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Click chemistry in carbon nanoreactors†

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Copper-nanoparticle catalytic centres anchored at the graphitic step-edges within hollow carbon nanoreactors exhibit superior activity and stability in cycloaddition reactions as compared to catalytic centres outside the nanoreactors. Nanoscale confinement enables efficient recycling of the catalyst in preparative-scale synthesis without significant changes in activity.

Confinement of molecules by restricting the available spatial volume down to the nanoscale provides a powerful methodology to control their physical properties and chemical reactivity.[1–4] Over the past three decades, a variety of molecular nanocontainers, including cyclodextrins, cavitands, calixarenes, cucurbiturils and supramolecular/coordination cages,[5] have been developed to replicate enzymatic-type nanoscale confinement, which drastically alters concentration, pressure and alignment of reactants and lowers the activation barriers of chemical reactions as compared to the bulk phase (solution or gas).[1]

Typically, molecular containers are synthetically tailored for a particular class of guest-molecules and consequently require intricate design and lengthy preparation. Furthermore, their thermal and chemical stabilities limit their applications to a narrow range of conditions, due to the chemically reactive functional groups of the host container (*e.g.* –OH, $-NH_2$). In contrast, hollow carbon nanostructures possess extremely high mechanical, chemical and thermal stability and the ability to encapsulate the widest spectrum of guest-molecules due to ubiquitous van der Waals forces. The diameters of carbon nanotubes (CNT) can be readily selected to provide the optimum confinement for the reactants of a particular chemical reaction, which can be studied at either the macroscale[6–8] or the nanoscale.[9–11] However, the use of CNT, whose internal diameters are typically in the range of 1–10 nm, in preparative scale reactions may result in substantial resistance to the transport of reactants and products to and from CNT, thus significantly thwarting kinetics of reactions[12,13] and in some cases totally precluding extraction of the products from within the internal cavity.[14] Hollow graphitised carbon nanofibres (GNF) being significantly wider than CNT (internal diameters typically above 50 nm) and always readily accessible to molecules, solve this problem of transport resistance.[15,16] However, despite the fact that the size of GNF significantly exceeds the typical dimensions of small organic molecules, which is expected to lead to the loss of confinement effects, it has been recently demonstrated that their unique internal structure consisting of a succession of 3–4 nm high steps formed by rolled-up sheets of graphene provides effective "anchoring points" for molecules and nanoparticles[17] and thus creates localised nanoscale reaction environments, different from the bulk phase, while still allowing effective transport of molecules through the tubular structure of GNF.[15,16]

In this study, we demonstrate for the first time that confinement in carbon nanoreactors has a remarkable stabilising effect on catalytic centres relative to catalysts deposited on the outer surfaces or dispersed in solution. Our novel nanoreactor catalysts can be readily recycled with retention of high catalytic activity, thus highlighting the importance of nanoreactors in preparative synthesis. Small dodecanethiolate-capped copper nanoparticles (CuNP, S1 and S2, ESI†)[18] were chosen as catalysts and inserted into the inner channel of GNF using *n*-hexane and supercritical CO_2 (S3, ESI†). The resulting composite structure (designated CuNP@GNF) contains the majority (>90%) of the nanoparticles immobilised at the corrugated internal step-edges of the nanofibres as demonstrated by high resolution transmission electron microscopy (HR-TEM, Fig. 1a–c, e and Fig. S3, ESI†). In a control experiment, CuNP were deposited onto the exterior of GNF (CuNP/GNF). Systematic comparison enables discrimination between the effects of support and confinement.

The use of CuNP in catalysis is highly attractive due to the low cost of both precursors and the bulk metal (relative to the other noble metals) and the plethora of carbon–carbon and carbon–heteroatom (oxygen, nitrogen, sulphur, selenium) bond-forming reactions catalysed by nanoscale copper.[19] For example, CuNP are very effective in the Huisgen cycloaddition of azides to alkynes,[20,21] which was selected as a model reaction in our study to assess the use of GNF as nanoreactors (Table 1).

