation. Gonzalo Prieto *et al.*, recently reviewed the main hollow material architectures and the advantages of using them as catalysts.⁸¹ The most common configurations of hollow materials can be summarized as being single shell (Figure 29a), single shell embedded with nanoparticles (Figure 29b), yolk-shell or core-shell (Figure 29c), rattle-type (Figure 29d), multi-

shell (Figure 29e) and nanoparticles within double-shell (Figure 29f). These configurations enable the materials to have diverse chemical compositions. For example, the shell composition can be based on metals, metal oxides, alloys, MOFs, carbon nitrides, porphyrins, polymers, etc; and they can have sizes in the micrometre or nanometre ranges. These tuneable nano environments can enhance the catalytic activity and the selectivity of reactions using similar principles to those in confinement within pores but with the potential for creating more diverse nanoreactor architectures. Such improvements in reaction efficiency are fundamental in the Green Chemistry context. In this section, we will highlight some examples of confinement by encapsulation in catalysis using these main hollow materials configurations, which are relevant in the context of green and sustainable chemistry.



Figure 29. Most common hollow material configurations: (a) single shell, (b) multi-shells, (c) yolk-shell or core-shell, (d) rattle-type, (e) yolk multishelled particle with additional intershell nanoparticle cargo. Reproduced from reference 81.

2.6.3.1 Single-shell hollow particles

Single-shell hollow particles are the simplest example of hollow materials. The reactants diffuse from the bulk solution through the pores of the shell and are confined in the available inner void space. Since there is no other active site, their outer and inner surfaces are responsible for the catalytic activity. This higher specific surface area, compared with their solid counterparts, can lead to higher reaction rates. For instance, our group studied the catalytic activity of iron oxide nanoshells in the oxidation of styrene to benzaldehyde using molecular oxygen (Scheme 17).²²⁷ The nanoshells gave significantly higher conversions than non-hollow NPs (84% versus 49-53%), despite a lower selectivity to benzaldehyde (65% versus 78-81%). The nanoshells were also etched, and the etched nanoshells gave higher styrene conversion (73%) and benzaldehyde

selectivity (73%) than the non-etched NPs, providing evidence of the benefit of exposing the inner surfaces as reaction sites. The confined system was able to carry out the challenging oxidation of styrene using molecular oxygen, with high conversion and considerable selectivity to the partially oxidized product.



Scheme 17. Styrene oxidation and its possible products. The reaction was performed by Rak *et al.*²²⁷ with high benzaldehyde selectivity inside hollow iron oxide nanoshells.

A study reported by Bin Qiao *et al.* demonstrated that PdCu single-shell nano boxes exhibit superior catalytic activity and reaction kinetics for the Cr(VI) reduction by HCOOH when compared with solid PdCu nanoparticles.²²⁸ The higher activity was associated with the active sites available on the surfaces of the material that enhanced the atom utilization and the collision frequency through the confinement of reactants. Time-dependent UV-vis spectra measured at different temperatures showed lower activation energy of the reaction inside the PdCu nano boxes.

Rabia Jamil *et al.* also observed improved catalytic activity within single-shell hollow structures.²²⁹ The performance of solid Pt-Ni NPs and hollow nano boxes were compared in the electrooxidation of methanol in fuel cells. Pt-Ni hollow nano boxes presented higher Pt % utilization and higher rate constants than the solid Pt-Ni NPs, which was confirmed by cyclic voltammetry measurements. It suggested that the inner surfaces of the hollow material participated in the reaction. While not explicitly explored, the rate enhancement may also have been influenced by a confinement effect within the nanovessels, which increased the supply of oxygenic species to the Ni and Pt sites and enhanced the activity of the catalyst.

In a study using Au nanocubes, Nazemi *et al.* were able to obtain high ammonia yields and faradaic efficiencies in the electrochemical reduction of nitrogen under ambient conditions.²³⁰ The authors compared the catalytic efficiency of the Au nanocages with solid Au nanoparticles of various shapes. The Au nanocages (Figure 30) gave higher activity, which was associated with the confinement of N_2 molecules within the cage. This confinement increased the frequency of

collisions and the contact time of N_2 molecules with the catalyst, therefore facilitating the conversion of N_2 to NH_3 .



Figure 30. Electrochemical synthesis of ammonia from N_2 and H_2O under ambient conditions using pore-size-controlled hollow gold nanocatalysts. Adapted with permission from reference 230.

Hollow nanocubes were also applied by the Du group in electrochemistry.²³¹ The cages were template-made and the walls consisted of nanosheets of cobalt and molybdenum oxides and sulfides (CoMoO_x, CoMoS_x, and CoS_x). The high electrochemical surface area and charge transfer capability of the nanosheets were explored in water splitting reactions. The catalyst was used as the anode and commercial Pt/C as the cathode. The cell voltage required for the process of the reaction was 1.58 V, 32 mV less than the voltage required by the commercial IrO₂/Pt/C couple. XPS analysis demonstrated that the strong electronic interaction between the interfaces of the oxides and sulfides influenced the adsorption energy of oxygen-containing intermediates, which improved the catalytic performance and stability of the catalysts.

In another recent study, Li and co-workers explored the catalytic activity of a high-density atomic Pt nanobox in the direct C–H bond borylation of toluene (Scheme 18).²³² The nanoboxes achieved 99% conversion in 10 h at 120 °C, while the commercial Pt/C catalyst converted less than 70% under the same conditions. The Pt nanoboxes also presented better stability compared with the homogeneous catalysts. The improved performance was attributed to both the high-density of atomic Pt species and the facilitated mass transfer and molecular diffusion within the hollow structures.



Scheme 18. C-H bond boryation of toluene, as performed by Li and co-workers inside Pt nanoboxes.²³²

2.6.3.2 Single-shell embedded with nanoparticles

Pores or channels within the shell increase their surface area and allow the incorporation of nanoparticles inside them, forming hierarchical hollow materials (Figure 29b). This configuration also enables a synergistic effect between the shell and embedded nanoparticles, contributing to the enhanced catalytic performance of the materials. Nanoparticles well-embedded in the pores are not as easily leached as from the external surface of a support, so this deactivation pathway is effectively suppressed in this type of architecture.

An illustrative study of the oxygen reduction reaction (ORR) with Fe_2O_3 nanoparticles dispersed in the mesoporous shell of an N-doped carbon hollow microsphere was published by Xiao *et al.*¹⁶⁴ The authors demonstrated that, compared with a series of hollow materials used as control samples, the Fe₂O₃ nanoparticles in the shell of N-doped carbon hollow microspheres exhibited higher activity and good electrochemical durability. This system provided a current density 18.5% higher than the commercial catalyst Pt/C. In addition, DFT calculations showed that the higher ORR activity was a result of the confinement in the microspheres, which lowered the reaction energy and facilitated the adsorption of O₂ molecules.

Another application for this architecture was the oxidative carbonylation of methanol to dimethyl carbonate, studied by Li and co-workers.²³³ Among different catalysts based on carbon spheres and Cu nanoparticles, the one with Cu nanoparticles located in the mesopores of a carbon shell achieved the best catalytic activity. This improvement was associated with the better confinement of Cu nanoparticles and the high degree of Cu dispersion.

In a study using the cavities of MOFs, Kuang *et coll*. evaluated the performance of Pt catalysts in the selective hydrogenation of cinnamaldehyde to cinnamic alcohol (Scheme 19) under mild conditions.²³⁴ The authors embedded the metal in two different matrices: a flexible one (Pt@ZIF-8), and a rigid one (Pt@ZIF-71). Carbon (20%)-matrixed platinum (Pt/C-20%) and PVP-stabilized

Pt NPs (Pt-PVP) were also tested as reference catalysts. The hollow catalysts gave lower cinnamaldehyde conversions but higher cinnamic alcohol selectivities. Between the MOF-based catalysts, the flexible one exhibited higher catalytic activity and lower selectivity than the rigid structure. Although confinement decreased the diffusion of the substrate through Pt NPs, leading to lower conversions, it successfully inhibited the excessive hydrogenation of the substrate, leading to higher selectivities. The hypothesis was confirmed by constructing additional MOF shells on top of Pt@ZIF-8 and Pt@ZIF-71 to confine exposed Pt NPs, which again provided lower conversions and improved selectivities.



Scheme 19. Reduction of cinnamaldehyde to cinnamic alcohol, reaction performed by Kuang *et coll*. with high selectivities inside Pt-containing MOF structures.²³⁴

Choi & Oh also studied catalysts in MOF matrices.²³⁵ They incorporated PdCo NPs in the structures of MOFs HZIF and HCS. The catalysts PdCo@HZIF and PdCo@HCS were applied in the reduction of 4-nitrophenol to 4-aminophenol (Scheme 20) and, compared with the non-hollow control materials, PdCo@HZIF and PdCo@HCS exhibited superior catalytic activities due to their unique structural features. The higher activities were attributed to facilitated mass transport through the hollow and porous shells and to the highly dispersed and confined incorporation of active bimetallic PdCo nanoparticles, which did not agglomerate and leach.



Scheme 20. Reduction of 4-nitrophenol to 4-aminiphenol, reaction performed by Choi & Oh inside PdCo-containing MOFs.²³⁵

2.6.3.3 Yolk-shell and rattle-type hollow nanoparticles

Both yolk-shell and rattle-type configurations are hierarchical structures where the active site is encapsulated inside a hollow porous shell. The only difference between these configurations is the structure of the core: while the core of a yolk-shell architecture is a single solid particle (Figure 29c), rattle-type is made from dispersed nanoparticles inside the shell (Figure 29d). The

encapsulation of the outer shell provides a confined nano environment where species can be well isolated and effectively stabilized. For instance, a recent study by Ma *et coll*. compared the activity of Ni NPs immobilized both inside (rattle-type encapsulation) and outside the hollow silica spheres.²³⁶ The catalysts were used in the dry reforming of methane and the particles confined inside the hollow spheres gave higher conversions due to a higher dispersion of Ni particles and increased coke resistance.

Several other studies in the literature have also taken advantage of the higher concentration of species between nuclei and shells in yolk-shell structures. For example, the Xie group obtained high ethanol and acetaldehyde conversion and selectivity towards hydrogen production by low-temperature ethanol steam reforming, known as the LT-ESR reaction.²³⁷ The catalyst used was a yolk-shell material composed of a CeO₂ nucleus and a Beta zeolite shell containing small Pt NPs on its interior surface, in a rattle-type fashion (Figure 31). The limited diffusion inside the zeolite shells created an over-concentration of species in the interior of the catalyst, and both Pt and CeO₂ worked synergistically to improve H₂ selectivity and completely convert the substrates.



Figure 31. TEM images of CeO2@Pt-Beta at different magnifications. Reproduced from reference 237.

Another example is the work of Song *et al.*, which demonstrates the excellent catalytic activity of Pd-Fe NPs encapsulated in mesoporous silica (Pd-Fe@mSiO₂) on the hydrogenation of a variety of olefins under ambient conditions.²³⁸ Almost quantitative conversions of the olefins were obtained over only a few minutes (Table 3). The authors compared the activity of Pd-Fe@mSiO₂ with commercial Pd/C and Pd nanoparticles loaded on the outside of Fe@mSiO₂, denoted Fe@mSiO₂/Pd. On the first four cycles, the catalytic activity of Pd-Fe@m-SiO₂ was nearly the same as that of Fe@m-SiO₂/Pd, but higher than that of commercial Pd/C. However, after 20 cycles, aggregation and detachment of Pd nanoparticles were observed for Fe@mesoSiO₂/Pd and Pd/C,

while the catalytic activity of Pd–Fe@m-SiO₂ was fully retained. The superior activity was attributed to the yolk-shell structure, which prevented the aggregation and deactivation of the catalyst and increased the local substrate concentration around the Pd NPs.

Table 3. Scope of t	he hydrogenation	of olefins with	h Pd-Fe@meso-SiO ₂ .	Reaction	conditions:	olefins (2	.5 mmol),	Pd-
Fe@meso-SiO ₂ (5.0	ng), ethanol (5 ml	L), 25 1C, under	r 1.0 MPa H2 atmosph	ere. Data f	rom referenc	ce 238.		

Pd-Fe@meso-SiO ₂						
$H_2, 25^{\circ}C$						
Entry	Olefin	Product	Time (min)	Conv. (%) ^a	TOF (h^{-1})	
1	\bigcirc		15	>99	7883	
2	\bigcirc		15	0	-	
3	H ₃ C	H ₃ C	10	>99	11824	
4	MeO	MeO	10	>99	11824	
5			25	>99	4730	
6	\bigcirc	\bigcirc	40	>99	2956	
7	cı	ci	10	>99	11824	

^a Conversion was determined by GC, and the identity was ascertained by GC-MS. ^b 5.0 mg Fe@meso-SiO₂ was adopted as a catalyst. ^cNo dechlorination product was detected and the selectivity for 1-chloro-4-ethylbenzene.

Cabelloa & Davoglio demonstrated that the confinement of reactants in a yolk-shell structure of MnO₂ hollow nanocages with encapsulated PtAu bimetallic nanoparticles reduced the diffusion of intermediate species to the bulk solution.²³⁹ This led to a higher overall reaction efficiency for the oxygen reduction and glycerol electro-oxidation reactions.

The Do group investigated the effect of shell thickness and void size by comparing different yolkshell structures of $Fe_3O_4@SiO_2$ in the degradation of acetaminophen, an emerging pollutant.²⁴⁰ It was demonstrated that materials with larger hollow void spaces and thinner silica shells performed better. This observation was attributed to the higher quantity of acetaminophen molecules that could be confined next to the Fe₃O₄ cores in larger voids. The Ren group reported a similar observation for the oxidative carbonylation of methanol to dimethyl carbonate.²⁴¹ It was found that larger void space in rattle-type Cu NPs on porous hollow carbon spheres structures led to higher activities compared to yolk-shell copper in hollow carbon spheres.

Another important feature of yolk-shell and rattle-type core-shell particles is the tunable composition of both the core and shell, allowing the effective integration of different components. These can promote synergistic interactions between the core and shell and enhance catalytic activity. Sanchez-Ballester *et al.* observed the existence of a synergistic effect for CO oxidation; the authors used a nanostructured polyaniline (PANI) matrix as a platform to create different yolk-shell compositions (Figure 32).²⁴² The catalysts tested were: PANI nanocapsules loaded with Cu ions, Cu-yolk, Cu-yolk in Cu-shell, Cu-yolk in Au-shell, a physical mixture of Cu-yolks and Au-shells, and commercial Cu NPs. The hierarchical structure Cu-yolk in Au-shell gave the most effective catalyst, converting 82% of the substrate at 300 °C after 53 minutes. It was followed by the physical mixture of Cu-yolk and Au-shell (about one-third of the activity), then the pure Cu systems with lower activities. These results showed that both Cu and Au are important for the reaction to happen and that the confinement of Cu and Au together is responsible for the highest catalytic activity.



Figure 32. Representation of the polyaniline nanostructure PANI, used by Sanchez-Ballester *et al.* to support Cu and Au NPs for confined CO oxidation reactions. Reproduced from reference 242.

Another example has been demonstrated by Zhang *et al.*, in which a yolk-shell material with Pt-CeO₂ core and UiO-66-NH₂ MOF shell showed superior catalytic activity than Pt@UiO66-NH₂ for the hydrogenation of furfural (Scheme 21).²⁴³ The authors were able to confirm, by hydrogen temperature-programmed reduction, that Pt and CeO₂ possessed a strong interaction that modulated the d-band center and surface electron density of Pt, which led to the enhancement of the catalytic activity. The relativity towards the two hydrogenation products was dependent on the thickness of the MOF shell, having the thickest shell (30 nm) provided >99% selectivity towards furfuryl alcohol.



Scheme 21. Furfural hydrogenation, the reaction performed by Zhang et al. in Pt/CeO2@MOF catalysts.²⁴³

Furthermore, the tunable structure of the yolk-shell and rattle-type configurations, *i.e.* space between the core and shell, as well as the thickness and pore size of the shell can influence the selectivity of reactions. The Tsubaki group observed that a core-shell structure of Zn-Cr oxide and zeolite SAPO-34 gave notably higher light olefin yields and lower CO₂ selectivity for the methanol-synthesis and methanol-to-olefin reactions that proceed as part of the Fischer–Tropsch process, compared with the physical mixture of both.²¹³ DFT calculations demonstrated that the SAPO-34 shells protected the Zn–Cr cores and limited the water gas shift (WGS) reaction as the adsorption energies of water are much higher on the SAPO-34 shell than on the Zn–Cr core. The yolk-shell structure also allowed better mass transfer and diffusion for a better synergistic effect. Furthermore, the confinement effect of the encapsulated catalyst inhibited side reactions and enhanced the light olefin selectivity (Figure 33).



Figure 33. The two different mass transfer routes over the Zn–Cr physical mixture catalyst and capsule catalyst. Reproduced from reference 213.

A final example selected with this architecture is a work of the Güttel group showing that cobaltbased core-shell catalysts ($Co_3O_4@mSiO_2$) provided higher methane selectivity in the CO_2 hydrogenation reaction than the simple supported system. Such higher activity was attributed to the confinement effect existing in the yolk-shell structure, which increased the probability for readsorption of CO on cobalt and favoured its methanation. However, for CO methanation, the coreshell catalyst was not efficient because the confinement of CO molecules improves the rate of C-O dissociation, causing deactivation by coking.²⁴⁴ This highlights the necessity of understanding the molecular scale mechanistic processes to optimize the design of these catalysts for a given catalytic application, as demonstrated by the theoretical works reviewed in section 2.5.1 of this thesis.

2.6.3.4 Double and multi-shelled hollow nanoparticles

A hollow multi-shelled structure, as the name implies, is a material configuration with at least two shells of different sizes. This is similar to the structure of an onion, with an exterior shell protecting the interior ones (Figure 29e). This configuration provides a large surface area with abundant reaction sites when the inner shells are catalytically active surfaces. Dan Wang and co-workers reported an interesting review of the correlation of the structure of hollow multi-shelled materials and their performance.²⁴⁵ In the context of encapsulation, the isolated chambers in this architecture

are able to provide additional free volume where confinement effects can also be observed. The multi-shelled structures also contribute to regulating mass transport, reducing effective diffusion distances for intermediate charges, ions, and molecules; and allow for multiple scattering of electromagnetic waves (Figure 34).



Figure 34. Schematic of the multiple scattering of light by multi-shelled hollow materials. Reproduced from reference 245.

An illustrative study was reported by the Yu group, comparing the performance of Bi_2WO_6 nanoparticles, single- and double-shelled Bi_2WO_6 , broken microspheres and triple-shelled Bi_2O_3/Bi_2WO_6 hollow structures for the photodegradation of Rhodamine $B.^{246}$ Combined with H_2O_2 , triple-shelled Bi_2O_3/Bi_2WO_6 (Figure 35) had a 16-fold increase in activity when compared to Bi_2WO_6 nanoparticles in the degradation of the dye. This higher activity was attributed to the hierarchic structure enabling multiple light reflections and scattering patterns inside the material, a key advantage in this photocatalytic process. The confined environment with an abundant presence of active sites also increased the probability of effective collisions.

The Zhang group recently reported the performance of hollow multi-shell CuO micro boxes for the electroreduction of CO_2 to ethylene.²³⁸ The CuO micro boxes presented higher catalytic activity than solid CuO particles, which were used as the control experiment. The higher electrocatalytic activity was associated with faster electron transfer processes and the increased adsorption of CO_2 molecules. The reaction was studied in different electrolytes (K₂SO₄, KHCO₃, and K₂HPO₄), and a higher faradaic efficiency was measured when the counter anion could not form a buffer (K₂SO₄) to neutralize the OH⁻ species that are generated near the catalyst/electrolyte


Figure 35. (a) and (b) SEM and TEM images of BWO-MSH. (c) HRTEM image of the BWO-MSH. (d) HAADF-STEM element mapping. Reproduced from reference 246.

interface, demonstrating the important role of these species. This high conversion efficiency of CO_2 to C_2H_4 was attributed to the confinement of the OH⁻ species within the CuO micro boxes. The higher OH⁻ concentration accelerated the CO₂ electroreduction pathways. Another relevant work was reported by Dong and co-workers, who evaluated the activity of Ce-Mn nanoparticles and a series of hollow spheres containing Ce and Mn with different numbers of shells for the selective catalytic reduction of NO to NH_3 .²⁴⁷ Catalytic activity in these systems increased with the number of shells, with the triple-shelled hollow material providing the best performance, followed by the double-shelled, single-shelled, and then the nanoparticles not contained within a shell. The activity of the materials was correlated with their structural configuration. The hollow materials confined NO molecules inside them, increasing the probability of effective collisions between NO molecules and the active sites. A higher number of shells provided more active surface area, hence enhancing the catalytic activity.

