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CHEMICAL REACTIONS INSIDE CARBON NANOTUBES

Scott A. Miners, MSci

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Abstract

The work presented in this thesis describes the development and application of strategies to evaluate the influence of extreme confinement within narrow single-walled carbon nanotubes (SWNT) on the pathways of preparative chemical reactions. Methodologies to reduce carbon nanotube length were critically assessed in order to aid the access and egress of reactants and products to and from the SWNT internal channel during confined reactions. A reliable procedure for the encapsulation of organic molecules within carbon nanotubes was developed utilising a novel fractional distillation procedure which exploits the effect of nanoscale confinement on the phase behaviour of liquids. Confinement of the halogenation of *N*-phenylacetamide within SWNT demonstrated, for the first time, that narrow SWNT are effective hosts for chemical reactions on a preparative scale in the absence of metallic catalysts. The selective formation of the *para*-brominated regioisomer improved from 68 to 97% as a direct result of confinement. Furthermore, the confinement of a range of azide-alkyne 1,3-dipolar cycloaddition reactions within SWNT showed a consistent increase in selectivity for the 1,4-triazole (up to a 55% increase). The magnitude of this effect can be tuned by varying the SWNT diameter or the steric bulk of the reactant substituents. In addition to the dominant steric factors, the results herein suggest that the electronic properties of carbon nanotubes induce an additional, more subtle influence on selectivity. Investigating the autocatalytic Soai reaction in the presence of carbon nanotubes demonstrated, on a fundamental level, that the helicity of SWNT induces an effect on the formation of chiral molecules. Since carbon nanotubes exist as a racemic mixture of *P* and *M* enantiomers, their presence has a symmetrising effect whereby an enantioselective Soai reaction affording 90% *ee* becomes racemic upon the addition of (6,5)-SWNT. These results clearly demonstrate the ability of carbon nanotubes to influence the properties of preparative chemical reactions.

Publications

Much of the work presented in this thesis has been published in peer-reviewed journals.

- (1) Graham A. Rance, Scott A. Miners, Thomas W. Chamberlain and Andrei N. Khlobystov, "The effect of carbon nanotubes on chiral chemical reactions," *Chemical Physics Letters*, 2013, **557**, 10-14.
- (2) Scott A. Miners, Graham A. Rance and Andrei N. Khlobystov, "Regioselective control of aromatic halogenation reactions in carbon nanotube nanoreactors," *Chemical Communications*, 2013, **49**, 5586-5588.
- (3) Scott A. Miners, Graham A. Rance, Alessandro La Torre, Stephen M. Kenny and Andrei N. Khlobystov, "Controlled oxidative cutting of carbon nanotubes catalysed by silver nanoparticles," *Journal of Materials Chemistry C*, 2014, **2**, 8357-8363.
- (4) Scott A. Miners, Graham A. Rance and Andrei N. Khlobystov, "Chemical reactions confined within carbon nanotubes," *Chem. Soc. Rev.*, *submitted*.
- (5) Scott A. Miners, Graham A. Rance and Andrei N. Khlobystov, "Cycloaddition reactions inside carbon nanotubes," *manuscript in preparation*.

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List of Acronyms, abbreviations and symbols

Acronym, abbreviation or symbol	Definition
@	[...] encapsulated within [...]
AD	Arc discharge
AgNP	Silver nanoparticle(s)
AuNP	Gold nanoparticle(s)
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
C ₆ D ₆	Deuterated benzene
CB	Carbon black, amorphous (commercial support)
CDCl ₃	Deuterated chloroform
CNT	Carbon nanotube(s)
CoMoCAT	Cobalt/Molybdenum-catalysed
Cp	Cyclopentadiene
Cp*	Pentamethylcyclopentadiene
CuNP	Copper nanoparticle(s)
CVD	Chemical vapour deposition
d _{crit}	Critical van der Waals dimension
DFT	Density functional theory
DMSO- <i>d</i> ₆	Deuterated dimethylsulfoxide
d _{NT}	Nanotube diameter
d _{NT} ^{int}	Van der Waals diameter of nanotube internal cavity
dopa	3,4-dihydroxyphenylalanine
DWNT	Double-walled carbon nanotube(s)
E _A	Activation energy
EDG	Electron-donating group
EDX	Energy-dispersive X-ray
<i>ee</i>	Enantiomeric excess
E _{EXT}	Energy required for extraction from CNT internal cavity
EWG	Electron-withdrawing group
FeNP	Iron nanoparticle(s)
FMO	Frontier molecule orbital
GCMS	Gas chromatography mass spectrometry
GNF	Graphitised carbon nanofibre
HiPCO	High pressure carbon monoxide disproportionation
HMOR	H-mordenite zeolite
HOMO	Highest occupied molecular orbital
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
I _D :I _G	Intensity ratio of the D and G bands in Raman spectroscopy

ⁱ Pr	Iso-propyl
IR	Infrared
L _{FG}	Length of functional group
L _{NT}	Length of carbon nanotube
LUMO	Lowest unoccupied molecular orbital
m/z	Mass/charge ratio
M ₁₀₀₀ /wt%	Mass residual remaining at 1000°C after air oxidation
mp	Melting point
MWNT	Multi-walled carbon nanotube(s)
NiONP	Nickel oxide nanoparticle(s)
NMR	Nuclear magnetic resonance
NP	Nanoparticle(s)
NT	Nanotube(s)
PdNP	Palladium nanoparticle(s)
PTFE	Poly(tetrafluoroethylene)
PyHCl ₂ Br	Pyridinium dichlorobromate
R _f	Retention factor
S _{1,4}	Selectivity for the 1,4-triazole
ⁱ S _{1,4}	Selectivity for the 1,4-triazole in the initial extraction
^T S _{1,4}	Selectivity for the 1,4-triazole after total extraction
SPR	Surface plasmon resonance
SWNT	Single-walled carbon nanotube(s)
^t Bu	Tertiary-butyl
TEM	Transmission electron microscopy
TGA	Thermogravimetric analysis
TLC	Thin layer chromatography
T _{ox}	Temperature of oxidation
t _{ox}	Duration of oxidation
UV-vis	Ultraviolet-visible

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1. Chemical reactions confined within carbon nanotubes

1.1. Chemical reactions in confined space

One of the most important aims of a chemist is to develop, understand and apply new methodologies to control reaction pathways and thus the outcome of chemical reactions. Historically, a myriad of methods have been developed to achieve this by the understanding and careful control of temperature, pressure, solvation, concentration, charge transfer and other variables and hence our capacity to manipulate chemical transformations is ever improving. One such tool, only adopted more recently by synthetic chemists, is the confinement of guest species within a supramolecular host. Restricting the available spatial volume down to the nanoscale can affect the physical properties of molecules, for instance the phase behaviour of confined water,¹ as well as the underlying mechanisms and thermodynamics of subsequent chemical transformations.² This offers increased reaction rates, improved selectivity and often facilitates milder reaction conditions. This approach, demonstrated so elegantly by the unparalleled efficiency of enzymes, has received increasing interest from chemists attempting to wield such control over synthetic chemical transformations.^{2, 3}

Conceptually, nanoscale confinement can influence reaction pathways through various pairwise interactions between the host nanostructure and either the reactant, transition state or product of a reaction (**Table 1.1**), while interactions with the confined catalyst also become important in catalysed processes. Favourable interactions between the host nanoreactor and encapsulated reactants can increase the local concentration or effective pressure, as compared to the bulk phase, thus increasing reaction rates.⁴ Stabilisation of transition states by favourable interactions with the host nanoreactor can act to reduce the activation energy barrier, also improving reaction kinetics.⁵ Electronic interactions between

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metal catalysts and the host nanostructure can subtly alter the electronic state, and thus catalytic activity.⁶ Furthermore, the anchoring of catalysts to a nanostructured support can stabilise the catalyst to sintering, coalescence and poisoning, thus prolonging activity. Moreover, the confined space within nanoreactors can enhance selectivity by altering the relative stability of one product over another.^{7,8} Alternatively, unfavourable interactions with product molecules may aid the efficient egress of product molecules back into the bulk phase,⁹ reducing the local concentration of products, thereby improving kinetics and facilitating higher catalytic turnover.

Table 1.1 The potential effects of confinement in nanoreactors on chemical reactions, described by pairwise interactions of the nanoreactor with reactants, transition states, products and catalysts respectively.

Reactant	Transition state	Product	Catalyst
Increased local concentration - increased reaction rate	Stabilisation of transition state, reducing activation energy barrier	Confined space promotes selective formation of one product over another	Enhanced stability of catalyst, thus prolonging activity
Arrangement of reactants facilitates desired reaction		Unfavourable interactions facilitate egress of product molecules	Electron transfer alters catalytic activity
Charge transfer effects acting to reduce activation energy		improving kinetics and turnover	

While some interactions offer merely practical advantages, such as prolonged catalyst stability and recyclability, many of these interactions have the potential to alter the underlying thermodynamics of the desired reaction. Indeed, consideration of a reaction profile in confinement highlights potentially drastic differences compared to the same reaction in the bulk phase (**Figure 1.1a**). By altering the stability of reactants, transition states and products, the activation energy barrier and overall enthalpy of the desired reaction can be profoundly influenced by nanoscale confinement. For instance, the Menshutkin amine alkylation reaction is predicted to be promoted within narrow SWNT, by the stabilisation of charge-separated products by the highly polarisable host carbon nanotube, thus reducing both the activation energy and endothermicity of the reaction.⁵ By the same principle, confinement can induce selectivity in an otherwise unselective reaction if specific

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interactions with one product over another introduces a significant discrepancy between the energy barriers to the formation of multiple products (**Figure 1.1b**).

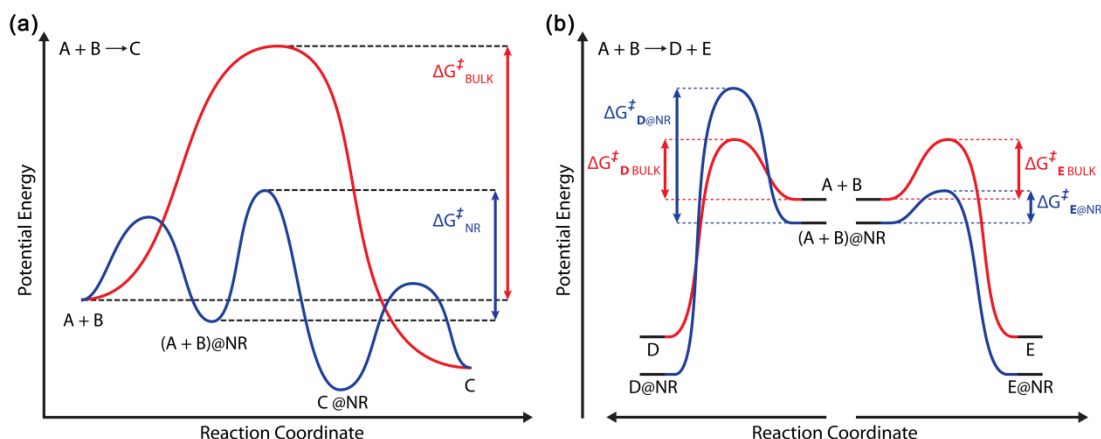


Figure 1.1 Reaction energy profiles comparing hypothetical reactions in the bulk phase (red) and confined at the nanoscale (blue) within a nanoreactor (@NR) (a) Reaction of A and B to form product C. There are more stages to the confined process due to the necessary encapsulation of reactants and release of products. Crucially, the stabilisation of the transition state by the host nanoreactor can act to decrease the energy barrier to the formation of product C ($\Delta G^{\ddagger}$, Gibbs free energy of activation). (b) The unselective reaction of A and B to form both D and E. The identical energy barriers to the formation of each product are altered by selective interactions to either stabilise one product (E@NR) or destabilise another (D@NR). This makes the formation of one product favoured within the nanoreactor (product E), affording increased selectivity in confinement. Adapted from Koblenz *et al.*¹⁰

Depending strongly on the specific encapsulated species and nanoreactor morphology, the influence of nanoscale confinement acting to increase or decrease the potential energy of reactants, transition states and products, is extremely difficult to predict, as is the effect of such changes on the outcome of a given reaction. In addition to thermodynamics, the kinetics of confined reactions require more complex consideration than traditional bulk phase reactions. The confined reaction involves multiple steps, namely the encapsulation of reactants, subsequent confined reaction and extraction of products, each of which introduces an energy barrier and enthalpy change. In the hypothetical example given (**Figure 1.1a**), each of the energy barriers is reduced in comparison to the bulk phase, facilitating a potentially enhanced reaction rate upon confinement. However, the overall kinetics of confined reactions depend on a summation of each step and most crucially, the energy barrier to the rate-determining step coupled with any diffusion limitations. For instance, even

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if the confined reaction has a reduced activation energy compared to the bulk phase reaction facilitating enhanced rates, the observed reaction kinetics may still be significantly retarded upon confinement if reactant encapsulation or product extraction steps are slow due to a high energy barrier or diffusion limitation.¹⁰ Therefore, the effect of nanoscale confinement on a reaction can be complex and is often critically dependent on a multitude of factors, most principally the specific reaction species and nanoscale host.

A range of both natural and synthetic supramolecular structures, including cyclodextrins, cavitands, zeolites and supramolecular co-ordination cages have been demonstrated as effective hosts for a variety of chemical reactions offering enhancements in kinetics and selectivity.^{2, 10-12} Supported by this more established field of molecular encapsulation, carbon nanotubes have more recently become recognised as effective nanoscale hosts for chemical reactions. Carbon nanotubes (CNT) possess many interesting properties which present huge potential when considered as nanoreactors.³ High thermal stability¹³ (up to 2800°C in vacuum and 700°C in air) and mechanical robustness^{13, 14} (10-100 times that of steel) can allow confined reactions to be carried out under harsher conditions without risking damage to the host CNT. Although shown to be susceptible to functionalisation by certain reagents,¹⁵ carbon nanotubes are relatively inert structures, remaining unreactive under most reaction conditions as a desirable host should. Furthermore, the curvature of the sp²-hybridised carbon lattice in CNT causes the concave interior surface of the nanotube to be even less reactive than the convex exterior due to the distortion of π -orbitals.¹⁶ The synthesis of carbon nanotubes on the bulk scale is facile in comparison to most molecular host structures and is becoming increasingly controlled;^{17, 18} for instance, varying synthetic parameters allows the nanotube diameter to be tuned to suit the desired guest species.¹⁹ Lastly, the encapsulation of species within carbon nanotubes relies solely on ubiquitous van der Waals interactions^{20, 21} which are almost universal and, due to the intimate contact between the guest-molecule and the host CNT, can be of considerable magnitude

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(e.g. energy of encapsulation for C₆₀ within SWNT can be as high as 3 eV per molecule).²² This highlights the potential of carbon nanotubes to host a plethora of chemical reactions.

The term carbon nanotube can encompass a range of related structures of varying morphology, each with distinct properties, which are important to distinguish in the context of confined reactions. The simplest such nanostructure is the single-walled carbon nanotube (SWNT, **Figure 1.2a**), consisting of a single sheet of sp²-hybridised carbon, rolled into a cylinder. These structures are typically very narrow, with diameters from 0.7 - 2 nm, and possess an extremely high surface area. Double-walled carbon nanotubes (DWNT) are similar in dimensions to SWNT, but with an additional concentric CNT layer. Due to the narrow diameters, confinement effects can be more pronounced within SWNT, and to a certain extent DWNT, as a consequence of the more intimate host-guest contact. However, these extremely narrow structures may present problems with access and egress of molecules to and from the interior cavity. Therefore, the most commonly used carbon nanoreactor is the wider multi-walled carbon nanotube (MWNT, **Figure 1.2b**) consisting of several concentric CNT. MWNT are more robust structures than SWNT with larger internal diameters (typically 4 - 20 nm), thus providing more readily accessible interior cavities; however, the less intimate host-guest contact can reduce the effect of confinement on encapsulated species and reactions. A further class of carbon nanostructure is the graphitised carbon nanofibre (GNF, **Figure 1.2c**), with a structure not strictly identical to carbon nanotubes despite them often being described in the literature as wide MWNT. These nanostructures consist of graphitic truncated cones, stacked together to form a large cylindrical nanostructure with an internal cavity typically between 50 - 100 nm in diameter and often including graphitised outer layers of sp²-hybridised carbon enveloping the stacked cones. While the large internal volume means access to the internal channel is almost unrestricted, confined species can experience a significantly reduced effect of confinement compared to SWNT, unless enhanced local confinement is observed at the internal corrugated substructure consisting of few nm high step-edges.

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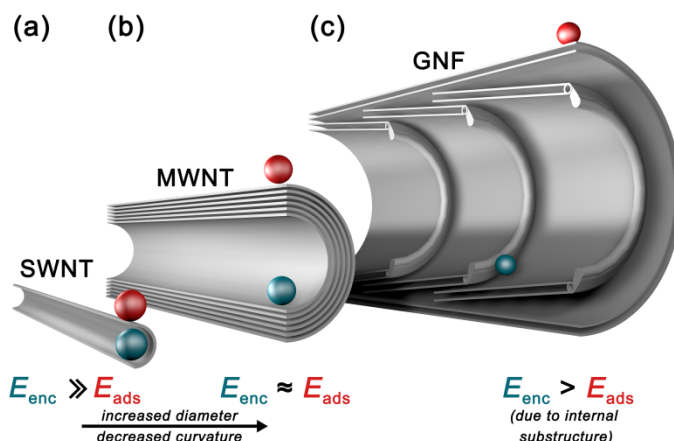


Figure 1.2 (a-c) Cross-section schematics of the three main carbon nanotube morphologies (not to scale) showing encapsulated (blue) and externally adsorbed (red) species. Each grey surface represents a sheet of sp^2 -hybridised carbon. (a) Single-walled carbon nanotube (SWNT), (b) multi-walled carbon nanotube (MWNT) and (c) graphitised carbon nanofibre (GNF) where the confined species tend to reside at the internal step-edges caused by the cup-stacked structure, providing local confinement. The difference between the energy of encapsulation (E_{enc} , blue) and the energy of external adsorption (E_{ads} , red) often exhibits a general trend depending on the curvature of the graphitic surface and thus, carbon nanotube diameter. For narrow CNT, the drastic difference in curvature between the concave inner and convex outer surfaces results in the energy of encapsulation being considerably larger than that of adsorption ($E_{enc} > E_{ads}$) due to a more intimate contact and hence greater van der Waals interaction. However, as CNT diameter increases (*i.e.* reduced curvature) this difference is reduced until the internal and external interaction energies become commensurate. This general trend for carbon nanotubes does not always hold true for GNF whereby, despite the large diameter, the internal step-edge substructure provides an increased van der Waals interaction in comparison to the smooth external surface.

Due to the diverse range of carbon nanotube morphologies available and the potential advantages of these novel nanostructures as nanoscale hosts, there has been growing interest over the past decade in the use of carbon nanotubes as nanoreactors.^{3, 23-28} However, before evaluating the results of confining chemical reactions within carbon nanotubes, consideration of the general experimental methodologies used to conduct such confined reactions and to reliably evaluate the effects of confinement is critical. Firstly, the reaction locus must be accurately controlled in order to ensure that the reaction occurs within the carbon nanotube. Clearly, for catalytic reactions, the reaction locus can be strongly inferred by defining the location of the catalyst and transmission electron microscopy allows accurate determination of nanoparticle catalyst location in relation to the host nanotube. However, synthetic procedures to direct the selective encapsulation of catalysts within nanotubes, while significantly improved in recent years, still show varying success in some cases. The inherent inhomogeneity of both carbon nanotubes and catalyst nanoparticles inevitably

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results in a proportion of the catalyst remaining adsorbed on the external surface of the carbon nanotube, making it difficult to reliably appraise the properties of encapsulated nanoparticles in preparative synthesis. However, through rigorous statistical measurement of catalyst location, including TEM tilt series and tomographic reconstruction, coupled with optimisation of encapsulation methodologies, it is possible to study trends in chemical properties and reactivity as a result of confinement within carbon nanotubes.

In order to unambiguously determine the effect of confinement within carbon nanotubes on a reaction, whether probing catalytic activity, reaction selectivity or reactant properties, direct comparison is required with a corresponding reaction where confinement effects are not present. The specific nature of this comparison varies between studies, and is always an important factor to consider when appraising the effect of confinement. If possible, the most reliable comparison (*i.e.* the least number of variables) is between that of identical catalyst particles reliably dispersed internally and externally on identical carbon nanotubes. However, the nature of the different synthetic procedures required to achieve this control over catalyst location can result in other variables being introduced, such as the oxidation or chemical functionalisation of the nanotube surface. Alternatively, in order to explore the effect of specific interactions with the CNT nanostructure, direct comparison can be made between catalyst particles encapsulated within CNT and dispersed on alternative carbonaceous supports, such as activated carbon. Although practical when considering potential improvements to industrially relevant processes, both the nature of the non-covalent host-guest interactions and spatial confinement of the catalyst are altered in this case, making the determination of confinement effects less reliable. In some cases, a confined nanoparticle catalyst is compared to a nanoparticle suspension in the absence of carbon nanotubes. This allows the interaction with the carbon nanotube surface to be directly studied, however, the difference between an internally confined and externally adsorbed catalyst is not probed directly. Lastly, a comparison can also be made between a nanoparticle catalyst confined within carbon nanotubes and a comparable bulk scale catalyst; however,

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this is the least useful methodology as nanoparticulate catalysts exhibit drastically altered properties to that of the bulk so the effect of confinement within the CNT could not be determined. Ideally, a combination of these methodologies allows more reliable conclusions to be drawn on the fundamental interactions behind potentially complex confinement phenomena by separately probing the individual components which comprise the overall effect of confinement. This approach, therefore, yields the most informative studies in the field. Unfortunately, there is no uniform approach to encapsulation procedures or methods to measure the activity or selectivity of confined catalysts and therefore, consideration of methodology is vitally important when comparing the results of different studies within this field.

1.2. **Chemical reactions inside catalytic carbon nanoreactors**

In spite of the experimental and methodological inconsistencies in the primary literature, numerous excellent studies have been conducted exploring the application of confinement within carbon nanotubes to preparative-scale catalysis. A broad range of chemical reactions (**Table 1.2**) have been studied, summarised herein, providing enhanced control over catalysts and reaction pathways via the confinement effects described in **Table 1.1**. Indeed, one area of catalysis where carbon nanotubes have an advantage over other porous nanostructures is the potential to influence the electronic structure, and thus reduction/oxidation behaviour, of catalyst particles.^{29, 30} This is of particular relevance to carbon nanoreactors, because such phenomena are predicted to be greater for species encapsulated within CNT than externally adsorbed due to the effect of curvature on π -orbital distortion. The unique nanoscale environment within CNT can alter the electronic state of catalyst particles, the magnitude and direction of which is dependent on both catalyst and carbon nanotube and this, in turn, affects catalytic behaviour. Again, whether confinement is an advantage or disadvantage for a particular catalytic process depends on the reaction mechanism and interactions with the specific catalyst and/or reaction species.⁶ This potential to control underlying catalytic

1. *Chemical reactions confined within carbon nanotubes*

activity, coupled with the industrial relevance of metallic oxidation and reduction reactions, led much of the early investigations into carbon nanoreactors to focus on oxidation and reduction reactions, studying the effects of confinement on various transition metal catalysts for a range of hydrogenation and oxidation reactions.

Table 1.2 Summary of preparative reactions confined within carbon nanotubes, including parameters such as carbon nanotube type and internal cavity diameter (d_{NT}^{INT}), catalyst species and nanoparticle diameter (d_{NP}) and the main reported result of confinement within CNT on the outcome of the reaction.

Ref	Reaction Class	Substrate	CNT	d_{NT}^{INT} /nm	Catalyst	d_{NP} /nm	Result of confinement
31	Hydrogenation	Benzene	MWNT	5-10	Pd	1-8	Higher activity than comparable activated carbon and zeolite supports.
32	Hydrogenation	Benzene	MWNT	4-8	Ni	3-7	4.6-fold increase in activity.
33, 34	Hydrogenation	α -ketoester	MWNT	8-10	Pt	3.5	10-fold increase in activity. Enhanced effect of chiral modifier on enantioselectivity. Sensitive to hydrophobic effects.
35	Hydrogenation	α,β -unsaturated acids	MWNT	5-10	Pd	5	Up to 2-fold increase in activity. Enhanced effect of chiral modifier on enantioselectivity.
36	Hydrogenation	Cinnamaldehyde	GNF	20-60	Pd	4-6	Increased selectivity for hydrocinnamaldehyde.
37	Hydrogenation	Cinnamaldehyde	MWNT	10 & 60-100	Pt	2-5	Increased selectivity for cinnamyl alcohol.
38, 39	Hydrogenation	Cinnamaldehyde	GNF	40	PtRu	1.5-3	3-fold increased activity. Cinnamyl alcohol selectivity increased from 35 to 95%.
40	Hydrogenation	Cinnamaldehyde & 1,3-butadiene	MWNT	2-5 & 5-10	Au	1.5-5	90-fold enhancement in TOF. Increased selectivity for hydrocinnamaldehyde.
41	Hydrogenation	Olefins & carbonyls	SWNT	1.5	Ru	1	3-fold reduction in TOF in comparison to activated carbon. Enhanced catalyst stability.
42, 43	Hydrogenation	Methyl acetate	MWNT	4-10 & 20-30	Cu	7-10	Enhanced activity. Subtle effect on selectivity. Narrower MWNT have greater effect.
44	Hydrogenation	CO (syn gas)	MWNT	4-8	Fe	4-8	33% improvement in activity. 50% higher selectivity for C_{5+} hydrocarbons.
45	Hydrogenation	CO (syn gas)	MWNT	5-12	Fe	7-9	Higher selectivity for C_{5+} hydrocarbons. Greater catalyst stability.
46	Hydrogenation	CO (syn gas)	MWNT	8-15	Co	5-10	Higher selectivity for C_{5+} olefins.
47	Hydrogenation	CO (syn gas)	MWNT	10-20	FeN	5-10	Higher catalytic activity.
48	Hydrogenation	CO (syn gas)	MWNT	4-8	RhMn	1-2	10-fold enhancement in activity.

Table 1.2 (*continued*)

Ref	Reaction Class	Substrate	CNT	d_{NT}^{INT}/nm	Catalyst	d_{NP}/nm	Result of confinement
49	Hydrogenation	CO (syn gas)	MWNT	4-8	FeN	4-10	Control of selectivity for hydrocarbon chain length by K and Mn additives.
50	Oxidation	CH ₄	MWNT	4-10	Ni	5-11	Higher activity and catalyst stability.
51	Oxidation	CO	MWNT GNF	⁷ 40	Au	2, 7 & 19	Generally lower activity than externally supported catalysts.
52	Oxidation	CO	MWNT	4-8	Ru	1.8	High catalyst stability and wider operating temperature.
53	Oxidation	Benzyl alcohol	MWNT	ca. 10	MnO ₂	2-4	Higher catalytic activity.
54	Oxidation	Styrene	MWNT	ca. 20	Co	10-15	Increased conversion (50 to 93%) and selectivity for styrene oxide (69 to 93%).
55, 56	Oxidation	Styrene	GNF	ca. 40-70	Cu(salen)	-	Slightly reduced activity. Enhanced recyclability and catalyst separation.
57	Oxidation	Propylene	DWNT MWNT	1-1.5 4-8	TiO ₂	0.2	8-fold enhancement in activity within DWNT.
58	Oxidation	Silane	GNF	ca. 50	Au	6	Drastic change in selectivity towards disiloxane dimer.
59	Oxidation	Toluene	DWNT	1-1.5	Pt	1	Enhanced catalytic activity. Stabilised catalyst.
60	Hydroxylation	Benzene	DWNT MWNT	1-1.5 4-8	PdV	<1-1.5 2-4	Reaction rate improved, particularly within narrow DWNT.
9	Hydroxylation	Benzene	DWNT	1-1.5	Re	<1.5	4-fold enhancement in activity. Enrichment of reactants quantified.
61	Oxidative dehydrogenation	Ethylbenzene	MWNT	4-8	CeO ₂	2-6	Enhanced activity. Reduced CNT length subtly improves conversion.
62	Oxidative dehydrogenation	Ethylbenzene	MWNT	4-8	CeMn	2	Enhanced activity.
63	Oxidation	Cyclohexane	MWNT	ca. 10 nm	Au	3-5	4-fold increase in activity. Slight improvement to cyclohexanol selectivity.
64	NH ₃ synthesis	N ₂ + H ₂	MWNT	4-8	Ru	2-5	Reduced activity in comparison to RuNP adsorbed externally on NT.

Table 1.2 (continued)

Ref	Reaction Class	Substrate	CNT	d_{NT}^{INT}/nm	Catalyst	d_{NP}/nm	Result of confinement
⁶⁵	Decomposition	NH ₃	GNF	20-50	FeCo	11-15	Enhanced catalyst stability. Turnover rate not affected.
⁶⁶	Decomposition	NH ₃	MWNT	10	Ru	2	Effect of confinement not directly probed, due to incomparable catalyst composition.
⁷	Hydrosilylation	Alkynes	GNF	ca. 30-60	Rh	3	Altered regioselectivity for dehydrogenative silylation products, dependant on aromaticity.
⁴	Hydrosilylation	Alkynes	GNF	ca. 40-70	Pt	3	Selective 3.2-fold concentration and thus rate enhancement for aromatic reactants.
⁶⁷	Hydrosilylation	Alkynes	DWNT MWNT GNF	1-2 3-8 40-70	Rh ₄ (CO) ₁₂	-	Regioselectivity altered, magnitude dependent on carbon nanostructure.
⁶⁸	Cycloaddition	Alkyne + azide	GNF	ca. 30-60	Cu	3	Higher catalyst stability and recyclability.
⁶⁹	Cross-coupling	Aryl iodide + aryl boronic acid	GNF	ca. 40-70	Pd	5-9	Enhanced yield and cross-coupling selectivity, depending on reactant substituents.
⁷⁰	Photo-degradation	Methylene blue	MWNT	5 & 11	CdS	4 & 8.5	Activity subtly reduced compared to externally supported catalyst. Higher catalyst stability.
⁷¹	Electrochemical oxidation	Methanol	MWNT	80	Pt	2-4	Enhanced catalytic activity. Greater stability and recyclability.
⁷²	Electrochemical reduction	Oxygen	MWNT	ca. 20	Fe	ca. 15-20	Confinement stabilises catalyst. Reaction occurs at external CNT surface, but confined catalyst alters NT catalytic properties.
⁷³	Electrochemical reduction	Oxygen	SWNT	1.4	P	<1	Confinement stabilises catalyst. Reaction occurs at external CNT surface, but confined catalyst alters NT catalytic properties.
⁷⁴	Electrochemical oxidation	Hydrazine	MWNT	10-15	NiFe	10-15	Confinement stabilises catalyst. Reaction occurs at external CNT surface, but confined catalyst alters NT catalytic properties.
⁷⁵	Nucleophilic substitution	Cp ^{Mn} Mn(CO) ₃	SWNT	1.4	-	-	Nucleophilic attack of oxidised intermediate by MeCN solvent is completely precluded.
⁷⁶	H [•] hydrogenation	1-heptene	SWNT	1.4	-	-	Reduced rate of hydrogenation for confined alkene.

1.2.1. Hydrogenation

The hydrogenation of benzene catalysed by both palladium³¹ and nickel oxide³² nanoparticles (NP) confined within MWNT showed increased catalytic activity as a result of confinement. Such encapsulated PdNP showed higher activity than comparable nanoparticles on both activated carbon and within zeolite porous solids and furthermore, the confined nickel species exhibited a 4.6-fold improvement over the same nanoparticles adsorbed on the exterior of the nanotube, directly confirming the influence of confinement. Temperature programmed reduction measurements of the nickel catalysts indicate the reason for this improvement in catalytic activity. It was found that the confined NiONP is more readily reduced than the externally adsorbed catalysts (at approximately 150°C and 200°C respectively), both of which are more easily reduced than bulk nickel oxide (395°C).³² Clearly, the intimate contact of the catalyst with the internal surface of CNT offers control over the electron density on the metal, thus improving catalytic activity.

The PtNP-catalysed hydrogenation of α -ketoesters showed analogous improvements in catalytic activity as a result of confinement within MWNT, increasing by an order of magnitude.³³ The direct comparison of catalyst particles both confined within, and externally adsorbed on, MWNT with those adsorbed on commercially available activated carbon rather elegantly demonstrates the general trend commonly observed for various reactions within carbon nanoreactors (**Figure 1.3**). The nanotube support provides an improvement in activity in comparison to an amorphous carbon support; however, this enhancement is further amplified when the catalyst is confined within the nanotube.

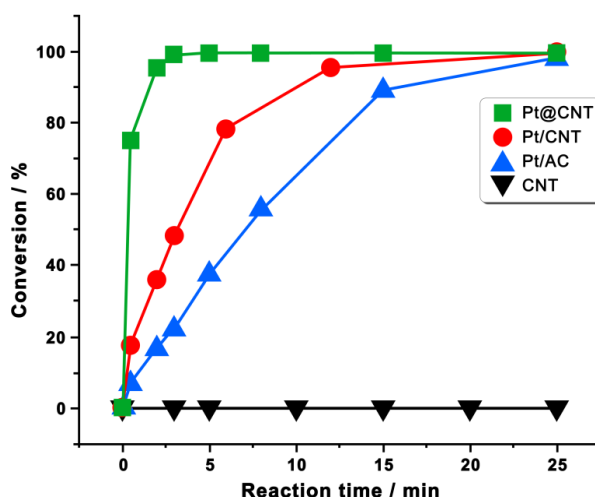
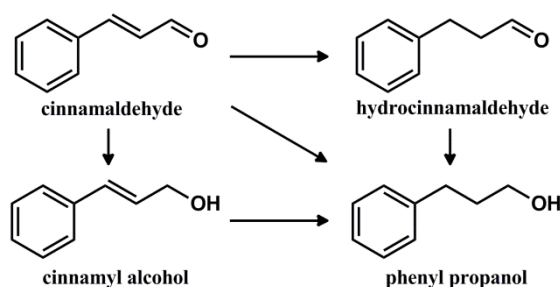


Figure 1.3 The asymmetric hydrogenation of ethyl pyruvate in the presence of MWNT (▼), PtNP on activated carbon (▲, Pt/AC), PtNP adsorbed on the exterior of MWNT (●, Pt/CNT) and PtNP encapsulated within MWNT (■, Pt@CNT). Reproduced from Chen *et al.*³³

It is proposed that this increased activity within CNT is partially due to favourable interaction between the host nanotube and the reactant (**Table 1.1**), whereby the effective local concentration of reactant molecules within the internal cavity of the CNT is enriched relative to that in the bulk solution causing a subsequent change to the rate of the confined reaction. Such a phenomenon is often quite general, not relying on any specific interactions, and thus can affect other aspects of the reaction aside from kinetics. For instance, the enantiomeric excess of a chiral product, a measure of the extent to which the product mixture contains an excess of one particular enantiomer, can also be influenced by confinement. Traditional solution-phase hydrogenation of ethyl pyruvate in the presence of the chiral auxiliary cinchonidine affords up to 75% enantiomeric excess; however, when this reaction occurs within the CNT, the observed enantiomeric excess reaches 96%. This is similarly attributed to an enrichment of cinchonidine within the CNT amplifying its enantioselective effect, and is found to be further influenced by hydrophobic effects³⁴ driving the organic reactants into the CNT from aqueous solution.³⁵ In the related asymmetric hydrogenation of α,β -unsaturated carboxylic acids, confinement of palladium nanoparticles within MWNT similarly enhances catalytic activity and enantiomeric excess consistently for a range of substrates by the same means.³⁶

1. *Chemical reactions inside carbon nanotubes*

Further control of selectivity by pairwise interactions with the CNT (**Table 1.1**) was the aim of various studies into the selective hydrogenation of cinnamaldehyde, which possesses both alkene and carbonyl moieties susceptible to reduction. This, therefore, gives rise to the potential reduction of either the C=C bond to form hydrocinnamaldehyde, the C=O bond to produce cinnamyl alcohol or the stepwise reduction of both to afford phenyl propanol (**Scheme 1.1**).



Scheme 1.1 The hydrogenation of cinnamaldehyde. Selective hydrogenation of the carbonyl affords cinnamyl alcohol, while selective alkene hydrogenation produces hydrocinnamaldehyde. The reduction of both bonds results in the formation of phenyl propanol.

While the most desirable product in this reaction is cinnamyl alcohol, an important product in the food, fragrance and pharmaceutical industry, the reduction of the C=C is more facile giving generally poor cinnamyl alcohol yields. This unselective reaction is sensitive to a range of factors and as such, is a common model reaction with which to study selectivity effects in catalysis.³⁷ Early studies on palladium nanoparticles within GNF exhibited a slight shift towards the selective reduction of the C=C bond to produce hydrocinnamaldehyde.³⁸ Confinement of platinum nanoparticles was claimed to induce the selective formation of cinnamyl alcohol in contrast to the externally adsorbed PtNP, which promoted the complete reduction to phenyl propanol; however, this indirect comparison utilised CNT of different diameter and morphology.³⁹ This highlights a common problem in the field, as direct systematic comparison across different carbon nanotubes is extremely difficult, if not impossible, due to the inherently inhomogeneous morphology and surface functionalisation of these nanostructures. The confinement of platinum-ruthenium alloyed nanoparticles within GNF was shown to induce an increased selectivity for cinnamyl alcohol; the

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selectivity of the confined catalyst reaching 95% in comparison to 35% for the nanoparticles suspension in the absence of GNF.^{40, 41} Along with these considerable changes to selectivity, almost all confined catalysts described showed enhanced activity as a consequence of nanoscale confinement. Indeed, the calculated turnover frequency (TOF) for gold nanoparticles in the hydrogenation cinnamaldehyde was reported to increase 90-fold upon confinement within MWNT, despite only 40% of AuNP estimated to be encapsulated.⁴²

All hydrogenation reactions discussed so far, and indeed the majority of reactions within CNT to date, have been studied within MWNT or GNF possessing relatively accessible inner cavities, *i.e.* at least an order of magnitude larger than a typical organic molecule. Significantly narrower SWNT are often expected to impose greater confinement effects because their internal cavity dimensions (van der Waals internal diameter ~ 1 nm) are commensurate to that of a typical organic molecule (*e.g.* critical van der Waals diameter of benzene ~ 0.7 nm). However, practical problems of molecular transport were expected and as such, examples of catalysis within such narrow carbon nanotubes are limited. The first experimental example of metal catalysis within SWNT was recently demonstrated over a range of hydrogenation reactions catalysed by encapsulated ruthenium nanoparticles.⁴³ A particularly novel aspect of this work is the use of RuNP@SWNT as a catalyst within a continuous flow reactor, allowing convenient scale up to preparative synthesis. The reduction reactions of olefins, butyraldehyde and cinnamaldehyde were conducted with the catalyst showing good activity and in some cases selectivity. For example, the selective hydrogenation of cinnamaldehyde to hydrocinnamaldehyde afforded 99% selectivity at 70% conversion. The catalyst confined within SWNT generally exhibited a reduced turnover frequency in comparison to comparable commercial porous carbon supports (32 and 103 min⁻¹ respectively), attributed to transport resistance within the extremely narrow one-dimensional internal cavity of the SWNT. However, confinement within SWNT imposed a significant stabilising effect on the RuNP, which remained active and unchanged

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for over 24 hours at elevated temperatures where unsupported metal nanoparticles rapidly coalesced.

The confinement of methyl acetate hydrogenation within CNT also exhibited a dependence on nanotube diameter. The hydrogenation of methyl acetate, a low-cost and readily available by-product of various industrial processes, is a novel synthetic route to ethanol, methanol and ethyl acetate. Confined copper nanoparticles showed a slightly enhanced catalytic effect in this reaction compared to comparable nanoparticle catalysts.^{44, 45} Interestingly, MWNT of internal diameter 7 (± 3) nm and 25 (± 5) nm were compared and the highest conversion values were observed within the narrower CNT.⁴⁵ These examples of methyl acetate and cinnamaldehyde hydrogenation within narrow MWNT and SWNT respectively demonstrate the concept that greater confinement effects may be possible within narrower CNT, with the potential drawback of reduced diffusion relative to wider CNT. It is, therefore, important to identify the optimum CNT host for a given chemical process representing a compromise between these two factors. Indeed, the concept of transport resistance, whereby the movement of confined species is hindered by the extreme spatial confinement within narrow CNT, requires further consideration in light of recent contrasting results. The field of nanofluidics, describing the phase behaviour and dynamics of substances at the nanoscale (*i.e.* confined within CNT), repeatedly produces unexpected results.^{1, 46-48} For instance, it has been suggested that the transport of molecules within the internal channels of CNT may be entirely unhindered by their extreme length and narrow diameter.^{47, 49-51} This is in stark contrast with some experimental studies reporting reduced conversion of reactions within narrow CNT due to transport resistance.^{43, 52} However, this review aims to highlight the potential ambiguity in attributing kinetic observations for confined reactions to any sole factor, as this depends critically on multiple aspects such as diffusion, local concentration, catalytic activity or a complex combination thereof.

1.2.2. *Syn gas conversion*

A particularly important family of hydrogenation reactions are the gas-to-liquid strategies to convert syn gas, a mixture of carbon monoxide and hydrogen, to synthetic liquid fuels, the most well-established of which being the Fischer-Tropsch process.⁵³ This can provide an attractive means of recycling gaseous waste products into useful longer-chain hydrocarbons, particularly for transport fuels.⁵⁴ In addition, the renewable production of syn gas from biomass,⁵⁵ or captured CO₂ can be readily integrated within this strategy in the hope of producing a renewable fuel source.⁵⁶ The conversion of carbon monoxide and hydrogen to hydrocarbons is typically rather complex involving multiple parallel synthetic pathways, the activity and selectivity of which are dependent on a multitude of experimental conditions and catalyst properties. Therefore, it has been a popular reaction with which to probe the effects of nanoscale confinement within CNT.

The confinement of iron nanoparticles within MWNT by both Chen *et al.*⁵⁷ and Dalai *et al.*⁵⁸ initially demonstrated the potential advantages of confinement in the Fischer-Tropsch process. The FeNP@MWNT catalyst exhibited superior activity than FeNP externally adsorbed on both CNT and activated carbon supports, with the confined catalyst affording 1.4 and 2.4-fold improvements in CO conversion respectively.⁵⁷ This enhanced activity is attributed to the more facile reduction of the iron oxide species within CNT, as supported by temperature programmed reduction measurements whereby the reduction temperature of the encapsulated iron oxide was 80°C lower than that of comparable nanoparticles on the CNT exterior. The stability of the iron nanoparticles towards sintering was also improved in both cases due to the intimate contact with the CNT interior. In addition to the effect of the CNT host on the catalyst particles, the unique reaction environment within MWNT also afforded a higher selectivity for long-chain hydrocarbons. The yield of desirable C₅₊ products showed an approximately 50% increase due to confinement within CNT, accompanied by a corresponding reduction in undesirable methanol yields. This observation was attributed to the increased contact time between

1. Chemical reactions inside carbon nanotubes

reactive intermediates and the active catalyst, as a consequence of spatial restrictions within the nanotube, which could promote carbon chain growth.^{57, 58} Similar trends upon confinement were also observed for cobalt⁵⁹ and iron nitride⁶⁰ nanoparticles.

An improved selectivity for C₂ oxygenates, predominantly ethanol, during the Fischer-Tropsch process is clearly desirable in providing a convenient, low-sulfur fuel more directly. Pan and coworkers studied the reduction of syn gas catalysed by rhodium-manganese alloy nanoparticles confined within MWNT. Consistent with many of the reported reactions, the confined catalyst exhibited a 10-fold enhancement in catalytic activity, due in part to an increased local pressure of H₂ within the pores of the MWNT.⁶¹ However, more interestingly, the confined catalyst also demonstrated a remarkable 16-fold increase in selectivity for C₂ oxygenates (mainly ethanol) (**Figure 1.4**).

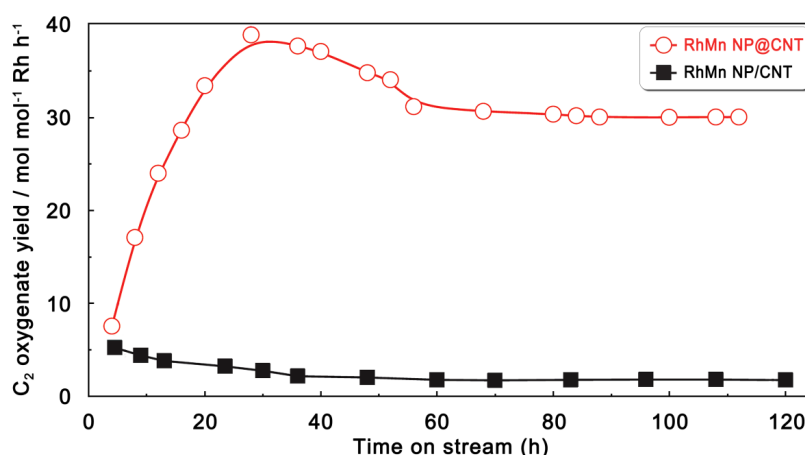


Figure 1.4 The formation of C₂ oxygenates in the hydrogenation of carbon monoxide as a function of time on stream at 320°C. The considerable difference in selectivity is clear between RhMn nanoparticles externally adsorbed on MWNT (black ■) and RhMn nanoparticles confined within MWNT (red, ○). Adapted from Pan *et al.*⁶¹

This drastic increase in selectivity is proposed to be the result of two synergistic effects of confinement. Raman spectroscopy indicates an interaction between manganese and oxygen atoms of CO for the confined nanoparticles which, crucially, is not present for the nanoparticles on the CNT exterior. It is proposed that charge transfer from the Mn to the CNT takes place when the nanoparticles are in contact with the electron-deficient CNT interior, causing the Mn atoms to more readily bind to a lone pair of electrons on the O atom

1. Chemical reactions inside carbon nanotubes

of CO. This not only strengthens the binding of CO to the RhMn catalyst, but also forces the adsorbed CO to align along the catalyst surface, a geometry which facilitates CO dissociation leading to the selective formation of C₂ oxygenates. In contrast, the comparatively electron-rich external surface of the CNT has the opposite effect for the supported catalyst. Hence, two major steps in the formation of ethanol, namely the dissociative adsorption of CO and subsequent hydrogenation, are both promoted by confinement within MWNT. It is the combination of tuned catalyst-CO interactions and increased local pressure of hydrogen which affords the drastic changes to selectivity and activity respectively. This example highlights the potential of confinement within carbon nanotubes to expand the already versatile field of transition metal catalysis allowing the design of catalysts exhibiting as yet unseen activity and/or selectivity. For instance, the novel synergistic effects of confinement within carbon nanotubes combined with the known methods of controlling catalytic activity could, in principle, provide the perfect catalyst for a chemical process. Indeed, this additional variable may necessitate the repeated study of previously investigated phenomena, such as the effect of catalyst additives, in combination with confinement within CNT in the pursuit of optimisation. For example, the effect of both Mn and K additives on the conversion of syn gas to various olefins was studied for iron nitride nanoparticles (FeNNP) within MWNT, where Mn was found to promote the formation of light olefins (C₂-C₄) and K found to enhance selectivity for C₅₊ products.⁶²

In a related chemical process, confined catalysts have also been applied to the *formation* of syn gas. Clearly, all syn gas conversion strategies require an affordable and renewable source of syn gas, for which multiple routes are viable. One such process, methane dry reforming, combines methane with carbon dioxide to produce syn gas, thus consuming two greenhouse gases in the process. Ma *et al.* found that NiONP@MWNT showed enhanced catalytic activity due to the more facile reduction of confined NiONP,⁶³ a relatively common phenomenon found to improve the catalysis of the majority of the aforementioned hydrogenation reactions.

1.2.3. Oxidation

Similarly to hydrogenation, oxidation reactions have been a particular focus of carbon nanoreactor research due to the ability of CNT hosts to influence the electronic properties of metal catalysts whereby, for instance, confined catalysts exhibit enhanced catalytic activity in the oxidation of carbon monoxide,⁶⁴ hydrocarbons^{9, 65} and alcohols.⁶⁶ The oxidation of benzyl alcohol to benzaldehyde can be catalysed by birnessite, a manganese dioxide mineral with intercalated potassium ions, and nanoparticles of this structure were encapsulated within MWNT by Yang and coworkers.⁶⁶ Analogous to previously mentioned studies, the confinement of this catalyst subtly altered the electron density on the catalyst, making the rate determining step, the reduction of Mn^{4+} species, more facile and improving the catalytic activity. The oxidation of toluene catalysed by PtNP further emphasises the importance of the carbon nanotube host in achieving such results.⁶⁷ The direct comparison of PtNP encapsulated within both CNT and a zeolite H-mordenite, possessing linear cavities of comparable diameter to CNT, shows that inorganic nanoscale hosts do not necessarily induce the same confinement effects (**Figure 1.5**). This infers that generic nanoscale confinement is not the sole cause of such increased catalytic activity and specific interactions with the carbon nanostructure are integral for controlling the properties of the catalyst.

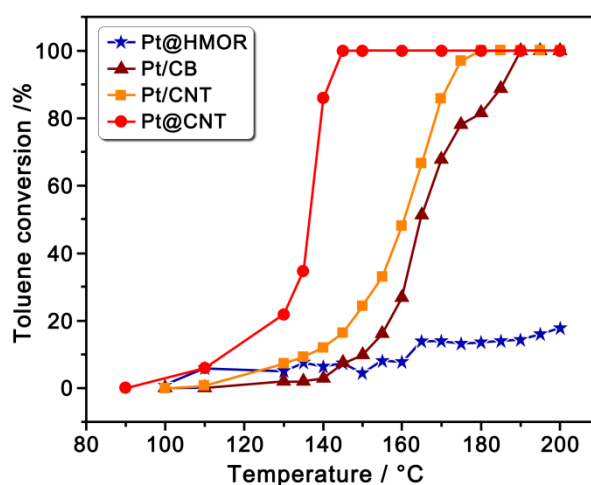


Figure 1.5 Toluene oxidation by molecular oxygen catalysed by platinum nanoparticles on a range of nanoscale supports. PtNP confined within CNT (Pt@CNT, ●) show enhanced activity in direct comparison with comparable PtNP adsorbed externally on CNT (Pt/CNT, ■), adsorbed on a commercially available amorphous carbon support (Pt/CB, ▲) and confined within H-mordenite zeolite (Pt/HMOR, ★). Adapted from Zhang *et al.*⁶⁷

1. Chemical reactions inside carbon nanotubes

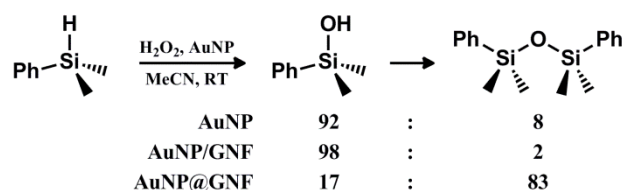
Shi and coworkers investigated the effect of cobalt nanoparticles encapsulated within MWNT on the liquid-phase oxidation of styrene, which can lead to multiple products including styrene oxide, benzaldehyde and phenylacetaldehyde. Confinement within MWNT increased the observed conversion from 50 to 93% and enhanced the catalyst stability, while also improving selectivity for styrene oxide from 69 to 93%.⁶⁸ Lebedeva *et al.* studied the effect of encapsulation within GNF on the activity and stability of Cu^{II}(salen) complexes.⁶⁹ The anchoring of such molecular catalysts to carbon nanostructures allows heterogenisation of previously homogeneous catalysts allowing facile catalyst separation. The non-covalent interactions with the host GNF were vastly improved by introducing the C₆₀ moiety in the structure of the catalyst, which also had a moderately favourable influence on catalytic activity by electron withdrawing effects.⁷⁰ While confinement slightly reduces the reaction rate, the covalent linking of the Cu(salen) catalyst to C₆₀, in combination with non-covalent anchoring within a carbon nanostructured host, provides a heterogeneous catalyst of superior activity, notably improved stability over multiple catalytic cycles and facile catalyst separation by filtration.

The epoxidation of propylene, while not an unselective reaction, was also found to be affected by nanoscale confinement. The confinement of small titania nanoparticles (TiO₂NP) within narrow, double-walled carbon nanotubes (inner diameter 1.0 - 1.5 nm) afforded a remarkable 8-fold increase in catalytic activity.⁷¹ This considerable improvement in conversion provides evidence that greater confinement effects may be possible within narrow diameter CNT. Raman spectroscopy of the TiO₂NP@DWNT shows a red shift of the G⁺ band by 3.5 - 8.5 cm⁻¹, relative to empty DWNT, which can be attributed to electron transfer from titanium dioxide to the CNT.⁷² This partial electron transfer from titanium dioxide to the CNT was only observed for the encapsulated nanoparticles demonstrating that, due to the increased curvature of such a narrow CNT, there is a greater discrepancy between the environment at the interior and exterior surface.¹⁶ Indeed, this work made a direct comparison between the catalytic activity of TiO₂NP confined within narrow DWNT

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(internal diameter 1.0 - 1.5 nm) and wider MWNT (internal diameter 4 - 8 nm). The rate of formation of propylene oxide was measured as 54 and 3.7 g_{PO} kg_{cat}⁻¹ h⁻¹ for DWNT and MWNT respectively, showing a drastic 14-fold increase upon confinement within the narrower carbon nanotube.⁷¹

The gold-catalysed oxidation of silane by hydrogen peroxide suggests that narrow diameter carbon nanostructures are not always necessary in order to observe striking changes in reactivity. The oxidation of dimethylphenylsilane affords dimethylphenylsilanol which can then undergo dimerisation to produce bis(dimethylphenyl)disiloxane (**Scheme 1.2**). The confinement of AuNP within graphitised carbon nanofibres (GNF) induces a drastic change in the ratio of products, causing a switch in selectivity in favour of the disiloxane.⁷³ This observation can be attributed to concentration effects, whereby the increased local concentration of reactants within the GNF accelerates the reaction kinetics and hence, the build-up of the silanol intermediate accelerates its subsequent dimerisation.



Scheme 1.2 Gold nanoparticle catalysed oxidation of dimethylphenylsilane by H₂O₂ to produce dimethylphenylsilanol, followed by dimerisation to afford bis(dimethylphenyl)disiloxane. AuNP confined within GNF induce a drastic change in the ratio of products.⁷³

As part of the recently increasing investigation into narrower carbon nanostructures the liquid-phase hydroxylation of benzene was studied within DWNT catalysed by both rhenium⁹ and platinum-vanadium alloy nanoparticles.⁷⁴ The Pt-V NP within DWNT exhibited twice the catalytic activity of the same nanoparticles within wider MWNT⁷⁴ due, potentially, to the greater extent of confinement, and more intimate contact with the nanoscale host. The same reaction catalysed by ReNP@DWNT showed a 4-fold increase in conversion due to nanoscale confinement.⁹ This work utilised, for the first time, *in situ* monitoring of the confined reaction by solid state NMR spectroscopy techniques. ¹³C magic

1. Chemical reactions inside carbon nanotubes

angle spinning NMR spectroscopy allowed the spectroscopic discrimination of benzene reactant molecules confined within DWNT to those of the bulk solution, showing an up-field shift of 13 ppm upon encapsulation, attributable to shielding by the CNT⁷⁵ consistent with previous reports.⁷⁶ This spectroscopic probe of the local environment allows the dynamic measurement of molecular encapsulation within CNT. Quantitative measurements show that the benzene reactant is preferentially encapsulated over the acetic acid solvent, due to hydrophobic effects,³⁴ causing an enrichment of reactant molecules within the CNT, accelerating the reaction. In combination, hydroxylation of benzene affords phenol which is less hydrophobic than the reactant, and thus is preferentially expelled from the CNT back into bulk solution (**Figure 1.6**). This example rather elegantly demonstrates the concept of synergistic confinement effects for reactions within carbon nanoreactors. Favourable hydrophobic interactions with benzene increase the confined reactant concentration and conversely, unfavourable interactions with phenol reduce the confined product concentration. Therefore, these two influences work in co-operation to drive the hydroxylation reaction forward, improving reaction rates.

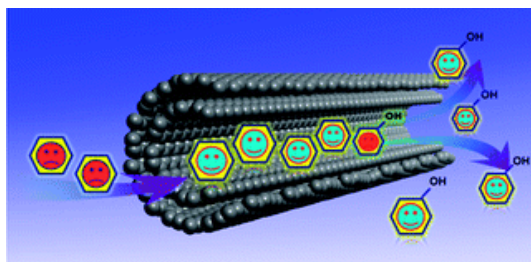


Figure 1.6 Synergistic confinement effects in the hydroxylation of benzene within DWNT. The hydrophobic enrichment of the benzene reactant within the CNT and the preferential expulsion of the phenol product is schematically represented by the abstract concept of molecular emotion. Reproduced from Zhang *et al.*⁹

Zhang and co-workers have investigated the application of carbon nanoreactor methodologies to the oxidative dehydrogenation of ethylbenzene with CO₂ to produce styrene.^{77, 78} In addition to the commonly observed increase in catalytic activity, these studies also address the need to study the influence of carbon nanotube morphology on confined chemical reactions. Although many studies have investigated the effect of CNT diameter on

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encapsulated reactions, this work probes the effect of CNT length. Clearly diffusion and molecular motion in confined space is important in understanding how chemical reactions proceed and is, therefore, integral to the design of efficient carbon nanoreactors. However, while the influence of CNT length is thought to be important, few experimental studies have been completed. This study confirmed that reactions confined within MWNT which have undergone shortening procedures proceed at an increased rate; however, this effect was surprisingly subtle, with an improvement in styrene yield of only 5% upon a two-fold reduction of the average CNT length from 300 to 150 nm.⁷⁷ This result, coupled with the growing examples of reactions within narrow carbon nanotubes^{8, 9, 43, 71, 74} infers that the accessibility of the CNT cavity may not be as much of an inhibiting factor as once presumed.

1.2.4. Ammonia synthesis and decomposition

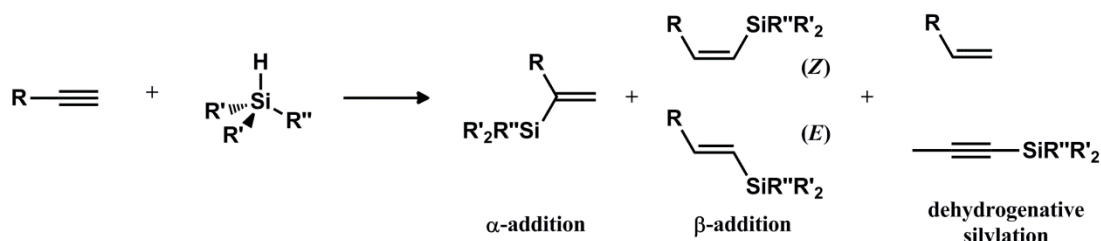
The study of confined catalysts for the decomposition of ammonia showed no discernible effect of confinement on activity, although catalyst particles were stabilised within CNT.^{79, 80} However, the ruthenium-catalysed synthesis of ammonia was also investigated within MWNT and in this case, confinement induced a 2-fold reduction in catalytic activity.⁸¹ As with the development of any new methodology, it is important to report and explain the results where confinement has a negative effect, in order to better understand and develop the approach. The synthesis of ammonia is known to be sensitive to the electron density of the catalyst, whereby higher electron density facilitates the rate determining N₂ dissociation step. Therefore, in light of this result, it is suggested that the electron density on the confined RuNP is reduced by charge transfer to the host CNT, consistent with previous reports on analogous confined iron catalysts,^{57, 61} causing a decrease in the catalytic activity of the confined RuNP towards ammonia synthesis. This important result demonstrates that the effect of confinement within carbon nanotubes can be an advantage or a hindrance depending on the underlying interactions with the CNT, the specific reaction mechanism and the desired outcome. While this is clearly not an attractive catalyst for ammonia synthesis, this work has provided an important experimental probe into the charge transfer between

metal nanoparticles and the host carbon nanotube, allowing a more well-informed approach to further development of carbon nanoreactor methodology.