Our control experiments revealed that the addition of benzyl azide **2a** to *para*-nitrophenylacetylene **1a** proceeds only in the

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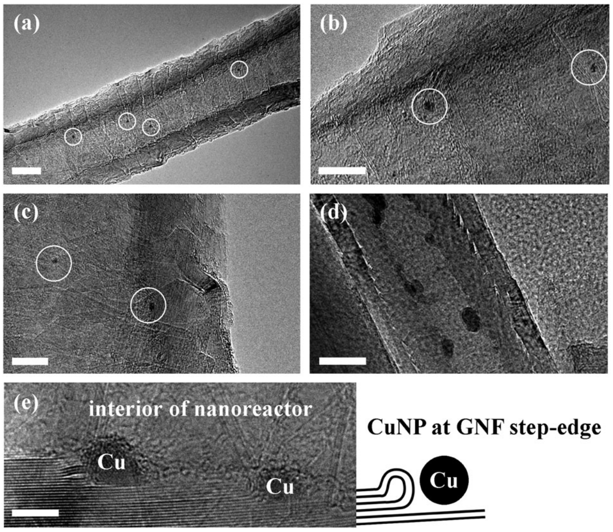


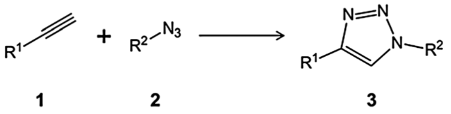
Fig. 1 HR-TEM of CuNP@GNF. CuNP (∼3 nm) immobilised at the step-edges (a–c) increase in size following catalysis (d) or thermal treatment (e), but remain within the GNF inner channel. White circles guide the eye to the location of small CuNP. Scale bars are 20 (a and d), 10 (b and c) and 5 nm (e).

presence of copper, as we found no products of cycloaddition in empty GNF under our experimental conditions (entry 1, Table 1). In the presence of CuNP dispersed in solution the cycloaddition afforded solely the 1,4-regioisomer of 1-benzyl-4-(4-nitrophenyl)-1*H*-[1,2,3]-triazole **3a**, in near quantitative conversion (entry 2). The regioselectivity is unaffected by the source of copper,[22] with a range of copper–silver alloy nanoparticles (entries 3–5 and S2, ESI†) and molecular salts (entry 7) showing remarkable regioselectivity and activity similar to pure CuNP. Further experiments showed that the reaction can be performed under a range of different experimental conditions (entries 8 and 9) and is suitable for a wide variety of aromatic and aliphatic azides and alkynes (entries 10–17), clearly showing the Hammett rule (S5, ESI†). All of these measurements indicate that the CuNP-catalysed Huisgen cycloaddition is a stable, reproducible reaction suitable for the evaluation of nanoreactors and for studying the catalytic properties of confined catalysts. We, thus, monitored the addition of **2a** to **1a** using ^{1}H NMR spectroscopy and compared the selectivity, activity and recyclability of CuNP, CuNP/GNF and CuNP@GNF catalysts (Fig. 2).

Firstly, the sole 1,4-regioisomer was afforded under all experimental conditions investigated for nanoreactors. This represents the principal example of the cycloaddition reaction conducted inside hollow carbon nanostructures and implies that the constrained steric environment imposed by the graphitic step-edge of GNF has no effect on the regioselectivity of the reaction. This contrasts with our previous observations for hydrosilylation reactions where confinement at the GNF step-edges resulted in different reaction pathways.[16]

Secondly, the rate of formation of the 1,2,3-triazole product is significantly higher for CuNP@GNF (commensurate with CuNP) relative to CuNP/GNF (Fig. 2a). This result is surprising as catalysts deposited on the outer surface of nanoreactors are more accessible to reactant molecules than those embedded within nanoreactors. The increased reaction rate and improved conversion for CuNP@GNF can be attributed to an increased local concentration effect. Both reactants **1** and **2** possess aromatic groups enabling specific van der Waals interactions with the graphitic step-edges within GNF leading to heightened

