Electronic Supporting Information file

Regioselective control of aromatic halogenation reactions using carbon nanotube nanoreactors

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

S1 Transmission Electron Microscopy

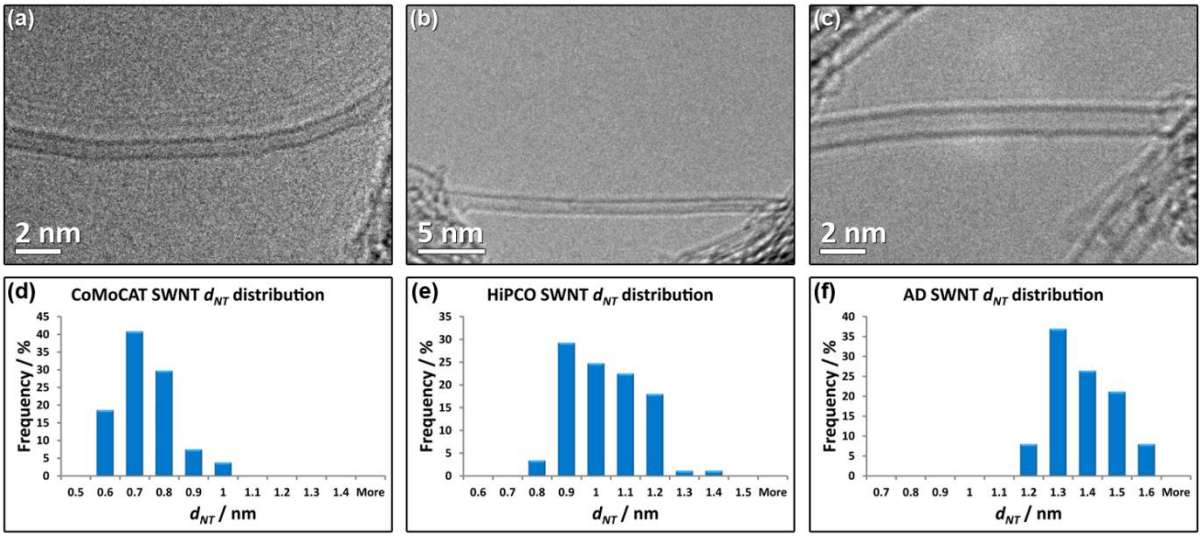


Figure S1. Transmission electron micrographs (a-c) of SWNT produced by CoMoCAT, HiPCO and arc discharge (AD) respectively coupled with nanotube diameter distribution histograms (d-f) for CoMoCAT, HiPCO and AD SWNT respectively.

d_{NT} values plotted in Figure S1 are van der Waals internal cavity diameters, based on the average nanotube diameter with the Van der Waals diameter of carbon atom (3.06 Å)[S1] subtracted.

S2 Experimental

General

N-phenylacetamide was purchased from Sigma-Aldrich, UK and recrystallised from toluene.[S2] Pyridinium dichlorobromate was synthesised according to literature precedent described by H. A. Muathen.[S3] HiPCO SWNT (Lot No. R2172) was purchased from Unidym© and purified by methods described below. CoMoCAT SWNT (Lot No. MKBF6413V, (6,5)-SWNT) were purchased from Sigma-Aldrich Chemicals, UK and AD SWNT (Lot No. CSCA) were purchased from Helix Material Solutions, TX, USA. CoMoCAT SWNT were heated at 520˚C for 6 minutes immediately before use and AD SWNT were heated at 380˚C for 35 minutes immediately before use. All nanotubes were also thoroughly dried immediately prior to use by heating at 250˚C for 30 minutes.

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. ^{1}H NMR spectra were obtained using a Bruker AV(III)-400 (400.07 MHz) spectrometer using 64 scans at 298K using DMSO-d_6 as the solvent. HRTEM imaging was performed using a JEOL 2100F transmission electron microscope (field emission electron gun source, information limit 0.19 nm) operated at an accelerating voltage of 100 kV. TEM specimens were prepared by casting several drops of a

methanolic suspension of the nanotubes onto a copper-grid mounted "lacey" carbon film and dried under a stream of nitrogen. Water was purified (> 18 MΩ cm) using a Barnstead NANOPure II system. All heat treatment was carried out in a tube furnace under air atmosphere unless otherwise stated.