1.2.5. Hydrosilylation

In order to better understand how molecular interactions of the host CNT with reactants and products of confined reactions can affect reaction selectivity, Solomonsz *et al.* used the hydrosilylation of alkynes as a probe reaction within various carbon nanostructures, predominantly graphitised carbon nanofibres (GNF).^{4, 7, 82} These carbon nanostructures (**Figure 1.2**) possess a wide internal cavity allowing facile diffusion, along with smaller internal 'step-edge' sites due to the folding of 'cup-stacked' graphitic layers for local confinement effects.⁸³ The hydrosilylation of terminal alkynes affords a mixture of products by a complex mechanism, including the α -addition product, two geometric isomers of β -addition (*Z* and *E*) and two products of dehydrogenative silylation (**Scheme 1.3**). In the reaction of aliphatic triethylsilane and phenylacetylene, rhodium nanoparticles within GNF showed a 3-fold increase in dehydrogenative hydrosilylation products at the expense of the β -(*Z*) isomer (5.8-fold decrease) relative to externally adsorbed RhNP.⁷ This is attributed to the selective enrichment of the aromatic alkyne reactant within the GNF due to non-covalent π - π interactions, which accelerates the subsequent β -H elimination reactions. Aliphatic alkynes exhibiting no such interactions produced no change in selectivity upon confinement, confirming the necessity of aromaticity to increase local alkyne concentration. Interestingly, when an aromatic silane is used, not only is the observed selectivity change reduced, but the trend is reversed. A 2.6-fold *increase* in selectivity for the β -(*Z*) isomer is reported upon confinement, due to the shifting of the equilibrium between reactive intermediates by varying geometry-dictated π - π interactions with the graphitic surface.

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Scheme 1.3 Alkyne hydrosilylation potentially forming a mixture including the α -addition product, two geometric isomers of β -addition (*Z* and *E*) and two products of dehydrogenative silylation (vinyl and alkynylsilane).

The role of non-covalent aromatic interactions in controlling confined reaction selectivity was further investigated by competitive hydrosilylation reactions where the alkyne is able to react with either an aliphatic or aromatic silane within the reaction mixture.⁴ Upon confinement, there is a 3.2-fold increase in the ratio of products from the aromatic silane reaction relative to the aliphatic reaction due to the locally enriched concentration of aromatic silane molecules within the GNF. Although local concentration effects are often utilised to explain reactivity trends within carbon nanoreactors, this work provided the first experimental quantification of such effects; evidently, the concentration of aromatic reactants can be selectively enriched 3-fold within GNF relative to aliphatic analogues. The magnitude of this enrichment is likely to vary significantly depending on the specific reactant and the morphology of the carbon nanostructure. For instance, the strength of π - π interactions will differ depending on molecular structure and indeed, the shortening of the host GNF in this reaction was reported to offer enhanced confinement effects resulting in a 4-fold enrichment of aromatic reactants and a 4-fold increase in selectivity for β -H elimination. The group continued their investigation into the influence of CNT morphology on the outcome of confined chemical reactions with a comparison of carbon nanoreactors of varying diameter in rhodium-catalysed alkyne hydrosilylation.⁸² The complex mixture of products formed in this reaction allowed the often synergistic influences of both CNT-catalyst and CNT-reactant interactions to be individually probed. It was demonstrated that the interaction of the $\text{Rh}_4(\text{CO})_{12}$ catalysts with each carbon nanostructure (DWNT, MWNT and GNF) caused a universal 2-fold increase in selectivity for the (*E*) isomer of β -addition

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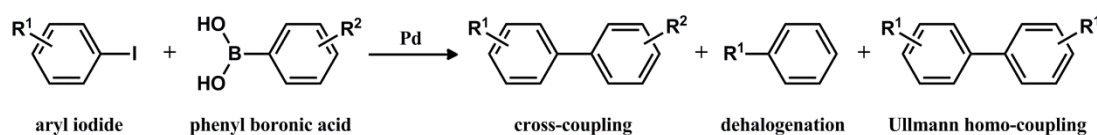
irrespective of adsorption on the internal or external nanotube surface. In addition, comparing the increase in selectivity for the products of dehydrogenative silylation over those of (Z)- β -addition upon confinement allows the extent of increased local reactant concentration within the CNT to be probed. A greater change in this product ratio was exhibited upon confinement within wider GNF (8-fold), due to the more accessible internal volume coupled with the unique internal structure providing local confinement, whereas the reduced effect of confinement observed within DWNT (4-fold change in this product ratio) was attributed to the expected diffusion limitations within narrower DWNT.

1.2.6. Cycloaddition and cross-coupling

The study of well-known organic chemistry transformations within carbon nanoreactors provides a convenient probe into the influence of confinement, drawing on the detailed mechanistic knowledge of such reactions. As such, the copper-catalysed azide-alkyne cycloaddition reaction between terminal alkynes and benzylazide was investigated by Rance *et al.* catalysed by copper nanoparticles (CuNP) within GNF.⁸⁴ Although confinement has influenced the selectivity of other catalytic reactions, in this case, the 1,4-triazole regioisomer is solely afforded under all experimental conditions due to copper catalysis. This implies either that the constrained environment within GNF has no effect on selectivity, or that any subtle influence is overcome by the strongly regioselective influence of the copper catalyst. Instead, this work focuses on the activity of the confined catalyst, showing that the CuNP confined within GNF are much more active than externally adsorbed CuNP, despite showing a slight decrease in activity relative to CuNP in solution. However, the advantage of nanoscale confinement is eminently clear when the recyclability of the catalyst is appraised. After repeated experimental cycles, both free CuNP and externally adsorbed CuNP/GNF are depleted due to dissolution of copper, leading to a steadily reducing catalytic activity. In contrast, the encapsulated particles exhibit remarkable stability after repeated cycles, with minimal loss of catalytic activity, in support of previous reports for both batch and continuous reactions within CNT and related nanostructures.^{58, 61, 63, 67, 85-87}

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The palladium catalysed Suzuki-Miyaura cross-coupling reaction, a staple of synthetic organic chemistry, was investigated within GNF by Cornelio *et al.*⁸⁷ Subtle enhancements in activity and selectivity for the cross-coupled product (**Scheme 1.4**) are observed upon confinement, depending on the aryl iodide substituent, suggesting that the crucial oxidative addition step occurs at the GNF step-edge and is therefore subject to the influence of the host nanostructure.



Scheme 1.4 The palladium catalysed Suzuki-Miyaura cross-coupling of aryl iodides and phenylboronic acids leading to the products of cross-coupling, dehalogenation and Ullmann homo-coupling.

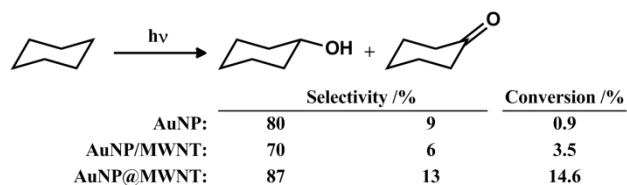
The systematic investigation of substituent effects in both reactants provides improved understanding of the relative affinities of reactants for the confined environment at the GNF step-edge in relation to both steric and electronic factors. For instance, sterically demanding aryl iodides do not appear to be stabilised by confinement within GNF, exhibiting a slightly higher conversion than PdNP on the GNF exterior due to the unrestrained environment around the supported catalyst. Competitive reactions where a boronic acid reactant can couple with two aryl iodide reactants show more pronounced shifts in selectivity due to confinement. This highlights the importance of less sterically-congested and higher aromaticity reactants in order to maximise the favourable interactions within the GNF interior and observe the greatest confinement effects.

1.2.7. Photocatalytic reactions

There have been recent reports of utilising nanoparticulate catalysts encapsulated within CNT for photocatalytic reactions exploiting spatial confinement effects coupled with the interesting electronic properties of carbon nanotubes.^{85, 86} The gold-catalysed photocatalytic oxidation of cyclohexane was demonstrated within MWNT, showing a 4-fold increase in conversion due to the confinement of AuNP (**Scheme 1.5, Figure 1.7a**).⁸⁵ In addition, the

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confined reaction exhibited quantitative selectivity towards the two main products whereas the reaction catalysed by AuNP externally adsorbed on MWNT seemingly afforded a measurable proportion of unidentified side product.



Scheme 1.5 Gold catalysed photocatalytic oxidation of cyclohexane to afford cyclohexanol and cyclohexanone. The relative yields of each product are comparable for all gold catalysts, although confinement of the AuNP within MWNT clearly increases the conversion.

This reaction was carried out under ambient conditions using visible light irradiation and air as the oxidant. The AuNP photocatalytically reduces atmospheric oxygen, producing H_2O_2 which then affords the active $\text{OH}^\bullet$ radical oxidant in the presence of a radical initiator. The intimate interaction of the confined AuNP with the host CNT shows a remarkable 3-fold increase on the measured photocurrent (**Figure 1.7b**) indicating the advantage of CNT hosts in the separation of photo-induced excitons by electron transfer from the AuNP to the CNT, consistent with previous reports.⁸⁸

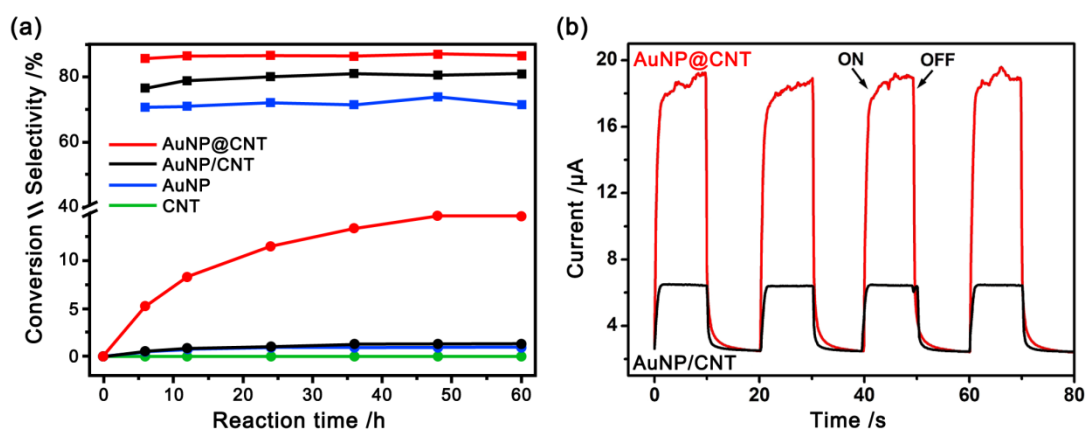


Figure 1.7 (a) Cyclohexane conversion and cyclohexanol selectivity in the photocatalytic oxidation of cyclohexane catalysed by various gold nanoparticle (AuNP) - carbon nanotube (CNT) composite materials showing the effect of confinement by comparison of AuNP@CNT with AuNP/CNT. (b) The photocurrent response for both AuNP@CNT (red) and AuNP/CNT (black) showing the effect of confinement on the measured photocurrent. Adapted from Liu *et al.*⁸⁵

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Cui *et al.* studied the effects of confinement within MWNT on cadmium sulfide nanoparticles by investigation of the photocatalytic degradation of methylene blue.⁸⁶ The CdS-CNT composite materials exhibited an approximately 2-fold increase in photocatalytic degradation compared to unsupported CdS demonstrating the advantages of carbon nanotubes in such processes, despite the CNT having no discernible effect on the process directly. The confined catalyst demonstrates considerably higher recyclability and stability against photocorrosion; however, the externally adsorbed CdS showed subtly higher activity in this reaction than the confined catalyst. The authors attribute this to the absorption of light by the carbon nanotube, reducing the incident light on the confined CdS catalyst. This is expected to a certain extent as a single graphitic layer has been found to absorb around 2% of incident white light,⁸⁹ so multi-walled carbon nanotubes could conceivably reduce the light intensity for confined particles. However, it should be noted that this is contradictory to the observation in the previous example for AuNP@MWNT whereby no measurable drop in photocatalytic activity was observed upon confinement.⁸⁵ Alternatively, the subtle reduction in activity for the confined catalyst could potentially be due to the large nanoparticulate CdS blocking the internal channels in the CdS@CNT material, reducing the diffusion of reactant towards the catalyst and retarding reaction kinetics. Indeed, either of these factors have the potential to drastically reduce the observed activity and if present, could in fact be completely obscuring any hypothetical improvement in underlying catalytic activity due to confinement, a summation of which results in the observed slight decrease in conversion for the confined catalyst reported in this study. This highlights the ambiguity in assessing the underlying interactions which dictate the overall behaviour of confined reactions as it is often extremely difficult to distinguish the separate influence of multiple, potentially synergistic or antagonistic, effects of confinement from the overall observed result. For instance, if the influence of increased local concentration acts to improve conversion by 10-fold, but in addition, the inherent catalytic activity is reduced by 2-fold, the overall observed result will be a 5-fold increase, and the underlying interactions may not be fully

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understood. Uncovering such mixed influences can, therefore, facilitate further optimisation of these catalytic systems; however, this is not always possible.

1.2.8. Electrochemical reactions

The growing examples of control over the reduction and oxidation behaviour of catalysts and the markedly improved stability and recyclability afforded by confinement within CNT have inspired the recent development of similarly confined catalysts in electrochemical reactions including methanol⁹⁰ and hydrazine⁹¹ oxidation, oxygen reduction,^{92, 93} and nucleophilic substitution.⁹⁴ Both the activity and stability of platinum nanoparticles in the electrocatalytic oxidation of methanol was improved upon confinement within MWNT.⁹⁰ The advantages over comparable PtNP externally adsorbed on either MWNT or activated carbon (AC) supports were clear, particularly with respect to catalyst durability, where the PtNP@CNT catalyst showed a 9% reduction in current density after 600 cycles, compared to 45 and 74% for PtNP/CNT and PtNP/AC respectively. This work demonstrates the potential advantages of metallic nanoparticles confined within CNT for improved electrocatalytic efficiency and durability in fuel cell applications. The use of less expensive nickel-iron alloy nanoparticles encapsulated within MWNT was also investigated for applications in direct hydrazine oxidation fuel cells.⁹¹ In an attempt to replace expensive platinum catalysts for the oxygen reduction reaction in fuel cells, carbon nanotube supports have been investigated as potential catalysts in this extremely useful process.^{92, 93} The oxygen reduction reaction does not typically occur within the carbon nanotube in these cases as the inner cavity is relatively inaccessible⁹² and thus, the CNT is not truly acting as a nanoreactor. However, in this case, the encapsulation of iron nanoparticles⁹² and phosphorus⁹³ dopants alters the electronic properties and catalytic activity of the carbon nanotube external surface, demonstrating the influence that confined species can have on the host carbon nanotube and highlighting the symbiotic nature of such host-guest interactions.²¹ Indeed, such modification of CNT properties by guest species has, for instance, facilitated vastly improved electrochemical sensing.⁹⁵

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A novel demonstration of electrochemical carbon nanoreactors was reported by McSweeney *et al.* by the encapsulation of methylcyclopentadienyl manganese tricarbonyl, $\text{Cp}^{\text{Me}}\text{Mn}(\text{CO})_3$, within narrow SWNT.⁹⁴ Firstly, the high electrical conductivity of the SWNT drastically increases the active interface with the redox active molecule, thus decidedly improving the electrochemical sensitivity. More interestingly, the confinement of this manganese complex within narrow SWNT alters the pathway of its electrochemically induced reaction with acetonitrile. Typically, this complex, once oxidised at 0.8 V, undergoes rapid and irreversible nucleophilic substitution of carbonyl ligands for acetonitrile solvent molecules. However, the extreme confinement within SWNT completely precludes this mechanism, allowing the corresponding reduction at 0.75 V to be observed (**Figure 1.8**). This intriguing example demonstrates the potential of exploiting multiple properties of carbon nanotubes in order to control chemical reaction pathways, acting as both nano-electrode and nanoreactor.

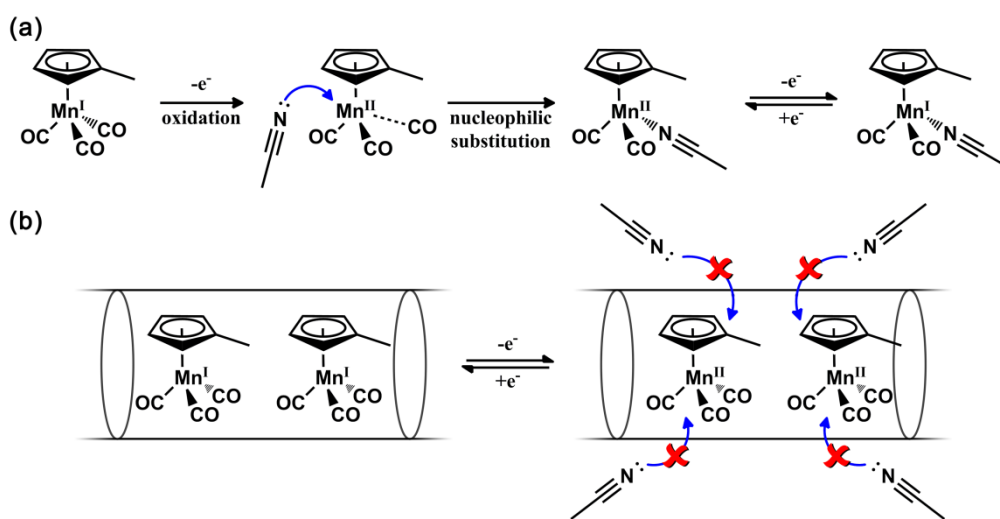


Figure 1.8 (a) The bulk phase electrochemical oxidation of $\text{Cp}^{\text{Me}}\text{Mn}^{\text{I}}(\text{CO})_3$ followed by the irreversible nucleophilic substitution of CO for a solvent acetonitrile molecule. (b) Confined within SWNT, the nucleophilic attack is precluded, allowing the corresponding reduction to the original complex.⁹⁴

1.2.9. *Extreme spatial confinement in narrow carbon nanotubes*

In brief, this review has detailed various examples where the properties of the catalyst can be tuned by confinement. This is often coupled with additional advantages that confinement within carbon nanotubes can invoke, such as increased local concentration, preferential orientation of reactants and more efficient recyclability of catalysts (**Table 1.3**).

Table 1.3 Summary of the potential advantages and disadvantages of the confinement of chemical reactions within carbon nanotubes.

Advantages of nanoscale confinement	Disadvantages of nanoscale confinement
Local concentration of reactants increased, improving reaction rates.	Diffusion rates are often low for both reactants in, and products from, the nanoreactor.
Selectivity control by steric confinement.	Confined reaction is often more complex, with multiple stages, making it difficult to monitor kinetics, particularly in light of diffusion factors.
Catalytic activity increased due to electron transfer.	Catalytic activity reduced due to electron transfer.
Catalyst stability improved affording prolonged activity, recyclability and a wider range of operating conditions.	Blockage of the internal channel by catalyst particles.
Activation energy barrier decreased by stabilisation of transition states.	Blockage of the internal channel by macromolecular product, impeding turnover and potentially precluding product extraction/separation.
Molecular motion altered in confinement potentially increasing catalyst contact time and altering selectivity.	
Product templation during self-assembly processes.	
Control of reactant/product concentrations by non-covalent interactions or the hydrophobic effect.	
Efficient egress of product back into the bulk phase facilitating higher turnover and kinetics.	
Facile catalyst separation.	

Sometimes it is difficult to deconvolute complex mixtures of such synergistic influences and thus, the underlying interactions behind such confinement effects are not always fully understood. However, it has been shown that even when metallic catalysts are neglected, the host carbon nanotube can have a direct effect upon confined reactions. This approach of probing the direct interactions between the host carbon nanotube and the molecular species of a reaction, allows the intrinsic influence of the host CNT to be discerned without interference from catalyst particles. For instance, in catalytic nanoreactors, the effect of charge transfer between the host CNT and metallic catalysts may completely obscure more

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subtle steric or charge transfer effects imposed by the CNT on the reactants or transition state, with the latter remaining undiscovered.

There have been few examples of this approach in comparison to confined catalytic reactions; however, the potential is clearly demonstrated. The first examples of such confined chemical transformations were only conducted on an analytical scale under observation by transmission electron microscopy.⁹⁶⁻⁹⁹ The oligomerisation of C_{60} fullerene epoxide was conducted within narrow SWNT, whereby the templation effect of the host SWNT induced the formation of strictly linear oligomers, in comparison to the statistical formation of highly branched oligomers in solution (Figure 1.9).⁹⁶ This was the first demonstration of confinement within carbon nanotubes altering the outcome of a chemical reaction, affording a linear product largely inaccessible by other means. Comparable TEM observations of fullerene dimerisation under electron beam irradiation further indicate the novel reaction environment within such narrow reaction vessels.⁹⁹

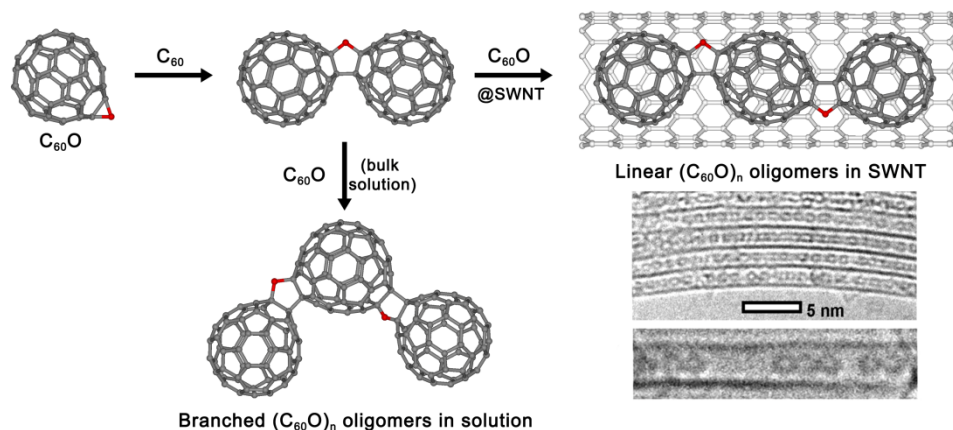


Figure 1.9 Fullerene epoxide ($C_{60}O$) oligomerisation both confined within SWNT, affording linear oligomers, and in bulk solution, producing a random distribution of highly branched structures. Inset are transmission electron micrographs showing the C_{60} epoxide oligomers encapsulated within SWNT upon formation. This work demonstrates the power of confinement within SWNT to alter the pathways of chemical transformations, affording products inaccessible by other means.

More recently, similar confinement effects have been utilised in the SWNT-templated formation of graphene nanoribbons.^{97, 98, 100} Graphene nanoribbons, linear quasi-1D graphene, show promise for interesting applications in electronic devices, yet controlled

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synthesis has proved difficult. A source of carbon, such as tetrathiafulvalene, confined within SWNT was shown to self-assemble into sulfur-terminated graphene nanoribbons upon initiation by heat or electron beam irradiation (**Figure 1.10**). This further demonstrates how the underlying thermodynamics of chemical reactions are affected by extreme confinement, where the relative stability of products within SWNT is drastically different to that in the bulk phase. The strong van der Waals interactions between the host CNT and the products in these examples can inhibit the extraction of the product,⁹⁶⁻⁹⁸ precluding preparative synthesis. However, the power of confinement within narrow SWNT over the outcome of chemical reactions is plainly demonstrated and the direct influence of the host CNT is explicit in the absence of metallic catalyst highlighting the potential for further work in this area.

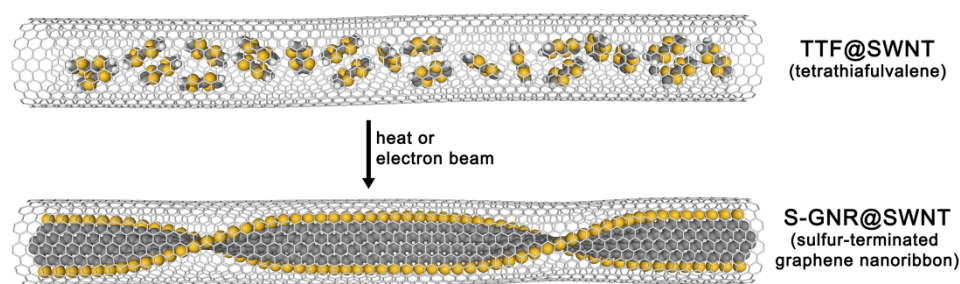


Figure 1.10 Carbon nanotube templated synthesis of sulfur-terminated graphene nanoribbons (S-GNR) from tetrathiafulvalene (TTF) within narrow SWNT by initiation from heat or electron beam irradiation.

The investigation of molecular physisorption on, and in, SWNT using temperature programmed desorption methods allowed the study of a simple alkene hydrogenation reaction by Kondratyuk and Yates.⁵² Observing the multiple desorption processes for physisorbed 1-heptene molecules on SWNT, the different adsorption sites were assigned; for example, adsorbed externally, at interstitial 'groove' sites or encapsulated within the internal cavity. The free radical hydrogenation of 1-heptene was studied within this experimental setup, inferring that the reactivity of the confined alkene is reduced by 3-fold in comparison to molecules adsorbed in interstitial groove sites. However, this may not be due to a reduction in the inherent reactivity, but merely kinetic diffusion limitations. In this case, the highly reactive atomic hydrogen will take longer to reach the confined alkene due to the

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steric barrier of the host CNT, thus being increasingly likely to react with the nanotube before reaching the hydrocarbon.

In support of these few experimental studies, theoretical studies of simple chemical reactions within carbon nanotubes have predicted that confinement can significantly alter reaction pathways even in the absence of catalysts. The deuterium exchange of molecular hydrogen was considered by Lu *et al.* and the reaction was expected to be favoured within SWNT of various diameters.^{101, 102} This was attributed to either a preferential co-linear alignment of the H₂ along the CNT axis, stabilising interactions with the transition state, or increased reactive collisions due to reflected collisions with the CNT walls. As previously mentioned, the Menshutkin S_N2 amine alkylation reaction is predicted to be promoted within narrow SWNT whereby the highly polarisable carbon nanotube host stabilises the emergence of a large dipole moment, reducing the endothermicity of the process.⁵ The C-H activation of small alkanes is expected to be more facile within narrow SWNT, with a reduction in the calculated E_A of between 4 and 10 kJ mol⁻¹ upon confinement, depending on nanotube diameter.¹⁰³ In contrast, confinement has been predicted to exhibit a negative influence on reactivity in the S_N2 chlorine exchange reaction.¹⁰⁴ Stabilising C-H-- π interactions exist between the CNT wall and both the reactant and transition state in this example. However, the magnitude of this stabilisation is less pronounced for the transition state than for the reactant, making the activation energy for the confined reaction higher than in the bulk gas phase.¹⁰⁴ The regioselectivity of a classic Diels-Alder cycloaddition reaction was investigated by molecular dynamics simulation within narrow SWNT.¹⁰⁵ Confinement is predicted to promote the formation of the 1,4-cycloadduct at the expense of the more thermodynamically stable 9,10-cycloadduct, due to a steric-induced energy penalty of 42 kJ mol⁻¹ to the formation of the latter in the restricted internal cavity of CNT, although this effect is critically dependent on diameter.

1.3. Aim and objectives

This work aims to investigate the use of narrow carbon nanotubes (1 – 2 nm diameter) for the confinement of preparative chemical reactions, directly probing the effects of extreme confinement within carbon nanotubes on the pathways of organic transformations. Interactions at the nanoscale between the host carbon nanotube and the molecular species of organic chemical reactions will be examined and their potential influence on the outcome of such reactions investigated. The confinement of well-known organic chemical reactions within carbon nanotube will enable the effects of nanoscale confinement on reaction pathways, particularly selectivity, to be explored directly.

In order to achieve this, a number of practical problems must be overcome. Reliable practical methods must be developed for the encapsulation of various organic compounds. The reaction locus should be controlled, ensuring that reactions occur exclusively within the carbon nanotube. Previous examples of reactions inside carbon nanotubes can define the exact location of reactions by transmission electron microscopy analysis locating catalytic centres, because the catalyst is essential for the reaction to proceed.⁷³ However, organic transformations in the absence of catalysts will readily proceed in the bulk phase, so careful control experiments must be developed and utilised to ascertain the effect of confinement. The extraction of product molecules from the internal channels of SWNT must be probed in order to ensure that products can be recovered and thus reactions can be preparative. To this end, in light of reports where macromolecular products (*e.g.* polymers, oligomers and nanoribbons) demonstrating strong host-guest interactions were not able to be extracted from SWNT,^{96, 97} small organic species will be investigated in order to reduce the van der Waals interactions with the CNT interior. In summary, this work aims to demonstrate the suitability of narrow carbon nanotubes as hosts for preparative chemical reactions in the absence of metallic catalysts and furthermore, to harness direct interactions between the host carbon nanotube and confined organic compounds to offer new mechanisms for control of reaction pathways.

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2. Controlling carbon nanotube length

2.1. Background

Since the discovery of carbon nanotubes, many wide-ranging applications have been proposed relating to their remarkable properties.¹ For each potential application, the delay between inception and realisation is governed by our understanding and manipulation of the properties of carbon nanotubes and how this influences their effectiveness for a particular task. This remains true when developing carbon nanotubes for use as hosts for chemical reactions and, therefore, the effect of various nanotube properties, such as diameter, length, morphology and chirality, is an important consideration.

For instance, the diameter of a carbon nanotube host can have a profound effect on how encapsulated molecules are arranged within their restricted internal volume, as demonstrated by the diameter-dependent arrangement of fullerene molecules within single-walled carbon nanotubes.^{2, 3} In this study, it was discovered that a narrow internal nanotube cavity (1.1 nm), very similar to the van der Waals diameter of the encapsulated C₆₀ fullerene molecules (1 nm), forces the molecules to remain in a linear arrangement. Additionally, as nanotube diameter is increased, the fullerene molecules adopt an alternative molecular packing arrangement, such as a double helix, in order to minimise intermolecular separation and maximise van der Waals contact. As carbon nanotube synthesis procedures offer control over diameter,⁴ certain properties of a guest molecule can be controlled in this way by careful choice of a suitable nanotube. Similarly, when using confinement within carbon nanotubes to influence a reaction pathway, the nanotube diameter offers a means to vary the extent of confinement depending on the geometry and steric bulk of a reaction species.

The inherently high aspect ratio of carbon nanotubes, while advantageous for applications such as spinning fibres,⁵ may prove to be a disadvantage when the narrow internal cavity is used to host chemical reactions. The length-dependent transport resistance

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of reactants to, and products from, the internal cavity of carbon nanotubes is expected to decrease diffusion rates and thus the observed rate of the confined reactions. Rao *et al.* studied the catalytic dehydrogenation of ethylbenzene in carbon nanotubes and found that a two-fold reduction in mean nanotube length, from approximately 300 nm to 150 nm, improves the absolute yield from 23 to 28%, representing a relative improvement of 20%.⁶ Clearly, nanotube length should be a consideration for carbon nanotube nanoreactors; however, unlike diameter, the length of carbon nanotubes is difficult to control during traditional synthesis procedures. The "bottom-up" approach to carbon nanotube synthesis from molecular precursors could, in theory, allow the fabrication of a specific length, diameter and chirality of carbon nanotube;⁷ yet, these approaches, while promising, are still in their infancy and cannot reliably produce CNT on a scale necessary for use as nanoreactors. Therefore, a reliable scalable method for the controlled cutting of as-produced long carbon nanotubes using "top-down" approaches is critically needed.

Besides carbon nanoreactors, controlling nanotube length will also be advantageous for a range of other potential applications. Generally, the solubility, and thus processability, of carbon nanotubes in conventional solvents is hampered by their extreme length;⁸ thus, an improvement in this respect would aid the development of CNT in a vast plethora of functional devices.⁹ Control of CNT length will be particularly important in harnessing the attractive electronic properties of carbon nanotubes in functional devices such as flexible energy storage,¹⁰ computers¹¹ and thermoacoustic speakers.¹² From biological and environmental perspectives, the toxicity of carbon nanotubes is increased as a function of length due to the heightened propensity for provoking an immune response.¹³⁻¹⁵ Thus, the use of carbon nanotubes as drug delivery agents will first require effective methods of shortening carbon nanotubes.

To date, a number of different experimental methodologies have been developed to control the length of carbon nanotubes and these can be classified conceptually into two general approaches (**Figure 2.1**).

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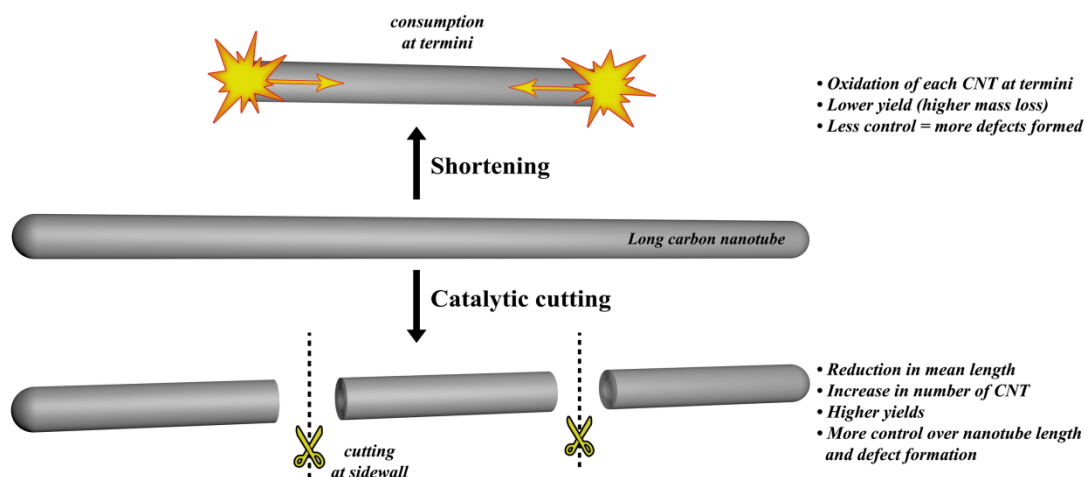


Figure 2.1 Schematic representing the two conceptual methodologies for decreasing mean nanotube length, shortening and cutting.

Shortening carbon nanotubes decreases the length of each carbon nanotube by a continuous reaction at the nanotube termini, proceeding along the length of the nanotube, similar to that of a lit fuse. In this way, the number of nanotubes does not change significantly; however, each original nanotube becomes shorter. Using this approach, a 50% reduction in nanotube length requires 50% mass loss and thus, these methods generally afford much lower yields. Alternatively, each carbon nanotube can be cut at a point along the nanotube sidewall, which decreases the mean nanotube length without significant loss of carbon by increasing the number of carbon nanotubes. While cutting often occurs simultaneously during methods which also shorten, the use of a catalyst to promote cutting over shortening has the potential to offer a greater degree of control over nanotube length with maximal yields.

Although methods of shortening nanotubes offer no spatial control and can, therefore, attack the nanotube at any point along the nanotube, the carbon atoms at the nanotube termini are more reactive than those of the nanotube sidewall due to the increased strain caused by curvature.¹⁶ For instance, while the planar arrangement of sp^2 -hybridised carbon in graphite or graphene is rather chemically inert, the strain induced when forming a curved structure, such as a fullerene or nanotube, causes the sp^2 -hybridised carbon to be

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more reactive towards functionalisation.¹⁷ This deviation from planar sp^2 -hybridised graphitic carbon creates a distorted distribution of p_z -orbital electron density on either side of the surface, with the majority of the orbitals existing on the exohedral surface of a convex structure such as carbon nanotubes. Considering carbon nanotubes, the curvature is more acute at the closed end-caps than along the sidewall (**Figure 2.1**) and therefore, the exohedral π -bonding orbitals at the termini are more diffuse, making them more readily available for attack than those along the nanotube sidewall. This means that during any chemical reaction with carbon nanotubes, the attacking species tends to react primarily at the nanotube termini,^{18, 19} relieving the strained geometry to a more stable sp^3 -hybridised carbon in the form a particular functional group.¹⁸ In the case of oxidation, this commonly leads to the shortening of carbon nanotubes and was initially demonstrated most simply by oxidation in air,^{8, 20} or carbon dioxide.²¹ These methods are uncontrolled and therefore oxidation tends to occur at the more reactive areas, whether at nanotube termini or pre-existing defect sites, leading to a random distribution of nanotube lengths and morphologies, typically with low yields. Furthermore, the use of CO_2 can result in the detrimental narrowing of multi-walled carbon nanotubes, through stripping of the outer layers.²¹ This could be because mildly oxidising CO_2 is slow to oxidise the carbon and as each graphitic layer is opened, the radicals created are the least stable and most reactive loci for further oxidation, leaving the inner layers temporarily intact.

Mechanical methods, such as ball milling^{22, 23} and diamond abrasion,²⁴ use mechanical stress to break the carbon nanotubes. Though effective at reducing the mean nanotube length, these methods are known to significantly damage the nanotube sidewall structure producing amorphous carbon which is difficult to separate from the shortened nanotubes.²³ Various solution based methods have been explored whereby reagents, such as nitric acid,²⁵⁻²⁷ a mixture of sulfuric and nitric acids,²⁸ "piranha" solution (a mixture of sulfuric acid and hydrogen peroxide),²⁹ potassium permanganate^{30, 31} or even ozone,³² can attack the carbon nanotube producing shorter mean nanotube lengths. While each method

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successfully shortens CNT, the oxidation often remains uncontrolled, occurring randomly at all points of the nanotube, which typically results in many instances of incomplete cutting leaving defects in the nanotube sidewall and a broad distribution of nanotube lengths.

Due to the inherently varied morphology of carbon nanotubes, the exact mechanism for many of the processes is not known and may not be constant for different instances depending on the local functionalisation of the nanotube. For instance, the oxidation by nitric acid occurring at the nanotube termini, compared with simultaneous oxidation at a pre-existing carbonyl-functionalised defect site is unlikely to be identical. However, viable mechanisms have been proposed such as that for the oxidation of carbon nanotubes in potassium permanganate solution.³³ It has been proposed that this could proceed along a similar mechanistic pathway to that of olefin oxidation by the permanganate anion (**Figure 2.2**).^{34, 35} This mechanism shows the attack of a pristine nanotube with perfect sp^2 -hybridised structure; however, alternative mechanisms are possible where the oxidant attacks a defect such as a methyl group formed sparingly by sonication or pre-existing from synthesis procedures, resulting in the addition of a carboxyl group and the cleavage of a nanotube carbon bond.³⁶ These examples demonstrate just two proposed mechanisms among a plethora of viable possibilities considering the inhomogeneous nature of carbon nanotube samples and the variety of procedures studied.

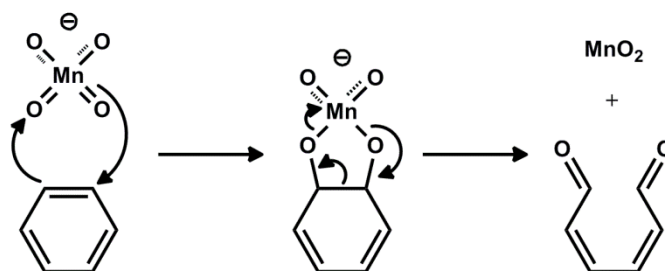


Figure 2.2 Proposed mechanism for the oxidation of carbon nanotubes by potassium permanganate. Here the sp^2 -hybridised carbon nanotube lattice is represented by one aromatic ring for simplicity, demonstrating the cleavage of a carbon-carbon bond.

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As shown in **Figure 2.1**, cutting of carbon nanotubes uses more controlled reactivity, leading to a more controlled reduction in length while minimising unwanted damage to the nanotube sidewall. Some highly controlled nanotube cutting methods have been developed using the electron beam during transmission electron microscopy imaging,^{37, 38} lithography,³⁹ or scanning probe microscopy⁴⁰ procedures. In these processes, the electron beam energy is used directly to break the carbon-carbon bonds of the nanotube, while also utilising the precise focussing of the beam to ensure the nanotube is only damaged at the point of cutting which produces short carbon nanotubes with nanoscale precision. However, these methods are inherently non-scalable and involve the use of time and cost intensive instrumentation.

A similarly controlled approach involves catalytic oxidation whereby a catalyst reduces the energy required for carbon nanotube oxidation locally causing selective cutting of the nanotube within the vicinity of the catalytic centre while leaving the majority of the nanotube sidewall intact. This gives greater control over the resulting nanotube length distribution and minimises detrimental defect formation while also representing a scalable process using common laboratory techniques. The fluorination of nanotubes has been shown to occur in rings around the circumference of the nanotube which can locally weaken the nanotube, allowing etching of the carbon by either pyrolysis⁴¹ or mild piranha solution.⁴² A safer, more convenient and effective method is the use of catalytic metal and metal oxide nanoparticles, such as nickel oxide (NiONP),⁴³ iron (FeNP)⁴⁴ or silver (AgNP),^{44, 45} dispersed on the nanotube surface. In these procedures, metallic or metallic oxide nanoparticles are formed on the nanotube surface before high temperature conditions facilitate carbon nanotube oxidation catalysed locally by the nanoparticle.

The most significant practical limitation to the current reports on cutting carbon nanotubes relates to the applicability of each individual approach. As carbon nanotubes are inherently inhomogeneous in terms of their physical characteristics, such as length, diameter, number of walls, chirality and concentration of sidewall defects, it is unreasonable to assume that any reported cutting method will be applicable to any given carbon nanotube sample.

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Unfortunately, when a cutting method is unsuccessful for a particular set of carbon nanotubes this result often remains unreported, meaning the limitations of each method are not widely known or directly comparable. A small number of studies directly compare different methods of nanotube cutting to assess their relative success,^{31, 46} but there has been no comprehensive study comparing the applicability of various published cutting processes for controlling the length of one particular type of nanotubes. This would allow the advantages and disadvantages of each method, in terms of cutting efficiency and structural damage to the nanotube, to be directly compared, allowing the ideal procedure for a specific application to be chosen accordingly.

2.2. Aim and Objectives

The aim of this study is to control the length distribution of carbon nanotubes. This will be achieved by firstly, comparing a range of popular procedures for cutting CNT and determining the most effective method and secondly, by assessing, for the most successful method, how readily it can be applied to a range of carbon nanostructures. In this way, the most effective and widely applicable method can be ascertained.

The nanotube cutting procedures appraised herein (**Figure 2.3**) were chosen owing to their relative ease of scalability and potential applicability to the majority of research laboratories. These methods include chemical oxidation using mixed acids (Method 1),^{25, 28} "piranha" solution (Method 2)²⁹ and potassium permanganate (Method 3)³⁰ as well as air oxidation catalysed by nanoparticles of nickel oxide (Method 4)⁴³ and silver (Method 5)⁴⁴ grown *in situ* during catalyst preparation. As a direct comparison, the air oxidation of CNT catalysed by preformed (*ex situ*) silver nanoparticles (Method 6)⁴⁵ was also considered. This investigation will require a common batch of carbon nanotubes to allow systematic comparison.

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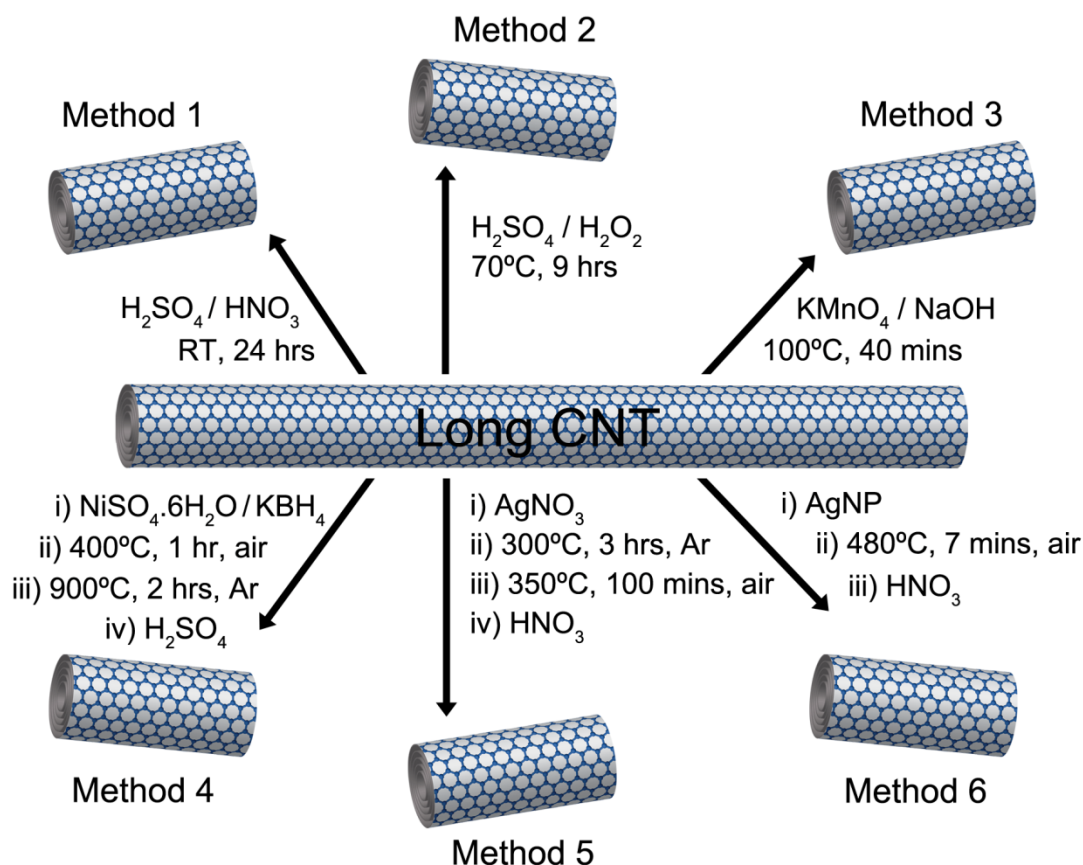


Figure 2.3 Schematic representation of the chosen protocols for cutting CNT (Methods 1-6) with an experimental summary for each.

The overall success of any given method will be evaluated by two main criteria, namely the extent to which the nanotubes are reduced in length and the amount of damage to the nanotube sidewall. The ideal procedure would therefore reduce the average length of the CNT by a large and controllable proportion ($>75\%$ reduction) with minimal introduction of defects in the nanotube ($<10\%$ increase in $I_D:I_G$). Nanotube length is to be measured by statistical analysis of nanotube length from transmission electron microscopy (TEM). The extent of damage to the nanotube sidewall subsequent to each procedure can be evaluated using various spectroscopic techniques, principally Raman spectroscopy but also including IR and UV-visible spectroscopies. Raman spectroscopy measures the energy of vibrational modes of a molecule under excitation from a laser radiation source. In the case of carbon nanotubes this gives rise to three main diagnostic vibrational modes; namely, the G and D modes and the radial breathing mode.⁴⁷ Comparing the intensity of the G band, originating

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from the in-plane vibration of an ideal lattice of sp^2 -hybridised carbon, to that of the D band, originating from disorder from an ideal sp^2 -hybridised lattice often in the form of sp^3 -hybridised defects, provides a direct, quantifiable indication of the number of defects in the carbon nanotube. Lastly, the radial breathing mode, unique to nanotubes, is a radial expansion-contraction of the nanotube, the frequency of which is dependent on nanotube diameter and therefore is typically only observed for SWNT.

The procedure deemed most efficient will be applied to the cutting of a range of hollow carbon nanostructures synthesised by either arc discharge (AD) or chemical vapour deposition (CVD) and possessing a diverse range of structural characteristics, such as length, diameter, internal and external structures.

2.3. Results and Discussion

2.3.1. *Comparison of literature protocols*

The six methods chosen were applied to the cutting of CVD MWNT because these nanotubes possess dimensions (mean external diameter of 15 ± 7 nm and length of 3250 ± 1600 nm, as measured by TEM) and physical properties analogous to many carbon nanotubes typically discussed in the literature. The conceptual methodology behind this investigation involved the application of each literature protocol to the same batch of CVD MWNT followed by analysis of the resultant materials by TEM to quantify average nanotube length, and various spectroscopic techniques to assess structural changes to the nanotube as a result of the procedure.

A typical procedure for the oxidation of MWNT by mixed acids (Method 1)²⁵ involved the addition of CVD MWNT to a 3:1 mixture of concentrated sulfuric and nitric acids. This mixture was chosen as it has been previously demonstrated to exfoliate graphite.⁴⁸ A black suspension was created by room temperature ultrasonication for 24 hours, allowing local sonochemistry to form vacancy defect sites in the nanotube sidewall, which

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are susceptible to further attack by the oxidising nitric acid. The black powder was recovered by filtration through a polytetrafluoroethylene (PTFE) membrane (0.2 μ m pore), and neutralised with a dilute sodium hydroxide solution. The oxidation by piranha solution (Method 2)²⁹ was completed by addition of CVD MWNT to piranha solution (5:1 vol. mixture of 96% sulfuric acid and 30% hydrogen peroxide solutions) at 70°C immediately forming a black suspension and stirring the mixture for 9 hours while the reaction showed evolution of a gas. Piranha solution is a particularly aggressive and corrosive mixture and appropriate safety precautions were taken to shield from potential exposure. The black powder was then recovered from the diluted solution by filtration and washed with water until neutral. Oxidation in potassium permanganate solution (Method 3)³⁰ involved the suspension of MWNT in an aqueous alkaline potassium permanganate solution by brief ultrasonication to form a dark purple suspension before stirring the mixture at reflux for 40 minutes. Upon cooling to room temperature, sodium sulfite and dilute sulfuric acid were added before continued stirring at room temperature to remove excess manganese(IV) oxide. The black solid was isolated by filtration and washed with hydrochloric acid to remove residual manganese as a brown solution.

The general methodology for oxidation of carbon nanotubes catalysed by metallic nanoparticles was the dispersion of nanoparticles on the MWNT surface, followed by the catalysed oxidation at elevated temperature, before finally removing the metallic particles to afford a black powder. The difference between the three methods is either the nature of nanoparticle-nanotube composite synthesis (*in situ* or *ex situ*), or the nature of the nanoparticle used (nickel oxide or silver). The *in situ* prepared materials are formed directly adsorbed to the MWNT surface, by co-ordination of a metal salt precursor to the CNT followed by high temperature decomposition to form metallic nanoparticles. Whereas *ex situ* methods involve the preparation of dodecanethiol-stabilised nanoparticles before dispersion on the MWNT surface.

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Oxidation catalysed by nickel oxide nanoparticles (Method 4)⁴³ was carried out by solution phase adsorption of nickel(II) sulfate hexahydrate on the nanotube surface followed by the addition of potassium borohydride to reduce the nickel to metallic nanoparticles. The resultant black powder composite material was heated at 400°C in air to oxidise the nickel nanoparticles to form the catalytically active nickel oxide nanoparticles. The material was then heated to 900°C under an argon atmosphere for 2 hours where the nickel oxide particles oxidise the carbon of MWNT to form carbon monoxide and metallic nickel, causing the nanotube to be cut. Washing the black powder with sulfuric acid removes nickel as a blue solution.

An alternative catalyst is silver as it is known to catalyse the oxidation of hydrocarbon compounds.⁴⁹⁻⁵¹ Oxidative cutting catalysed by silver nanoparticles produced *in situ* (Method 5)⁴⁴ is similar to that of NiONP. A silver salt precursor was dispersed on MWNT from aqueous silver nitrate solution at 100°C leaving a black powder which, upon heating under argon at 300°C, decomposed to form metallic silver nanoparticles releasing nitrogen dioxide and oxygen. Heating the resultant black composite material at 350°C for 100 minutes in air results in AgNP-catalysed oxidative cutting of the nanotube. Remaining silver nanoparticles are removed by washing with dilute nitric acid, at a concentration which does not cause measurable oxidation of the nanotubes, before isolating the black powder by filtration.

The air oxidation catalysed by AgNP produced *ex situ* (Method 6,⁴⁵ **Figure 2.4**) differs from Method 5 mainly by method of nanoparticle-nanotube composite preparation. While the *in situ* synthesis approach forms nanoparticles in the presence of MWNT from pre-adsorbed metal precursors co-ordinating to acidic functional group defects on the nanotube, the *ex situ* synthesis uses standard colloidal techniques to prepare stabilised AgNP which can then be uniformly dispersed on the nanotube surface from solution. This method has the potential to offer more control over nanoparticle size, morphology and dispersion on the nanotube surface and thus, more control over nanotube length subsequent to oxidative

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cutting. Initially, nanoparticles are synthesised by a modified Brust-Schiffrin reduction⁵² first described by Kang and Kim.⁵³ This synthetic method involves a silver nitrate precursor, an alkanethiol stabiliser molecule, comprising of a thiol group which effectively co-ordinates to the metallic silver atoms of the growing nanoparticle core, along with a large alkyl chain which aids solvation in organic media as well as preventing aggregation by steric repulsion. The silver is then reduced by the addition of sodium borohydride at room temperature to form metallic nanoparticles which are subsequently stabilised by dodecanethiol. The ratio of alkanethiol to silver offers a convenient control of nanoparticle size. Recrystallisation from acetone affords a dark brown precipitate isolable by filtration. UV-visible spectroscopy confirms the formation of nanoparticles by the presence of a surface plasmon resonance at 435 nm. This absorbance, due to the collective oscillation of the conduction band electrons on the nanoparticle surface, is diagnostic of noble metal nanoparticles.⁵⁴ Statistical analysis of transmission electron micrographs showed the discrete particles to have an average diameter of 7.3 (± 1.7) nm.

The second stage involved the self-assembly of silver nanoparticle/MWNT composite material, by ultrasonication of CVD MWNT in a solution of AgNP, allowing the nanoparticles to adsorb on the nanotube surface. In order to ensure sufficient uptake of nanoparticles by the nanotube, a nanoparticle to nanotube mass ratio of 1:1 was used which, being greater than the maximum loading ratio, ensured reproducible saturation of the nanotube surface with nanoparticles. Filtration and washing with dichloromethane removed excess AgNP not adsorbed to the MWNT, to afford a black solid composite material with residual metal mass (at 1000°C, as measured by thermogravimetric analysis) of 29% indicating considerable uptake of AgNP by MWNT. The composite material also exhibited primary oxidation in air at 472°C, considerably reduced compared to as-received MWNT (589°C) demonstrating the effective catalytic oxidation of carbon due to AgNP.

The final stage was the preparative oxidative cutting process, whereby the composite material was heated in air at 480°C for 7 minutes resulting in a 32% mass loss. This

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temperature was chosen as it is sufficient for catalytic oxidation (being above 472°C), yet not high enough to allow the uncatalysed, and therefore uncontrolled, oxidation of MWNT (being less than 589°C). Heating at this temperature for 7 minutes afforded a mass loss of 32% suggesting that catalytic oxidation had occurred, while remaining low enough to ensure an acceptable yield. The resultant black powder was dispersed in nitric acid by ultrasonication to remove silver before being filtered and washed with water.

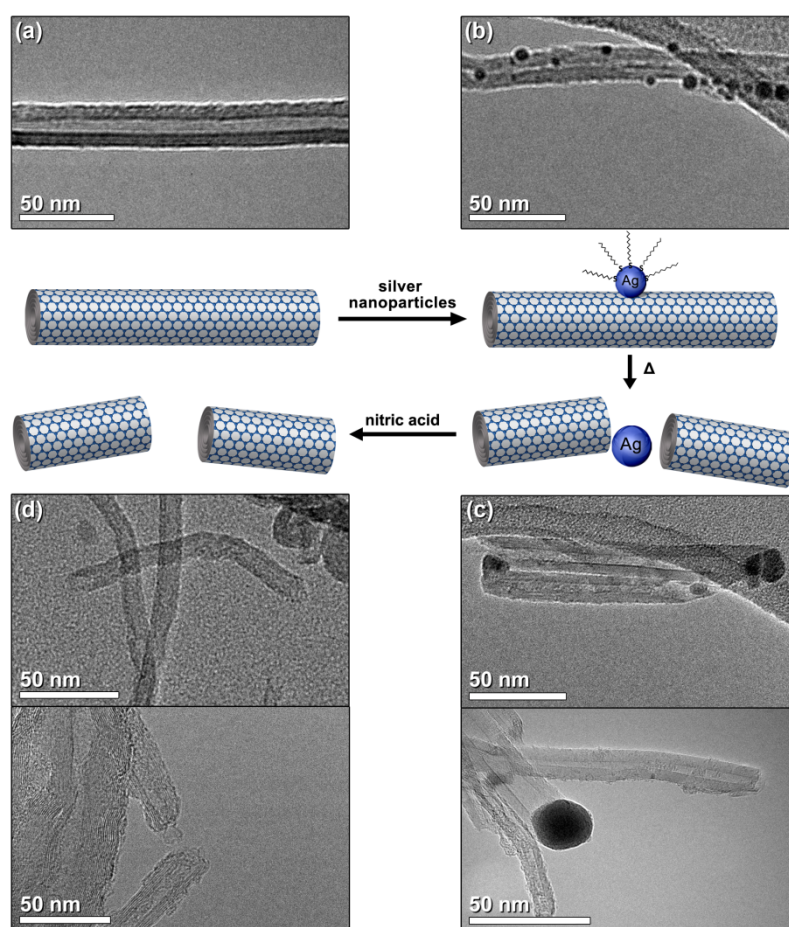


Figure 2.4 Schematic representation of each stage of the AgNP-catalysed oxidative cutting of MWNT accompanied with representative transmission electron micrographs, showing: (a) as-received CVD MWNT; (b) AgNP-dispersed on the external surface of CVD MWNT by ultrasonication; (c) the resulting cut MWNT after heating the AgNP/MWNT composite material in air showing metallic nanoparticles remaining at the recently cut MWNT termini; and (d) the cut MWNT after removal of silver by nitric acid washing.

Whilst the exact mechanism of silver-catalysed oxidation of carbon nanotubes remains unclear, silver is known to both co-ordinate effectively with aromatic molecules⁵⁵ and

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catalyse the oxidation of hydrocarbon compounds.^{49, 50} Therefore, a mechanism is tentatively proposed whereby the π -bonds of carbon nanotubes co-ordinate to silver cations, following the Dewar-Chatt-Duncanson model,^{56, 57} thus reducing the strength of the bond and facilitating oxidation at a lower temperature (**Figure 2.5**).

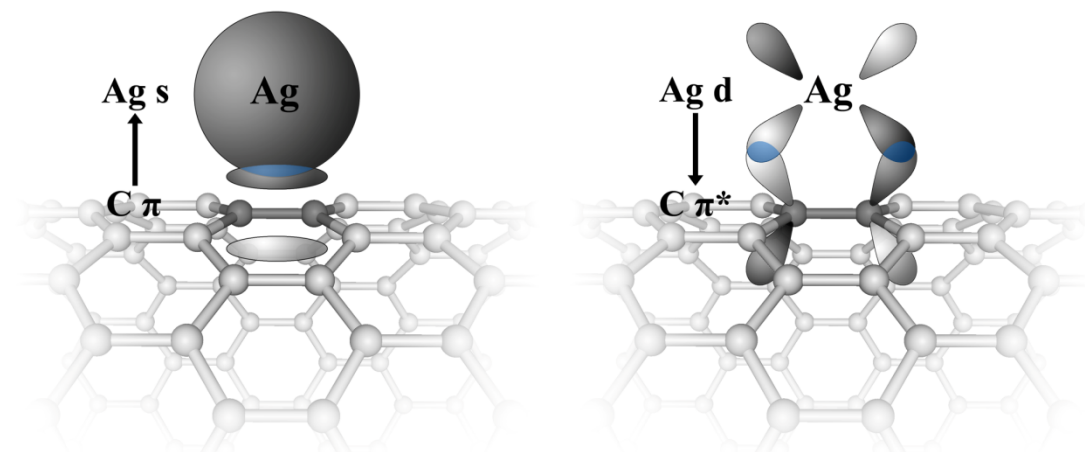


Figure 2.5 Schematic representation of the two potential, synergistic bonding interactions between silver cations and the π system of a carbon nanotube describing (a) the donation of electrons from the occupied nanotube π -bonding orbital to the vacant 5s orbital of $\text{Ag}^{(I)}$ and (b) the back-donation of electrons from an occupied $\text{Ag}^{(I)}$ d-orbital to the vacant π^* antibonding orbital of a nanotube carbon-carbon bond. Both interactions contribute to an overall reduction in bond order, making the weaker carbon bond more susceptible to oxidative cleavage.

