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ADDITIVE
SOFT- & HARDWARE FÜR TECHNIK & WISSENSCHAFT

CASE STUDIES

Water-Filled Single-Wall Carbon Nanotubes as Molecular Nanovalves

Molecular dynamics simulations were used to study stability of water inside single-wall carbon nanotubes (water-SWNTs) in various gas atmospheres below 0.1MPa. It is found that the resistivity of water-SWNTs exhibits a significant increase in gas atmospheres below a critical temperature T_c, at which a particular type of atmospheric gas molecule enters the SWNTs in an on–off fashion. On the basis of this phenomenon, it is proposed that water-SWNTs can be used to fabricate a new type of molecular nanovalve. The process of the water ejection from the inside of the SWNTs triggered by the entering gas molecules is observed below T_c.
The water ejected from the inside of the SWNTs is located around the open ends of the SWNTs, where it is able to reversibly re-enter the SWNTs. Such process is possible when the gas-molecule-SWNT interactions have a comparable strength to that of the water–SWNT interactions. Then, water and gases are competing with each other to fill the SWNTs. Evidently, gases with stronger attractive interactions with the SWNT walls are more stable inside the SWNTs, and therefore have higher T_c.
The filling–ejecting transition mentioned above were carried out on a system of an open SWNT, water, methane and neon using NTV ensemble at T = 200 K. The interaction potentials were based on the TIP3P model for water and Lennard-Jones (LJ) sphere models for carbon, methane and neon.
The coexistent cases are given in Fig. 1. It is shown that the water cluster was gradually forced out from the SWNT by the entering methane molecules (Fig. 1a). In contrast, for Ne with a weaker gas–SWNT interaction potential (about 1/2 of that of methane), such replacement was not observed (Fig. 1b), confirming qualitatively the observed phenomena in the present experiments.

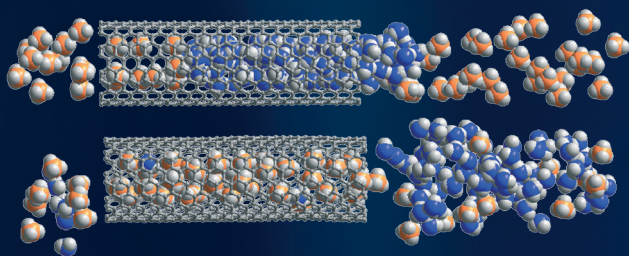References: Maniwa et al., Nature Materials (2007), 6, 135.

Figure 1a. MD simulations for the coexistent systems of water and methane molecules. Initially the water clusters are located inside the SWNT. After 300 ps, methane molecules enter the SWNT at 200 K.
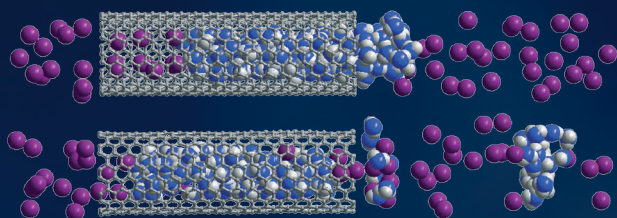

Figure 1b. MD simulations of filling-ejecting phenomena for the coexistent systems of water and Ne molecules.

Importance of local energy minima in drug analogs studies

(4s,5s)-4-methyl-5-phenyl-4,5-dihydro-1,3-oxazol-2-amine (U4EA) is an analog of dextroamphetamine expressing similar stimulant effects and similar toxicity. This fact suggests that both compounds bind with the same receptor, so significant structural analogy between the two compounds is expected. U4EA has one rotatable bond, shown in red (Fig. 2a) while dextroamphetamine has two. Global energy minimum search was performed using AM1-COSMO method by MO-G in SCIGRESS (Fig. 2a and 2b). An attempt to superimpose both structures shows very little analogy apart from the phenyl ring (Fig. 2c). A second calculation was performed on dextroamphetamine. The initial geometry was prepared by removing the part of the U4EA molecule shown in green (Fig. 2d), and adding hydrogens. A local energy minimum calculation by AM1-COSMO yielded structure shown in Fig. 2e. This structure overlaps very well (Fig. 2f) with the global energy minimum geometry of U4EA, proving that those two compounds might target the same receptor. The important conclusions from this study are:
For flexible drugs the lowest energy conformers are not always the active ones.
The choice of initial geometry submitted to geometry optimization calculations is of very high importance in computational drug studies.
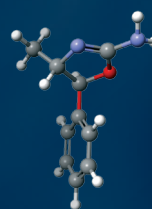
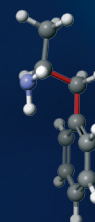

Figure 2a. U4EA lowest energy conformer.