Multi-shelled systems were also employed by the Peng group; the researchers used a LaNiO₃ double-shelled nanocage catalyst for CO oxidation and compared it to LaNiO₃ nanoparticles, pure

NiO, and La₂O₃.²⁴⁸ The LaNiO₃ double-shelled nanocages presented superior catalytic activity at low temperatures and the highest reaction rate. The superior performance was mainly attributed to the structural configuration of the material. This configuration allowed the catalyst to act as a nanoreactor, and to store and confine the reactants inside it.

All these examples highlight that multi-shelled materials may be used as powerful platforms affording higher surface area, the ability to confine greater numbers of molecules, the ability to control diffusion and multiple scattering of light within these materials. These designs enabled increased catalytic outcomes.

2.6.3.5 Nanoparticles within double shells

Materials with this configuration present the same advantages as multi-shelled ones, but the presence of confined nanoparticles between the shells enables synergistic effects to occur, hence more opportunities to improve catalytic activity (Figure 29f). Yin *et al.* studied the photocatalytic hydrogenation of nitroarenes by comparing the photocatalytic activity of Ag_2O and Ag nanoparticles supported on double-shell hollow SiO_2 spheres in various configurations: confined between the silica shells with space, confined between the silica shells without space, and supported on top of the outer shell (Figure 36).²⁴⁹ The Ag_2O and Ag nanoparticles confined between the hollow SiO_2 shells with space achieved the highest yields and selectivity towards aniline in organic and aqueous media. Using molecular dynamics simulations, it was shown that the confined nano space significantly improved the collision probability of nitrobenzene and hydronium ions.

Zhao *et al.* studied the photodegradation of tetracycline within Ag nanoparticles confined in double-shell hollow TiO₂ photocatalysts as well as hollow TiO₂, Ag-decorated TiO₂, and Ag NPs confined within double-shelled TiO₂.²⁵⁰ The catalyst composed of confined Ag NPs achieved the degradation of tetracycline and excellent recyclability. The high catalytic activity was associated with the double-shell structure of the material and confinement effects. Electrochemical Impedance Spectroscopy (EIS) Nyquist plots and time-resolved transient photoluminescence showed that the confinement of Ag nanoparticles between the shells improved the lifetime of photogenerated charge carriers by inhibiting their recombination. Liang and co-workers reported an interesting study about the catalytic activity of hollow platinum nanocages that were encapsulated in porous carbon nitride for the hydrogenation of various nitroaromatics.²⁵¹ They first



Figure 36. Hydrogenation of nitroarenes. Hydrogenation model of photocatalysts with and without confined nanospace as well as unconfined bare Ag/Ag₂O. a) SiO₂-Ag/Ag₂O/void@SiO₂ catalysts with confined nanospace: high activity and selectivity are achieved in the reduction of nitroarenes under visible-light irradiation; b) SiO₂-Ag/Ag₂O@SiO₂ catalysts without confined nanospace: moderate activity and selectivity are obtained; c) SiO₂/void@SiO₂-Ag/Ag₂O catalysts (unconfined bare Ag/Ag₂O): poor activity or selectivity are observed. Reproduced from reference 249.

tested the activity of this catalyst for the transfer hydrogenation of 4-nitrophenol (4-NP) and achieved >99% conversion and selectivity in only a few minutes. The material was further tested with another 23 nitroaromatics with different functional groups and completed the catalytic transfer hydrogenation for all of them within 10 min. The enhanced activity of the material was also attributed to its structural features. The material contained super thin walls with about six platinum atoms of thickness, hence high atom utilization efficiency and accelerated electron transfers. Furthermore, the synergistic effect between the iron oxides and Pt improved the catalytic activity.

Collectively these examples provide evidence for the ability to use hollow shells as effective catalytic systems for a variety of transformations of relevance to green chemistry, from targeted synthesis to the remediation of pollutants. Although confinement effects have been observed for all the presented structures, the heterogeneity of architectures and compositions of encapsulated

systems poses a challenge in understanding and generalizing the mechanistic factors responsible for the improvement of catalytic activity. Future works will with no doubt focus on rationalizing such effects towards the development and optimization of catalytically active hollow shell systems.

2.6.4 Outlooks of confinement for more sustainable catalysis

The examples highlighted in this section truly showcase that confined systems can make more with less, hence they are a valuable tool to create greener catalytic systems.

It is apparent that the confinement of reactants, intermediates, and catalysts can lead to remarkable improvements in the efficiencies of an array of chemical transformations. Proof of principle examples have been highlighted here for systems where the confinement occurs within pores or cavities of solid porous materials, and inside hollow solid materials. While the nature of confinement varies between these diverse systems, all demonstrate the importance of interfaces and the co-location of reactants, catalysts, and intermediates in governing improvements in reaction efficiency. The precise control over diffusion effects as well as the geometry of transition states are also powerful ways to achieve higher activities and selectivities.

Advances in the use of confinement for green chemistry will rely on a greater understanding of the roles of geometrical and electronic effects in different reaction systems. This understanding is challenging due to the uniqueness of each combination of reactants and catalysts, which make generalization and predictions difficult to make. As demonstrated particularly on section 2.6.1, confinement effects are powerful but need to be designed for the peculiarities. Enzymes, for instance, are the perfect example of confined systems that can be achieved if reaction spaces and intermolecular interactions are optimized for a given catalytic process. Being able to design *a priori* such spaces will be a substantial step forward in the development of more reactive, selective, and specific catalytic systems. Hence, we see computational chemistry playing an invaluable role in the future of confined catalysis.

Systems that are confined within solid porous or hollow materials face a bottleneck which is the synthesis of the materials themselves. Small scales and low reproducibilities are common in the world of nanomaterial synthesis, specially for hierarchical structures. These represent challenges to the full understanding and optimization of processes and limit the large-scale impact of confined

systems. Therefore, we understand larger scale nanoparticle synthesis to be a key factor in the wide application of confined catalysis withing porous and hollow structures.

Nevertheless, confinement provides an excellent tool for the high-level control of chemical reactions that cannot be provided within bulk homogeneous solutions. Understanding, harnessing, and utilising this effect will pave the way for a quantum leap in the development of more active and selective catalytic processes, a key cornerstone for green chemistry in the 21st century.

The design strategies to make hollow core-shell silica nanoreactors presented on section 2.1 will be applied to develop a confined catalytic system in chapter 5 of this thesis.

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3

Photocatalysis meets magnetism: Designing magnetically recoverable supports for visible-light photocatalysis

3.1 Preamble

The previous chapter gave the theoretical basis that will be applied throughout this chapter and the following ones. The design of silica nanostructures detailed in Chapter 2 is used here to develop dense silica core-shell structures as supports for magnetic visible-light photocatalysis. The challenges in combining magnetism and photocatalytic properties highlighted in the previous chapter are addressed here, being the core-shell structure key to enabling a systematic study of the effect of light absorption by the support in photocatalytic activity.

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Terra, J. C.; Desgranges, A.; Monnereau, C.; Sanchez, E. H.; De Toro, J. A.; Amara, Z.; Moores, A., Photocatalysis meets magnetism: designing magnetically recoverable supports for visible-light photocatalysis. *ACS Appl. Mater. Inter.* **2020**, *12* (22), 24895-24904.

3.2 Abstract

While magnetic supports have been widely used to immobilize homogeneous catalysts in organic chemistry, this strategy has so far found very little application in photocatalysis. This is because magnetic supports are dark-colored, therefore propense to compete for photon absorption. We have developed a series of core-shell Fe (0) @ silica nanoparticles as supports for immobilizing the photosensitizer Ru(bpy)₃²⁺, featuring various silica shell thicknesses – 16-34 nm of SiO₂ – on 9 nm Fe cores. The supports and the resulting photocatalytic systems were studied for their magnetic, optical and catalytic properties in the context of the photo-oxidation of citronellol, and we found that thicker silica shells lead to higher catalytic activity. We correlated this effect, as well as Ru(bpy)₃²⁺ fluorescence and singlet oxygen generation, to the absorption properties of the supports. We were able to reuse our optimal system 3 times with minimal loss of activity and achieved turnover numbers largely surpassing the performance of homogeneous Ru(bpy)₃²⁺. This work highlights the role of material design in the conception of new supports for applications in heterogeneous photocatalysis.

3.3 Introduction

The chemical industry has historically relied on thermal convection as a means to deliver energy to chemical processes, while Nature – the greatest photochemist – relies on photons emitted by the Sun for some of its most fundamental processes. Over a century ago, Giacomo Ciamician¹ prophesized a future society that would be powered by sunlight photochemistry instead of fossil fuels, but only in the last decades we have witnessed the development of synthetic technologies enabling this vision.^{2, 3} Visible light (vis-light) is particularly appealing in the context of catalysis, since it composes a large portion of sunlight and affords energy levels of interest for chemical transformations.^{4, 5} Also, the development of inexpensive LEDs emitting in this regime allows to design efficient photoreactors at accessible cost.⁶ Photosensitizers (PS) or photocatalysts are defined as compounds able to harvest vis-light and convert its energy to trigger photochemical reactions.⁷ Upon absorption of vis-light, they reach excited states (PS^{*}), which feed either redox pathways or energy transfers.⁴ In both of these, highly reactive species or intermediates are generated, opening pathways for new reactivity and highly atom and energy efficient processes.

Among organometallic and organic PSs, Ru and Ir complexes stand out, as they can very efficiently populate and stabilize long-lived triplet states, and thus be exploited for vis-light photochemistry.⁸ Ru(II) tris(bipyridine) [Ru(bpy)₃²⁺] is a celebrated example, which features a strong metal-to-ligand charge transfer (MLCT) absorption band at 452 nm and enhanced stability.⁴ In particular, Ru(bpy)₃²⁺ has been reported as an active photocatalyst capable of generating singlet oxygen (¹O₂), which is a powerful metastable oxidant with extremely rich reactivity.^{9, 10} Singlet oxygen is well-known for its reactions with alkenes,¹¹ but it can also oxidize amines,¹² sulphides and phosphines.⁹ It is viewed as a key method in the total synthesis toolbox,⁹ as exemplified with the semi-synthesis of Artemisin, a major malaria drug.¹³ It has also been extensively applied to photodynamic therapy,^{14, 15} as it is a powerful oxidant of cellular constituents such as nucleic acids, lipids and amino-acids.¹⁶

PSs are typically used in solution, where they are homogeneously dispersed and intrinsically difficult to recycle. Immobilization of photocatalysts on solid supports is a popular avenue to address this challenge,¹⁷ as illustrated by PS anchorage onto silica via silane coupling agents.¹⁸⁻²⁰ Recently, the Amara group reported an alternative approach, relying on electrostatic interactions to anchor $Ru(bpy)_3^{2+}$ onto silica without the need for surface functionalization.^{21, 22} Yet, classical recycling of solid supported catalysts also has its limitations, including the reliance on sometimes unpractical filtrations. In other contexts, catalyst immobilization onto magnetic supports has been developed to circumvent these issues, providing means to use an external magnet for separation.²³⁻ ²⁶ This strategy has a great potential in photochemistry,²⁷ as it would offer superior processing options such as simpler recycling. In flow chemistry applications, magnetic supports can provide improved control on residence times (including spatio-temporal control),²⁸ and allow the development of moving catalytic beds, which prevent flow clogging²⁹ and improve light penetration.²¹ However, creating magnetic supports for vis-light catalysis is an intrinsically challenging approach as magnetic nanoparticles, which are typically based on iron, cobalt or nickel, are dark colored³⁰⁻³² and will compete with the PS for vis-light absorption. To avoid this shortcoming, we proposed to coat magnetic nanoparticles with a high refractive index material to limit its vis-light absorption. Yet, such a coating would dilute and compromise the magnetic properties of the resulting hybrid nanoparticles. For this reason, we selected Fe (0) as a high spin density material (*e.g.* more than twice larger than its ferrimagnetic oxides)³³ to form the core of this architecture. For the shell, silica was selected as a well-understood and versatile material, known as a suitable platform for PS immobilization^{18-20, 34, 35}. It is also stable towards oxidizing media²⁵ and can change the optical properties of the support due to its low vis-light absorption. Furthermore, the extensively developed sol-gel chemistry of silica provides a manifold to the precise construction of the shell.³⁶ In this article, we demonstrate as a proof-of-concept that novel silica-coated Fe (0) nanoparticles can act as magnetic supports for photocatalysis. These were used to immobilize Ru(bpy)₃²⁺ and then evaluated as photocatalytic systems for the generation of ¹O₂ in the model Schenck-ene photo-oxidation of citronellol, a multi-ton scale process performed in the fragrance industry.³⁷ We studied the magnetic and photocatalytic properties of the resulting materials and performed a detailed photophysical study in order to understand the optical properties of the supports. We obtained a system which is not only comparable to the homogeneous PS in terms of reaction rates, but also more stable and more easily recyclable.

3.4 Results and discussion

Iron cores were synthesized according to the procedure developed by Sun and co-workers.³⁸ For silica deposition, among the many existing methodologies³⁹⁻⁴³ we took inspiration from the protocol pioneered by Rossi et al.²⁵ relying on a reverse microemulsion method, which allows precise coating of individual nanoparticles with uniform and thickness-tunable shells.^{25, 44} To date. such a strategy had yet to be applied for Fe (0) coating. First, we produced oleylamine-capped Fe nanoparticles of 8.6 ± 1.4 nm with excellent size control (Figure 42 in section 3.8.1) and added them to a surfactant-stabilized microemulsion of ammonium hydroxide in cyclohexane. TEOS was then added to the mixture and underwent hydrolysis inside the aqueous phase, specifically on the surface of the Fe nanoparticles, at the water-oil interface. As Fe nanoparticles were coated with silica, they became more hydrophilic and migrated into the interior of the micelles, where full coating was eventually achieved. The number of Fe nanoparticles was optimized to match the number of micelles (section 3.8.2) so that the formation of core-free or multi-nuclei particles was minimized. Gradual additions of small amounts of TEOS allowed for the shell to be built layer by layer,⁴⁰ until the desired thickness. The resulting nanomaterials were analyzed by TEM and confirmed to be core-shell structures (Figure 37). Higher magnification (inset on Figure 37a and Figure 44) revealed a thin intermediate shell between the darker Fe (0) cores and the lighter silica shells, which was attributed to iron oxide formed by partial oxidation of the cores during the silica

coating step, which happened in non-degassed water.³⁸ Silica shells of 15.9 ± 1.0 , 26.7 ± 1.4 , 28.4 ± 2.0 and 34.1 ± 4.5 nm were obtained after 3, 6, 9 and 12 TEOS additions, respectively (section 3.8.4). Materials were named Fe@SiO₂^{TX}, being X the number of TEOS additions. Plain silica nanoparticles were prepared as positive controls by the same microemulsion method, but in the absence of the magnetic cores. Such SiO₂ NPs were grown to achieve comparable size to Fe@SiO₂^{T3}, which happened upon 12 additions of TEOS (section 3.8.5).



Figure 37. TEM images of silica-coated materials $Fe@SiO_2^{TX}$ (X=3, 6, 9, 12). Insert in the center is a higher magnification image of a $Fe@SiO_2^{T3}$ particle.

XPS spectra of fresh materials $\text{Fe}@\text{SiO}_2^{\text{TX}}$ (X=3-12) all featured pure silica only. This is consistent with the fact that all shells are thicker than the analytical penetration depth of XPS. We performed etching with an argon flow on $\text{Fe}@\text{SiO}_2^{\text{T3}}$, which uncovered Fe XPS signals from the core in a depth profile analysis (Figure 48). Fe $2p_{3/2}$ spectra were deconvoluted and featured the Fe (0) peak at 707 eV and magnetite phase multiplet splitting signals from 708 to 715 eV (Figure 49).⁴⁵

Magnetic measurements were also obtained for the synthesized nanoparticles. Zero-field cooled (ZFC) curves (Figure 50) showed that all $Fe@SiO_2^{TX}$ (X=3-12) have the same blocking temperature (50 K), hence the same anisotropy, confirming that the magnetic cores are virtually identical in size. From the blocking temperature of the magnetically isolated NPs and assuming the anisotropy constant of bulk Fe (K = 45 kJ m⁻³), the diameter of the cores was estimated to be around 9 nm, which is in agreement with the results obtained by TEM (8.6 ± 1.4 nm). Additionally, considering that the Fe (0) core diameter is in fact smaller than the TEM measurements due to partial oxidation, the result can be interpreted as proving an enhanced magnetic anisotropy of the core due to exchange-coupling of Fe (0) with the magnetite shell, a phenomenon frequently observed in composite nanomagnets comprising materials with different anisotropies.^{46, 47} The field-cooled (FC) magnetization curves show the FC-ZFC irreversibility typically observed in ensembles of uniformly-sized, isolated magnetic particles. The mass-normalized hysteresis loops (Figure 38) confirmed that addition of extra layers of silica decreases the overall magnetic response of the nanomaterials. The loops were measured after field-cooling in 5 Tesla from room temperature, resulting in strong horizontal shifts H_E (exchange bias effect, with H_E \sim 1.5 kOe), confirming the exchange coupling between the metallic Fe core (ferromagnetic) and the magnetite shell (ferrimagnetic), as observed by TEM and XPS. Exchange bias and coercivity values (Table 5), which is proportional to the anisotropy barrier, show no significant difference through the series, pointing out again the similarity of the composite magnetic cores.

With this series of magnetic supports in hand, we moved to $Ru(bpy)_3^{2+}$ immobilization (3.8.8). Upon immobilizing a PS such as $Ru(bpy)_3^{2+}$ on a surface, the distance between two neighbouring photoactive centers is a crucial parameter to control because PSs can self-quench when they are in close proximity.⁴⁸ Therefore, we compared in this entire study samples which had the same [quantity of immobilized PS]/[BET surface area] ratios, and surface coverage was defined as the percentage of the surface area of the support occupied by the immobilized PS (sections 3.8.9 and



Figure 38. Hysteresis loops at 5 K measured for all supports after cooling in a field H = 50 kOe from room temperature.

3.8.10). A fixed surface coverage of 10% was defined for immobilization of PS on the materials based on our previous experiences with similar systems.²² EDS mapping was also performed, but Ru mapping did not afford significant data due to the low Ru concentration in the material (0.005 atomic%), which is below the detection limit of the experimental setup (section 3.8.11).

To benchmark the reactivity of these magnetic photocatalytic systems in ${}^{1}O_{2}$ chemistry, the materials were tested on the photo-oxidation of citronellol (reaction scheme on Figure 39). Reactions were carried out in a jacketed reactor cooled down with water at 20 °C, surrounded by LED strips and with a bubbling O₂ balloon (section 3.8.12). Figure 39 shows conversions for this reaction within 2 h with Fe@SiO₂^{TX}@Ru as catalysts, as well as the positive controls SiO₂@Ru and homogeneous Ru(bpy)₃²⁺. Homogeneous catalysis afforded 92% conversion, while 63 to 71% conversion were obtained when Ru(bpy)₃²⁺ was immobilized on non-magnetic silica nanoparticles, showing that immobilization itself did affect reactivity.

To aid in the comparison among the different supports, we introduced a hindering effect factor [100% (1 - (conversion on $\text{Fe@SiO}_2^{\text{TX}})/(\text{conversion on SiO}_2))$] (dotted line on Figure 39). It represents the reduction in percentage of conversion when compared to the positive control SiO₂@Ru. Interestingly, for X=12, the thickest silica shell we grew on Fe (0) cores, hindering

effect is essentially zero, meaning $Fe@SiO_2^{T12}@Ru$ reacted similarly to $SiO_2@Ru$. It suggests that, for this system, the presence of the colored core does not significantly affect photocatalysis in our reaction conditions. Upon moving to thinner shell samples $Fe@SiO_2^{TX}@Ru$ (X=3, 6 or 9), photocatalysis became increasingly affected, likely because Fe core absorption became more significant. Yet, this effect remained modest and did not severely hamper long-term catalytic efficiency since we reached a conversion of 63%, even for X=3. There is, therefore, a trend of increased photocatalytic activity as silica thickness increases, even though it is not highly pronounced in our reaction conditions specifically (*i.e.* $Fe@SiO_2^{T3}@Ru$ is about 88% as efficient as $Fe@SiO_2^{T12}@Ru$ in terms of TON after 2 h, with a maximum hindering factor of 12% across the series).



