ChemComm

RSC Publishing

COMMUNICATION

View Article Online
View Journal | View Issue

Regioselective control of aromatic halogenation reactions in carbon nanotube nanoreactors†

Cite this: *Chem. Commun.*, 2013, **49**, 5586

Received 3rd April 2013,
Accepted 8th May 2013

DOI: 10.1039/c3cc42414f

www.rsc.org/chemcomm

Scott A. Miners, Graham A. Rance and Andrei N. Khlobystov*

The use of single-walled carbon nanotubes as effective nanoreactors for preparative chemical reactions has been demonstrated for the first time. Extreme spatial confinement of reactant molecules inside nanotubes has been shown to drastically affect both the regioselectivity and kinetics of aromatic halogenation reactions.

The confinement of guest molecules within host containers provides a novel way to control the properties of the guest, manipulate reaction pathways and govern the outcome of chemical reactions. In recent decades, the reactions of molecules encapsulated within various nanoreactors, such as cyclodextrins, cavitands, calixarenes, supramolecular/coordination cages and zeolites, have been shown to be drastically altered by confinement, where concentration, pressure, reactant alignment and thus activation energy barriers become critically influenced by the host.[1] However, the use of hollow carbon nanostructures, such as single-walled carbon nanotubes (SWNT), as containers for confined reactions has yet to be explored; these structures, which possess two nanoscopic and one macroscopic dimensions (1D), bridge the gap between previously studied molecular containers (0D) and porous solids (3D).

SWNT possess a cylindrical cavity of tunable size which permits the encapsulation of a wide range of guest molecules through ubiquitous van der Waals forces. Furthermore, as SWNT exhibit high mechanical, chemical and thermal stability, reactions inside carbon nanotubes can be carried out under a wider range of conditions than is possible with existing nanoreactor systems.[2] Previous studies have shown that the regioselectivity and activity of metal-catalysed reactions are affected by confinement inside carbon nanostructures,[3–7] however metal-free reactions represent a more direct way to study the confinement effects induced by the nanotube itself. Few such reactions have been carried out within carbon nanotubes to date, but notable examples include the formation of linear structures, such as fullerene[8] and fullerene epoxide oligomers,[9] graphene nanoribbons[10,11] and the transformation of $Fe(C_{60}Me_5)Cp$ into C_{70}.[12] It is important to note, however, that due to the significant van der Waals attraction between the one-dimensional host and high molecular weight incarcerated guests, such as those formed in the oligomerisation reactions, extraction and recovery of the formed product is not possible and as such no preparative reactions using SWNT have been performed so far. A more attractive approach would be to probe well-known transformations of small molecules, where inherently weaker intermolecular forces are present, thus minimising the detrimental issue of product recovery. In this study, we have investigated the influence of confinement in narrow carbon nanotubes on aromatic halogenation reactions and demonstrate for the first time regioselective control of preparative chemical reactions using single-walled carbon nanoreactors.

The bromination of *N*-phenylacetamide by pyridiniumdichlorobromate ($PyHCl_2Br$)[13] in solution reliably and reproducibly forms an unselective (68 : 32) mixture of *N*-(4-bromophenyl)acetamide (*para*-regioisomer) and *N*-(2-bromophenyl)acetamide (*ortho*-regioisomer) respectively. This reaction is therefore an ideal probe to study the effect of confinement on regioselectivity. The *para*-selective bromination of *N*-phenylacetamide due to spatial confinement within cyclodextrin cavities[14] has been previously demonstrated and attributed to the site selective electrophilic attack of the incarcerated aromatic guest directed by the truncated conical shape of the cyclodextrin host. As SWNT have cylindrical cavities analogous to cyclodextrins, a similar effect of confinement is expected to be possible in carbon nanotubes.

However, in order to demonstrate selectivity, it is integral that a nanotube of suitable diameter be used which can successfully discriminate between the formation of *para*- and *ortho*-products. Geometric considerations showed single-walled carbon nanotubes produced by the HiPCO[15] process to have the most suitable diameters for this purpose (Fig. 1b).