Table 1 The Huisgen cycloaddition of azides to alkynes[a]



	Catalyst	R^1	R^2	Product	*t*/h	Yield (%)
1	GNF	*p*-NO$_2$Ph **1a**	Bn **2a**	**3a**	168	0
2	CuNP	**1a**	**2a**	**3a**	48	96
3	Cu$_{0.75}$Ag$_{0.25}$NP	**1a**	**2a**	**3a**	24	83
4	Cu$_{0.50}$Ag$_{0.50}$NP	**1a**	**2a**	**3a**	24	99
5	Cu$_{0.25}$Ag$_{0.75}$NP	**1a**	**2a**	**3a**	24	99
6	AgNP	**1a**	**2a**	**3a**	168	0
7	CuI	**1a**	**2a**	**3a**	24	95
8	CuNP^b	**1a**	**2a**	**3a**	4	96
9	CuNP^c	**1a**	**2a**	**3a**	168	67
10	CuNP	*p*-BrPh **1b**	**2a**	**3b**	48	94
11	CuNP	Ph **1c**	**2a**	**3c**	144	99
12	CuNP	*p*-MeOPh **1d**	**2a**	**3d**	144	95
13	CuNP	*p*-NH$_2$Ph **1e**	**2a**	**3e**	144	94
14	CuNP	Cy **1f**	**2a**	**3f**	24	93
15	CuNP	C_8H_{17} **1g**	**2a**	**3g**	66	97
16	CuNP	OHCH$_2$ **1h**	**2a**	**3h**	66	99
17	CuNP	**1a**	C_6H_{13} **2b**	**3i**	72	99

[a] Standard conditions: alkyne (0.1 mmol), azide (0.1 mmol), catalyst (2.5 mol% Cu), triethylamine (0.15 mmol), C_6D_6 (1.4 mL), 40 °C (S4, ESI). [b] 80 °C. [c] MeOD.

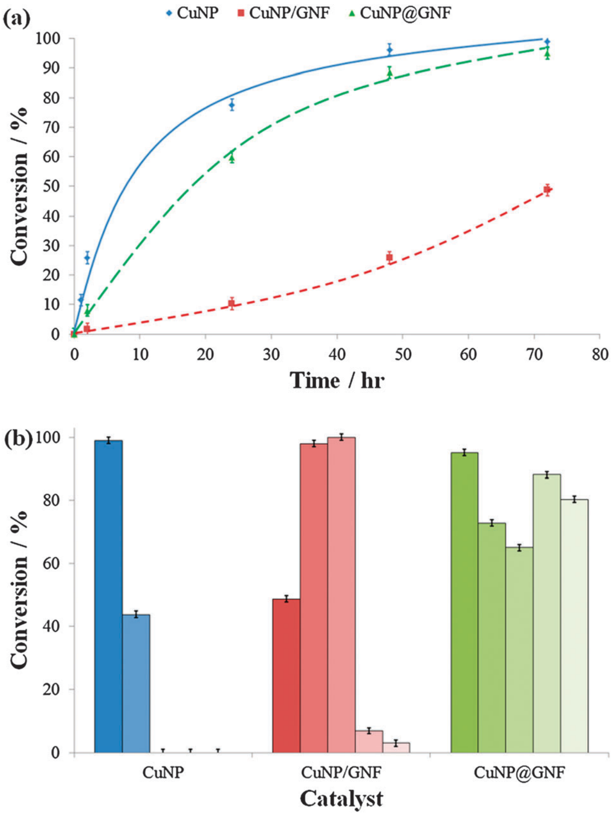
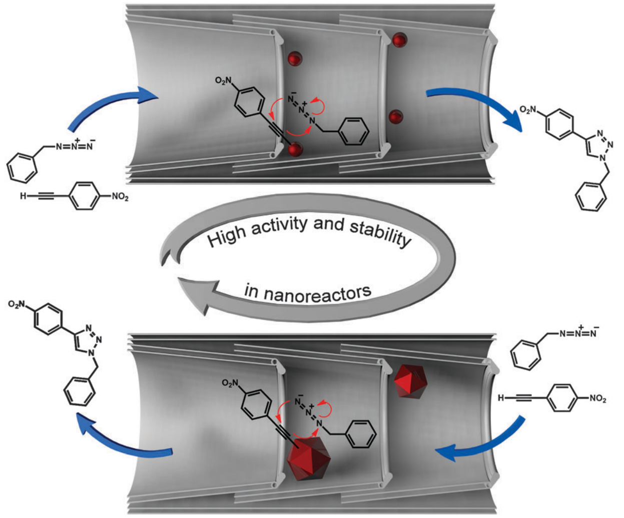