Figure 39. Catalytic results for the oxidation of citronellol with $Ru(bpy)_3^{2+}$ immobilized on different supports. Blue bars (left ordinate) reflect the GC conversion for the reactions after 2h in acetonitrile at 20°C, 0.05 mol% catalyst load, with shining vislight LEDs and bubbling O₂ (section 3.8.12). Hindering effect indexes (orange dotted line, right ordinate) provide a metric for the negative effect of the presence the dark magnetic core in the support, reflecting the percentage of conversion lost when compared to the positive control SiO₂@Ru [100% (1 - (conversion on Fe@SiO₂^{TX})/(conversion on SiO₂))].

Hence, we selected $\text{Fe@SiO}_2^{\text{T3}}$ @Ru as our catalyst of choice to investigate recyclability, as it featured the highest magnetization. Reaction time was extended to 4 h and 85% conversion was obtained. The catalyst was stable to reuse, with a slight decrease of activity on the third cycle (section 3.8.13). Noteworthy, cumulative TON for the process reaches 7671 after five recycling steps, while it is limited to 1840 for the homogeneous process.

After investigating the catalytic performance of our systems, we turned to spectrophotometric experiments as an effort to better understand their optical properties. We measured the absolute luminescence quantum yields (QY) for the $Fe@SiO_2^{TX}@Ru$ series, $SiO_2@Ru$ and homogenous $Ru(bpy)_3^{2+}$ (Figure 40, blue bars). An initial QY drop was observed from $Ru(bpy)_3^{2+}$ to $SiO_2@Ru$, as a result of immobilization, and then a systematic decrease within the $Fe@SiO_2^{TX}@Ru$ series, with poorer results as the shell became thinner. This trend is in agreement with the catalytic results for citronellol oxidation. We also plotted in Figure 40 (orange bars) the vis-light (455 nm) absorbance of $Fe@SiO_2^{TX}$ materials and SiO_2 , prior to PS immobilization (section 3.8.14). As we would expect, light absorption by the supports decreased as silica-to-iron ratio increased, which is consistent with the idea that the darker particles absorbed more vis-light. A strong inverse correlation between the QY of supported PS and support light absorption was observed. This suggests that the QY of the $Fe@SiO_2^{TX}@Ru$ series was primarily affected by support absorption.

To test this hypothesis, $Ru(bpy)_3^{2+}$ luminescence lifetimes measurements (section 3.8.15) under anaerobic conditions were undertaken. Lifetimes remained similar for all systems, on the order of 900-1000 ns, regardless of the presence or nature of a support. This constitutes a strong evidence that immobilization in itself did not significantly affect the radiative and non-radiative processes occurring at the $Ru(bpy)_3^{2+}$ level, confirming that the apparent drop of photosensitization quantum yields in supported systems results primarily from competitive absorption by the support.



Figure 40. Orange bars, left ordinate: absorbance at 450 nm of suspensions of the different supports (without PS). Blue bars, right ordinate: absolute QY in air-free conditions for a $Ru(bpy)_3^{2+}$ solution, as well as for $Ru(bpy)_3^{2+}$ immobilized on silica NPs or Fe@SiO₂^{TX}. All the measurements were carried out in acetonitrile solutions or suspensions. In both cases, concentrations respected the ratio of mass of material used for catalytic tests.

With this spectroscopic data in hand, we proceeded to study the formation of ${}^{1}O_{2}$, the active species in catalysis. We measured the characteristic phosphorescence of ${}^{1}O_{2}$ through a near IR study under aerobic conditions (section 3.8.16) and found the same trend of increasing ${}^{1}O_{2}$ formation for increasing silica layering on the supports, except for Fe@SiO₂^{T12}@Ru and SiO₂@Ru, which provided low ${}^{1}O_{2}$ phosphorescence signals. Those two supports featured however much more textured surfaces (section 3.8.9), which may have caused longer residence times for ${}^{1}O_{2}$ species in close proximity the silica walls, and thus higher quenching rates with silanol groups.⁴⁹ Singlet oxygen generation can also be detected and quantified using a quencher, such as anthracene dipropionic acid (ADPA).^{50, 51} Figure 41 shows kinetic monitoring of the ADPA oxidation reaction in the presence of our photocatalysts, as well as decay factors (in brackets) (section 3.8.17). ADPA decomposition rates increased as the silica layer grew larger, confirming that supports with lower vis-light absorption afforded more effective photocatalysts (in terms of TOF).


Figure 41. ADPA decomposition tests carried out with suspensions of the catalysts in acetonitrile. The amount of material was adjusted in each cuvette to give the same $Ru(bpy)_{3^{2+}}$ concentration. Light was irradiated at 390 nm and collected at 500 nm. Spectra were obtained at specific reaction times, areas under the curves integrated and compared to initial area.

Overall, across the series of catalysts we studied, we observed a strong reverse correlation between the support's contribution to light absorption on the one hand, and both the luminescence QY of the PS and ${}^{1}O_{2}$ generation (ADPA) trends on the other. This strongly suggests that support's absorption is the primary cause of catalyst efficiency loss in such supported systems, and demonstrates the importance of using absorption reduction strategies, such as the one proposed herein. Notably, we noticed that the absorption reduction observed as the silica shell grew was caused by an increase in the ability of the particles to scatter light (section 3.8.18). Additionally, QY and ${}^{1}O_{2}$ generation were also strongly correlated, even though PS^{*} quenching by either luminescence or ${}^{1}O_{2}$ generation are competing pathways. We thus measured the luminescence of Ru(bpy)₃²⁺ in degassed (pure luminescence) and oxygenated conditions (luminescence + ${}^{1}O_{2}$ formation) and observed a consistent ~40% reduction of luminescence intensity when O₂ is introduced for all our photocatalysts (section 3.8.19). This means that immobilization of the catalyst onto the support neither significantly modifies the kinetics of luminescence nor the energy transfer to oxygen. Formation of PS^{*} is thus the critical element in all systems, and the catalytic efficiency of this process is only affected by competitive absorbance from the support. Once PS^{*} was formed, catalysis proceeded readily with similar efficacy across the studied systems.

3.5 Conclusion

In conclusion, we have shown that it is possible to obtain photocatalytic supports with magnetic tractability by coating dark-colored magnetic NPs in order to decrease their light absorption. We have developed a methodology for tailoring magnetic supports to obtain versatile materials which we will subsequently adapt to different setups (*e.g.* various PSs and flow conditions). The materials were successfully used in the photo-oxidation of citronellol and recycled to afford a high cumulative TON. We have systematically demonstrated that light absorption is the key element in producing effective supports, a phenomenon that has been largely overlooked in photocatalysis. From photophysical studies, we demonstrated that thicker silica shells do lower the absorption of vis-light by the Fe core, which results in increased catalytic activity in terms of TOF. We explained this feature by showing that PS photoexcitation was the key step in the process. This work features a proof of concept that magnetic tractability and photocatalytic activity are compatible features and provides insights on the effective design of heterogenized photocatalytic systems.

3.6 Experimental

All the chemicals were purchased from Sigma Aldrich and used as received, unless specified.

Fe NPs synthesis: the procedure is a direct adaptation of the method reported by the Sun group.³⁸ All the glassware was dried overnight in the oven and all the solvents degassed by 3 freeze-pumpthaw cycles and stored with molecular sieves. 20 mL of octadecene and 0.3 mL of oleylamine were added to a 100 mL 3-neck RBF with a condenser attached to it (water running at 2°C) and bubbled with argon for 30 minutes. The RBF was then wrapped in aluminum foil and heated up to 180°C while magnetically stirring at 1600 rpm with a constant argon flow. 15 min after the temperature was reached, the Ar inlet and outlet were temporarily closed and 0.7 mL of Fe(CO)₅ were quickly injected into the hot mixture. Smoke was observed inside the condenser and, once the smoke settled, the Ar inlet and outlet were reset on top of the condenser. The reaction for 20 minutes at 180°C, before heating was stopped, and the aluminum foil removed to reveal a darkcolored suspension. The resulting mixture was left to cool down to rt under Ar flow and then transferred via a canula to a 250 mL Schlenk flask under Ar. The reaction flask with the stir bar was washed 3 times with 15 mL hexanes to recover the residual product. Once in the Schlenk flask, the suspension was placed in a hot water bath and the volatiles were evaporated under reduced pressure until the volume was decreased to about 15 mL. Then 25 mL of ethanol were added. The particles were magnetically separated from the solvent, which was removed with a syringe. The particles were washed again with 45 mL of hexanes and 90 mL of ethanol was added to precipitate them. These were magnetically separated again from the solvent which was removed with a syringe. Residual volatiles were removed under reduced pressure. The dry particles were dispersed in 15 mL of cyclohexane and stored in a flask under Ar in the freezer for further use.

Silica coating: the procedure was inspired mainly by the work of Fu *et coll*.⁴⁰ for iron oxide coating. 110 mL of dry cyclohexane and 5 mL of IGEPAL CO-520 were added to a 250 mL 2-neck dry RBF and bubbled with Ar for 30 min. The flask was then sealed and placed on a sonicating bath for 10 min. Then the mixture was agitated under 900 rpm magnetic stirring and constant Ar flow and the following components were added, in this order: 0.25 mL of NH4OH solution (28%), 1.25 mL of the prepared Fe NPs solution in cyclohexane (allowed to warm up to rt) and 0.25 mL or TEOS (tetraethyl orthosilicate). Daily additions of 0.25 mL were made to the reaction mixture until the desired product was obtained (3 additions for T3, 6 for T6 and so on). After the last addition, the reaction ran for additional 24h and the product was washed twice with 200 mL ethanol and once with 100 mL of distilled water. The washed NPs were transferred with a minimal water content to a vial, which was frozen and freeze-dried, resulting in the final silica-coated iron NPs.

 $Ru(bpy)_3^{2+}$ immobilization: a typical experiment for supporting Ru(bpy)_3^{2+} on T12 at 10% surface coverage is described: a stock solution containing 10.0 mg of [Ru(bpy)_3]Cl₂.6H₂O in 10 mL of Mili-Q water was prepared. 237 µL of this solution was added to 50 mg of T12 fresh out of the freeze-dryer in a vial, to which 2.5 mL of Mili-Q water were added. The suspension was sonicated for 5 min and then magnetically stirred at 1200 rpm for 2h. The final material was washed three times with 50 mL of Mili-Q water and freeze-dried. The supernatant was collected and analyzed by UV-Vis to verify the absence of residual (non-grafted) PS. The same procedures were followed for all materials, always maintaining 50 mg of support and 2.5 mL total for the suspensions. The only changing parameter was the amount of stock solution added. Table 4 shows the amount of stock solution needed to give 10% surface coverage, which reflects different concentrations per mass of support because of varying surface areas.

Table 4. Volume of stock solution (μ L) necessary for synthesizing 50 mg of catalysts as well as the catalyst load per mass of support to give 10% surface coverage.

	T12	T9	T6	Т3	SiO ₂
Volume of stock solution (µL)	237	197	70	103	245
PS per mass of support $(mg \cdot g^{-1})$	4.73	3.94	1.40	2.05	4.89

Characterization techniques: a) TEM (transmission electron microscopy) - samples were dispersed in ethanol and deposited onto a Cu grid with a carbon backing. The images were taken on a Tecnai F-20 with an accelerating voltage of 200 kV. Particle sizes were measured using ImageJ software over a minimum sample size of 100 particles. b) XPS (X-ray photoelectron spectroscopy) - samples were analysed on a Fischer Scientific K α spectrometer using a spot size of 200 µm, running 5 survey scans at 200 mV for 50 ms residence times, and 5-20 scans for specific elements, also at residence times of 50 ms. Deconvolution and peak positions were determined using CasaXPS® processing software. c) SQUID (superconducting quantum interference device) magnetometry was performed using an MPMS-Evercool system by Quantum Design. The temperature dependence of low-field (H = 50 Oe) magnetization was measured upon heating from 5 K at 2 K/min following conventional zero-field and field-cooling protocols (ZFC and FC curves). The magnetic response at 5 K was registered after cooling in a field H = 50 kOe in order to probe possible exchange-bias effects. d) EDS: experiments were carried out in a Thermo Scientific Talos F200X S/TEM operated at 200 keV, with high brightness XFEG Schottky source. EDS carried out with a SuperX G2 energy dispersive spectroscopy detector comprising four windowless SSDs, dwell time 20 µs per pixel and probe current 236 pA. Data was processed using Gatan Digital Micrograph® software. e) Spectrophotometry: Absorption spectra were measured using a Shimadzu UV-2600 equipped with an integration sphere ISR-2600 Plus, using 1 cm square cuvettes. Emission spectra were measured using Horiba-Jobin-Yvon Fluorolog-3 fluorometer equipped with a three-slit double-grating excitation and emission monochromator with dispersions of 2.1 nm·mm-1 (1200 grooves·mm-1). Steady-state luminescence spectra were obtained upon excitation by unpolarized light from a 450 W xenon continuous wave (CW) lamp and detected at

an angle of 90° for measurements either by using a Hamamatsu R928 (visible luminescence) or by using a nitrogen-cooled InGAs detector (¹O₂ phosphorescence in the NIR). Spectra were corrected for both excitation source light-intensity variation and PhotoMultiplier spectral responses. Luminescence quantum yield measurements for $Ru(bpy)_3^{2+}$ were performed in an integration sphere, using the previously published general methodology as reported by De Mello and coworkers.⁵² Briefly, dilute solutions of each sample were introduced into an open capillary quartz tube, equipped with a Young's valve, and thoroughly degassed by four consecutive freeze-pumpthaw cycles. The inserted tube was then placed into the cavity of a GMP G8 integration sphere and measurements of the different lamp and emission signals were performed. In order to minimize differences between the peak intensities of the lamp and emission profiles, and also to ensure that the collected signal remained in the linear range of the detector, density filters (0.5%) were used to attenuate the intensity of the lamp profile. Irradiation wavelength was 400 nm. Luminescence lifetime measurements were performed in acetonitrile at 298K on a Horiba-Jobin-Yvon Fluorolog-3® spectrofluorometer, equipped with a NanoLED 440L source operating at 440 nm with 250 ps pulses, with a repetition rate of 10 kHz. Emission decay was probed at 600 nm, using a iHR320 emission monochromator with 1200 groves.mm-1 gratings and a R928 detector connected to a FluoroHubA+ TCSPC controller. Degassed samples were prepared in quartz cuvette equipped with a Young's valve, by three consecutive freeze-pump-thaw cycles. Luminescence decay curves were fitted with the decay analysis software (DAS) program, using either mono or biexponential decay model. Reliability of the measurement was ascertained by the χ^2 test, which was found close to 1 in all cases. ¹O₂ generation measurements were performed in a 3 mL open quartz cuvette (1 x 1 x 3 cm). All solutions were set at a similar concentrations of $Ru(bpy)_3^{2+}$ (0.3 mmol L⁻¹). In order to maximize ¹O₂ lifetime and phosphorescence signal d₃-AcCN was used as a solvent in all cases. Luminescence signal centered at 1270 nm was recorded in the same irradiation conditions for all samples (excitation wavelength: 400 nm; excitation slits: 3 nm, emission slits: 14 nm, sum of 4 consecutive scans between 1250 and 1310 nm, integration interval of 1 nm, integration time of 1s) allowing a direct comparison of the integrated signal. For comparison of ¹O₂ generation efficiency using a ADPA as a scavenger, 2 mL of freshly prepared acetonitrile solutions of anthracene-9.10dipropionic acid and of $Ru(bpy)_3^{2+}$ (in solution or in suspension with the different supported systems, 0.3 mmol·L-1) were placed in a three ml open quartz cuvette (1 x 1 x 3 cm) and stirred at 60 rpm for the whole irradiation period. Suspensions of nanoparticles with the same $Ru(bpy)_3^{2+}$

concentration (0.30 mmol L⁻¹) were prepared as well as an ADPA solution of absorbance around 0.1. The cuvettes were filled with 1 mL of the NP suspension and 1 mL of the ADPA solution. Irradiation wavelength was centred at 400 nm (corresponding to the main band associated with PS absorbance), entrance slits were set at 7 nm opening. This setup ensured a constant irradiation power throughout all the irradiations experiments. Conversion of the ADPA scavenger upon reaction with the photogenerated oxygen was followed by regular measurement of the luminescence signal of the latter (considering it linearly proportional to its concentration, which is valid in the investigated range of absorbance) consecutive to an excitation performed at 350 nm, allowing to plot its evolution vs irradiation time. Fitting of the resulting plot is described in full in section 3.8.17.

Catalytic tests: citronellol oxidation tests were run with β-citronellol using orthodimethoxybenzene as an internal standard, using acetonitrile as a solvent and magnetic stirring at 1600 rpm. The reactions were ran using a 125 mL 3-neck jacketed reactor with a condenser attached to it and running water at 20°C. A thermometer was attached to one of the necks to read the internal temperature of the system, which constantly stayed between 20 and 25°C. A balloon filed with molecular oxygen was connected to a needle whose tip touched the bottom of the flask, allowing the gas to bubble through the system at atmospheric pressure. LED strips (MINGER White Strip Light LED 6000K Bright White Daylight) were positioned around the flask on a cylindrical support of about 30 cm diameter and 10 cm height, (Figure 57). The reactor and the LED framework were covered with in aluminum foil. In a typical procedure, 15.0 mg of β citronellol and 12.0 mg of ortho-dimethoxybenzene were dissolved in 20 mL of acetonitrile and the resulting mixture was transferred in the reactor. Part of the solvent would be used to suspend about 16.0 mg of T3-supported $Ru(bpy)_3^{2+}$, for instance, with the aid of sonication and added to the reactor. The reaction ran for 4 h and aliquots were taken, guenched with 1.2 molar equivalent of triphenylphosphine and injected for GC analysis at time zero and at every hour. The final crude products were also quenched with triphenylphosphine, concentrated in a rotary evaporator, and dissolved in CDCl₃ for ¹H NMR spectroscopy analysis (section 3.8.12).

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3.8 Appendix A

3.8.1 TEM images of Fe NPs

The following images showcase the monodisperse Fe NPs used as the magnetic core for producing all the supports used in this work. For the purposes of this imaging, the particles were submitted to a controlled oxidation treatment with trimethylamine N-oxide in order to create a protecting iron oxide shell that would allow minimal sample modification upon exposure to air during grid deposition and manipulation.



Figure 42. TEM images of uncoated Fe NPs which were submitted to controlled surface oxidation for imaging purposes.

3.8.2 Optimization of ratios for silica coating

A key parameter for controlling the reverse microemulsion mechanism is the perfect match of the number of micelles with the number of particles added. An excess of particles causes the formation of silica-coated joint multi-nuclei, and an excess of micelles cause the formation of core-free silica particles. The starting point for the definition of the parameter of this work was the work of Ding and co-workers.¹ The number of Fe particles, however, cannot be compared since they are added in the form of NPs suspensions, so the ratio NH₄OH/surfactant had to be adjusted to vary the number of micelles. This study was done in smaller batches and the volumes of Fe NPs suspensions and surfactant were fixed to 100 μ L and 0.5 mL, respectively, while the volume of NH₄OH (28%) was varied from 100 to 25 μ L. Images of the resulting materials are found in Figure 43. Based on the images, 25 μ L was selected as the optimal volume of NH₄OH for providing high degree of

individual coating, with minimal formation of core-free particles. Once optimized, the procedure was scaled up by a factor of 10 to produce the supports used in this work.





3.8.3 Additional TEM images

These are additional TEM images of the Fe@SiO₂^{TX} materials.

On the first image on the left, the higher magnification allows the visualization of a layer of iron oxide between the Fe (0) core and the silica shells. The presence of this layer of was confirmed by XPS analysis and it likely comes from the silica coating step, which happens in water.