The materials resulting from each of the six methods were characterised by complementary microscopy (**Figure 2.6**, **Figure 2.7** and **Table 2.1**) and spectroscopy methods (**Table 2.1**). The most powerful analytical method was transmission electron microscopy, allowing direct observation and measurement of individual carbon nanotubes from each sample. Qualitative analysis revealed that each method had been successful in reducing the length of CVD MWNT (**Figure 2.6** & **Figure 2.7**). The nanotubes were visibly shortened in all cases as, before each procedure, the vast majority of nanotubes extended beyond the frame of measurement due to their extreme length (**Figure 2.6a-b**) whereas, after each treatment, there were often instances where both termini of an individual nanotube were visible, demonstrating a clear reduction in length (**Figure 2.6c-d**).

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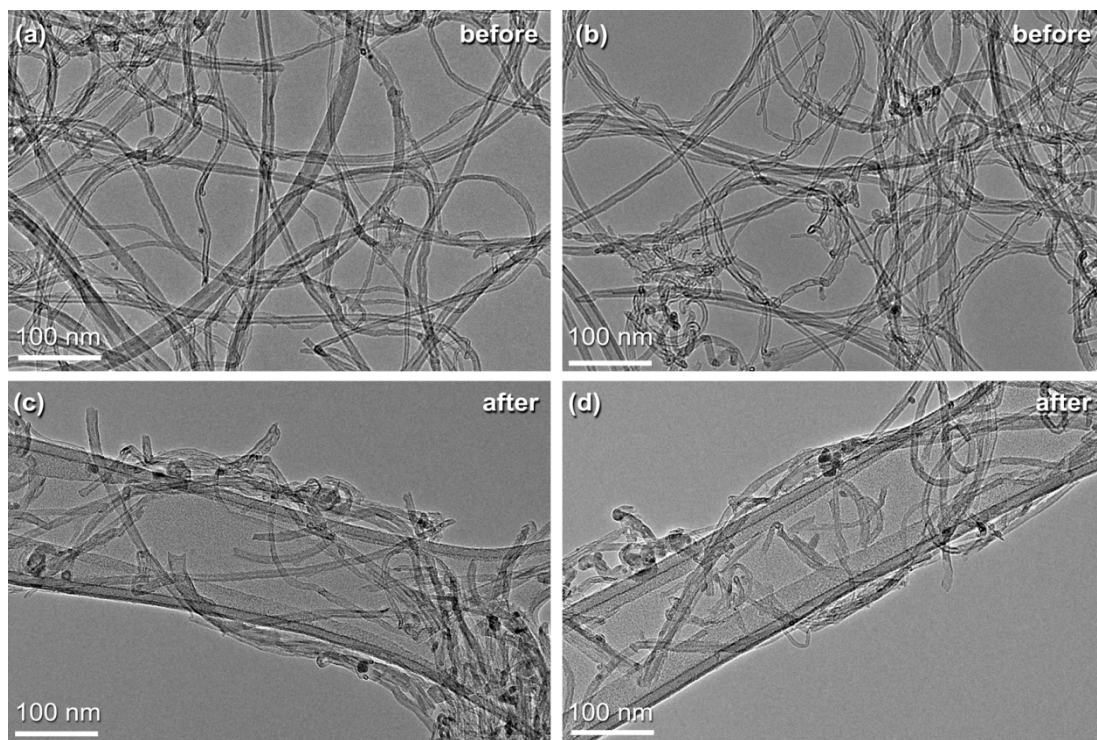


Figure 2.6 Transmission electron micrographs before (a-b) and after (c-d) the air oxidation of CVD MWNT catalysed by *ex situ* AgNP demonstrate the reduction in length in many instances while retaining their tubular morphology. Prior to the procedure, the vast majority of MWNT exhibit extreme length extending beyond the frame, whereas subsequent to oxidative cutting, there are many instances where both termini of a nanotube are visible due to a significant reduction in nanotube length. No visible corrugations or large vacancy defects have formed as a consequence of the procedure and the decrease in average nanotube diameter from 14.4 ± 6.0 nm to 12.4 ± 3.7 nm is within the standard deviation of the measurement. The carbon nanotubes are adhered to an amorphous carbon film support for analysis.

To allow detailed quantitative comparison of each procedure, statistical analysis of carbon nanotube length was measured from the electron micrographs (**Figure 2.7** and **Table 2.1**), and coupled with Raman spectroscopy measurements to quantify changes to nanotube morphology (**Table 2.1**).

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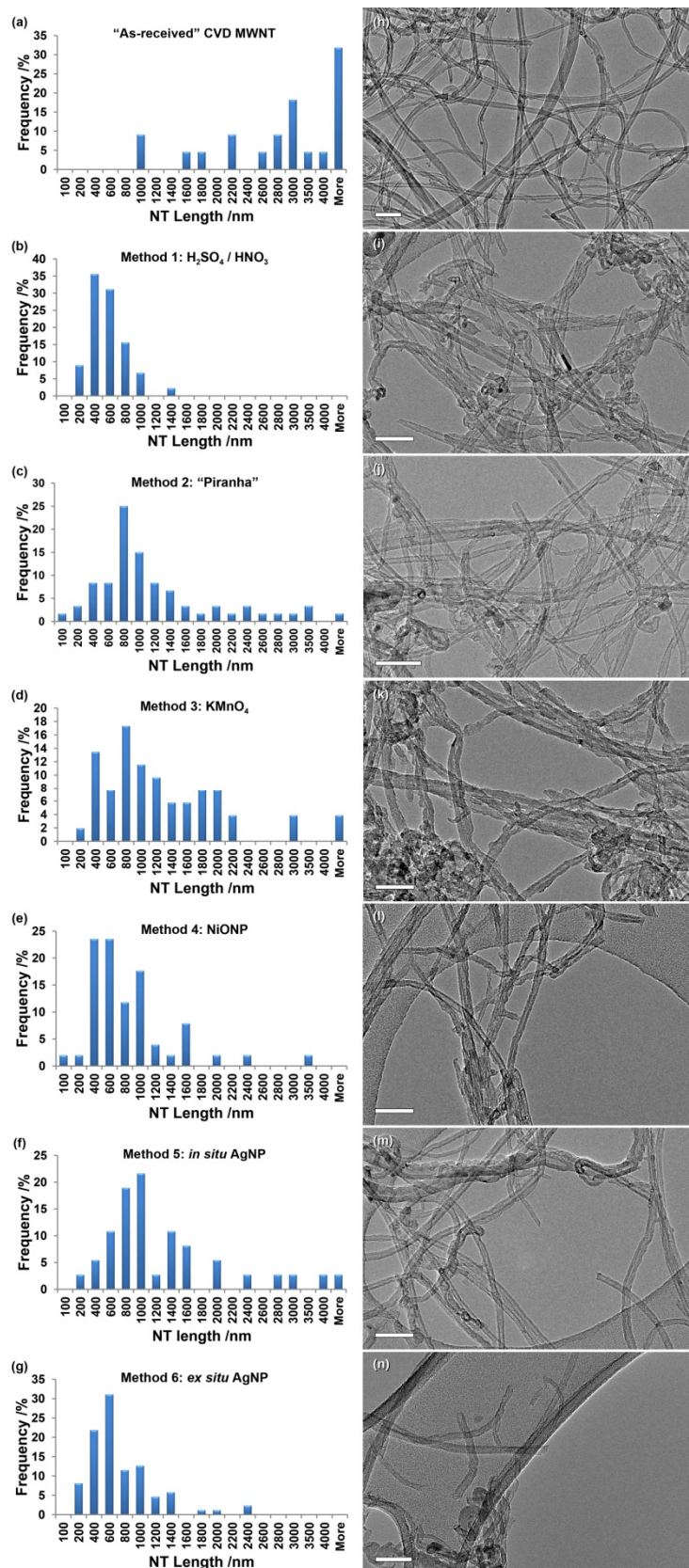


Figure 2.7 Nanotube length (L_{NT}) distribution histograms (a-g) as measured by statistical analysis of transmission electron micrographs, along with a representative electron micrograph (h-n), for the treatment of CVD MWNT with Methods 1-6 respectively. Scale bars are 50 nm.

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Table 2.1 Evaluation of different methods for cutting CVD MWNT. L_{NT} indicates the mean length of CVD MWNT subsequent to each treatment, as determined by statistical analysis of transmission electron micrographs. ΔL_{NT} describes the percentage decrease in nanotube length relative to the as-received CVD MWNT. $I_D:I_G$ and $\Delta(I_D:I_G)$ refer respectively to the mean ratio and change in mean ratio of D to G bands as determined by Raman spectroscopy. $I_D:I_G$ gives a direct quantitative indication of the extent of disorder in a lattice of sp^2 -hybridised carbon and thus the extent of carbon nanotube functionalisation or damage introduced during each procedure.

Method	L_{NT}/nm	$\Delta L_{NT}/\%$	$I_D:I_G$	$\Delta(I_D:I_G)/\%$
"As-received" CVD MWNT	3250±1600	-	0.791	-
Method 1: Oxidation: H_2SO_4/HNO_3 ^{25, 28}	478±243	-85	0.881	+11
Method 2: Oxidation: "piranha" solution ²⁹	1130±862	-65	0.863	+9
Method 3: Oxidation: $KMnO_4$ ³⁰	1250±986	-61	1.185	+50
Method 4: Air oxidation by NiONP catalyst ⁴³	787±586	-76	0.956	+21
Method 5: Air oxidation by <i>in situ</i> AgNP catalyst ⁴⁴	1350±1450	-58	0.814	+2
Method 6: Air oxidation by <i>ex situ</i> AgNP catalyst ⁴⁵	634±436	-81	0.801	+1

This systematic comparison confirmed that all of the methods evaluated were successful in reducing the mean length of CVD MWNT. The greatest reductions in mean length are achieved by sonication in mixed acids (Method 1) and oxidation *via ex situ* silver nanoparticle catalysis (Method 6), giving reductions in mean length of 85 and 81% respectively. The nanotube length analysis (**Figure 2.7**) shows that cutting with both mixed acid and oxidation *via ex situ* AgNP give the most uniform nanotube length distributions, indicating that these two methods exhibit much better control over nanotube length than the alternative methods which typically result in wider length distributions.

The change in intensity ratio of D to G bands, as measured by Raman spectroscopy (**Table 2.1**), gives a direct indication of the extent of disorder in the nanotubes subsequent to the cutting process. Cutting carbon nanotubes will inevitably result in an increase in the extent of disorder, quantified by an increase in $I_D:I_G$, as many of the methods studied introduce oxygen containing functional groups to the nanotube termini and sidewalls in order to stabilise highly reactive carbon radicals created by carbon-carbon bond cleavage. Indeed, these data demonstrate that the magnitude of this increase is variable up to 50% (Method 3). However, while mixed acid cutting showed a clear 11% increase in $I_D:I_G$, the smallest increase was observed for oxidation in air catalysed by *ex situ* AgNP which showed a

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negligible increase (0.01), within standard deviation of measurements in triplicate (± 0.02). Thus, oxidation in air catalysed by *ex situ* AgNP (Method 6) represents the best method for producing short nanotubes with minimal introduction of defects.

To elucidate, in more detail, how the structural and functional properties of the carbon nanotubes may have been affected specifically by air oxidation catalysed by *ex situ* AgNP, these carbon nanotubes were further characterised by comparative analytical techniques (**Figure 2.8**).

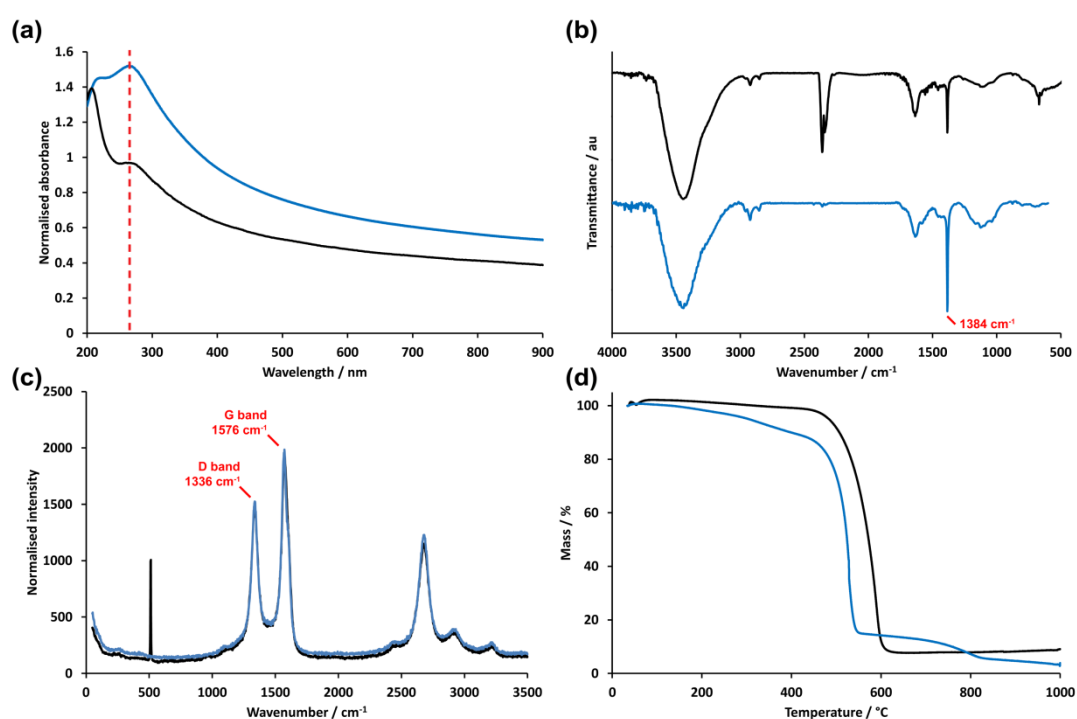


Figure 2.8 Spectroscopic and gravimetric analysis of CVD MWNT prior (black) and subsequent to (blue) cutting by air oxidation catalysed by *ex situ* AgNP (Method 6). (a) UV-vis spectroscopy shows no shift in the position of the π -plasmon absorbance at 264 nm, indicated by the red dotted line. (b) Infrared spectroscopy indicates minimal changes to CNT functionalisation except a stronger band at 1384 cm^{-1} , which might suggest a slight increase in functionalisation as a result of the procedure but could also be due to a molecular impurity common to KBr (peak at 2360 cm^{-1} due to atmospheric CO_2). (c) Raman spectrum shows no discernible change in $I_D:I_G$ ratio (spectrum normalised to G band, peak at 520 cm^{-1} corresponds to the silicon support). (d) Thermogravimetric analysis showing a slight reduction in oxidation temperature from 589°C to 528°C . Mass loss at 750°C is likely to correspond to decomposition of silver oxide, indicating that some silver has remained after HNO_3 washing and this may be the cause of the reduction in oxidation temperature. It is important to note that residual mass at 1000°C are not comparable in this case, as the final HNO_3 washing may have altered the mass of iron remaining from nanotube synthesis.

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UV-visible spectra of carbon nanotubes typically exhibit a π plasmon absorbance between 155-310 nm associated with the collective excitation of nanotube π electrons, which provides an indication of the extent of conjugation and also correlates with carbon nanotube diameter.⁵⁸ CVD MWNT subsequent to AgNP-catalysed air oxidation shows a constant π plasmon absorbance at 264 nm indicating no measurable change in the extent of conjugation. Infrared spectroscopy shows little change in functionalisation aside from an increase in intensity of the peak at 1384 cm^{-1} , which may be due to the C-O stretch in oxygen-containing functional groups such as ethers, esters or alcohols,⁵⁹ or possibly a disorder-induced phonon absorbance band.⁶⁰ Both of these possibilities suggest that the nanotube may have become slightly functionalised as a result of the catalytic oxidation. However, in contrast, Raman spectroscopy shows negligible change in the intensity ratio between D and G bands at 1336 and 1576 cm^{-1} respectively inferring minimal sidewall damage due to the oxidation procedure. Raman spectroscopy is the more reliable technique in this regard as there is a possibility that the sharp peak observed in the IR spectrum is due to a molecular impurity in the KBr used in the measurement. Therefore, it is concluded that minimal sidewall functionalisation of the CNT has taken place during the procedure. Thermogravimetric analysis shows a subtle decrease in the primary oxidation temperature from 589°C to 528°C as a consequence of oxidation. Typically, this often suggests that the CNT may have been further functionalised, but in this case, this is likely to be caused by a small amount of catalytic silver remaining in the sample.

These combined spectroscopic and microscopic analysis techniques show that the structural and functional characteristics of the nanotubes remain largely unaffected by catalytic oxidation which is critical for their use as nanoscale reaction vessels as well in functional devices. Therefore, considering all available evidence, this study indicates that oxidation in air catalysed by *ex situ* silver nanoparticles is the most effective method for shortening MWNT as it results in one of the most marked decreases in mean length (to $643 \pm 436\text{ nm}$) with a narrow diameter distribution, while also causing minimal sidewall damage.

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2.3.2. Method optimisation: alternative metallic nanoparticles

A range of transition metals are known to catalyse hydrocarbon oxidation⁶¹ and may also be applicable to the oxidation of carbon nanotubes; therefore, it is important to evaluate and compare different types of nanoparticles in nanotube cutting applications. Indeed, Wang *et al.*⁴⁴ demonstrated that iron nanoparticles also showed catalytic behaviour towards carbon nanotube oxidation, reducing the oxidation temperature by 190°C; however, the authors concluded that iron is less efficient than silver in this process, affording less control over nanotube length distributions. In light of this, a range of nanoparticulate catalysts (Au, Cu and PdNP) were synthesised and assessed for their ability to catalyse the oxidative cutting of CVD MWNT. As silver was known to be effective, the surrounding elements in the periodic table were chosen due to their similar electronic configuration and therefore comparable reactivity. Conveniently, a common synthetic procedure was known allowing the synthesis of dodecanethiol-stabilised nanoparticles of comparable diameter for each metal.⁶² This biphasic Brust-Schiffrin⁵² synthetic procedure yielded dark brown solid gold, copper and palladium nanoparticles. Gold nanoparticles exhibited a characteristic surface plasmon resonance at 523 nm and nanoparticle diameter was measured by statistical TEM analysis to be 2.2 (± 0.7) nm. Analogous measurements of copper and palladium nanoparticles found diameters of 2.6 (± 1.4) nm and 1.2 (± 0.3) nm respectively. The stabilised nanoparticles were dispersed on the surface of CVD MWNT by sonication in dichloromethane, analogous to that described previously. As the affinity of the nanotubes for each nanoparticle is likely to vary, a NP to NT mass ratio of 1:1 was used during the ultrasonication to allow maximum loading of each nanoparticle on the nanotubes. This led to varied metal loading on CVD MWNT, showing a trend seemingly dependant on the polarisability of the metal (**Table 2.2**), following precedent by Rance *et al.*⁶³, with the highest loading for gold, and lowest for copper.

Each metal was shown by thermogravimetric analysis to catalyse the oxidation of carbon nanotubes as indicated by reduced oxidation temperatures (**Figure 2.9**, **Table 2.2**).

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This reduced oxidation temperature was used for the oxidation in air catalysed by each metal, and the resultant black solid was washed with dilute nitric acid. Although this stage had limited success in removing gold and palladium nanoparticles, it was carried out in each case to provide reliable comparison.

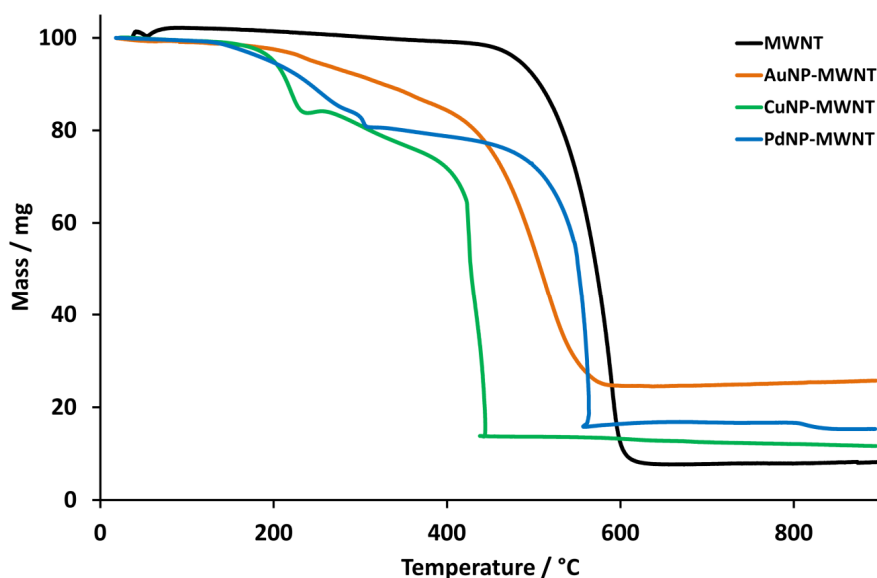


Figure 2.9 Thermogravimetric analysis of the composite materials comprising of gold (orange), copper, (green) and palladium (blue) metallic nanoparticles dispersed on CVD MWNT (black) showing the reduced oxidation temperature of each composite material relative to as received CVD MWNT.

Table 2.2 Thermogravimetric analysis of composite materials comprising of metal nanoparticles on CVD MWNT showing the oxidation temperature (T_{ox}), the reduction in oxidation temperature relative to as-received CVD MWNT (ΔT_{ox}) and the metal loading (M) as measured using TGA by the mass remaining at 900°C (corrected by subtracting the residual metal from CVD MWNT synthesis). Raman spectroscopic data for CVD MWNT subsequent to oxidation catalysed by metal nanoparticles, detailing the frequency and relative intensity of D and G bands as well as the percentage change in this value relative to as-received CVD MWNT.

Material	$T_{ox} / ^\circ\text{C}$	$\Delta T_{ox} / ^\circ\text{C}$	M / wt.%	D / cm^{-1}	G / cm^{-1}	$I_D:I_G$	$\Delta(I_D:I_G) / \%$
CVD-MWNT	589	-	-	1335.7±3.8	1576.2±1.7	0.791±0.020	-
AuNP-CVD MWNT	512	-77	17	1340.2±1.7	1578.2±3.0	0.867±0.045	+9.6
CuNP-CVD MWNT	439	-150	3	1341.3±3.5	1576.7±1.5	0.828±0.123	+4.7 ^a
PdNP – CVD MWNT	559	-30	7	1343.8±2.6	1580.2±1.7	0.908±0.045	+14.8

^a Value within standard deviation of measurements in triplicate.

TEM analysis of carbon nanotubes subsequent to air oxidation (**Figure 2.10a-d**), indicates that both gold and copper nanoparticles show no oxidative cutting behaviour at the

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temperature of primary oxidation as indicated by TGA. All observed nanotubes retain their extreme length extending beyond the frame of measurement. While the nanoparticles do not catalytically cut the nanotubes, they instead become preferentially encapsulated within the CNT internal cavity showing no further catalytic activity once encapsulated. However, palladium nanoparticles show some evidence of nanotube length reduction (**Figure 2.10e-f**). Multiple instances were observed of short nanotubes (average length 390 ± 305 nm), often with PdNP remaining at or near the cut nanotube termini suggesting cutting by catalytic oxidation. However, while there were instances of very short nanotubes, approximately 50% of the nanotubes remained extremely long and were, as such, not included in this length analysis because the nanotubes extended beyond the frame of measurement. It is important to highlight while comparing these three metals that the nanotube oxidation temperature was reduced by varying degrees depending on the metal; therefore, the difference in catalytic cutting behaviour may be partly a result of temperature. For instance, palladium was the only metal of the three to show catalytic cutting behaviour, while also showing the smallest reduction in CNT oxidation temperature of 30°C (**Table 2.2**). Due to CNT inhomogeneity, oxidation can be a broad feature (**Figure 2.9**) occurring over a temperature range (*ca.* 500-600°C). Therefore, a reduction of the peak oxidation temperature by 30°C leaves the *catalytic* oxidation well within the temperature range of uncatalysed oxidation. In light of this, it is not necessarily clear whether the observed reduction in length is entirely a result of PdNP catalysis or partly due to non-catalysed oxidation at elevated temperature. Indeed, it may be the case that the enhanced catalytic activity of palladium is also due to this elevated temperature. In a practical sense, the reduced efficiency of palladium as compared to silver, coupled with the comparatively higher cost of palladium makes this a non-viable alternative.

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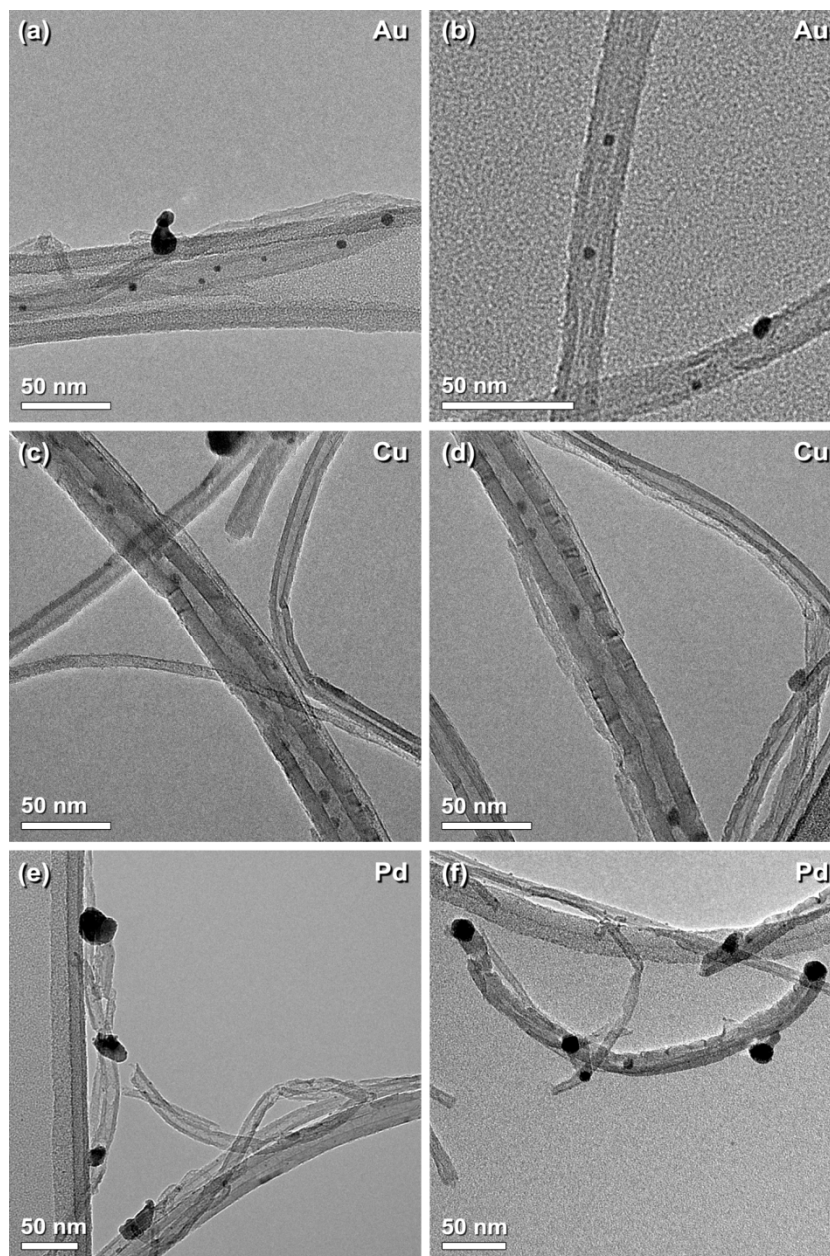


Figure 2.10 Transmission electron micrographs showing CVD MWNT subsequent to air oxidation in the presence of (a, b) gold, (c, d) copper, and (e, f) palladium nanoparticles. AuNP and CuNP appear unsuccessful in cutting carbon nanotubes, instead becoming encapsulated within the CNT internal cavity, while PdNP shows oxidative cutting behaviour similar to that of AgNP.

Interestingly, a correlation between the catalysed oxidation temperature for each metal and the change in $I_D:I_G$ as a consequence of oxidation (**Table 2.2**, **Figure 2.11**) indicates that higher temperature oxidation generally introduces a greater number of nanotube defects. This suggests that the success of AgNP in this procedure, resulting in shortened CNT with negligible introduction of defects, is due to the high activity of the metal at a reduced oxidation temperature.

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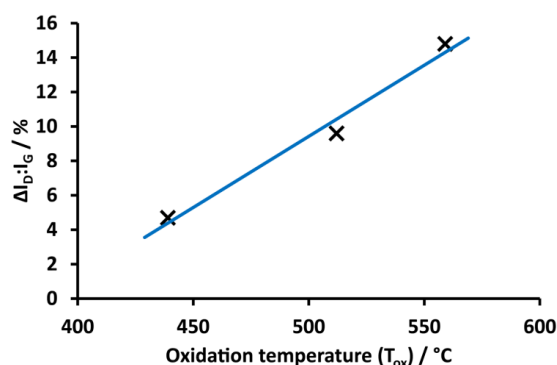


Figure 2.11 Plot showing the correlation between percentage increase in $I_D:I_G$ with temperature of oxidation (T_{ox}) for the oxidative cutting in air catalysed by copper, gold and palladium (at 439, 512 and 559°C respectively).

After comparison to alternative metals including gold, copper and palladium, it has been shown that, consistent with previous reports,⁴⁴ silver nanoparticles appear to be the most suitable catalyst found for carbon nanotube oxidation.

2.3.3. Application of silver-catalysed oxidation to a range of carbon nanostructures

To explore the versatility of this approach, the *ex situ* AgNP-catalysed oxidation procedure was systematically applied to a range of nanostructured carbon materials (**Table 2.3**, **Figure 2.13** and **Figure 2.14**). It is important to note that, as the carbon nanostructures investigated were manufactured by a variety of methods, all nanotubes were pre-treated by sonication in hydrochloric acid before being collected by vacuum filtration, in order to enable direct comparison of different nanotube samples. This non-oxidative and non-destructive process removes any accessible metal particles along with some graphitic impurities, which may interfere with the desired catalytic oxidation, whilst not damaging or functionalising the nanotubes.⁶⁴

In a typical experiment, black solid carbon nanostructure (CNS) was added to dodecanethiol-stabilised silver nanoparticles ($d_{NP} = 7.3 \pm 1.7$ nm) synthesised by a modified Brust-Schiffrin reduction (see **Section 2.5.7**) in dichloromethane at a concentration of 1 mg ml^{-1} , and using a CNS:AgNP mass ratio of 1:1. Ultrasonication for 30 minutes effected

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saturation of the nanostructure surface with nanoparticles, and excess nanoparticles were removed during filtration by washing with dichloromethane, to yield a black solid nanoparticle/carbon nanostructure composite material. Thermogravimetric analysis indicated the oxidation temperature of each composite and this value was used for catalytic oxidative cutting in air. The rate of oxidation varied for each nanostructure and therefore, the duration of oxidation was varied in order to achieve approximately 35-50% mass loss (see **Section 2.5.9, Table 2.5**). This range was chosen as it represented sufficient mass loss to ensure that oxidation had occurred, while not allowing excess oxidation to significantly reduce yield and introduce nanostructure damage. The black powder remaining subsequent to catalytic oxidation was suspended in dilute nitric acid by ultrasonication for 30 minutes to remove residual silver before being isolated by filtration, washed with copious water and dried *in vacuo* to yield black solid carbon nanostructure.

The nanostructure length analysis was carried out by careful statistical analysis of transmission electron micrographs (**Figure 2.12**). SWNT are known to exist in bundles making measurement of individual nanotubes incredibly challenging and therefore the length of the SWNT bundles was measured (**Figure 2.12a-b**) when it was not possible to accurately measure individual nanotubes. Assuming that no individual SWNT can be longer than the bundle, the measurements of L_{NT} for SWNT samples do not discriminate between bundles and isolated nanotubes and thus, represent the maximum length of a single nanotube within a given bundle, consistent with previous studies.⁶⁵

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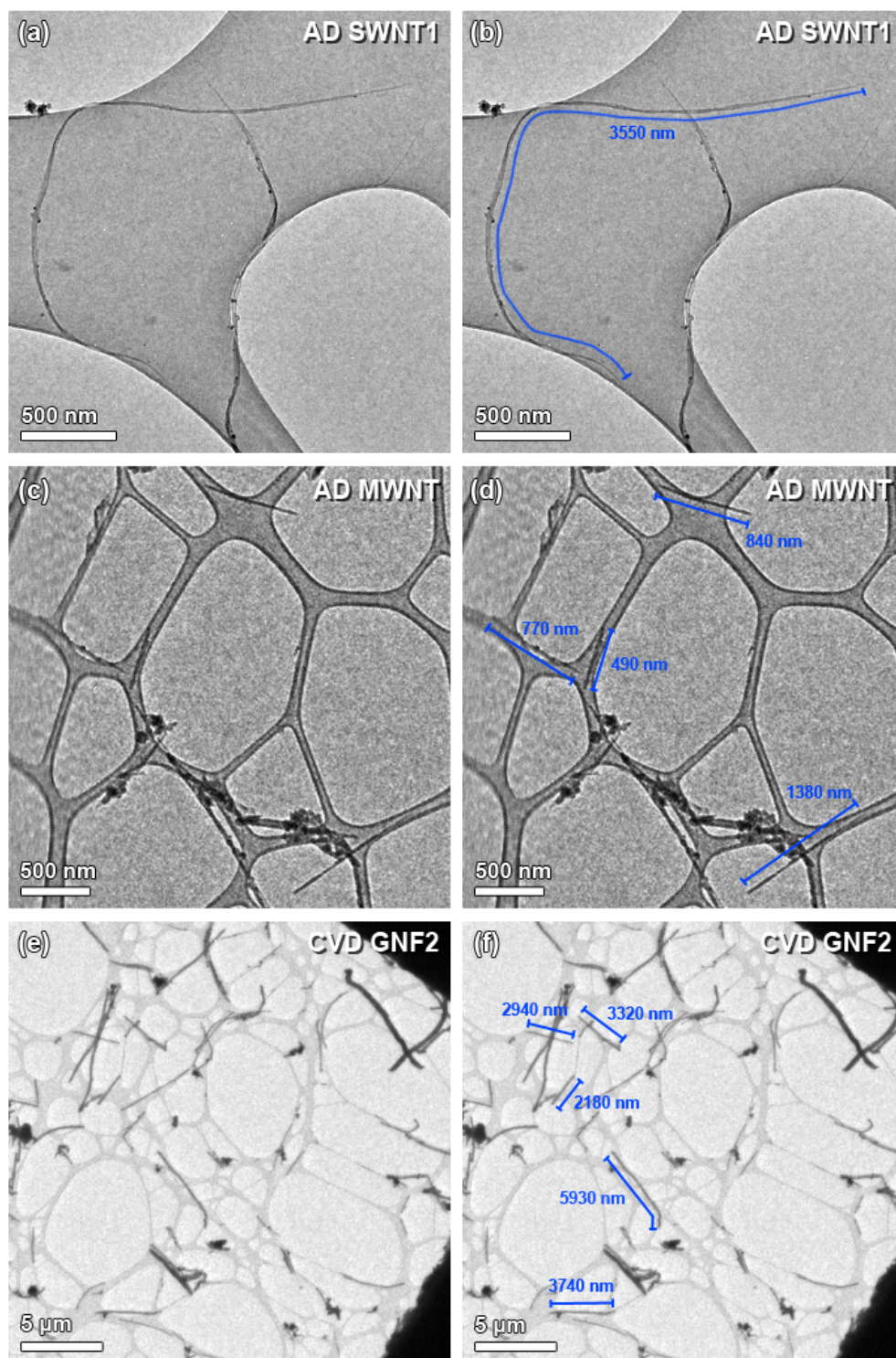


Figure 2.12 Representative transmission electron micrographs showing (a) AD SWNT1, (c) AD MWNT, (e) CVD GNF2 and examples of the typical procedure for measuring carbon nanostructure length (b, d and f respectively).

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Table 2.3 Evaluation of the controlled cutting of a range of carbon nanostructures (single-walled carbon nanotubes, SWNT; multi-walled carbon nanotubes, MWNT; graphitised nanofibres, GNF) using the *ex situ* AgNP-catalysed oxidation procedure. Nanotube diameter (d_{NT}), mean initial length (L_{NT}) and change in mean length after cutting (ΔL_{NT}) as determined by TEM; change in oxidation temperature catalysed by AgNP (ΔT_{ox}) and catalyst loading (Ag/ wt.%) as measured by TGA; mean ratio ($I_D:I_G$) and change in mean ratio ($\Delta I_D:I_G$) of D to G bands as attained from Raman spectroscopy.

Carbon Nanostructure	d_{NT} / nm	L_{NT} / nm	ΔL_{NT} / %	ΔT_{ox} / °C	Ag / wt.% ^a	$I_D:I_G$	$\Delta(I_D:I_G)$
CoMoCAT SWNT	0.7±0.1	2499±1338 ^b	-45	-84	21	0.113±0.011	+0.034
HiPCO SWNT	1.0±0.1	3589±1638 ^b	-28	-56	6	0.159±0.011	+0.009 ^c
AD SWNT1	1.3±0.1	2434± 849 ^b	-28	-31	12	0.038±0.003	+0.008
AD SWNT2	1.3±0.1	3195±1532 ^b	-4	-108	42	0.016±0.002	-0.004
CVD MWNT	14.4±6.0	3251±1601	-80	-117	21	0.791±0.028	+0.010 ^c
AD MWNT	19.0±5.8	2563±1513	-34	-111	36	0.147±0.012	+0.005 ^c
CVD GNF1	96±32	7586±7538	-75	-263	22	0.225±0.049	+0.104
CVD GNF2	115±37	5102±5084	-46	-250	30	0.154±0.058	+0.254

^a Silver loading is corrected to account for residual metal content from carbon nanotube synthesis catalyst and represents the maximum uptake of nanoparticles by carbon nanostructures from organic suspension. ^b SWNT length measurements do not discriminate bundles and isolated carbon nanotubes. ^c Values within standard deviation of measurements in triplicate.

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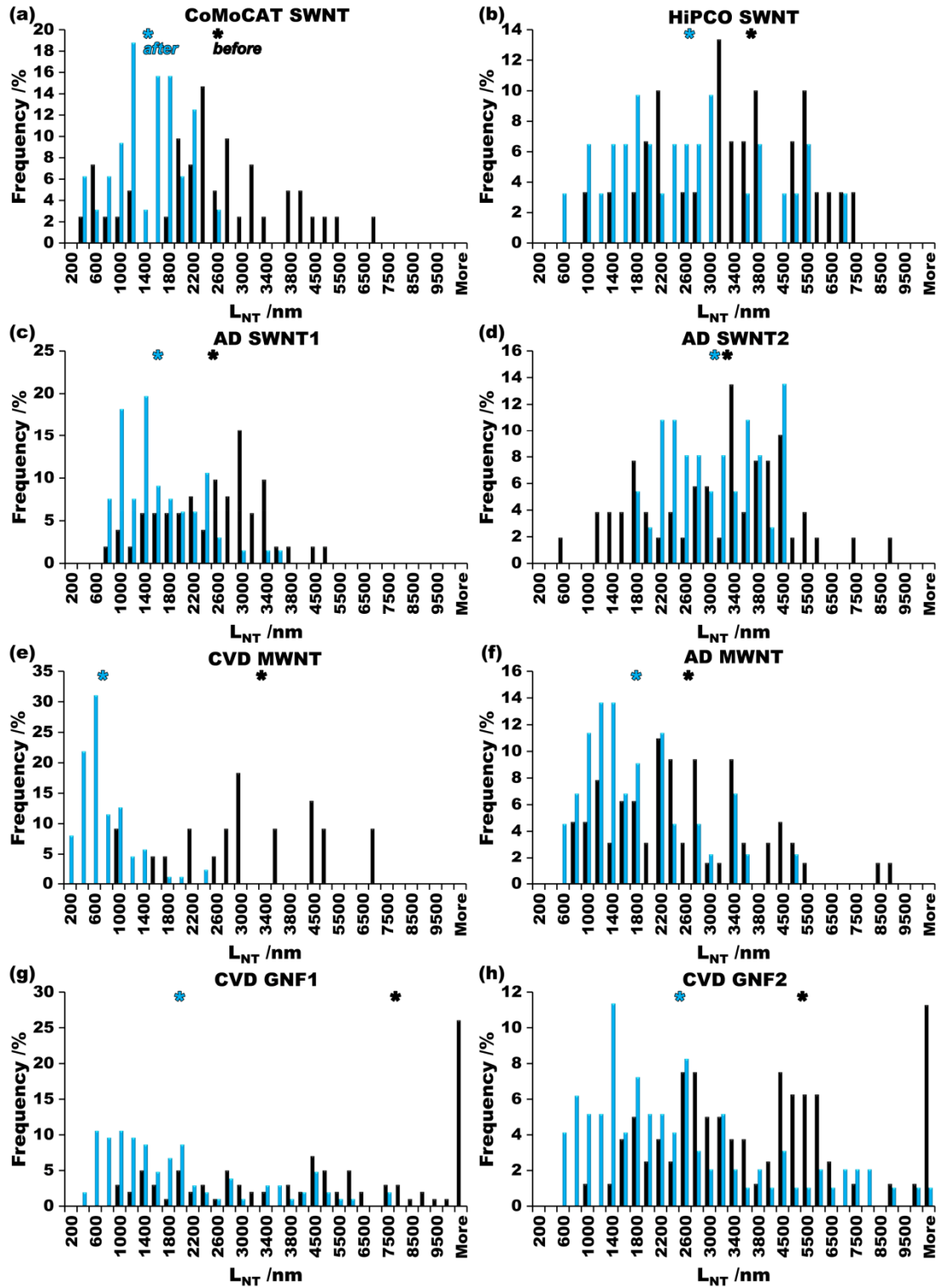


Figure 2.13 Histogram showing the distribution of nanotube length (L_{NT}) before (black) and after (blue) the cutting procedure for each carbon nanostructure (a-h). Asterisks denote mean values of L_{NT} .

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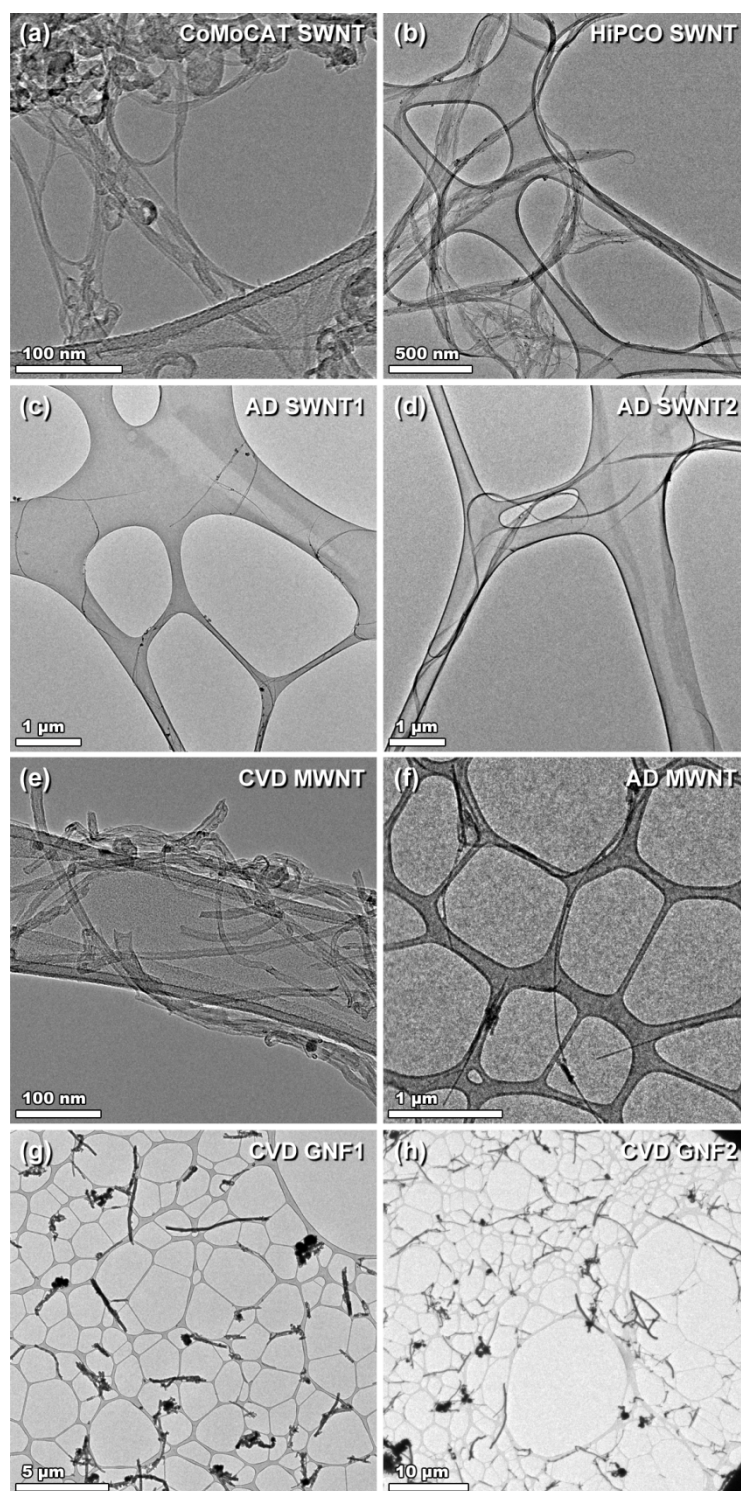


Figure 2.14 Representative transmission electron micrographs showing each carbon nanostructure subsequent to silver nanoparticle-catalysed oxidation. (a) CoMoCAT SWNT, (b) HiPCO SWNT, (c) AD SWNT1, (d) AD SWNT2, (e) CVD MWNT, (f) AD MWNT, (g) CVD GNF1 and (h) CVD GNF2.

Careful microscopic analysis of carbon nanotube length subsequent to silver-catalysed air oxidation demonstrates that this method is highly effective for the controlled cutting of a wide spectrum of carbon nanostructures, with the mean length clearly decreasing by 28-80%

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in all but one case. These experiments were carried out without any further specific optimisation for each nanostructure, clearly showing how easily this procedure could potentially be applied to alternative carbon nanomaterials beyond those employed in this study. Further analysis indicates that larger diameter multi-walled carbon nanostructures (MWNT and GNF) are more effectively shortened (34-80%) than narrower SWNT (28-45%). This could be attributed to the inherently higher polarisability of wider nanostructures exhibiting stronger interactions with catalyst nanoparticles. In addition, carbon nanostructures manufactured by the CVD process were more drastically reduced in length (up to 80%) than those synthesised by arc-discharge (up to 34%).

A particularly pertinent comparison is that of AD SWNT2, produced by arc-discharge and possessing a near perfect sidewall structure ($I_D:I_G = 0.016$), to AD SWNT1 which shares many attributes with AD SWNT2 (i.e. manufacturing process and diameter) but with a higher proportion of defects ($I_D:I_G = 0.038$). While AD SWNT2 remained unaffected by this cutting procedure, AD SWNT1 was successfully shortened by 28%. These measurements, therefore, indicate that the presence of initial defects is the most important factor influencing how effectively nanotubes are shortened by AgNP-catalysed oxidation. Indeed, as wider multi-walled carbon nanostructures tend to have more defects than SWNT,⁶⁶ the observation of wider nanostructures being more successfully cut may simply be related to a greater concentration of initial defects. Furthermore, CVD synthesis produces less structurally pristine carbon nanotubes than arc discharge methods;⁶⁷ this is due to the lower temperatures employed in the CVD process which do not facilitate the structural rearrangements of carbon atoms in the sidewall structure, which occur more readily during the higher temperature arc discharge process.⁶⁸ The importance of nanotube defects is demonstrated across the entire range of nanotubes studied by a correlation between nanotube $I_D:I_G$ ratio and the extent of cutting (**Figure 2.15**), where nanotubes with a higher degree of "disorder" in the form of deviation from a perfect sp^2 lattice (i.e. defects) tend to be shortened more effectively.

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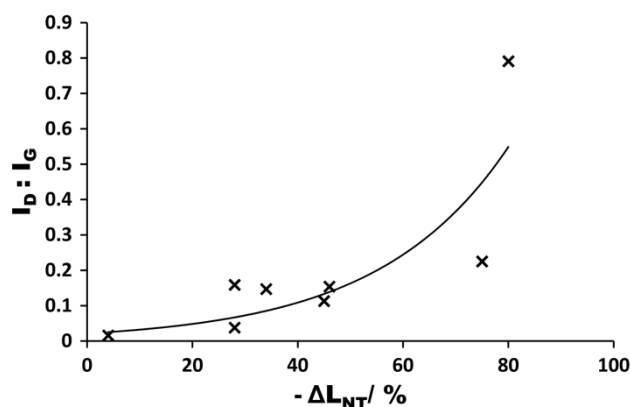


Figure 2.15 Plot showing the correlation between the mean percentage reduction in nanotube length ($-\Delta L_{NT}$) as measured by TEM and initial $I_D:I_G$ ratio as determined by Raman spectroscopy, showing that nanotubes with a higher proportion of initial defects tend to be shortened to a larger extent.

It is clear that defects in the nanotube sidewall play an important mechanistic role in nanoparticle catalysed oxidative cutting. It has been proposed in previous studies of alternative oxidation methods that pre-existing defect sites, as the most reactive areas of the nanotube, would be the initial sites for oxidative cutting and functionalisation.³¹ Furthermore, the difference between a mild and aggressive cutting method is often defined by whether the procedure introduces new defects or simply etches carbon around pre-existing sites.²⁹ For silver nanoparticle catalysed oxidation, nanotube defects could either play a direct mechanistic role, providing oxygen *via* functional groups such as carboxyl, hydroxyl or ethers, or alternatively, nanotube defects could indirectly aid the process by improving nanoparticle-nanotube interactions. The latter could be facilitated by defects providing efficient anchoring points for nanoparticle surface co-ordination; which is supported by a 13% increase in the $I_D:I_G$ ratio for the composite, prior to catalytic oxidation, as a result of interactions between AgNP and carbon nanotubes (**Figure 2.16**). As is common when studying the chemistry of carbon nanotubes, the diverse range of morphologies and surface functionalisation exhibited by nanotubes within any given sample makes it difficult to draw unambiguous conclusions on a detailed mechanistic level.

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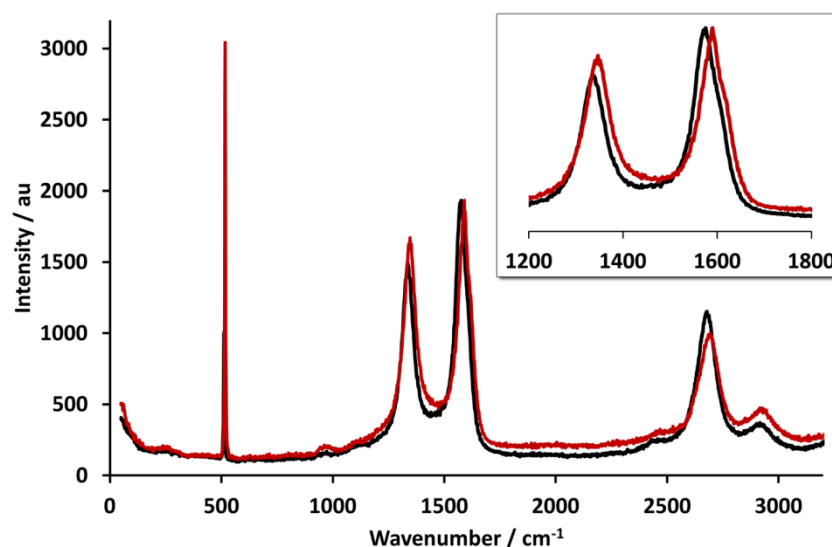


Figure 2.16 Normalised Raman spectra comparing CVD MWNT prior to the procedure (black) and the AgNP-CVD MWNT composite (red) showing the effect of the AgNP on the carbon nanotube. The ratio of the D band (1336 cm^{-1}) to the G band (1576 cm^{-1}) increases by 13% (see expanded inset) as a consequence of depositing silver nanoparticles on the surface, suggesting that silver nanoparticles preferentially aggregate around defect sites⁶⁹ due to a more efficient interaction. Furthermore, the position of the G band is shifted from 1576 cm^{-1} to 1590 cm^{-1} as a consequence of surface adsorbed silver nanoparticles. This upfield shift is indicative of charge transfer from the nanotube to the nanoparticle,⁷⁰ supporting the mechanistic hypothesis described in **Figure 2.5**.

Previous studies have indicated that pre-treatment of carbon nanotubes with nitric acid is required to increase the surface functionalisation and aid the cutting process.^{25, 26, 28, 31, 43–46}

Although these findings suggest that this would indeed improve the result in terms of producing shorter nanotubes, these results actually demonstrate that this pre-treatment is not necessary for the majority of carbon nanotubes when using silver-catalysed oxidation. This would be particularly important for applications where the introduction of additional defects would be undesirable. From a personal perspective, when aiming to utilise CNT as nanoscale reaction vessels, any changes to the chemical functionality of the nanotube surface can have a drastic effect on the reactivity of the nanotube^{18, 19} meaning the resultant structures may undergo unwanted side reactions interfering with the desired chemical process. More generally, various advanced nanotube devices are currently in development aiming to utilise their extraordinary properties; however, the presence of too many defects in these nanostructures can degrade their intrinsic properties.^{66, 71} In particular, the use of carbon nanotubes in nanoscale electronic devices⁷² will require nanotubes of controlled length with

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pristine structures⁹ and as such, minimising nanotube defects while controlling length represents an important step towards integrating carbon nanotubes into this new generation of functional devices.

2.4. Conclusions

This systematic study of various literature protocols for shortening carbon nanotubes has shown that the most effective method for cutting multi-walled carbon nanotubes manufactured by the CVD process is oxidation in air catalysed by pre-formed silver nanoparticles. Combined microscopy and spectroscopic analysis indicates that, of the six methods compared, AgNP-catalysed oxidation in air significantly reduces the length of carbon nanotubes (up to 80%) with minimal damage to the nanotube sidewall.

This method can be readily applied to a variety of carbon nanostructures, including SWNT, MWNT and GNF, possessing the broadest spectrum of structural attributes (diameter, length, internal and external structure). The procedure is most effective for (i) larger diameter carbon nanostructures (MWNT and GNF) and (ii) those produced by the CVD process. Furthermore, there is a clear correlation between the concentration of initial defects and the extent of oxidative cutting, showing that nanotube defects play the most important role in the process. The oxidation in air catalysed by silver nanoparticles, which does not require the use of expensive, specialist equipment or hazardous chemicals, has proved effective, reliable and easily applicable to various carbon nanomaterials and thus represents a highly versatile method for controlling the length of carbon nanotubes. Nanotubes of controlled length produced by this process may become essential for application of carbon nanostructures as nanoscale reactors to contain chemical reactions, particularly affecting the kinetics in these systems by improving diffusion rates of reactants into, and products out from such nanoreactors. Additionally, carbon nanostructures of controlled length will be important in the development of the new generation of functional devices such as computers,¹¹ energy storage devices¹⁰ and drug delivery systems.¹³⁻¹⁵

2.5. Experimental

2.5.1. General

All reagents were purchased from Sigma-Aldrich, UK and used without further purification. Carbon nanotubes were purchased from a range of commercial suppliers (**Table 2.4**). Thermogravimetric analysis (TGA) was performed using a TA Instruments SDT Q600 under a flow of air at a rate of 100 mL min⁻¹ at a heating rate of 10°C min⁻¹ from room temperature to 1000°C, unless specified otherwise. Infra-red (IR) spectra were measured as potassium bromide discs using a Nicolet 380 FT-IR spectrometer over the range 4000-400 cm⁻¹. Raman spectroscopy was conducted by Dr. Graham Rance using a HoribaJY LabRAM HR spectrometer with a laser wavelength of 532 nm. Samples were dropcast from methanolic solutions onto Si(100) wafers and a minimum of five spectra recorded from different areas of the sample. UV-vis spectra were recorded in solution using 1 cm quartz cuvettes using a Perkin-Elmer Lambda 25 UV-vis spectrophotometer at a scan rate of 240 nm min⁻¹ over the range 190-900 nm. The position and intensity of the absorbance maximum was obtained using the “find peaks” function in UV WinLab ES software with the threshold set at 0.01. Transmission electron microscopy (TEM) was performed by Professor Andrei Khlobystov or Dr. Alessandro La Torre using a JEOL 2100F TEM (field emission gun source, information limit <0.19 nm) at room temperature. Analysis of both carbon nanotube diameter and length as well as nanoparticle diameter (d_{NT} , L_{NT} and d_{NP} respectively) was conducted using Gatan DigitalMicrograph software. Energy dispersive X-ray (EDX) analysis was performed by Professor Andrei Khlobystov using an Oxford Instruments INCA 560 X-ray microanalysis system. TEM samples were prepared *via* drop-drying methanolic solutions onto copper grid mounted “lacey” carbon films.

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Table 2.4 List of carbon nanostructures used throughout this study along with details and commercial suppliers.

Carbon nanostructure	Synthesis method	d_{NT} / nm	Commercial name	Commercial Supplier
CoMoCAT SWNT	CVD	0.7±0.1	6,5-SWeNT	Sigma Aldrich, UK
HiPCO SWNT	CVD	1.0±0.1	HiPCO SWNT	Unidym Inc., CA, USA
AD SWNT1	AD	1.3±0.1	Helix SWNT	Helix Materials Solutions, TX, USA
AD SWNT2	AD	1.3±0.1	P2 SWNT	Carbon Solutions Inc., CA, USA
CVD MWNT	CVD	14.4±6.0	PD30L520 MWNT	Nanolab, MA, USA
AD MWNT	AD	19.0±5.8	MER MWNT	MER Corporation, AZ, USA
CVD GNF1	CVD	96±32	PR24 GNF	Applied Sciences, OH, USA
CVD GNF2	CVD	115±37	PR19 GNF	Applied Sciences, OH, USA

2.5.2. Chemical oxidation of CVD MWNT using H_2SO_4/HNO_3 (Method 1)

CVD MWNT (25 mg) were suspended in a mixture of concentrated sulfuric acid (75 mL) and concentrated nitric acid (25 mL) with ultrasonication for 24 hours. The suspension was then diluted with deionised water (500 mL) and the solid collected by vacuum filtration (0.2 μ m pore size PTFE membrane), washed with aqueous sodium hydroxide (1M, 50mL) and copious deionised water and dried *in vacuo* to yield a black solid (23.0 mg, 7% mass loss).

Raman (532 nm) ν/cm^{-1} 1341.2 ±4.0 (D), 1574.3 ±7.0 (G), $I_D:I_G = 0.881 \pm 0.030$;

TEM (200 kV) L_{NT}/nm 478 ±243 (180-1300 nm).

2.5.3. Chemical oxidation of CVD MWNT using piranha solution (Method 2)

CVD MWNT (25 mg) were suspended in a mixture of sulfuric acid (96%, 25 mL) and hydrogen peroxide (30%, 5 mL) and stirred at 70°C for 9 hours. The suspension was diluted in deionised water (500 mL) and the solid collected by vacuum filtration (0.2 μ m pore size PTFE membrane), washed with copious deionised water until the filtrate exhibited a neutral pH. The black solid was then washed with ethanol (25 mL) and dried *in vacuo* to yield a black solid (22.4 mg, 10% mass loss).

Raman (532 nm) ν/cm^{-1} 1345.6 ±1.8 (D), 1581.7 ±2.6 (G), $I_D:I_G = 0.863 \pm 0.038$;

TEM (200 kV) L_{NT}/nm 1127 ±862 (100-4300 nm).

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2.5.4. Chemical oxidation using KMnO_4 (Method 3)

CVD MWNT (25 mg) were suspended in a mixture of aqueous potassium permanganate (0.3 M, 20 mL) and aqueous sodium hydroxide (0.1M, 10 mL) with ultrasonication for 20 minutes before stirring at reflux for 40 minutes. To the stirred solution was added sodium hydrogen sulphite (0.7 g) and sulfuric acid (1M, 0.1 mL) and the mixture was stirred under reflux for a further 19 hours. The solid was collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed sequentially with sodium hydroxide (0.01M, 50 mL), hydrochloric acid (5M, 50 mL) and copious deionised water and finally dried *in vacuo* to yield a black solid (2.0 mg, 92% mass loss).