Fig. 2 The comparative (a) kinetics and (b) recyclability over five cycles (measured as the conversion at 72 h) for the copper catalysts dispersed in solution (CuNP), deposited on the surface (CuNP/GNF) or inserted in nanoreactors (CuNP@GNF).



Scheme 1 The retention of high catalytic activity after multiple cycles using CuNP@GNF nanoreactors containing catalyst.

concentrations inside the nanoreactor cavity, relative to the bulk phase, and thus enhancement in kinetics of reactions.[15,16]

Thirdly and most significantly, the recyclability of CuNP@GNF nanoreactors relative to supported CuNP/GNF and free-standing CuNP catalysts is much greater. Whilst the catalytic activity of CuNP and CuNP/GNF decreases rapidly after one and three cycles, respectively, CuNP inside nanoreactors exhibit remarkably stable catalytic activity even after five cycles (Fig. 2b). HR-TEM imaging of the CuNP@GNF structures after several catalytic cycles clearly illustrates that the initial small CuNP undergo dynamic coalescence into much larger particles (∼20–30 nm, Fig. 1d and Fig. S6, ESI†), thus explaining the subtle variation in absolute activity across catalytic cycles, but critically remain anchored to the interior of GNF and are therefore available for subsequent reactions (Scheme 1). In contrast, under the same conditions CuNP are removed from the surfaces of nanofibres in CuNP/GNF (S6, ESI†), due to dissolution of copper in the reaction mixture, thus leading to a continuous and eventual total loss of catalytic centres after only three cycles. In a series of control experiments, CuNP were separately grown to a larger size (∼10–20 nm, Fig. S7, ESI†) inside and outside GNF prior to catalysis. These experiments confirmed that activity and recyclability of CuNP@GNF are not affected by the size of CuNP as long as they remain located inside nanoreactors (S7, ESI†) and further emphasised the importance of confinement of the catalytic centres within nanoreactors.

In conclusion, we have shown for the first time that carbon nanoreactors provide an excellent environment for cycloaddition reactions. The kinetics of reactions are accelerated and conversion rates improved in nanoreactors relative to catalysts deposited on the outer surfaces. Most significantly, catalytic centres embedded in the nanoreactor cavity are stabilised by interactions with the nanoscale graphitic step-edges, which prevent the loss of catalyst during reactions, thus allowing efficient recycling of CuNP@GNF with retention of high catalytic activity cycle after cycle. This methodology can be transferred to other types of reactions as the Brust–Schiffrin reductive synthesis of nanoparticles is applicable to a wide range of catalytically active transition metals, which can be readily inserted into GNF nanoreactors using the methodology described for CuNP in this study. Our findings broaden the spectrum of preparative chemical transformations in carbon nanoreactors which present an ideal catalyst system for further exploration of the effects of nanoscale confinement on chemical processes, ensuring high selectivity, activity and recyclability of catalytic centres. Current development of nanotubes and hollow nanofibres as nanoreactors is very timely, as their recently demonstrated applications as magnetically controlled pipettes,[23] liquid chromatographers[24] and cellular endoscopes[25] are fundamentally changing the way chemists study and make molecules.