In order to ensure that the bromination reaction, known to readily occur in the absence of nanotubes, was conducted within the SWNT hollow interior, it was essential that one of the reactants be encapsulated prior to the reaction. After extensively testing possible methods of reactant encapsulation the most effective method was found to be immersion of open nanotubes in molten *N*-phenylacetamide; the nanotubes becoming spontaneously filled with the reactant due to capillary forces. This has proven to be an

School of Chemistry, The University of Nottingham, University Park, Nottingham, NG7 2RD, UK. E-mail: Andrei.Khlobystov@Nottingham.ac.uk; Fax: +44 (0)115 9513563; Tel: +44 (0)115 9513917

† Electronic supplementary information (ESI) available: Experimental detail and theoretical calculations. See DOI: 10.1039/c3cc42414f

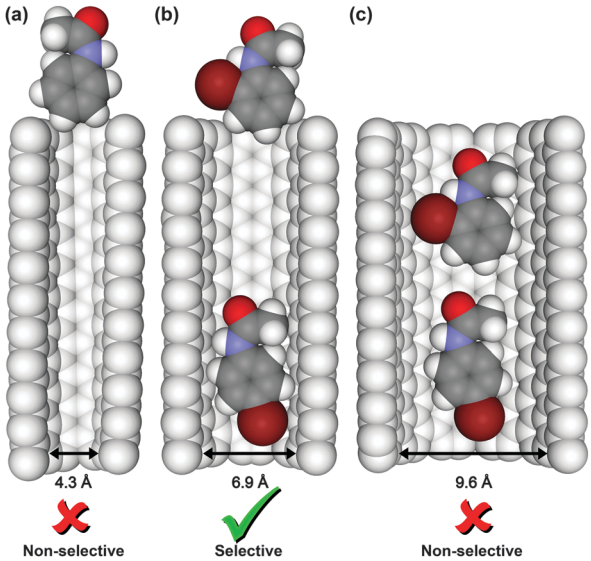

Fig. 1 Comparison of the van der Waals diameter of the internal cavity (d_{NT}) of three types of nanotubes to the critical van der Waals diameter ($d_{critical}$) of reactant and product molecules. (a) CoMoCAT SWNT (d_{NT} = 4.3 Å), too narrow to allow confinement of the reactant ($d_{critical}$ = 6.9 Å); (b) HiPCO SWNT (d_{NT} = 6.9 Å), allowing the formation of *para*- but not *ortho*-product and (c) wider AD SWNT (arc discharge) (d_{NT} = 9.6 Å) freely allowing the formation of both products. (S1, ESI†)

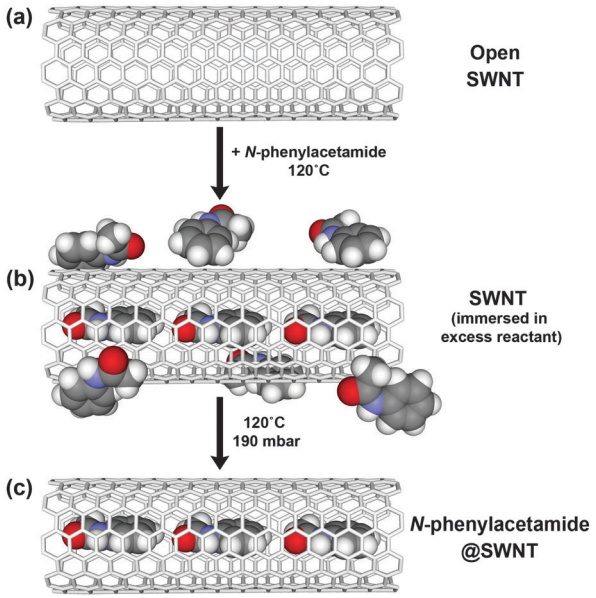

Fig. 2 Schematic representation of the molten encapsulation and fractional distillation procedure to remove excess external molecules leaving *N*-phenylacetamide@SWNT.

effective method as virtually all molecular liquids have a surface tension below the 200 mN m^{-1} threshold for efficient encapsulation.[16] However, as immersion requires a significant excess of molten *N*-phenylacetamide, this method, although highly effective in filling nanotubes, unfortunately produces an excess of *N*-phenylacetamide adsorbed on SWNT which must be removed prior to the reaction. Several studies of the dynamics of molecules, particularly water, confined within narrow SWNT have predicted that encapsulated guests would exhibit drastically different behaviour to that of the bulk phase due to arrangement in pseudo-1D arrays. For example, both the melting[17] and boiling point[18] of water have been calculated to be significantly elevated by confinement in narrow SWNT. We therefore exploited this principle and developed a novel fractional distillation procedure (Fig. 2) to separate the excess external *N*-phenylacetamide from the confined molecules.