Raman (532 nm) v/cm^{-1} 1345.6 ± 1.3 (D), 1579.4 ± 1.5 (G), $I_D:I_G = 1.185 \pm 0.050$;

TEM (200 kV) L_{NT}/nm 1254 ± 986 (180-5070 nm).

2.5.5. Air oxidation of CVD MWNT catalysed by NiONP (Method 4)

CVD MWNT (25 mg) were suspended in nitric acid (3M, 53 mL) by ultrasonication for 15 minutes and stirred at reflux for 5 hours. The black solid was collected by vacuum filtration (0.5 μm pore size PTFE membrane), washed sequentially with deionised water (50 mL), sodium hydroxide (1M, 50 mL), hydrochloric acid (1M, 50 mL) and copious deionised water to yield a black solid (24.5 mg, 2% mass loss). To the black solid suspended in ethanol (5 mL) was added an aqueous solution of nickel(II) sulfate hexahydrate (0.085M, 5 mL) and the mixture stirred vigorously while an aqueous solution of potassium borohydride (0.085 M, 5 mL) was injected and stirred for a further 50 minutes. The solid was collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed with deionised water (200 mL) and dried at 120°C in air for 2 hours. The black solid was heated in air to 400°C at a rate of $10^\circ\text{C min}^{-1}$ and held at 400°C for 1 hour. A flow of argon was introduced and the sample was heated to 900°C at a rate of $10^\circ\text{C min}^{-1}$ and held at 900°C for 2 hours before cooling to room temperature. The black powder was suspended in sulfuric acid (5M, 1 mg mL^{-1}) with sonication for 15 minutes before the solid was collected by vacuum filtration (0.2 μm pore

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size PTFE membrane), washed sequentially with aqueous sulfuric acid (1M, 500 mL) and copious deionised water and dried *in vacuo* to yield a black solid (4.0 mg, 84% mass loss).

Raman (532 nm) ν/cm^{-1} 1337.2 $\pm$ 4.6 (D), 1573.2 $\pm$ 6.6 (G), $I_D:I_G = 0.956 \pm 0.050$;

TEM (200 kV) L_{NT}/nm 787 $\pm$ 586 (80-3450 nm).

2.5.6. Air oxidation of CVD MWNT catalysed by *in situ* AgNP (Method 5)

CVD MWNT (25 mg) were suspended in nitric acid (5M, 50 mL) and stirred at reflux for 5 hours. The suspension was diluted with deionised water (300 mL) and the solid was collected by vacuum filtration (0.5 μm pore size PTFE membrane), washed sequentially with sodium hydroxide (1M, 50 mL), hydrochloric acid (1M, 50 mL), deionised water (200 mL) and acetone (50 mL) and dried *in vacuo* to yield a black solid (24.2 mg, 3% mass loss). The nanotubes were suspended in an aqueous solution of silver nitrate (0.005 M, 1.42 mL) and the suspension stirred at 40°C for 90 minutes, before the mixture was dried at 100°C for 90 minutes to yield a black solid (21.6 mg). The composite material was heated under a flow of argon to 300°C at a rate of 3°C min⁻¹ and held at 300°C for 3 hours, before cooling to room temperature under argon. The sample was then heated under argon to 350°C at a rate of 3°C min⁻¹ and air was then flowed across the sample at 350°C for a further 100 minutes before cooling in air. The nanotube sample was then sonicated in nitric acid (2M, 1 mg mL⁻¹), the black solid collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed with copious deionised water and dried *in vacuo* to yield a black solid (12.0 mg, 52% mass loss).

Raman (532 nm) ν/cm^{-1} 1337.6 $\pm$ 4.1 (D), 1579.3 $\pm$ 10.6 (G), $I_D:I_G = 0.814 \pm 0.070$;

TEM (200 kV) L_{NT}/nm 1353 $\pm$ 1446 (200-8600 nm).

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2.5.7. Air oxidation of CVD MWNT catalysed by ex situ AgNP (Method 6)

2.5.7.1. Synthesis of AgNP

To silver nitrate (153 mg) in ethanol (30 mL) was added dropwise dodecanethiol (0.1 mL) and the combined mixture stirred for 10 minutes at room temperature. To this was added dropwise a saturated solution of sodium borohydride in ethanol (60 mL) and the combined mixture vigorously stirred at room temperature for 2 hours. To the mixture was added acetone (100 mL) and the solution stored in the freezer at -20°C overnight affording a solid precipitate which was collected by vacuum filtration (0.5 µm pore size PTFE membrane), washed sequentially with toluene (10 mL), acetone (200 mL), methanol (200 mL) and dried *in vacuo* to yield a brown solid (171 mg).

UV/vis (toluene) λ_{max} /nm 435.0; **TEM** (200 kV) d_{NP} /nm 7.3 ± 1.7 (4.7-11.5 nm).

2.5.7.2. Self-assembly of AgNP-CVD MWNT composite material

CVD MWNT (20 mg) was dispersed in concentrated hydrochloric acid (20 mL) with ultrasonication for 30 minutes. The nanotube suspension was then diluted with water (200 mL), the solid collected by vacuum filtration (0.2 µm pore size PTFE membrane), washed sequentially with water (500 mL) and acetone (100 mL) before being dried *in vacuo*. To the resulting carbon nanotube powder (10 mg) was added a suspension of the silver nanoparticles (10 mg) in dichloromethane (10 mL) and the mixture was sonicated for 30 minutes. The solid was collected by vacuum filtration (0.2 µm pore size PTFE membrane), washed with dichloromethane (10 mL) and dried *in vacuo*.

TGA (air): T_{ox} /°C 472, M_{1000} /wt% 29.0.

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2.5.7.3. Oxidation in air catalysed by ex situ AgNP

The carbon nanotube composite material was heated in air at 480°C for 7 minutes resulting in a 32% reduction in mass. The resultant black powder was suspended in nitric acid (2M, 0.5 mg mL⁻¹) with ultrasonication for 30 minutes. This suspension was then diluted with water (50 mL), the solid collected by vacuum filtration (0.2 µm pore size PTFE membrane), washed sequentially with water (20 mL) and acetone (20 mL) and dried *in vacuo* to yield a black solid (1.2 mg, 88% mass loss).

UV-vis (H₂O) λ /nm 264.3; **IR** (KBr) ν /cm⁻¹ 1384 ($\nu_{C=C}$), 1636 ($\nu_{C=C}$); **TGA** (air) T_{ox}/°C 528, M₁₀₀₀/wt% 3.3; **TEM** (200 kV) L_{NT}/nm 634 ±436 (125-2330 nm), d_{NT}/nm 12.4 ±3.7 (6.9-26.8 nm); **Raman** (532 nm) ν /cm⁻¹ 1336.2 ±1.5 (D), 1571.6 ±2.3 (G), I_D:I_G = 0.801 ±0.028.

2.5.8. Alternative metals for ex situ nanoparticle-catalysed oxidation of CVD

MWNT

2.5.8.1. Synthesis of gold nanoparticles

To a solution of tetrachloroauric acid trihydrate (79 mg, 0.2 mmol) in deionised water (30 mL) was added a colourless solution of tetraoctylammonium bromide (219 mg, 0.4 mmol) in dry toluene (60 mL) to give a biphasic solution. Upon addition of dodecanethiol (48 µL, 0.2 mmol) in toluene (5 mL) a slight yellow colour was observed. A solution of sodium borohydride (76 mg, 2 mmol) in deionised water (30 mL) was added rapidly in one portion and the reaction mixture turned dark brown. The mixture was left stirring at room temperature for 20 hours. The organic layer was separated and washed repeatedly with water before being dried over sodium sulfate and filtered through cotton wool. The solvent was removed *in vacuo* and the dark solid dissolved in toluene (3 mL) and precipitated by the addition of ethanol (350 mL) at -18°C for 20 hours. The solid was collected by vacuum filtration (0.2 µm pore size PTFE membrane) to yield dark brown solid nanoparticles (42 mg).

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IR (KBr) ν/cm^{-1} 2851 ($\nu_{\text{C-H}}$), 2872 ($\nu_{\text{C-H}}$), 2921 ($\nu_{\text{C-H}}$) and 2956 ($\nu_{\text{C-H}}$); **UV/vis** (toluene)

$\lambda_{\text{max}}/\text{nm}$ 522.8; **TEM** (200 kV) d_{NP}/nm 2.2 ± 0.7 (1.2-4.4 nm).

2.5.8.2. Synthesis of copper nanoparticles

To a solution of copper nitrate hemipentahydrate (279 mg, 1.2 mmol) in deionised water (120 mL) was added a colourless solution of tetraoctylammonium bromide (4.36 g, 8.00 mmol) in dry toluene (320 mL) to give a biphasic solution. Upon addition of dodecanethiol (432 μL , 1.8 mmol) in toluene (5 mL) a slight yellow colour was observed. A solution of sodium borohydride (752 mg, 20 mmol) in deionised water (100 mL) was added dropwise and the reaction mixture turned dark brown. The mixture was left stirring at room temperature for 20 hours. The organic layer was separated and washed repeatedly with water before being dried over sodium sulfate and filtered through cotton wool. The solvent was removed *in vacuo* and the dark solid dissolved in toluene (3 mL) and precipitated by the addition of ethanol (350 mL) at -18°C for 20 hours. The solid was collected by vacuum filtration (0.2 μm pore size PTFE membrane) to yield dark brown solid nanoparticles (119 mg).

IR (KBr) ν/cm^{-1} 2850 ($\nu_{\text{C-H}}$), 2874 ($\nu_{\text{C-H}}$), 2919 ($\nu_{\text{C-H}}$) and 2955 ($\nu_{\text{C-H}}$); **UV/vis** (toluene)

$\lambda_{\text{max}}/\text{nm}$ 279.0; **TEM** (200 kV) d_{NP}/nm 2.6 ± 1.4 (0.8-10.0 nm).

2.5.8.3. Synthesis of palladium nanoparticles

To a solution of potassium tetrachloropalladate (150 mg, 0.46 mmol) in deionised water (25 mL) was added a colourless solution of tetraoctylammonium bromide (375 mg, 0.69 mmol) in dry toluene (125 mL) to give a biphasic solution. Upon addition of dodecanethiol (110 μL , 0.46 mmol) in toluene (5 mL) a slight yellow colour was observed. A solution of sodium borohydride (175 mg, 4.6 mmol) in deionised water (10 mL) was added rapidly in one portion and the reaction mixture turned dark brown. The mixture was left stirring at room temperature for 20 hours. The organic layer was separated and washed repeatedly with

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water before being dried over sodium sulfate and filtered through cotton wool. The solvent was removed *in vacuo* and the dark solid dissolved in toluene (3 mL) and precipitated by the addition of ethanol (350 mL) at -18°C for 20 hours. The solid was collected by vacuum filtration (0.2 µm pore size PTFE membrane) to yield dark brown solid nanoparticles (105 mg).

IR (KBr) ν/cm^{-1} 2851 ($\nu_{\text{C-H}}$), 2870 ($\nu_{\text{C-H}}$), 2921 ($\nu_{\text{C-H}}$) and 2956 ($\nu_{\text{C-H}}$); **UV/vis** (toluene)

$\lambda_{\text{max}}/\text{nm}$ 420.1; **TEM** (200 kV) d_{NP}/nm 1.2 ± 0.3 (0.6-1.7 nm).

2.5.8.4. Preparation of nanoparticle-nanotube composite materials

CVD MWNT (10 mg) were added to a suspension of metal nanoparticles (10 mg) in dichloromethane (10 mL) and the mixture was sonicated for 30 minutes. The solid was collected by vacuum filtration (0.2 µm pore size PTFE membrane), washed with dichloromethane (10 mL) and dried *in vacuo* to yield a black solid (9, 19 and 15 mg for composites of CVD MWNT and Au, Cu and PdNP respectively).

2.5.8.5. CVD MWNT oxidation in air catalysed by metallic nanoparticles

The carbon nanotube composite material (10 mg) was heated in air for 5 minutes at 515, 440 or 560°C for Au, Cu and PdNP respectively. The resultant black powder was suspended in nitric acid (2M, 0.5 mg mL⁻¹) by ultrasonication for 30 minutes. This suspension was then diluted with water (50 mL), the solid collected by vacuum filtration (0.2 µm pore size PTFE membrane), washed sequentially with water (20 mL) and acetone (20 mL) and dried *in vacuo* to yield a black solid (8.4, 6.3 and 5.2 mg for composites of CVD MWNT and Au, Cu and PdNP respectively).

2.5.9. Oxidation of carbon nanostructures using ex situ silver nanoparticles

Carbon nanostructures (20 mg) were dispersed in concentrated hydrochloric acid (20 mL) using an ultrasonic bath at room temperature for 30 minutes. The nanotube suspension was

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then diluted with water (200 mL), collected by vacuum filtration (0.2 μm pore size PTFE membrane) and washed sequentially with water (500 mL) and acetone (100 mL) before being dried *in vacuo*. To the resulting black powder (10 mg) was added a suspension of dodecanethiol-stabilised silver nanoparticles (10 mg) (see 2.5.7.1) in dichloromethane (10 mL) and the mixture was sonicated for 30 minutes. The solid was collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed with dichloromethane (10 mL) and dried *in vacuo*. The composite material was heated in air at a prescribed temperature until approximately 30-50% mass loss was observed (see Table 2.5 for details). The resultant black powder was suspended in nitric acid (2M, 0.5 mg mL⁻¹) with ultrasonication for 30 minutes. This suspension was then diluted in water (50 mL), the solid collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed sequentially with water (20 mL) and acetone (20 mL) and dried *in vacuo* to yield a black solid. Black solid carbon nanomaterials produced were characterised by thermogravimetric analysis (Table 2.5), Raman spectroscopy (Table 2.6), and transmission electron microscopy (Section 2.3.3, Figure 2.13, Figure 2.14 and Table 2.3).

Table 2.5 Thermogravimetric analysis for various carbon nanostructures showing the oxidation temperature (T_{ox}), the change in oxidation temperature facilitated by pre-formed silver nanoparticles (ΔT_{ox}) and the loading of silver nanoparticles. Experimental heating temperature (T_{exp}) and duration (t_{exp}) are also described for each carbon nanostructure.

Carbon nanostructure	$T_{\text{ox}} / ^\circ\text{C}$	$\Delta T_{\text{ox}} / ^\circ\text{C}$	Ag / wt.% ^a	$T_{\text{exp}} / ^\circ\text{C}$	$t_{\text{exp}} / \text{mins}$	Mass loss / %
CoMoCAT SWNT	563	-84	20.7	480	14	42
HiPCO SWNT	499	-56	6.2	440	14	45
AD SWNT1	457	-31	12.2	425	14	36
AD SWNT2	725	-108	42.4	620	7	28
CVD MWNT	589	-117	20.6	480	7	32
AD MWNT	727	-111	36.3	600	10	48
CVD GNF1	761	-263	22.0	440	35	37
CVD GNF2	733	-250	29.7	440	28	39

^a Metal loading is corrected to account for residual metal content associated with carbon nanotube synthesis catalyst.

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Table 2.6 Raman spectroscopic analysis for various carbon nanostructures prior to the cutting procedure including the absolute shifts in both D and G band frequencies (ΔD and ΔG respectively) and the absolute change in $I_D:I_G$ ratio subsequent to oxidation in air catalysed by silver nanoparticles.

Carbon nanostructure	D / cm^{-1}	ΔD / cm^{-1}	G / cm^{-1}	ΔG / cm^{-1}	$I_D:I_G$	$\Delta(I_D:I_G)$
CoMoCAT SWNT	1303.2 $\pm$ 1.5	+1.4	1578.7 $\pm$ 3.1	-6.0	0.113 $\pm$ 0.011	+0.034
HiPCO SWNT	1320.2 $\pm$ 0.9	+2.5	1577.7 $\pm$ 2.3	0.0	0.159 $\pm$ 0.006	+0.009 ^a
AD SWNT1	1329.2 $\pm$ 1.7	+4.0	1581.2 $\pm$ 1.5	+3.5	0.038 $\pm$ 0.003	+0.008
AD SWNT2	1338.7 $\pm$ 2.3	+0.5	1586.2 $\pm$ 0.9	+1.0	0.016 $\pm$ 0.002	-0.004
CVD MWNT	1335.7 $\pm$ 3.8	+0.5	1576.2 $\pm$ 1.7	-4.5	0.791 $\pm$ 0.020	+0.010 ^a
AD MWNT	1346.8 $\pm$ 0.0	-1.5	1577.2 $\pm$ 1.7	-2.0	0.147 $\pm$ 0.012	+0.005 ^a
CVD GNF1	1335.2 $\pm$ 0.9	+1.5	1563.6 $\pm$ 2.3	-0.5	0.225 $\pm$ 0.049	+0.104
CVD GNF2	1337.2 $\pm$ 2.3	+8.4	1564.1 $\pm$ 2.3	+7.3	0.154 $\pm$ 0.038	+0.051

^a Values within standard deviation of measurements in triplicate

2.6. References

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3. Regioselective aromatic halogenation inside carbon nanotubes

3.1. Aromatic substitution in confinement

To date, there have been no experimental studies reporting the sole use of carbon nanotubes as containers for preparative chemical reactions. Although the term preparative is often associated with scale, many preparative chemical syntheses are developed and conducted on the microscale through necessity (*e.g.* due to cost),¹ and therefore a preparative chemical reaction is any reaction which affords isolable products and can, in principle, be scaled using common laboratory equipment. Promising results have been observed for carbon nanotube hosts in metal-catalysed reactions,²⁻⁴ as well as analogous nanoscale molecular hosts,⁵ highlighting the importance of studying the unusual reaction environment provided by the interior cavity of carbon nanotubes. The few examples of non-preparative, non-catalysed chemical reactions within CNT^{6, 7} have shown the potential of this area of research with the CNT directly influencing the pathway of the reaction and the products afforded. However, severe product inhibition, where the product molecules experience strong interactions with the CNT, has made product extraction impossible in these cases. For carbon nanotubes to be utilised as nanoscale hosts in practical synthetic applications, it must first be experimentally demonstrated that chemical transformations can be conducted within carbon nanotubes on a preparative scale, allowing the extraction of useful products. Conceptually, carbon nanotubes are able to host a wide range of organic chemical reactions; however, advances in the field of carbon nanoreactors are dependent on the development of convenient and easily adaptable practical methodologies for confining such reactions. Therefore, it is essential, as a proof-of-principle study, to conduct a simple chemical reaction confined within carbon nanotubes on a preparative scale.

The first foreseen hurdle to overcome when attempting to confine organic reactions within CNT is determining and controlling the reaction locus (*i.e.* where the reaction occurs).

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The use of metallic catalysts facilitates direct electron microscopy determination of the catalyst location and thus, the reaction locus can be accurately defined as the reaction can only occur in the presence of the catalyst under the applied experimental conditions.^{8, 9} However, the use of catalyst particles does not allow the influence of the CNT host-guest interactions on the mechanisms of organic transformations to be studied directly and thus, is not considered within this investigation. Current electron microscopy techniques do not allow the direct visualisation of small organic molecules within carbon nanotubes due to the low stability of typical functional groups (*e.g.* C-H, C-C bonds) under electron beam irradiation.¹⁰ Moreover, the encapsulated species is additionally obscured by the carbon atoms that comprise the surrounding carbon nanotube. Therefore, a possible method to indirectly determine the local environment of a reaction is to study the potential effects of confinement on selectivity. Under this framework, any observed effect can be attributed to the confinement of the reaction and thus, the reaction becomes a *probe* with which to study the *effects of confinement* within narrow carbon nanotubes. In order to do this, the chosen model reaction must be an unselective reaction producing a mixture of products in solution, with selectivity readily modified through changes to the reaction environment.

While this pioneering investigation into organic chemical reactions inside CNT could be achieved with any unselective reaction, it is logical to study a well-known and synthetically useful organic transformation allowing comparison to a wealth of previous examples. One such reaction is the electrophilic substitution reaction, particularly halogenation, of simple aromatic molecules. Halogenated organic compounds are both synthetically important intermediates, specifically in the manufacture of agrochemicals, pharmaceuticals and flame-retardants, and commercial commodities in their own right, being utilised as antitumor, antibacterial, antifungal, antiviral and antioxidising agents.¹¹ The position of electrophilic attack on aromatic molecules varies and is influenced by effects such as the steric bulk or electronically directing nature of functional groups, as well as solvent polarity and other experimental conditions.¹²

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Due to the sensitivity and wide functional group tolerance, this reaction is a common model reaction chosen when studying novel reaction environments and, as such, aromatic substitution reactions have been studied previously within molecular containers (*e.g.* cyclodextrins). Cyclodextrins are naturally occurring polysaccharides, the most common being α , β and γ -cyclodextrin consisting of six, seven and eight glucosidic monomer units respectively. The use of these supramolecular structures as molecular hosts has been demonstrated for a number of molecules and reactions.¹³ Small aromatic molecules are readily encapsulated within the internal void, particularly in aqueous media, and such nanoscale confinement can, for example, drastically alter the selectivity and kinetics of subsequent electrophilic substitution reactions.⁵ The selective *para*-chlorination of anisole has been demonstrated within cyclodextrins and a clear correlation was established between regioselectivity and increasing molar equivalents of α -cyclodextrin in solution.¹⁴ Dumanski *et al.* further developed this methodology when studying the bromination of both *N*-phenylacetamide (**Figure 3.1**) and anisole within α -cyclodextrin, achieving near-quantitative selectivity for the *para*-regioisomer in each case.¹⁵

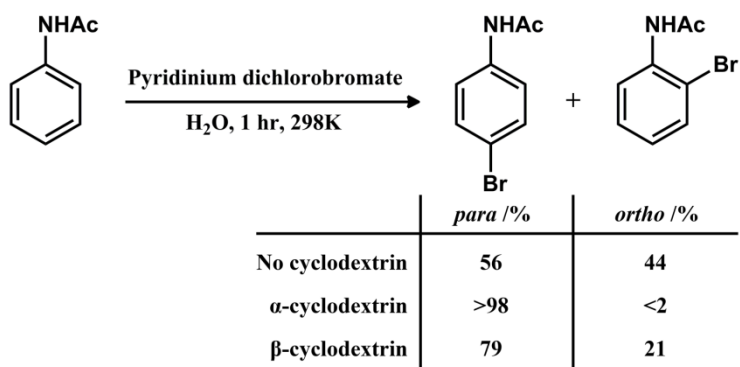


Figure 3.1 Electrophilic bromination of *N*-phenylacetamide by pyridinium dichlorobromate to form a mixture of both *para*- and *ortho*-brominated products. Confinement within α -cyclodextrin improves the *para*-selectivity from 56 to >98%. The less extreme steric confinement within β -cyclodextrin affords a less pronounced influence on regioselectivity.

The arrangement of the aromatic reactant molecule within the cyclodextrin cavity is postulated to block the electrophilic attack at the *ortho* position, thus promoting the formation of the *para*-brominated product (**Figure 3.2a**). These results within molecular

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nanoreactors offer great promise for the confinement of such reactions within carbon nanotubes, as the principles of size and shape selectivity should be comparable within similarly sized hosts, potentially offering analogous improvements in *para*-selectivity within CNT (**Figure 3.2b**).

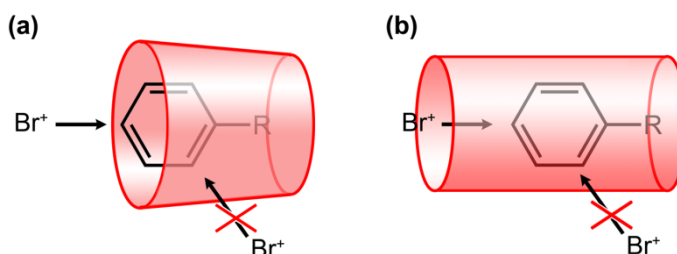


Figure 3.2 Schematic representation of the hypothesised shape-selective electrophilic bromination of a substituted aromatic molecule confined within (a) cyclodextrin and (b) a narrow SWNT. In both cases, the schematic demonstrates that the nanoscale host can block electrophilic attack at the *ortho* position, promoting the formation of the *para*-brominated product.

3.2. Aim and Objectives

The aim of this study is to demonstrate, for the first time, that organic chemical reactions can be conducted within the internal cavity of narrow carbon nanotubes on a preparative scale. It is the intention of this work to establish how nanoscale confinement can influence reaction pathways, particularly by offering enhanced control of selectivity. Practical methods will be explored and optimised with the aim of developing a universal approach for the confinement of organic chemical reactions. Such practical considerations include the efficient encapsulation of reactants, facile extraction of products and ensuring the reaction occurs predominantly within the CNT cavity and not in solution or adsorbed on the nanotube surface.

The electrophilic halogenation of aromatic molecules has been chosen as the model reaction. This simple transformation, involving just a small aromatic molecule and halogenating agent, offers the most convenient and promising probe for the potential of carbon nanotubes to host preparative reactions. Crucially, aromatic substitution can be unselective, resulting in the formation of a mixture of regioisomeric products, namely *ortho*,

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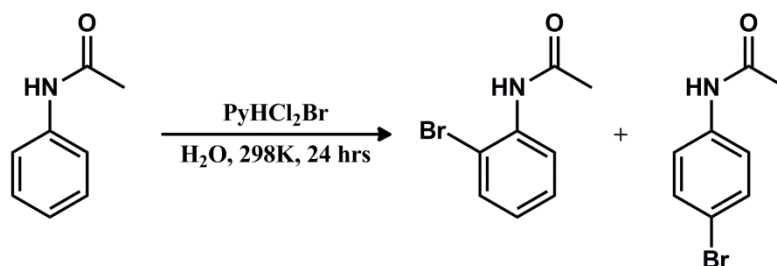
meta and *para*-substituted products, allowing the effect of confinement within CNT on regioselectivity to be probed. A suitable aromatic reactant, halogenating agent and conditions will be required to provide an unselective mixture of isomers. Only non-covalent interactions such as π - π interactions between the aromatic guest and conjugated CNT host will be utilised to facilitate encapsulation and thus, ensure that the reaction occurs in the CNT. It is also surmised that halogenated aromatic molecules, being much smaller (*i.e.* shorter in length) than the graphitised nanoribbon or fullerene oligomer products previously formed within SWNT, will experience much weaker non-covalent interactions with the nanotube sidewall and therefore facilitate the quantitative egress of product molecules from the nanotube.

The specific effects of confinement observed in this novel area of research could prove unexpected and wide-ranging. However, based on results observed using molecular nanoreactors,^{14, 15} the foremost hypothesis for the confinement of such reactions within carbon nanotubes is an increase in selectivity in favour of the more linear *para*-regioisomers (**Figure 3.2**).

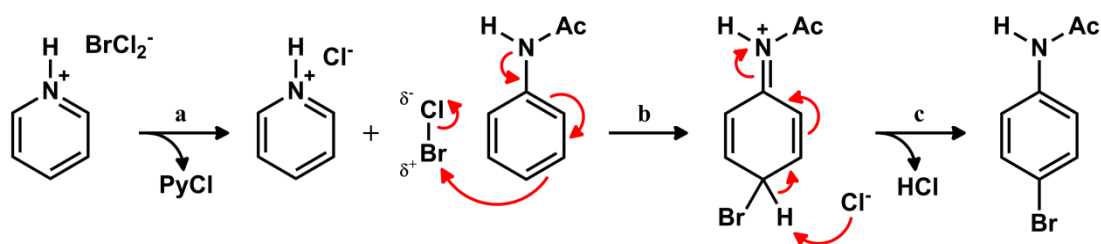
3.3. Results and Discussion

A suitable model reaction for appraisal within the CNT cavity should proceed to form an unselective mixture of mono-halogenated regioisomers, thus enabling any effect of confinement within carbon nanotubes on the reaction selectivity to be readily observed. The choice of both aromatic functional group and halogenating agent are paramount in the search for such a reaction.¹⁶ For instance, the bromination of aniline typically affords 2,4,6-tribromoaniline due to the high reactivity of the aromatic reactant and, furthermore, the use of molecular bromine as the halogenating agent for many aromatic substrates often selectively affords the *para*-brominated product. In addition, aromatic functional groups often have *ortho*-, *meta*- or *para*-directing properties, further influencing the distribution of products,¹⁷ and such effects must not be too strong so as to override any potential influence of confinement. Preliminary investigations into a suitable model reaction found that the bromination of *N*-phenylacetamide by pyridinium dichlorobromate (PyHCl₂Br) afforded an unselective mixture of *ortho*- and *para*- monobrominated products (**Schemes 3.1 and 3.2**), with a 68% selectivity for the *para*-regioisomer. The reactions of alternative aromatic reactants (such as anisole^{15, 18} and toluene¹⁹⁻²¹) and alternative brominating agents (such as *N*-bromosuccinimide,^{22, 23} Br₂, NaBrO₃¹⁹ and BrNO₃²⁰), although reported to be unselective to varying degrees, all afforded equal or higher selectivity for the *para*-isomer in our preliminary experiments and were, therefore, not considered further for this investigation into the effect of confinement within CNT. An additional consideration is the structure of the brominating agent in the context of extreme confinement. For instance, the active bromine source formed *in situ* from pyridinium dichlorobromate is the much smaller Br-Cl species (**Scheme 3.2**), which reduces the chance that bulky groups could block the CNT internal channel and halt the progress of the confined reaction.

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Scheme 3.1 Bromination of *N*-phenylacetamide by pyridinium dichlorobromate to afford a mixture of both *ortho*- and *para*- monobrominated regioisomers in the ratio of approximately 3:7.



Scheme 3.2 Mechanism of electrophilic bromination of *N*-phenylacetamide by pyridinium dichlorobromate involving: (a) the formation of the BrCl brominating agent, a source of Br⁺, and by product pyridinium chloride (PyCl); (b) the electrophilic aromatic bromination of *N*-phenylacetamide; and (c) the formation of final product, *N*-(4-bromophenyl)acetamide and by product, HCl.

In a typical experiment, an aqueous solution of *N*-phenylacetamide and pyridinium dichlorobromate (0.6 equivalents) was stirred at room temperature for 24 hours before being quenched with an excess of sodium bisulfite. Although all of the brominating agent has typically reacted after 1-2 hours, the extended reaction duration ensured sufficient conversion of reactions confined within CNT to allow reliable measurement by spectroscopic means and therefore direct comparison. A reduced stoichiometry of brominating agent (0.6 equivalents) was used in order to ensure that no polybromination occurs in order to simplify the analysis of product mixtures. Products were extracted from the crude aqueous mixture into diethyl ether, washed with water and dried to yield a white solid. ¹H NMR spectroscopy of the product mixture showed an approximate 30 : 70 ratio of *ortho*-brominated and *para*-brominated products respectively, by comparison of peak integrals at 7.11 (1H, *ortho*) and 7.46 (2H, *para*) ppm corresponding to the aromatic proton environments *para*- and *meta*- to the acetamide respectively. This aromatic bromination reaction, therefore, represents a suitable reaction with which to complete the preliminary investigation into the effect of extreme confinement within SWNT.

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The high cost of carbon nanotubes, coupled with the limited cavity volume per unit mass, limits the scale on which chemical reactions within CNT can be conducted, *i.e.* the mass of carbon nanotubes required to confine a reaction on a sufficiently large scale to produce 10-100 mg of product is not economically viable at the present time. Thus, we must analyse the effect of confinement within CNT on regioselectivity for reactions on a smaller scale than typical laboratory experiments. In light of this necessity, the effect of varying reaction scale on the regioselectivity of *N*-phenylacetamide bromination was determined across the range of 3.7 μmol to 0.2 mmol and found to show no trend and little variation (standard deviation $\pm 3\%$), confirming that reaction scale has no measurable effect on the regioselectivity of this reaction.

Before the halogenation of *N*-phenylacetamide can be confined within a carbon nanotube, a suitable nanotube host must be chosen. The results of Dumanski *et al.* for this reaction within cyclodextrins suggest that host diameter is an important consideration.¹⁵ Regioselectivity varied between different sizes of cyclodextrin host and the greatest shift in selectivity was observed within α -cyclodextrin, which has a crystallographic diameter of approximately 0.84 nm. It is logical to utilise a carbon nanotube of comparable diameter in the hope of inducing similar shifts in regioselectivity as a consequence of confinement. Synthetic procedures for the production of carbon nanotubes are continually being developed offering improved control over carbon nanotube diameter²⁴ and as such, carbon nanotubes are commercially available with a relatively monodisperse diameter range. Single-walled carbon nanotubes produced by high pressure carbon monoxide disproportionation (HiPCO) yield carbon nanotubes with an approximate crystallographic diameter (d_{NT}) of 1.0 (± 0.1) nm.²⁵ Therefore, taking into account the van der Waals atomic radii,²⁶ the diameter of the internal cavity ($d_{\text{NT}}^{\text{int}}$) is 0.69 nm. Simple three-dimensional geometric consideration of such a carbon nanotube (**Figure 3.3**) shows that the preferred *para*-brominated *N*-phenylacetamide product (critical van der Waals dimension, $d_{\text{crit}} = 0.69$ nm) could be encapsulated within the internal cavity; however, the most stable conformation of the *ortho*-

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regioisomer ($d_{\text{crit}} = 0.79 \text{ nm}$) cannot. As such, HiPCO SWNT are suitable hosts to investigate the influence of confinement on *N*-phenylacetamide halogenation reactions, and it is hypothesised that such confinement will promote the formation of the *para*-brominated product at the expense of the *ortho*-regioisomer by utilising this concept of size exclusion.

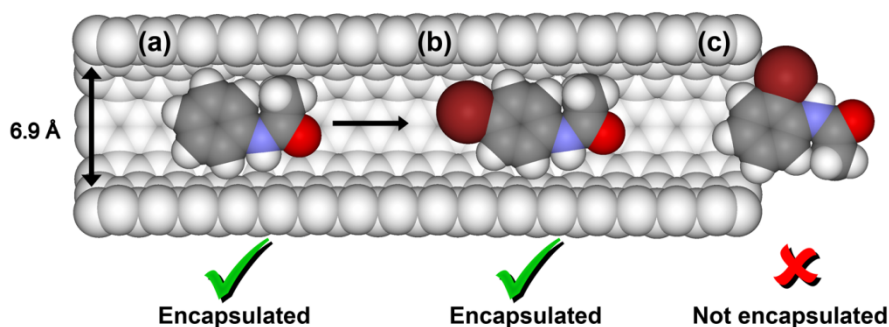


Figure 3.3 Schematic three-dimensional representation of reaction species in relation to an average HiPCO SWNT. (a) *N*-phenylacetamide reactant and (b) *para*-brominated product are able to fit within the nanotube internal cavity, whereas (c) the *ortho*-brominated product is unable to fit within the nanotube in its most stable conformation. This size exclusion is the basis of the hypothesised increase in selectivity for the *para*-brominated product as a consequence of confinement within SWNT.

In order to probe the effect of confinement within HiPCO SWNT on the regioselectivity of this bromination reaction, it is firstly important to determine whether the external surface of the SWNT would have any influence on the reaction. Preliminary control experiments were conducted, whereby HiPCO SWNT powder was simply added to the reaction mixture, with no effort made to encapsulate any reaction species. The addition of HiPCO SWNT induced no change in the regioselectivity of the bromination reaction, which repeatedly afforded an approximately 70:30 mixture of *para*- and *ortho*-brominated products respectively. Confirming that the CNT external surface has no effect on the regioselectivity of the model reaction is very important in allowing any observed shifts in selectivity for reactions within the CNT to be more reliably attributed to confinement.

The next practical consideration for the confinement of this organic chemical reaction within CNT is how to ensure that bromination, known to readily proceed in solution, instead occurs within the CNT cavity. Breslow and co-workers pioneered the use of the hydrophobic effect to promote confined reactions within cyclodextrins.²⁷⁻²⁹ It was shown

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that reactions of non-polar organic molecules in water were accelerated by the addition of aromatic hosts, because the hydrophobic properties of the molecules encouraged their encapsulation which, in turn, increased the local concentration of confined reactants and improved the reaction kinetics. Similar interactions have been observed with carbon nanotubes,^{30, 31} so the hydrophobic effect is also applicable to organic chemical reactions within CNT. Similarly, due to the poor aqueous solubility of the aromatic reactant, it is reasonable to surmise that, if either reactant is encapsulated within the carbon nanotube, the diffusion into the surrounding solution under experimental conditions will be slow. Therefore, if the majority of reactant molecules are situated within the CNT cavity prior to the addition of the halogenating agent in aqueous solution, then this may ensure that the majority of the bromination reaction occurs within the CNT. This was identified as the most suitable approach to allow the effect of confinement on this reaction to be probed.

Conceptually, such a methodology can be approached in one of three ways; namely, the prior encapsulation of either reactant followed by the addition to an aqueous solution of the corresponding reactant (**Figure 3.4a & b**), or the simultaneous encapsulation of both reactants prior to the reaction (**Figure 3.4c**). The simultaneous encapsulation of both reactants has the potential to introduce various complications. For instance, one reactant may have a higher affinity towards encapsulation, leading to uneven stoichiometry inside the CNT. Secondly, the order of encapsulation may not be statistical, instead forming local linear arrays of one reactant unable to react with the corresponding reactant. Thirdly, the two reactants may react in solution before effectively confined, prohibiting the study of the confined reaction. As such, initial investigation was focussed on the former strategy, the prior encapsulation of a single reactant, before the addition of the second reactant in aqueous solution.

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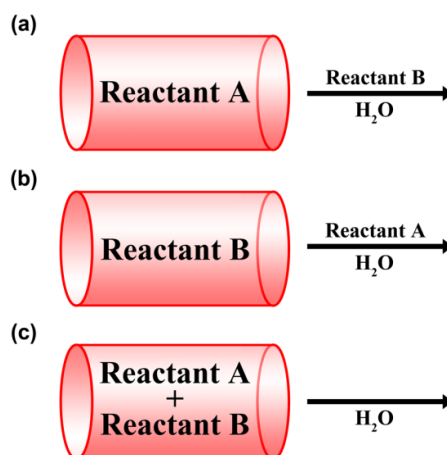


Figure 3.4 Schematic representation of the three potential approaches to the confinement of a simple chemical reaction, $A + B \rightarrow \text{products}$. (a-b) the prior encapsulation of either reactant A or B (respectively) before the addition of a solution of the corresponding reactant or (c) the simultaneous encapsulation of both reactants prior to suspension in solvent at experimental conditions to initiate reaction.

3.3.1. *Reactant encapsulation procedure*

The hollow structure of carbon nanotubes, and thus their ability to encapsulate guest species, has stimulated scientific imagination since their discovery in the late 20th century. As such, previous research efforts have focussed on encapsulating guest species within these nanoscale hosts and probing the effect of such confinement on the properties of both the guest species and host nanotube.³¹⁻³⁵ Guest species have included fullerenes, organometallic complexes, octasiloxane cages, low molecular weight polymers, ionic salts and small molecular species, such as iodine. The method of encapsulation varies depending on the physical properties of the guest but can be categorised into three general approaches, namely gas, liquid or solution-phase encapsulation.

For guest species which are stable in the gas or vapour phase, a mixture of the guest molecule and open CNT can be sealed and heated above the boiling point of the guest, allowing the highly mobile gaseous guest species to enter the nanotube through the open termini or sidewall defects. This process has been studied in detail for C₆₀ fullerene³⁶ and a moderate energy barrier to encapsulation must be overcome (0.3 eV), but the energy gain upon encapsulation is typically much larger due to enhanced van der Waals interactions

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depending on whether the host cavity diameter is approximately commensurate with the guest.³¹

If a guest species remains stable in the liquid phase, the immersion of carbon nanotubes can result in spontaneous filling according to the Young-Laplace law.³⁷ This empirical law states that, for a carbon nanotube of <4 nm diameter, liquids with surface tension below 200 mN m⁻¹ are efficiently drawn into the carbon nanotube cavity.³⁸ This behaviour is conceptually similar to the classical fluidics phenomenon of capillary force; however, this analogy may be misleading as such classical continuum approximations break down within CNT below 10 nm and therefore nanoscale liquids can exhibit unexpected behavior.³⁷

When an intended guest species cannot be melted or sublimed, encapsulation has been demonstrated from solution. This method tends to be less efficient than filling from either gas or liquid phase due to the presence, and particular abundance, of solvent molecules in a typical solution.^{31, 35} However, when the intended guest species cannot be encapsulated using the former two methods, the solution phase remains a viable approach. Due to this potential complication, investigations into encapsulating the reactants of the aromatic bromination reaction initially focussed on gas or liquid phase encapsulation procedures.

When choosing which reactant to encapsulate, *N*-phenylacetamide or pyridinium dichlorobromate, the physical properties and thermal stability of each should be carefully considered. In order to utilise existing gas or liquid phase encapsulation, the intended guest species must be stable in the intended phase. While both reactants are solid at room temperature, *N*-phenylacetamide is entirely covalent in nature and is, therefore, expected to be more thermally stable and less reactive at elevated temperatures. Although pyridinium dichlorobromate (Py⁺HCl₂Br⁻) has a measurable melting point,¹⁸ its thermal stability is less well-understood relative to *N*-phenylacetamide. Additionally, the active brominating agent is likely to be a bromine chloride complex¹⁸ and therefore, if pyridinium dichlorobromate were

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to be encapsulated prior to the reaction, the presence of unwanted side products (*e.g.* pyridinium derivative) could present complications within the narrow SWNT cavity. *N*-phenylacetamide has proven stable in both the liquid and gas phase, with a recorded melting point of 115°C,³⁹ and a boiling point of 304°C,^{40, 41} suggesting that this molecule can be readily manipulated at elevated temperatures without decomposition. Therefore, investigation was focussed towards the liquid or gas phase encapsulation of *N*-phenylacetamide within HiPCO SWNT.

The initial attempts at the *gas* phase encapsulation, by heating SWNT with gaseous *N*-phenylacetamide were unsuccessful, as were attempts at encapsulation from the *solution* phase, by gradual and repeated removal of solvent at reduced pressure. In an attempt to promote the spontaneous encapsulation of *N*-phenylacetamide from solution utilising the hydrophobic effect, the ionic strength was increased by the addition of lithium chloride,²⁹ which still remained unsuccessful. As previously mentioned, encapsulation from the solution phase is complicated by the presence and abundance of solvent molecules and this may explain the limited success with these methodologies. It was found that the most effective method to ensure CNT are efficiently filled with *N*-phenylacetamide, was the immersion of opened SWNT in an excess of molten *N*-phenylacetamide. This method proved very effective because virtually all molecular liquids exhibit a surface tension below the 200 mN m⁻¹ threshold for spontaneous encapsulation by capillary forces, and the elevated temperature required to melt the reactant readily provides sufficient energy to encourage diffusion into the CNT internal channels. However, as immersion requires a significant excess of molten *N*-phenylacetamide, this method, although highly effective at filling the carbon nanotubes, unfortunately produces an abundance of *N*-phenylacetamide molecules externally adsorbed on the SWNT (**Figure 3.5b**) which must be removed prior to the reaction. If the excess of external reactant remains, then the measured selectivity will not be representative of the reaction within carbon nanotubes because the majority of the reaction will have occurred externally or in bulk solution.

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In order to selectively remove the externally adsorbed molecules, leaving the encapsulated molecules within the CNT cavity, a difference between the two environments must be identified and exploited. Several studies of molecules, particularly water, confined within narrow SWNT have predicted that encapsulated guest species will exhibit drastically different phase behaviour to that of the bulk material, due to arrangement in pseudo-1D arrays and stronger non-covalent interactions with the surrounding SWNT sidewall. For example, both the melting⁴² and boiling point^{43, 44} of water have been calculated to be significantly elevated by confinement in narrow SWNT. Assuming a similar phenomenon is also exhibited by *N*-phenylacetamide, this principle could be exploited, using a novel fractional distillation procedure (**Figure 3.5**), to separate externally adsorbed *N*-phenylacetamide from the encapsulated molecules. Therefore, assuming that the boiling point of the confined material will be higher than that of the bulk, heating the mixture (**Figure 3.5b**) at the known boiling point of bulk *N*-phenylacetamide should remove the externally adsorbed molecules into the gas phase leaving only the *N*-phenylacetamide molecules confined within the SWNT (**Figure 3.5c**).

Typically, opened HiPCO SWNT were immersed in molten *N*-phenylacetamide and briefly agitated to allow the efficient filling of the SWNT cavity. The mixture was then heated under reduced pressure until the sample mass reduced to the desired value, typically requiring 5-12 hours, yielding a black *N*-phenylacetamide/SWNT composite powder.

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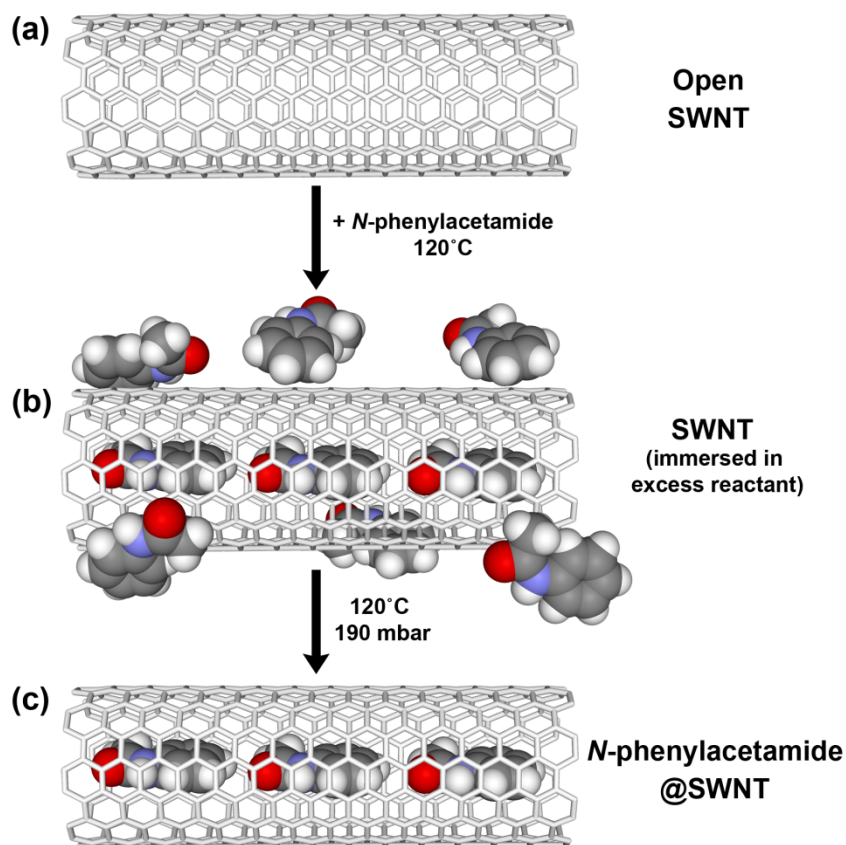


Figure 3.5 Schematic representation of the encapsulation of *N*-phenylacetamide reactant within (a) opened HiPCO SWNT, by immersion of SWNT in the molten reactant to afford (b) efficiently filled SWNT with an excess of reactants externally adsorbed. The selective removal of excess external reactant by fractional distillation at reduced pressure gradually yields (c) the desired *N*-phenylacetamide@SWNT material.

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3.3.2. Regioselectivity of aromatic bromination in confinement

Due to the ambiguity regarding characterisation of organic molecules confined within SWNT,^{45, 46} the most reliable means by which to infer that the majority of reactant molecules are confined within SWNT is by carrying out the bromination reaction with pyridinium dichlorobromate. If the encapsulation methodology is effective in ensuring that the majority of reactant molecules are held within the SWNT cavity, and the hypothesis concerning the effect of confinement within CNT on reaction selectivity is correct, then an increase in selectivity for the *para*-brominated product should be observed.

A typical bromination reaction confined within SWNT involved the addition of the "*N*-phenylacetamide@SWNT" black powder to an aqueous solution of pyridinium dichlorobromate and stirring vigorously at room temperature for 24 hours. After quenching the reaction with excess sodium bisulfite, organic products were extracted with diethyl ether, washed with water, dried over sodium sulfate and filtered through cotton wool. Removal of solvent at reduced pressure yields a white solid mixture of brominated *N*-phenylacetamide. The ratio of *ortho*- to *para*-brominated products was determined from ¹H NMR spectroscopy by comparison of peak integrals at 7.11 (1H, *ortho*) and 7.46 (2H, *para*) ppm corresponding to the proton environments at the 4 and 3/5 positions respectively.

It is important to note, at this early stage in the investigation, that the extraction of molecular products from the carbon nanotube was possible by simply washing with organic solvent, as evidenced by the detection of products from the confined reaction by NMR spectroscopy. This confirmed the hypothesis that confined reactions producing small molecular products, which therefore experience weaker interactions with the nanotube sidewall, could be carried out within carbon nanotubes on a preparative scale with products being extracted and isolated.

The procedure described repeatedly afforded mono-brominated product mixtures with selectivity for the *para*-brominated product varying between 68 and 97% (**Table 3.1**).

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This represents the first experimental evidence that the confinement of aromatic bromination reactions within narrow SWNT has the potential to alter the regioselective outcome of a reaction on a preparative scale. Crucially, such confinement increases the selectivity for the more linear *para*-regioisomer, albeit to varying degrees, supporting the hypothesis that extreme steric confinement within narrow carbon nanotubes can invoke size and shape selectivity principles to affect the outcome of chemical reactions.

Table 3.1 The effect of confinement within HiPCO SWNT on the regioselective bromination of *N*-phenylacetamide. Selectivity determined from ^1H NMR spectroscopy with a standard deviation of $\pm 3\%$.

Carbon nanotube	Product ratio / %	
	<i>para</i>	<i>ortho</i>
None	68	32
HiPCO SWNT (closed)	69	31
HiPCO SWNT (open) ^a	97	3

^a The *para*-selectivity for these reactions varied (68-97%) depending on the relative success of the encapsulation procedure so the maximum selectivity achieved with optimised conditions is shown here to better represent the confined reaction (**Figure 3.6**).

Although confinement reliably increases selectivity for the *para* isomer, the magnitude of this increase in selectivity showed large variation. This is most probably due to the difficulty in accurately defining and controlling the conditions under which the fractional distillation procedure takes place, as well as the inherent inhomogeneity of carbon nanotube morphology even within a single batch. For instance, while all efforts were made to keep experimental variables constant, slight variations in the temperature, pressure or duration of the fractional distillation procedure often result in a varied proportion of *N*-phenylacetamide still remaining on the external surface of the SWNT. While reactant molecules remaining within the SWNT may react with comparatively higher *para*-selectivity, those not encapsulated will react to afford the unselective mixture of products observed in bulk solution and therefore, the overall measured regioselectivity of the reaction critically depends on the ratio of reactant molecules encapsulated within the SWNT to those externally

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adsorbed. Indeed, the fractional distillation procedure was developed to increase this ratio by selectively removing unencapsulated reactant molecules. Therefore, it is hypothesised that the increase in *para*-selectivity upon confinement is controlled by the extent to which the fractional distillation procedure has been completed (*i.e.* the proportion of the remaining reactant molecules which are encapsulated). As the fractional distillation proceeds, the overall mass of *N*-phenylacetamide decreases, yet the absolute mass of reactant encapsulated within the SWNT should remain approximately constant. Therefore the proportion of the reactant encapsulated gradually increases and, by sampling the "*N*-phenylacetamide@SWNT" material at different stages throughout the fractional distillation procedure, it is hypothesised that the observed selectivity for the *para*-regioisomer will increase as the fractional distillation proceeds. By measuring the regioselectivity of the bromination of *N*-phenylacetamide at ten points throughout this procedure, the point at which the confined reaction becomes dominant over the reaction outside the SWNT can be determined (**Figure 3.6**). A clear increase in *para*-selectivity is demonstrated as the excess *N*-phenylacetamide is gradually removed from the SWNT surface, with *para*-selectivity ranging up to 97% within SWNT.

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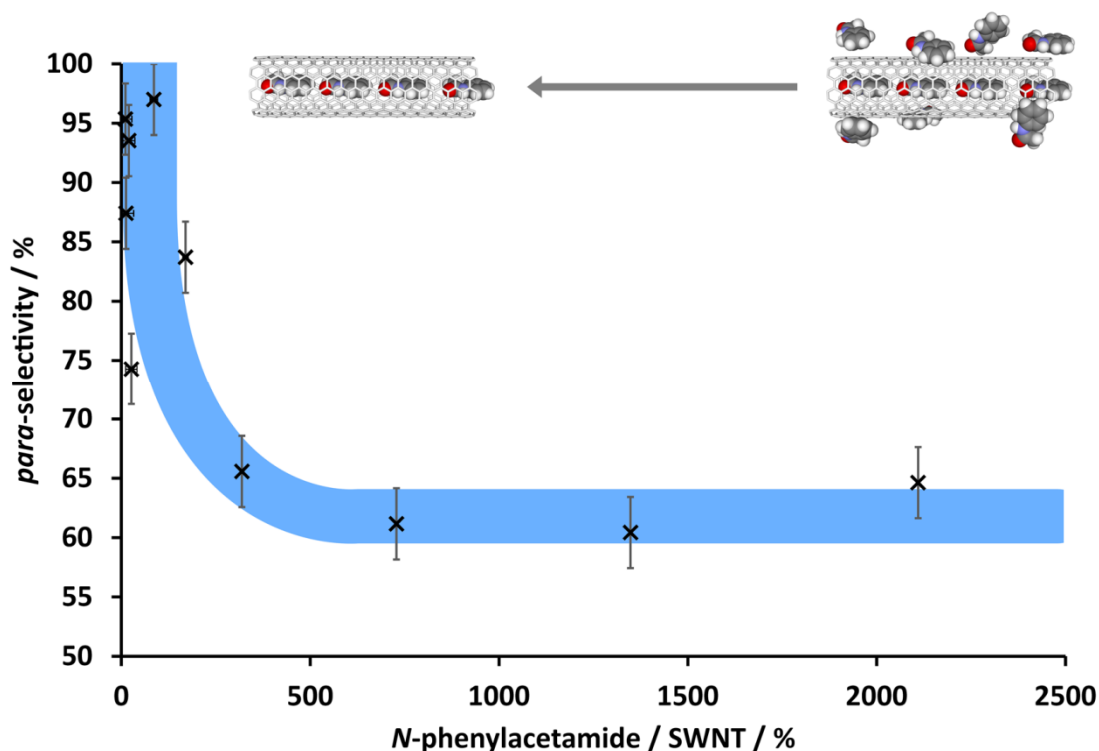


Figure 3.6 The *para*-selectivity of the bromination of *N*-phenylacetamide with pyridinium dichlorobromate confined within HiPCO SWNT, as a function of reactant/SWNT mass ratio. The gradual, selective removal of externally adsorbed reactant molecules (from right to left) decreases this mass ratio, thus increasing the proportion of reactant molecules within the SWNT. As a greater proportion of reactant molecules are encapsulated within SWNT, a greater proportion of the bromination occurs in confinement, and the observed selectivity for the *para*-brominated regioisomer increases up to 97%. Error bars represent the error and standard deviation ($\pm 3\%$) of selectivity values determined from ^1H NMR spectroscopy.

Analysis of the trend in regioselectivity as a function of reactant/SWNT ratio gives an indication of the balance between the confined reaction and the reaction in bulk solution. When the mass of *N*-phenylacetamide is greater in proportion to the mass of the host SWNT (**Figure 3.6**, right), the majority of the reactants must be adsorbed on the external surface of the SWNT due to the finite capacity of such a SWNT host. Therefore, the majority of the reaction must occur externally, in bulk solution, affording regioselectivity as expected in the absence of a SWNT host. Although a finite mass of *N*-phenylacetamide will be encapsulated, the external excess dominates the competition between internal and external reactions and the effect of confinement is not observed. It is only when the external excess of *N*-phenylacetamide molecules is removed, that the regioselectivity of the confined reaction is

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detected (**Table 3.1**), because the confined reaction becomes comparable and eventually dominant (**Figure 3.6**, left).

3.3.3. *Effect of host nanotube diameter*

In order to determine how readily the developed methodology could be applied to alternative reactions, the sensitivity of the observed confinement effects to common CNT variables, such as host carbon nanotube diameter, should be studied. The effect of such extreme confinement on regioselectivity is expected to be sensitive to the diameter of the host carbon nanotube because it is the size and shape of the product molecules in relation to the SWNT internal cavity which forms the basis of the induced selectivity. Therefore, it is hypothesised that as the diameter increases, the effect of confinement on the regioselectivity of aromatic halogenation will be diminished because the volume available for the reaction will increase, thus allowing both products to form freely.

The sensitivity of the observed change in selectivity to varying SWNT diameter is difficult to predict because so few experimental studies have been conducted on organic transformations within narrow carbon nanotubes. For instance, the regioselectivity within a SWNT may gradually decrease as SWNT diameter is increased, or there may be a more acute change to the effect of confinement. Molecular dynamics simulations of the Diels-Alder cycloaddition of 9-anthraldehyde with *N*-substituted maleimides predicted that stereoselectivity can be affected by the extreme steric confinement within SWNT. However, the effect of such confinement within SWNT on stereoselectivity is predicted to be significantly reduced when the host SWNT increases from 1.08 to 1.22 nm. While this example represents a different reaction studied only theoretically, this suggests that the observed regioselectivity for aromatic halogenation may be very sensitive to the diameter of the host SWNT and therefore experimental studies are important.

A range of single-walled carbon nanotubes of varying diameter were selected in addition to the HiPCO SWNT used in the initial investigation into regioselective aromatic

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bromination. SWNT synthesised by the CoMoCAT⁴⁷ process exhibit a diameter (d_{NT}) of 0.7 nm (internal cavity diameter, $d_{\text{NT}}^{\text{int}}$, of 0.43 nm), providing the opportunity to study a narrower host nanotube offering more extreme spatial confinement. SWNT produced by the arc discharge (AD SWNT) process exhibit a larger diameter of 1.3 nm ($d_{\text{NT}}^{\text{int}} = 0.96$ nm) providing less extreme confinement. It is not common to distinguish between the crystallographic nanotube diameter (d_{NT}) and the internal cavity diameter ($d_{\text{NT}}^{\text{int}}$) for single-walled carbon nanotubes; however, when considering reactions under such extreme confinement within SWNT, the internal volume is critical and therefore the van der Waals radii of the CNT carbon atoms must be taken into account to give a more accurate measure of the available internal volume (**Figure 3.7**).

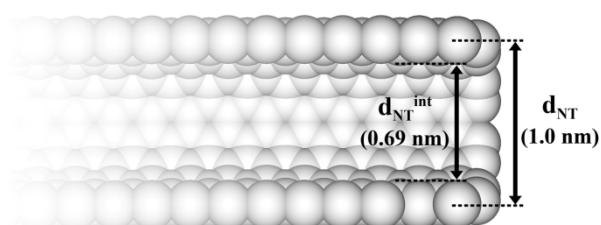


Figure 3.7 Schematic of HiPCO SWNT demonstrating both the crystallographic nanotube diameter (d_{NT}), as measured by statistical analysis of transmission electron micrographs, between carbon atom nuclei in comparison to the van der Waals diameter of the nanotube internal cavity ($d_{\text{NT}}^{\text{int}}$) which takes into account the van der Waals radii of CNT carbon atoms to give a more accurate measure of the internal volume available for confined reactions.