Figure 44. Additional TEM images for the Fe@SiO₂ materials.

3.8.4 Thickness of the silica layers

Thicknesses of the silica layers were measured according to the following histograms. The change in color of the materials was also clear to the naked eye, as one can see in the photo in Figure 46.



Figure 45. Histograms of measurements of silica thickness. Particles dimensions were measured in various TEM images (including the ones on Fig. 44) using ImageJ[®].



Figure 46. Photos of the different supports for comparison with a suspension of Fe NPs.

3.8.5 TEM images of SiO₂ NPs (positive control)

 SiO_2 nanoparticles were produced using the same microemulsion method, but without the addition of the iron core. The particles were grown until they reached comparable size to T3.



Figure 47. TEM images of SiO₂ particles used as blanks.

3.8.6 XPS depth profile



Figure 48. Combined deconvoluted Fe 2p_{3/2} signals from material T3 plotted according to etching time.

ETCHED LEVEL 1 (120s)



ETCHED LEVEL 3 (360s)





ETCHED LEVEL 4 (480s)



Figure 49. Detailed deconvolution of Fe $2p_{3/2}$ XPS signals for various etching levels of material T3.



3.8.7 Exchange bias and coercivity values

Figure 50. Normalized ZFC-magnetization curve for sample $Fe@SiO_2^{TX}$ (measured in H = 50 Oe). Blocking temperature is defined as the maximum in the curve.

Coercitivity and exchange bias values on Table 5 were extracted from Figure 50. The small variation in those parameters across the series of materials implicate the similarity of the magnetic cores.

Table 5.	Coercitivity	and exchange	bias valu	ues (kOe).

	Fe@SiO ₂ ^{T3}	Fe@SiO2 ^{T6}	Fe@SiO ₂ ^{T9}	Fe@SiO2 ^{T12}
Coercivity (KOe)	1.64	2.05	1.48	1.27
Exchange bias (kOe)	2.23	2.10	2.19	1.78

3.8.8 Ru(bpy)₃²⁺ immobilization

 $Ru(bpy)_3^{2+}$ was immobilized on the surface of the supports by the stirring the materials in an aqueous solution of $Ru(bpy)_3^{2+}$ containing the amount of photosensitizer desired to give 10% surface coverage on the support. The effectiveness of the immobilization could be immediately realized at the end of the process, when the strongly orange initial solution had turned transparent and the supports, that originally featured shades of grey, had turned yellowish. Visible-light absorption spectra of the aqueous solutions before and after immobilization are shown on Figure

52. The absence of the signal peaking at 452 nm for the remaining solutions suggest full removal of $\text{Ru}(\text{bpy})_3^{2+}$ from the solution, therefore 100% immobilization efficacy was assumed for all materials.



Figure 51. Photos of the materials obtained by grafting $Ru(bpy)_3^{2+}$ at 10% surface coverage on each of the supports. The yellow color becomes more evident as the silica layer increases.



Figure 52. UV-Vis of stock solutions used for $Ru(bpy)_{3^{2+}}$ immobilization of the remaining solution, after separation of the material with grafted $Ru(bpy)_{3^{2+}}$. The stock solutions were diluted by a factor of 2 for these measurements.

3.8.9 BET Surface Area

All the materials had surface areas higher than the estimated values for smooth silica spheres with iron cores (approximated taking into consideration the dimeters of silica and iron for each material and the densities of amorphous silica and bulk Fe). Surface area decreases from T3 to T6, which is expected due to particle size increase, but the values unexpectedly increase with size for T9 and T12. Such data is initially counter-intuitive, since surface/volume ratio drops as a function of particle size. Yet, close analysis of TEM images (Figure 44) provided a rational to justify this trend, as the surface of the nanosupports go from being fairly smooth (T3 and T6), to becoming rougher and more textured as more silica layers are added (T9 and T12). Since the growth of the shells was carried out on a step-by-step mechanism, it is likely that irregularities on the surfaces would be carried along and magnified when additional external layers were deposited. The inversion point when the roughness of the surface becomes more important than particle size in defining the surface area lies somewhere between 6 and 9 silica layers.



Figure 53. Expected and measured BET surface areas (m²·g) for the series of supports, including the blank SiO₂ NPs.

3.8.10 Surface coverage

Surface coverage is defined as the percentage of area of the support covered by photosensitizer. In order to define that, one needs the BET surface areas of the supports (section 3.8.9) and the area occupied by a single photosensitizer molecule, which can be multiplied by Avogadro's number to give the area occupied by mol of photosensitizer. The area occupied by an ion of PS was considered to be a circle of diameter equal to the distance between two farthest atoms on a structure (found on software Avogadro[®]), added by the van der Waals radii of the two atoms in the extremities.

Area of one Ru(bpy)₃²⁺ ion: $A = \pi r^2 = \pi (1.425 \text{ nm})^2 = 6.38 \text{ nm}^2$

Area of occupied by one mol of $\text{Ru}(\text{bpy})_3^{2+}$ ions: $A = (6.38nm^2)(6.022.10^{23}mol^{-1}) = 3.84.10^6 m^2 mol^{-1}$

Surface coverage = $\left(\frac{(n \, Ru(bpy)_3^{2+})[mol](3.84.10^6)[m^2mol^{-1}]}{(surface area of support)[m^2g^{-1}](mass of support)[g]}\right)(100\%)$



Figure 54. $Ru(bpy)_{3^{2+}}$ structure and measurement of its radius, which allowed the determination of surface coverage.

3.8.11 EDS Mapping

The material $Fe@SiO_2^{T3}@Ru$ was analyzed by TEM and elemental mapping was achieved by energy-dispersive X-ray (EDS) spectroscopy (Figure 55). This analysis could confirm the presence of an Fe-rich core, covered with a layer of SiO₂. Ru mapping could not give significant data, since the expected percentage is not within the detection limits of the experimental setup.



Figure 55. TEM imaging and EDS elemental mapping for a Fe@SiO₂^{T3}@Ru particle (from top left, clockwise: BF-TEM, O-EDS, Si-EDS, Ru-EDS, Fe-EDS and overlay of EDS for O, Si, Ru and Fe).

Table 6. Expected (theoretical) atomic percentage and experimental quantification obtained by EDS for the red square in the BF-TEM image above.

	EXPECTED atomic %	EXPERIMENTAL atomic %
Si	31.85	25.7
0	65.80	72.9
Fe	2.34	1.3
Ru	0.054	0.16



3.8.12 Citronellol oxidation tests

Figure 56. Detailed mechanism of the citronellol photo-oxidation reaction.

Citronellol oxidation tests were performed for 2h in acetonitrile at 0.05 mol% of catalyst, with shining LED lights at 25°C and bubbling O_2 through the solvent during the reaction (setup in Figure 57). The results obtained through time for $Ru(bpy)_3^{2+}$ immobilized on the various supports are detailed on Figure 58.

Conversion was calculated by GC-MS, a sample chromatogram in presented on Figure 59, the ratio between the internal standard and the reactant peak areas was monitored and checked again the spectra at time zero for the calculation of conversion. NMR spectroscopy was used for yield calculation; a sample spectrum is presented on Figure 60. In all cases close to 100% mass balance between final products and unreacted starting material indicated the absence of secondary products.



Figure 57. Photoreactor setup.











Figure 59. Sample gas chromatogram for a crude reaction product showing the internal standard, remaining reagent, the two product peaks and also the oxidized and non-oxidized forms of the quenching agent.



Figure 60. NMR spectrum of the selected region for yield calculation.

3.8.13 Catalyst recycling

Recycling tests were carried out using material T3 as a support. The reaction was allowed to proceed to 4h at the same conditions used for the support screening tests: 0.05 mol% of Ru, at 20° C in acetonitrile, O₂ 1 atm and LED light irradiation.



Figure 61. Kinetics of citronellol oxidation at optimized conditions for of catalysis using $Fe@SiO_2^{T3}@Ru$, with control experiments.

3.8.14 Absorption spectra

The following absorption spectra were obtained in a UV-Vis spectrophotometer equipped with an integrating sphere. It, therefore, accounts for all transmitted and reflected photons.



Figure 62. Absorption spectra for $Fe@SiO_2^{TX}$ (X=3, 6, 9, 12) and SiO₂ nanoparticles recorded in a UV-Vis spectrophotometer equipped with an integrating sphere. Experiments were carried out in acetonitrile suspensions, under stirring, containing amount of material that respected the same ratios used in catalysis.

3.8.15 Role of total Fe content versus silica thickness

Since the amount of PS per mass of support varies in the catalytic systems due to surface area changes, the amount of particles added to perform each catalytic test also changes, therefore creating a possible source of bias. For example, T3 and T12: in a typical replicate of citronellol oxidation (15 mg of citronellol, 0.096 mmol), 18.3 mg of T3 would be added to the reactor, while T12 would require only 7.59 mg to ensure the same catalyst load (0.05 mol%). It is true that more Fe is added to the reactor when using T3, but it is also true that each extra Fe core added comes coated with SiO₂, so extra amounts of both Fe and SiO₂ are added. The extra amount of Fe will indeed increase light absorption, but the extra amount of silica will likewise decrease light adsorption. We have estimated the mass percentage of the core and of the shell in each system and calculated the absolute masses of Fe and of SiO₂ for each of the catalytic tests (Table 7 and Table

8). The total masses of Fe and SiO_2 were plotted against our absorbance data (Figure 62). Absorbance data was also plotted against the thickness of the silica shell, which reflects neither the amount of Fe nor the amount of SiO_2 in the media, but the intrinsic relationship between those two parameters.



Figure 63. Relationships between total mass of Fe, total mass of SiO₂, shell thickness and vis-light absorbance.

The plots presented above show no correlation between the mass of Fe (or SiO_2) and the absorbance of light by the systems, while the correlation to the thickness of the silica shell is clear. The strong correlation between absorbance and silica thickness, shows that the dominating factor is not the absolute amount of Fe or SiO₂, but actually the amount of Fe relative to SiO₂, which is directly related to the thickness of the silica layer, and systematically varied by changing this parameter throughout all the experiments, which consistently corroborate among themselves.

It is possible, however, that the presence of a larger number of particles in the system (*e.g.* comparing T3 to T12) results in a larger number of inter-particle interactions, such as inter-particle scattering or shielding, but our data shows that this is not the dominating factor at our working conditions. For all our experiments, we made sure to work on concentrations that provided perfectly clear suspensions. Such inter-particle interactions would become more apparent if we had worked in highly concentrated suspensions, which would significantly deviate from "ideal behaviour".

	Shell	Particle	Core	Particle	Core	Shell	Core	Shell	Core	Shell
	thickness ¹	diameter ¹	diameter ²	volume	volume	volume ³	mass ⁴	mass ⁵	mass	mass
	nm	nm	nm	nm ³	nm ³	nm ³	g	g	%	%
Т3	15.4	38.2	7.4	2.92E+04	2.12E+02	2.90E+04	1.68E-18	7.68E-17	2.14	97.86
T6	23.7	57.7	10.3	1.01E+05	5.72E+02	1.00E+05	4.52E-18	2.65E-16	1.68	98.32
Т9	28.4	65.8	9.0	1.49E+05	3.82E+02	1.49E+05	3.02E-18	3.94E-16	0.76	99.24
T12	32.3	73.8	9.2	2.10E+05	4.08E+02	2.10E+05	3.22E-18	5.57E-16	0.58	99.42

Table 7. Estimative of the mass percentage of the components of each support

¹from measurements of over 100 particles using ImageJ®

²difference between the average particle diameter and twice the average thickness

³difference between particle volume and core volume

⁴assuming the density of metallic iron = $7.90E^{-21}$ g·nm⁻³

⁵assuming the density of amorphous silica = $2.65E^{-21}$ g·nm⁻³

Table 8. Calculations of total masses of Fe and SiO2 in each catalytic system

	Surface	PS per area	PS per mass	Catalyst mass	Core mass	Shell mass	Shell	Absorbance
	area	of support ¹	of support ²	in reactor ³	in reactor ⁴	in reactor ⁴	thickness	at 455 nm ⁵
	m ² •g ⁻¹	mmol·m ²	mmol∙g ⁻¹	mg	mg	mg	nm	-
Т3	105	2.50E-05	2.63E-03	18.3	0.39	17.90	15.4	0.2391
T6	72	2.50E-05	1.80E-03	26.7	0.45	26.22	23.7	0.1395
Т9	202	2.50E-05	5.05E-03	9.5	0.07	9.43	28.4	0.0779
T12	243	2.50E-05	6.08E-03	7.9	0.05	7.86	32.3	0.0532

¹for 10% surface coverage, given a mol of Ru(bpy)₃²⁺ occupies 3.84E+6 m² (section 3.8.10)

²according to the specific surface areas

³to give 0.05 mol% of Ru(bpy)₃²⁺ using 15 mg of substrate

⁴using percentages calculated in previous table

⁵from Fig. 62



3.8.16 Luminescence lifetime measurements

Figure 64. $Ru(bpy)_{3^{2+}}$ luminescence decay curves for Fe@SiO₂^{TX}@Ru (X= 3, 6, 9, 12) and SiO₂@Ru.

	Lifetime (ns)	Standard deviation
Ru(bpy) ₃ ²⁺	973	2.74
SiO ₂ @Ru	1147	5.15
Fe@SiO ₂ ^{T3} @Ru	1023	5.30
Fe@SiO ₂ ^{T6} @Ru	1119	6.30
Fe@SiO ₂ ^{T9} @Ru	906	8.11
Fe@SiO ₂ ^{T12} @Ru	943	9.38

Table 9. Detailed Ru(bpy)₃²⁺ luminescence lifetime measurements.

3.8.17 Singlet oxygen phosphorescence

The characteristic phosphorescence of ${}^{1}O_{2}$ was monitored through a near IR study under aerobic conditions. Figure 65 shows the acquired ${}^{1}O_{2}$ phosphorescence spectra, which confirms the generation of ${}^{1}O_{2}$ under these conditions. The intensity of the emission signal increases from Fe@SiO₂^{T3}@Ru to Fe@SiO₂^{T9}@Ru following the trend observed in QY, and thus reflecting the same screening effect of the silica shell responsible for fluorescence QY evolution. The last two materials, however, gave lower ${}^{1}O_{2}$ signals than expected, in contrast with the evolution previously observed with Ru(bpy)₃²⁺ luminescence QY. Interestingly, a similarity between those two supports is that both were made from 12 TEOS additions. Such number of additions gave them highly irregular surfaces, since surface irregularities are magnified as additional silica layers are built (*e.g.* noticeable on Fig. 44 and large BET surface areas, Fig. 53). We postulate that mean free path of the photosensitized ${}^{1}O_{2}$ is limited by the surface irregularities, which increases its residence time in proximity to the surface of the support. Such surface is silanol-rich, which quenches ${}^{1}O_{2}$ species. Such fact may account for a less efficient sensitization and emission of ${}^{1}O_{2}$ observed in these systems.



Figure 65. ${}^{1}O_{2}$ phosphorescence measured for suspensions of the photocatalysts in deuterated acetonitrile. All measurements were carried out with suspensions and the amount of material was adjusted so that the concentration of Ru(bpy)₃²⁺ was the same in each cuvette. Light irradiated at 418 nm and collected from 1225 to 1325 nm.

3.8.18 ADPA decomposition fitting

ADPA data was fitted on Origin[®] using the exponential decay function. The plots are presented in Figure 66 and the detailed parameters on Table 10. Decay factors on Figure 41 were calculated as $1/t_1$ to give a constant that can be directly multiplied by the exponential factor.



Figure 66. ADPA decomposition data fitting.

Table 10. Fitting p	parameters.
---------------------	-------------

Equation	$\mathbf{y} = \mathbf{A}$.1*exp(x/t1)) + y0		
Adj. R-Square	0.98911	0.98342	0.98786	0.99457	0.99906
		Value	Standar	d Error	
С	y0	9.40664	2.71563		
С	A1	90.138	4.72193		
С	t1	-1.01713	0.14559		
D	y0	8.85114	4.33945		
D	A1	90.24286	5.94355		
D	t1	-1.78724	0.32138		
E	y0	7.92556	4.20187		
E	A1	90.97136	5.24317		
E	t1	-2.19069	0.3407		
F	y0	-5.04462	5.84929		
F	A1	105.3523	6.16002		
F	t1	-4.03775	0.5497		
G	y0	-10.4591	4.27034		
G	A1	110.6117	4.10139		
G	t1	-6.3364	0.47401		

3.8.19 Light scattering measurements

Scattering measurements were carried out by shining 450 nm light on cuvettes containing suspensions of $Fe@SiO_2^{TX}$ (before PS immobilization) and collecting photons of the same wavelength at a detector positioned perpendicularly to the pathway of the incident light. As anticipated, the thicker the silica shell, the more the corresponding $Fe@SiO_2^{TX}$ was able to scatter light. $Fe@SiO_2^{T3}$ and $Fe@SiO_2^{T6}$ – the two strongest light-absorbing supports – scattered light fairly poorly, while $Fe@SiO_2^{T9}$ and $Fe@SiO_2^{T12}$ scattered light with a similar intensity to SiO₂, a similar trend seen for the hindering effect index. This hints that efficient scattering positively affects photocatalytic activity.



Figure 67. Left side: Light scattering of supports before PS immobilization. Light irradiated and collected at 450 nm, samples consisted of 0.5 mg·mL⁻¹ suspensions of Fe@SiO₂^{TX} in acetonitrile. Right side: scheme of experimental setup.

3.8.20 Luminescence in presence and absence of O₂

Table 11. Integrated area under $Ru(bpy)_{3^{2+}}$ luminescence curves and ratio in the presence and in the absence of O₂, with similar $Ru(bpy)_{3^{2+}}$ concentrations and spectrofluorometer settings in all cases.

	Luminescence in degassed	Luminescence in	DATIO
	conditions	oxygenated conditions	KATIO
Fe@SiO ₂ ^{T3} @Ru	1.20E+09	7.50E+08	1.6
Fe@SiO ₂ ^{T6} @Ru	2.91E+09	2.03E+09	1.4
Fe@SiO ₂ ^{T9} @Ru	4.02E+09	2.90E+09	1.4
Fe@SiO ₂ ^{T12} @Ru	3.24E+09	2.32E+09	1.4
SiO ₂ @Ru	3.81E+09	2.76E+09	1.4
Ru(bpy) ₃ ²⁺	1.28E+09	7.51E+08	1.7

4

Photocatalysis on magnetic supports for single oxygen generation: Role of immobilization and photobleaching

4.1 Preamble

Silica-coated magnetic supports were developed in the previous chapter and proved capable of combining magnetic properties with photocatalytic activity. In this chapter, those same supports are tested with a different photosensitizer and a different immobilization method to demonstrate the versatility of the support.

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Terra, J. C.; Desgranges, A.; Amara, Z.; Moores, A., Photocatalysis on magnetic supports for singlet oxygen generation: Role of immobilization and photobleaching. *Catal. Today* **2023**, *407*, 52-58.

4.2 Abstract

Organometallic photosensitizers are very efficient triplet sensitizers that have found wide use in photocatalysis, but they are scarce, toxic, and expensive. Organic fluorophores have also been used in several systems, but they can suffer from lower efficiency and sensitivity to photobleaching. In this work, we immobilized ruthenium (II) tris(bipyridine) and rose bengal on magnetic nanosupports and compared their activity and photostability in the singlet oxygen mediated photo-oxidation of citronellol. Both systems can perform the transformation with equivalent turnover frequencies and be magnetically recovered. We studied their long-term stability and found photobleaching to be a major cause of photocatalyst deactivation over time for both systems, and we were able to improve their photostability upon immobilization on solid supports.