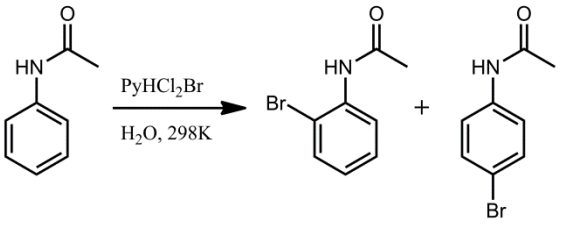
HiPCO SWNT purification

HiPCO SWNT (151 mg) was heated at 380˚C for 30 minutes in air to yield annealed nanotubes (106 mg, 30% mass loss) which was suspended in concentrated (12M) hydrochloric acid (1 mg mL^{-1}) and sonicated at room temperature for 30 minutes. The black suspension was diluted in ice (300 ml) and the solid collected by vacuum filtration (0.2 μm pore size PTFE membrane), washed sequentially with water, sodium hydroxide (1M), hydrochloric acid (1M), water and acetone and finally dried *in vacuo* to yield purified HiPCO SWNT (47 mg). Overall yield of purification: 31%. Thermogravimetric analysis showed a peak oxidation temperature of 410˚C with a residual mass of 6.5%.

General encapsulation and fractional distillation

To molten *N*-phenylacetamide (100 mg, 120˚C) was added purified HiPCO SWNT (5 mg) and the mixture 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 (which typically required 5-12 hours) to yield 5-10 mg black *N*-phenylacetamide/SWNT composite powder.

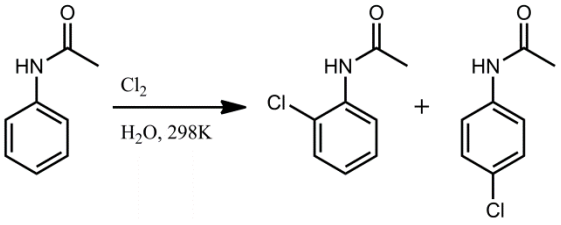
Bromination of *N*-phenylacetamide@SWNT



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. *Ortho-para* ratios were determined by integration of peaks at 7.11 (1H *ortho*) and 7.46 (2H, *para*) ppm. Conversion values can vary depending on experimental conditions reaching 100% in the optimum cases. The high conversion observed for these encapsulated reactions suggests facile extraction of product molecules from within the carbon nanoreactor. Our current hypothesis for this phenomenon is related to the ambiphilic nature of the products of this reaction; the energy of solvation in bulk solvent is similar to the energy of encapsulation and therefore the release of halogenated product molecules relies on simple diffusion.

^{1}H NMR (DMSO-d_6) δ_H/ppm *N*-phenylacetamide: 9.91 (s, 1H, N*H*), 7.57 (dt, 2H, *J* = 8.8, 1.1 Hz, Ar*H*), 7.28 (tt, 2H, *J* = 8.4, 1.8 Hz, Ar*H*), 7.02 (tt, 1H, *J* = 7.5, 1.2 Hz, Ar*H*), 2.04 (s, 3H, CH_3). *N*-(4-bromophenyl)acetamide: 10.05 (s,1H, N*H*), 7.55 (dt, 2H, *J* = 8.8, 2.2 Hz, Ar*H*), 7.46 (dt, 2H, *J* = 8.8, 2.2 Hz, Ar*H*), 2.04 (s, 3H, CH_3). *N*-(2-bromophenyl)acetamide: 9.45 (s, 1H, N*H*), 7.64 (dd, 1H, *J* = 8.0, 1.1 Hz, Ar*H*), 7.59 (dd, 1H, *J* = 8.0, 1.1 Hz, Ar*H*), 7.35 (td, 1H, *J* = 7.7, 1.1 Hz, Ar*H*), 7.11 (td, 1H, *J* = 7.7, 1.1 Hz, Ar*H*), 2.08 (s, 3H, CH_3). Values consistent with literature analogues.[S4]

Chlorination of *N*-phenylacetamide@SWNT

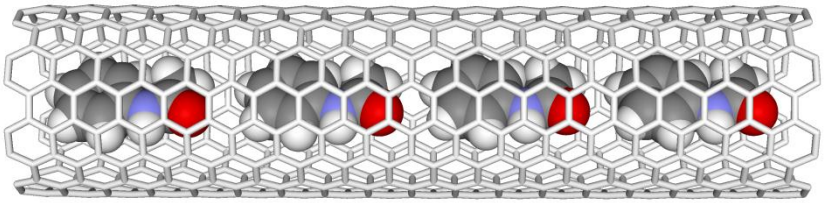


Through a stirred aqueous suspension of *N*-phenylacetamide@SWNT (4.66 mg in 4 mL) was bubbled an excess of chlorine gas for 90 minutes at room temperature. The suspension was then flushed with nitrogen for 12 hours before extracting with diethyl ether (2 x 4 mL), washed with water (2 x 10 mL), dried over anhydrous sodium sulfate, filtered and dried *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 assure consistent stoichiometry of chlorine. *Ortho-para* ratios were determined by integration of peaks at 7.19 (1H *ortho*) and 7.61 (2H, *para*) ppm. Conversion was 100% in all cases due to the excess of chlorinating agent.

