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Dissolution-driven convection in reactive systems

Abstract

Dissolution-driven convection develops when a buoyantly unstable density stratification builds in the gravity field upon dissolution of a species into a host fluid. This phenomenon has regained interest in the context of CO₂ sequestration in oil fields or saline aquifers because it accelerates the mixing between CO, and the host phase, thereby improving the safety of the storage process. Our objective is to understand to what extent the properties of such convective dissolution depend on the chemical composition of the storage site. Chemical reactions can indeed impact convection as they affect concentrations and thus the density stratification in the host phase, at the origin of convection. Using combined theoretical, numerical and experimental approaches, we show that a chemical reaction between the dissolving species and a reactant dissolved in the host phase can either accelerate or slow down the development of convection compared to the nonreactive case. We classify the various possible cases as a function of the contributions to density and diffusion coefficients of the chemical species involved. We also discuss the impact of chemistry on the interfacial flux of the dissolving species.

Keywords

Fluid dynamics, convection, physical chemistry, CO_2 sequestration

1. Introduction

The interplay between chemistry and fluid flows can produce a wide range of complex dynamics [1, 2]. Indeed, chemical species can sometimes be more than simple passive tracers entrained by fluid flows when variations in solute concentrations change the physical properties of the fluid such as density, viscosity, or surface tension. By modifying the local concentrations, reactions and diffusion can create dynamic spatial gradients of composition, which in turn alter physical properties of the flow and can induce convective flows. In particular, convection can develop due to gradients of density, when a denser fluid lies on top of a less dense one in the gravity field. This convection, resulting from a hydrodynamic instability, accelerates the transport of the solutes compared to the case of pure diffusive transport for which no flow motion is present. Such convective flows can thus be interesting in applications requiring mixing of chemicals, such as during CO₂ sequestration in geological formations for instance.

To mitigate climate change, Carbon Capture and Sequestration (CCS) is considered as one of the mandatory measures needed to reduce the increase in concentration of this greenhouse gas in the atmosphere. CO_2 is captured at the exhaust of plants and injected into soils in old mine or oil fields as well as in saline aquifers, widely distributed around the globe. When CO_2 is injected in an aquifer, it is less dense than brine (saline water) and hence first rises up to the impermeable cap rock constraining the fluid due to gravity currents before starting to dissolve into the brine located below, as shown in Fig. 1. As CO_2 increases the density of the aqueous solution upon dissolution, an unstable density stratification forms in the brine, where a boundary layer of denser brine rich in CO₂ grows over time. After an onset time depending on the physical parameters, the two-layer stratification becomes unstable and convection sets in, creating fingers of CO₂-rich brine sinking in the host phase. This convective instability improves the safety of the sequestration as it transports the dissolved CO₂ downwards, further away from potential pathways to escape to the atmosphere [3-5]. Furthermore, geochemical reactions may occur between dissolved acidic CO_2 and minerals dissolved in the brine [5-7]. These reactions can modify the density profile in the aqueous phase, and thereby the unstable density gradient that triggers convective motions. As an example, it has been shown that a reaction between CO₂ and the solid porous matrix of the aquifer can slow down the onset of the convective instability, because it consumes the species at the very origin of convection [6, 7]. The impact of reactive processes involving species in solution on the transport dynamics of CO_2 is, however, still poorly understood.

In this context, our goal is to understand and classify the effects of reactions involving species in solution on the properties of dissolution-driven convection, by means of combined theoretical, numerical and experimental approaches.

2. Model

We consider an isothermal and isotropic twodimensional system with the gravity field gpointing downwards along the vertical z axis, as shown in Fig.2. Two partially miscible phases are placed in contact along a horizontal interface in a porous medium. Phase A dissolves with a finite solubility A₀ into the fluid phase located below, called in this study ``host" phase or solution. The concentration of A at the interface is considered to be equal to A₀ at all times (assumption of local chemical equilibrium). The interface is assumed to remain in time at the same position z = 0. In this situation, the model can focus on the dynamics in the host phase only. The host phase contains



Figure 1: Convective dissolution taking place during CO, sequestration in a saline aquifer

a reactant B initially present in concentration $B_{0.}$ Species A and B react according to the simple kinetic scheme A + B→C to produce another solute C. The interface is assumed to be impermeable to the solvent and to solutes B and C. All three species A, B and C can contribute to changes in the density of the host phase.



Figure 2: Model system

The equations describing the dynamics in the reactive host phase are nondimensionalized with the following scales: concentration A_0 , time $t_c=1/(qA_0)$, length $l_c=\sqrt{(D_A/(qA_0))}$, velocity $u_c=\phi\sqrt{(D_AqA_0)}$, pressure $p_c=\phi D\mu/\kappa$, density $p_c=\phi D_A\mu/(g\kappa l_c)$), where q is the kinetic constant of the reaction, D_A the diffusion coefficient of A, ϕ the porosity of the medium, μ the viscosity of the host phase, κ the permeability of the porous matrix, q the norm of the gravity.