4.3 Introduction

Performing chemical reactions with the energy of visible light is a trick long known by Nature¹ and, more recently, mastered by chemists in many areas, such as organic synthesis.² Visible light is interesting because it is safe, abundant,³ and can be generated at low energy expense using LEDs.⁴ It is also especially useful for organic synthesis because it does not have enough energy to cause C-C bond degradation and lead to side reactions, a common issue in UV photochemistry.² Dyes used as photosensitizers for visible-light photocatalysis can absorb visible photons and transfer the energy to molecules of interest. Molecular oxygen is an example of a molecule that can be photoactivated to form a powerful oxidant, namely singlet oxygen (¹O₂).⁵

Ruthenium (II) tris(bipyridine) $[Ru(bpy)_3^{2+}]$ is the state-of-art example of an organometallic photosensitizer that easily accesses an excited triplet state bearing adequate energy to readily generate 1O_2 . Notably, the MLCT in $Ru(bpy)_3^{2+}$ makes the gap between the first excited singlet and triplet states so small that intersystem crossing occurs in the femtosecond scale and almost quantitatively.⁶ We have previously reported the immobilization of $Ru(bpy)_3^{2+}$ on magnetically recoverable supports (core-shell Fe@SiO₂ NPs).⁷

As the chemical industry, including the pharmaceutical sector, is increasingly attracted to photochemical solutions to synthetic challenges, we need to develop robust alternatives for their recovery. While we have established a proof of concept in the past with our Fe@SiO₂ nanosupports
using $Ru(bpy)_{3^{2+}}$, we were interested in validating and comparing such an approach for another photocatalyst. This step is essential towards designing powerful systems for larger-scale use.

Given the drawbacks associated with precious metals, organic fluorophores have also been immobilized on supports in various contexts.⁸⁻¹¹ We decided to expand our work to the use of Rose Bengal (RB), an inexpensive dye that has been increasingly present in the photocatalysis literature during the last decade.¹² The heavy halogens in its structure approximate the excited singlet and triplet energy states,¹³ giving RB a system intercrossing rate (ϕ_{ISC}) of 0.77.¹² Although lower than the ϕ_{ISC} of Ru(bpy)₃²⁺, it is significantly high for an organic photosensitizer. RB has been extensively used for singlet oxygen photocatalysis.¹²⁻¹⁴ Some recent examples include RB-generated singlet oxygen participating in the formation of peroxo radicals¹⁵⁻¹⁷ or directly being added across π bonds.¹⁸⁻²⁰ Within the latter category, the photo-oxidation of citronellol has already been reported to happen with RB catalysis.^{21, 22} Organic fluorophores are, however, generally less stable to photobleaching than organometallic ones, but this photostability can be improved with different strategies.²³ For instance, the Heinrichs and the Machese groups have observed improved rose bengal photostability upon immobilization on mesoporous silica.^{24, 25}

Photobleaching is the irreversible light-induced transformation of a photosensitizer into a new molecule that does not absorb light or is less photoactive than the original dye. This phenomenon is complex and can happen through oxygen-dependent or oxygen-independent pathways, or via a combination of both.²³ In other words, the same light irradiation required to excite a photocatalyst can also cause its decomposition., while photogenerated oxygen species can oxidize the photosensitizer itself. Thus, the efficiency of a photocatalytic system strongly depends on its photobleaching mechanisms.

In this context, we used Fe@SiO₂ nanoparticles to support both a metal-based (Ru(bpy)₃²⁺) and a metal-free (RB) photosensitizer, and RB-decorated Fe@SiO₂ nanocatalysts were applied for the photo-oxidation of citronellol. These systems allowed us to study photobleaching and the effect of photosensitizer immobilization in different contexts. We found that photobleaching deactivates both RB and Ru(bpy)₃²⁺ systems, and that immobilization on the supports increased the photostability of the dyes.

4.4 Experimental

All chemicals were acquired from Sigma-Aldrich and used as received unless specified.

Synthesis of supports

The supports were synthesized according to the methodology published in our previous report.⁷ In summary, we prepared oleylamine-capped Fe(0) nanospheres (diameter 8.6 ± 1.4 nm) by the thermal decomposition of Fe(CO)₅²⁶ and coated those NPs with silica shells using a reverse microemulsion method.²⁷ The thickness of the silica shells was controlled by gradual additions of the silicon source TEOS.²⁸ We obtained a set of Fe@SiO₂ supports with varying shell thicknesses, which were named according to the number of TEOS additions (X additions of 0.25 mL of TEOS) required to form the final shell (Scheme 22). The supports were named Fe@SiO₂^{TX} (X = 3, 6, 9, or 12). Silica NPs were also made as blanks following the same reverse microemulsion methodology (12 TEOS additions) but in the absence of Fe cores.



Scheme 22. Preparation of supports.

The supports were characterized with transmission electron microscopy (TEM) by dispersing the powders in ethanol and drop-casting onto a Cu grid with carbon backing. The images were taken using a Thermo Scientific Talos F200X TEM. Particle sizes were measured using ImageJ[®].

Rose bengal immobilization

The supports were then used to anchor the photosensitizer rose bengal (RB) using a covalent immobilization strategy adapted from Heyne *et coll.*.²⁹ It consists of functionalizing the silica surface with aminopropyl groups, which are then used to form an amide bond with the carboxylic acid in RB using a carbodiimide coupling agent (Scheme 23).



Scheme 23. Preparation of supported photocatalysts.

First, Fe@SiO₂ NPs fresh out of a desiccator (50 mg) were dispersed in 2-propanol (50 mL) and sonicated for 5 min. We then added NH₄OH 28% (5 mL) and stirred the mixture for 20 min. Following this, we added (3-aminopropyl)triethylsilane (APTES, 25μ L) and set the suspension to stir at RT for 3 h. The amine-functionalized supports were washed by centrifugation (10,000 rpm) three times with 2-propanol (40 mL x 3) and dispersed in 10 mL of a 2-(N-morpholino)ethanesulfonic acid (MES) buffer of pH 6 (0.1 M MES solution, pH adjusted with 0.1 M NaOH).

On a separate container, we added an RB solution of concentration 1.0 mg mL⁻¹ (130, 89, 245, 300 and 310 μ L for T3, T6, T9, T12, and SiO₂ NPs; respectively) to react with the coupling agent 1-

ethyl-3-(3-(dimethylamino)-propyl) carbodiimide hydrochloride (EDC, 40 mg) in 15 mL of the MES buffer pH 6 for at RT under stirring for 20 min. The amount of RB per support was normalized by the BET surface area of each support. We estimated the surface occupied by a single RB molecule and calculated the number of mols of RB molecules needed to provide a surface coverage of 10% of RB on Fe@SiO₂, as we had previously done for Ru(bpy)₃²⁺ immobilization.⁷ The 10% surface coverage was fixed for all catalysts based on our previous experience with similar systems^{7, 30} (details in section 4.8.1). The suspension of amine-functionalized supports was then added to the modified RB solution and allowed to react under stirring at RT for another 3 h in a vial wrapped in aluminum foil. The obtained materials were washed by centrifugation (10,000 rpm) three times with DI water (40 mL x 3), resulting in pink precipitates and clear supernatants. The materials were lyophilized, and we named them RB/Fe@SiO₂^{TX}. The supernatants were analyzed by UV-Vis spectrophotometry to verify the absence of RB's absorption band at 560 nm.

Ruthenium (II) tris(bipyridine) immobilization

The immobilization of Ruthenium (II) tris(bipyridine) was done by suspending the supports in aqueous solutions of the photosensitizer and stirring at RT overnight, as represented in Scheme 23. The detailed methodology has been reported in our previous paper.⁷

Citronellol photo-oxidation

The reaction was carried out in a 125 mL three-neck jacketed reactor with a condenser attached to it. LED strips (MINGER White Strip Light LED 6000K bright white daylight) were placed around the reactor on a cylindrical support with 30 cm diameter and 10 cm height. The complete system was covered with aluminum foil. In a typical experiment, citronellol (30 mg, 0.18 mmol) was dissolved in 2-propanol (20 mL) with 1,3-dimethoxybenzene (15 mg, 0.11 mmol) and catalyst at 0.015 mol% of RB (1.5 μ M *i.e.* 7.21, 10.49, 3.74, 3.11 and 3.00 mg of T3, T6, T9, T12, and SiO₂; respectively). The mixture was sonicated for 5 min and left to react for 4h with 1200 rpm magnetic stirring, constant flow of bubbling O₂ at 1 atm, LED illumination, and water chilling at 20°C. Substrate conversion and product yields were followed by GC-MS (Agilent technologies 7890A coupled with Agilent technologies 5975C inert XL MSD with triple-axis detector) and ¹H NMR spectroscopy (Bruker AVIIIHD 500 MHz).

Reuse tests were carried out with catalyst RB/Fe@SiO $_2^{T3}$. The catalyst was recovered magnetically using a neodymium magnet, washed by centrifugation with DI water, lyophilized, and reused in the reactor with fresh substrate at the same conditions as the initial catalytic tests.

Photobleaching and leaching experiments

Luminescence decay over time was measured on an Agilent Cary Eclipse fluorescence spectrophotometer. The catalysts (homogeneous and immobilized) were submitted to reaction conditions (solvent, temperature, light irradiation, and O₂), but in the absence of substrate. The photoluminescence of RB and Ru(bpy)₃²⁺ were measured prior to submission to light irradiation and O₂ (t = 0 min), and upon submission to bleaching conditions at time intervals (30 or 60 min) for 8 hours. The same experiments were also carried out in oxygen-free conditions (solvents degassed with 3 freeze-pump-thaw cycles and under argon atmosphere) for a period of 4h. All experiments were carried out with 20 mL of solvent (2-propanol or acetonitrile), and catalyst concentrations according to optimized reaction conditions: $1.5 \,\mu$ M (*i.e.* 7.21 mg of RB/Fe@SiO₂^{T3}) or 4.80 mg of Ru(bpy)₃/Fe@SiO₂^{T3}) and 5.0 μ M of Ru(bpy)₃²⁺ (*i.e.* 16 mg of Ru(bpy)₃/Fe@SiO₂^{T3}). We excited the RB systems at 545 nm (10 nm slit) and collected emission from 560 to 900 nm (5 nm slit); homogenous RB aliquots were diluted 4 times for spectroscopic measurements to respect the Lambert-Beer quantification region. Ru(bpy)₃²⁺ systems were excited at 452 nm (20 nm slit) and we collected emissions from 490 to 900 nm (20 nm slit).

4.5 Results and discussion

$RB/Fe@SiO_2^{TX}$ as photocatalysts for the oxidation of citronellol

Representative TEM images of the $Fe@SiO_2^{TX}$ supports used to immobilize both photosensitizers are shown in Figure 68. These images exhibit the high monodispersity of the nanoparticulate system. Photos of the supports (Figure 69) showcase the change in color with the change in thickness of the silica coverage. The colors go systematically from dark to light gray, indicating a reduction in the absorption of light by the dark Fe cores as silica layers are added.



Figure 68. Representative TEM images of supports $Fe@SiO_2^{TX}$ (from left to right, X = 3, 6, 9, and 12).



Figure 69. Photos of materials Fe@SiO₂^{TX} before RB immobilization.

We immobilized RB on the supports by a covalent bond immobilization strategy, as depicted in Scheme 23. First, the silica surface was functionalized with aminoethyl groups and RB was modified with 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) on the carboxylate ending. The amino groups on the silica surface act as nucleophiles and substitute the EDC group on RB, covalently anchoring the photosensitizer to the functionalized silica surface.

The RB-decorated catalysts were then tested in the photo-oxidation of citronellol, which is the key step in the synthesis of rose oxide, a 100 tons scale/year product of the fragrance industry.³¹ The reaction was run for 4 h in 2-propanol at 20 °C, LED illumination, and bubbling oxygen gas at atmospheric pressure. RB was added at 0.015 mol% related to the substrate citronellol. The reaction and optimized conditions are summarized in Scheme 24, while citronellol conversions obtained using each material are shown in Figure 70.



Scheme 24. Citronellol oxidation reaction scheme and conditions



Figure 70. Photocatalytic results of the oxidation of citronellol with rose bengal immobilized on different supports. Bars reflect the GC conversion for the reactions after 4h in 2-propanol at 20 °C, 0.015 mol% catalyst load, with vis-light LEDs and bubbling O₂ at 1 atm. The pink dotted line (scale on the left side) shows the hindering effect index, a metric of the negative effect on the photocatalytic activity due to the absorption of light by the Fe core. It shows the percentage of conversion reduction when compared to the positive control RB/SiO₂, index zero. The hindering effect is calculated by [100 (1 – (conversion on RB/Fe@SiO₂^{TX} / conversion on RB/SiO₂)].

We observed a general trend of increased catalytic activity with thicker silica shells. While homogeneous RB (0.015 mol%) converted 96% of the substrate in 4 h, RB/SiO₂ converted 89%; and RB/Fe@SiO₂ systems gave conversions ranging from 76 to 89% in the same reaction conditions. The reduction from 96% for homogeneous RB to 89% when it is supported on pure silica nanoparticles can be attributed to the reduced mass transfer intrinsic to heterogeneous systems,³² or even a change in catalyst conformation upon immobilization. The hindering effect index (dotted line on Figure 70) was introduced to measure the detrimental effect of the Fe cores on the catalytic activity of each system. This parameter was defined as [100 (1 – (conversion on

RB/Fe@SiO₂^{TX}/conversion on RB/SiO₂))], hence it represents the percentage reduction of conversion using catalyst RB/Fe@SiO₂^{TX} when compared to the positive control RB/SiO₂, where the Fe core is absent (hindering effect index zero). We can observe a minimal hindering effect of 1-4% for the supports with higher silica content (T9 and T12), suggesting that the amount of silica in those supports was enough to block most of the absorption of photons by the dark-colored Fe core, rendering the systems almost as active as RB/SiO₂. On the other hand, a higher hindering effect (12-15%) was observed for the supports with lower silica content T3 and T6; indicating that silica shielding in those systems does not completely block photon absorption by the core but still renders the system photoactive. The reduced hindering effect when RB is supported on NPs with higher silica content can be explained by the scattering ability of the silica coverage. These shells scatter part of the visible-light photons that would otherwise be absorbed by the dark Fe core. This effect can be observed not only from the color of the nanoparticles themselves (Figure 69) but also through photophysical measurements on those same supports, as we previously demonstrated.⁷

Although covering the Fe cores leads to increased photoactivity, it also reduces the magnetic response of the supports. Using neodymium magnets in our setup, we only succeeded in magnetically recovering the lowest silica content $RB/Fe@SiO_2^{T3}$ catalysts. When testing the recycled catalyst $RB/Fe@SiO_2^{T3}$, we observed a drastic reduction from 76% conversion using the fresh catalyst to about 36% in the first reuse cycle.

Similar results were previously obtained by us when using the photocatalytic system $Ru(bpy)_3/Fe@SiO_2^{TX}$ for this same reaction, but the stability of the photocatalytic system was much higher.⁷ We catalyzed the oxidation of citronellol with $Ru(bpy)_3^{2+}$ at a higher catalytic loading (0.05 mol%) and obtained 92% conversion with homogeneous $Ru(bpy)_3^{2+}$ within 2 h, and conversions of 63-72% using $Ru(bpy)_3/Fe@SiO_2^{TX}$ (X = 3-12). A similar trend of hindering effects was found (0-11% from $Ru(bpy)_3/Fe@SiO_2^{T12}$ to $Ru(bpy)_3/Fe@SiO_2^{T3}$), indicating this is an effect that is intrinsic to the supports and not the photosensitizers. The thinnest silica shell $Ru(bpy)_3/Fe@SiO_2^{T3}$ was also the only magnetically recoverable catalyst, and the reaction with $Ru(bpy)_3/Fe@SiO_2^{T3}$ pushed to 4 h afforded 85% conversion. The $Ru(bpy)_3^{2+}$ system, contrary to RB, was stable to reuse for 3 cycles of 4 h with minimal loss in activity, and for 5 cycles with a reduction to 65% conversion in the 5th cycle. Although $Ru(bpy)_3^{2+}$ was stable to reuse and RB was

not, both afforded very similar total turnover numbers under our conditions due to the different catalytic loads employed $(7671 \text{ for } \text{Ru}(\text{bpy})_3^{2+} \text{ and } 7647 \text{ for } \text{RB})$.

Intrigued by the distinct behaviour of our two systems, we then moved into studying their photostability under our reaction conditions, *i.e.* when exposed to light irradiation and oxygen.

Photostability of the catalytic systems

In this section, we investigated the stability of our supported $Ru(bpy)_3^{2+}$ and RB photocatalytic systems towards light exposure in the presence of oxygen. This study consisted of adding homogeneous RB and $Ru(bpy)_3^{2+}$ as well as immobilized RB/Fe@SiO₂^{T3} and $Ru(bpy)_3$ /Fe@SiO₂^{T3} to a photoreactor under their respective optimized catalytic conditions for citronellol oxidation (RB 1.5 µM in 2-propanol and $Ru(bpy)_3^{2+}$ 5.0 µM in acetonitrile; Figure 71a, b) but in the absence of the substrate citronellol. For reference, the $Ru(bpy)_3^{2+}$ systems were also submitted the same conditions as RB in another test ($Ru(bpy)_3^{2+}$ 1.5 µM in 2-propanol, Figure 71c). We monitored the luminescence over an extended time period (8 h) to account for photobleaching.

The luminescence decay profiles in Figure 71 show different behaviours for the two photosensitizers, but similar ones for the same photosensitizer in different conditions, *i.e.* $\operatorname{Ru}(\operatorname{bpy})_3^{2+}$. Homogeneous RB (lighter pink curve in Figure 71a) showed a slow and steady decrease to 55% in 4 h and to 30% in 8 h. Supported RB (darker pink curve in Figure 71a) suffered a similar steady decrease in luminescence, going to 67% in 4 h and 49% in 8 h. Conversely, homogeneous $\operatorname{Ru}(\operatorname{bpy})_3^{2+}$ in both conditions (lighter orange curves in Figure 71a and b) went through a steep drop to 20-30% photoluminescence within the first hour of exposure, followed by relatively stable curves up to 8 h. Supported $\operatorname{Ru}(\operatorname{bpy})_3^{2+}$ (darker orange curves in Figure 71a and b) showed a slight drop to 80-90% luminescence within 30 min, followed by stable emission profiles up to 8 h. In a 24 h period of exposure to light and oxygen, the supported $\operatorname{Ru}(\operatorname{bpy})_3^{2+}$ systems in acetonitrile still conserved 72% of their initial luminescence intensity. This piece of data demonstrates that immobilization led to stabilization against photobleaching for both photosensitizers. In fact, immobilization of dyes is known to increase their stability against bleaching for two main reasons: oligomerization is prevented, hence reduced risk of self-quenching; and bimolecular degradation events are less frequent.^{33, 34}



Figure 71. Photobleaching of a) RB under its optimized reaction conditions, b) Ru(bpy)32+ under its optimized catalytic conditions, and c) Ru(bpy)32+ under RB's conditions for comparison. The results are plotted by percentage of the initial luminescence of each system. Darker curves represent the photoluminescence of supported photosensitizers and lighter curves represent the luminescence of homogeneous systems. Photobleaching was measured by comparing the luminescence of a fresh solution or suspension of the photocatalyst with their luminescence over time when submitted to LED lights at 20°C with O₂ bubbling at 1 atm. Mimicking optimized reaction conditions, the reactors contained 20 mL of 1.5 μM of RB and $Ru(bpy)_{3^{2+}}$ in 2-propanol (a and c) or 5.0 μM of $Ru(bpy)_{3^{2+}}$ in acetonitrile (b).

Moreover, a comparison of the two immobilized catalysts showcased the superior photostability of Ru(bpy)₃/Fe@SiO₂^{T3} over RB/Fe@SiO₂^{T3}. It corroborates the fact that the former remained photoactive upon catalystic recycling while the latter did not; it also points to photobleaching as an important route of catalyst deactivation in our systems. The photobleaching kinetics also demonstrate that Ru(bpy)₃²⁺ felt a more intense stabilization effect against photobleaching than RB upon immobilization, which could stem from the different immobilization strategies that were illustrated in Scheme 23. While Ru(bpy)₃²⁺ is ionically directly attached to the support with the possibility of multiple points of contact, hence closer to the surface; RB is attached to the surface by relatively flexible spacers (aminoethyl groups), with a single point of contact. This immobilization approach approximates the RB system to an interphase catalytic system: the photosensitizer is in a mobile phase, which is attached to a stationary phase, the support. These systems are considered intermediates between homogeneous and heterogeneous catalytic conditions.³⁵ Thus, although both systems are heterogenized, immobilized RB still slightly resembles a homogeneous system because of its increased mobility in solution, which is probably the reason why this system is more susceptible to photobleaching than immobilized Ru(bpy)₃²⁺.