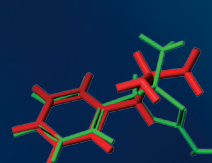Figure 2b. Dextroamphetamine lowest energy conformer.

Figure 2c. Overlap of lowest energy conformers of U4EA and dextroamphetamine.
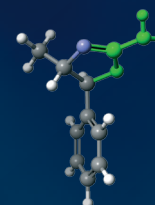

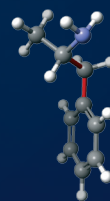Figure 2d. Preparation of initial geometry for dextroamphetamine local minumim search.

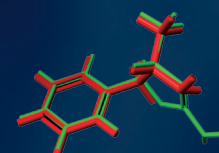Figure 2e. Local energy minimum of dextroamphetamine.

Figure 2f. Overlap of the non-minimum energy conformer of dextroamphetamine with lowest energy conformer of U4EA.

Molecular Dynamics Simulations of an Antiferroelectric Liquid Crystalline Molecule

Molecular dynamics simulations were carried out for an antiferroelectric liquid crystalline molecule, (S)-4-[1-methylheptyloxycarbonyl] phenyl 4'-octyloxybiphenyl-4-carboxylate (MHPOBC), to analyze its conformational property in smectic liquid crystalline phases. The simulation reproduces a phase transition through the solid-S_mC_x-S_mA-isotropic states. The MHPOBC molecules in the solid-S_mC_x phase are packed in a tilted layered structure, while in the S_mA-isotropic phase the molecular tilt disappears producing a fluid like conformation.

The simulations were carried out on a system of 64 MHPOBC molecules under periodic boundary conditions using NTP ensemble at various temperatures and DREIDING and OPLS force-field parameters.

The molecular dynamics simulation reproduces the X-ray structure at 298K (Fig. 3a) and this is identified as the solid phase. At 400K (Fig. 3b), the biphenyl group is packed in an alternately tilted structure of the S_mC_x phase. At 450K (Fig. 3c) the tilted later structure disappears as the molecules uniaxially align along the layer direction. The molecules take on more elongated conformations and this phase is identified as the S_mA phase. The average molecular bend angle in this phase agrees with ^{13}C-NMR and ^{2}H-NMR experimental data. At 750K (Fig. 3d), the MHPOBC molecules undergo free rotational and translational motion as well as internal bond rotation. The orientation correlation function has a computed value of zero. This phase is thus identified as the fluid like isotropic state.

The program is therefore capable of generating the four distinct phases (solid, S_mC_x, S_mA and isotropic) of the MHPOBC liquid crystal.

References: Torumi et al., Molecular Crystals and Liquid Crystals (2003), 402, Number 1, 1.

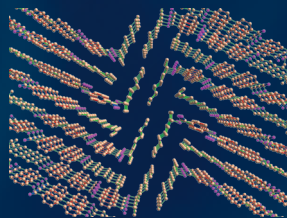
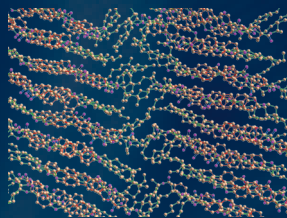Figure 3a. Structure of MHPOBC liquid crystal system from MD simulation at 298K.

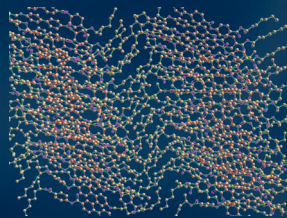Figure 3b. Structure of system at 400K representing the S_mC_x phase.

Figure 3c. Structure of system at 450K. The molecules take on a more elongated shape representing the S_mA phase.
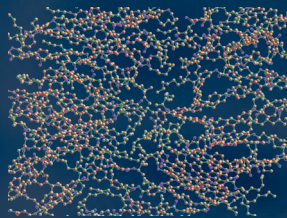

Figure 3d. Structure of system at 750K. The MHPOBC molecules undergo free motion and inteArnal bond rotation representing the fluid like isotropic state.