In an attempt to predict the outcome of aromatic bromination within each of the three SWNT, the critical van der Waals dimensions (d_{crit}) of the reactant and regioisomeric products were considered in relation to the internal cavity volume for each host nanotube (**Figure 3.8**). The critical diameter of the guest species is the maximum van der Waals dimension perpendicular to the largest dimension, which dictates the smallest diameter carbon nanotube required to encapsulate the molecule. It is hypothesised that the CoMoCAT SWNT are too narrow to allow the encapsulation of the reactant (*i.e.* $d_{\text{crit}} > d_{\text{NT}}^{\text{int}}$) and therefore, the reaction cannot occur within the nanotube internal cavity. This narrow SWNT is expected to induce no selectivity, affording the unselective mixture observed in bulk solution. Conversely, the wider AD SWNT provides sufficient internal volume for both the

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para-brominated ($d_{\text{crit}} = 0.69 \text{ nm}$) and *ortho*-brominated ($d_{\text{crit}} = 0.79 \text{ nm}$) regioisomers to be encapsulated (*i.e.* $d_{\text{crit}} < d_{\text{NT}}^{\text{int}}$). Thus, the size exclusion principles exploited within HiPCO SWNT will not be as effective within AD SWNT, providing reduced selectivity. Therefore, the confined reaction is expected to exhibit lower regioselectivity than that observed within HiPCO SWNT. The greatest regioselectivity is expected within HiPCO SWNT because the internal cavity provides sufficient volume for the *para*-regioisomer to form ($d_{\text{crit}} \approx d_{\text{NT}}^{\text{int}}$), but insufficient volume for the *ortho*-regioisomer ($d_{\text{crit}} > d_{\text{NT}}^{\text{int}}$).

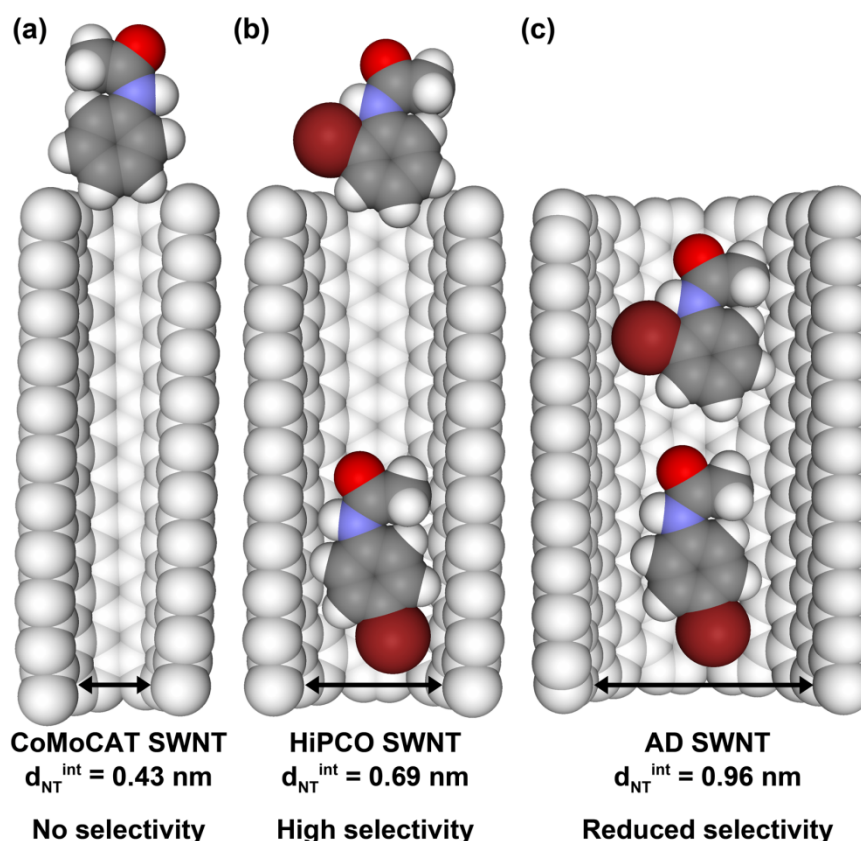


Figure 3.8 Comparison of the van der Waals diameter of the internal cavity ($d_{\text{NT}}^{\text{int}}$) of the three appraised SWNT to the critical dimension (d_{crit}) of the reactant and product molecules forming the basis of the hypothesised effect of confinement on regioselectivity. (a) CoMoCAT SWNT ($d_{\text{NT}}^{\text{int}} = 0.43 \text{ nm}$) is too narrow to allow the encapsulation of the *N*-phenylacetamide reactant ($d_{\text{crit}} = 0.69 \text{ nm}$); (b) HiPCO SWNT ($d_{\text{NT}}^{\text{int}} = 0.69 \text{ nm}$) allows the formation of the *para*-product ($d_{\text{crit}} = 0.69 \text{ nm}$) but not the *ortho*-product ($d_{\text{crit}} = 0.79 \text{ nm}$); and (c) wider AD SWNT ($d_{\text{NT}}^{\text{int}} = 0.96 \text{ nm}$) freely allows the formation of both products.

In order to test these hypotheses, the procedure developed for the encapsulation of *N*-phenylacetamide within HiPCO and the subsequent reaction with pyridinium

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dichlorobromate (**Sections 3.3.1 and 3.3.2**) was repeated using both CoMoCAT SWNT and AD SWNT and the resultant regioselectivity compared (**Table 3.2**).

Table 3.2 The effect of confinement within single-walled carbon nanotubes on the regioselective bromination of *N*-phenylacetamide. Selectivity determined from ^1H NMR spectroscopy with a standard deviation of $\pm 3\%$.

Carbon nanotube	$d_{\text{NT}}^{\text{int}} / \text{nm}$	Product ratio / %	
		<i>para</i>	<i>ortho</i>
None	n/a	68	32
CoMoCAT SWNT	0.43	70	30
HiPCO SWNT	0.69	97	3
AD SWNT	0.96	69	31

The hypotheses were found to be largely correct, in that the greatest selectivity was observed within HiPCO SWNT. As expected, the regioselectivity observed for CoMoCAT SWNT is identical, within the error of the measurement, to that observed in bulk solution because the SWNT is too narrow to allow the confined reaction which, instead, occurs in solution surrounding the SWNT. The regioselectivity observed within AD SWNT is also identical to that of bulk solution, which is particularly interesting because this SWNT is only 0.3 nm wider than the HiPCO SWNT, within which the greatest regioselectivity is attained. This result demonstrates the critical importance of carbon nanotube diameter when influencing the pathways of chemical reactions by extreme confinement. This particular conclusion offers the first experimental evidence in support of the theoretical simulations of Smith *et al.* whereby it was predicted that an increase in nanotube diameter of merely 0.14 nm will significantly reduce the effect of confinement on the regioselectivity of Diels-Alder cycloaddition reactions.⁴⁸

It has been demonstrated that consideration of the host nanotube diameter is a critical concern when attempting the confinement of any chemical reactions within narrow carbon nanotubes when aiming to influence the reaction pathway. Additionally, this systematic comparison of different carbon nanotubes provides valuable control experiments

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which prove that the significant improvement in *para*-selectivity observed within HiPCO SWNT is not due to any interaction with the SWNT exterior, but is instead a result of extreme and precise confinement controlled by matching the size and shape of the reaction products with the nanotube cavity.

3.3.4. *Estimation of kinetic parameters in confinement from selectivity data*

The kinetics of reactions confined within SWNT are complicated and difficult to study directly. The observed rate of reaction is a product of multiple steps along the reaction coordinate, including the diffusion of reactants into the CNT, the rate of the confined reaction and the rate of diffusion of products from the CNT internal cavity. This is further complicated by the inhomogeneity of carbon nanotubes which can mean that diffusion rates into and out from the internal cavity may not be consistent. Diffusion limitations often contribute to slower *observed* reaction kinetics for reactions within narrow SWNT,⁴⁹ as was found in this study, where the conversion of aromatic halogenation within HiPCO SWNT is typically lower than the corresponding reaction in bulk solution, with values ranging from 11 - 95% depending on specific experimental conditions. A final complication arises when studying non metal-catalysed organic reactions which are known to occur readily in solution, because the observed rate of reaction is the result of two competing reaction environments, namely within the SWNT internal cavity and in the surrounding solution. Due to these complications, it is difficult to reliably measure the kinetics of confined reactions directly; however, it is possible to gain some understanding of the confined reaction kinetics indirectly through detailed analysis of regioselectivity.

This approach has been used previously by Breslow and Campbell when studying the chlorination of anisole in α -cyclodextrin.¹⁴ It was found that an unusually high *para*-selectivity was observed despite only 72% of the anisole reactant being bound within the host. Logically, this leads to the conclusion that the reaction is accelerated by confinement due to a favourable interaction, leading to improved kinetics compared to the reaction in bulk

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solution. To evaluate the relative kinetics of *N*-phenylacetamide bromination within SWNT, a similar approach was taken as part of this study.

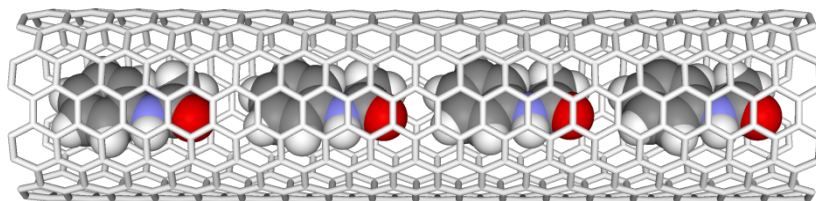
By comparing the observed regioselectivity in each experiment to the known regioselectivity of the reaction in bulk solution, it is possible to estimate the proportion of the reaction which occurred inside the SWNT. The bromination of *N*-phenylacetamide in bulk solution is known to afford a mixture of regioisomers with 68% *para*-selectivity. If it is assumed that a reactant molecule within HiPCO SWNT cannot react to form the *ortho*-product due to extreme confinement (**Figure 3.8**) and thus affords 100% *para*-selectivity, then it is possible to attain an indirect measure of the relative reaction rates in confinement and in solution. If, for example, the observed *para*-selectivity of a particular reaction was 84%, it can be inferred that approximately 50% of the reaction occurred in bulk solution (affording a 68:32 mixture of *para:ortho* regioisomers) and 50% of the reaction occurred in confinement (affording 100% *para*-regioisomer). The subsequent extraction and combination of the two product mixtures yielding an overall 84% *para*-selectivity.

In analogy to the work of Breslow and Campbell,¹⁴ where the percentage of reactant in confinement was determined empirically, the proportion of *N*-phenylacetamide within HiPCO SWNT must be estimated. While this cannot be reliably measured experimentally, because no quantitative spectroscopic techniques allow discrimination of organic molecules within the CNT to those of the bulk, the mass of encapsulated reactant prior to the reaction can be approximated based on experimental mass values. In order to do this, the capacity of the SWNT to host the reactant must be estimated. Geometrical consideration of the reactant molecules aligned within an average HiPCO SWNT (**Table 3.3**) allow the maximum capacity of the host SWNT for *N*-phenylacetamide to be estimated based on the approximate mass of HiPCO SWNT required to encapsulate a reactant molecule. It is estimated that a given mass of HiPCO SWNT can encapsulate 7.6% by mass of *N*-phenylacetamide. This represents the maximum mass of *N*-phenylacetamide able to be confined within a given mass of HiPCO SWNT and therefore, it can be assumed that any remaining *N*-phenylacetamide

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beyond this threshold must be outside the SWNT cavity. Based on the known mass of SWNT and the measured mass of *N*-phenylacetamide, the proportion of the reactant encapsulated within the SWNT prior to the reaction can now be estimated.

Table 3.3 Calculation for the maximum percentage, by mass, of *N*-phenylacetamide reactant able to be encapsulated within a given mass of HiPCO SWNT. This is based on an idealised (8, 8) SWNT assumed to be representative of the average HiPCO SWNT. As CNT purity is assumed to be 100%, this calculated value represents the *maximum* capacity because impurities and structural imperfections within a CNT sample will reduce the relative capacity.



Mass of <i>N</i> -phenylacetamide molecule:	135.2 g mol ⁻¹
Carbon atoms required to encapsulate one <i>N</i> -phenylacetamide molecule:	148
Mass of carbon required to encapsulate one <i>N</i> -phenylacetamide molecule:	148 x 12 = 1776 g mol ⁻¹
Mass % of reactant molecular able to be encapsulated in SWNT:	135/1776 = 7.6%

If the approximated proportion of reactant encapsulated within the SWNT prior to the reaction is presumed to be the proportion of the reaction to occur in confinement, this neglects to account for any catalytic turnover whereby product molecules are expelled and reactant molecules diffuse into the SWNT to react. However, comparison of the calculated regioselectivity based on this assumption (**Table 3.4** & **Table 3.5**), to the experimentally observed regioselectivity (**Figure 3.6**), will indicate the influence of diffusion and allow a deeper understanding of reaction kinetics in confinement.

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Table 3.4 Example calculation, for a representative reaction, of the expected theoretical regioselectivity of *N*-phenylacetamide bromination based on the experimental sample mass, calculated HiPCO SWNT capacity for the reactant, known regioselectivity in bulk solution and postulated regioselectivity in confinement.

Known product ratio of reaction in bulk solution	= 68% <i>para</i> : 32% <i>ortho</i>
Mass of SWNT	= 4.897 mg
Mass of <i>N</i> -phenylacetamide	= 3.243 mg
<i>N</i> -phenylacetamide/SWNT	= 66%
Max. calculated <i>N</i> -phenylacetamide mass inside SWNT ^[a]	= 4.897 mg × 7.6% = 0.372 mg (11.5%)
<i>N</i> -phenylacetamide mass outside SWNT	= 3.243 mg – 0.372 mg = 2.871 mg (88.5%)
Calculated <i>para</i> -product formed outside nanotube ^[b]	= 88.5% × 68% = 60.2%
Calculated <i>para</i> -product formed inside nanotube ^[c]	= 11.5%
Calculated total <i>para</i> -product	= 60.2 + 11.5 = 71.7%
Calculated <i>ortho</i> -product	= 88.5% × 32% = 28.3%

^[a] Maximum percentage, by mass, of *N*-phenylacetamide able to be encapsulated in a given mass of HiPCO SWNT, 7.6%, taken from previous approximation (**Table 3.3**). ^[b] The bromination of *N*-phenylacetamide in bulk solution (88.5% of reactant molecules in this case) is known to form an unselective mixture with 68% *para*-selectivity. ^[c] Calculation based on assumption that all truly encapsulated *N*-phenylacetamide molecules (11.5% of reactant molecules in this case) can only react to form the *para*-product.

Table 3.5 Table showing the large discrepancy between the experimentally observed regioselectivity and that expected based on the theoretical calculations described in **Table 3.4**.

	Product ratio / %	
	<i>para</i>	<i>ortho</i>
Calculated	72	28
Experimental	97	3

It is found that in most cases, particularly those exhibiting high regioselectivity, the observed *para*-selectivity is higher than expected, based on the mass of reactant encapsulated prior to the reaction, *e.g.* already reaching 97% when just a minority of reactant molecules are encapsulated (**Table 3.4**). Indeed, when the trend of increasing regioselectivity with decreasing *N*-phenylacetamide/SWNT ratio is examined (**Figure 3.6**), the curve is much more gradual than expected based on the finite capacity of the SWNT for the reactant and apparent excess of externally adsorbed reactant. This suggests, not only that reactant molecules diffuse into the nanotube during the reaction (*i.e.* catalytic turnover), but that the rate of the confined reaction is accelerated compared to that of the reaction in bulk solution.

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To clarify this point, the flow of logic can be reversed; whereby the proportion of the reaction to occur in confinement is calculated based on the observed *ortho*-product formation (Table 3.6) which suggests, in this case, that over 90% of the reaction occurred in confinement, despite only 11.5% of the reactant able to be encapsulated at any point.

Table 3.6 Example calculation of the expected proportion of the reaction which occurred in confinement based on the observed *ortho*-selectivity. This calculation follows the reverse logic of the previous calculation in order to clarify the point that a much larger proportion of the reaction seems to have occurred within the SWNT than expected based on the finite capacity of the SWNT for the reactant molecules.

Observed <i>ortho</i> -formation:	= 3% <i>ortho</i>
Estimated proportion of reaction occurring outside SWNT ^[a]	= 3% <i>ortho</i> / 0.32 = 9.4%
Proportion of reaction occurring inside SWNT	= 100 - 9.4 = 90.6 %
Mass of <i>N</i> -phenylacetamide	= 3.24 mg
Max. calculated <i>N</i> -phenylacetamide mass <i>inside</i> SWNT ^[b]	= 4.90 mg × 7.6% = 0.372 mg (11.5%)
Proportion of reactant initially encapsulated within SWNT	= 0.372 / 3.24 = 11.5%

[a] Assuming that all *ortho*-product observed must have formed outside SWNT and also afforded the corresponding *para*-isomer in ratio of 68:32, based on the known regioselectivity in bulk solution. ^[b] Maximum percentage, by mass, of *N*-phenylacetamide able to be encapsulated in a given mass of HiPCO SWNT, 7.6%, from Table 3.3.

The diffusion of organic molecules into, and out from, narrow carbon nanotubes is not fully understood; however, it is expected to be partially dictated by the competitive interactions of the organic molecules with either solvent or the pseudo-solvation environment of the nanotube internal channel.³⁵ For instance, if the guest molecule experiences a stronger interaction with the nanotube than with solvent (*e.g.* non-polar molecule in water), encapsulation is more energetically favourable. In this case, it is likely to result in the diffusion of guest molecules to the CNT from bulk solution. This phenomenon, previously applied to molecular nanoreactors and referred to as the hydrophobic effect,^{28, 29} can readily be applied to carbon nanotubes in aqueous suspension and explains the potential driving force for the diffusion of *N*-phenylacetamide molecules into the SWNT from aqueous solution throughout the course of the reaction.

The theoretical simulations of Halls and Schlegel analysed the confinement of the Menshutkin S_N2 reaction within narrow SWNT and predicted that such nanoscale

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confinement would substantially increase the reaction rate.⁵⁰ It was shown that the highly polarisable carbon nanotubes can stabilise the charge separated transition state which significantly lowers the activation energy and endothermicity when compared to the reaction in the gas phase. The bromination of *N*-phenylacetamide also involves a transition state with a large charge separation (*i.e.* high dipole moment) and therefore, it is reasonable to surmise that the highly polarisable host SWNT could stabilise this transition state, thus reducing the activation energy barrier and accelerating the reaction rate for the formation of the *para*-product within HiPCO SWNT (**Figure 3.9**).

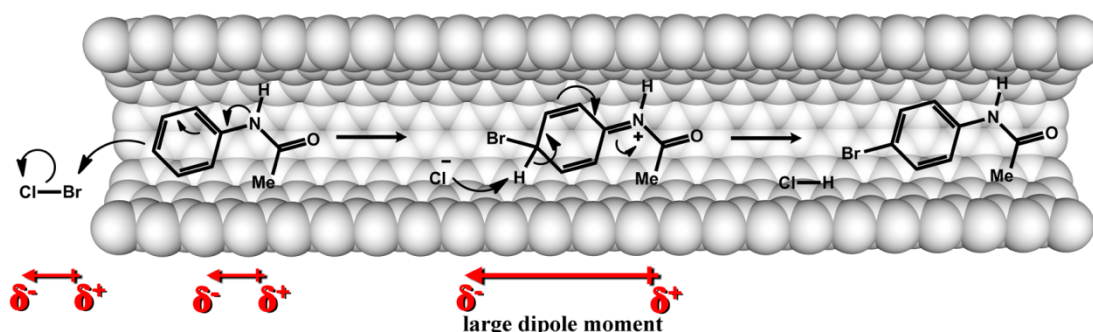


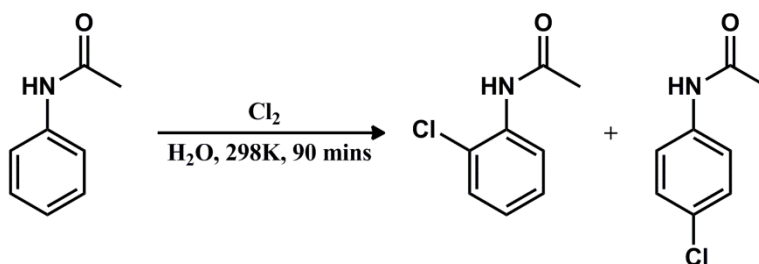
Figure 3.9 Schematic representation of the mechanism of *N*-phenylacetamide bromination confined within a HiPCO SWNT showing the formation of a transition state with a high dipole moment. This transition state dipole can be stabilised by the highly polarisable host nanotube, thus lowering the activation energy barrier and accelerating the reaction inside the nanotube.

3.3.5. Regioselectivity of aromatic chlorination in confinement

In order to assess whether the observed increase in bromination at the *para*-position of *N*-phenylacetamide is a general phenomenon and how readily this concept may be applied to alternative reactions, the analogous chlorination reaction (**Scheme 3.3**) was also studied within HiPCO SWNT. By investigating an alternative halogenation reaction using the same aromatic reactant, the encapsulation procedure can remain constant. It is important to determine whether the improvement in selectivity for the *para*-regioisomer is a general phenomenon based on size and shape selectivity and thus, whether the effect of confinement on the regioselectivity of chlorination is comparable to that for bromination. Molecular chlorine was chosen as a suitable chlorinating agent as it affords an unselective mixture of

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both *ortho*- and *para*-substituted regioisomers. While the chloro- adduct is comparable in steric bulk to the bromo-, the halogenating agents are significantly different (Cl_2 cf. PyHCl_2Br), and this comparison may therefore indicate whether any specific interactions are necessary and how readily the concept of carbon nanotube nanoreactors can be applied to a range of organic transformations.



Scheme 3.3 Chlorination of *N*-phenylacetamide by chlorine gas to afford an unselective mixture of both *ortho*- and *para*-monochlorinated regioisomers.

In a typical chlorination reaction, an excess of chlorine gas was bubbled through an aqueous solution of *N*-phenylacetamide at room temperature for 90 minutes. The flask was flushed with nitrogen for 12 hours, to remove excess chlorine gas, and organic products were extracted with diethyl ether, washed with water, dried over sodium sulfate and all solvent was removed at reduced pressure to yield a white solid. ^1H NMR spectroscopy of the product mixture allowed the regioselectivity to be determined by comparison of peak integrals at 7.19 (1H, *ortho*) and 7.61 ppm (2H, *para*) ppm corresponding to the environments at the 4 and 2 positions respectively. This reaction, in the absence of SWNT, afforded an unselective (85:15, *ortho*:*para*) mixture. The analogous reaction confined within HiPCO SWNT was completed by encapsulating the *N*-phenylacetamide reactant within HiPCO SWNT using the liquid-phase immersion and fractional distillation procedure described previously. In order to keep the chlorine concentration constant and directly comparable between the confined reaction and the control reaction in bulk solution, the two reactions were carried out simultaneously and in parallel. This was achieved by splitting the chlorine gas flow between two reaction flasks, one containing an aqueous solution of *N*-phenylacetamide and the other containing an aqueous suspension of *N*-phenylacetamide@HiPCO SWNT. This parallel

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comparison allows the effect of confinement within HiPCO SWNT on the regioselectivity of this chlorination reaction to be directly observed (**Table 3.7**).

Table 3.7 The effect of confinement within HiPCO SWNT on the regioselectivity of *N*-phenylacetamide chlorination. Conditions were not optimised.

Reaction	Product ratio / %	
	<i>para</i>	<i>ortho</i>
No SWNT	15	85
<i>N</i> -phenylacetamide@HiPCO SWNT	42	58

A clear increase in regioselectivity in favour of the *para*-regioisomer is demonstrated as a consequence of confinement within HiPCO SWNT. This supports the hypothesis that the selectivity induced by extreme confinement of aromatic halogenation within SWNT is a general phenomenon not reliant on any specific interactions and only size and shape exclusion principles control the increase in *para*-selectivity in each case. Although the host SWNT seemingly exhibits a less pronounced change to the regioselectivity of chlorination than for bromination, the result for chlorination was not optimised and as such, reliable conclusions cannot be drawn from the magnitude of selectivity increase. As the observed regioselectivity for bromination was directly related to the proportion of reactant encapsulated and therefore showed variation depending on sample mass (**Figure 3.6**), it seems reasonable to assume that such behaviour should be similar for chlorination. However, while the magnitude of this change in selectivity is not important, the shift in favour of the *para*-chlorinated product indicates that the concept of size and shape selectivity within SWNT can be utilised for molecules of comparable size and shape irrespective of their chemical structure.

3.4. Conclusions

Single walled carbon nanotubes have been demonstrated as effective nanoscale hosts for preparative organic reactions. Novel methodologies have been developed for the encapsulation of small organic reactants and the confinement of non metal-catalysed organic reactions within narrow SWNT. The encapsulation of small organic molecules has been demonstrated for *N*-phenylacetamide using a previously developed liquid-phase method coupled with a novel fractional distillation procedure in order to selectively remove excess externally adsorbed reactant molecules. This procedure exploits the hypothesised effect of extreme confinement on the phase behaviour of guest molecules to differentiate between the confined environment and the surrounding bulk liquid.

It has been shown that the confinement of aromatic halogenation reactions within HiPCO SWNT in aqueous suspension significantly increases selectivity for the *para*-substituted regioisomer. The confined bromination of *N*-phenylacetamide affords the *para*-brominated regioisomer with up to 97% selectivity as opposed to 68% selectivity in bulk solution. The chlorination of *N*-phenylacetamide demonstrates a similar shift in regioselectivity in favour of the *para*-chlorinated regioisomer, from 15 to 42%, as a result of nanoscale confinement within HiPCO SWNT, although these conditions were not optimised. These increases in *para*-selectivity have been found to be a consequence of extreme and precise confinement within the internal cavity of HiPCO SWNT, by precluding attack at the *ortho*-position due to the precise arrangement of reactant molecules in confined space.

The effect of confinement on the regioselectivity of aromatic bromination was found to be critically dependent on the diameter of the host carbon nanotube. A nanotube of suitable diameter must be chosen, based on the critical dimensions of the intended guest molecules, in order to host the desired reaction and impose size and shape selectivity between two possible isomeric products. The reported increases in selectivity for the *para*-regioisomer were only observed when the optimum confinement was achieved within

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HiPCO SWNT; altering the diameter by 0.3 nm afforded no change to the observed selectivity upon confinement.

The extraction of products has proven facile in these reactions due to the weak van der Waals interactions between the encapsulated product molecules and the host nanotube, meaning that traditional extraction into organic solvent is effective. This highlights the potential for carbon nanotubes to host a wide range of chemical reactions on a preparative scale, since no specific interactions are required to encapsulate reactants other than ubiquitous van der Waals forces.

By careful analysis of the regioselectivity in confinement, along with the mass ratio of host nanotube to guest reactant, it has been concluded that the rate of aromatic bromination within HiPCO SWNT is significantly increased relative to that of the bulk solution. It is inferred that reactants diffuse into the carbon nanotubes due to the hydrophobic effect, and the highly polarisable carbon nanotube stabilises the transition state dipole moment, thus accelerating the confined reaction, in accordance with previous theoretical reports.⁵⁰

The methodologies developed in this study could, in principle, be applied to the confinement within narrow SWNT of a vast library of preparative organic chemical reactions where steric confinement can influence selectivity.⁵ This study highlights the significance of carbon nanoreactors in organic synthesis, particularly as this unique reaction environment has been shown to permit the formation of species inaccessible by any other means.²

3.5. Experimental

3.5.1. General

All glassware was cleaned with a mixture of hydrochloric and nitric acid (3:1 v/v, 'aqua regia') and rinsed thoroughly with deionised water, cleaned with potassium hydroxide in isopropyl alcohol and finally rinsed thoroughly with deionised water. Water was purified ($> 18 \text{ M}\Omega \text{ cm}$) using a Barnstead NANOPure II system. ^1H NMR spectra were obtained using a Bruker AV(III)400 (400 MHz) spectrometer at 298K using 64 scans in deuterated dimethylsulfoxide ($\text{DMSO-}d_6$). All heat treatment was carried out in a tube furnace under air atmosphere unless otherwise stated. Transmission electron microscopy was performed by Professor Andrei Khlobystov using a JEOL 2100F TEM (field emission gun source, information limit $< 0.19 \text{ nm}$) at room temperature. Samples were prepared *via* drop-drying methanolic solutions onto copper grid mounted "lacey" carbon films. Nanotube diameter measurements were conducted from statistical analysis of transmission electron micrographs using Gatan DigitalMicrograph software. All molecular measurements (d_{crit}) were carried out using the Accelrys DS ViewerPro 6.0 software, by simple geometry optimisation and measurement of inter-nuclei distance, also taking into account the van der Waals radii.²⁶ All reagents were purchased from Sigma-Aldrich, UK and used without further purification unless otherwise specified. *N*-phenylacetamide was recrystallised from toluene.⁵¹ Pyridinium dichlorobromate was synthesised according to the literature precedent described by Muathen.¹⁸

3.5.2. Carbon nanotube sources and pre-treatment

Carbon nanotubes were purchased from commercial suppliers and all were pre-treated by air oxidation in order to oxidatively remove the nanotube end-caps, providing access to the internal cavity. Conditions varied for this procedure (**Table 3.8**).

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Table 3.8 Description and commercial source for each carbon nanotube used. The conditions used during oxidative pre-treatment including temperature (T_{ox}) and duration (t_{ox}) are provided, and mean nanotube diameter (d_{NT}) was measured by statistical analysis of transmission electron micrographs.

d_{NT} / nm	Synthesis	Commercial name	Commercial Supplier	Lot no.	T_{ox} / °C	t_{ox} / mins
0.69±0.1	CoMoCAT	(6,5)-SWNT	Sigma-Aldrich Chemicals, UK	MKBF 6413V	520	6
1.0±0.1	CVD	HiPCO SWNT ^a	Unidym Inc., CA, USA	R2172	380	30
1.3±0.1	Arc discharge	Helix SWNT	Helix Materials Solutions, TX, USA	CSCA	380	35

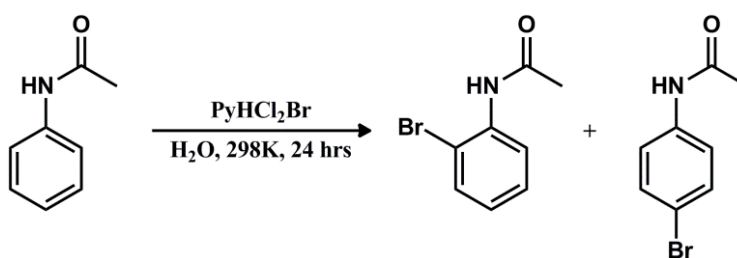
^a HiPCO SWNT were additionally purified prior to use by protocol detailed by manufacturer.

Additionally, all carbon nanotubes were dried thoroughly at 250°C for 30 minutes immediately prior to use.

3.5.3. Encapsulation of *N*-phenylacetamide within SWNT

To molten *N*-phenylacetamide (100 mg, 120°C) was immediately added purified SWNT (5 mg). The mixture was briefly agitated and left for 5 minutes to allow complete immersion. The mixture was then heated at 120°C under reduced pressure (190 mbar) until the sample mass reduced to the desired value (typically requiring 5-12 hours) to yield black *N*-phenylacetamide/SWNT composite powder (5-10 mg).

3.5.4. Bromination of *N*-phenylacetamide@SWNT



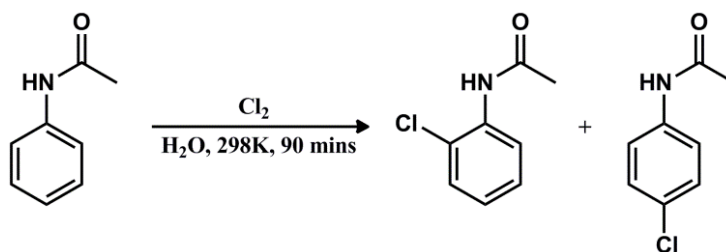
To an aqueous solution of pyridinium dichlorobromate (0.6 equivalents, 1.5 mmol dm⁻³) was added *N*-phenylacetamide@SWNT (e.g. 5.5 mg, of which 5 mg is SWNT) and the suspension stirred vigorously for 24 hours at room temperature. The reaction was quenched by the addition of excess sodium bisulfite and extracted with diethyl ether (2 x 0.9 mL). The organic solution was washed with water (2 x 2 mL), dried over anhydrous sodium sulfate, filtered and dried *in vacuo* to yield a white solid mixture of brominated products. The ratio of

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ortho- and *para*- regioisomers was determined from ^1H NMR spectroscopy by comparing diagnostic peak integrals at 7.11 (1H, *ortho*) and 7.46 (2H, *para*) ppm (underlined below).

^1H NMR (DMSO- d_6) δ_{H} /ppm *N*-phenylacetamide: 9.91 (s, 1H, NH), 7.57 (dt, 2H, $J = 8.8$, 1.1 Hz, *Ar* H2, H6), 7.28 (tt, 2H, $J = 8.4$, 1.8 Hz, *Ar* H3, H5), 7.02 (tt, 1H, $J = 7.5$, 1.2 Hz, *Ar* H4), 2.04 (s, 3H, CH₃). *N*-(4-bromophenyl)acetamide: 10.05 (s, 1H, NH), 7.55 (dt, 2H, $J = 8.8$, 2.2 Hz, *Ar* H2, H6), 7.46 (dt, 2H, $J = 8.8$, 2.2 Hz, *Ar* H3, H5), 2.04 (s, 3H, CH₃). *N*-(2-bromophenyl)acetamide: 9.45 (s, 1H, NH), 7.64 (dd, 1H, $J = 8.0$, 1.1 Hz, *Ar* H2), 7.59 (dd, 1H, $J = 8.0$, 1.1 Hz, *Ar* H3), 7.35 (td, 1H, $J = 7.7$, 1.1 Hz, *Ar* H5), 7.11 (td, 1H, $J = 7.7$, 1.1 Hz, *Ar* H4), 2.08 (s, 3H, CH₃). Aromatic proton environments numbered relative to the acetamide position. Values consistent with literature analogues.¹⁵

3.5.5. Chlorination of *N*-phenylacetamide



Through a stirred aqueous suspension of *N*-phenylacetamide@SWNT (4.66 mg in 4 mL) was bubbled an excess of chlorine gas for 90 minutes at room temperature. Chlorine gas was generated by addition of manganese dioxide (43.5 g) to concentrated hydrochloric acid (4 equiv.). The suspension was then flushed with nitrogen for 12 hours, extracted into diethyl ether (2 x 4 mL), washed with water (2 x 10 mL), dried over anhydrous sodium sulfate and filtered through cotton wool. Solvent was removed *in vacuo* to yield a white solid mixture of chlorinated products. The reaction was carried out alongside a simultaneous control experiment (in the absence of nanotubes) in order to ensure consistent chlorine stoichiometry. The ratio of *ortho*- and *para*- regioisomers was determined from ^1H NMR spectroscopy by comparison of diagnostic peak integrals at 7.19 (1H, *ortho*) and 7.61 (2H, *para*) ppm (underlined below).

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¹H NMR (DMSO-*d*₆) δ_{H} /ppm ***N*-(4-chlorophenyl)acetamide**: 10.06 (s, 1H, NH), 7.61 (dt, 2H, $J = 8.8, 2.0$ Hz, ArH), 7.35 (dt, 2H, $J = 8.8, 2.0$ Hz, ArH), 2.11 (s, 3H, CH₃). ***N*-(2-chlorophenyl)acetamide**: 9.51 (s, 1H, NH), 7.70 (dd, 1H, $J = 8.4, 1.2$ Hz, ArH), 7.49 (dd, 1H, $J = 8.4, 1.2$ Hz, ArH), 7.32 (td, 1H, $J = 7.8, 1.4$ Hz, ArH), 7.19 (td, 1H, $J = 7.6, 1.2$ Hz, ArH), 2.11 (s, 3H, CH₃). Values consistent with literature analogues.⁵²

3.6. References

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4. Cycloaddition reactions inside carbon nanotubes

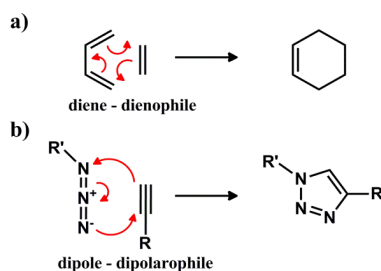
4.1. Background

It has been shown in the previous chapter that the outcome of simple chemical transformations can be drastically influenced by confinement within narrow carbon nanotubes. The reactions studied thus far could be considered pseudo-unimolecular given the discrepancy between the molecular size of the reactants (*e.g.* arene reacting with Br^+). It was essential to first test the hypothesis that confinement can influence preparative reactions inside carbon nanotubes using simple reactions in an attempt to minimise or negate the potential complications of bimolecular arrangement or diffusion. However, the study of truly bimolecular reactions, where both reactants are of commensurate size, will further extend the boundaries of this CNT nanoreactor methodology and allow a more detailed examination of the steric effects induced by nanoscale confinement inside carbon containers. One class of bimolecular chemical reactions which offers broad functional group tolerance, while also remaining synthetically useful, is the cycloaddition reaction.

4.1.1. Cycloaddition

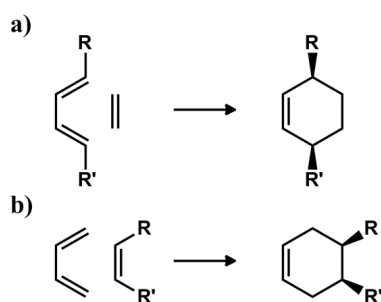
Cycloaddition reactions are defined as those reactions whereby two or more reactants combine to form a stable cyclic molecule, during which no fragments are eliminated and σ bonds are formed but not broken.¹ This encompasses reactions such as the Diels-Alder reaction,^{2, 3} dimerisation of olefins⁴ and 1,3-dipolar cycloaddition reactions,⁵⁻⁸ and such reactions have proven to be immensely useful in all areas of synthetic chemistry. In particular, the Diels-Alder reaction offers a powerful method for producing 6-membered rings with good control over regio- and stereochemistry and 1,3-dipolar cycloaddition represents a convenient and adaptable approach to the regio- and stereoselective synthesis of 5-membered heterocycles (**Scheme 4.1**).

4. Cycloaddition reactions inside carbon nanotubes



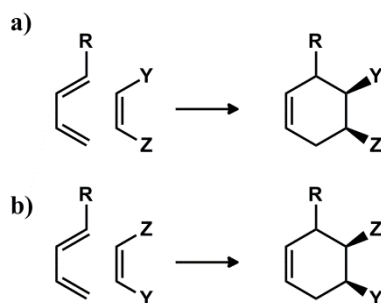
Scheme 4.1 Simple examples of cycloaddition reactions demonstrating the concerted formation of cycloadducts. a) The Diels-Alder (4 + 2) cycloaddition of 1,3-butadiene (diene) with ethene (dienophile) to form cyclohexene. b) The 1,3-dipolar (3 + 2) cycloaddition of an azide (dipole) with an alkyne (dipolarophile) to form a 1,2,3-triazole.

The Diels-Alder cycloaddition reaction broadly describes the (4 + 2) cycloaddition of a conjugated diene with a dienophile, commonly a substituted alkene or alkyne, but also including more complex π -systems such as C_{60} fullerenes⁹ and carbon nanotubes.¹⁰ Although the mechanism of the Diels-Alder reaction is debated,^{11, 12} the prevailing opinion is that it proceeds *via* a concerted reaction pathway where the reactant stereochemistry is preserved in the products (**Scheme 4.2**). However, reactions involving asymmetric reactants can give rise to regioisomerism as a result of the two possible molecular arrangements of the diene and dienophile (**Scheme 4.3**).



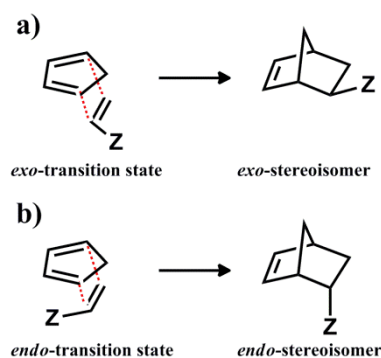
Scheme 4.2 Stereospecificity exhibited in Diels-Alder reactions, whereby a) *trans-trans* geometry of the diene and (b) the *cis-* geometry of the dienophile both result in the formation of a cyclohexene derivative with *syn*-stereochemistry.

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Scheme 4.3 Schematic demonstrating the potential regioisomerism during Diels-Alder cycloaddition of asymmetric reactants, (a & b) showing the two potential arrangements of reactants leading to two regioisomers.

The Diels-Alder reaction of cyclic dienes can give rise to further stereoisomerism resulting in the potential formation of both *endo* and *exo* bicyclic stereoisomers (**Scheme 4.4**). Interactions between the dienophile functional group (Z) and the π -system of the diene often stabilise the *endo*-transition state, thus accelerating the relative reaction rate leading to the favoured formation of the *endo* stereoisomer;¹³ however, steric congestion can counteract this effect¹⁴ making the *endo/exo* stereochemical outcome of complex Diels-Alder cycloadditions more difficult to predict.

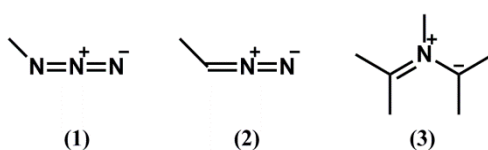


Scheme 4.4 Stereoisomerism resulting from the Diels-Alder cycloaddition of a cyclic diene. (a) *exo*-transition state leads to the formation of the *exo* stereoisomer, whereas (b) the *endo*-transition state proceeds to form the *endo* stereoisomer. The red dotted line represents the developing bonding interaction.

1,3-dipolar cycloaddition reactions can occur between any 1,3-dipole and a dipolarophile. A 1,3-dipole is a molecule where four π electrons are distributed amongst three atoms such as an azide, diazoalkane or azomethine ylide (**Scheme 4.5**). Dipolarophiles, which can be almost any π bonded molecule, are most commonly alkenes and alkynes but carbonyls,

4. Cycloaddition reactions inside carbon nanotubes

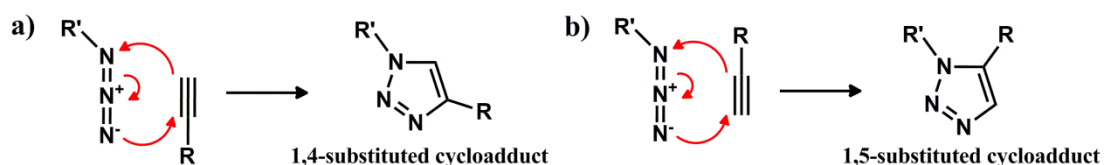
imines, C₆₀ fullerenes¹⁵ and even carbon nanotubes^{16, 17} can also undergo 1,3-dipolar cycloaddition. Thus, this methodology can easily be applied to form a vast array of heterocyclic compounds.¹⁸ The great success of 1,3-dipolar cycloaddition reactions, particularly azide-alkyne cycloaddition, is a result of the efficiency, adaptability and reliability of the process. As such, these reactions have found widespread applications, as evidenced by extensive literature reviews,^{5, 6, 19, 20} in areas of natural product synthesis, polymer and materials science^{21, 22} as well as *in vivo* biochemical applications.^{23, 24}



Scheme 4.5 Examples of 1,3-dipoles such as (1) azides, (2) diazoalkanes or (3) azomethine ylides.

4.1.2. Regioselectivity of cycloaddition reactions

1,3-dipolar cycloaddition reactions can give rise to two regioisomers depending on the bonding arrangement of dipole and dipolarophile (**Scheme 4.6**). The regioselectivity of these reactions is influenced by both steric and electronic effects, both of which can be modulated by catalysts to control the selectivity of such reactions.²⁵ In the reaction of 1,3-dipoles with alkenes, the potential formation of diastereomers must be considered, and the use of chiral reactants can give rise to enantiomeric products;²⁵ however, this chapter focuses on azide-alkyne 1,3-dipolar cycloaddition so this concept will not be discussed further.



Scheme 4.6 Potential regioisomers in 1,3-dipolar cycloaddition reactions, demonstrated by an azide-alkyne cycloaddition, depending on the arrangement of reactants in the transition state leading to (a) 1,4-substituted triazole or (b) a 1,5-substituted triazole.

The regioselectivity of cycloaddition reactions is well-predicted by both the Woodward-Hoffmann rules²⁶ and frontier molecular orbital (FMO) theory.^{1, 27} These theoretical

4. Cycloaddition reactions inside carbon nanotubes

approaches can approximately predict the reactivity of pericyclic cycloaddition reactions based on the energy and symmetry of the reactant molecular orbitals. The preferred reaction pathway will occur *via* the more stable transition state; thus, comparing the energy levels of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of the reactants can indicate the most energetically favourable bonding interaction (**Figure 4.1**). Such considerations offer an insight into the relative kinetics of cycloaddition reactions as this energy corresponds approximately to the enthalpy of formation of isomeric cycloadducts, thus underpinning the thermodynamics of the process.

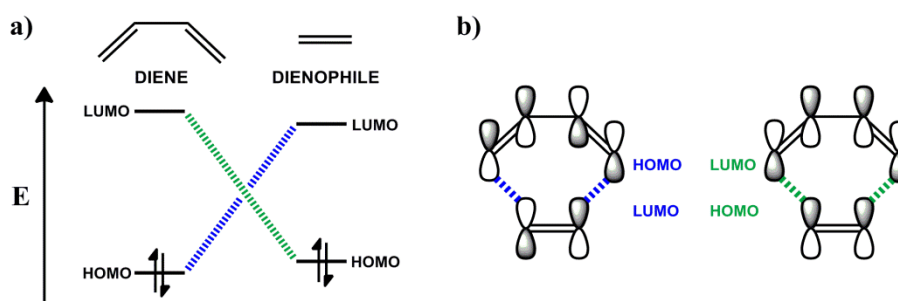


Figure 4.1 Frontier molecular orbital considerations for the Diels-Alder cycloaddition reaction, although such considerations apply to all concerted cycloaddition reactions. (a) The relative energies of the HOMO and LUMO molecular orbitals of both diene and dienophile indicate the two potential bonding interactions. The more favourable interaction is that with the smallest ΔE value; however, when these values are comparable (as shown), the two interactions compete and must be considered simultaneously. (b) The symmetry consideration for each bonding interaction showing the matched polarity required for an allowed bonding overlap.

The application of FMO theory to 1,3-dipolar cycloaddition reactions by Sustmann²⁸ defined three classes of reaction based on the dominant orbital interaction (**Figure 4.2**) and this model clearly demonstrates the influence that substituent electronic properties can have on the kinetics of such reactions.

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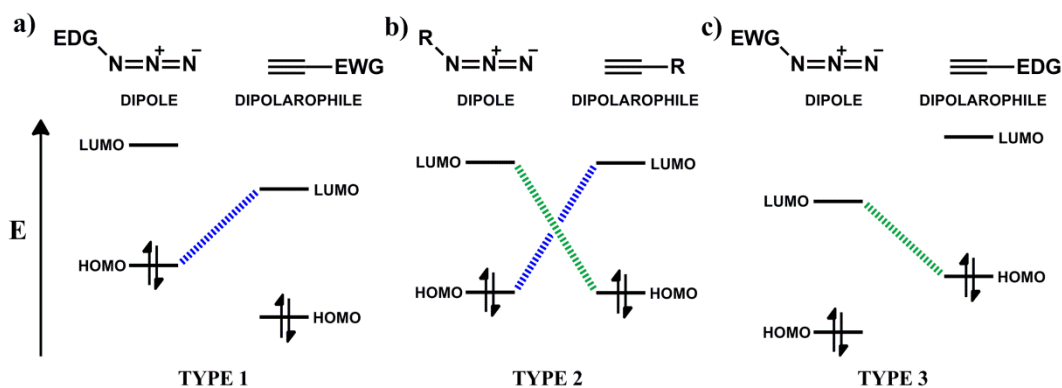


Figure 4.2 The three potential classes of 1,3-dipolar cycloaddition reactions depending on the relative molecular orbital energies and thus, dominant bonding interaction. (a) Type 1 is dominated by the dipole^{HOMO}-dipolarophile^{LUMO} interactions, (b) type 2 is a mixture of both competing bonding interactions and (c) type 3 is dominated by the dipolarophile^{HOMO}-dipole^{LUMO} interaction.

While reactivity is described by relative orbital energies, the regioselectivity of such cycloaddition reactions depends not only on which molecular orbitals will overlap in a bonding interaction, but also the arrangement of each reactant in the corresponding transition state. The arrangement of each reactant in the transition state for a reaction in solution is presumably statistical, unless an additional influence, such as asymmetric substituents of varying steric bulk or electronic properties, causes one particular transition state to be more energetically favourable. Specifically, substituent electronic properties can influence the regioselectivity of cycloaddition reaction by altering the relative orbital coefficients on each atom for the frontier molecular orbitals. In this way, the relative contribution from the atomic orbitals of each atom to the molecular orbital of the reactant may vary depending on the substituent. Hence, the most favourable interaction, resulting in the most stabilised transition state, will occur when the coefficients are of commensurate magnitude (**Figure 4.3**). Hence, the regioselectivity of cycloaddition reactions can, to an extent, be controlled by substituent electronic effects.^{29, 30}

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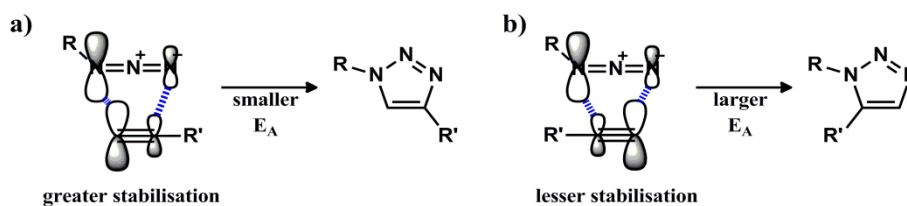
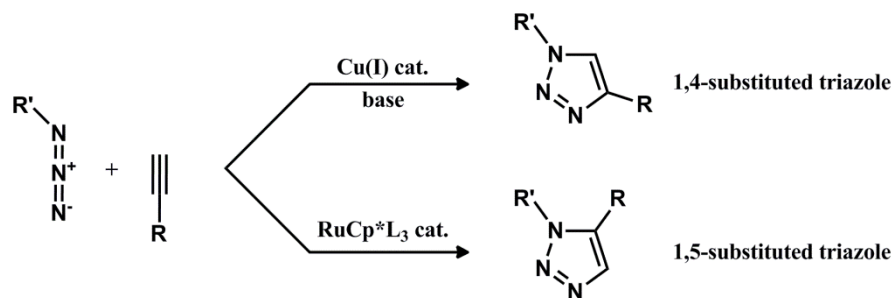


Figure 4.3 Schematic representation showing (a) a more stable bonding interaction (blue dashed line), due to the overlap of molecular orbitals between atoms with comparable orbital coefficients, than in (b) where the orbital coefficients are mismatched. This subtle stabilisation of the two regioisomeric transition states can lead to a comparatively lower activation energy for one isomer, in this case the 1,4-triazole (a), leading to its favoured formation.

4.1.3. Controlling selectivity: metal catalysis

Although the reactivity and selectivity of cycloaddition reactions can be rationalised by molecular orbital energy and symmetry considerations, extensive research has aimed to achieve precise control over the outcome of these widely useful synthetic transformations. Initially, the influence of substituent steric and electronic effects discussed previously has been harnessed to control the regioselectivity of 1,3-dipolar cycloaddition reactions, utilising electron-withdrawing groups³⁰ or severely strained alkynes.³¹ However, these methods exploiting specific functionalisation have clear limitations in functional group tolerance and therefore do not adhere to the convenient concepts of combinatorial click chemistry. Logically, much effort has been focussed on controlling selectivity *via* metal catalysis.^{32, 33} For example, the use of copper-based Lewis acid catalysts for Diels-Alder reactions,³⁴ various catalysts based on boron, aluminium, magnesium, titanium or nickel to enhance the 1,3-dipolar cycloaddition of nitrones,²⁵ and the well-known regioselective copper^{32, 33} or ruthenium^{35, 36} catalysed azide-alkyne cycloaddition (**Scheme 4.7**). As an extension to the homogeneous copper catalysis of azide-alkyne cycloaddition, the regioselectivity offered by copper catalysis has been combined with the advantages of nanoscale supports, such as metal organic frameworks,³⁷⁻³⁹ zeolites⁴⁰⁻⁴³ and carbon nanotubes,⁴⁴ to provide improved catalyst recyclability in the heterogeneous catalysis of 1,3-dipolar cycloaddition reactions.

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Scheme 4.7 Metal-catalysed azide-alkyne 1,3-dipolar cycloaddition to yield the 1,4- or 1,5-substituted triazoles selectively. Copper(I) catalysis, in the presence of a base, affords the 1,4-triazole with much improved reaction rates and regioselectivity^{19, 45} via the formation of a copper acetylide and subsequent complexation of the azide at the proximal nitrogen, promoting attack of the proximal carbon by the terminal nitrogen.¹⁸ Conversely, ruthenium(II) catalysts, often containing a Cp* ligand,⁴⁶ have been shown to afford the corresponding 1,5-triazole with high regioselectivity.^{35, 36} Crucially, both of these catalytic mechanisms are believed to be stepwise; thus, these reactions are no longer concerted pericyclic reactions and the previous consideration of frontier molecular orbital theory no longer applies.

These complementary catalytic reactions are effective and convenient, and as such, have found widespread applications in synthetic organic chemistry. However, the relative scarcity of ruthenium⁴⁷ is seen as a limiting factor in industrial applications, and the toxicity of copper limits the use of this potentially useful catalysed reaction for biological applications, particularly *in vivo*.⁴⁸ These reasons have led to the search for alternative approaches to controlling regioselectivity.

4.1.4. Controlling selectivity: confinement

A more general approach to improving reaction kinetics while also controlling the regioselectivity of cycloaddition reactions in the absence of metallic catalysts is spatial confinement at the nanoscale. Using this strategy, the various confinement effects described previously can be utilised to influence reaction pathways. For instance, an azide-alkyne cycloaddition reaction known to afford an enzyme-inhibitor used to treat HIV was synthesised by Whiting *et al.* using a templating effect within a pocket of a protease enzyme. The presence of the templating enzyme accelerated the reaction and improved the selectivity for the 1,4-triazole from 66 to 95%.⁴⁹

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The reaction kinetics of Diels-Alder cycloaddition reactions have also been improved significantly by nanoscale confinement within molecular nanoreactors. The reaction of *p*-benzoquinone and cyclohexadiene within a self-assembled, dimeric, spherical capsule⁵⁰ exhibited a 170-fold rate enhancement compared to the reaction in conventional solvent,⁵¹ due to an increase in the effective concentration of the reactants in confinement. More modest rate improvements of 20 to 60-fold were also achieved for the cycloaddition of substituted anthracenes to various maleimides within a cavitand molecular capsule.⁵² In addition to rate enhancements, regioselectivity can be drastically affected by supramolecular hosts, as demonstrated by the Diels-Alder reaction of *N*-cyclohexylmaleimide with 9-hydroxymethylanthracene. Within an octahedral self-assembled palladium cage⁵³ the 1,4-cycloadduct is formed exclusively, in stark contrast to the same reaction in bulk solution whereby only the more thermodynamically stable 9,10-cycloadduct is formed (**Figure 4.4**).⁵⁴ This drastic shift in regioselectivity is related to the steric confinement of the reactants, holding them in an orientation which simultaneously encourages 1,4-cycloaddition and precludes 9,10-cycloaddition.

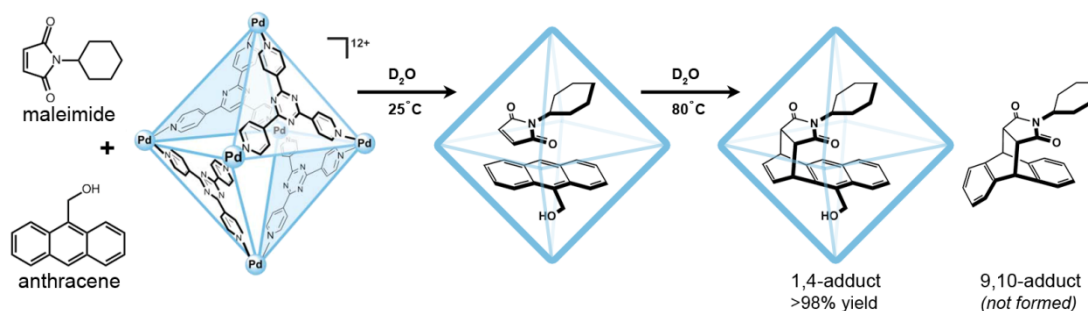


Figure 4.4 Schematic showing the Diels-Alder reaction of *N*-cyclohexylmaleimide with 9-hydroxymethylanthracene within an octahedral supramolecular host cage to afford the 1,4-cycloadduct exclusively.⁵⁴ In solution, only the thermodynamically more stable 9,10-cycloadduct is formed.

1,3-dipolar cycloaddition reactions confined within supramolecular hosts have also demonstrated superior control over reactivity. The cylindrical, dimeric cavitand capsule developed by Rebek and coworkers^{55, 56} is capable of encapsulating two mono-substituted aromatic guests simultaneously. When both phenyl azide and phenylacetylene are

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encapsulated, the polar functional groups remain near the centre of the capsule due to interactions with the hydrogen-bonded "seam" of the capsule, ensuring that the reactants remain in a bonding arrangement. The reaction of phenyl azide and phenylacetylene in bulk mesitylene proceeds very slowly to produce an approximately equal mixture of the two regioisomeric triazoles. However, confined within the cavitand capsule, the 1,4-triazole is exclusively formed after around 3-4 days, with a calculated 240-fold rate increase (**Figure 4.5**). This impressive regioselectivity is due to the reactant arrangement encouraging the 1,4-triazole bonding interaction, and the fixed geometry of the host capsule sterically precluding the alternative 1,5-triazole formation. The rate acceleration is due to an increase in the effective local concentration of reactants within the nanoreactor. Crucially, while this self-assembled capsule could theoretically allow high catalytic turnover, where products are released and additional reactants enter, the 1,4-triazole product remains encapsulated due to a strong host-guest interaction. This product inhibition gradually slows the reaction to a halt as all available nanoreactor hosts become irreversibly saturated with product molecules.

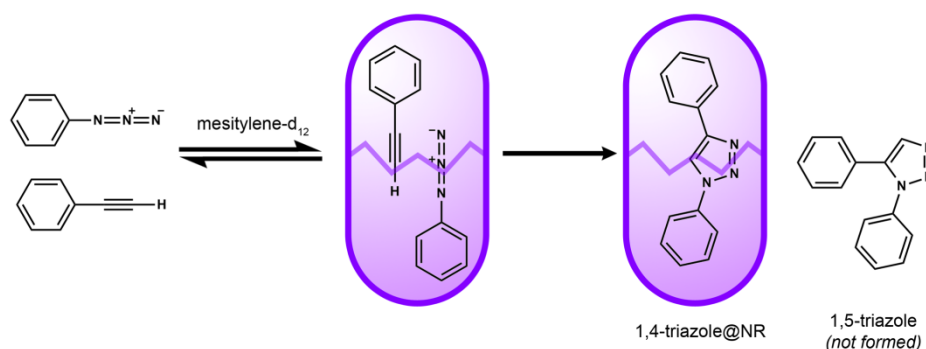


Figure 4.5 Schematic showing the reaction of phenyl azide with phenylacetylene confined within a dimeric cavitand nanoreactor, forming the 1,4-triazole exclusively at an accelerated rate compared with the reaction in free solution where a mixture of both 1,4- and 1,5-triazoles are formed.

Comparable regioselectivity is observed for the azide-alkyne cycloaddition of amidoalkyl-substrates encapsulated within a concurbituril nanoreactor. The previously unselective azide-alkyne cycloaddition affords the 1,4-substituted triazole exclusively in acidic aqueous solution containing the molecular host, with an observed 10^5 -fold rate acceleration; however, the release of products from the concurbituril is found to be the rate-limiting step, as is

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common in such systems.^{57, 58} Similar, yet less pronounced, changes in regioselectivity and kinetics have been achieved within a polyoxamolybdate cage.⁵⁹ While these results show the potential of polyoxametallate cages as hosts for chemical reactions, in this case, the azide functionality is covalently fixed to the nanoreactor and therefore does not represent a potentially preparative methodology. Kawamichi *et al.* demonstrated azide-alkyne cycloaddition confined within a crystalline porous co-ordination network showing increased selectivity for the 1,4-triazole for previously unselective cycloaddition reactions.⁶⁰ Furthermore, the templation of a polymer nanoreactor around the intended regioisomeric product has been demonstrated to be an effective way of producing a nanoreactor to host subsequent selective formation of complex triazoles.⁶¹ This polymer nanoreactor utilises only non-covalent interactions in an attempt to be more generally applicable; however, the host nanoreactor is specifically designed to synthesise one particular triazole.