With these scales, the reaction-diffusionconvection equations describing the spatiotemporal evolution of the solute concentrations c_A , c_B , c_C in the host phase become:

$$\frac{\partial c_i}{\partial t} + (\boldsymbol{u} \cdot \boldsymbol{\nabla})c_i = \delta_i \nabla^2 c_i + f(c_i), \qquad (i = A, B, C) \quad (1)$$

with $\delta_i = D_i/D_A$ the ratio of the diffusion coefficients and $f(c_i)$ the reaction rate equal to $-c_A c_B$ for reactants A and B and $+c_A c_B$ for product C. The flow velocity **u** is computed using Darcy's equation for an incompressible fluid flow:

$$\boldsymbol{u} = -\boldsymbol{\nabla} p + \rho \boldsymbol{e}_{\boldsymbol{z}}, \qquad \boldsymbol{\nabla} \cdot \boldsymbol{u} = \boldsymbol{0}, \tag{2}$$

where e_z is a unit vector pointing along the vertical z axis, p is the pressure and ρ the density

of the host fluid. The equations for the solute concentrations (1) and for the fluid flow (2) are coupled via an equation of state for the density ρ of the host fluid:

$$\rho = \sum_{i=A,B,C} R_i c_i, \tag{3}$$

expressing the fact that the density profile in the solution depends on the concentration profiles. Here $R_i = \rho_0 \alpha_i g \kappa l_c / (\phi \mu D_A)$ are the Rayleigh numbers quantifying the contributions of the different species to the density of the solution, ρ_0 is the density of the solvent and $\alpha_i = \frac{1}{\rho_0} \frac{\partial \tilde{\rho}}{\partial c_i}$ is the solutal expansion coefficient of species *i* with tildes denoting dimensional variables. The dimensionless parameters of the model are δ_B , δ_C , R_A , R_B and R_C , depending on the nature of the chemicals involved, as well as the ratio $\beta = B_0/A_0$ between the initial concentration B_0 of reactant B dissolved in the host fluid and the solubility A_0 of A in the host phase.

3. Classification of the reaction-diffusion density profiles

The type of density stratification in the host fluid existing in the reaction-diffusion (RD) regime, i.e. before convection sets in, helps us predict different scenarios for the onset of convection. We thus theoretically compute RD density profiles along the vertical axis z and classify them in a parameter space spanned by the diffusivity and Rayleigh number ratios. While only two different types of density profiles can develop in the non-reactive case (monotonically decreasing or increasing along z), eight different types of profiles can be observed in the reactive case [8], as shown in Fig. 3. The coupling between dissolution and diffusion on the one hand, and chemistry on the other hand, thus multiplies the number of possible scenarios for the development of buoyancy-driven instabilities. This enlarged complexity can be explained by the increased number of parameters as three species A, B and C are involved in the dynamics instead of only one in the non-reactive case.



Figure 3: Classification of RD density profiles in the parameter space $(\delta_{il} \delta_{cr} R_{jl} / R_c)$ adapted from Loodts *et al.* [8]. (a) For $R_A > 0$ (species A increases the density of the solution), four types of density profiles are possible: I: monotonically decreasing along z; II: minimum at the reaction front, indicated as a dashed line; III: minimum below the reaction front; IV: minimum at the reaction front followed by a maximum below. (b) For $R_A < 0$ (species A decreases the density of the solution), four other types of density profiles are possible: V: maximum at the reaction front; VI: monotonically increasing along z; VII: maximum at the reaction front followed by a minimum below; VIII: maximum below the reaction front.

4. Effects of reactions on the convective dynamics

On the basis of this classification, we now analyze how reactions affect the convective dynamics by using a linear stability analysis and numerical simulations. We here consider more specifically $R_A = 1 > 0$, i.e. species A increases the density of the solution, and all diffusion coefficients equal (line $\delta_B / \delta_C = 1$ in Fig. 3a). In this situation, it can be shown that the dynamics only depend on the initial dimensionless concentration β of reactant and on the difference $\Delta R_{CB} = R_C - R_B$ between the contributions to density of reactant B and product C [9, 10].

The fingering dynamics are illustrated in Fig. 4 in the non-reactive case and two specific reactive cases with $\beta=1$ and different ΔR_{CB} . Without reaction (Fig. 4a), fluid motion occurs because less dense fluid poor in dissolving species A tends to float up towards the surface while denser fluid rich in A sinks downwards in the form of fingers. In the presence of a reaction A+B→C, the other solutes B and C also contribute to the density of the host solution, thereby affecting the density stratification and thus the fluid flow [9, 10].