^{1}H NMR (DMSO-d_6) δ_H/ppm. *N*-(4-chlorophenyl)acetamide: 10.06 (s, 1H, N*H*), 7.61 (dt, 2H, *J* = 8.8, 2.0 Hz, Ar*H*), 7.35 (dt, 2H, *J* = 8.8, 2.0 Hz, Ar*H*), 2.11 (s, 3H, CH_3). *N*-(2-chlorophenyl)acetamide: 9.51 (s, 1H, N*H*), 7.70 (dd, 1H, *J* = 8.4, 1.2 Hz, Ar*H*), 7.49 (dd, 1H, *J* = 8.4, 1.2 Hz, Ar*H*), 7.32 (td, 1H, *J* = 7.8, 1.4 Hz, Ar*H*), 7.19 (td, 1H, *J* = 7.6, 1.2 Hz, Ar*H*), 2.11 (s, 3H, CH_3).Values consistent with literature analogues.[S5]

S3 Theoretical Calculations

Capacity of HiPCO SWNT for N-*phenylacetamide*



Mass of *N*-phenylacetamide molecule = 135.17 g mol^{-1}
Carbon atoms required to encapsulate one *N*-phenylacetamide molecule = 148
Mass of carbon required to encapsulate one *N*-phenylacetamide molecule = 148 x 12 = 1776 g mol^{-1}
Mass percentage of guest molecule in ideal *N*-phenylacetamide@SWNT sample = 135/(1776+135) = **7.1%**

Theoretical product ratios based on calculated SWNT capacity

Example calculation shown for one data point only.

Product ratio of background reaction in bulk solution	$= 68\%\ para : 32\%\ ortho$
Mass of SWNT	$= 4.897\ mg$
Mass of *N*-phenylacetamide	$= 3.243\ mg$
N-phenylacetamide/SWNT	$= 66\%$
Calculated (max.) amount of *N*-phenylacetamide ***in*** SWNT[a]	$= 4.897\ mg \times 7.1\% = 0.350\ mg\ (i.e.\ 10.8\%)$
Amount of *N*-phenylacetamide ***outside*** SWNT	$= 3.243\ mg - 0.350\ mg = 2.893\ mg\ (89.2\%)$
Calculated *para*-product formed ***outside*** nanotube[b]	$= 89.2\% \times 68\% = 60.7\%$
Calculated *para*-product formed ***inside*** nanotube[c]	$= 11\%$
Calculated total *para*-product	$= 60.7 + 11 = \mathbf{71.5}\%$
Calculated *ortho*-product	$= 89\% \times 32\% = \mathbf{28.5}\%$
Experimental *para*-product	$= \mathbf{97}\%$
Experimental *ortho*-product	$= \mathbf{3}\%$

[a] Maximum SWNT capacity value calculated as shown in **S3.1**.
[b] As the reaction of *N*-phenylacetamide outside the SWNT (89% of total *N*-phenylacetamide molecules) will form a known ratio (68%) of *para*-product.
[c] Calculation based on the assumption that all truly encapsulated *N*-phenylacetamide molecules (11% of total *N*-phenylacetamide molecules) can only form *para*-product.

Summary:	**Product Ratio / %**	
	para	***ortho***
Calculated	**71.5**	**28.5**
Experimental	**97**	**3**

The discrepancy between calculated and experimental product ratios suggests that the effect of confinement is greater than expected. This could be rationalised by diffusion into the nanotube combined with an accelerated confined reaction rate compared to the bulk. Although it is not possible to experimentally measure activation energy for this reaction, the hypothesised rate enhancement is consistent with a previous theoretical study where the activation energy of the Menshutkin reaction was calculated to be reduced by 60%, upon confinement within carbon nanotubes, providing exponential rate acceleration.[S6]

S4 References

S1 A. Bondi, *Journal of Physical Chemistry*, 1964, **68**, 441.
S2 W. L. F. Armarego, C. Chai, *Purification of Laboratory Chemicals*, Elsevier Science, Oxford, 2003, p. 83.
S3 H. A. Muathen, *Synthesis* 2002, 169.
S4 P. G. Dumanski, C. J. Easton, S. F. Lincoln, J. S. Simpson, *Australian Journal of Chemistry* 2003, **56**, 1107.
S5 B. S. Moon, H. Y. Choi, H. Y. Koh, D. Y. Chi, *Bull. Korean Chem. Soc.* 2011, **32**, 472.
S6 M. D. Halls, H. B. Schlegel, *Journal of Physical Chemistry B* 2002, **106**, 1921.