The potential of nanoscale confinement for controlling the outcome of cycloaddition reactions is clearly demonstrated by the examples discussed, and offers a powerful methodology for controlling these important organic reactions without the use of metallic catalysts. No nanoreactor has yet proven convenient and easily adaptable to a range of cycloaddition reactions, and therefore carbon nanotubes may represent ideal hosts for such reactions due to the non-specific host-guest interactions and tuneable size available from these novel nanostructures. Although no experimental studies of cycloaddition reactions within carbon nanotubes have yet been completed, recent molecular dynamics simulations by Smith *et al.* predict that the extreme spatial confinement exhibited by SWNT may induce drastic changes in the stereoselectivity of the Diels-Alder reaction.⁶² The regioselectivity of reactions between 9-anthraldehyde and both *N*-cyclohexyl- and *N*-phenyl- maleimides was simulated within SWNT of diameter 1.08 and 1.22 nm. The predicted products of these reactions were shown to be affected by nanotube confinement and highly dependent on nanotube diameter. Similar to the observation reported by Yoshizawa *et al.* within a supramolecular cage,⁵⁴ confinement within narrow carbon nanotubes is predicted to afford

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the 1,4-cycloadduct selectively over the more thermodynamically stable 9,10-cycloadduct for the aforementioned cycloaddition of anthracene and maleimide derivatives. An additional, sterically-induced energy penalty of 10 kcal mol⁻¹ for the formation of the 9,10-product promotes the selective formation of the 1,4-isomer. While it is predicted that this effect is quickly diminished when the nanotube diameter is increased by as little as 0.14 nm, it clearly demonstrates the potential control that confinement within carbon nanotubes may exert over cycloaddition reactions and highlights the importance of complementary experimental studies.

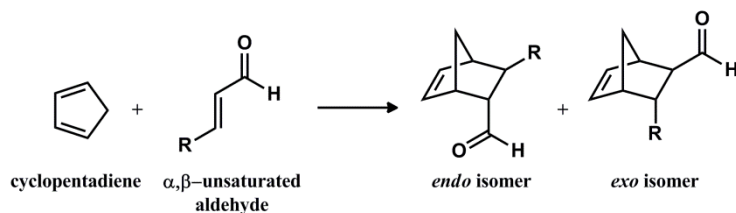
4.2. Aim and Objectives

The aim of this chapter is to study cycloaddition reactions confined within narrow carbon nanotubes in order to deduce the effect of extreme spatial confinement on the selectivity of such reactions. Due to the extensive studies and advanced understanding of both Diels-Alder reactions and 1,3-dipolar cycloaddition reactions, these two reactions have been selected as suitable model reactions to investigate within carbon nanotubes. Specific examples of each cycloaddition reaction must be identified which reliably afford a mixture of regioisomers in solution and thus allow the effect of confinement within SWNT on regioselectivity to be probed.

4.2.1. *Diels-Alder cycloaddition*

The reactions of cyclopentadiene with α,β -unsaturated aldehydes (**Scheme 4.8**) will be studied within narrow carbon nanotubes. The potential to vary the dienophile substituent may allow the *endo/exo* selectivity to be tuned in order to identify a suitably unselective reaction in solution, with which to probe the effect of confinement within SWNT.

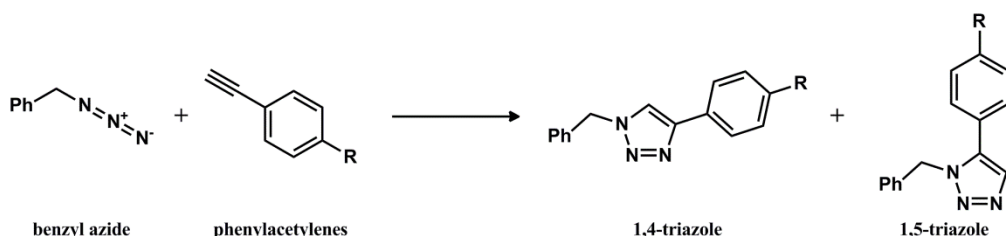
4. Cycloaddition reactions inside carbon nanotubes



Scheme 4.8 Diels-Alder cycloaddition reaction of cyclopentadiene with a substituted α,β -unsaturated aldehyde to form a mixture of both *endo* and *exo* isomers.

4.2.2. Azide-alkyne 1,3-dipolar cycloaddition

The 1,3-dipolar cycloaddition reactions of an aromatic azide with a selection of aromatic alkynes will be studied within carbon nanotubes of various diameters (**Scheme 4.9**).



Scheme 4.9 1,3-dipolar cycloaddition reaction of benzyl azide with various *para*-substituted phenylacetylene derivatives to form a mixture of both 1,4- and 1,5-triazoles.

Thermally initiated azide-alkyne cycloaddition reactions are well known to produce a mixture of both triazole regioisomers³² thus, allowing the effect of confinement within SWNT on reaction selectivity to be explored. While carbon nanotubes are known to react with alternative 1,3-dipoles, such as azomethine ylides^{16, 17} and nitrile imines,⁶³ there are seemingly no reports of the 1,3-dipolar cycloaddition of organic azides to carbon nanotubes and therefore, these substrates represent a suitable 1,3-dipole for use in this study. The variable functionality of the alkyne *para*-substituent allows convenient control over both the steric bulk and, through conjugation, the electron density of the alkyne. This study will attempt to ascertain how these factors affect the regioselectivity of these reactions while confined within carbon nanotubes. More specifically, the pseudo one-dimensional steric confinement experienced within CNT may influence the regioselectivity similarly to the 1,3-

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dipolar cycloaddition within a cavitand dimer,⁵⁵ promoting the formation of the more linear 1,4-triazole (**Figure 4.6**).

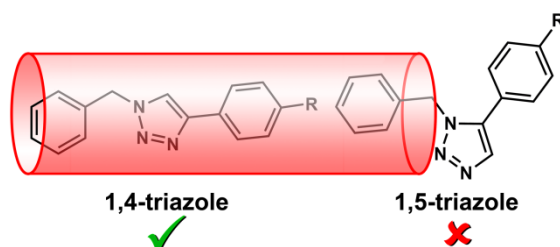


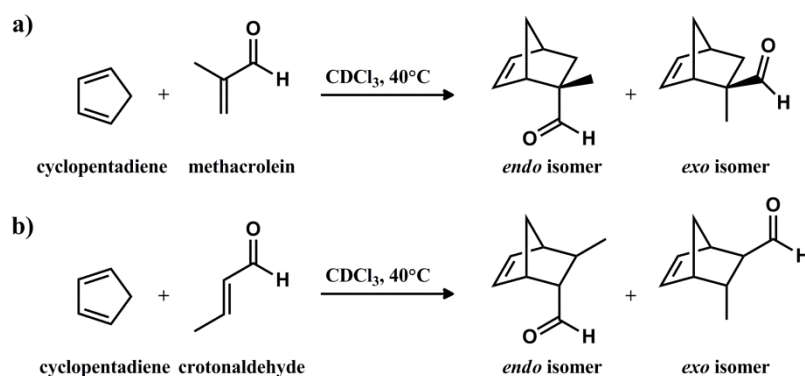
Figure 4.6 Hypothesised shape-selectivity for 1,3-dipolar cycloaddition reactions within narrow CNT. The more linear 1,4-triazole may be able to form confined in CNT, whereas the 1,5-triazole may not, resulting in an increase in selectivity for the 1,4-triazole as a result of nanotube encapsulation.

1,3-dipolar cycloaddition reactions have been shown to be sensitive to substituent electronic effects which influence both the kinetics, by altering molecular orbital energy levels, and the regioselectivity, by distorting the relative atomic orbital coefficients. Therefore, as encapsulation within SWNT can affect the HOMO/LUMO molecular orbital energy levels of the guest molecules,⁶⁴⁻⁶⁶ confinement within SWNT may change the regioselectivity or kinetics through analogous electronic effects in addition to the hypothesised steric confinement effects.

4.3. Results and Discussion

4.3.1. Diels-Alder cycloaddition

In order to assess the effect of host carbon nanotubes on the selectivity of Diels-Alder reactions, a suitable model reaction must be chosen which reliably affords a mixture of both *endo*- and *exo*-stereoisomers in the absence of nanotubes, and allows the convenient characterisation of the resultant product mixture. Preliminary investigations highlighted the Diels-Alder cycloaddition of cyclopentadiene to α,β -unsaturated aldehydes (**Scheme 4.10**) as a potentially suitable range of model reactions.



Scheme 4.10 Diels-Alder cycloaddition of cyclopentadiene to (a) methacrolein and (b) *E*-crotonaldehyde to form an unselective mixture of both *endo*- and *exo*-stereoisomers.

Cyclopentadiene (Cp) was chosen as it exhibits enhanced reactivity in cycloaddition reactions because the geometry is locked in a favourable *cis* formation.⁶⁷ Aldehyde reactants are suitable for this investigation because the carbonyl group exhibits strong secondary orbital interactions with the diene controlling selectivity to an extent, while the terminal proton also allows the distribution of isomeric products to be conveniently probed by ¹H NMR spectroscopy. As all three reactants are liquids, this will potentially allow the convenient encapsulation of the reactants inside SWNT by capillary methods analogous to those discussed in **Chapter 3**. Crucially, these reactions were found to afford an unselective mixture of both *endo*- and *exo*-isomers (**Table 4.1**). The *endo/exo* selectivity was previously demonstrated to be sensitive to catalysts such as thioureas and chiral Lewis acids as well as

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experimental conditions, such as temperature and solvent.^{68, 69} The sensitivity of this reaction suggests that the drastically altered reaction environment within carbon nanotubes is also likely to influence the reaction pathway. Finally, it is expected that the conjugation of the reactants may increase the strength of the π - π interaction with the nanotube interior, improving encapsulation; conversely, the loss of conjugation upon cycloaddition may decrease this interaction, conducive to the effective egress of products from the nanotube cavity. In light of the reported Diels-Alder cycloaddition to carbon nanotubes,¹⁰ the model reaction must occur under conditions whereby the carbon nanotube remains inert. The mild conditions of this reaction, coupled with the relatively low reactivity of the chosen reactants should ensure that no undesirable side-reactions occur with the CNT sidewall.

In a typical Diels-Alder reaction, a colourless solution of the aldehyde and cyclopentadiene in deuterated chloroform was stirred at 40°C. The stereoselectivity of each reaction was determined by ¹H NMR spectroscopy of the crude reaction mixture. The peak integrals of diagnostic aldehyde singlet proton environments were compared at 9.39 and 9.68 ppm for the *endo* and *exo* products of the methacrolein reaction respectively, and at 9.38 and 9.79 ppm for the *endo* and *exo* products of the crotonaldehyde reaction respectively.

The reaction of methacrolein with Cp in CDCl₃ demonstrated a 12% selectivity for the *endo* product with quantitative conversion after 48 hours (**Table 4.1, entry 1**). The analogous reaction of crotonaldehyde with Cp in CDCl₃ demonstrated a 68% selectivity for the *endo* product also with quantitative conversion. Before the effect of confinement within nanotubes on selectivity can be assessed, it must be confirmed that the external surface of carbon nanotubes does not alter the selectivity of these reaction. The addition of as-received SWNT to the reaction mixture, with no effort made to oxidatively open the SWNT, resulted in no change to the selectivity of either of the reactions studied relative to the reaction in the absence of SWNT (**Table 4.1, entries 4 and 7**).

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Table 4.1 Diels-Alder reactions of both methacrolein and crotonaldehyde with cyclopentadiene (Cp) in CDCl₃ at 40°C for 48-96 hr, comparing the conversion and selectivity for the *endo* isomer. SWNT d_{NT} = 1.3 nm. Selectivity values determined from ¹H NMR spectroscopy with an error of ±3%.

	Reaction	Conversion /%	<i>endo</i> selectivity /%
1	Methacrolein + Cp	100	12
2	Methacrolein + Cp@SWNT	100	8
3	Methacrolein@SWNT + Cp	5	15
4	Methacrolein + Cp + SWNT	100	12
5	Crotonaldehyde + Cp	100	68
6	Crotonaldehyde@SWNT + Cp	45	74
7	Crotonaldehyde + Cp + SWNT	100	68

As suitable model reactions have been found and standard conditions developed to produce an unselective mixture of *endo* and *exo* isomeric products, the effect of confinement within narrow SWNT on the selectivity of these Diels-Alder reactions can be assessed. In order to do this, a suitable host nanotube must be identified. The ideal nanotube is the SWNT with the minimum diameter while also providing sufficient internal capacity for the reaction to occur. SWNT synthesised by the arc discharge process with average diameter of 1.3 nm were found to satisfy these criteria, allowing both reactants and products to be encapsulated (**Figure 4.7**). It is important to note that narrower SWNT are commercially available (HiPCO SWNT, d_{NT} = 1.0 nm) and were also considered; however, these narrower SWNT did not allow the theoretical confinement of the cycloadducts, as their critical dimensions exceed 1 nm. As such, SWNT of 1 nm diameter were deemed to be too small to allow the confinement of these Diels-Alder reactions.

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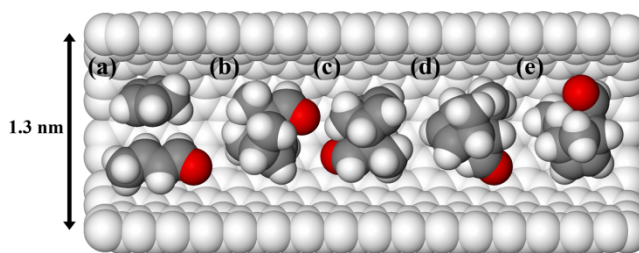


Figure 4.7 Schematic representation of the reaction species within the internal cavity of a SWNT ($d_{\text{NT}} = 1.3 \text{ nm}$). (a) Reactants: cyclopentadiene and α,β -unsaturated aldehyde (crotonaldehyde shown as an example). Stereoisomeric products of the cycloaddition of Cp to either methacrolein, (b) *endo* and (c) *exo* respectively, or crotonaldehyde, (d) *endo* and (e) *exo* respectively. All molecules shown are able to fit within the internal channel of the chosen SWNT, showing it is a suitable host for such reactions.

To explore the effect of confinement within SWNT on the selectivity of these Diels-Alder reactions, one of the reactants must be encapsulated within the SWNT prior to the reaction. As all three reactants are liquid at room temperature, with surface tension below the critical value of 200 mN m^{-1} for sufficient SWNT wetting, the immersion of opened nanotubes in the liquid causes the SWNT internal channels to be filled with the liquid spontaneously by capillary force, as discussed in **Chapter 3**. Typically, dried, opened SWNT powder was immersed in the liquid reactant at room temperature. The removal of excess reactant molecules not encapsulated within the nanotube interior was accomplished by filtration under a modest vacuum until the mixture resembled a dry black powder. The black 'reactant A'@CNT powder (where A = diene or dienophile) was then added to the colourless solution of reactant B (where B = dienophile or diene respectively) to form a black suspension upon stirring at 40°C . In order to analyse the selectivity of the reaction, the solid CNT was removed by filtration through cotton wool and the crude mixture analysed by ^1H NMR spectroscopy. This allowed the stereoselectivity of the two Diels-Alder reactions within carbon nanotubes to be compared to that observed in solution and thus the effect of confinement within SWNT on these reactions to be deduced (**Table 4.1**).

When cyclopentadiene (Cp) was encapsulated within the SWNT prior to the reaction with methacrolein (**Table 4.1, entry 2**), the conversion was quantitative with no significant change in selectivity relative to the reaction in bulk solution. When methacrolein is encapsulated in SWNT (**entry 3**), the selectivity of the same reaction with Cp is, again, not

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drastically affected; however, the conversion is 5%, a figure closer to that expected from previous observations for conversion of aromatic bromination within SWNT. This suggests that the encapsulation of Cp (**entry 2**) was unsuccessful in forcing the reaction to occur within the SWNT, and is therefore not suitable for evaluating the nanoscale confinement effects of such Diels-Alder reactions within SWNT. This is possibly because cyclopentadiene is not held strongly within the nanotube and therefore may readily diffuse out from the SWNT cavity giving results consistent with the unconfined reaction in bulk solution. Therefore, no further experiments were conducted by prior encapsulation of cyclopentadiene. The encapsulation of methacrolein (**entry 3**), showing significantly reduced conversion, is more likely to have occurred within the nanotube cavity; however, this reaction still shows minimal changes in *endo* selectivity (+3%) as a consequence of confinement within SWNT, which is within the error of NMR spectroscopic measurement.

The reaction of crotonaldehyde with Cp showed a slight increase in *endo* selectivity to 74% when encapsulated within the SWNT (**entry 6**), with a reduced conversion of 45%. This selectivity increase of 6%, compared to the reaction in solution, is slightly more significant than that observed for methacrolein yet still represents a minimal effect of confinement.

Understanding why no significant changes in selectivity have been observed requires more detailed scrutiny of how the reaction species might be orientated within the nanotube. Firstly, from consideration of the selectivity induced by steric confinement, it is evident when viewing the three-dimensional geometry of the various stereoisomers within SWNT (**Figure 4.8**) that there is sufficient volume within the nanotube for both isomers to form. Furthermore, due to their bicyclic structure, there appears to be little to distinguish between the isomers in terms of size or shape. This would explain why there are no drastic changes in the mixture of products formed in these reaction induced by size or shape selectivity within SWNT.

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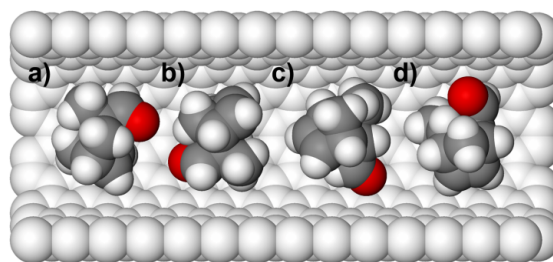


Figure 4.8 Schematic representation of the stereoisomers formed during the reactions of methacrolein and crotonaldehyde with cyclopentadiene. The a) *endo* and b) *exo* isomers formed from the methacrolein reaction as well as the c) *endo* and d) *exo* isomers formed from the crotonaldehyde reaction are shown confined within a SWNT of diameter 1.3 nm. No clear size or shape selectivity is evident from this schematic, potentially explaining why no significant changes in selectivity were observed as a consequence of spatial confinement.

It was hypothesised that the extreme confinement within carbon nanotubes may influence the reaction pathway by altering the electronic properties of the reaction species. However, the SWNT used ($d_{\text{NT}} = 1.3$ nm) appear slightly too large for the encapsulated reactants to experience significant interactions, and it is therefore possible that a more "snug fit" might invoke such a change due to improved charge transfer. Unfortunately, as previously discussed, a SWNT of smaller diameter ($d_{\text{NT}} = 1.0$ nm) is too small to allow products to form, based on the critical van der Waals dimensions of the product molecules, and a SWNT of intermediate diameter is not commercially available due to the limited control of nanotube diameter in current nanotube synthesis procedures.

In conclusion, these experiments have shown the selectivity of the Diels-Alder reactions of both methacrolein and crotonaldehyde with cyclopentadiene is not drastically affected by confinement in SWNT. Only slight improvements in the *endo*-selectivity of up to 6% were observed. It is postulated that this is due to the geometry of the products being largely indistinguishable in terms of size or shape, and thus the spatial confinement experienced within the carbon nanotube does not significantly favour the formation of either isomer. In light of these findings, the 1,3-dipolar cycloaddition reaction was chosen as a more appropriate model reaction to study, allowing more variation in functionalisation and therefore providing further understanding of the reaction environment within the cavity of a carbon nanotube.

4.3.2. 1,3-dipolar cycloaddition

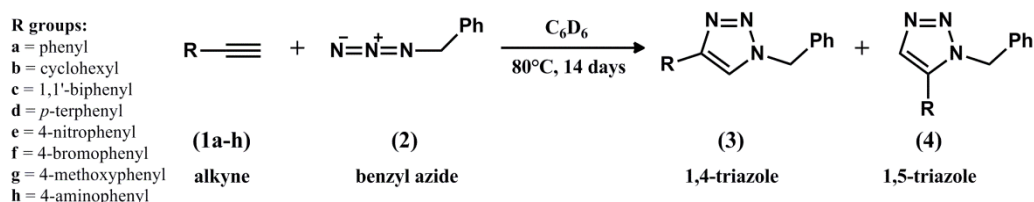
4.3.2.1. Azide-alkyne cycloaddition within SWNT

In order to determine the effect of confinement within SWNT on the regioselectivity of the 1,3-dipolar cycloaddition, a range of reactions and conditions must be identified which reliably afford an unselective mixture of products. Thermally initiated azide-alkyne 1,3-dipolar cycloaddition reactions are slow but typically produce a mixture of both the 1,4- and 1,5-triazoles, and are known to have wide functional group tolerance.³² As there is such a wide library of known organic azides and alkynes, the search was narrowed by only considering benzyl azide. Benzyl azide, possessing an aromatic ring, is likely to have reasonably strong interactions with the nanotube sidewalls facilitating the confined reaction. Specifically, benzyl azide was chosen over the more commonly studied phenyl azide because benzyl azide, possessing a benzylic methylene bridge, is less reactive and therefore safer to handle as it is less prone to decomposition into the corresponding nitrene than the conjugated phenyl azide.^{70, 71} It has been reported that nitrenes, often formed *in situ* from reactive azide precursors, can undergo [2+1] cycloaddition with the sidewall of carbon nanotubes.⁷² This would be a particularly detrimental process when attempting cycloaddition within nanotubes, as the azide reactant would be consumed. Indeed, preliminary azide-alkyne cycloaddition reactions of phenyl azide in the presence of carbon nanotubes did not afford the intended triazole products, indicating that phenyl azide is too unstable for the intended study of confined reactions. Additionally, the benzylic protons of benzyl azide offer a convenient spectroscopic probe for analysing the relative product distribution by ¹H NMR spectroscopy, typically appearing in an otherwise unobscured region around 5 ppm.

The 1,3-dipolar cycloaddition of benzyl azide (**2**) with terminal alkynes (**1a-h**) under thermal initiation is generally slow, so elevated temperature and extended duration were required to achieve reasonable conversion. In a typical reaction, a solution of benzyl azide and substituted alkyne in deuterated benzene was stirred at 80°C for 14 days. Upon cooling,

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the regioselectivity was determined by ^1H NMR spectroscopy of the crude reaction mixture, comparing peak integrals for diagnostic peaks corresponding to the benzylic protons in the region of 4.8 to 5.1 ppm. The appraised reactions (**Scheme 4.11**) of benzyl azide (**2**) with various alkynes (**1a-h**) were found to afford a mixture of both the 1,4- (**3**) and 1,5- (**4**) substituted triazoles, with selectivity for the 1,4-triazole ranging from 8 to 62%.



Scheme 4.11 The thermally initiated 1,3-dipolar cycloaddition of benzyl azide (**2**) to a range of substituted aromatic alkynes (**1a-h**) to afford a mixture of both 1,4- (**3**) and 1,5- (**4**) substituted triazoles.

In order to compare the regioselectivity of the chosen reactions within SWNT to that in solution, suitable SWNT must be chosen and conditions found whereby these reaction can be confined within them. This study initially focussed on the reaction of benzyl azide with phenylacetylene as a means of developing these methodologies. In order to ensure that the majority of the reaction, which is known to occur in solution, instead occurs inside the SWNT inner channel, one reactant is encapsulated within the SWNT prior to addition to a solution of the corresponding reactant. As discussed in **Chapter 3**, one of the most effective ways of efficiently encapsulating molecular guests inside carbon nanotubes is by the immersion of opened SWNT in the pure liquid compound. In the cycloaddition of benzyl azide to phenylacetylene, both reactants are liquids at room temperature, allowing convenient liquid phase encapsulation within SWNT. Also, the relatively high vapour pressure of both reactants at room temperature facilitates the selective removal of excess reactant externally adsorbed on the nanotube by a fractional distillation procedure (**Chapter 3**),⁷³ leaving only reactant@SWNT.

The encapsulation of both phenylacetylene and benzyl azide was attempted independently within SWNT of diameter 1.3 nm. This diameter SWNT was found to have

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sufficient internal volume to allow the encapsulation of both the reactants and the products of this cycloaddition reaction, and was therefore deemed suitable for this preliminary investigation. Typically, encapsulation of the chosen reactant was achieved by immersion of the opened SWNT in the reactant at room temperature. Excess reactant not encapsulated within the SWNT cavity was left to slowly evaporate at room temperature over seven days to afford a black 'reactant@SWNT' solid. These conditions were chosen in an attempt to offer the most control over the procedure of removing excess reactant, because the process of reactant evaporation would be slow and controlled, with easily reproducible conditions.

In order to ascertain both whether the reactant had been efficiently encapsulated using this procedure, and whether the confinement of this 1,3-dipolar cycloaddition reaction would induce any changes to the regioselectivity as hypothesised, the 'reactant@SWNT' solid was added to the corresponding reactant (benzyl azide or phenylacetylene accordingly) in deuterated benzene and stirred at 80°C for 14 days. The crude product mixture was analysed by ^1H NMR spectroscopy immediately after removal of the black SWNT solid by filtration through cotton wool. Additionally, in order to ensure that all product molecules were extracted from the SWNT, the black SWNT solid was washed three times sequentially by ultrasonication in chloroform. The colourless solutions were combined, the solvent removed at reduced pressure and the mixture analysed by ^1H NMR spectroscopy in order to determine the regioselectivity after complete extraction of products.

It was hypothesised that the 1,4-triazole, exhibiting a more linear conformation, would be more stable inside a narrow carbon nanotube and, therefore, selectivity for the 1,4-triazole would increase as a consequence of confinement within a nanotube. Analogous studies within cavitand capsules demonstrated a similar observation.⁵⁵ Indeed, density functional theory (DFT) calculations for 1,3-dipolar cycloaddition within the cavitand capsule revealed that steric confinement and non-covalent host-guest interactions stabilise the transition state leading to the 1,4-triazole, while simultaneously destabilising the transition state leading to the 1,5-regioisomer.⁶⁶ Therefore, confinement can cause the energy

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barrier to the formation of each isomer to be drastically different leading to significantly increased selectivity for the 1,4-triazole. Initial investigations within carbon nanotubes showed this hypothesis to be correct, to a small extent, as confinement in SWNT improved the selectivity for the 1,4-regioisomer in the reaction of phenylacetylene (**1a**) with benzyl azide by 7% (**Table 4.2**).

Table 4.2 Selectivity for the 1,4-triazole (**3a**, $S_{1,4}$) in the reaction of phenylacetylene with benzyl azide both in solution and confined within single-walled carbon nanotubes.

Ph—C≡CH + N⁺=N=N⁻CH₂Ph $\xrightarrow[80^{\circ}\text{C}, 14 \text{ days}]{\text{C}_6\text{D}_6}$ Ph-C(=N)-N=CH-CH₂Ph + Ph-C(=N)-N=CH-CH₂Ph

(1a) (2) (3a) (4a)

	Reactant encapsulated	$d_{\text{NT}} / \text{nm}^{\text{a}}$	$S_{1,4} / \%^{\text{b}}$	$\Delta S_{1,4} / \%$
1	n/a	No SWNT	44	-
2	Phenylacetylene (1a)	1.3	51	+7
3	Benzyl azide (2)	1.3	51	+7

^a mean nanotube diameter as determined by statistical analysis of transmission electron micrographs. ^b reaction selectivity determined by ¹H NMR spectroscopy

It is important to note that the encapsulation of either reactant prior to the reaction results in identical regioselectivity. This shows that there is no difference, in terms of fundamental reactivity, between the two practical approaches. However, the fact that identical conditions were equally successful for both reactants is likely a result of the comparable physical properties of the two reactants, *e.g.* melting point, boiling point and vapour pressure. The efficacy of encapsulation for alternative reactants may vary widely depending on the inherent properties of each molecule, *e.g.* melting and boiling point, thermal or chemical stability, and therefore, for ease of methodology and valid comparison, all subsequent reactions were carried out by prior encapsulation of benzyl azide.

The conversion of these 1,3-dipolar cycloaddition reactions was determined from ¹H NMR spectroscopy of the crude reaction mixture comparing peak integrals of products to diagnostic singlet peaks from the benzyl azide and alkyne reactants (*ca.* 3.67 and 2.72-2.83 ppm respectively). Reactions confined within SWNT exhibited conversion between 4 and 18%. Although these values are lower than those for reactions in bulk

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solution, for which 24-80% conversion was typically observed, the observed kinetics of confined reactions is dependent on many factors such as diffusion and accurate stoichiometry. For this reason, conversion values were not considered further. However, it was important to confirm that selectivity does not vary as a function of conversion during these 1,3-dipolar cycloaddition reactions in order to maintain the reliability of our comparisons at slightly different conversions. Control experiments, whereby selectivity was measured at six points throughout the reaction, showed a standard deviation in selectivity of less than 2% consistently, confirming the validity of selectivity comparison at different levels of conversion.

In order to gain insight into the importance of aromaticity in the confinement of organic chemical reactions within carbon nanotubes, the confined reactions of benzyl azide with phenylacetylene and aliphatic analogue cyclohexylacetylene were directly compared. The effect of confinement within SWNT on the regioselectivity of cyclohexylacetylene cycloaddition was less pronounced, showing a 2% increase in selectivity for the 1,4-triazole which is within the error of ^1H NMR spectroscopic measurements (**Table 4.3**).

Table 4.3 Reactivity comparison for the cycloaddition of both cyclohexylacetylene and phenylacetylene to benzyl azide confined within SWNT of 1.3 nm diameter, showing the selectivity for the 1,4-triazole in the absence of carbon nanotubes ($S_{1,4}$) and the change in this value as a consequence of confinement ($\Delta S_{1,4}$).

	Alkyne	$d_{\text{NT}} / \text{nm}^{\text{a}}$	$S_{1,4} / \%^{\text{b}}$	$\Delta S_{1,4} / \%$
1	Cyclohexylacetylene (1b)	No SWNT	58	-
2	Cyclohexylacetylene (1b)	1.3	60	+2
3	Phenylacetylene (1a)	No SWNT	44	-
4	Phenylacetylene (1a)	1.3	51	+7

Initially, this result suggests that confinement of organic chemical reactions within CNT is more effective for aromatic substrates. As the aliphatic alkyne will exhibit much weaker intermolecular interactions with the aromatic carbon nanotube, there may be a reduced

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driving force for the diffusion of the reactant into the SWNT inner cavity. This would result in a reduced proportion of cycloaddition reactions occurring within SWNT, and therefore account for the observed selectivity values being much closer to that seen in bulk solution. However, there are various alternative explanations for this result. Although comparable in size, the increased flexibility of the cyclohexyl ring may reduce the effect of confinement within SWNT, allowing conformational rearrangements to facilitate energetically favourable transition states for both regioisomers. This steric reasoning could account for the reduced effect of steric confinement on the selectivity of the reaction, and suggests that reactants should be chosen which have limited flexibility, allowing reactant arrangement within narrow SWNT to be better predicted and further influenced by confinement. Alternatively, if the effect of confinement observed for phenylacetylene is, in part, due to close interactions with the nanotube sidewall altering the electronic properties of the reactant, then reduced interaction between the aliphatic alkyne and the nanotube sidewall could also account for the reduced effect of confinement in this case.

4.3.2.2. Tuning the extent of steric confinement: host SWNT diameter

The 1,3-dipolar cycloaddition of benzyl azide to phenylacetylene within SWNT of 1.3 nm diameter has demonstrated a subtle increase in the selectivity for the 1,4-triazole as a consequence of nanoscale confinement. Based on previous observations for similar reactions within molecular nanoreactors,⁵⁵ greater changes in selectivity were expected and therefore, it is postulated that the effects of confinement within carbon nanotubes on regioselectivity can be amplified by increasing the *extent* of confinement. As SWNT of 1.3 nm diameter have sufficient internal capacity for both the 1,4- and 1,5-triazoles to be encapsulated in their most stable conformation, it is possible that, by reducing the nanotube diameter, the effects of confinement can be increased and evidenced by a further increased selectivity for the 1,4-triazole. A previous investigation into aromatic halogenation reactions within SWNT (**Chapter 3**) showed a clear trend whereby the effect of confinement on selectivity was

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critically dependent on nanotube diameter. In this case, confinement within SWNT which were too narrow to allow encapsulation showed no effect, and confinement within SWNT which were wide enough to allow the formation of both regioisomers also afforded no observable change to regioselectivity. An analogous study was therefore conducted on the effect of varying the host SWNT diameter on the regioselectivity of 1,3-dipolar cycloaddition (**Table 4.4**). Benzyl azide was encapsulated within SWNT of average diameter 1.0, 1.3 and 2.0 nm using the aforementioned general procedure, and added to a solution of phenylacetylene under the standard conditions defined previously.

Table 4.4 Selectivity for the 1,4-triazole (**3a**, $S_{1,4}$) in the reaction of phenylacetylene with benzyl azide confined within carbon nanotubes of varying diameter (d_{NT}).

$\text{Ph}-\text{C}\equiv\text{C} + \text{N}^-\text{N}^+=\text{N}-\text{CH}_2\text{Ph} \xrightarrow[80^\circ\text{C}, 14 \text{ days}]{\text{C}_6\text{D}_6} \text{Ph}-\text{C}_4\text{H}_3\text{N}_3-\text{CH}_2\text{Ph} + \text{Ph}-\text{C}_4\text{H}_3\text{N}_3-\text{CH}_2\text{Ph}$			
(1a)	(2)	(3a)	(4a)
	d_{NT} / nm	$S_{1,4} / \%$	$\Delta S_{1,4} / \%$
1	No NT	44	-
2	1.0	47	+3
3	1.3	51	+7
4	2.0	50	+6

Confinement within each of the SWNT induced an increase in selectivity for the 1,4-triazole, further supporting the hypothesis that nanoscale confinement favours the formation of the 1,4-regioisomer. There is a subtle trend in the magnitude of the selectivity increase ($\Delta S_{1,4}$), whereby the optimum confinement, *i.e.* that which causes the greatest increase in selectivity, is observed for SWNT of 1.3 nm diameter (**Table 4.4**, entry 3), and deviation of SWNT diameter from this value affords a less pronounced change in selectivity (**Table 4.4**, entries 2 and 4).

In order to rationalise these observations, the geometry of each triazole must be considered in relation to the nanotube internal cavity, and such analysis reveals that the results shown in **Table 4.4** are not quite as expected. The most pronounced change in selectivity would be expected within a SWNT which can host the 1,4-triazole whilst

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providing insufficient capacity to host the 1,5-triazole (**Figure 4.9a**). SWNT of 1.0 nm diameter fulfil these criteria; however, a more subtle change in selectivity is observed in this case (entry 2), suggesting that the greater proportion of the reaction may be occurring in solution. Conversely, in SWNT of 1.3 nm diameter, where both regioisomers can freely be encapsulated (**Figure 4.9b**), a less pronounced increase in selectivity for the 1,4-isomer is expected; however, a larger increase in selectivity is observed in this case (entry 3).

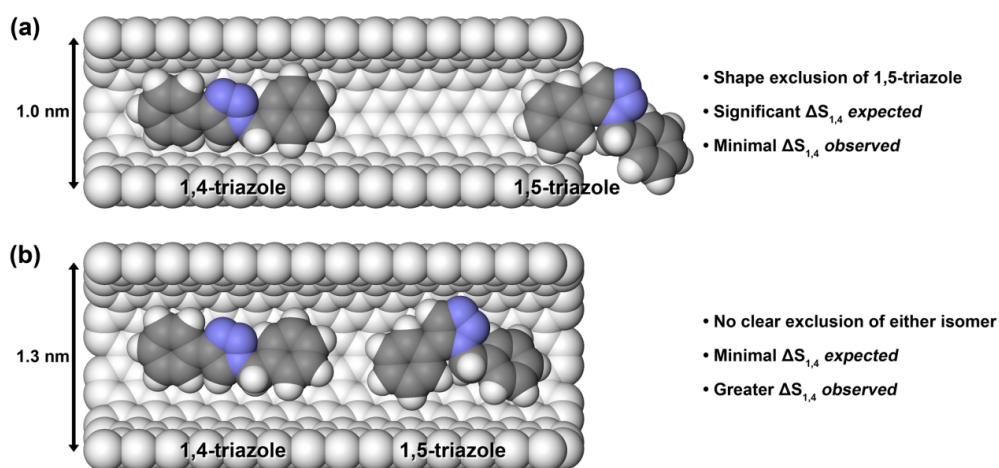


Figure 4.9 Three-dimensional representation of the geometry of the 1,4- and 1,5-triazole regioisomers confined within carbon nanotubes of (a) 1.0 nm and (b) 1.3 nm diameter. (a) The narrower SWNT does not appear to allow the confinement of the 1,5-triazole in its most stable conformation, so a larger $\Delta S_{1,4}$ is expected compared to (b) the wider SWNT, where both products can fit within the SWNT cavity in their most stable conformations. However, the opposite is observed and the greater $\Delta S_{1,4}$ occurs within the wider SWNT suggesting that *product* geometry is not the crucial consideration for this confined reaction.

Due to the modest changes in selectivity observed, particularly when compared to the error of these measurements, it is difficult to draw conclusions reliably and further investigation may be required to confirm these conclusions. Nevertheless, these observations suggest that, for the confined reaction to occur, a larger internal cavity is required than that expected based on product geometry alone. It seems logical that the minimum volume required for a reaction to occur depends most crucially on the critical dimension of the largest species along the reaction pathway. In many simple reactions, such as aromatic halogenation, the critical dimension may not vary significantly throughout the reaction profile and as such, consideration of product geometry alone will suffice. However, for reactions such as

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cycloaddition, which involve considerable geometric rearrangements while traversing the reaction coordinate, consideration of the geometry of the transition state is imperative.

4.3.2.3. Tuning the extent of steric confinement: guest alkyne steric bulk

An alternative approach to tuning the extent of steric confinement for cycloaddition reactions is to alter the steric bulk of the reaction species, while keeping the diameter of the host nanotube constant. A series of alkyne reactants were selected which exhibited varying degrees of steric bulk, through functionalisation at the *para*-position of phenylacetylene. By functionalising at the *para*-position, the steric bulk directly adjacent to the reacting alkyne, often quantified by Tolman cone angle,⁷⁴ remains constant due to the aromatic ring. This allows us to study the indirect steric influence of extreme spatial confinement without complication from steric effects in the vicinity of the reaction centre. By *para*-functionalisation of phenylacetylene in one dimension, with aromatic groups which exhibit limited flexibility, the steric bulk is more easily defined and understood in relation to the limited internal volume of the carbon nanotube. These considerations, coupled with a constant Tolman cone angle, mean that a more useful quantification of functional group steric bulk is the length of the functional group (L_{FG}). These values are measured from the carbon atom nucleus to which the functional group is bonded, to the outermost atom, including the van der Waals radius. The regioselectivity of the reactions of each of the appraised alkynes with benzyl azide within SWNT of varying diameter was compared to the reaction in solution in order to ascertain the effect of nanoscale confinement in each case (Table 4.5).

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Table 4.5 Selectivity for the 1,4-triazole ($S_{1,4}$) in the reactions of a range of substituted alkynes of varying steric bulk with benzyl azide both in solution (No NT) and confined in carbon nanotubes of various diameters (d_{NT}). The steric bulk of the alkyne functional group is quantified by L_{FG} , the length of the functional group including the van der Waals atomic radii.

R groups:
a = phenyl
c = 1,1'-biphenyl
d = *p*-terphenyl

(1a, c & d) (2) (3) (4)

	Alkyne R Group	L_{FG} / nm	d_{NT} / nm	No NT	Confined within NT	
				$S_{1,4}$ / %	$S_{1,4}$ / %	$\Delta S_{1,4}$ / %
1	Phenyl (1a)	0.6	1.3	44	51	+7
2	1,1'-biphenyl (1c)	1.1	1.3	8	63	+55
3	Phenyl (1a)	0.6	2.0	44	50	+6
4	1,1'-biphenyl (1c)	1.1	2.0	8	46	+38
5	<i>p</i> -terphenyl (1d)	1.5	2.0	11	36	+25

Generally, increasing the steric bulk of the alkyne reactant within the same diameter nanotube produced considerably larger increases in 1,4-selectivity ($\Delta S_{1,4}$), up to a 55% shift (**Table 4.5, entry 2**). As the steric bulk is increased within a CNT of a given diameter, the transition state and products experience a greater degree of spatial confinement which results in a more pronounced increase in selectivity for the 1,4-triazole (*e.g.* 1,1'-biphenyl *cf.* phenyl). Conversely, when the reaction species are smaller, in relation to the CNT cavity and thus experience less extreme spatial confinement, there is a less pronounced change in selectivity as a consequence of confinement (**entry 3**). In this way, by varying the steric bulk of reactant functional groups, the extent of confinement can be tuned to achieve optimum confinement and thus greater control over reaction selectivity.

It must be acknowledged that, by increasing the steric bulk of the alkyne in this way, the aromaticity has also been increased and thus, the non-covalent interaction of the alkyne with the SWNT will undoubtedly be enhanced, further facilitating the confined reaction. However, the influence of these two variables is not easily deconvoluted.

4.3.2.4. Investigating the electronic effects of confinement

As described earlier (**Section 4.1.2**), cycloaddition reactions are sensitive to both steric and electronic effects as explained by frontier molecular orbital theory. Substituents of varying electronic properties can influence both kinetics, by shifting the frontier molecular orbital energy levels (**Figure 4.2**), and regioselectivity, by inducing an asymmetric distribution of the frontier molecular orbital density across the atoms involved in the reaction (**Figure 4.3**). Carbon nanotubes, due to their novel electronic properties, have been shown to exhibit interesting effects when species are in intimate contact with either the internal or external surface of the nanotube.^{65, 75, 76} For these reasons, the electronic influence of the host SWNT on the selectivity of 1,3-dipolar cycloaddition within SWNT was investigated by further variation of the alkyne substituent. Again, in order to keep the relative steric bulk (L_{FG}) as constant as possible, particularly with minimal steric hindrance around the reaction centre, phenylacetylene derivatives with various *para*-substituents were chosen ranging from the electron-withdrawing nitro group to the electron-donating amine (**Table 4.6**). The regioselectivity of the cycloaddition of each alkyne with benzyl azide confined within SWNT was compared to each reaction in solution in order to ascertain the effect of the host nanotube. For ease and validity of comparison, benzyl azide was encapsulated within SWNT of 1.3 nm diameter before addition to a solution of each alkyne under standard conditions.

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Table 4.6 Selectivity for the 1,4-triazole (**3**) ($S_{1,4}$) in the reactions of benzyl azide and a range of substituted alkynes, of varying electronic properties, confined within carbon nanotubes of 1.3 nm diameter. Electronic properties vary between the electron-withdrawing nitro group to the electron-donating amine group and this is quantified by the Hammett constant.⁷⁷ The steric bulk, quantified by the length of the functional group (L_{FG}) does not vary significantly.

R groups:
a = phenyl
e = 4-nitrophenyl
f = 4-bromophenyl
g = 4-methoxyphenyl
h = 4-aminophenyl

$R-C\equiv C-H + N=N=N-CH_2-Ph \xrightarrow[80^\circ C, 14 \text{ days}]{C_6D_6} R-1,4-triazole-CH_2-Ph + R-1,5-triazole-CH_2-Ph$

	Alkyne R Group	Hammett constant	L_{FG} / nm	No NT	Confined within NT	
				$S_{1,4} / \%$	$S_{1,4} / \%$	$\Delta S_{1,4} / \%$
1	4-nitrophenyl (1e)	+0.78	0.8	62	80	+18
2	4-bromophenyl (1f)	+0.23	0.8	51	66	+15
3	Phenyl (1a)	0	0.6	44	51	+7
4	4-methoxyphenyl (1g)	-0.27	0.8	42	49	+7
5	4-aminophenyl (1h)	-0.66	0.7	40	40	0

In the absence of carbon nanotubes, the appraised cycloaddition reactions exhibit a clear, yet subtle trend in regioselectivity related to the alkyne electronic properties, whereby electron-withdrawing substituents increase the selectivity for the 1,4-triazole (**Figure 4.10**, black line). Electron withdrawing groups tend to increase the relative molecular orbital coefficients on the terminal alkyne carbon atom, which introduces a slightly more favoured orbital overlap with the azide benzylic nitrogen, thus stabilising the transition state leading to the 1,4-triazole. As *para*-substituents can influence the regioselectivity by subtle distortion of molecular orbitals, the external influence of a carbon nanotube host on the confined molecular orbitals has the potential to offer additional influence through a similar mechanism.

Confinement within SWNT increased the 1,4-triazole selectivity in all but one case, up to an 18% shift in the most extreme instance. Furthermore, the trend in unconfined regioselectivity as a function of alkyne electron-withdrawing nature appears to be amplified by confinement within SWNT (**Figure 4.10**, blue line). The greatest enhancement in $S_{1,4}$ upon confinement was observed for the alkyne with the most electron-withdrawing *para*-substituent (18% increase for 4-nitrophenylacetylene).

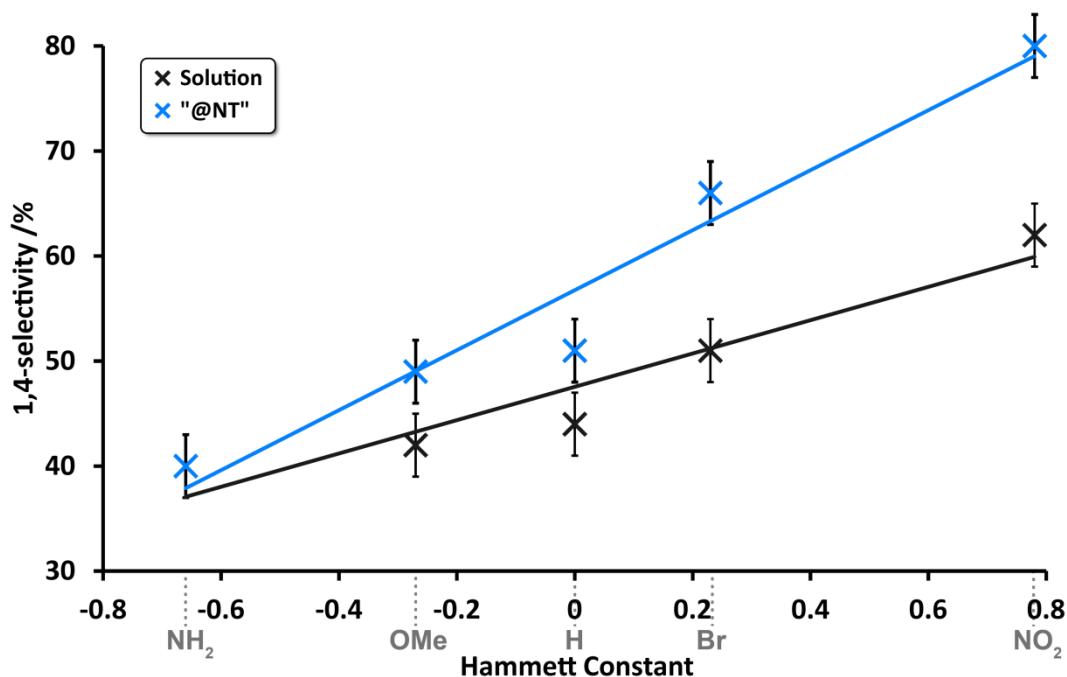


Figure 4.10 Plot of selectivity for the 1,4-triazole against the Hammett constant for each alkyne aromatic *para*-substituent in the 1,3-dipolar cycloaddition of benzyl azide to a range of alkynes both in solution (black) and confined within a SWNT (blue) of 1.3 nm diameter. A clear correlation shows that an increase in alkyne electron-withdrawing nature (more positive Hammett constant) results in a greater 1,4-selectivity. Crucially, this trend is amplified by confinement within SWNT. The trend lines, shown here merely to guide the eye, have approximate gradients of 16 and 29 for the reactions in solution and within SWNT respectively. Error bars show the $\pm 3\%$ error in ^1H NMR measurements.

It is important to note that the overall steric bulk of each of the appraised functional groups is similar (L_{FG} , **Table 4.6**) and any slight variation certainly cannot account for the observed correlation. Based on previous experiments (**Table 4.4**, **Table 4.5**), a small increase in selectivity for the 1,4-triazole is expected due to steric confinement, which should remain approximately constant for each of the appraised alkynes. The varying influence of the host SWNT in these reactions therefore suggests that electronic effects induced by the nanotube can partially contribute to the observed increases in selectivity for the 1,4-triazole in confinement in combination with the known steric effects.

The Hammett constant used to describe each functional group gives a measure of the dipole moment of the alkyne, providing both direction and magnitude. It is this dipole moment which dictates the electron density on the alkyne bond and thus, indirectly, the selectivity of the reaction. The high polarisability of carbon nanotubes allows stabilisation of

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guest species with high charge-separation (*e.g.* high dipole moment) which effectively increases the dipole moment.⁷⁸ The high dipole moment of the guest molecule induces this response from the polarisable host carbon nanotube and therefore the magnitude of this stabilisation varies depending on the magnitude of the intrinsic dipole moment of the molecule. In this way, encapsulated molecules with a high dipole moment will exhibit an even greater dipole moment due to confinement, whereas guest molecules with a lower dipole moment will be influenced to a lesser extent (**Figure 4.11**). In the case of an electron-deficient alkyne (*e.g.* 4-nitrophenylacetylene), an increase to the dipole moment due to confinement within CNT will further reduce electron density on the alkyne, thus promoting the formation of the 1,4-triazole to a greater extent. Whereas a less electron-deficient alkyne with a lower dipole moment (*e.g.* 4-bromophenylacetylene) will experience a less pronounced increase in dipole moment upon confinement, and thus will exhibit a smaller increase in selectivity for the 1,4-triazole by comparison. Conversely, for alkynes with electron-donating substituents, exhibiting a dipole moment in the opposite direction, an increase in dipole moment due to confinement will further *increase* the electron density on the alkyne, thus, reducing selectivity for the 1,4-triazole. Therefore, in this way, confinement within carbon nanotubes effectively amplifies the underlying substituent electronic effects, resulting in an increase to the gradient of the trend demonstrated (**Figure 4.10**).

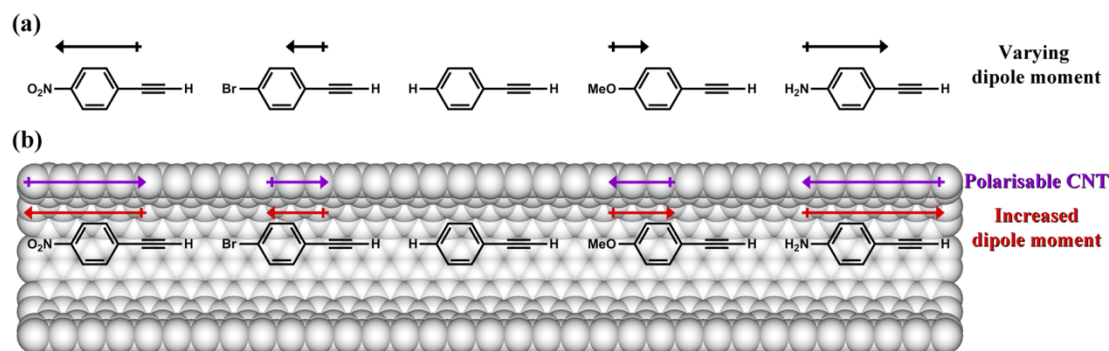


Figure 4.11 Schematic representation of the dipole moments for the appraised alkynes both (a) in solution, and (b) confined within a SWNT. The highly polarisable host carbon nanotube stabilises the partially charge-separated species, effectively increasing the guest alkyne dipole moment (red) in comparison to the same alkyne in bulk solution (black). In this way, the extent to which the carbon nanotube influences the electronic properties of the confined molecule, and thus the regioselectivity of the reaction, depends on the initial dipole moment (*i.e.* extent to which the *para*-substituent is electron-withdrawing or donating).

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Within this dipole-dependent postulation, it might be expected that the reaction of 4-aminophenylacetylene within carbon nanotubes would afford a lower $S_{1,4}$ value than that of the bulk solution. However, in addition to the postulated *electronic* effect, the subtle effect of *steric* confinement will act to increase the selectivity for the 1,4-triazole equally for each of the appraised alkynes, as concluded from previous observations (Table 4.4, Table 4.5). The observed effect of confinement on selectivity is likely to reflect a balance between both steric and electronic effects. Therefore, the net zero change in selectivity upon confinement for the reaction of 4-aminophenylacetylene may be a result of competition between electronic effects, acting to subtly reduce $S_{1,4}$, and steric effects, acting to subtly increase $S_{1,4}$ (Figure 4.12).

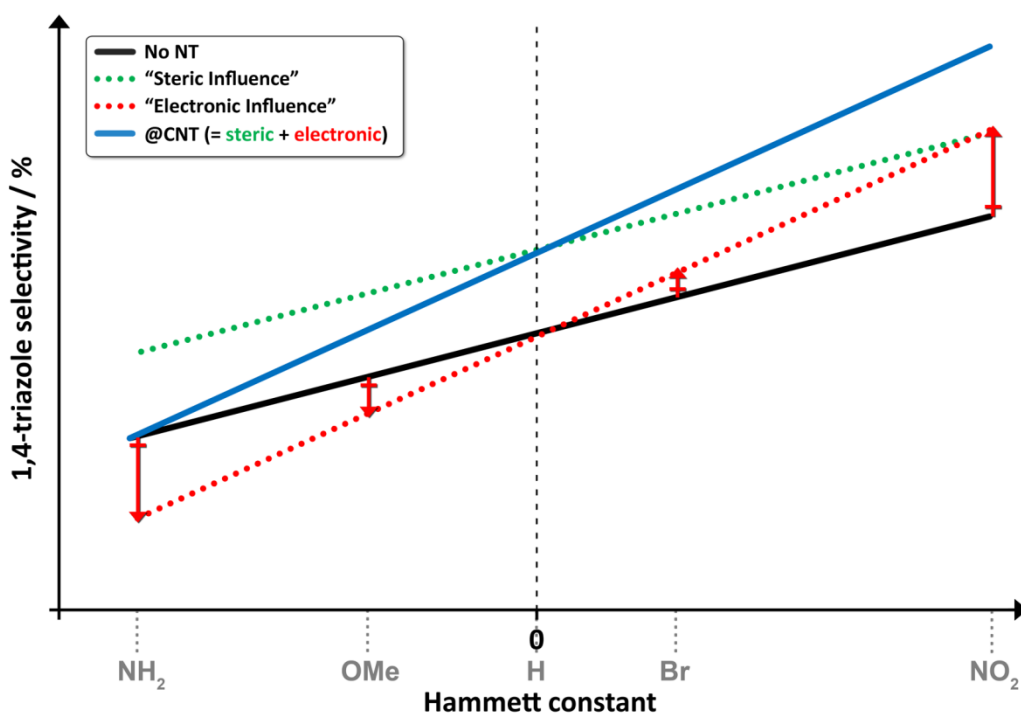


Figure 4.12 Schematic representation of the postulated combination of steric and electronic confinement effect in relation to the observed experimental trends. Solid lines denote experimental trends, dotted lines represent the postulated hypothetical deconvolution. It is proposed that a subtle influence of steric confinement acts to increase selectivity for the 1,4-triazole to a similar degree for each of the appraised alkynes (green). In combination, the electronic effect of confinement within carbon nanotubes (red) acts to alter regioselectivity in different directions, depending on the electron-withdrawing or donating nature of the alkyne substituent, and to varying degrees, depending on the alkyne dipole moment. The combination of these two influences accounts for the observed trend in regioselectivity in confinement (blue) as a function of alkyne electronic properties.

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In addition, the influence of specific alkyne interactions with the carbon nanotube must be considered in relation to regioselectivity. For instance, primary amines are known to interact with the carbon nanotube exterior surface^{79, 80} and although these interactions may be transient, depending on the properties of both the nanotube and amine, the effect of such interactions on reactions within CNT must be considered. While the net zero change in selectivity for the reaction of 4-aminophenylacetylene as a consequence of confinement could be a consequence of competing steric and electronic influences, as described, it is also possible that specific amine-CNT interactions may inhibit the confined reaction. If the amine interacts strongly with the nanotube external surface (*i.e.* the first surface it will most likely diffuse to) and is, therefore, not allowed to freely diffuse into the nanotube, then this would result in the reaction occurring mostly outside the nanotube cavity thus affording identical regioselectivity to that observed in bulk solution. While the strength of the interaction between the specific carbon nanotube and amine is not accurately known, such an interaction could still account for a reduced diffusion of alkyne molecules into the CNT cavity in this case.

In order to gain further insight into this specific example and highlight any reactivity or interactions not associated with the desired azide-alkyne cycloaddition, a control experiment was conducted whereby the aminoalkyne was heated in the presence of SWNT under experimental conditions, but in the absence of any azide (see **Section 4.5.9** for details). The SWNT remaining after this experiment were characterised by Raman spectroscopy showing a 43% increase in $I_D:I_G$ demonstrating an increase in nanotube disorder. Carbon nanotubes are stable under experimental conditions, so no increase in $I_D:I_G$ is expected. Therefore, such a measurable increase can reasonably be attributed to a considerable interaction with the amine which could certainly influence the confinement of this particular reaction within CNT.

In whichever way the underlying electronic effects of the nanotube are influencing these reactions, it still remains clear that, if the optimum extent of steric confinement is

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achieved, it can invoke a much more significant change in selectivity than the observed electronic effects. The $\Delta S_{1,4}$ observed as a consequence of electronic effects (up to 18%) remains much smaller than that observed when the extent of steric confinement is tuned (up to 55%). The conclusion that, even within narrow carbon nanotubes, steric effects are typically dominant over electronic effects is supported by the solution phase studies of Huisgen.⁸¹

4.3.2.5. Product extraction

When analysing the effect of confinement on the selectivity of cycloaddition reactions, it is of utmost importance that the product mixture analysed is a true representation of the confined reaction. Typical reaction work up procedures must include the removal of solid CNT from solution in order to allow solution-phase analysis of the product mixture. However, previous studies into reactions confined within molecular nanoreactors have highlighted the potential problems of product inhibition, whereby the product molecule can become irreversibly bound within the host cavity and difficult to remove.⁵⁵ In order to circumvent this practical limitation, previous studies have utilised *in situ* analysis of the confined product mixture, made possible by the solubility of molecular nanoreactors. However, the extremely limited solubility of carbon nanotubes, coupled with the restricted sensitivity of solid state NMR spectroscopy and complications arising from paramagnetic impurities within carbon nanotubes, necessitates the solution-phase analysis of product mixtures after the removal of all CNT solid. It is, therefore, imperative that all organic material (*i.e.* reactant and product) is removed from the nanotube prior to analysis in order to be confident that spectroscopy measurements accurately represent the outcome of the confined reaction.

To quantitatively extract the triazole products in this case, the carbon nanotube solid required consecutive washing, up to three times, with sonication in a small amount of organic solvent. It was shown that additional washing of the nanotube beyond this did not

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extract any additional organic products within the detection limits of NMR spectroscopy and sensitivity of TLC. Furthermore, EDX spectroscopic analysis of the CNT remaining after this procedure showed no remaining encapsulated products within the limits of detection (Figure 4.13).

