The Confined Space Inside Carbon Nanotubes can Dictate the Stereo- and Regioselectivity of Diels-Alder reactions

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Supplementary material

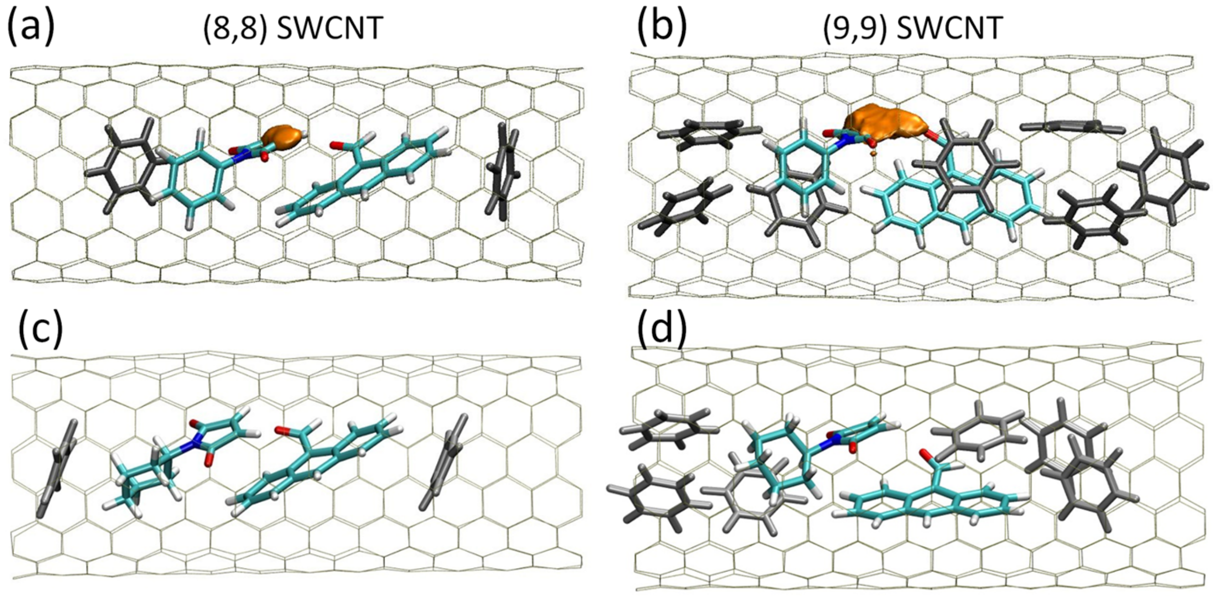

Figure S1. Average position of the reactants **(a)**-**(b)** N-phenylmaleimide/9-anthraldehyde and **(c)**-**(d)** N-cyclohexylmaleimide/9-anthraldehyde within (8,8) SWCNTs (**(a)**,**(c)**) and (9,9) SWCNTs (**(b)**,**(d)**) during 4ns molecular dynamics simulation. The gold surface shows the 95% probability surface for the reacting carbons on the maleimide. Surrounding benzene molecules are shown in

Computational methods

All ab initio geometry optimisations and energy calculations were done using Møller-Plesset second order perturbation theory (MP2)[1] with a 6-31+G* basis set, using Gaussian03[2] with the opt=tight convergence criteria. Transition states were found using the synchronous transit-guided quasi-Newton (STQN) method.[3] For both the ground and transition state optimisations, numerous initial guesses of the geometry were used to ensure the correct final state was found (Figure S2).

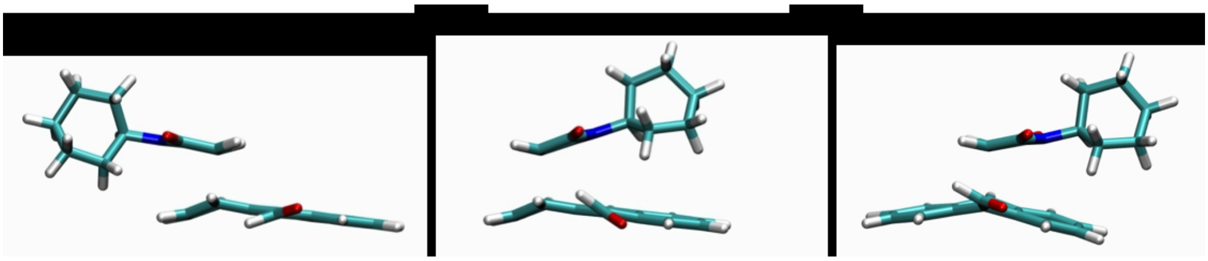

Figure S2: Optimized gas phase transition states of possible products from the Diels-Alder reaction between 9-anthraldehyde with N-cyclohexylmaleimide. **(left)** 1,4-exo adduct **(centre)** 1,4-endo adduct and **(right)** 9,10-adduct. Level of theory MP2 with 6-31+G* basis set.