If $\Delta R_{CB} = 1$ (C is denser than B), the density profile is monotonically decreasing (zone I in Fig. 3a) and convection develops faster than in the non-reactive case (Fig. 4b). If $\Delta R_{CB} =$ -1 (C is less dense than B), the density profile developing in the host phase has a minimum where locally, less dense fluid lies on top of denser one in the gravity field (zone II in Fig. 3a). Due to this local buoyantly stable zone, the instability develops more slowly than in the non-reactive case (Fig. 4c).

In order to generalize these observations to other values of parameters, we measure the growth rate σ of the instability as a function of the parameters ΔR_{CB} and β . Taking into account these results and the classification of the RD density profiles (Fig. 3), we divide the ΔR_{CB} axis in three zones Ia, Ib and II as illustrated in Fig. 5.

In zone II ($\angle R_{CB} < 0$), the growth rate σ is smaller than its non-reactive counterpart because the minimum in the RD density profile acts as a stabilizing barrier and slows down the development of convection. Zone I ($\angle R_{CB} \ge 0$), corresponding to monotonic RD density



Figure 4: Density field at three successive times (from top to bottom) computed from numerical simulations ($R_A = 1, \delta_B = \delta_C = 1$).



Figure 5: Growth rate σ of the instability as a function of ΔR_{CB} and β with typical RD density profiles as insets. The dashed line corresponds to the non-reactive case. Figure adapted from Loodts *et al.* [10].

profiles, is further subdivided in zones Ib and Ia depending on whether σ is smaller or larger than its non-reactive counterpart. In zone Ib corresponding to small positive values of ΔR_{CB} , reactions slow down the development of convection. We can better understand this stabilizing effect of reactions in zone Ib when $\Delta R_{CB} = 0$: the consumption of B is exactly compensated by the production of C in terms of density, but the species A, which increases the density, is consumed by the chemical reaction. In zone Ia, C is dense enough to more than compensate for the consumption of A, so that convection develops faster than in the non-reactive case. Furthermore, for all values of ΔR_{CR} , increasing the initial concentration β of reactant amplifies the stabilizing or destabilizing effect of reaction. We can thus tune the properties of the dissolution-driven convection either by modifying the nature of the reactant (impacting ΔR_{CB}) or the initial quantity of the reactant (impacting β) [10-12].

5. Experiments on the convective dissolution of CO₂ into aqueous alkaline solutions

To validate those theoretical predictions, we perform experiments in quasi-two-dimensional systems, more specifically vertical Hele-Shaw cells made of two transparent glass plates separated by a small gap. Pure gaseous CO_2 is injected through the top of the cell at atmospheric pressure and flows above aqueous solutions containing various chemicals. Dynamics occurring within the transparent fluids are visualized with the help of a schlieren technique, which tracks dynamical changes in refractive index related to density gradients in the solutions.

We experimentally study the convection developing upon dissolution of gaseous CO_2 into reactive aqueous solutions of CsOH, KOH, NaOH and LiOH of increasing concentration. As shown in Fig.6, we observe that convection arises sooner and develops faster when (1) the concentration of the base is increased in the



Figure 6: Convective fingering patterns recorded at a time t = 13 min when CO₂ dissolves into solutions of CsOH, KOH, NaOH and LiOH in increasing concentrations [13]. The dimensions of the pictures are 12 cm x 7 cm.

aqueous solution; (2) the counter ion of the hydroxide is replaced with an element located further down in the alkali metal column (Li⁺ < $Na^+ < K^+ < Cs^+$). Indeed, the reaction between dissolved CO₂ and the base MOH (with M⁺ an alkali metal) modifies the density stratification in the solution and thus the development rate of the dissolution-driven convection [13]. Additionnaly, changing the counter-ion M⁺ of the base also modifies the density profile, through a combination of solutal and differential diffusivity effects. These experimental findings highlight that chemical reactions between CO₂ and a reactant dissolved into the host aqueous phase can accelerate the development of dissolution-driven convection and thus the mixing between both CO₂ and aqueous phases.

7. Conclusion

In conclusion, our work has contributed to a better understanding of the influence of chemical reactions on the development of dissolutiondriven convection. Our theoretical classification has shown that reactions can accelerate or slow down the development of convection, depending on the parameters of the problem, in particular the relative contributions to density of the reactants and the product. We have illustrated the case where reactions increase the growth rate of the instability with laboratory experiments on the convective dissolution of gaseous CO_2 into aqueous alkaline solutions of MOH. Our results thus help understand the fundamental physicochemical processes impacting transport in fluids, which are important for various industrial applications, in particular CO₂ sequestration in geological formations. Dissolution-driven convection can improve the safety of the sequestration by transporting dissolved CO₂ faster downwards, further away from faults, fracks and other pathways for a potential escape to the atmosphere. As reactions affect the time scales for the development of convection, it would be possible to control convective dissolution with chemistry, by selecting the most appropriate storage site from a geochemical point of view.