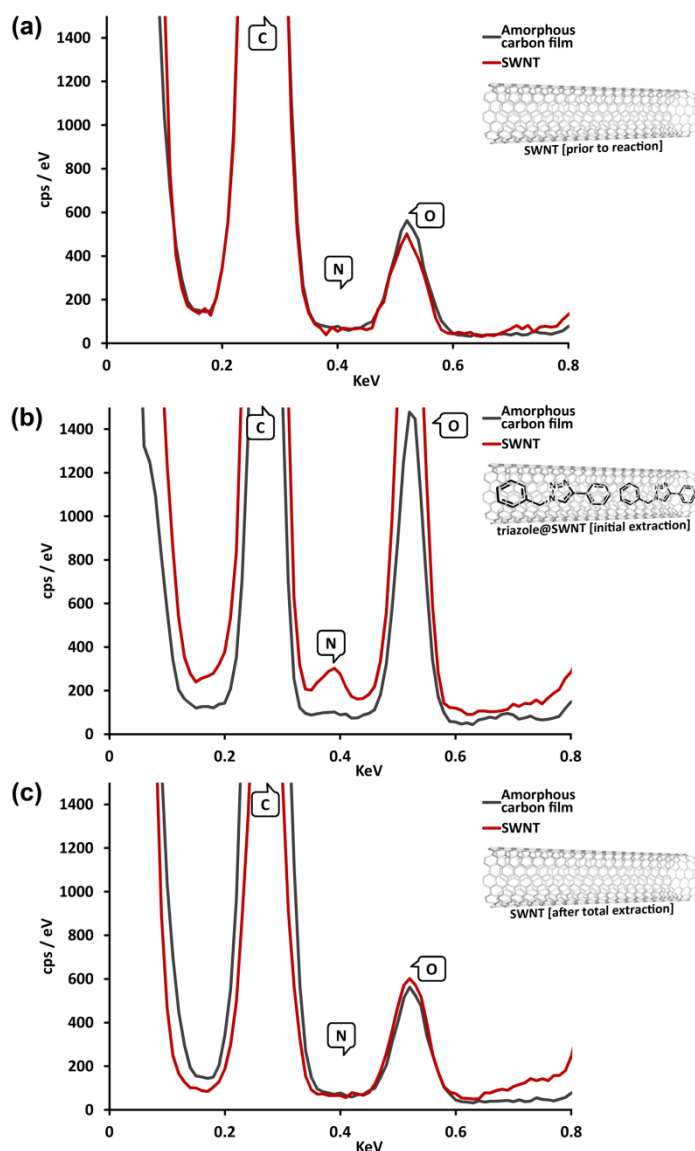


Figure 4.13 Energy dispersive x-ray spectra of SWNT ($d_{NT} = 1.3$ nm). (a) Prior to the addition of any organic molecules, no nitrogen is detected, as expected. (b) Immediately subsequent to the initial extraction procedure, a clear peak at 0.4 KeV is observed corresponding to the nitrogen atoms of either benzyl azide reactant or triazole products. (c) Subsequent to the complete extraction procedure, no nitrogen is detected, demonstrating the quantitative extraction of organic molecules within the limits of detection by EDX spectroscopy. In each case, the spectrum of a SWNT bundle (red) is compared to the spectrum of the amorphous carbon background (black), the difference in which indicates the signal observed due to the SWNT sample.

4. Cycloaddition reactions inside carbon nanotubes

The complete extraction of products was found to be particularly important when studying the selectivity of confined cycloaddition reactions because the measured distribution of products in the extracted solution varied when comparing product mixtures from consecutive extraction stages (**Table 4.7**). It was shown that the apparent 1,4-triazole selectivity values for the initial extraction aliquots were, in many cases, positively skewed when compared to the overall product mixtures after complete extraction.

Table 4.7 Selectivity for the 1,4-triazole ($S_{1,4}$) after initial ($^iS_{1,4}$) and total ($^TS_{1,4}$) product extraction, consistently showing deceptively high values for $\Delta S_{1,4}$ in the initial extraction, potentially due to a selective retention of the 1,5-triazole by the nanotube.

	Alkyne R' Group	d_{NT} / nm	No NT	Initial extraction		Total extraction	
			$S_{1,4}$ / %	$^iS_{1,4}$ / %	$\Delta S_{1,4}$ / %	$^TS_{1,4}$ / %	$\Delta S_{1,4}$ / %
1	Phenyl (1a)	1.0	44	45	+1	47	+3
2	Phenyl (1a)	1.3	44	72	+28	51	+7
3	Phenyl (1a)	2.0	44	45	+1	50	+6
4	Cyclohexyl (1b)	1.3	58	60	+2	60	+2
5	1,1'-biphenyl (1c)	1.3	8	63	+55	63	+55
6	1,1'-biphenyl (1c)	2.0	8	76	+68	46	+38
7	<i>p</i> -terphenyl (1d)	2.0	11	34	+23	36	+25
8	4-nitrophenyl (1e)	1.3	62	85	+23	80	+18
9	4-bromophenyl (1f)	1.3	51	82	+31	66	+15
10	4-methoxyphenyl (1g)	1.3	42	61	+19	49	+7
11	4-aminophenyl (1h)	1.3	40	39	-1	40	0

In almost all cases, the selectivity for the 1,4-triazole is greater in the initial extraction, suggesting that the 1,5-triazole is selectively withheld from solution due to stronger interactions with the nanotube leading to a reduced diffusion rate out of the nanotube cavity. This results in deceptively high values for 1,4-triazole selectivity, which tend to decrease slightly after total extraction. This complication must always be considered for reactions confined within any nanoscale host, because the additional stage of product extraction may involve an energy barrier which must be overcome. However, selective interactions between the host nanotube and isomeric products may, if strong enough, provide a novel means of *in*

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situ product separation, affording further control over the resulting products but not by directly influencing the reaction pathway.

The selective interaction of the 1,5-triazole with the carbon nanotube is supported by preliminary calculations whereby the energy change as a consequence of encapsulation within a (10,10) SWNT was calculated for both regioisomers. The stabilisation energy of the nanotube for each isomer was calculated by comparison of the triazole encapsulated within a SWNT to the total energy of each independent component. The energy change upon encapsulation (*i.e.* the energy required for extraction, E_{EXT}) was predicted to be over 1 eV (23 kcal mol⁻¹) larger for the 1,5-triazole. This supports the experimental observation that the 1,5-triazole is selectively retained within the nanotube due to a stronger interaction with the nanotube than the comparable 1,4-triazole.

To summarise the experimentally observed effects of confinement on the regioselectivity of azide-alkyne cycloaddition reactions, the activation energy for the 1,4-triazole within SWNT has been found to be smaller than that for the 1,5-triazole resulting in an increased selectivity for the 1,4-regioisomer. Furthermore, the 1,5-triazole, once formed, experiences stronger interactions with the host SWNT, and therefore, the energy required to extract (E_{EXT}) the 1,5-triazole is greater than that for the 1,4-regioisomer (**Figure 4.14**). If these conclusions are correct, the changes to both E_A and ΔH due to confinement within carbon nanotubes, means that the two competing 1,3-dipolar cycloaddition reactions no longer adhere to the Bell-Evans-Polanyi principle.^{82, 83} This states that, for reactions of a similar family, a linear correlation usually exists between activation energy and the enthalpy of the reaction, so that the more stable product exhibits the smaller activation energy. The current understanding of these two competitive reactions within narrow carbon nanotubes suggests that this is not the case (**Figure 4.14**) and therefore confinement within carbon nanotubes can fundamentally alter the underlying properties of a chemical reaction, exhibiting behaviour not observed in traditional bulk scale transformations.

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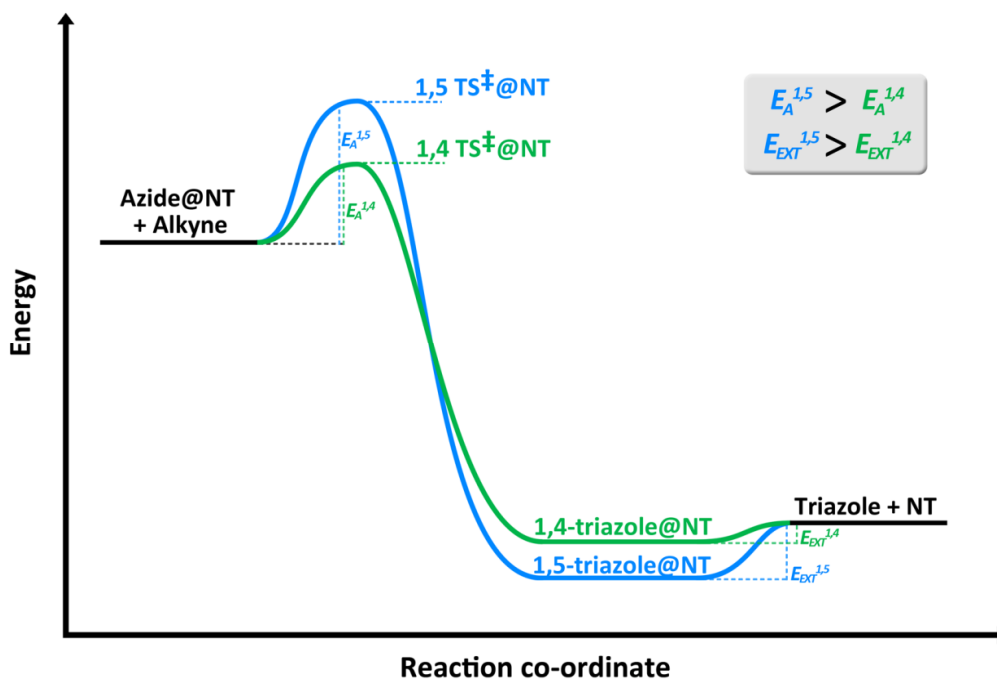


Figure 4.14 Schematic representation of the reaction profile for azide-alkyne cycloaddition reaction within SWNT showing the competitive formation of both the 1,4-triazole (green) and the 1,5-triazole (blue). The activation energy (E_A) for the formation of the 1,4-triazole is believed to be smaller than that for the 1,5-triazole due to the combined confinement effects discussed. However, when the 1,5-triazole forms, it exhibits stronger interactions with the host SWNT and thus, the energy required to extract (E_{EXT}) the 1,5-triazole is greater than that required for the 1,4-triazole.

4.4. Conclusions

The Diels-Alder cycloaddition of cyclopentadiene to both methacrolein and crotonaldehyde showed measurable, yet minimal increases in *endo* selectivity (up to 6%) as a consequence of confinement within narrow carbon nanotubes. It was postulated that no drastic effect was observed because there was no clear mechanism of size or shape selectivity within carbon nanotubes due to the similar size and shape of the isomeric transition states.

The 1,3-dipolar cycloaddition of various alkynes to benzyl azide has been studied within the internal cavity of narrow carbon nanotubes, showing consistent increases in selectivity for the 1,4-triazole (up to 55%) due to confinement within SWNT. As hypothesised, the more linear 1,4-triazole is favoured within the SWNT cavity in almost all cases, although there is reason to believe that this is not entirely due to steric confinement. It was shown that the extent of confinement can be tuned by varying the SWNT diameter or the steric bulk of reactant substituents in order to maximise the effect of confinement on selectivity. In many examples, measurable increases in 1,4-triazole selectivity were observed whilst the host nanotube cavity provided sufficient volume for both products to be encapsulated freely. This suggests that, to understand the mechanism of size or shape selectivity induced by the nanotube, the geometry of the regioisomeric transition states can be the most important consideration.

A clear correlation between the electron-withdrawing nature of alkyne substituents and the increase in 1,4-triazole selectivity within SWNT suggests that the electronic properties of carbon nanotubes are providing an additional subtle influence on selectivity. It is postulated that the highly polarisable host CNT stabilises the alkyne dipole moment, effectively increasing the partial charge separation. This phenomenon acts to amplify the underlying trend in regioselectivity by decreasing the alkyne electron density for electron-deficient alkynes and increasing the electron density for electron-rich alkynes. Therefore, confined cycloaddition reactions are influenced by a balance of both steric and electronic

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factors induced by confinement within carbon nanotubes. Indeed, it is expected that these two influences can be additive or opposing, affording the observed selectivity. However, from these results, it appears that steric effects can induce the greatest change in selectivity; the most sterically constricted reaction showing an increase in selectivity for the 1,4-triazole of 55%, compared with an 18% increase for the most electron-withdrawing.

It was found that, although the formation of the 1,5-triazole is less favoured within SWNT, once formed, this isomer can be selectively withheld from solution by stronger interactions with the SWNT cavity. This demonstrates that efficient extraction of products is critical, but this also highlights an additional potential method offering further control over product distribution if this effect could be harnessed.

Whilst the selectivity results discussed do not compare with those obtained by copper-catalysed click reactions, this study clearly indicates the profound effect that simple confinement within carbon nanotubes can have on organic chemical reactions. The effect of steric confinement on reaction pathways has been further explored and is better understood. The great potential of utilising other novel properties of carbon nanotubes, such as their electronic influence on encapsulated guests, to control chemical transformations has also been demonstrated.

4.5. Experimental

4.5.1. General

All glassware was cleaned with a mixture of hydrochloric and nitric acid (3:1 v/v, 'aqua regia') and rinsed thoroughly with deionised water, cleaned with potassium hydroxide in isopropyl alcohol and finally rinsed thoroughly with deionised water. Water was purified ($> 18 \text{ M}\Omega \text{ cm}$) using a Barnstead NANOPure II system. ^1H NMR spectra were obtained using a Bruker AV(III)400 (400.07 MHz) spectrometer at 298K using 64 scans in either C_6D_6 or CDCl_3 . All heat treatment was carried out in a tube furnace under air atmosphere unless otherwise stated. Thermogravimetric analysis was performed using a TA Instruments SDT Q600 under a flow of air at a rate of 100 mL min^{-1} at a heating rate of $10^\circ\text{C min}^{-1}$ from room temperature to 1000°C . Transmission electron microscopy was performed by Professor Andrei Khlobystov using a JEOL 2100F TEM (field emission gun source, information limit $< 0.19 \text{ nm}$) at room temperature. Nanotube diameter measurements were conducted using Gatan DigitalMicrograph software. Energy dispersive X-ray spectroscopy was performed by Dr. Michael Fay using an Oxford Instruments INCA 560 X-ray microanalysis system. Samples were prepared *via* drop-drying methanolic solutions onto a copper grid mounted "lacey" carbon films. Raman spectroscopy was conducted by Dr. Graham Rance using a HoribaJY LabRAM HR spectrometer with a laser wavelength of 532 nm. Samples were dropcast from methanolic solutions onto Si(100) wafers and a minimum of five spectra recorded from different areas of the sample. GC-MS was completed by Dr. Mick Cooper using a VG Autospec in EI^+ mode. The Diels-Alder reactivity experiments were carried out by Mr. Rhys Lodge. All reagents were purchased from Sigma-Aldrich, UK and used without further purification unless otherwise specified. Benzyl azide (**2**)⁸⁴ and alkynes 4-ethynyl-1,1'-biphenyl (**1c**),⁸⁵ 4-ethynyl-*p*-terphenyl (**1d**),⁸⁶ 1-ethynyl-4-nitrobenzene (**1e**),⁸⁷ and 1-bromo-4-ethynylbenzene (**1f**)⁸⁸ were synthesised according to literature protocols.

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4.5.2. Carbon nanotube sources and pre-treatment

Carbon nanotubes were purchased from commercial suppliers and all were pre-treated by air oxidation in order to oxidatively remove the nanotube end-caps and provide access to the internal cavity. Conditions varied for this procedure (**Table 4.8**).

Table 4.8 Description of each carbon nanotube used and commercial source. Conditions used during oxidative pre-treatment including temperature (T_{ox}) and duration (t_{ox}) are provided, and mean nanotube diameter (d_{NT}) was measured by statistical analysis of transmission electron micrographs.

d_{NT} / nm	Synthesis	Commercial name	Commercial Supplier	Lot no.	T_{ox} / °C	t_{ox} / mins
1.0±0.1	CVD	HiPCO SWNT	Unidym Inc., CA, USA	R2172	380	30
1.3±0.1	Arc discharge	Helix SWNT	Helix Materials Solutions, TX, USA	CSCA	380	30
2.0±0.4	CVD	SWNT	Timesnano, Chengdu, China		570	8

Additionally, all carbon nanotubes were dried thoroughly at 250°C for 30 minutes immediately prior to use.

4.5.3. Synthesis of cyclopentadiene

Cyclopentadiene was prepared from dicyclopentadiene by cracking at 180°C, according to literature precedent,^{89, 90} and was stored at -20°C prior to use to inhibit dimerisation.

¹H NMR (300 MHz) δ /ppm 6.59 (m, 2H), 6.50 (m, 2H), 3.01 (s, 2H).

4.5.4. Diels-Alder cycloaddition of methacrolein to cyclopentadiene

To a solution of cyclopentadiene (28 mg, 0.42 mmol) in CDCl₃ (0.5 mL), was added methacrolein (25 mg, 0.36 mmol) and the mixture stirred at 40°C for 48 - 96 hours.

The crude product mixture was analysed by ¹H NMR spectroscopy to determine the selectivity and conversion. *Endo/exo* selectivity was determined by comparing the peak integrals at 9.39 ppm (*endo*) and 9.68 ppm (*exo*) corresponding to the aldehyde proton environments of each isomer. The ¹H NMR chemical shifts showed good agreement with known literature values⁹¹ confirming the identity of each isomer.

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4.5.5. Diels-Alder cycloaddition of *E*-crotonaldehyde to cyclopentadiene

To a solution of cyclopentadiene (28 mg, 0.42 mmol) in CDCl₃ (0.5 mL), was added *E*-crotonaldehyde (25 mg, 0.36 mmol) and the mixture stirred at 40°C for 48 - 96 hours.

The crude product mixture was analysed by ¹H NMR spectroscopy to determine the selectivity and conversion. *Endo/exo* selectivity was determined by comparing the peak integrals at 9.38 ppm (*endo*) and 9.79 ppm (*exo*) corresponding to the aldehyde protons of each isomer. The ¹H NMR chemical shifts showed good agreement with known literature values⁹² confirming the identity of each isomer.

4.5.6. Encapsulation of cyclopentadiene, methacrolein and crotonaldehyde in SWNT

SWNT (5 mg) were dried thoroughly at 250°C in air before immediate addition to the liquid reactant (cyclopentadiene, methacrolein or crotonaldehyde) (2 mL) on a filter membrane (0.2 µm pore, PTFE) and the mixture was briefly agitated before leaving for 1 minute to allow sufficient nanotube filling by capillary wetting. A mild vacuum was applied, using a water aspirator, in order to facilitate the removal of excess liquid reactant, until the black suspension resembled a dry black powder (typically around 15 minutes).

For Diels-Alder reactions inside SWNT, the black "reactant A"@SWNT solid was added, in place of the corresponding liquid reactant, to the CDCl₃ solution of reactant B following the procedures described in Sections 4.5.4 and 4.5.5.

4.5.7. 1,3-dipolar cycloaddition of benzyl azide (2) to alkynes (1a-h)

To deuterated benzene (1.6 mL), was added benzyl azide (14 µL, 0.113 mmol) and the alkyne (0.113 mmol) and the solution was stirred at 80°C for 14 days. The product distribution was determined from ¹H NMR spectroscopy (C₆D₆) of the crude reaction mixtures comparing diagnostic peaks in the region of 4.8 to 5.1 ppm corresponding to the

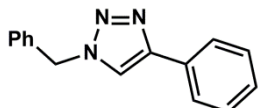
4. Cycloaddition reactions inside carbon nanotubes

1,4- and 1,5-triazoles (specific spectroscopic detail given below, diagnostic peaks underlined). Where necessary, the identification of each regioisomer was confirmed by regioselective synthesis and isolation of the respective triazole.

Cycloaddition of benzyl azide to phenylacetylene (1a)

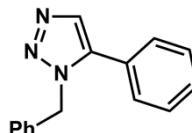
(3a)

1-benzyl-4-phenyl-1H-1,2,3-triazole



(4a)

1-benzyl-5-phenyl-1H-1,2,3-triazole

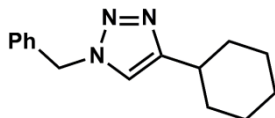


The regioselectivity was determined from ^1H NMR spectroscopy (C_6D_6) by comparing peak integrals at 4.83 ppm (s, 2H) and 5.03 ppm (s, 2H), consistent with literature reports for the 1,4-triazole (**3a**)⁴⁴ and 1,5-triazole (**4a**)^{35, 93, 94} respectively.

Cycloaddition of benzyl azide to cyclohexylacetylene (1b)

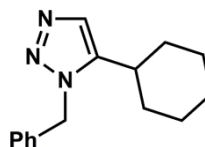
(3b)

1-benzyl-4-cyclohexyl-1H-1,2,3-triazole



(4b)

1-benzyl-5-cyclohexyl-1H-1,2,3-triazole



The regioselectivity was determined from ^1H NMR spectroscopy (C_6D_6) by comparing peak integrals for the 1,4-triazole (**3b**) at 4.86 ppm (s, 2H), consistent with literature reports,⁴⁴ and the 1,5-triazole (**4b**) at 5.00 ppm (s, 2H). The identity of the 1,5-triazole (**4b**) was confirmed by regioselective synthesis, isolation and characterisation.

Regioselective synthesis of 1-benzyl-5-cyclohexyl-1H-1,2,3-triazole (4b)

Synthetic procedure based on analogous procedures described by Zhang *et al.*³⁵ using standard Schlenk line techniques under an argon atmosphere. An orange solution of cyclohexylacetylene (13 μL , 0.1 mmol), benzyl azide (14 μL , 0.1 mmol) and $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ (5.2 mg) in deuterated benzene (5 mL) was stirred at 80°C for 4 hours

4. Cycloaddition reactions inside carbon nanotubes

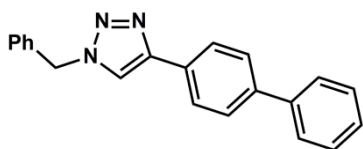
under argon atmosphere. Product isolated by flash chromatography (1:2, dichloromethane: petroleum ether) to yield a colourless oil (3 mg, 11% yield).

¹H NMR (C₆D₆) δ_{H} /ppm 7.46 (s, 1H), 7.00-6.92 (m, 3H), 6.92-6.88 (m, 2H), 5.00 (s, 2H), 2.18-2.08 (m, 1H), 1.48-1.35 (m, 6H), 1.00-0.87 (m, 4H); **¹H NMR (CDCl₃)** δ_{H} /ppm 7.48 (s, 1H), 7.36-7.28 (m, 3H), 7.18-7.13 (m, 2H), 5.52 (s, 2H), 2.54-2.45 (m, 1H), 1.79-1.64 (m, 6H), 1.35-1.18 (m, 4H); **¹³C NMR (CDCl₃)** δ_{H} /ppm 131.06, 128.88, 128.21, 127.04, 51.62, 33.42, 32.74, 26.05, 25.54; **HRMS** m/z calculated for C₁₅H₁₉N₃ 242.1652, found 242.1652 [M+H].

Cycloaddition of benzyl azide to 4-ethynyl-1,1'-biphenyl (1c)

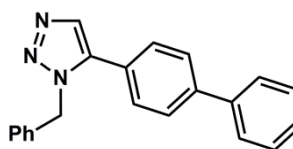
(3c)

4-(1,1'-biphenyl-4-yl)-1-benzyl-1,2,3-triazole



(4c)

5-(1,1'-biphenyl-4-yl)-1-benzyl-1,2,3-triazole



The regioselectivity was determined from ¹H NMR spectroscopy (C₆D₆) by comparing peak integrals at 4.87 ppm (s, 2H) for the 1,4-triazole (**3c**), consistent with literature reports,⁹⁵ and 5.11 ppm (s, 2H) for the 1,5-triazole (**4c**). The identity of the 1,5-triazole (**4c**) was confirmed by regioselective synthesis, isolation and characterisation.

Regioselective synthesis of 5-(1,1'-biphenyl-4-yl)-1-benzyl-1,2,3-triazole (4c)

Synthetic procedure based on analogous procedures described by Zhang *et al.*³⁵ using standard Schlenk line techniques under an argon atmosphere. To a mixture of 4-ethynyl-1,1'-biphenyl (18 mg) and Cp*RuCl(PPh₃)₂ (5 mg), was added a solution of benzyl azide (15 mg, 1.1 equiv.) in deuterated benzene (1.6 mL, degassed). The orange solution was stirred at 80°C under argon for 4 hours. Product isolated by flash chromatography (3:7, ethylacetate: hexane) to yield a white solid (9.9 mg, 31% yield).

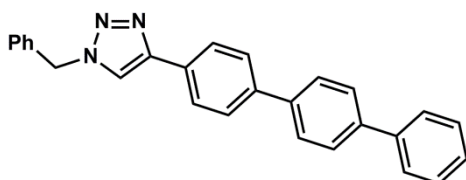
4. Cycloaddition reactions inside carbon nanotubes

R_f 0.31 (3:7, ethylacetate: hexane); **mp** 136-139°C; **¹H NMR (C₆D₆)** δ_H/ppm 7.71 (s, 1H), 7.39-7.34 (m, 2H), 7.27-7.13 (m, 5H), 6.98-6.89 (m, 7H), 5.11 (s, 2H); **¹H NMR (CDCl₃)** δ_H/ppm 7.80 (s, 1H), 7.68-7.59 (m, 4H), 7.48 (tt, 2H), 7.40 (tt, 1H), 7.36-7.29 (m, 5H), 7.15-7.11 (m, 2H), 5.61 (s, 2H); **¹³C NMR (CDCl₃)** δ_H/ppm 142.36, 139.86, 137.92, 135.53, 133.27, 129.26, 128.96, 128.88, 128.19, 127.96, 127.58, 127.12, 127.06, 125.65, 51.88; **HRMS** *m/z* calculated for C₂₁H₁₇N₃ 312.1495, found 312.1498 [M+H].

Cycloaddition of benzyl azide to 4-ethynyl-1,1':4,1''-terphenyl (1d)

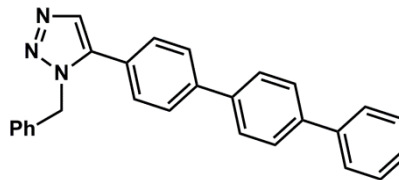
(3d)

4-(1,1':4',1''-terphenyl-4-yl)-1-benzyl-1,2,3-triazole



(4d)

5-(1,1':4',1''-terphenyl-4-yl)-1-benzyl-1,2,3-triazole



The regioselectivity was determined from ¹H NMR spectroscopy (C₆D₆) by comparing peak integrals at 4.89 ppm (s, 2H) and 5.13 ppm (s, 2H) for the 1,4-triazole (**3d**) and 1,5-triazole (**4d**) respectively. The identity of the 1,5-triazole (**4d**) was confirmed by regioselective synthesis, isolation and characterisation. Regioselective synthesis and isolation of the 1,4-triazole (**3d**) could not be achieved despite attempts following well-known synthetic protocols.^{44, 96, 97} However, the relative chemical shift of the diagnostic benzylic proton environment is not expected to vary significantly between the fully characterised biphenyl-functionalised 1,4-triazole (**3c**) at 4.87 ppm and the terphenyl-functionalised 1,4-triazole (**3d**), so the peak observed at 4.89 ppm in the crude mixture was assigned as the expected 1,4-triazole (**3d**).

Regioselective synthesis of 5-(1,1':4',1''-terphenyl-4-yl)-1-benzyl-1,2,3-triazole (4d)

Synthetic procedure is based on analogous procedures described by Zhang *et al.*³⁵ using standard Schlenk line techniques under an argon atmosphere. To a mixture of 4-ethynyl-*p*-terphenyl (26 mg) and Cp*RuCl(PPh₃)₂ (5 mg), was added a solution of benzyl

4. Cycloaddition reactions inside carbon nanotubes

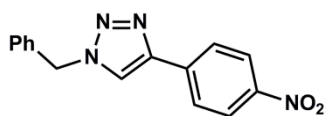
azide (15 mg, 1.1 equiv.) in deuterated benzene (1.6 mL, degassed). The orange solution was stirred at 80°C under argon for 4 hours. The product was isolated by flash chromatography (3:7, ethylacetate:hexane), yielding a white solid (5.3 mg, 13% yield).

R_f 0.23 (3:7, ethylacetate:hexane); **mp** 230-233°C; **¹H NMR (C₆D₆)** δ_H/ppm 7.74 (s, 1H), 7.55-7.50 (m, 4H), 7.46-7.41 (m, 2H), 7.34-7.08 (m, 5H), 7.04-6.88 (m, 7H), 5.13 (s, 2H); **¹H NMR (CDCl₃)** δ_H/ppm 7.82 (s, 1H), 7.74-7.64 (m, 8H), 7.49 (t, 2H), 7.42-7.30 (m, 6H), 7.16-7.12 (m, 2H), 5.62 (s, 2H); **¹³C NMR (CDCl₃)** δ_H/ppm 141.82, 140.87, 140.41, 138.68, 137.90, 135.56, 133.32, 129.31, 128.89, 128.88, 128.20, 127.69, 127.56, 127.44, 127.42, 127.13, 127.04, 125.74, 51.89; **HRMS** *m/z* calculated for C₂₇H₂₁N₃ 388.1808, found 388.1807 [M+H].

Cycloaddition of benzyl azide to 1-ethynyl-4-nitrobenzene (1e)

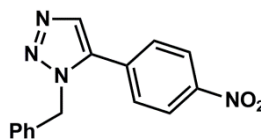
(3e)

1-benzyl-4-(4-nitrophenyl)-1H-1,2,3-triazole



(4e)

1-benzyl-5-(4-nitrophenyl)-1H-1,2,3-triazole

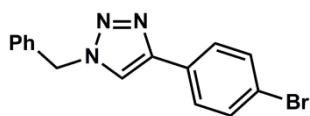


The regioselectivity was determined from ¹H NMR spectroscopy (C₆D₆) by comparing peak integrals at 4.79 ppm (s, 2H) and 4.91 ppm (s, 2H), consistent with literature reports for the 1,4-triazole (3e)⁴⁴ and 1,5-triazole (4e)^{93, 94} respectively.

Cycloaddition of benzyl azide to 1-bromo-4-ethynylbenzene (1f)

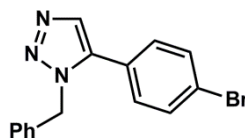
(3f)

1-benzyl-4-(4-bromophenyl)-1H-1,2,3-triazole



(4f)

1-benzyl-5-(4-bromophenyl)-1H-1,2,3-triazole



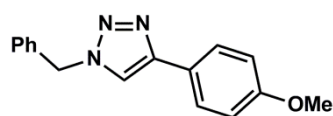
The regioselectivity was determined from ¹H NMR spectroscopy (C₆D₆) by comparing peak integrals at 4.81 ppm (s, 2H) and 4.93 ppm (s, 2H), consistent with literature reports for the 1,4-triazole (3f)⁴⁴ and 1,5-triazole (4f)^{93, 94} respectively.

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Cycloaddition of benzyl azide to 1-ethynyl-4-methoxybenzene (1g)

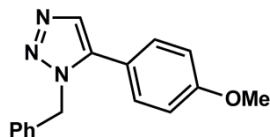
(3g)

1-benzyl-4-(4-methoxyphenyl)-1,2,3-triazole



(4g)

1-benzyl-5-(4-methoxyphenyl)-1,2,3-triazole

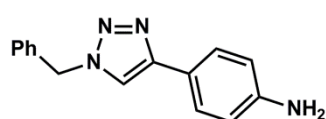


The regioselectivity was determined from ^1H NMR spectroscopy (C_6D_6) by comparing peak integrals at 4.86 ppm (s, 2H) and 5.08 ppm (s, 2H), consistent with literature reports for the 1,4-triazole (**3g**)⁴⁴ and 1,5-triazole (**4g**)^{93, 94} respectively.

Cycloaddition of benzyl azide to 4-ethynylaniline (1h)

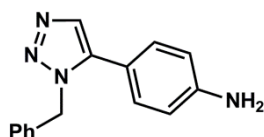
(3h)

4-(1-benzyl-1H-1,2,3-triazol-4-yl)aniline



(4h)

4-(1-benzyl-1H-1,2,3-triazol-5-yl)aniline



The regioselectivity was determined from ^1H NMR spectroscopy (C_6D_6) by comparing peak integrals at 4.83 ppm (s, 2H) for the 1,4-triazole (**3h**), consistent with literature reports,⁴⁴ and 5.10 ppm (s, 2H) for the 1,5-triazole (**4h**).

The identity of the 1,5-triazole (**4h**) could not be confirmed by regioselective synthesis and isolation despite attempts applying the analogous ruthenium-catalysed protocol described by Zhang *et al.*³⁵ However, literature reports confirming the identity of the 1,4-triazole (**3h**) coupled with the expected relative chemical shift values when compared to structural analogues (**3a-g** cf. **4a-g**), it is highly likely that the peak observed at 5.10 ppm in the crude mixture is due to the expected 1,5-triazole (**4h**).

4. Cycloaddition reactions inside carbon nanotubes

4.5.8. 1,3-dipolar cycloaddition of benzyl azide (2) to substituted alkynes (1a-h) confined within single-walled carbon nanotubes

Pre-treated, dried SWNT (see **Section 4.5.2**) (5.0 mg) were immediately immersed in benzyl azide (300 μ L) on a PTFE membrane (0.2 μ m pore size) and left at room temperature and pressure for 7 days to allow excess benzyl azide to evaporate, affording a black benzyl azide@SWNT powder (4.85 - 5.25 mg). To the benzyl azide@SWNT solid was added the substituted alkyne solution (45 μ mol) in deuterated benzene (1.6 mL) and the mixture stirred at 80°C for 14 days. The carbon nanotube black solid was removed by filtration through cotton wool, and washed in chloroform (15 mL) with 15 minutes sonication. The filtration and washing stages were repeated three times consecutively, and all solvent aliquots were combined before solvent removal *in vacuo*. Regioselectivity was determined from ^1H NMR spectroscopy (C_6D_6) of the crude mixture by comparing diagnostic peaks between 4.8 and 5.1 ppm as detailed in **Section 4.5.7**.

4.5.9. Control: 4-aminophenylacetylene interaction with SWNT

SWNT (Helix SWNT, $d_{\text{NT}} = 1.3$ nm) was pre-treated as described in **Section 4.5.2**.

Raman (532 nm) v/cm^{-1} 1333.2 $\pm$ 3.2 (D), 1583.2 $\pm$ 3.8 (G), $I_{\text{D}}:I_{\text{G}} = 0.048 \pm 0.012$

The SWNT black solid (5 mg) was added to a solution of 4-aminophenylacetylene (12 mg) in deuterated benzene (5 mL) and the black suspension stirred at 80°C for 14 days. The mixture was cooled to room temperature and black solid was removed by filtration (PTFE, 0.2 μ m pore) and washed with benzene (10 mL). Black solid nanotube powder (filtrand) was analysed by Raman spectroscopy.

Raman (532 nm) v/cm^{-1} 1337.1 $\pm$ 1.3 (D), 1587.9 $\pm$ 0.8 (G), $I_{\text{D}}:I_{\text{G}} = 0.069 \pm 0.011$. A relative increase in $I_{\text{D}}:I_{\text{G}}$ of 43% as a result of experimental conditions in the presence of 4-aminophenylacetylene.

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5. Chiral chemical reactions on carbon nanotubes

5.1. Carbon nanotubes and chirality

As carbon nanotubes are becoming rapidly established as nanoscale containers for a wide range of chemical reactions,¹⁻³ the influence of various structural parameters of the host nanotube, such as diameter,⁴ length⁵ and surface morphology, on chemical reactions is currently being investigated. The extreme spatial confinement experienced by molecules within narrow carbon nanotubes has been shown to alter the outcome of chemical reactions by size and shape selectivity (**Chapter 3**).⁶ Furthermore, the electronic properties of the host carbon nanotube, particularly its inherent polarisability, have been utilised to influence the regioselectivity of chemical transformations (**Chapter 4**) by stabilising the dipole moment of encapsulated molecules. However, the effect of one important property of carbon nanotubes, their intrinsic helicity, on chemical reactivity has yet to be explored.

The helicity of carbon nanotubes emerges as a result of the wrapping of a graphene sheet along a particular chiral vector C_h (**Figure 5.1**). The length of C_h , which determines the circumference of the resulting nanotube, is defined by indices (n, m) related to the graphene lattice vectors a_1 and a_2 . However, the *direction* of C_h determines which side the graphene sheet is curled inward to form a cylinder and results in two distinct helical twists, denoted P (right-handed or plus) and M (left-handed or minus). Although synthetic conditions can be varied to offer control over the distribution of diameters⁷ and even, to a certain extent, chiral indices,⁸ the statistical nature of these two potential 'roll-up' vectors results in the formation of a racemic mixture of both P and M enantiomers for any chiral nanotube.⁹

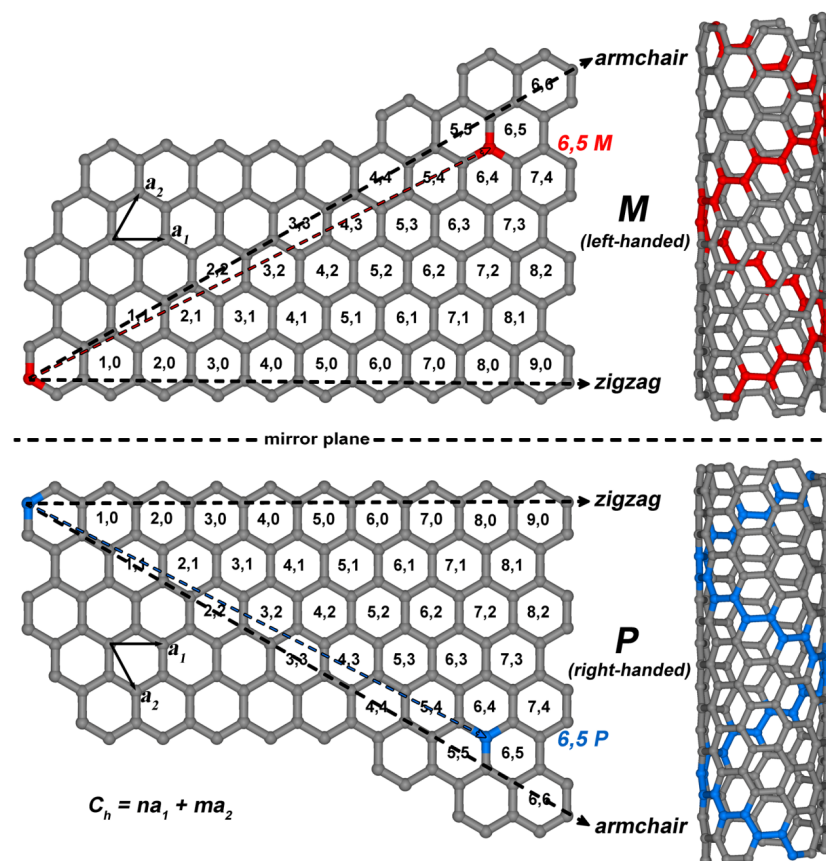
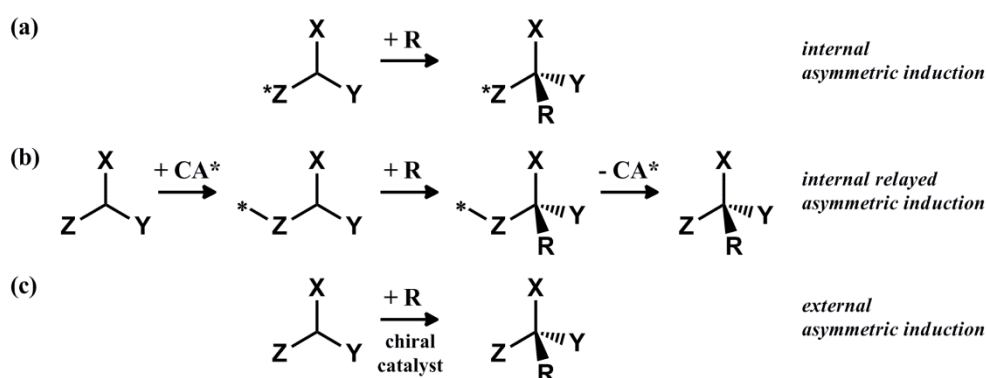


Figure 5.1 The chirality and helicity of carbon nanotubes are defined by the magnitude and direction, respectively, of the roll-up vector, C_h (defined by chiral indices, n and m). Aside from the highly symmetric zig-zag ($m=0$) and arm-chair ($n=m$) structures, all intermediate carbon nanotubes are chiral. Each chiral nanotube structure can exist as either *P* (right handed, blue) or *M* (left-handed, red) enantiomers and macroscopic quantities of CNT material contain a racemic mixture of the two. The carbon nanotubes shown are the representative enantiomers of (6,5)-SWNT, where the coloured carbon atoms highlight the direction of the helical twist in each enantiomer.

Controlling the stereochemical outcome of a chemical reaction is a common concern of synthetic chemists due to the prevalence of chiral centres in important natural products and the different properties exhibited by otherwise seemingly indistinguishable enantiomers. This subtle difference can be extremely important in pharmaceuticals; for instance, sufferers of Parkinson's disease are treated with a chiral amino acid 3,4-dihydroxyphenylalanine (DOPA). However, only (*S*)-DOPA is effective at treating nerve degeneration, while (*R*)-DOPA is both ineffective and toxic.¹⁰ For these reasons, the isolation of enantiomerically pure compounds represents a key challenge for industry. The difficulties in separating these near-identical enantiomers, and the inherent 50% inefficiency involved in such post-synthetic purification, has lead to the development of multiple methods to achieve

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enantioselective control over the *synthesis* of chiral compounds.¹¹ One such method, termed asymmetric induction, involves the addition of an enantiomerically pure chiral auxiliary to direct the synthesis of stereoisomeric products by promoting the selective formation of a single enantiomer. This can be achieved through "internal" asymmetric induction, by the covalent addition of a chiral centre to a reactant (**Scheme 5.1a-b**), or through "external" asymmetric induction, by a chiral catalyst or ligand influencing the transition state (**Scheme 5.1c**).¹² Internal strategies can involve the covalent bonding of a chirally active moiety as a permanent component of the product or, alternatively, the chiral functional group can be removed in an additional final synthetic step (relayed asymmetric induction). The use of chiral *catalysts*, when possible, represents the most efficient protocol, minimising additional synthetic steps by negating the covalent functionalisation of reactants. For example, the asymmetric synthesis of the analgesic (*S*)-naproxen can be achieved with 97% enantiomeric excess by hydrogenation catalysed by a ruthenium catalyst containing the chiral (*S*)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) ligand.¹³



Scheme 5.1 The three strategies for asymmetric induction, distinguishing both internal (a, b) and external (c) methodologies. (a) Internal asymmetric induction achieved by the deliberate design of a suitable reactant with a covalently linked chiral moiety (Z^*) can be effective, but limits functionality. (b) Relayed asymmetric induction, by the temporary introduction and subsequent removal of a chiral auxiliary (CA^*), offers enhanced flexibility and functional group tolerance yet requires additional synthetic steps. (c) External asymmetric induction does not involve any covalent bonding of the chiral auxiliary, instead influencing the transition state through catalyst co-ordination. Therefore, this represents the most adaptable and efficient strategy. Chiral moieties are denoted by an asterisk.

Autocatalysis is the process by which the product of a reaction can also act as a catalyst for the same reaction. This concept can also apply to asymmetric syntheses, whereby an

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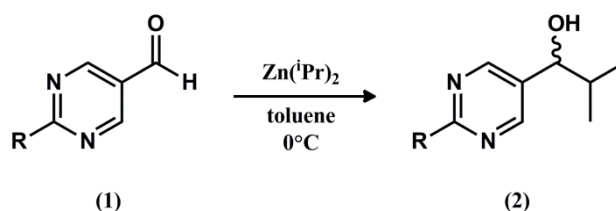
enantiomerically pure product molecule can catalyse the enantioselective formation of the corresponding enantiomer.¹⁴ This phenomenon means that the addition of a catalytic amount of the intended pure enantiomer will induce the asymmetric autocatalytic synthesis of the same enantiomer with high enantiomeric excess. Indeed, certain examples of these reactions are extremely sensitive to any chiral material in the reaction mixture, whereby chiral molecules,¹⁵ inorganic crystals,^{14, 16, 17} circularly polarised light¹⁸ and even isotopic substitution¹⁹ have been shown to induce high enantioselectivity through asymmetric autocatalysis.

When no chiral influence is present in the reaction mixture, asymmetric autocatalytic reactions can still exhibit high enantiomeric excess by the process of spontaneous symmetry breaking. This occurs when the initial formation of products happens, by chance, to produce a slight excess of one enantiomer, which then catalyses the enantioselective formation of that single enantiomer. This concept is not considered for traditional, bulk scale chiral chemical reactions because the large number of product molecules being formed throughout the reaction always tend toward a statistical racemate. However, in the initial stages of a reaction, when far fewer product molecules have been formed, there may, by chance, be a slight excess of one particular enantiomer. Asymmetric autocatalysis can amplify this *slight* enantiomeric excess throughout the course of the reaction to afford much higher enantiomeric excess.²⁰ It should be highlighted that, without any external chiral influence promoting the formation of one particular enantiomer, the chance of spontaneous symmetry breaking inducing the enantioselective formation of either isomer is equal. Therefore, one reaction of this kind may product the (*R*)-enantiomer selectively, while repetition of the identical reaction may, by chance, produce the (*S*)-enantiomer selectively.

Since the addition of chiral substances can influence the enantiomeric outcome of chemical reactions, it seems reasonable that the intimate contact between chiral carbon nanotubes and adjacent reactant molecules or transition states could also influence the stereochemistry of reactions. The enantioselective amplification exhibited in certain

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asymmetric autocatalytic reactions makes these reactions particularly sensitive to chiral surfaces. Indeed, the asymmetric autocatalytic alkylation of pyrimidine-5-carbaldehyde with diisopropyl zinc, referred to as the Soai reaction, has been used to determine the chirality of saturated quaternary and tertiary hydrocarbons which were indistinguishable by traditional optical techniques.²¹ In this way, the asymmetric autocatalytic Soai reaction (**Scheme 5.2**) is an effective probe to investigate novel chiral auxiliaries and this makes such systems the ideal reactions with which to probe the effect of carbon nanotube helicity on chiral chemical reactions.



Scheme 5.2 The Soai reaction. The asymmetric autocatalytic alkylation of pyrimidine-5-carbaldehydes (1) by diisopropyl zinc to afford a chiral pyrimidyl alkanol (2).

5.2. Aim and Objectives

The aim of this study is to investigate the effect of carbon nanotube helicity on the stereochemical outcome of chiral chemical reactions. The effect of chiral single-walled carbon nanotubes on the relative formation of enantiomers in the autocatalytic Soai reaction will be investigated. These reactions (**Scheme 5.2**), developed by Kenso Soai and coworkers,²² involve the alkylation of pyrimidine-5-carbaldehydes with diisopropyl zinc. The asymmetric autocatalysis underpinning this reaction causes enantiomeric amplification, often leading to high enantiomeric excess. This study will attempt to rationalise any observed effect on the enantiomeric outcome of the reaction by consideration of the fundamental interactions between the carbon nanotube and the species involved in the reaction. For instance, it is possible that the chiral surface of the CNT may exhibit selective non-covalent interactions with one enantiomer of the autocatalyst, thus promoting enhanced enantioselectivity. In addition, more transient non-covalent interactions between the CNT

surface and either reactant may increase the local concentration of molecules, causing a discrepancy between relative reaction rates in bulk solution and in the vicinity of the carbon nanotube. Such a phenomenon could amplify the observed effect of any subtle influences of the carbon nanotube.

5.3. Results and Discussion

5.3.1. Method development

In order to investigate the effect of carbon nanotube helicity on chiral chemical reactions, a suitable reaction must be identified under conditions which exhibit high sensitivity to chiral surfaces. While the Soai reaction (**Scheme 5.2**) represents a suitable range of reactions for this investigation, the sensitivity of the reaction is highly dependent on the nature of the pyrimidine R group *para* to the aldehyde. Previous reports suggest that the tertiary-butyl alkynyl group, C₂^tBu, provides the highest level of enantioselective amplification^{23, 24} and this is expected to offer the highest sensitivity to chiral surfaces. In order to confirm this and identify the most suitable reactant for this study, preliminary reactivity studies were carried out for a small selection of pyrimidine-5-carbaldehydes and the enantiomeric excess was determined (**Table 5.1**).

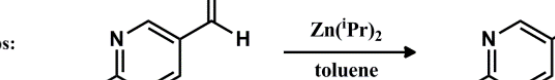
In a typical Soai alkylation reaction, enantiomeric amplification is encouraged by the stepwise addition of reactant and catalyst in increasing quantities. A solution of diisopropyl zinc (1 eq.) in toluene was added dropwise to pyrimidine-5-carbaldehyde (0.25 eq.) at 0°C and the mixture was stirred for 1 hour at 0°C followed by 23 hours at room temperature. Then, an additional portion of diisopropyl zinc (3 eq.), toluene and pyrimidine-5-carbaldehyde (**1**) (1 eq.) was added dropwise to the mixture at 0°C and stirred at 0°C for 1 hour, followed by 23 hours at room temperature. A third portion of diisopropyl zinc (3 eq.) and pyrimidine-5-carbaldehyde (**1**) (4 eq.) was then added dropwise to the reaction mixture and stirred at 0°C for 1 hour followed by 23 hours at room temperature. The

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reaction was then quenched with dilute hydrochloric acid and neutralised with an aqueous solution of sodium bicarbonate. The crude product was extracted with chloroform and dried over sodium sulfate. The solvent was removed at reduced pressure and the crude residue was purified by flash chromatography to yield pyrimidyl alkanol (**2**) as a pale microcrystalline solid. Yields ranged from 40 - 98% depending on the specific autocatalyst employed in the reaction and exhibited varying degrees of enantiomeric excess (**Table 5.1**). Specific rotation ($[\alpha]_D$), determined by polarimetry, and enantiomeric excess (ee), determined from high performance liquid chromatography (HPLC) using a chiral stationary phase, showed a strong correlation (see **Section 5.5.4** for details).

Table 5.1 The effect of pyrimidine-5-carbaldehyde R group on the enantioselectivity of the asymmetric autocatalytic alkylation reaction. The mean magnitude of specific rotation ($[\alpha]_D$) and mean enantiomeric excess (ee) were determined from a minimum of two experiments.

R groups:
a) H
b) Me
c) C₂^tBu



(1a-c)
(2a-c)

R group	$[\alpha]_D / ^\circ$	$ee / \%$
H (1a)	2.4 ± 1.1	0.2 ± 0.1
Me (1b)	1.0 ± 1.1	0.9 ± 0.8
C ₂ ^t Bu (1c)	31.3 ± 0.5	90.2 ± 2.0

The alkylation of pyrimidine-5-carbaldehyde with either hydrogen (**1a**) or methyl (**1b**) substituents, under the conditions of the autocatalytic Soai reaction, exhibited no clear enantiomeric excess ($<1\%$ ee). Although asymmetric autocatalysis occurs during these reactions, the racemic products formed catalyse the continued formation of each enantiomer in equal quantities affording an overall racemate as the reaction progresses. However, consistent with previous reports,^{23, 24} C₂^tBu-carbaldehyde (**1c**) exhibits spontaneous symmetry breaking which, coupled with a large enantioselective amplification *via* asymmetric autocatalysis, affords a product mixture with high enantiomeric excess ($ee = 90 \pm 2\%$). Mechanistic reasoning for this varied behaviour has seen little investigation and remains unknown.²³ It must be highlighted that, although this reaction reliably affords

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high enantioselectivity, the specific enantiomeric outcome of each reaction is governed by chance. While both the (*R*)- or (*S*)-enantiomer are equally likely to form selectively, it is the *magnitude* of the enantiomeric excess (*ee*) which gives a measure of the asymmetric autocatalysis and indicates the sensitivity of the reaction. The asymmetric autocatalytic Soai alkylation of C₂¹Bu-carbaldehyde (**1c**) is expected to be most sensitive to chiral induction and, therefore, the most suitable reaction to study the effect of carbon nanotube helicity on chiral chemical reactions.

In order to assess the effect of carbon nanotube helicity on the Soai reaction, a suitable carbon nanotube should be chosen. While the majority of carbon nanotubes are produced as a complex mixture of chiralities (**Figure 5.1**), single-walled carbon nanotubes enriched with chiral (6,5)-SWNT (*ca.* 50% abundance) are commercially available, as synthesised by the CoMoCAT process.²⁵ While the chirality of SWNT can be controlled to a certain extent, these SWNT presumably exist as a racemic mixture of both *P* and *M* enantiomers as no synthetic procedure has yet been developed to control carbon nanotube helicity. Thermogravimetric analysis (TGA) (**Figure 5.2a**) indicates that (6,5)-SWNT contain approximately 9% residual mass due to cobalt and molybdenum catalyst particles remaining from synthesis. In order to directly probe the influence of the carbon nanotube surface on the reaction, it was important to firstly ensure that no such impurity present in the carbon nanotube could affect the outcome of the Soai reaction. Analysis of the carbon nanotubes by transmission electron microscopy (TEM) (**Figure 5.2b-d**) showed that the catalyst particles were present as spherical nanoparticles (1 - 5 nm in diameter) completely encased in several layers of graphitic carbon and therefore inaccessible to the reactants of the Soai reaction.

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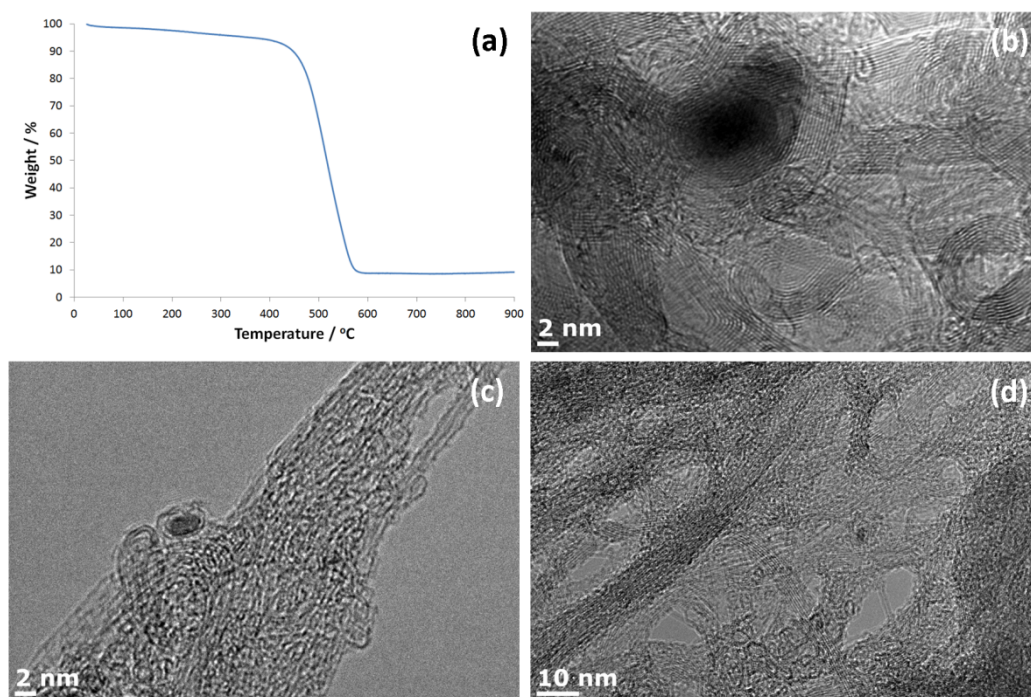


Figure 5.2 a) TGA and (b-d) TEM analysis of the as-received (6,5)-SWNT, indicating the presence of approximately 9% residual metal catalyst, encased within shells of graphitic carbon.

Despite TEM analysis indicating the presence of presumably inert catalyst particles, attempts were made to remove all accessible metal from the carbon nanotubes and highlight any potential influence on the reactivity of the Soai reaction from metallic catalyst particles. Control experiments (**Section 5.5.5**), whereby the accessible residual catalyst particles were removed by treatment with either hydrochloric or nitric acid, indicated that the presence of catalyst particles plays no role in the enantiomeric outcome of the Soai reaction.

5.3.2. The effect of SWNT on the Soai reaction

In order to assess the effect of carbon nanotube helicity on the asymmetric autocatalytic Soai alkylation reaction, a small quantity of (6,5)-SWNT (1.9 mg/ mmol autocatalyst) was added to a range of Soai reactions under standard conditions (see **Section 5.5.3**), and the enantiomeric excess was compared (**Table 5.2**).

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Table 5.2 The effect of (6,5)-SWNT (1.9 mg/ mmol autocatalyst) on the magnitude of specific rotation ($[\alpha]_D$) and enantiomeric excess (ee) of the Soai products. The mean $[\alpha]_D$ and ee values were obtained from a minimum of two experiments.

R	CNT	$[\alpha]_D / ^\circ$	$ee / \%$
H (1a)	none	2.4 ± 1.1	0.2 ± 0.1
H (1a)	(6,5)-SWNT	2.5 ± 0.3	0.3 ± 0.3
Me (1b)	none	1.0 ± 1.1	0.9 ± 0.8
Me (1b)	(6,5)-SWNT	0.6 ± 0.6	0.5 ± 0.3
C ₂ H ₅ (1c)	none	31.3 ± 0.5	90.2 ± 2.0
C ₂ H ₅ (1c)	(6,5)-SWNT	13.6 ± 7.7	37.1 ± 23.2

For carbaldehydes with hydrogen and methyl substituents (**1a** and **1b**), the presence of (6,5)-SWNT showed no effect on the enantiomeric excess of the Soai reaction within the error of the measurements. This is expected if the SWNT sample is presumed to exist as an equal mixture of both *P* and *M* enantiomers, because each nanotube enantiomer would influence the formation of either (*R*) or (*S*) optical isomers in equal proportions. If an excess of either *P* or *M* nanotubes were prevalent in the SWNT sample, desymmetrisation of the racemic Soai reaction could be expected, affording an increased enantiomeric excess in favour of either the (*R*) or (*S*)-optical isomer. However, due to the current practical limitations to carbon nanotube synthesis and processing, this hypothesis cannot be directly tested.

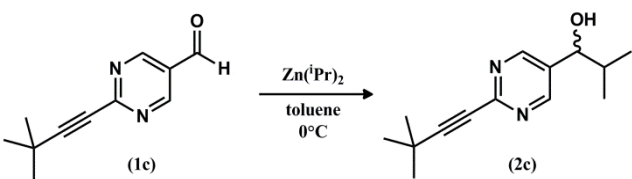
In contrast, the addition of (6,5)-SWNT to the Soai alkylation of carbaldehyde **1c**, which undergoes spontaneous symmetry breaking, caused a significant decrease in the enantiomeric excess of the alkanol product mixture (**2c**), reducing from 90 to 37%. This demonstrates, for the first time, that the helicity of carbon nanotubes can affect the chirality of chemical reactions. The racemic mixture of *P* and *M* nanotube enantiomers interferes with the spontaneous symmetry breaking and enantiomeric amplification phenomena to afford a more equal mixture of optical isomers. Whilst the symmetrisation of the products of the Soai

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reaction is often synthetically undesirable, these observations demonstrate the key principle that the helicity of carbon nanotubes can be used to control the enantiomeric outcome of chiral chemical reactions. However, in this case, the equal mixture of both *P* and *M* carbon nanotubes translates its racemic nature into the formation of racemic products, overcoming the effect of spontaneous symmetry breaking.

In order to confirm that the carbon nanotube surface was the cause of this change in enantiomeric excess, the proportion of carbon nanotubes was varied from 0 to 9.5 mg mmol⁻¹ (Table 5.3). If the SWNT surface causes the symmetrisation, a correlation should be observed between mass of carbon nanotube and enantiomeric excess.

Table 5.3 Effect of mass of (6,5)-SWNT (m_{SWNT} /mg mmol⁻¹ autocatalyst) on the enantiomeric excess (*ee*) of the products of the Soai reaction (2c). The mean $[\alpha]_{\text{D}}$ and $|ee|$ values were obtained from a minimum of two experiments.

		
m_{SWNT} /mg mmol ⁻¹	$[\alpha]_{\text{D}}$ / °	$ ee $ / %
0	31.3 ± 0.5	90.2 ± 2.0
1.0	28.2 ± 0.7	85.4 ± 1.5
1.9	13.6 ± 7.7	37.1 ± 23.2
3.8	5.4 ± 1.8	14.7 ± 4.9
5.7	2.5 ± 2.9	7.5 ± 8.0
9.5	1.9 ± 1.5	5.5 ± 4.9

An increased proportion of carbon nanotubes in this reaction showed an even greater effect on the enantiomeric excess of the products, reducing from 90 to 5.5% when 9.5 mg SWNT/ mmol autocatalyst was present. This demonstrates that, in sufficient quantities, a racemic mixture of *P* and *M* carbon nanotubes can completely desymmetrise the enantioselective Soai reaction within the error of the measurement (Figure 5.3).