As the fractional distillation proceeds, the proportion of external *N*-phenylacetamide decreases relative to the confined molecules. By sampling the *N*-phenylacetamide@SWNT at different stages of fractional distillation, we are able to study confinement effects by measuring the *para*-selectivity of the subsequent bromination reaction (Fig. 3).

The plot demonstrates a clear increase in selectivity towards the *para*-product as the excess *N*-phenylacetamide is removed from the SWNT surface (up to 97% *para*-selectivity), confirming that confinement in SWNT, similarly to cyclodextrins, promotes the formation of the *para*-product. A control experiment with closed nanotubes, where the reactant is not able to enter the SWNT cavities, showed no increased yield of the *para*-product (entry 2, Table 1) compared to solution (entry 1) confirming that the open SWNT do act as nanoreactors (entry 3).

The regioselective outcome of the reaction is determined by the precise match between the nanotube diameter and the diameters of reactants/products. Since the diameters of SWNT are largely dependent on their method of production, we conducted a series of experiments with nanotubes produced by arc discharge (AD) and CoMoCAT techniques whose average diameters are respectively wider and narrower than that of HiPCO SWNT. The use of narrower CoMoCAT SWNT (average van der Waals diameter of nanotube internal cavity d_{NT} = 4.3 Å, entry 4, Table 1) resulted in no change in *para*-selectivity relative to the reaction in solution (entry 1), consistent with the insufficient diameters of these nanotubes to encapsulate *N*-phenylacetamide reactant molecules (Fig. 1a). Using wider AD SWNT (d_{NT} = 9.6 Å, entry 5) also gave no change in selectivity as the nanotube diameter is large enough for both products to form with no size discrimination (Fig. 1c). This comparison of different nanotubes proves that the significant improvement in *para*-selectivity observed in HiPCO SWNT is not due to any interaction with the nanotube exterior, but instead a result of extreme and precise confinement controlled by matching the size and shape of the reaction products with the nanotube.

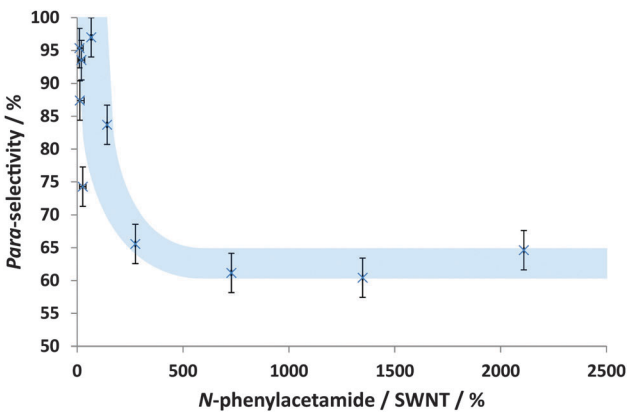

Fig. 3 Plot of *para*-selectivity against *N*-phenylacetamide/SWNT mass ratio showing the onset of confinement effects as the mass ratio of *N*-phenylacetamide to SWNT decreases.

Table 1 Effect of confinement in nanotubes on the regioselective halogenation of *N*-phenylacetamide

	Carbon nanotube	Halogenation agent	Product ratio/% *Para*	*Ortho*
1	None	$PyCl_2Br$[a]	68	32
2	HiPCO SWNT (closed)	$PyCl_2Br$	69	31
3	HiPCO SWNT	$PyCl_2Br$	97	3
4	CoMoCAT SWNT	$PyCl_2Br$	70	30
5	AD SWNT	$PyCl_2Br$	69	31
6	None	Cl_2[b]	15	85
7	HiPCO SWNT	Cl_2	42	58

[a] Standard conditions: *N*-phenylacetamide (1.0 eq.), $PyCl_2Br$ (0.6 eq. 1.5 mmol dm^{-3}), H_2O, RT, 24 h. [b] Standard conditions: *N*-phenylacetamide (1.0 eq.), Cl_2 (1000-fold excess), H_2O, RT, 90 min (S2, ESI†).