Since oxygen sensitization can generate singlet oxygen and reactive oxygen species (ROS)³⁶ that may lead to photobleaching pathways, we carried out experiments under oxygen-free conditions to investigate the role of ROS. The results can be found in Figure 73 in the appendix for this chapter; they illustrate how the role of O_2 in photobleaching mechanisms is highly dependent on the interplay between the nature of the photosensitizer and the solvent. Although not investigated here, the presence of amine groups on the surface of silica could also influence photobleaching; these groups were added in excess and they may form radical cations upon visible light excitation.³⁷ Additionally, an important implication of these results when it comes to catalysis is in the absolute luminescence intensity values (Figure 74). Light absorption by the supports decreases the initial luminescence intensity of the immobilized photosensitizers. In the case of Ru(bpy)₃²⁺, with the intense drop in luminescence in the first hour, this initial decrease is compensated over time by the stabilization upon immobilization is too drastic to be compensated over time by bleaching stabilization. We also measured catalyst leaching in our systems (section 4.8.4)

and, although present for $Ru(bpy)_3/Fe@SiO_2^{T3}$, our results suggest that it is a minor cause of deactivation in these systems.

4.6 Conclusions

This work investigated basic photochemistry concepts using a benchmark metal-based and a benchmark metal-free photosensitizer. Photosensitizers have different behaviours that can be influenced by several factors including their structure (organometallic or metal-free), interaction with solvents, self-quenching threshold concentrations, quantum yields, immobilization strategies (for supported catalysis), and others.

Nevertheless, we were able to immobilize RB by covalent anchoring on silica-covered iron NPs (Fe@SiO₂) and use it as a photocatalyst, as we had previously shown for Ru(bpy)₃²⁺ immobilized on the same supports by ionic interactions. The heterogeneous catalyst RB/Fe@SiO₂^{T3} was able to perform the singlet-oxygen photo-oxidation of citronellol and it could be recovered from the solution with a magnet. Photoluminescence decay studies showed that photobleaching is an important route of catalyst deactivation in these systems. Immobilizing the photosensitizers on the supports did not only make them easier to separate but also significantly improved their photostability.

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4.8 Appendix B

4.8.1 Surface coverage of photosensitizer on the support

We defined surface coverage as a means to fix the distance between the photosensitizers on the surface of a support and allow comparison between different supports. This was calculated by using the area occupied by a molecule of RB and the BET are of the support. The area of a RB molecule was considered to be that of a circle of diameter equal to the distance between the two farthest atoms on the structure (measured on Avogadro[®]), added by the can der Waalls radii of the two atoms in the extremities.

Area of one RB molecule: $A = \pi r^2 = \pi (1.443nm)^2 = 6.54 nm^2$

Area occupied by one mol of RB molecules: $A = (6.54nm^2) \cdot (6.022 \cdot 10^{23}mol^{-1}) = 3.94 \cdot 10^6 m^2 \cdot mol^{-1}$

 $Surface \ coverage = \left(\frac{(nRB)[mol] \cdot (3.94 \cdot 10^6)[m^2 \cdot mol^{-1}]}{(surface \ area \ of \ support)[m^2 \cdot g^{-1}](mass \ of \ support)[g]}\right)$



Figure 72. RB structure and measurement of its radius used in the definition of surface coverage.

4.8.2 The role of O₂ in photobleaching of the studied systems

The same photobleaching studied reported in the article in Figure 4 were also carried out under oxygen-free conditions. For that, the solutions or suspensions were degassed with 3 freeze-pump-thaw cycles, the reactor was set under vacuum and then filled with argon, and the experiment was performed under argon bubbling at 1 atm (analogous of O_2 bubbling used for catalysis and photobleaching studies). Results are plotted in

Figure 73 Figure 74.

RB in 2-propanol and $Ru(bpy)_3^{2+}$ in acetonitrile under oxygen-free conditions presented more photobleaching than the analogous tests in the presence of ROS, suggesting that oxygen-dependent photobleaching pathways are not significant for our systems. On the contrary, these results indicate that oxygen sensitization inhibits bleaching mechanisms in those cases, likely because they compete with each other to quench triplet state photosensitizer molecules. Renn *et al.* (J. Molec. Phys, 2006, 104, 409-414) found a similar effect in a study of the photochemistry of ionic organic fluorophores embedded in PMMA; the authors suggested that the role of oxygen in those systems is not to oxidize the fluorophores (photobleach), but rather to quench the excited photosensitizer and consequently improve photostability. On the other hand, $Ru(bpy)_3^{2+}$ in 2-propanol suffered higher bleaching in the presence of ROS, suggesting that bleaching by oxidation of the photosensitizer is likely to dominate in this case.

Another interesting observation is that, under our optimized catalytic conditions (RB in 2-propanol and Ru(bpy)₃²⁺ on acetonitrile), the behaviour of the supported and unsupported systems was very similar in oxygen-free conditions: a steep drop in luminescence in the first 30 minutes for homogeneous RB and Ru(bpy)₃²⁺, and a slow and steady decrease for supported RB and Ru(bpy)₃²⁺. Upon the addition of oxygen, we saw similar changes for the immobilized catalysts, but not for the homogeneous ones. Additionally, although O₂ has the opposite effect in the Ru(bpy)₃²⁺ in 2-propanol system, it is still more evident in the homogeneous case than in the heterogeneous one. The low impact of ROS on the immobilized catalysts is probably related to the quenching of ¹O₂ by the surface OH groups of silica since the oscillators of O-H bonds are known to quench ¹O₂ by electronic-to-vibronic energy transfers. (Bregnhoj *et al.*, Phys. Chem. Chem. Phys., 2016, 18, 22946-22961).



Figure 73. Photobleaching under O2 (filled circles) and under argon (empty circles) of a) RB under its optimized reaction conditions, b) $Ru(bpy)_3^{2+}$ under its optimized catalytic conditions, and c) Ru(bpy)32+ under RB's conditions for comparison. The results are plotted by percentage of the initial luminescence of each system. Darker curves represent the photoluminescence of supported photosensitizers and lighter curves represent the luminescence of homogeneous systems. Photobleaching was measured by comparing the luminescence of a fresh solution or suspension of the photocatalyst with their luminescence over time when submitted to LED lights at 20°C with either O2 or argon bubbling at 1 atm. Mimicking optimized reaction conditions, the reactors contained 20 mL of 1.5 μ M of RB in 2-propanol (a and c) or 5.0 μ M of Ru(bpy)₃²⁺ in acetonitrile (b).



4.8.3 Luminescence decay by absolute intensity





Figure 74. Photobleaching of catalytic systems based on RB (a), and $Ru(bpy)_{3^{2+}}$ in 2-propanol (b) and acetonitrile (c), reported by the absolute intensity of luminescence. Darker curves represent the photoluminescence of supported photosensitizers and lighter curves represent the luminescence of homogeneous systems. Full circles show experiments carried out in the presence of oxygen and empty circles, in an argon atmosphere. Photobleaching was measured by comparing the luminescence of a fresh solution or suspension of the photocatalyst with their luminescence over time when submitted to LED lights at 20°C with either O2 bubbling at 1 atm or under argon. Mimicking optimized reaction conditions, the reactors contained 20 mL of 1.5 µM of RB in 2propanol or 5.0 μ M of Ru(bpy)₃²⁺ in acetonitrile.

4.8.4 Catalyst leaching

Leaching was assessed by celite-filtering the heterogeneous photocatalysts after 4h of reaction and measuring the luminescence of the solutions. This luminescence of leached $\text{Ru}(\text{bpy})_3^{2+}$ was 15.1% of the luminescence of a fresh 5.0 μ M Ru(bpy)_{3²⁺} solution in acetonitrile; the luminescence of leached RB was 1.39% of the luminescence of a fresh 1.5 μ M RB solution in 2-propanol. Since the system with more leaching and less photobleaching (*i.e.* immobilized Ru(bpy)_{3²⁺}) was the most stable to reuse, we see leaching as a minor catalyst deactivation route in the studied systems.

The percentage is calculated based on the homogeneous solutions because luminescence intensity decreases upon immobilization (Figure 74). Since the leached species are not immobilized, their luminescence needs to be compared with that of the non-immobilized photosensitizers.

The distinct leaching profiles can be rationalized by the immobilization methods: $Ru(bpy)_3^{2+}$ was attached to the surface of the NPs by ionic interactions because the photosensitizer is a cation and silica is negatively charged at close-to-neutral pH (Kosmulski *et al.*, Adv. Colloid Interface Sci., 2020, 275). The latter, on the other hand, is anionic and was attached to ethylamine-functionalized silica surfaces by the amine groups. The ionic attachment of $Ru(bpy)_{3^{2+}}$ to the slightly negative silica surface seems to be less robust than the covalent attachment of RB to functionalized silica.



4.8.5 Linearity of the luminescence measurements

Figure 75. Luminescence of $Ru(bpy)_{3^{2+}}$ and RB over the range of concentrations used in the measurements for the photobleaching experiments.

5

Trapping hydrogen: Confined catalysis for improved hydrogen borrowing selectivity

5.1 Preamble

In the two previous chapters, we demonstrated how silica coating can improve magnetic photocatalytic systems and studied the effect of support absorption on photocatalytic activity. Moving away from magnetic photocatalysis, this chapter presents another context in which silica shells play a decisive role: confined catalysis. Here, hollow core-shell nanostructures are created using the concepts outlined in Chapter 2, and the concept of confined catalysis also explored in Chapter 2 is applied using this system. We use yolk-shell nanostructures to catalyze the alcohol amination reaction and demonstrate how controlled etching of the shells gives rich morphologies that can be tuned to maximize the yield and selectivity of the process.

This chapter is adapted from an article submitted as a working paper that has not yet been peerreview. All co-authors gave permission to reprint.

Terra, J. C. S.; DeWolfe, J.; Valdez, J. A.; Moores, A., Trapping hydrogen: Confined catalysis for improved hydrogen borrowing selectivity. *ChemRxiv*. **2022**. DOI 10.26434/chemrxiv-2022-24j10

5.2 Abstract

Alcohol amination via hydrogen borrowing is an established method for the clean and simple alkylation of amines with alcohols, which are stable and available in bulk; it also does not require the addition of hydrogen to reduce the imines or the use of coupling agents. A common problem however in those systems is the need to employ additives to prevent stagnation of the product at the imine stage, which indicates inefficient usage of the borrowed hydrogen atoms. In this work, we designed a catalyst series to demonstrate that confined environments can assist with improved selectivity. To this end, we encapsulated Al₂O₃/Ru(OH)_x nanocatalysts inside mesoporous silica in a yolk-shell architecture and were able to trap the hydrogens to increase the amine yield from 12% to 82%, with a 3-fold increase in selectivity without the need of any additive; we found the presence of mesopores in the silica shells to be essential to enable access to the catalytic sites and the yolk-shell gap size to be the key parameter influencing the reactivity of the catalytic system. To the best of our knowledge, this is the first report of a confined hydrogen borrowing reaction, an approach that can be extended to the other types of cascade reactions that produce labile intermediates.

5.3 Introduction

Hydrogenations are present in at least a quarter of all chemical processes.¹ They can happen either through direct hydrogenation, when H₂ is the source of hydrogen atoms; or through transfer hydrogenation, when the hydrogen atoms come from a non-H₂ source.² The latter process, although less atom economical, has the advantage of not relying on hazardous pressurized hydrogen gas.³ A unique type of hydrogen transfer happens when the hydrogen source does not only donate hydrogen atoms but is also involved in an intermediate reaction within the cycle. The *in-situ* formed intermediate can then be hydrogenated in the following step, as it happens in the alcohol amination process (Scheme 25). First, the catalyst oxidizes an alcohol molecule, "borrowing" two hydrogen atoms. The alcohol, now activated as a carbonyl, condenses with an amine or ammonia to form the corresponding imine. Lastly, the catalyst returns the hydrogens to reduce the imine, forming a substituted amine. This is a typical hydrogen borrowing process, also known as

hydrogen auto-transfer.^{4, 5} Alcohol amination is particularly interesting because it gives access to substituted amines from alcohols, which are stable, available, and possibly bio-sourced.⁶



Scheme 25 Amination of alcohols through the hydrogen borrowing mechanism.

An effective hydrogen borrowing catalyst needs to both withdraw and return the hydrogen atoms within the catalytic cycle, so the same system is bound to perform the antagonistic tasks of dehydrogenation and hydrogenation. The first catalysts for alcohol amination were published in 1981 by Grigg *et al.*, using Rh and Ir triphenylphosphine complexes,⁷ and by Watanabe and co-workers, using a Ru triphenylphosphine coordination compound.⁸ Although there are now systems in the literature based on abundant metals,⁹ Ru and Ir catalysts still dominate the alcohol amination literature.⁶

Many alcohol amination catalytic systems are assisted by base additives. Fujita *et al.* for instance reported a [Cp*IrCl₂]₂/K₂CO₃ system that could quantitatively catalyze the coupling of aniline and benzyl alcohol to give the secondary amine (Entry 1, Table 12).¹⁰ The Crabtree and Eisenstein groups performed Density Function Theory (DFT) studies on Fujita's system and found the central role of carbonate as a ligand that accepts a hydride in the alcohol oxidation step, and then returns it to reduce the imine.¹¹ They found that, although the catalyst has the challenging task of performing the two mirroring reactions, the overall process moves forward effectively for two

main reasons: 1) alcohol dehydrogenation via proton transfer followed by β -hydride elimination is preferred over amine oxidation, and 2) the imine is more easily hydrogenated than the aldehyde. The authors also found that the catalyst is not involved in the carbonyl-amine condensation step. The Lang group published an interesting study on a solid catalyst made by pyrolyzing carbon power loaded with *cis*-Ru(phen)₂Cl₂, which formed Ru NPs supported on N-doped carbon.¹² The authors reacted aniline **1** and benzyl alcohol **2** to obtain full selectivity to the secondary amine **3** using KOH as an auxiliary base (Entry 2, Table 12). When NaOH was used as the base, the system gave full selectivity to the corresponding imine **4**. Lang *et coll*. related this phenomenon to the larger radius of K⁺, which could coordinate to the C=N bond on the imine and elongate it, facilitating the hydrogenation step. Using this catalyst based on Ru NPs on N-doped carbon and switching the base between KOH and NaOH, the authors were able to tune the reactivity using several substrates to give either the amine, through the full hydrogen auto-transfer mechanism, or the imine, through what they called the acceptorless hydrogenation coupling reaction.

The use of auxiliaries is however a drawback in the context of Green Chemistry, especially toxic ones like strong inorganic bases. It goes against atom economy (principle 2), as well as principles 3 and 5 which call for less hazardous syntheses and the use of benign auxiliaries.¹³ A very robust auxiliary-free heterogeneous system for alcohol amination is the one developed by the Mizuno group, based on $Ru(OH)_x$ deposited on alumina (Entry 3, Table 12);¹⁴ the authors obtained 90% selectivity to the secondary amine **3** in the reaction of aniline **1** and benzyl alcohol **2**, having the corresponding imine **4** as the sole by-product. Also in the absence of an additional base, our group has catalyzed the alcohol amination reaction with plasma-made Ni/Cu mixed ferrite nanoparticles (Entry 4, Table 12).¹⁵ Although no base was added to the system, the addition of isopropanol as a sacrificial source of hydrogens was essential to improve the selectivity of the system to form the amine, suggesting that stagnation of the cycle at the imine stage might be associated with low availability of hydrogen.



Table 12. Alcohol amination conditions from the literature for the coupling of aniline (1) and benzyl alcohol (2).

[a] mol% of 1; [b] based on 1; [c] under microwave radiation; [d] 10% of total solvent volume.

In fact, the proton and the hydride "borrowed" by the catalyst can recombine and form a labile H₂ ligand, which could detach from the metal center and leave the liquid phase as H₂ gas due to its low solubility in organic solvents.¹⁶ The Crabtree group studied a Ru-catalyzed alcohol amination reaction system and found through DFT studies that H₂ release or retention is decisive in the formation of the substituted amine.¹⁷ Such a finding was corroborated by H₂ detection experiments which showed that low amine selectivity was accompanied by the presence of free H₂ in solution. Cascade reactions such as the N-alkylation of amines with alcohols are indeed challenging processes due to the antagonist tasks given to the catalyst. Mattey et al. took a literal approach and compartmentalized the process in a flow system; the oxidation and reduction pathways were carried out separately by different biocatalysts but interconnected in a flow reactor.¹⁸ Another way to compartmentalize incompatible catalytic systems for cascade reactions is to use hierarchical nanostructures, which can work as multicomponent nanoreactors.¹⁹ These nanoreactors can also induce the retention of intermediates in the proximity of catalytic centers, a strategy that can as well be applied to push the completion of cascade reactions.²⁰ Species confined in nanopores, for instance, have been shown to have slower diffusion rates when compared to the same species in bulk solutions. Such an effect can stem from the similar dimensions of the molecules and the pore openings, which enhances molecule-wall interactions and may even increase the viscosity of confined fluids.²¹ Dong *et al.* used single-molecule fluorescence to study the oxidation of amplex red in 2-3 nm wide cylindrical pores and found diffusion rates of intermediates inside the pores to be 5 orders of magnitude lower than the diffusion in the bulk solution.²² The lower diffusion caused an enrichment of intermediates around the catalytic site, which increased reaction rates. Our group has also worked with catalysis confined in mesopores, more specifically the cascade coupling of an amine, an aldehyde, and an alkyne inside the pores of mesoporous silica MCM-41;²³ the system benefited from the slow diffusion and hence high concentration inside the pores of both released Cu⁺ ions and *in-situ* generated intermediates.

Confined reactions have been used in various contexts to make catalytic systems greener and more efficient,²⁴ but this strategy has not yet been applied to hydrogen borrowing. In this context, here we report for the first time a nanoconfined hydrogen borrowing catalytic system. To the best of our knowledge, we systematically demonstrate for the first time the strategy of trapping a gas intermediate within a nanostructure to improve a cascade reaction system. We created yolk-shell structures by encapsulating nanoparticulated $Ru(OH)_x/Al_2O_3$ in mesoporous silica shells, and applied them as catalysts for alcohol amination. By controlling the morphology of the porous shells and the yolk-shell voids, we were able to tune the selectivity of the system towards the secondary amine without the use of any additive.

5.4 Results and discussion

Our goal was to design a heterogeneous catalyst for the hydrogen borrowing reaction featuring a confined space, hence we were inspired by Mizuno's $Ru(OH)_x/Al_2O_3$ system¹⁴ as a simple and robust core for our design. Commercial spherical alumina NPs (diameter 37.8 ± 25.5 nm, PDI 0.4, details in section 5.8.1) were modified by being dispersed in water with $RuCl_3.3H_2O$ (1 wt% of Ru) and stirred overnight at pH 13.2 (step 1, Scheme 26). The construction of the yolk-shell architecture was based on the methodology reported by Yin and co-workers.^{25,26} The resulting dark gray powder $Ru(OH)_x/Al_2O_3$ was refluxed with PVP (M_w 55,000) to create a sacrificial template layer (step 2, Scheme 26), which was then covered with silica using the Stöber method (step 3, Scheme 26). The silica-coated material was refluxed with PVP (M_w 10,000) to create a second protective layer (step 4, Scheme 26); this second protective layer allowed internal and controlled etching of the silica structure upon treatment with a concentrated NaOH solution (step 5, Scheme

26). Base etching was tested at varied times (2, 3, 4, 5, and 6 h), affording materials $Ru(OH)_x/Al_2O_3@pSiO_2$ E2, E3, E4, E5, and E6. Finally, the catalysts were pyrolyzed at 550 °C (step 6, Scheme 26) to remove template residues, giving materials $Ru(OH)_x/Al_2O_3@pSiO_2$ E2P, E3P, E4P, E5P, and E6P. As a control we also pyrolyzed the non-etched silica-coated material (skipping step 5 in Scheme 26), providing material E0P.



Scheme 26. Multi-step procedure for catalyst synthesis.