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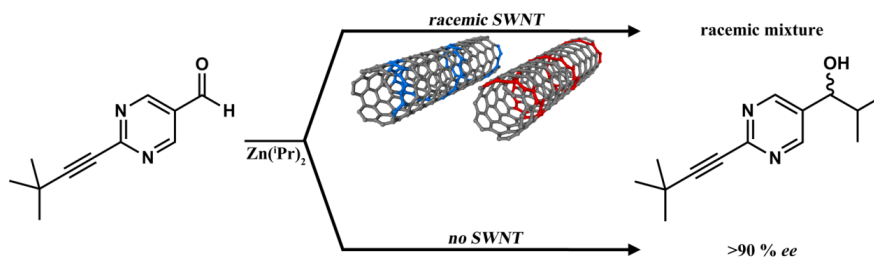


Figure 5.3 The effect of a racemic mixture of both *P* and *M* (6,5)-SWNT on the enantiomeric excess (*ee*) of products formed in the Soai reaction.

A strong correlation is evident between the extent of reaction symmetrisation and the amount of carbon nanotubes (**Figure 5.4**). Therefore, the greater the proportion of molecules able to react at the SWNT surface, the lower the enantiomeric excess of the resultant product mixture. This confirms that the observed symmetrisation of the Soai reaction is due to an interaction with the carbon nanotube surface.

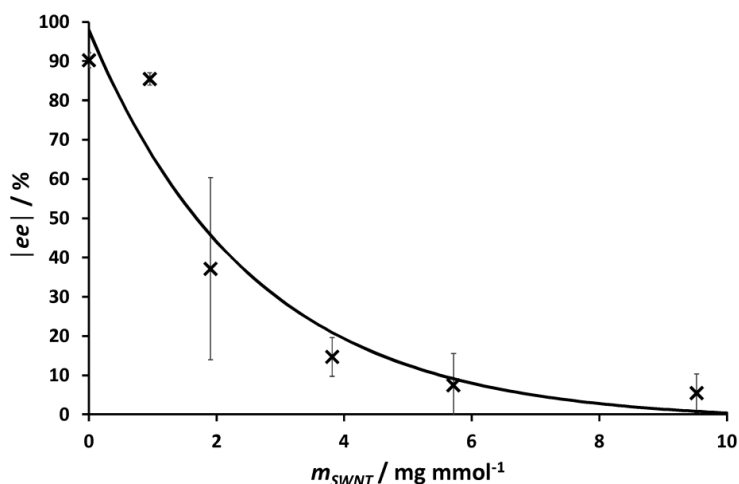


Figure 5.4 The effect of (6,5)-SWNT mass (m_{SWNT}) on the mean magnitude of enantiomeric excess ($|ee|$) for the products of the Soai reaction (**2c**). An increased proportion of SWNT mass, and thus SWNT surface area, invokes a greater degree of symmetrisation of the Soai reaction (*i.e.* lower *ee*). Vertical bars represent the standard deviation from repeated experiments.

5.3.3. Mechanistic investigation

In order to harness the potential power of carbon nanotube helicity for controlling chiral chemical reactions, the mechanism by which the SWNT surface influences the enantioselectivity of the Soai reaction must be understood.

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There are two potential mechanisms by which the surface of carbon nanotubes can influence the properties of this classic reaction (**Figure 5.5**). The first (**Figure 5.5a**) involves the non-covalent interaction of pyrimidine nitrogen atoms with the sp^2 -carbon atoms of the SWNT external surface, before subsequent reaction with $Zn(iPr)_2$. This mechanism draws parallels with a previous study reporting the use of chiral quartz crystal to template the enantiomeric distribution of Soai products,¹⁶ which postulated that the adsorption of pyrimidine-5-carbaldehyde onto the chiral facets of the inorganic crystals, prior to the reaction with $Zn(iPr)_2$, can trigger asymmetry in the autocatalytic reaction. An alternative mechanism is also postulated (**Figure 5.5b**), involving the co-ordination of $Zn(iPr)_2$ to the chiral SWNT exterior surface, followed by the reaction of pyrimidine-5-carbaldehyde (**1c**) with the $Zn(iPr)_2$ -SWNT complex.

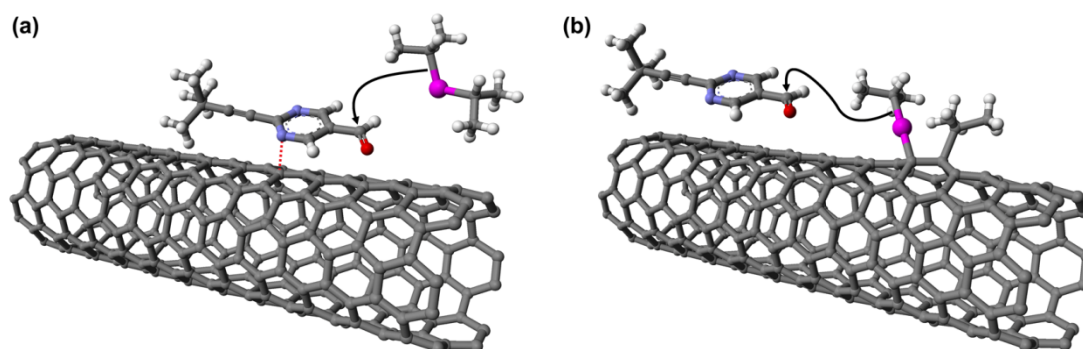


Figure 5.5 The proposed mechanisms for the Soai reaction in the presence of (6,5)-SWNT. (a) The non-covalent interaction of pyrimidine nitrogen atoms with the carbon nanotube, before subsequent attack of $Zn(iPr)_2$. (b) The co-ordination of achiral $Zn(iPr)_2$ to the chiral SWNT exterior surface followed by the reaction of pyrimidine-5-carbaldehyde (**1c**) with the $Zn(iPr)_2$ -SWNT complex.

Considering the first postulated mechanism (**Figure 5.5a**), the non-covalent interaction of nitrogen atoms with the external surface of carbon nanotubes is well-known.^{26, 27} In order to probe the strength of this interaction for the specific reactant and SWNT, adsorption measurements were completed (see **Section 5.5.6** for details). (6,5)-SWNT were added to a solution of pyrimidine-5-carbaldehyde (**1c**) in toluene and the combined suspension sonicated at room temperature for 1 hour. The black nanotube powder was removed from suspension by syringe filtration, and the solvent was removed at reduced pressure. The mass

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of pyrimidine-5-carbaldehyde (**1c**) recovered (88%) gives a measure of the mass adsorbed onto the carbon nanotubes by subtraction (12%). This indicates that 1 mg of (6,5)-SWNT can adsorb 1.2 μmol of carbaldehyde (**1c**) under these conditions, highlighting the strength of interaction between the reactant and the SWNT surface, and supporting the viability of the proposed mechanism.

Both postulated mechanisms could account for the direct translation of carbon nanotube helicity (present as a racemic mixture in these experiments) into the chirality of the Soai products. However, it may be possible to distinguish the most likely process by considering the differences between the two proposed pathways. One such difference is that the co-ordination of $\text{Zn}(\text{iPr})_2$ to carbon nanotubes (**Figure 5.5b**) must involve the transformation of SWNT sp^2 -carbon atoms into sp^3 , analogous to SWNT alkylation with organometallic reagents.^{28, 29} On the contrary, the interaction of the pyrimidine-5-carbaldehyde with the SWNT (**Figure 5.5a**) is non-covalent and hence, the covalent structure of the nanotube remains unaffected. Therefore, complementary electron microscopy and spectroscopy were conducted on the SWNT recovered from the reaction in order to determine which of these was the case and thus, gain mechanistic insight into the process (**Figure 5.6**). Comparison of the peak intensity for the D and G bands from Raman spectroscopy of the SWNT gives a measure of disorder in a carbon nanotube sample. If co-ordination of the Zn species to the CNT sidewall occurs, an increase in this ratio is expected as the proportion of sp^3 -carbon atoms within the graphitic lattice increases. In addition, transmission electron microscopy (TEM) and energy dispersive X-ray (EDX) spectroscopy can characterise the structure of the carbon nanotubes subsequent to the reaction to determine whether Zn co-ordination has occurred.

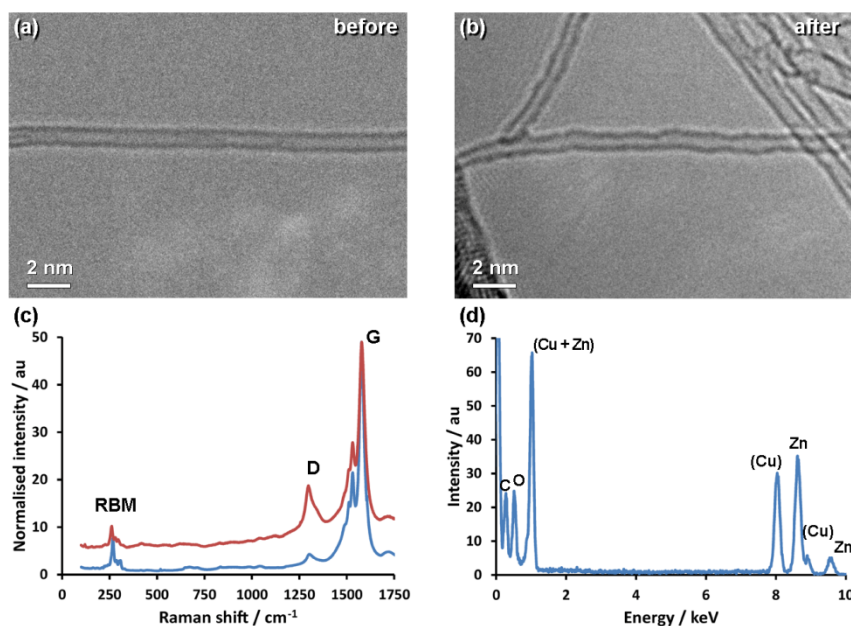


Figure 5.6 (6,5)-SWNT Characterisation both prior, and subsequent, to the Soai reaction. Transmission electron micrographs of (6,5)-SWNT (a) as received and (b) subsequent to the Soai reaction indicate a clear increase in sidewall corrugation. (c) Raman spectra of the SWNT before (blue) and after (red) the reaction indicate an increase in $I_D:I_G$ associated with an increase in lattice disorder due to the conversion of sp^2 -carbon to sp^3 . (d) Energy dispersive X-ray (EDX) spectroscopy of the SWNT subsequent to the reaction confirms the presence of Zn in the nanotube sample. Cu peaks are from the sample support and TEM assembly.

Raman spectroscopy (**Figure 5.6c**) indicates a notable increase in $I_D:I_G$ from 0.10 to 0.33, consistent with the covalent functionalisation of the CNT. TEM (**Figure 5.6a-b**) shows that the SWNT are more dispersed (less bundled) and contain more surface structural defects after the reaction. EDX spectroscopy (**Figure 5.6d**) confirms the presence of Zn dispersed on the SWNT surface at both the atomic scale and as ZnO nanoparticles formed *in situ* during the Soai reaction (**Figure 5.7**).

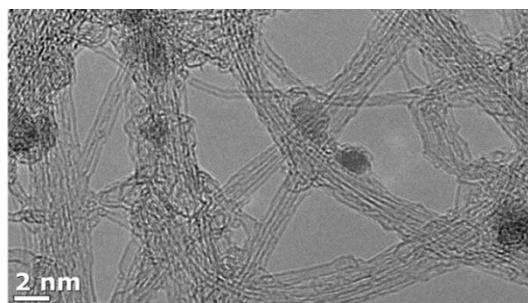


Figure 5.7 Transmission electron micrographs of 6,5-SWNT subsequent to the Soai reaction, showing the morphology of the ZnO nanoparticles formed *in situ*, in support of the corresponding EDX spectroscopy.

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Similar changes in SWNT properties were observed following a control reaction in the absence of the carbaldehyde. Each of these observations is consistent with the formation of a $\text{Zn}(\text{iPr})_2$ -SWNT complex during the reaction (**Figure 5.5b**). Therefore, it is postulated that the Zn species co-ordinates to the SWNT surface and the reaction of the carbaldehyde with the intermediate $\text{Zn}(\text{iPr})_2$ -SWNT complex acts to translate the axial chirality of the carbon nanotube into the enantioselective formation of chiral products. However, the racemic nature of the SWNT in these reactions invokes the formation of a racemic mixture of enantiomeric products, counteracting the spontaneous symmetry breaking and enantiomeric amplification of the Soai reaction.

5.3.3.1. Investigation of CNT surface curvature: SWNT vs MWNT

Evidently, the external surface of the carbon nanotube is important in influencing the enantiomeric outcome of the Soai reaction. As both reactivity and molecular interactions with carbon nanotubes are typically highly dependent on carbon nanotube diameter,³⁰⁻³³ the effect of narrow SWNT was compared to much wider MWNT to better understand the underlying surface interactions involved in this reaction. While MWNT possess the same *P* and *M* enantiomers as SWNT, the diameter is significantly larger. Therefore, MWNT, exhibiting an average external diameter of 14 ($\pm$ 6) nm, represent a significantly less curved sp^2 -carbon surface than (6,5)-SWNT with a diameter of 0.7 nm. A reduction in the surface curvature consequently reduces the sp^2 -carbon pyramidalisation angle and thus, the availability of the CNT p_z orbitals for potential bonding with $\text{Zn}(\text{iPr})_2$. Therefore, it is hypothesised that the influence of MWNT on the enantioselectivity of the Soai reaction will be less pronounced in comparison to SWNT. The addition of MWNT to the Soai reaction of carbaldehyde (**1c**) under the standard conditions described for SWNT allows direct comparison of the influence of these two carbon nanostructures on the outcome of this chiral reaction (**Table 5.4**).

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Table 5.4 The effect of carbon nanotubes (9.5 mg/ mmol autocatalyst) on the enantiomeric excess (*ee*) of the products of the Soai reaction (**2c**). The mean $[\alpha]_D$ and $|ee|$ values were obtained from a minimum of two experiments.

Carbon nanotube	$[\alpha]_D / ^\circ$	$ ee / \%$
none	31.3 ± 0.5	90.2 ± 2.0
MWNT	30.4 ± 1.8	82.9 ± 2.5
(6,5)-SWNT	1.9 ± 1.5	5.5 ± 4.9

Similar to previous observations for (6,5)-SWNT, the presence of MWNT acts to reduce the enantiomeric excess of the product mixture. Clearly, the racemic mixture of both *P* and *M* MWNT acts to translate its racemic nature into the products of the reaction, counteracting the effect of spontaneous symmetry breaking and reducing the enantioselectivity of the reaction. However, as hypothesised, the reduction of enantiomeric excess to 83% afforded by the presence of MWNT is much less pronounced than the near complete symmetrisation observed when SWNT are present in equal quantities. The precise reason behind this observation remains slightly ambiguous because the increased diameter of MWNT reduces not only the reactivity of the surface towards $\text{Zn}(\text{iPr})_2$, due to a substantial reduction in pyramidalisation angle, but also the surface area per unit mass, decreasing the available carbon surface with which the reaction species may interact. In support of this, the extent of MWNT alkylation and Zn complexation during the course of the reaction (**Figure 5.9**), while measurable, was significantly reduced in comparison to that observed for SWNT (**Figure 5.8**).

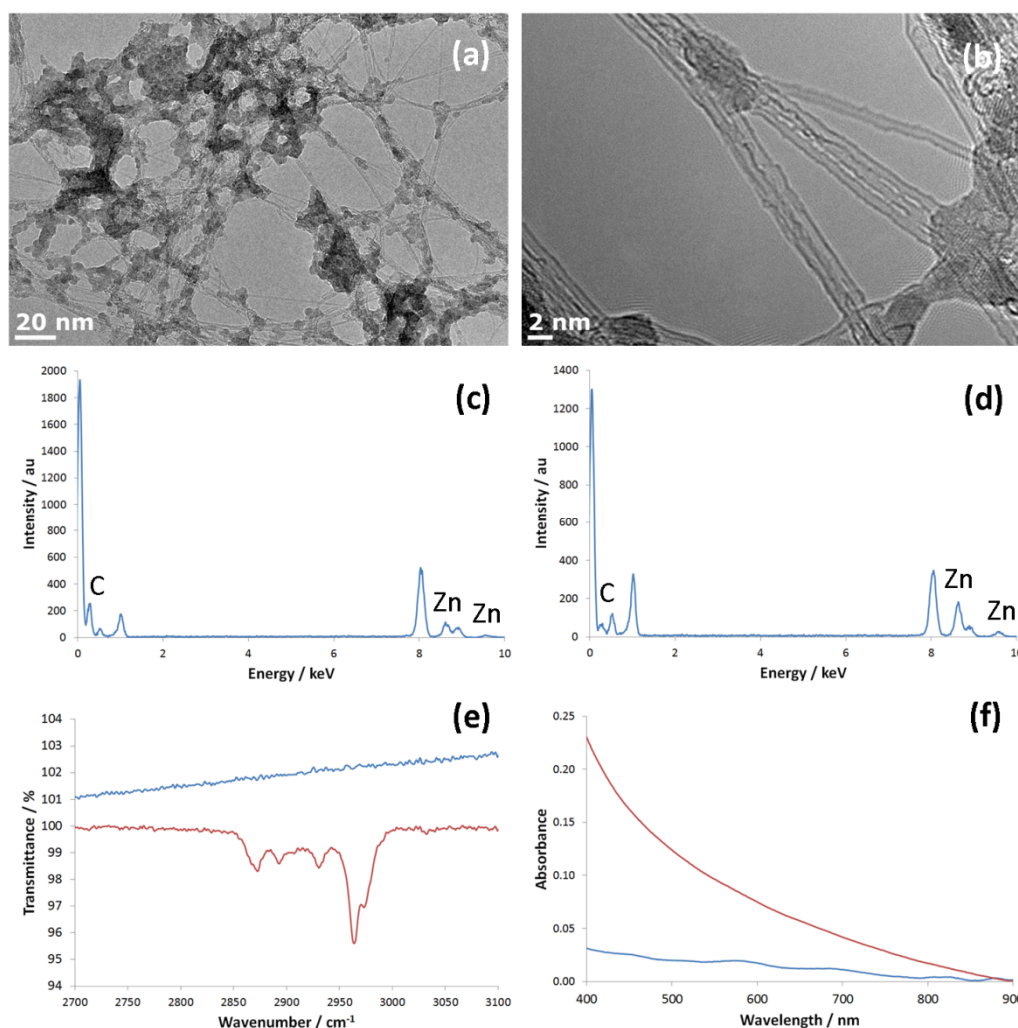


Figure 5.8 (a-b) TEM and (c-d) EDX spectroscopy analyses of the SWNT isolated from the reaction mixture subsequent to the Soai reaction and comparative (e) IR and (f) UV-vis spectroscopy studies of SWNT before (blue) and after (red) autocatalysis. TEM (a-b) shows the nanotubes to be highly corrugated, existing in moderately sized bundles (significantly smaller than those of the as-received sample), consistent with alkylation and the consequent accumulation of negative charge. The local EDX spectrum (c) of a seemingly clean bundle of nanotubes (*i.e.* no visible nanoparticles), shows the presence of Zn at the atomic level with a C:Zn ratio of 1:0.06. The global EDX spectrum (d) of a bundle of nanotubes with ZnO nanoparticles visibly adsorbed shows that the mean C:Zn ratio is 1:0.53. The presence of copper peaks is associated with the TEM column assembly. Comparison of the ATR-IR spectra (e) of the as-received SWNT (blue) and the isolated nanotubes after the Soai reaction (red) shows the introduction of numerous aliphatic C-H stretching vibrations in the region 3000-2850 cm^{-1} , consistent with nanotube alkylation. Comparison of the UV-vis spectra (f) of aqueous solutions of nanotubes before (blue) and after (red) the Soai reaction shows the loss of characteristic broad absorbances in the visible region, consistent with perturbation of π -bands as a result of nanotube functionalisation.

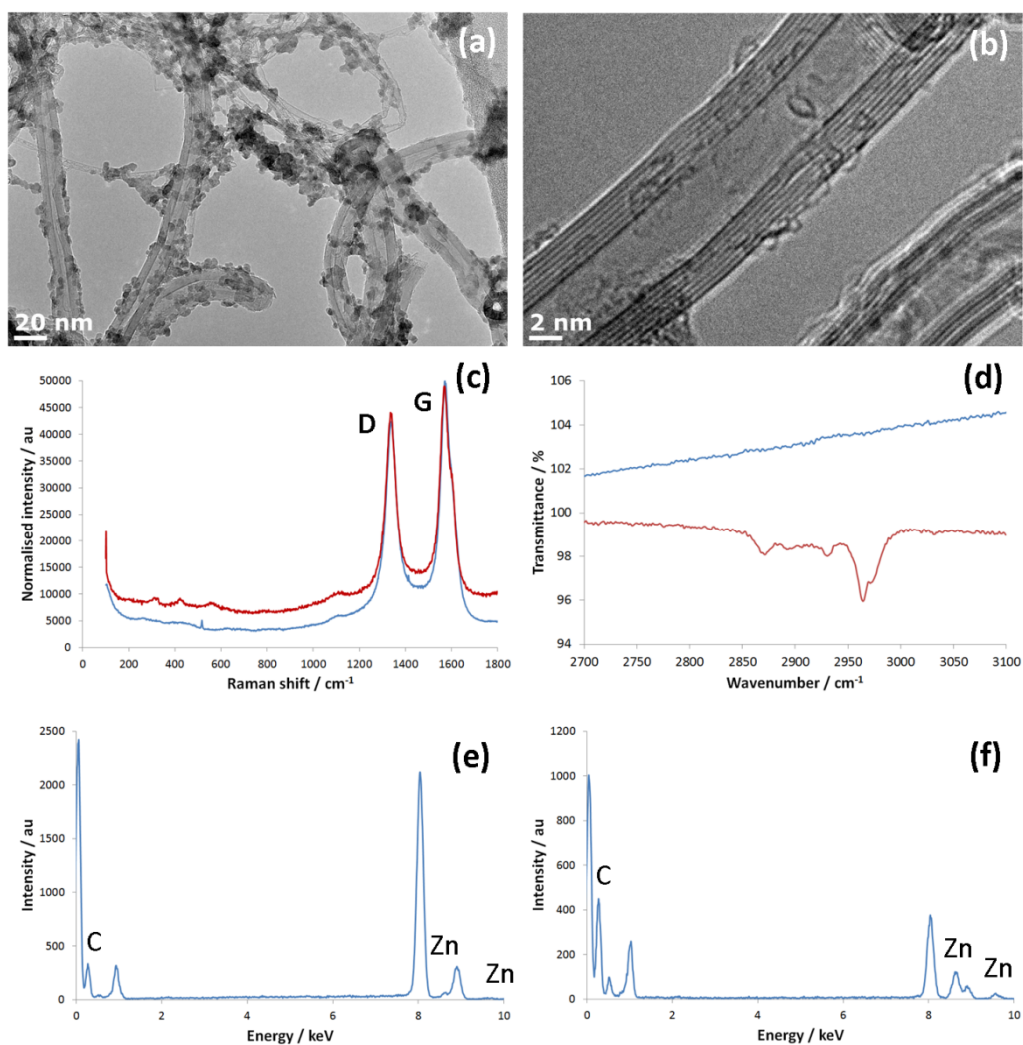


Figure 5.9 (a-b) TEM, (c) Raman, (d) IR and (e-f) EDX spectroscopic analysis of MWNT isolated from the reaction mixture subsequent to the Soai reaction. TEM analysis of MWNT (a-b) after the Soai reaction shows no evidence of the sidewall corrugation associated with significant alkylation. A small change in hybridisation was observed using Raman spectroscopy (c), determined by an increase in the I_D/I_G ratio from 0.85 to 0.91, before (blue) and after (red) the Soai reaction. The presence of aliphatic C-H stretching vibrations in the IR spectra (d) confirm the small, but measurable, alkylation of nanotubes. The local EDX spectrum (e) shows the presence of zinc at the atomic level, however the C:Zn ratio of 1:0.02 is considerably lower than that of the corresponding SWNT analogue. By analogy, the amount of Zn present in the global EDX spectrum (f) is also considerably lower than for SWNT, with C:Zn = 1:0.17. No significant changes in the UV-vis spectra of aqueous solutions of MWNT before and after the Soai reaction were observed.

5.4. Conclusions

This study has demonstrated, on a fundamental level, that the intrinsic helicity of carbon nanotubes has an effect on the formation of chiral molecules and can be translated into the products of the autocatalytic Soai reaction. Since carbon nanotubes exist as a racemic mixture of *P* and *M* enantiomers, their presence has a symmetrising effect on the chiral reaction explored. An enantioselective autocatalytic Soai reaction which undergoes spontaneous symmetry breaking to afford a 90% *ee* becomes effectively racemic upon the addition of (6,5)-SWNT in sufficient quantities, affording an *ee* of 5.5±5.0%. The importance of the carbon nanotube surface in this observation is highlighted by a clear correlation between the mass of carbon nanotubes and the extent of symmetrisation.

The nanotube surface forms an intermediate complex with the organometallic reagent which, in turn, reacts with the pyrimidine-5-carbaldehyde transposing the axial chirality of the SWNT into the formation of a chiral alkanol. This postulated mechanism is supported by an increase in $I_D:I_G$ from Raman spectroscopy, the detection of Zn remaining on the CNT by EDX spectroscopy and the corrugation of the CNT sidewall as evident from electron microscopy. In support of this mechanism, the presence of MWNT in the reaction has a similar, yet significantly reduced, symmetrising effect on the Soai reaction. This is to be expected as the reduced curvature of the wider MWNT is less reactive toward $Zn(iPr)_2$ functionalisation and thus, the organometallic intermediate forms less readily in comparison to much narrower SWNT.

This study is the first demonstration of the principle that the chirality of nanoscale carbon surfaces can be harnessed to control the chirality of products in organic chemical reactions. While this work established this principle by the symmetrisation of a chiral reaction, the logical progression is to induce chirality in a previously achiral chemical reaction using chemically and enantiomerically pure *P* or *M* carbon nanotubes.

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Methods of separation by helicity to prepare enantiomerically enriched carbon nanotubes are currently being developed.³⁴ Techniques such as density gradient ultracentrifugation,³⁵ where carbon nanotube enantiomers are separated by extensive centrifugation and by harnessing subtly different interactions with a chiral surfactant,³⁶⁻³⁹ have proven reasonably effective on a very small scale. In addition to the scale limitations in these procedures, caution must be exercised when considering such enantiomerically enriched CNT for applications to chiral chemical reactions, because the procedures inevitably leave some chiral surfactant impurities on the carbon nanotubes. These chiral impurities will interfere with the intended chiral reaction and hence, it will be difficult to unambiguously assign any altered reactivity directly to the presence of CNT. Therefore, the bulk scale use of chemically and enantiomerically pure carbon nanotubes to induce chirality in a previously symmetric reaction is not currently viable.

In light of this work, an investigation has since demonstrated that enantiomerically pure SWNT analogues can induce asymmetry in the Soai reaction.⁴⁰ While the production of enantiomerically pure CNT on the bulk scale is not viable, Hitosugi *et al.* recently synthesised finite polyaromatic hydrocarbon analogues of narrow carbon nanotubes and investigated their effect on the Soai reaction. It was found that the enantiomerically pure **P** and **M** structures induced the enantioselective formation of the alkanol product with corresponding (*R*) and (*S*) chirality respectively with >99.5% *ee* (**Figure 5.10**). This result holds great promise for the future application of enantiomerically pure carbon nanotubes to asymmetric synthesis.

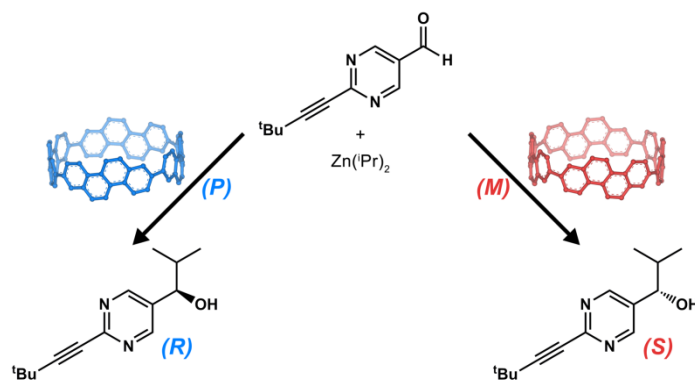


Figure 5.10 The effect of both *P* (blue) and *M* (red) enantiomers of (12,8)-[4]cyclo-2,8-chrysenylene,⁴¹⁻⁴³ on the outcome of the Soai reaction of carbaldehyde **1c**. The chrysenylene enantiomers act as finite length analogues of chiral carbon nanotubes with defined helicity and lead to the enantioselective formation of the alkanol product of the corresponding chirality, *i.e.* *P* and *M* helicity initiators afford (*R*) and (*S*) alkanol enantiomers respectively.

5.5. Experimental

5.5.1. General

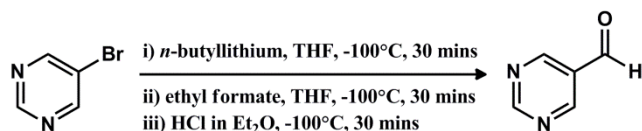
All reagents were purchased from Sigma-Aldrich, UK and used without further purification unless otherwise specified. Carbon nanotubes (6,5)-SWNT (Lot no. MKBF6413V) and PD30L520 MWNT (Lot no. 71310) were purchased from Sigma Aldrich, UK and Nanolab Inc., MA, USA respectively. All glassware was cleaned with a mixture of hydrochloric and nitric acid (3:1 v/v, 'aqua regia') and rinsed thoroughly with deionised water, cleaned with potassium hydroxide in isopropyl alcohol and finally rinsed thoroughly with deionised water to avoid contamination with chiral impurities. Water was purified ($> 18 \text{ M}\Omega \text{ cm}$) using a Barnstead NANOPure II system and toluene was distilled over calcium hydride. ^1H and ^{13}C NMR spectra were obtained using a Bruker DPX-300 spectrometer (300.13 and 75.48 MHz, respectively) at 293K using CDCl_3 as a solvent. Attenuated total reflectance infra-red (IR) spectra were measured by Dr. Graham Rance using a Nicolet 380 FT-IR spectrometer (spectral resolution of 0.9 cm^{-1}) over a range of $4000\text{--}600 \text{ cm}^{-1}$. UV-vis spectra were recorded in solution using 1 cm quartz cuvettes with a Perkin-Elmer Lambda 25 UV-vis spectrophotometer at a scan rate of 480 nm min^{-1} over a range of 400–900 nm. Mass spectrometry was conducted on a Bruker Apex IV using ESI in positive mode. Specific

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rotation was determined by polarimetry using a Bellingham Stanley ADP440 polarimeter at 22°C by Dr. Graham Rance. Samples were made up to a concentration of 1 g 100 mL⁻¹ in chloroform. Enantiomeric excess was calculated by HPLC analysis on a Shimadzu SPD-M20A using a chiral stationary phase by Dr. Thomas Chamberlain (Chiralcel OD-H: 4 x 250 mm, 254 nm UV detector, eluent is *n*-hexane/2-propanol = 19/1, flow rate is 1.0 mL min⁻¹). Retention times of 8.33, 9.85, 9.40, 10.10, 11.10 and 16.27 minutes were recorded for *S*-**2a**, *R*-**2a**, *S*-**2b**, *R*-**2b**, *S*-**2c** and *R*-**2c** respectively (see **Section 5.5.4**). Mean values of specific rotation and enantiomeric excess were obtained from a minimum of two experiments. Thermogravimetric analysis was performed using a TA-instruments SDT Q600 under a flow of air at a rate of 90 mL min⁻¹ at a heating rate of 10°C min⁻¹ from room temperature to 1000°C. Raman spectroscopy was conducted by Dr. Graham Rance using a HoribaJY LabRAM HR spectrometer (spectral resolution = 1.1 cm⁻¹/ pixel) with a laser wavelength of 532 nm. Samples were dropcast from methanolic solutions onto Si(100) wafers and a minimum of five spectra recorded from different areas of the sample. The spectra shown are representative of the averaged spectra. Transmission electron microscopy was performed by Professor Andrei Khlobystov using a JEOL 2100F TEM (field emission gun source, information limit < 0.19 nm) at room temperature. Energy dispersive X-ray spectroscopy was performed by Professor Andrei Khlobystov using an Oxford Instruments INCA 560 X-ray microanalysis system. Samples were prepared *via* drop-drying methanolic solutions onto copper grid mounted “lacey” carbon films. Spectra were recorded both “locally” (measuring a clean bundle of nanotubes suspended over a hole in the ‘lacey’ carbon film and, therefore, avoiding a contribution from the amorphous carbon support film) and “globally” (measuring a few μm² area) from a variety of areas of the sample and therefore permitting more quantitative analysis. The values quoted represent an average of at least three measurements.

5.5.2. Synthesis and characterisation of pyrimidine-5-carbaldehydes

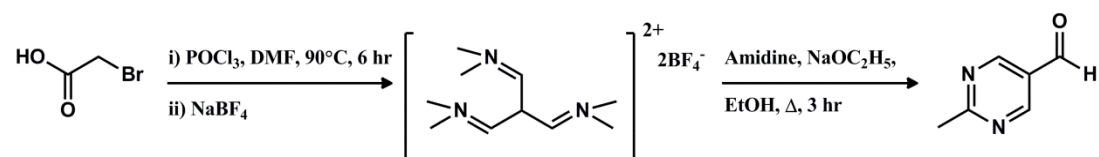
5.5.2.1. Synthesis and characterisation of 1a (R = H)



Synthetic procedure from literature protocol,⁴⁴ 51% yield.

1a pyrimidine-5-carbaldehyde: **R_f** 0.38 (diethyl ether); **m.p.** 39-41°C (lit. 38-41°C);⁴⁵ **¹H NMR** δ_H /ppm 9.87 (s, 1H), 9.01 (s, 1H), 8.86 (s, 2H); **¹³C NMR** δ_C /ppm 189.5, 161.8, 157.7, 128.5; **HRMS** m/z calculated for C₅H₅N₂O 109.0402, found 109.0336 [M+H]⁺.

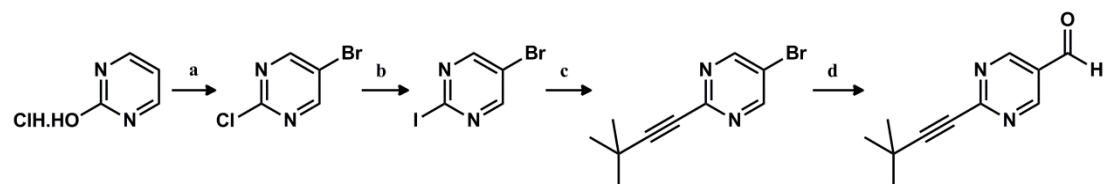
5.5.2.2. Synthesis and characterisation of 1b (R = Me)



Synthetic procedure from literature protocol,⁴⁴ 48 and 40% consecutive yields.

1b 2-methylpyrimidine-5-carbaldehyde: **R_f** 0.33 (ethyl acetate / hexane, 4 / 1); **m.p.** 65-68°C (lit. 68-69°C);⁴⁶ **¹H NMR** δ_H /ppm 10.13 (s, 1H), 9.10 (s, 2H), 2.87 (s, 3H); **¹³C NMR** δ_C /ppm 188.9, 173.2, 158.2, 29.7, 26.6; **HRMS** m/z calculated for C₆H₇N₂O 123.0558, found 123.0522 [M+H]⁺.

5.5.2.3. Synthesis and characterisation of 1c (R = C₂^tBu)



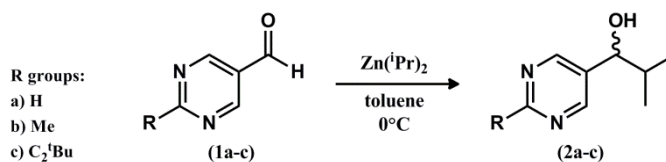
Synthesis of **1c**. (a) (i) Br₂, H₂O, 25°C, 1 hr, (ii) phosphorus oxychloride, dimethylaniline, Δ , 4 hr (32%);⁴⁷ (b) hydrogen iodide, DCM, 0°C, 5 hrs (85%);⁴⁸ (c) 3,3-dimethylbut-1-yne,

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$\text{PdCl}_2(\text{PPh}_3)_2$, CuI, dipea, toluene, 50°C , 16 hrs (99%),⁴⁹ (**d**) (i) *n*-butyllithium, THF, -100°C , 30 mins, (ii) ethyl formate, THF, -100°C , 30 mins, (iii) HCl in Et_2O , -100°C , 30 mins (54%).⁴⁹

1c 2-(3,3-dimethyl-1-butynyl)pyrimidine-5-carbaldehyde: R_f 0.30 (hexane / acetone, 6 / 1); **m.p.** $105\text{--}107^\circ\text{C}$; ^1H NMR δ_H/ppm 10.13 (s, 1H), 9.11 (s, 2H), 1.40 (s, 9H); ^{13}C NMR δ_C/ppm 188.3, 158.2, 156.4, 126.3, 103.1, 79.0, 30.2, 28.2; **HRMS** m/z calculated for $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}$ 189.1028, found 189.1058 $[\text{M}+\text{H}]^+$.

5.5.3. Asymmetric autocatalytic Soai alkylation reaction



To a mixture of the pyrimidine-5-carbaldehyde (**1**) (0.025 mmol) and carbon nanotubes (0-10 mg) at 0°C , was added, dropwise over the course of 15 minutes, a solution of diisopropyl zinc (0.1 mL, 1 mol dm^{-3} in toluene, 0.1 mmol) and the combined mixture was stirred at 0°C for 1 hour, followed by 23 hours at room temperature. To this was added dropwise a solution of diisopropyl zinc (0.3 mL, 1 mol dm^{-3} in toluene, 0.3 mmol) and toluene (0.75 mL) followed by the dropwise addition over 15 minutes of pyrimidine-5-carbaldehyde (**1**) (0.1 mmol) in toluene (0.75 mL) at 0°C . The mixture was stirred at 0°C for 1 hour, followed by 23 hours at room temperature. To this was added a solution of diisopropyl zinc (0.8 mL, 1 mol dm^{-3} in toluene, 0.8 mmol) and toluene (5 mL), followed by the dropwise addition over 15 minutes of pyrimidine-5-carbaldehyde (**1**) (0.4 mmol) in toluene (2 mL) and the combined mixture was stirred at 0°C for 1 hour and at room temperature for 23 hours. The black carbon nanotube solid was removed by syringe filtration (0.45 μm PTFE membrane). The reaction was quenched by dilute aqueous hydrochloric acid (10 mL, 1M), neutralised by an aqueous sodium bicarbonate solution (saturated). The crude product was extracted with chloroform and dried over sodium sulfate. The solvent was

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removed *in vacuo* and the crude residue was purified by flash chromatography (petroleum ether/ethyl acetate, 7/3) to yield pyrimidyl alkanol (**2**) as a pale microcrystalline solid. Yields ranged from 40 - 98% depending on the specific autocatalyst employed in the reaction. Specific rotation was determined by polarimetry and enantiomeric excess was calculated from HPLC.

2a 2-methyl-1-(pyrimidin-5-yl)propan-1-ol: **R_f** 0.29 (ethyl acetate); **¹H NMR** δ_H /ppm 9.03 (s, 1H), 8.65 (s, 2H), 4.48 (d, 1H, *J* = 6.0 Hz), 3.48 (br s, 1H), 1.97 (m, 1H), 0.95 (d, 3H, *J* = 6.9 Hz), 0.86 (d, 3H, *J* = 6.9 Hz); **¹³C NMR** δ_C /ppm 157.5, 155.3, 136.6, 75.1, 45.8, 35.2, 18.5, 17.5; **HRMS** *m/z* calculated for C₈H₁₃N₂O 153.1028, found 153.1018 [M+H]⁺.

2b 2-methyl-1-(2-methylpyrimidin-5-yl)propan-1-ol: **R_f** 0.16 (ethyl acetate); **¹H NMR** δ_H /ppm 8.55 (s, 2H), 4.44 (d, 1H, *J* = 6.3 Hz), 2.95 (br s, 1H), 2.69 (s, 3H), 1.97 (m, 1H), 0.97 (d, 3H, *J* = 6.6 Hz), 0.86 (d, 3H, *J* = 6.6 Hz); **¹³C NMR** δ_C /ppm 167.0, 155.5, 133.0, 75.3, 45.8, 35.1, 25.5, 18.4, 17.7; **HRMS** *m/z* calculated for C₉H₁₅N₂O 167.1184, found 167.1181 [M+H]⁺.

2c 2-methyl-1-(2-(3,3-dimethylbut-1-ynyl)pyrimidin-5-yl)propan-1-ol: **R_f** 0.26 (hexane / ethyl acetate, 7 / 3); **¹H NMR** δ_H /ppm 8.59 (s, 2H), 4.50 (d, 1H, *J* = 6.0 Hz), 2.77 (br s, 1H), 1.96 (m, 1H), 1.39 (s, 9H), 0.94 (d, 3H, *J* = 6.6 Hz), 0.86 (d, 3H, *J* = 6.8 Hz); **¹³C NMR** δ_C /ppm 155.6, 152.1, 134.33, 97.9, 78.4, 75.2, 35.2, 30.4, 27.9, 18.4, 17.4; **HRMS** *m/z* calculated for C₁₄H₂₁N₂O 233.1654, found 233.1653 [M+H]⁺.

5.5.4. HPLC and polarimetry analyses

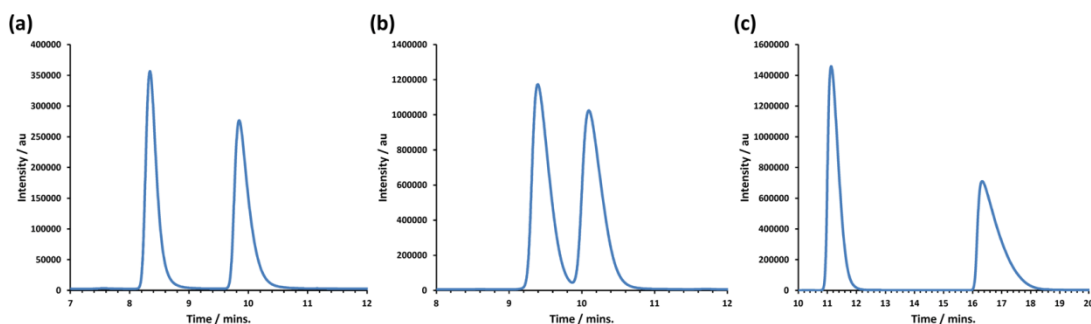


Figure 5.11 Typical HPLC traces for the products of the Soai reaction. (a) **2a**, where R = H; (b) **2b**, where R = Me; (c) **2c**, where R = C₂^tBu. In each case, the (*S*)- enantiomer has the lower retention time. Retention times /mins: *S*-**2a** (8.33), *R*-**2a** (9.85), *S*-**2b** (9.40), *R*-**2b** (10.10), *S*-**2c** (11.10) and *R*-**2c** (16.27).

Enantiomeric excess calculated from HPLC showed strong correlation with the specific rotation determined from polarimetry (**Figure 5.12**).

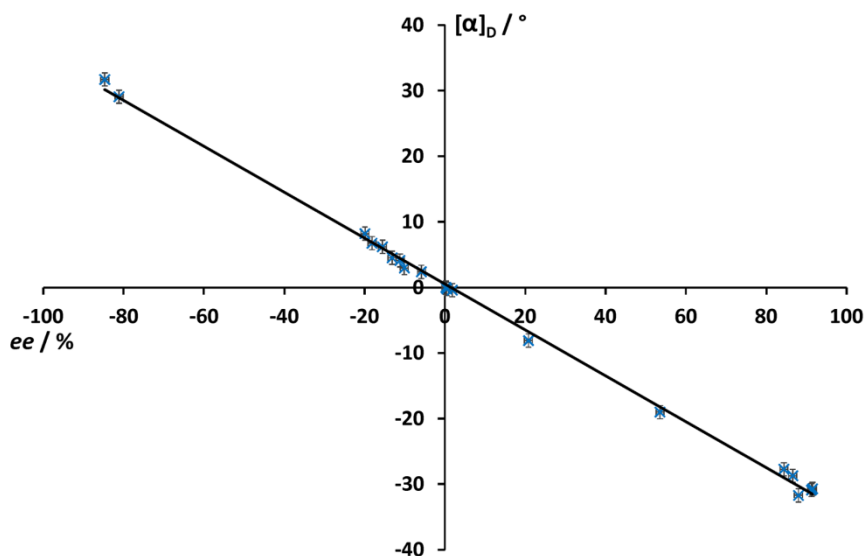


Figure 5.12 Correlation between enantiomeric excess (*ee*), determined from HPLC analysis, and specific rotation ([α]_D), determined from polarimetry, for **2c** where R = C₂^tBu. [α]_D = -0.35*ee*, R² = 0.99.

5.5.5. The effect of residual CNT metallic catalyst on the Soai reaction

Despite TEM and thermogravimetric analysis indicating the presence of presumably inert catalyst particles (**Figure 5.2**), attempts were made to remove all remaining metal from the carbon nanotubes. As-received SWNT were compared, by TGA and Raman spectroscopy, to those purified by two well-established literature protocols and the effect of each material on

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the Soai reaction was determined (under standard conditions) to highlight any potential influence on reactivity due to the metallic catalysts (**Table 5.5**). Procedure A, involves treatment with hydrochloric acid at room temperature to remove Co and procedure B comprised refluxing nitric acid to remove both Co and Mo.

Procedure A: To SWNT (20 mg, 6,5-SWNT) was added concentrated hydrochloric acid (20 mL) and the combined black suspension was sonicated at room temperature for 1 hr. The suspension was then poured into deionised water (200 mL) and the black solid recovered by vacuum filtration (0.2 μ m PTFE membrane), washed with sodium hydroxide (50 mL, 1M), hydrochloric acid (50 mL, 1M), deionised water (50 mL) and finally acetone (50 mL), sucked dry and further dried at room temperature over phosphorus pentoxide under vacuum.

Procedure B: To SWNT (20 mg, 6,5-SWNT) was added concentrated nitric acid (20 mL) and the combined black suspension sonicated at room temperature for 15 min and then heated at reflux for 1 hr. The suspension was then poured into deionised water (200 mL) and the black solid recovered by vacuum filtration (0.2 μ m PTFE membrane), washed with sodium hydroxide (50 mL, 1M), hydrochloric acid (50 mL, 1M), deionised water (50 mL) and finally acetone (50 mL), sucked dry and further dried at room temperature over phosphorus pentoxide under vacuum.

Table 5.5 The effect of CNT treatment procedures on $I_D:I_G$, as determined by Raman spectroscopy, residual metal mass (**M**) and the enantiomeric excess of products of the Soai reaction.

SWNT	$I_D:I_G$	M / wt. %	$ [\alpha]_D $ / °	$ ee $ / %
as-received	0.11	9.4	1.9 ± 1.5	5.5 ± 4.9
Procedure A	0.12	9.0	1.1	3.0
Procedure B	0.65	5.9	1.4	1.9

Procedure A induced no change to the residual metal content (within the error of the measurement), confirming that all cobalt metal is encased in graphitic carbon. As expected, there was no change to the enantiomeric outcome of the Soai reaction using this SWNT sample. Procedure B was sufficiently vigorous to chemically etch the graphitic carbon and

5. Chiral chemical reactions on carbon nanotubes

partially remove metallic particles, as evidenced by the decrease in residual metal content and considerable increase in $I_D:I_G$ relative to the as-received SWNT. However, no change to the *ee* of the Soai reaction was observed using these SWNT. Therefore, it is concluded that the presence of metallic catalysts has no effect on the autocatalytic reactions studied.

5.5.6. Adsorption of pyrimidine-5-carbaldehyde (**1c**) on CNT

Experimental procedure

To **1c** (10 mg) in toluene (10 mL) was added carbon nanotubes (5 mg) and the combined suspension sonicated at room temperature for 1 hour. The black nanotube solid was removed by syringe filtration (0.45 μ m PTFE membrane), the solvent removed *in vacuo* and the mass of recovered **1c** recorded (**Table 5.6**).

Table 5.6 The affinity of carbon nanotubes for pyrimidine-5-carbaldehyde (**1c**).

Carbon nanotube	1c recovered /mg	1c adsorbed /mg	Affinity / μ mol mg ⁻¹
(6,5)-SWNT	8.84	1.16	1.2
MWNT	6.11	3.89	4.1

Repeat experiments were within 5% of the original values displayed.

5.5.7. Isolation and characterisation of CNT after the Soai reaction

Both SWNT and MWNT were isolated subsequent to the reaction of carbaldehyde (**1c**) and characterised by complementary microscopy and spectroscopy (**Figure 5.8** and **Figure 5.9**). The experimental procedure was identical to that described in **Section 5.5.3**, however, the removal of CNT solid was carried out by vacuum filtration (0.2 μ m PTFE membrane) in order to isolate the CNT. The black CNT powder was then washed with toluene (10 mL), sucked dry and further dried at room temperature over phosphorus pentoxide under reduced pressure.

5.6. References

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6. Concluding remarks

As a relatively novel material, carbon nanotubes show promise for the advancement of many areas of science due to their interesting and often extraordinary physicochemical properties. These hollow carbon nanostructures possess internal cavities ranging from 1 to 100 nm which are capable of hosting the widest spectrum of molecular species. In addition, the attractive properties of carbon nanotubes, most notably their high mechanical, thermal and chemical stability, make these structures particularly suited to hosting chemical reactions. As such, the field of carbon nanotube nanoreactors has been growing in recent years with various studies demonstrating the influence that confinement within carbon nanotubes can have over the properties of encapsulated materials and their subsequent reactions. The spatial restriction within the cavity of carbon nanotubes has been shown to affect catalytic chemical reactions in a multitude of ways including: (i) influencing catalyst activity by tuning electronic properties, (ii) controlling catalyst morphology and stability, (iii) altering local concentration of reaction species, and (iv) the pre-arrangement of reactants to promote the selective formation of isomeric products. In practice, these influences are mostly observed as a complex mixture which is sometimes difficult to deconvolute and rationalise. Additionally, the extreme spatial restriction provided by narrow single-walled carbon nanotubes (SWNT) is less widely studied than larger multi-walled carbon nanotubes (MWNT). However, these narrow SWNT, being commensurate in size with many small organic molecules, may hold the most potential to influence reaction pathways due to the more intimate contact between reaction species and the nanotube sidewalls. Therefore, by neglecting the use of metallic catalysts, the interactions between the host carbon nanotube and the encapsulated species can be directly probed. This approach had been previously demonstrated in a series of pioneering studies showing the formation of large linear oligomers and nanostructures within SWNT; however, these were limited to an analytical scale by the strong van der Waals interactions between the host CNT and the products, inhibiting the extraction of products and precluding preparative synthesis. Therefore, the development of methodologies to conduct chemical

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reactions within narrow carbon nanotubes on a preparative scale represents a significant area of the field within which to further our collective understanding. This work aimed to develop such practical methodologies and demonstrate the suitability of narrow carbon nanotubes to not only host a range of chemical transformations but, ultimately, alter their outcome. By probing the direct interactions between the host carbon nanotube and the confined species, it was hoped that any such control exerted over reaction pathways could be rationalised.

As the encapsulation of small organic molecules within carbon nanotubes relies mostly on ubiquitous van der Waals interactions, an efficient and reliable method for promoting the confined reaction over the same reaction in the bulk phase is essential in order to study the effects of confinement. In an attempt to improve the efficiency of encapsulation, the controlled reduction in carbon nanotube length was investigated. This systematic comparison of six methods, both established and novel, evaluated both the effectiveness at reducing average CNT length and the extent to which the CNT lattice structure is altered by the procedure. It was found that the oxidative cutting of carbon nanotubes catalysed by silver nanoparticles was the most effective in that the length of carbon nanotubes was reduced significantly (by up to 80%) with minimal damage to the nanotube sidewall.

A novel method for encapsulating organic molecules within SWNT was developed for *N*-phenylacetamide combining reliable liquid phase encapsulation with a novel fractional distillation procedure to remove excess externally adsorbed molecules. This procedure exploits the effect of extreme confinement on the phase behaviour of guest molecules to differentiate between the confined environment and the surrounding bulk liquid due to the altered observed boiling point. The encapsulation of *N*-phenylacetamide allowed the study of aromatic halogenation within SWNT demonstrating, for the first time, that SWNT are effective hosts for chemical reactions on a preparative scale, even in the absence of metallic catalysts. Furthermore, it was shown that the extreme confinement within SWNT drastically increases selectivity for the *para*-substituted regioisomer. The confined bromination of *N*-phenylacetamide in aqueous suspension affords the *para*-brominated regioisomer with up

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to 97% selectivity as opposed to 68% selectivity in the absence of confinement. This remarkable observation was found to be a consequence of extreme and precise confinement within the SWNT internal cavity, precluding attack at the *ortho*-position due to the specific arrangement of reactant molecules in confined space. It was also found that, under such extreme nanoscale confinement, the diameter of the host CNT is critically important as varying this by just ± 0.3 nm afforded no such result. While this is seemingly dependent on correctly matching the dimensions of the host carbon nanotube with those of the encapsulated guest molecule, the concept remains broadly applicable to a range of reactions as no specific interactions are required and the host carbon nanotube can be readily selected to suit the desired reaction. This study also demonstrated that the extraction of small organic products from narrow SWNT is facile due to the weak van der Waals interactions between encapsulated molecules and the host nanotube which are easily overcome by interactions with an appropriate organic solvent.

The study of more complex Diels-Alder cycloaddition reactions within SWNT showed measurable, yet minimal changes to selectivity as a consequence of confinement. It was postulated that no drastic effect was observed because there was no clear mechanism of size or shape selectivity within carbon nanotubes, due to the similar size and shape of the isomeric transition states. The 1,3-dipolar cycloaddition of various alkynes to benzyl azide demonstrated a consistent increase in selectivity for the 1,4-triazole (up to 55% increase) due to confinement within carbon nanotubes. As hypothesised, the more linear 1,4-triazole is favoured within the SWNT cavity in almost all cases. It was shown that the extent of confinement can be tuned by varying either the SWNT diameter or the steric bulk of reactant substituents in order to maximise the effect of confinement on the selectivity of reaction products. In many examples, measurable increases in 1,4-triazole selectivity were observed whilst the host nanotube cavity provided sufficient volume for both products to be encapsulated freely, suggesting that, to understand the mechanism of size or shape selectivity induced by the nanotube, the geometry of the regioisomeric transition states may be the most

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important consideration. In addition to steric considerations, a clear correlation between the electron-withdrawing nature of alkyne substituents and the increase in 1,4-triazole selectivity within SWNT suggests that the electronic properties of carbon nanotubes are providing an additional subtle influence on the selectivity of the reaction products. It is postulated that the highly polarisable host CNT stabilises the alkyne dipole moment, effectively increasing the partial charge separation. This phenomenon acts to amplify the underlying trend in regioselectivity by decreasing the alkyne electron density for electron-deficient alkynes and increasing the electron density for electron-rich alkynes. Therefore, confined 1,3-dipolar cycloaddition reactions are influenced by a complex balance of both steric and electronic factors induced by confinement within carbon nanotubes. Indeed, it is expected that these two influences can be additive or opposing, affording the observed selectivity changes. However, these results suggest that steric effects can induce the greatest change in selectivity with the most sterically constricted reaction showing an increase in selectivity for the 1,4-triazole of 55%, compared to an 18% increase for the most electron-withdrawing.

Whilst the extraction of small aromatic products from aromatic halogenation reactions proved facile, the extraction of larger aromatic molecules (possessing multiple aromatic rings) by organic solvent proved less so. In the case of 1,3-dipolar cycloaddition, although the formation of the 1,5-triazole is less favoured within SWNT, once formed, this isomer can be selectively withheld from solution by stronger interactions with the SWNT cavity. This demonstrates that the efficient extraction of products is critical when measuring selectivity, but this also highlights a potentially novel method offering further control over product distribution if this effect could be harnessed. The profound effect that simple confinement within carbon nanotubes can have on organic chemical reactions was clearly indicated by this work. The host carbon nanotube not only acting as a steric barrier, templating chemical processes, but also subtly altering the electronic properties of confined species through the interaction with the highly polarisable host.

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In an attempt to harness additional properties of carbon nanotubes in order to control reaction pathways, the influence of the inherent helicity of chiral carbon nanotubes on the autocatalytic Soai reaction was investigated. Due to the current limitations of carbon nanotube separation and purification, a single enantiomer of a carbon nanotube cannot be used on a preparative scale; however, this work demonstrated on a fundamental level that the helicity of CNT has an effect on the formation of chiral molecules and can be translated into the products of the autocatalytic Soai reaction. Since carbon nanotubes exist as a racemic mixture of both *P* and *M* enantiomers, their presence has a symmetrising effect on this chiral reaction. An enantioselective autocatalytic Soai reaction which undergoes spontaneous symmetry breaking to afford 90% *ee* becomes effectively racemic upon the addition of (6,5) chiral SWNT. The importance of the carbon nanotube surface in this observation is highlighted by a clear correlation between the mass of carbon nanotubes and the extent of symmetrisation.

In conclusion, this study has involved (i) the development of practical methodologies for the encapsulation of organic molecules within SWNT and subsequent confined reactions, followed by (ii) the demonstration, for the first time, of simple chemical reactions confined within narrow SWNT on a preparative scale. The application of this methodology to a range of chemical reactions has led to the observations that: (iii) extreme spatial confinement within SWNT can drastically alter the regioselectivity of both aromatic substitution and cycloaddition reactions; (iv) the magnitude of such changes in selectivity can be controlled by tuning both CNT diameter and reactant morphology; (v) the electronic properties of the host CNT can invoke a subtle influence over the regioselectivity of confined cycloaddition reactions; and (vi) the inherent helicity of chiral carbon nanotubes can be translated into the chiral products of an asymmetric reaction. Consequently, the work presented in this thesis represents a genuine and significant contribution to the field of carbon nanotube nanoreactors.

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As the field of nanotechnology continues to grow, further developments will undoubtedly aid the advancement of carbon nanoreactors. For instance, improvements to carbon nanotube synthesis are expected to afford greater dictation of geometry and morphology in combination with more accurate and economical computational approaches to studying reactions confined within carbon nanotubes. Such developments will allow greater control of carbon nanotube diameter, surface functionality, chirality and helicity and improve our understanding of how underlying chemical concepts such as diffusion, phase behaviour and kinetics are influenced by nanoscale confinement within carbon nanotubes.

Furthermore, when contemplating the future research goals in this area, the progress made in all areas of carbon nanoreactors must be considered. Firstly, whilst a range of confinement effects have been experimentally demonstrated to date, it would be naïve to assume that all of the mechanisms by which confinement within carbon nanotubes can influence chemical reactions have been discovered. Further work should, therefore, be directed towards harnessing the interesting properties of these nanostructures towards controlling reaction pathways. For instance, using the optical and/or electronic properties of carbon nanotubes to control light-driven and/or electrochemical reactions holds great potential. Secondly, whilst various confinement effects have been experimentally demonstrated for specific, carefully selected reactions, a particular advantage of carbon nanoreactors is their wide potential applicability to a plethora of chemical processes. Therefore, our increasing understanding of these phenomena will allow the design of bespoke nanoreactors for a desired reaction utilising synergistic confinement effects in order to achieve the optimum environment for any chemical reaction. This, in turn, may lead to enhanced activity, selectivity, stability or a combination thereof depending on the desired outcome.

The logical direct extension to this work is the search for an industrially relevant application whereby confinement effects within carbon nanotubes can be harnessed to improve the synthesis of commercially significant molecules. However, the ultimate goal

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continuing within this field remains the confined preparative synthesis of a product or nanomaterial inaccessible by any other means, clearly demonstrating the potential of this novel reaction environment to afford unprecedented control over the outcome of chemical transformations. These developments, coupled with the known practical advantages of carbon nanotubes in synthetic chemistry, such as convenient catalyst recovery by filtration or magnetic separation, could potentially provide an effective and adaptable reaction environment to further the field of chemical science.