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Notes and references

1 A. N. Khlobystov, *ACS Nano*, 2011, **5**, 9306–9312.
2 D. A. Britz and A. N. Khlobystov, *Chem. Soc. Rev.*, 2006, **35**, 637–659.
3 P. Serp and E. Castillejos, *ChemCatChem*, 2010, **2**, 41–47.
4 X. Pan and X. Bao, *Acc. Chem. Res.*, 2011, **44**, 553–562.
5 *Molecular encapsulation: Organic reactions in constrained systems*, ed. U. D. Brinker and J.-L. Mieusset, Wiley, New York, 2010.
6 X. Pan, Z. Fan, W. Chen, Y. Ding, H. Luo and X. Bao, *Nat. Mater.*, 2007, **6**, 507–511.
7 W. Chen, Z. Fan, X. Pan and X. Bao, *J. Am. Chem. Soc.*, 2008, **130**, 9414–9419.
8 E. Castillejos, P.-J. Debouttiere, L. Roiban, A. Solhy, V. Martinez, Y. Kihn, O. Ersen, K. Philippot, B. Chaudret and P. Serp, *Angew. Chem.*, 2009, **121**, 2567–2571.
9 C. S. Allen, Y. Ito, A. W. Robertson, H. Shinohara and J. H. Warner, *ACS Nano*, 2011, **5**, 10084–10089.
10 A. Ilie, J. S. Bendall, K. Nagaoka, S. Egger, T. Nakayama and S. Crampin, *ACS Nano*, 2011, **5**, 2559–2569.
11 A. Ilie, S. Egger, S. Friedrichs, D.-J. ang and M. L. H. Green, *Appl. Phys. Lett.*, 2007, **91**, 253124.
12 S. Xu, W. Zhang, X. Liu, X. Han and X. Bao, *J. Am. Chem. Soc.*, 2009, **131**, 13722–13727.
13 D. A. Newsome and D. S. Scholl, *Nano Lett.*, 2006, **6**, 2150–2153.
14 D. A. Britz, A. N. Khlobystov, K. Porfyrakis, A. Ardavan and G. A. D. Briggs, *Chem. Commun.*, 2005, 37–39.
15 A. La Torre, M. C. Gimenez-Lopez, M. Fay, G. A. Rance, W. A. Solomonosz, T. W. Chamberlain, P. D. Brown and A. N. Khlobystov, *ACS Nano*, 2012, **6**, 2000–2007.
16 W. A. Solomonsz, G. A. Rance, M. Suyetin, A. La Torre, E. Bichoutskaia and A. N. Khlobystov, *Chem.–Eur. J.*, 2012, **18**, 13180–13187.
17 A. La Torre, M. Fay, G. A. Rance, M. C. Gimenez-Lopez, W. A. Solomonsz, P. D. Brown and A. N. Khlobystov, *Small*, 2012, **8**, 1222–1228.
18 M. Brust, M. Walker, D. Bethell, D. J. Schiffrin and R. Whyman, *J. Chem. Soc., Chem. Commun.*, 1994, 801–802.
19 B. C. Ranu, R. Dey, T. Chatterjee and S. Ahammed, *ChemSusChem*, 2012, **5**, 22–44.
20 F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Eur. J. Org. Chem.*, 2010, 1875–1884.
21 Z. F. Zhang, C. M. Dong, C. H. Yang, D. Hu, J. Long, L. Wang, H. Li, Y. Chen and D. L. Kong, *Adv. Synth. Catal.*, 2010, **352**, 1600–1604.
22 V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596–2599.
23 J. R. Freedman, D. Mattia, G. Korneva, Y. Gogotsi, G. Friedman and A. K. Fontecchio, *Appl. Phys. Lett.*, 2007, **90**, 103108.
24 R. Singhal, V. M. Mochalin, M. R. Lukatskaya, G. Friedman and Y. Gogotsi, *Sci. Rep.*, 2012, **2**, 510.
25 J. J. Niu, M. G. Schrlau, G. Friedman and Y. Gogotsi, *Small*, 2011, **7**, 540–545.