Similarly to the bromination, we have shown that selectivity of the chlorination reaction[19] increases from 15% of *para*-product in solution (entry 6, Table 1) to 42% due to confinement inside HiPCO SWNT (entry 7). Furthermore, conversion rates of *N*-phenylacetamide halogenation reach 100% in the optimum cases thus suggesting facile diffusion of products from nanoreactors.

Para-selectivity is expected to rise sharply as surface adsorbed *N*-phenylacetamide excess is removed by the fractional distillation. However, our measurements indicate a much more gradual increase in *para*-selectivity (Fig. 3) suggesting that not all *N*-phenylacetamide reactant molecules could possibly be encapsulated at any one time. Surprisingly, the measured selectivity for the *para*-product is higher than is expected from the calculated proportion of encapsulated *N*-phenylacetamide molecules at the start of the reaction, already reaching 97% when just a minority of reactant molecules are encapsulated (S3, ESI†). This observation suggests that the rate of the confined reaction is significantly accelerated compared to that of the bulk and reactant molecules are diffusing into the nanotube during the reaction. The theoretical simulations of Halls and Schlegel[20] predicted that nanotube confinement would substantially affect the Menshutkin S_N2 reaction and showed that the highly polarisable nanotube stabilised the charge separation in the transition state which significantly lowered the activation energy and endothermicity compared to the reaction in the gas phase. The aromatic bromination reaction mechanism (Fig. 4) also forms an intermediate with a large charge separation (*i.e.* high dipole moment) and it is therefore reasonable to surmise that the highly polarisable nanotube could stabilise this dipole, thus reducing activation energy barriers and accelerating the reaction rate for the *para*-product in nanotubes. The acceleration of confined reactions may explain the greater than expected selectivity towards the *para*-product even when not all *N*-phenylacetamide molecules are initially encapsulated in SWNT.

In conclusion, single-walled carbon nanotubes have been demonstrated as effective nanoreactors where nanoscale confinement significantly improves the selectivity and kinetics of aromatic halogenation reactions. We have demonstrated that the size of the host-nanotube cavity is of critical importance for effective control of selectivity where a suitable nanotube diameter can be readily selected to provide the optimum confinement for the reactants or products of a particular chemical reaction. Since no specific interactions are required to encapsulate reactants in SWNT other than ubiquitous van der Waals forces, the strategies developed for molecular containers such as cryptophanes, which possess the ability to bind small molecules from solution,[21,22] can be employed for carbon nanoreactors. Furthermore the enhanced thermal and chemical stability of the SWNT interior surface combined with the rich reactivity of the SWNT outer surface[23–25] open up opportunities for constructing bespoke recyclable nanoreactors[26] tailored for chemical processes leading to products unattainable by other means.[2]

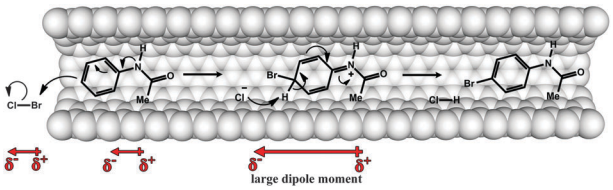

Fig. 4 Schematic representation of the bromination reaction mechanism in a SWNT showing the formation of an intermediate with a large dipole moment which is stabilised by a highly polarisable nanoreactor, thus lowering the activation barrier and accelerating the reaction in nanotubes.