To conduct the molecular dynamics simulations, initial coordinates of the (8,8) and (9,9) SWCNTs were generated using the TubeASP web site, with each tube approximately 2.8 nm in length. Each SWCNT was solvated in a 6 x 6 x 6 nm box of benzene (different simulations for each case) as pictured in Figure S3. The benzene molecules filled the simulation box including the interior space of the SWCNTs not occupied by the reactants or products. The parameters of all carbon atoms in the SWCNTs were set to be those of sp2-like aromatic carbons (type CA) in the CHARMM27 force field,[4] including bond, angle, and dihedral parameters and all charges of these atoms were set to 0, as has been validated by previous simulations.[5-7] The atoms in the SWCNTs were allowed to move (i.e. were not fixed). The reactants and products were also parameterised to be consistent with the CHARMM27 force field. This meant that charges were determined using the Merz-Singh-Kollman electrostatic fitting method[8,9] from an HF/6-31+G* calculation, while van der Waals and bond parameters were determined from similar atom types in the force field. The reactants and products were placed within the SWCNTs at a separation of approximately 0.4nm prior to conducting the simulations. An additional set of simulations with the reactants and products in a bulk 6 x 6 x 6 nm box of benzene (with no SWCNT) were also conducted. Simulations were conducted with a 1fs time-step using an NPT ensemble at a temperature of 300K and pressure of 1 atm controlled using Langevin dynamics and a Langevin piston using NAMD.[10] The pictures shown in Figure S2 represent the average positions of the reactants during 4 ns, after allowing 1 ns for system equilibration.

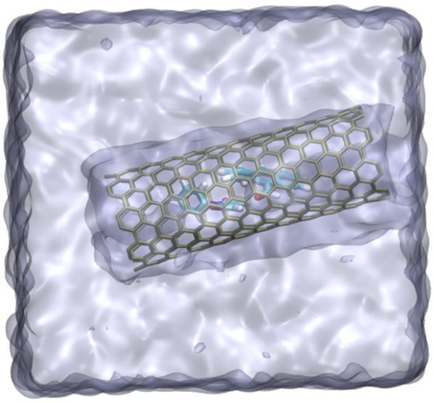

Figure S3: Simulation system. The SWCNT is shown in brown, the reactants as coloured atoms inside the SWCNT and the area sampled by benzene molecules as the blue surface.

Free energy profiles (potential of mean force) were constructed using the method of umbrella sampling.[11] In this the separation between the distance centre of mass of the 2 carbon atoms on each of the reactants that are going to participate in the Diels-Alder reaction is biased using a harmonic potential with force constant 5 kcal/molÅ^2, as pictured in Fig. S4. The centre of this potential was moved in 0.1 nm steps from a separation of 0.2 to 0.9nm, and 1 ns of equilibration and 3 ns of simulation was conducted at each position. The probability distributions were collectively analysed using the weighted histogram analysis method[12] using the implementation of Grossfield to determine the unbiased free energy profile. In order to calculate the free energy to remove the products from the SWCNTs, umbrella sampling was used to move the product from the centre of the tube into bulk in 25 steps separated by 0.1nm, each simulated for 1.4 ns. All other parameters were the same as the previously described umbrella sampling simulations.

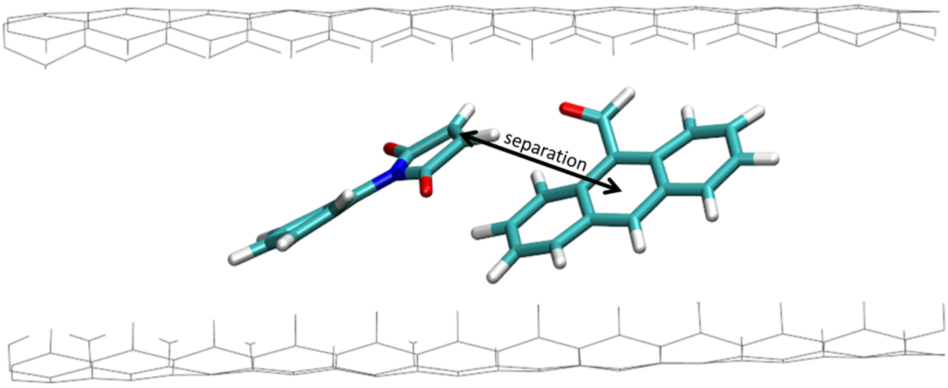

Figure S4: Umbrella sampling simulations. To calculate the free energy as a function of the separation of the reactants, the distance between the centre of mass of the carbons participating in each reaction was restrained to different distances in the molecular dynamics simulations. In this case, the separation is pictured for reactants forming the 9,10 product. Only some of the SWCNT is shown for context and the benzene molecules present in the simulations are not shown here.

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