The duration of the base treatment had a direct impact on the morphology of the silica shells, as evidenced by TEM images (Figure 76, additional images in Figure 83). The TEM micrographs were chosen as representatives of the final etched and pyrolyzed materials, showcasing the difference between the non-etched catalyst (material E0P, Figure 76a, d) and the etched materials (E2P, E3P, E4P, E5P, and E6P, Figure 76b, c, e, f, g-l). Using commercial Al₂O₃ (diameter 37.8 ± 25.5 nm, PDI 0.4) as the core, we were able to achieve reasonable control over the silica coating and observe clear overall trends. The progressive deterioration of the silica shells is noticeable from the thicker silica coating of on average 32 nm on E2P, which reduces to about 19 nm on E3P, and then to visibly thinner coatings of 9-11 nm after 3 hours of etching (materials E4P, E5P, and E6P, more evident on the higher magnification micrographs Figure 76d-f, j-l, detailed thickness measurements detailed in Figure 84). The progressive deterioration and thinning of the silica shells then evolve to their eventual full dissolution. Analysis of TEM images with 400-



Figure 76. TEM images of the following pyrolyzed catalysts: $Ru(OH)x/Al_2O_3@pSiO_2 EOP (a, g), E2P (b, h), E3P (c, i), E4P (d, j), E5P (e, k), E6P (f, l).$

600 particles per sample reveals a predominance of coated particles on samples etched for 2-5 h (E2P, E3P, E4P, and E5P present 10-20% uncoated particles), and a predominance of 70% of uncoated particles on material E6P, after 6 hours of etching (Figure 85). In addition, the silica shells become textured and the void between the yolk and the shell becomes more apparent after 3 hours of etching, as we will discuss further in this text.

The presence of Ru in the materials was confirmed by ICP-OES and XPS (Figure 86), but particles of Ru metal or oxide could not be consistently identified on TEM micrographs (Figure 87). This observation implies a high dispersion of Ru species throughout the Al₂O₃ surface, as previously observed by the Mizuno group.¹⁴ Also in accordance with Mizuno's findings, XPS analysis showed consistent Ru 3d_{5/2} signals around 281.6 eV, a shift to lower binding energy when compared to the parent material RuCl₃ (282.4 eV).²⁷ No significant shift in the Ru 3d_{5/2} signal was observed upon base treatment, confinement, or pyrolysis at 550 °C. The effect of pyrolysis was however noticeable on TGA. Template mass loss of 4-6% was observed on the non-pyrolyzed materials but disappeared after pyrolysis (Figure 89), proving the effectiveness of the thermal treatment in removing template remnants. The composition and morphology of the nanostructures were also confirmed by EDAX elemental mapping and nanotomography experiments. Elemental mapping confirmed that the core was composed of Al and O (Figure 77b and d) and the shells of Si and O (Figure 77c and d). The low Ru content (around 1 wt% as measured by ICP-OES for $Al_2O_3/Ru(OH)_x$) challenged the detection limits of the EDAX instrumentation but the dotted white circles indicating the alumina cores from the HAADF image (Figure 77e) aid in the visualization of the higher density of signal in these regions when compared to noise in the other regions of the micrograph. The image reconstructed by nanotomography (Figure 78, additional media in section 5.8.8) confirms the yolk-shell structure in three dimensions, showcasing the empty gap between the core and the shell and the porous texture of the silica layer.



Figure 77. EDAX mapping of material $Ru(OH)_x/Al_2O_3@pSiO_2 E5P$: a) HAADF image, b) Al mapping, c) Si mapping, d) O mapping, e) Ru mapping with the contour of alumina cores based on the HAADF image, and f) overlap with the HAADF image with Si and Ru mapping.



Figure 78 Nanotomography of material $Ru(OH)_x/Al_2O_3@pSiO_2 E5P$. The three-dimension image is shown in (a), followed by a two-dimensional intersect image in (b) showcasing the yolk-shell gap. The HAADF image is shown in (c). The threedimensional rotation video can be found in section 5.8.8.

We then studied the ability of the series of produced materials to catalyze the coupling of aniline 1 and benzyl alcohol 2 to produce the corresponding secondary amine 3 (complete alcohol amination mechanism) and imine 4 (incomplete alcohol amination, *i.e.* acceptorless hydrogenation). Pure alumina NPs gave a 10% yield of imine 4 and no amine 3 (Table 14, entry 2), pure silica NPs produced neither (Table 14, entry 3), and the unconfined catalytic system Al₂O₃/Ru(OH)_x afforded 25% imine 4 and 12% amine 3 (Figure 79). These results suggest that alumina contributes to the dehydrogenation step, which leads to imine formation; $Ru(OH)_x$ is essential for hydrogenation, which leads to the desired secondary amine; and silica does not play a direct catalytic role in the system, in agreement with the original findings of the Mizuno group.¹⁴ Moving on to the systems catalyzed under confined conditions (results in Figure 79), we can observe the strong effect of the catalyst's hierarchical structure and morphology. The confined and non-etched material gave lower yields than the unconfined $Ru(OH)_x/Al_2O_3$ system (*i.e.* 7.2% imine 4 and 2.8% amine 3 with EOP). The pyrolyzed and etched catalysts, on the other hand, showed a general trend of increasing yields and selectivities up to a maximum with E5P (5.2% imine 4 and 81.9% amine 3), followed by a decrease with E6P (23.2% imine 4 and 2.3% amine 3). The low activity of the non-etched material EOP indicates the importance of opening the porous structures of the shells to give access to the catalytic sites. On the same lines, non-pyrolyzed materials afforded yields of 21-24% of imine 4 and 4-20% of amine 3 (Table 14, entries 12-14), highlighting the importance of the pyrolysis step during the synthesis of the catalysts to expose the catalytic surface and allow the reactions to proceed. The drastic decrease in activity with catalyst E6P, on the other hand, showcases the importance of the presence of porous silica structures, which are mostly destroyed after 6 hours of base treatment.

The intermediate materials E2P, E3P, E4P, and E5P; although all pyrolyzed and etched, bearing open porous structures, and made mostly of silica-coated structures (80-90% of coated particles); still have distinct catalytic behaviours. E2P and E3P are less active than the unconfined system, while E4P and E5P have improved activity when compared to the unconfined system; the latter affording an impressive 94% selectivity to the desired product. Varying the etching time is a strategy that directly affects the morphology of the silica shells, so we looked deeper at their morphological features to better understand our catalytic systems.



Figure 79. GC yields on amine **3** and imine **4** obtained from the reaction between aniline **1** and benzyl alcohol **2** catalyzed by, from left of right: $Ru(OH)_x/Al_2O_3$ with no silica shell (unconfined), confined and pyrolyzed non-etched material EOP, and confined, catalyzed, and etched (2-6h) materials E2P, E3P, E4P, E5P, and E6P. The dotted line and numbers around the dots represent the selectivity to amine **3**. The only products observed were **3** and **4**. Reaction conditions: 0.25 mmol of aniline, 0.38 mmol of benzyl alcohol, 6 mL of mesitylene, 100 mg of catalyst, 135 °C, 18h, 1 atm of argon. Expanded results on Table 14.

The morphology of the materials was investigated using N₂ adsorption experiments. BET surface areas started at 53 m² g⁻¹ before any etching (E0P) and steadily increased to a maximum of 196 m² g⁻¹ after 3 hours of etching (*i.e.* almost a 3-fold increase); after this 3-hour etching threshold, we noticed a gradual decrease in BET surface area up to 137 m² g⁻¹ with 6 hours of etching (Figure 91a). Total pore volumes followed the same pattern, initially increasing with etching times, from 0.23 cm³ Å⁻¹ g⁻¹ before any etching (E0P), reaching a maximum 0.49 cm³ Å⁻¹ g⁻¹ after 3 hours of etching (*i.e.* over 100% increase in pore volume), followed by a continuous decrease up to 0.18 cm³ Å⁻¹ g⁻¹ with 6 hours of etching (Figure 91b). The initial increase in BET surface area and total pore volume is related to the opening of the silica structures upon base treatment. Longer etching times however caused a progressive deterioration of the silica shells and eventual complete collapse of the silica structures, as observed in TEM, hence the decrease in surface area and pore volume after 3 hours of base etching. It is interesting to note that the inflection point at 3 hours of etching was exactly the point at which the catalysts changed behaviour.

We also obtained DFT pore size distributions using data from N₂ adsorption experiments (Figure 80a-e). An important observation is the presence of mesoporosity (2-50 nm) upon etching, which did not exist in the non-etched material EOP (Figure 95). Moreover, there is a 3.8 nm main peak present in all etched samples, which we have shaded in light gray and labeled region A in Figure 80. Upon longer etching times, this peak persisted but became narrower, and peaks corresponding to larger mesopores (6-24 nm) progressively developed in the area we shaded in darker gray and labeled region B. In fact, the main peak in region A for E2P and E3P (Figure 80a,b) seems to be composed of an overlap of a taller 3.8 nm peak and shoulder peaks around 4-6 nm. With longer etching times (E4P, E5P, E6P, Figure 80c-e), the main peak was maintained and narrowed while the shoulder peaks shifted to region B in the plots. This movement suggests two types of porosity in our samples: one that was created early in the etching process and remained at 3.8 nm, and another type that was enlarged with progressive etching. Yolk-shell structures are indeed known to present two distinct porosity profiles in the same material: the pores within the shell structure and the yolk-shell voids.

While N_2 adsorption has the advantage of measuring the whole of the sample, it does not discriminate between the pores in the silica shells and the voids between the alumina yolk and the silica shell.²⁸⁻³⁰ This discrimination was done through manual measurements of yolk-shell voids in TEM images to obtain the histograms of yolk-shell void size distribution in Figure 80f-j (sample measurements in section 5.8.11). As opposed to N_2 adsorption, TEM measurements only represent a fraction of the sample, but we could selectively measure the yolk-shell voids. The analysis of both methods combined gave precious information about the morphology of our catalysts. The histograms built from measuring TEM micrographs (Figure 80f-j) are analogous to the N_2 adsorption plots but only account for yolk-shell voids, excluding the pores inside the silica shells.



Figure 80. a-e) DFT pore size distribution for the pyrolyzed materials $Ru(OH)_x/Al_2O_3@pSiO_2 EOP$ (non-etched), E2P, E3P, E4P, E5P, and E6P, in this order, obtained from N₂ adsorption experiments. f-j) yolk-shell gap sizes measured from TEM micrographs of the same pyrolyzed materials $Ru(OH)_x/Al_2O_3@pSiO_2 EOP$ (non-etched), E2P, E3P, E4P, E5P, and E6P, in this order. The shaded areas A (lighter gray) represents the small mesoporous range that comprises both pores in the silica shells and smaller yolk-shell gaps, while the shaded areas B (darker gray) represent larger mesopores which come mostly from yolk-shell gaps only.
These plots show an almost exclusive population of region A for E2P and E3P (Figure 80f, g), and a shift to region B for more etched samples (E4P, E5P, E6P, Figure 80h-j). This shift of the histograms to region B is consistent with the shift of the shoulder peaks in Figure 80a-e to region B, indicating that those shoulder peaks likely correspond to yolk-shell voids, which became larger with longer etching times. That leaves the taller peak at 3.8 nm for the pores within the silica shells, which are in the same order of magnitude as the observations of Zhang and co-workers for their protected silica-etching protocol.²⁶ However, contrary to the observations of Zhang *et al.* in their surface-protected SiO₂@void@SiO₂ system, longer base treatment did not cause a noticeable increase in the pore size within the silica shells, but instead it led to an opening of the void size in our surface-protected Al₂O₃@void@SiO₂ system. In our case, the shell porosity was developed up to around 3.8 nm, at which point the base was able to effectively access the interior of the structures and act from the inside out. The 3-hour mark was the limit at which internal etching became dominant over the etching of the pores in the shells. Larger cavities contribute less to surface area and pore volume, corroborating the fact that the 3-hour threshold is the inflection point at which pore volume and surface area begin to decrease in our series of materials.

It is interesting to note that the jump in catalytic activity and selectivity happens after the 3-hour etching mark, exactly when the surface area and total pore volumes inflected and the porosity profile showed the presence of larger yolk-shell voids (region B in Figure 80). With the more open structures, catalyst E4P brought the amine selectivity up to 74%, more than doubling the 30% observed for its counterpart E3P. Catalyst E5P, with even more open voids than E4P, was more efficient and afforded a selectivity of 94% to the complete alcohol amination product. Catalyst E6P, on the other hand, presented low yields and a 10-fold decrease in selectivity when compared to E5P, likely due to the dominance of uncoated particles in that case.

Two factors can influence the success of the hydrogenation step, as highlighted in Scheme 27: 1) the presence of imine molecules in the vicinity of the catalytic site, and 2) the retention of H₂ on the catalyst [MH₂]. The confined nanoreactor system in a mesoporous shell can address both factors. First, slower diffusion out of the system increases the residence time of the imine intermediate in the proximity of the metal. Second, slower diffusion of the labile H₂ ligand out of the confined cage can create a local concentration of H₂ molecules, favouring the reverse reaction in the equilibrium [MH₂] \Rightarrow [M] + H₂, as highlighted in the expanded catalytic cycle shown in

Scheme 27; the stability of the [MH₂] adduct is a key point in driving the reaction towards the formation of the amine.¹⁷



Scheme 27. Alcohol amination through the hydrogen borrowing mechanism, highlighting the role of H₂ retention.

In this context, we decided to investigate the release of H_2 gas in our systems in the presence and absence of the confining silica shell. For that, we removed gas aliquots of the headspace of our sealed reaction vials at the end of the reaction cycle and analyzed this headspace by GC-TCD to look for evidence of the lability of H_2 in two of our systems: one catalyzed by unconfined $Ru(OH)_x/Al_2O_3$, and another one catalyzed by confined E4P. We were able to detect H_2 in the first case, while no H_2 was detected in the latter (Figure 95). The presence of H_2 in the headspace of the unconfined system agreed with the findings of the Crabtree group¹⁷ that the loss of hydrogens atoms is related to low amine selectivity (unconfined $Ru(OH)_x/Al_2O_3$ system). The absence of H_2 in the headspace of the headspace of the confined reaction suggested that our confined catalyst was effective in

trapping the hydrogens, leading to a higher concentration of [MH₂] species in the nanoreactor and, consequently, more successful hydrogenations.

Given such catalytic results, it is clear that the confined yolk-shell structure can drive the reaction to high amine selectivities, and its morphology directly affects the outcome of the reaction. The presence of mesopores in the shells is important to allow access to the catalytic site, as shown by the low conversion of E0P, in which the lack of porosity barred access of the substrates to the catalytic sites. Mesopores may also be responsible for maintaining the hydrogen atoms inside the system as indicated by the H₂ measurements; this concentration effect also applies to the imine intermediate. Nanopores and nanochannels are known to have special diffusion patterns when compared to bulk systems. Due to the enhanced interaction of the diffusion stream with the walls of the porous structure, diffusion rates are greatly influenced by adsorption equilibria (moleculewall interactions), as well as molecule-molecule interactions which are also enhanced in confined spaces. Microporous systems experience molecule-wall interactions over the entire pore space, while mesoporous systems experience those interactions in the layers surrounding the walls but also contain a central region with bulk diffusion properties, where molecule-wall interactions are limited or inexistent.³¹ This mesoporous access to the reacting site can hence play a decisive role in systems like ours which rely on a balanced rate between the retention of intermediates in the catalytic site and the release of fully formed products.

Mesoporosity in the shells is however not enough to secure high conversions and selectivities in our system, as one can observe in the low activities of E2P and E3P (Figure 79). The higher catalytic activity observed for E4P and E5P happens when larger yolk-shell voids are created in the structures, which in our case takes place after the 3-hour etching threshold as observed in Figure 80. Thus, in addition to the mesoporous shells, those larger gaps in the 6-24 nm range seem to be a key feature positively affecting reactivity. While the mesoporous shells are responsible for slowing down the diffusion of intermediates, these yolk-shell voids are where the reaction happens; these spaces are the *de facto* nanoreactors, so it is reasonable to expect that their dimensions would powerfully affect reactivity. Our data shows that reaction spaces in the 2-6 nm range (region A in Figure 80, *i.e.* 80% of the measured voids in E2P and 69% of the voids measured in E3P, *versus* about 30% for E4P, E5P, and E6P) are unfavourable for the completion of the alcohol amination cycle in our system specifically. Given that the substrate molecules have flat dimensions in the

0.5-0.6 nm range and the product molecules have about 1 nm diameter, one can envisage the geometrical restrictions for movement within the nanoreactor. Although the concentration of intermediates in the vicinity of the active sites can improve the catalytic system, reactivity is controlled by an intricate diffusion balance since products also should be able to diffuse away. In this context, yolk-shell voids predominantly in region B of Figure 80, in fact mostly in the 6-16 nm range (56-59% for E4P, E5P, and E6P) were revealed as optimal nanoreactor dimensions for our system. E6P however behaved much like the unconfined system Al₂O₃/Ru(OH)_x, probably due to the high amount of destroyed silica shells. Hence, our results showed that, although the limited diffusion through the mesoporous shells is beneficial for this specific catalytic system, overly tight reaction spaces are detrimental.

Our system followed the so-called volcano behaviour: low catalytic activity was observed in tight spaces, which increased with the increasing nanospace size until a maximum catalytic activity, which then decayed when the space was too large and approached bulk (unconfined) behaviour. This is a common reactivity pattern in nanoconfined systems.^{32, 33}

5.5 Conclusions

Confined catalysis is a versatile concept with a wide range of applications. We produced yolk-shell $Al_2O_3/Ru(OH)_x@SiO_2$ structures with porous silica shells and varied yolk-shell gaps using the surface-protected etching methodology. We successfully used those materials to demonstrate the use of confinement to improve hydrogen borrowing by trapping the hydrogens atoms together with the catalysts and *in-situ* generated intermediates inside the mesoporous silica shells. We however found that trapping the intermediates is not enough to trigger the desired reactivity, as our system behaved optimally when the reaction space (*i.e.* the void between the alumina yolk and the silica shell) was mostly in the 6-16 nm range. Our results followed a volcano behaviour, with low activity at smaller yolk-shell gaps, maximum activity at the optimal gap size, and then decreased activity for particles that were over-etched and had lost the encapsulating silica layer. To the best of our knowledge, this is the first study of a confined hydrogen borrowing system, and we foresee confined systems playing a major role in the future not only in hydrogen borrowing reactions but also in cascade systems in general that can benefit from the trapping of labile intermediates.

5.6 Experimental

All chemicals used in this work were acquired from Sigma Aldrich and used as received unless specified.