Approximated transition state study by semiempirical methods applied to process optimization.

The reaction of methylnitrone with monofluoroallene proceeds in two directions yielding syn and anti addition products (Fig 4a). Syn product is the dominant one. The aim of the study was to predict possible ways of altering the proportions of the products. The difference in heats of formation of the syn and anti products is less than 0.1 kcal/mole (MO-G AM1 SCIGRESS), thus the thermodynamic control of the reaction direction is highly unlikely. AM1 calculations of syn and anti addition geometries were done by MO-G in SCIGRESS (Fig 4a, 4b, respectively). While the shape of frontier orbitals (solid surfaces) is almost identical in both cases, the appearance of electrostatic isopotential surfaces (dotted) is quite different. In case of anti-addition there is a +,+ interaction, that explains the observed yields. Repulsive electrostatic interactions may be decreased, as the solvent polarity increases giving a method of yield control in industrial applications.
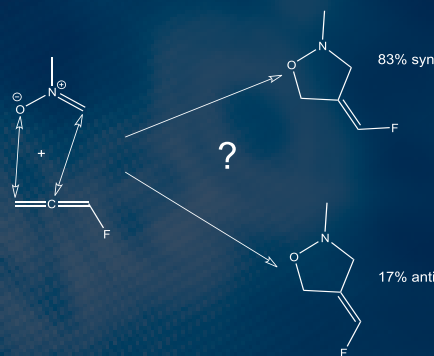

Figure 4a. The two reaction directions of methylnitrone monofluoroallene addition.
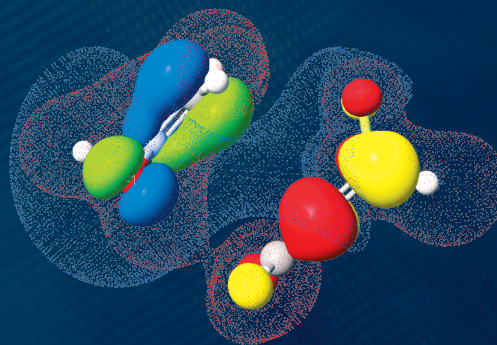

Figure 4b. Frontier orbitals and electrostatic isopotentials of syn-addition attack.
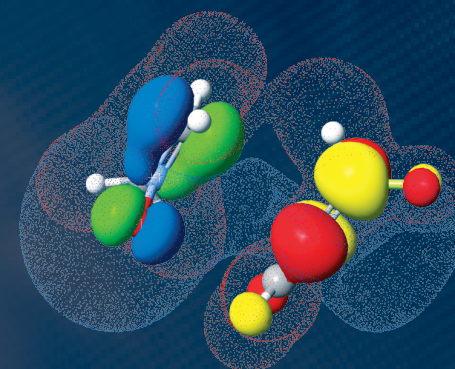

Figure 4c. Frontier orbitals and electrostatic isopotentials of anti-addition attack.

SCIGRESS

SCIGRESS is a leading computer-aided chemistry modeling package designed for computational chemists as well as experimental chemists conducting research in life sciences, materials and chemicals and undergraduate and graduate educators. Designed by chemists for use by chemists, SCIGRESS incorporates a wide range of modeling and analysis techniques, including many developed and validated by experts in computational chemistry. Chemists who need answers about realistic molecular systems can use SCIGRESS effectively without becoming experts in the details of computational techniques. SCIGRESS facilitates access to its methods by easy-to-use graphical interface which intuitively guides users through varying calculation methods and offers alternatives to balance accuracy and computational requirements. SCIGRESS can apply a wide range of computational models, from molecular mechanics through rigorous quantum electronic structure techniques, to all types of molecular systems, from organic molecules, to inorganics, polymers, materials systems (metals, oxides, ceramics, semiconductors), and whole proteins.