Notes and references

1 U. H. Brinker and J. L. Mieusset, in *Molecular Encapsulation: Organic Reactions in Constrained Systems*, John Wiley & Sons, 2010.
2 A. N. Khlobystov, *ACS Nano*, 2011, **5**, 9306.
3 (*a*) Z. J. Chen, Z. H. Guan, M. R. Li, Q. H. Yang and C. Li, *Angew. Chem., Int. Ed.*, 2011, **50**, 4913; (*b*) Q. H. Yang, D. H. Han, H. Q. Yang and C. Li, *Chem.–Asian J.*, 2008, **3**, 1214; (*c*) B. Li, S. Y. Bai, X. F. Wang, M. M. Zhong, Q. H. Yang and C. Li, *Angew. Chem., Int. Ed.*, 2012, **51**, 11517.
4 W. A. Solomonsz, G. A. Rance, M. Suyetin, A. La Torre, E. Bichoutskaia and A. N. Khlobystov, *Chem.–Eur. J.*, 2012, **18**, 13180.
5 A. La Torre, M. D. Gimenez-Lopez, M. W. Fay, G. A. Rance, W. A. Solomonsz, T. W. Chamberlain, P. D. Brown and A. N. Khlobystov, *ACS Nano*, 2012, **6**, 2000.
6 X. L. Pan and X. H. Bao, *Acc. Chem. Res.*, 2011, **44**, 553.
7 P. Serp and E. Castillejos, *ChemCatChem*, 2010, **2**, 41.
8 M. Koshino, Y. Niimi, E. Nakamura, H. Kataura, T. Okazaki, K. Suenaga and S. Iijima, *Nat. Chem.*, 2010, **2**, 117.
9 D. A. Britz, A. N. Khlobystov, K. Porfyrakis, A. Ardavan and G. A. D. Briggs, *Chem. Commun.*, 2005, 37.
10 A. Chuvilin, E. Bichoutskaia, M. C. Gimenez-Lopez, T. W. Chamberlain, G. A. Rance, N. Kuganathan, J. Biskupek, U. Kaiser and A. N. Khlobystov, *Nat. Mater.*, 2011, **10**, 687.
11 A. V. Talyzin, I. V. Anoshkin, A. V. Krasheninnikov, R. M. Nieminen, A. G. Nasibulin, H. Jiang and E. I. Kauppinen, *Nano Lett.*, 2011, **11**, 4352.
12 E. Nakamura, M. Koshino, T. Saito, Y. Niimi, K. Suenaga and Y. Matsuo, *J. Am. Chem. Soc.*, 2011, **133**, 14151.
13 H. A. Muathen, *Synthesis*, 2002, 169.
14 P. G. Dumanski, C. J. Easton, S. F. Lincoln and J. S. Simpson, *Aust. J. Chem.*, 2003, **56**, 1107.
15 P. Nikolaev, M. J. Bronikowski, R. K. Bradley, F. Rohmund, D. T. Colbert, K. A. Smith and R. E. Smalley, *Chem. Phys. Lett.*, 1999, **313**, 91.
16 E. Dujardin, T. W. Ebbesen, H. Hiura and K. Tanigaki, *Science*, 1994, **265**, 1850.
17 K. Koga, G. T. Gao, H. Tanaka and X. C. Zeng, *Nature*, 2001, **412**, 802.
18 V. V. Chaban and O. V. Prezhdo, *ACS Nano*, 2011, **5**, 5647.
19 R. Chênevert and G. Ampleman, *Can. J. Chem.*, 1987, **65**, 307.
20 M. D. Halls and H. B. Schlegel, *J. Phys. Chem. B*, 2002, **106**, 1921.
21 M. A. Little, J. Donkin, J. Fisher, M. A. Halcrow, J. Loder and M. J. Hardie, *Angew. Chem., Int. Ed.*, 2012, **51**, 764.
22 M. A. Little, M. A. Halcrow and M. J. Hardie, *Chem. Commun.*, 2013, **49**, 1512.
23 S. A. Hodge, M. K. Bayazit, K. S. Coleman and M. S. P. Shaffer, *Chem. Soc. Rev.*, 2012, **41**, 4409.
24 M. K. Bayazit and K. S. Coleman, *Chem.–Asian J.*, 2012, **7**, 2925.
25 A. Suri and K. S. Coleman, *J. Nanosci. Nanotechnol.*, 2012, **12**, 2929.
26 G. A. Rance, W. A. Solomonsz and A. N. Khlobystov, *Chem. Commun.*, 2013, **49**, 1067.