Synthesis of catalysts

The synthesis of our catalysts consists of 6 steps, according to the scheme in Figure 1. The steps are: 1) modification of Al_2O_3 with $Ru(OH)_x$, 2) templating, 3) silica coating, 4) surface protection, 5) etching with base, and 6) pyrolysis. We started from aluminum oxide NanoArc® AL-0405 99.5% (40-50 nm) acquired from Alfa Aesar as the core of our design. The alumina modification protocol was adapted from Mizuno and co-workers.¹⁴ First (step 1), we calcinated alumina NPs in a tube furnace, ramping to 550 °C at 8.75 °C min⁻¹ and holding at 550 °C for 3 h. Then, calcinated Al₂O₃ (4.0 g) was dispersed in DI water (200 mL) and sonicated with a probe at 20% amplitude for 5 min. In a separate container, we prepared a solution of RuCl₃.3H₂O (0.5 mmol, 103.6 mg) in DI water (50 mL) which was also sonicated with a probe at 20% amplitude for 5 min. We then combined the RuCl₃ with the suspension of alumina NPs and set it magnetically stir at 1000 rpm. With the aid of a pHmeter, the suspension was titrated with NaOH (1 mol L⁻¹) until pH 13.2. The initial pH of the suspensions was around 2.5 and the volume of base needed for the titration varied from 15 to 20 mL across different batches. The alkaline suspension was then stirred for 18h and then centrifuged. The resulting dark gray powder was redispersed in DI water (50 mL) and dialyzed for 48 h. After dialysis, the suspension was centrifugated (supernatant pH 6.5) and either redispersed in DI water (40 mL) for further modification or lyophilized to give a dark gray powder, labeled Al₂O₃/Ru(OH)_x. The next steps in the synthesis were adapted from the methodology of Yin and co-workers.^{25, 26} For templating (step 2), we prepared a solution containing 2.0 g of polyvinyl pyrrolidine (PVP) of molecular weight 55,000 in DI water (20 mL) and added to it a quarter of the previously prepared Al₂O₃/Ru(OH)_x suspension (10 mL). The suspension was sonicated with a probe at 20% amplitude for 5 min and refluxed for 3 h. After cooling down, the product was washed by centrifugation with DI water (4 x 40 mL) to remove the excess PVP 55k and resuspended in DI water (15 mL). For silica coating (step 3), the prepared suspension of Al₂O₃/Ru(OH)_x@PVP55 was added to a 1 L RBF containing anhydrous ethanol (500 mL), DI water (10 mL), and ammonium hydroxide 28-30% (25 mL). We set the suspension to stir magnetically at 1000 rpm and added 5.0 mL of tetraethyl orthosilicate (TEOS). We left the

suspension to stir for 18h, collected the silica-coated material Al₂O₃/Ru(OH)_x@PVP55@SiO₂ by centrifugation, and washed it once by centrifugation with DI water (40 mL). This is material E0, the non-etched catalyst. For surface protection (step 4), we prepared a solution containing 10.0 g of PVP 10,000 (i.e. PVP K15, purchased from Alfa Aesar) in DI water (200 mL). We then suspended the prepared material Al₂O₃/Ru(OH)_x@PVP55@SiO₂ in the PVP 10K solution and refluxed the suspension for 3 h. Moving to silica etching (step 5), once the suspension cooled down, we added to it a freshly-prepared solution of NaOH (1.5 g, micro-pearls acquired from Acros Organics) in DI water (5-10 mL). The alkaline suspension was stirred for various times (2-6 h) and then collected and washed once with DI water (40 mL) by centrifugation, redispersed in DI water (50 mL), and dialyzed for 48 h. After dialysis, the suspension was centrifugated pН (supernatant 6.5) and lyophilized to give а gray powder. labeled $Al_2O_3/Ru(OH)_x@PVP55@SiO_2EX (X = 2-6, the etching time in hours).$ Finally, the powders were then pyrolyzed (step 6) in a tube furnace under argon flow, ramping to 550 °C at 1 °C min⁻¹ and holding at 550 °C for 5 h. The resulting materials are the final etched and pyrolyzed catalysts used in this work, labeled $Al_2O_3/Ru(OH)_x@PVP55@SiO_2 EXP$ (X = 2-6, the etching time in hours). The non-etched material E0 was also pyrolyzed, giving material E0P.

Characterization of the catalysts

The Ru content on sample Al₂O₃/Ru(OH)_x was measured by inductively coupled plasma atomic emission spectroscopy (ICP-OES) on a Thermo iCap 6500 Duo Series Spectrometer. We digested the samples (around 10 mg, triplicate) suspending them in a mixture of concentrated HCl (3 mL) and HF (2 mL) in XP-1500 vessels and leaving them at RT for 30 min; then we introduced the sealed vessels in a microwave digestion system programmed to reach 180 °C in 20 min and hold for 10 min at 600 W. We carried out X-Ray photoelectron spectroscopy (XPS) on samples Al₂O₃/Ru(OH)_x, Al₂O₃/Ru(OH)_x pyrolyzed, and E5P on a Fischer Scientific K α X-Ray spectrometer with an excitation source of Al K α = 1486.6 eV. The binding energies were corrected by referencing the C 1s line to 284.80 eV. The spot size was 200 µm, running 5 survey scans at 200 mV for 50 ms residence times. Specific energy regions analyzed were Al 2p (5 scans, 85-65 eV), O 1s (3 scans, 545-525 eV), and overlapping C 1s and Ru 3d combined (10 scans, 298-276 eV), also at residence times of 50 ms. Deconvolution and peak positionS were determined using the CasaXPS software. We analyzed all samples by transmission electron microscopy (TEM) by deposing DI water suspensions onto a Cu grid with a carbon backing (Electron Microscopy Sciences). They were analyzed on a Thermo Scientific Talos F200X S/TEM operated at 200 keV, with high brightness XFEG Schottky source. Electron-dispersive X-ray spectroscopy (EDAX) was carried out with a SuperX G2 energy dispersive spectroscopy detector comprising four windowless SSDs, with a dwell time of 2 µs per scan for 20 min and a current probe of 500 pA. Data were processed using the software Velox[®]. Electron tomography was carried out using two STEM detectors: High angle annular dark field (HAADF) detector with a camera length of 200 mm. The datasets were obtained using the software SerialEM³⁴ and a tilt range of $\pm 60^{\circ}$ with a tilt step of 2° . The 3D reconstruction was performed using the software IMOD³⁵ with a SIRT algorithm with 10 iterations. The visualization and manipulation of the 3D volume tomography were done using UCSF software Chimera.³⁶ Thermogravimetric analysis (TGA) was carried out on a TA Instruments Q50 machine, sample weight 5-10 mg, heating from RT to 1000 °C at 20 °C min⁻¹, with N₂ flow at the beginning at air flow after 800 °C. N₂-sorption isotherms were measured on a Quantachrome instrument and used to determine porosity (density-functional theory, DFT), and surface area (Brunauer-Emmett-Teller, BET), samples were pre-treated at 100°C for 12 hours. Statistical analysis of yolk-shell voids was done by manually measuring about 100-200 voids with clearly identifiable limits in bright-field TEM images (8-17 micrographs in total depending on the sample); the measurements were done using ImageJ (section 5.8.11). Measurement of the silica shell thickness were carried out similarly, over 100-300 particles (Figure 84). Counting of shellfree particles was carried out using the ImageJ counting tool measuring 400-600 clearly identifiable particles over 4-8 bright-field TEM images, depending on sample (section 5.8.4).

Catalysis

All chemicals involved in the catalytic tests were stored over molecular sieves 3 Å. In a typical experiment, we added aniline (around 0.25 mmol), benzyl alcohol (0.38 mmol), catalyst (100 mg), and solvent mesitylene (6 mL) in an Anton-Paar microwave vial. The reaction mixture was bubbled with argon for 15 min, then sealed and sonicated for 5 min. We then set the vials in an oil bath at 135 °C and magnetic stirring at 1600 rpm. After 18 h, we placed the vials in ice to quench the reaction, centrifuged the contents, washed them out with acetone (2 x 10 mL), filtered the product with celite, added the external standard 1,4-dimethoxybenzene (500 μ L of a 0.41 mol L⁻¹ solution in acetone), and completed the volume to 25.00 mL. The crude was analyzed on an

Agilent 7890A gas chromatographer equipped with a flame ionization detector (GC-FID) and an HP-5ms 30 m x 250 μ m, 0.25 μ m film; the yields of the two main products N,1-diphenylmethanimine and N-benzylaniline were followed using a calibration curve built with the purchased pure products and the external standard. The H₂ released from reactions catalyzed by Al₂O₃/Ru(OH)_x and E4P were analyzed by injecting 100 μ L of the headspace of the sealed vials after 18 h of reaction in an Agilent 6890N gas chromatographer equipped with a thermal conductivity detector (GC-TDC) and using argon as the carrier gas; we used two columns (HP-Plot Q 30 m x 530 μ m, 40.0 μ m and HP Molsieve 5Å, 30 m x 530 μ m, 25.0 μ m) that were valve-switched after 11 min; splitless inlet at 200 °C, detector at 250 °C; oven held at 30 °C for 9 min, then ramped at 50 °C min⁻¹ to 120 °C and held for 8 min.

5.7 References

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5.8 Appendix C

5.8.1 Alumina NPs sizing



Figure 81. Histogram of alumina particle diameters measured from TEM images using Image J.



Figure 82. Measurement of alumina nanoparticles using Image J. The black lines represent the measured diameters.

5.8.2 Additional TEM images of confined materials pre-pyrolysis



Figure 83. TEM images of silica-coated, non-pyrolyzed material E0; and silica-coated, etched, and non-pyrolyzed materials E2, E3, E4, E5, and E6.



5.8.3 Measurement of the thickness of the silica shells

Figure 84. On the left, histograms of silica thickness measurements of E2P, E3P, E4P, E5P, and E6P. On the center and right, sample images showing the measurements with black lines on the silica shells.



5.8.4 Counting of coated and uncoated particles

Figure 85. Sample images of the counting procedure. Uncoated particles were assigned a yellow number and coated particles (even if partially coated) were assigned a white number.

Sample	Number of coated particles	Number of uncoated particles	Total of particles counted	Percentage of uncoated particles
E2P	411	55	466	12 %
E3P	433	52	485	11 %
E4P	422	121	543	22 %
E5P	368	58	426	14 %
E6P	206	486	692	72 %

Table 13. Total number of particles counted to obtain the percentage of silica coverage after varied etching times.



5.8.5 X-Ray Photoelectron Spectroscopy (XPS)

Figure 86. XPS spectra of unconfined $Al_2O_3/Ru(OH)_x$ pre (a) and post (b) pyrolysis as well as confined and pyrolyzed $Al_2O_3/Ru(OH)_x@pSiO_2 E5P$.



5.8.6 TEM images of non-confined materials

Figure 87. TEM images of unmodified Al_2O_3 NPs (a-c), and Ru-containing particles $Al_2O_3/Ru(OH)_x$ before (d-f) and after (g-h) pyrolysis.

5.8.7 Thermogravimetric analysis (TGA)



Figure 88. Thermogravimetric analysis profiles of the non-pyrolyzed and non-etched material RuOH/Al₂O₃@PVP@SiO₂@PVP as well as the etched materials pre and post-pyrolysis. Analyses were carried out from room temperature to 800 °C at a heating rate of 20 °C min⁻¹, starting under N₂ atmosphere and switching to compressed air at 550 °C.



Figure 89. Thermogravimetric analysis profiles highlighting the difference between the pre and post-pyrolysis materials. Analyses were carried out from room temperature to 800 °C at a heating rate of 20 °C min⁻¹, starting under N₂ atmosphere and switching to compressed air at 550 °C.

5.8.8 Nanotomography



Figure 90. Additional angles of the three-dimensional structure of E5P obtained through nanotomography.

Reference for download and visualization of the video:

Terra, Julio (2022): movie1 (1).mp4. figshare. Media. https://doi.org/10.6084/m9.figshare.21719987.v1

5.8.9 Catalysis results

Table 14. Expanded results for the alcohol amination reaction reaction between aniline and benzyl alcohol. The yields presented were obtained by GC-FID using 1,4-dimethoxy bezene as internal standard. Reaction conditions: 0.25 mmol of aniline, 0.38 mmol of benzyl alcohol, 6 mL of mesitylene, 100 mg of catalyst, 135 °C, 18h, 1 atm of argon.

Entry	Catalyst	Yield imine (%)	St. dev.	Yield amine (%)	St. dev.	Selectivity (%)
1	None	0.0	-	0.0	-	-
2	SiO ₂	0.0	-	0.0	-	-
3	Al ₂ O ₃	10.5	0.4	0.0	-	-
4	Ru(OH) _x /Al ₂ O ₃	25.4	0.1	12.4	2.2	33
5	Ru(OH)x/Al ₂ O ₃ Pyrolyzed	25.4	1.8	2.4	0.1	9
6	Ru(OH)x/Al2O3 @pSiO2 E0P	7.2	0.2	2.8	0.2	28
7	Ru(OH) _x /Al ₂ O ₃ @pSiO ₂ E2P	15.8	4.7	3.2	0.5	17
8	Ru(OH) _x /Al ₂ O ₃ @pSiO ₂ E3P	12.5	2.1	5.4	1.7	30
9	Ru(OH) _x /Al ₂ O ₃ @pSiO ₂ E4P	16.2	0.8	46.2	5.2	74
10	Ru(OH)x/Al2O3 @pSiO2 E5P	5.2	1.7	81.9	4.4	94
11	Ru(OH)x/Al2O3 @pSiO2 E6P	23.2	4.9	2.3	0.1	9
12	Ru(OH) _x /Al ₂ O ₃ @pSiO ₂ E4 (non P)	23.7	3.4	4.5	1.7	16
13	Ru(OH) _x /Al ₂ O ₃ @pSiO ₂ E5 (non P)	24.8	2.0	5.1	0.5	17
14	Ru(OH)x/Al2O3 @pSiO2 E6 (non P)	21.2	1.3	20.1	2.1	49

Conversion data is not available. The substrates had a close boiling point to the solvent (mesitylene), hence the difficulty for separation by GC given the high amount of solvent (6 mL) when compared to substrates (20-40 µL before reaction). The only peaks consistently observed and quantifiable were compared to standards and attributed to 1,4-dimethozybenzene, N-benzylaniline, and N-diphenylmethanimine.

5.8.10 Pore volume and surface area

Table S3. DFT total pore volumes and BET surface area for pyrolyzed materials, both non-etched and etched for different times.

Material	DFT Total Pore Volume	BET Surface Area		
	$(cm^3 g^{-1})$	$(m^2 g^{-1})$		
EOP	0.23	53		
E2P	0.36	134		
E3P	0.49	196		
E4P	0.25	162		
E5P	0.22	138		
E6P	0.18	137		



Figure 91. Evolution of a) BET surface area and b) DFT total pore volumes and according to etching time.



Figure 92. N2 sorption isotherms for pyrolyzed catalysts pre-etching (E0P) and etched for varied times (E2P, E3P, E4P, E5P, E6P).

5.8.11 Measurements of yolk-shell voids



Figure 93. TEM images of silica-coated, pyrolyzed material E0P; and silica-coated, etched, and pyrolyzed materials E2P, E3P, E4P, E5P, and E6P. The thick black lines display representative yolk-shell void sizes measured by ImageJ. The yellow arrows in the E2P micrographs was placed to help visualization of the measured lines in the voids. No measurements were done in E0P.



Figure 94. Histograms built from manually measuring yolk-shell voids in TEM images for samples E2P, E3P, E4P, E5P, and E6P using Image J.

5.8.12 Pore-size distribution pre-etching



Figure 95. Pore size distribution of material EOP (non-etched).



5.8.13 H₂ detection

 $\label{eq:Figure 96. GC-TCD analysis of headspace of model alcohol amination reaction catalyzed by (a) non-confined catalyst Ru(OH)_x /Al_2O_3, and (b) confined catalyst Ru(OH)_x /Al_2O_3@pSiO_2 E4P.$

6

Conclusions and future work

6.1 Conclusions

In this thesis, we have used silica-based nanocomposites and explored possibilities of core-shell designs to tackle different aspects of green chemistry through catalysis. We have specifically looked at magnetic supports for photocatalysis and confined catalysis, both using the core-shell design. The silica shells were fundamental in each case and this relatively simple addition completely changed the catalytic processes studied. The versatility of the silica shell architectures also allowed systematic studies and understanding of important parameters that brought improvement for the systems and better alignment with the principles of green chemistry.

We started by introducing silica chemistry, nanoarchitectures, and synthetic approaches. We then briefly reviewed photocatalysis and magnetic catalysis, highlighting the challenges in combining the two features and the possible advantages, specifically the possibility of designing highly efficient flow photocatalytic systems with magnetic stations for in-line catalyst recycling and enhanced light penetration. Still in the introductory chapter, we have extensively reviewed the field of confined catalysis in porous and encapsulated nanostructures for more sustainable catalysis, and we have shown with several examples from the literature that confined catalysis is a tool with enormous potential to be explored in green chemistry.

In chapter 3 we produced magnetic nanosupports to be used in visible light photocatalysis, having developed one of the few systems in the literature that combined those two properties to be used

in fine chemistry. Furthermore, the precise design of the silica nanoshells allowed, for the first time in the literature, a systematic demonstration of the effect of the absorption of light by supports in photocatalysis and how this competition for photons with the photosensitizer affects photocatalytic activity.

Chapter 4 expanded the system used in chapter 3 to a new photosensitizer, which operates in a different range of visible light and was immobilized onto the supports using another approach. This system was also magnetically recoverable and photoactive, showcasing the versatility of the silica-coated supports. The effect of light absorption was similar for this system, corroborating the fact that such an effect is indeed inherent to the supports themselves, independent of the photosensitizer or immobilization method. We also studied the photostability of the catalysts and confirmed that immobilization makes photosensitizers more resistant to photobleaching, but the extent of this stabilization might depend on certain factors including how the photosensitizers are attached to the surface of the support.

Chapters 3 and 4 together demonstrate the robustness and versatility of iron-coated silica nanoparticles as magnetically recoverable supports that are compatible with photocatalytic systems. This system can potentially be a platform for the immobilization of several different photosensitizers to perform all sorts of photochemical reactions.

The subject of study was then changed in chapter 5, in which we investigated confined catalysis but still took advantage of meticulously designed silica shells. We investigated the alcohol amination reaction, confirmed that the escape of borrowed hydrogens is a possible reason for low amine selectivities, and were able to improve this feature by trapping the reaction inside mesoporous silica shells, in a yolk-shell architecture. In our optimized systems, we observed an increase in amine yield from 12% to 82% and a 3-fold increase in selectivity when compared to our unconfined reference catalyst. More than developing an efficient catalytic system that produces substituted amines without any additives, we also systematically studied the effect of the hollow core-shell morphology and found that directly impacts reactivity. Mesoporosity in the silica shells was necessary for catalytic activity and an internal spacing of 6-16 nm between the nuclei and the shells provided optimal catalytic activity. In this study, we have developed a general approach that can be used for different hydrogen borrowing systems, as well as other cascade reactions.

Green chemistry is a vast field of study which it can be approached from different points of view and types of expertise. We approached it in a unique way throughout this thesis, demonstrating that the precise design of core-shell silica nanostructures can be used to improve catalytic systems in the search for greener chemical processes.

6.2 Suggestions for future work

Society depends on manufactured chemicals, but the current chemical industry relies heavily on non-renewable feedstocks, highly reactive and hazardous reactants, scarce precious metals, highly wasteful methods, and many times energy sources that unsustainably emit greenhouse gases. These practices have been challenged by the Green Chemistry community for decades and will continue to be, hence future work in the general field of catalysis for green chemistry is enormous, urgent, and necessary. There are also specific directions in which the projects outlined in this thesis can be furthered and made more impactful.

The supports developed in chapter 3 responded to a magnetic field in the whole range of silica coverage, but only the one with the least amount of silica (Fe@SiO $_2^{T3}$) could be recovered using simple neodymium magnets. This issue can be approached in three different parts: 1) the magnetic recovery setup, 2) the coating shell, or 3) the photosensitizer. First, a direct improvement without changing the photocatalytic system itself would be the use of more powerful magnetic setups. Second, one could look at the design of the shells, either changing their morphology or composition. One option is the development of porous silica shells to cover the magnetic nuclei instead of dense ones; the mesoporous shells would have a lower silica-to-iron mass ratio comparable volume, so they could potentially be active in shielding the core's absorption while adding less mass to be dragged during magnetic decantation. A second option would be the use of a more reflecting shell material such as titania (TiO₂) instead of silica, which could be equally or more shielding than the silica shells with thinner coatings; this approach comes however with the inconvenience of a less controlled sol-gel chemistry for titanium dioxide. Finally, one could explore photosensitizers that absorb infrared light, which would not suffer from competition with the high visible light absorbing magnetic nanoparticles; the coating of the magnetic nanoparticles could even be dispensed in this case, or thin layers could be used provide a functionalizable surface.

Chapter 4 could benefit from the exploration of a library of photosensitizers to test the effect of absorption wavelength. In addition, a more direct comparison and a more assertive conclusion would have been possible by comparing different photosensitizers immobilized by the same immobilization method; for instance, using a modified ruthenium (II) tris(bipyridine) structure that includes a site for covalent anchoring could clarify the question of the effect of immobilization on photobleaching.

Chapter 5 is a proof-of-concept study that tests one model reaction in the confined system, but it could be expanded to a large scope of alcohol amination substrates or other hydrogen borrowing systems. More broadly, the strategy has the potential to be a general method to improve cascade reaction systems that suffer from labile and gas intermediates that can easily detach from catalytic centers. This study would also benefit from theoretical calculations of diffusion rates under the different confined systems, but this step is made difficult by the heterogeneity of the nanoreactors which is inherited from the highly irregular alumina nuclei. An improvement on this aspect would be the utilization of less polydisperse nuclei, which could provide more regular coatings and spacings and hence and more accurate study of the effects of nanoconfinement on those systems.