SCIGRESS computational tools

- **Molecular Mechanics and Dynamics** – All elements; organics and inorganics; MM2 and MM3; adjustable mechanics parameters; conformational searching; energy maps; geometry optimization; molecular dynamics calculations.
- **MO-G** – Main group elements; organics and inorganics; AM1, PM3, PM5, MINDO/3, MNDO; d-orbitals for transition metals; COSMO solvent model; MOZYME for up to 20,000 atoms; ESR; IR spectra; heat of formation; free energy; transition state searching; intrinsic reaction coordinates; dynamic reaction coordinates; activation energy; polarizabilities; reactivity surfaces; dipole moments; partial charges; bond orders; potential energy surfaces; geometry optimization: excited states, open shell systems; intersystem crossing.
- **DGauss** – DFT calculations: optimum geometry; potential energy maps; vibrational frequencies and spectra; transition states; reaction pathways; molecular orbital energies; dipole, quadrupole, and octupole moments; polarizability; partial charges; NMR chemical shifts. Transition metals, pseudo potentials.
- **MD-ME** – advanced molecular dynamics simulations; ensembles: NEV, NTV, NPH and NTP; the time evolution of the equations of motion: Gear or Hernandez methods; temperature and pressure-controlled MD simulations: Parrinello-Rahman, velocity scaling and Nose methods; SHAKE and MATRIX algorithms for stretch-bond constraint. External fields: electrostatic, magnetic, gravitational, containing sphere and elastic energy correction. Non-equilibrium molecular dynamics for thermal conductivity calculations. Extensive potential library is comprised of numerous high-quality published potentials, including two-body, three-body and embedded atom models (EAM) covering crystals, metals, ceramics, semi-conductors, solutions, liquids, gases, organic systems, polymers and biomolecules. Electronegativity equalization method (EEM): calculation of the charge distribution during

simulation. Powerful analysis modules: thermodynamic properties as a function of time, the trajectory and animation of collective atomic configurations, mean square displacement and the self-diffusion coefficient, radial distribution function and running integration number, interference function calculates X-ray and neutron diffractions, Voronoi analysis, velocity auto-correlation function, modulus of elasticity, rotational auto-correlation function, viscosity coefficient.
- **CONFLEX** – Automated global minimum search, systematic and exhaustive generation of low energy conformers of a molecule of any shape, including rings; automatic and full characterization of optimum geometries, eliminating duplicates and stationary structures that are not minima.
- **ZINDO** – Predicts spectroscopic properties; d-orbitals, INDO and CNDO, organics and inorganics; atom partial charges, bond orders, UV-visible spectra; SCRF solvent modeling, reactivity surfaces.
- **MO-S (MOS-F)** – Predicts spectroscopic properties of both open and closed-shell molecules. Semiempirical methods: AM1, PM3, PM5, INDO/S, CNDO/S, CNDO/S2, CNDO/S3. RPA/CIS methods. Onsager solvation model.
- **LocalSCF** – A novel linear scaling quantum mechanics method able to calculate more than 100 000 atoms, designed for very fast calculations of electronic structure of proteins. MNDO, AM1, PM3, and PM5 semi-empirical Hamiltonians. COSMO continuum solvent model.
- **Spreadsheet** – Automated batch processing; research project management; tracking and annotation; scatter graphs; simple, multiple and step-wise regressions; QSAR & QSPR for ADME, logP, Rule-of-5. Handles thousands of molecules. Auto-docking module.

SCIGRESS Features

- Determination of total energy (DFT), heat of formation (semi-empirical methods) or strain energy (MM).
- Reaction mechanism determination via transition state searching and evaluation and visualization of intrinsic reaction coordinates.
- Determination of low energy conformations.
- Vibrational analysis including visualization of IR spectra and normal modes of vibration.
- Interactions with radiation including visualization of UV-visible spectra, and identification of molecular orbitals responsible for orbitals electronic transitions.
- 3D-visualization of electronic surfaces including orbitals, electron densities, and electrostatic surfaces.
- Molecular dynamics study and analysis of phase transitions, expansion, defects, compressibility, tensile strength, adsorption, absorption, and thermal conductivity.
- QSAR/QSPR analysis.
- Protein-ligand docking.
- Quantum chemistry of full proteins

SCIGRESS can transparently run and visualize results from the third party programs: ADF, GAMESS, Gaussian, PHASE, MOPAC2009, and CONFLEX6. SCIGRESS has been designed as a modular product to allow each user to choose only the components needed. The computational power may be extended by optional multi-core compute engines for Windows and Linux.

FUJITSU

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