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Mechanical unfolding of single oligorotaxanes using atomic force microscopy

Abstract

Nature leads the way in the design of biological molecular machines with specific functions in our bodies. But chemists are in hot pursuit, synthesizing highly sophisticated artificial molecular machines with well-defined folded Mechanically interlocked architectures. molecules, such as rotaxane, catenane or molecular knots, are very attractive for the design of molecular machine prototypes, enabling the controlled submolecular movement of their components. Using atomic force microscopy (AFM), we investigated here the mechanochemical properties of oligorotaxanes. These molecules are made of a flexible poly(ethylene oxide) thread containing electronrich 1,5-dioxynapthalene units and encircled by multiple tetracationic molecular rings. Thanks to donor-acceptor interactions, they display a serpentine-like folded conformation in solution. Individual oligorotaxane foldamers were trapped between a substrate and an AFM tip and were mechanically unfolded by singlemolecule force spectroscopy. Standard force experiments show the sequential breaking of intramolecular interactions. Real-time fluctuations between partially folded states were observed for the first time on a wholly synthetic molecule, evidencing the very fast (un)folding dynamics of those molecules. Pulling-relaxing experiments and dynamic force spectroscopy showed the remarkable ability of these synthetic oligorotaxanes to do work against a mechanical

load and their higher performance compared to natural folding proteins.

Keywords

Molecular machines, atomic force microscopy, single-molecule force spectroscopy

1. Introduction

1.1. Molecular machines

Biological molecular machines are known to carry out specific tasks in our bodies. Muscles contraction, cargo transport inside the cell along actin filaments or flagella rotary motions are few examples of natural molecular machineries with a specific function [1]. For a few decades, the domain of artificial molecular machines has gained a lot of attention. This field was even recognized by the Nobel committee which attributed the 2016 Nobel prize in chemistry conjointly to Jean-Pierre Sauvage, Ben Feringa and J. Fraser Stoddart for the design and synthesis of molecular machines. In 1959, Richard P. Feynman gave a very inspiring insight into the promise of these man-made molecular machines, even before chemists were able to synthesize them. In his lecture There's plenty of room at the bottom, he considered the immense possibilities of exploring the world at the nanoscale and the advantages of building wholly synthetic molecular machines [2]. "I can't see exactly what would happen, Feynman said, but I can hardly doubt that when we have some control of the arrangement of things on a small scale we will get an enormously greater range of possible properties that substances can have, and of different things that we can do".

In this contest for the control of molecular and sub-molecular motions at the nanoscale, mechanically interlocked molecules (MIMs) have gained a lot of attention [3]. These MIMs, such as rotaxanes and catenanes (Fig. 1), consist of several subcomponents interlaced together by mechanical bonds. As prototypes of artificial molecular machines, they enable the controlled movement and positioning of their component parts [4]. Under an external stimulus such as light irradiation or a change of solvent, each single machine is pulled out of its equilibrium state and is able to produce an effective work. The integration of those molecules into more complex architectures (such as polymer gels) can possibly lead to a macroscopic change of the material [5].



Figure 1. Mechanically interlocked molecules: (a) catenane, (b) rotaxane, (c) Borromean ring, (d) molecular knots. Adapted from reference [3].

1.2. Atomic force microscopy

Collecting information about the working processes of such molecules is crucial for the design of more efficient molecular devices. Atomic force microscopy (AFM)-based singlemolecule force spectroscopy (SMFS) has proved to be an elegant technique to obtain exquisite and detailed information about the structure, dynamics and operation of functional complex molecules and machines, as well as probing intra- and intermolecular interactions [6,7]. During a force spectroscopy experiment, the molecule of interest is trapped between a microscopic probe (AFM tip) and a substrate, its restoring force being measured during the mechanical stretching. AFM-based force spectroscopy has been widely used to unravel the behavior of natural biomolecules under mechanical load [6], to measure the binding interactions between molecular partners [8], to elucidate the mechanochemistry of biological machines [9], and to investigate the mechanochemical properties of mechanically interlocked molecules [10-12].

Beyond standard force spectroscopy, dynamic force spectroscopy focuses on the influence of the loading rate on the force required to break an interaction [13]. By increasing the loading rate, the interaction is pulled out-of-equilibrium and the rupture force increases. The relationship between the rupture force and the loading rate has been described by several models, namely Bell-Evans [14], Friddle-Noy-De Yoreo [15], and Dudko-Hummer-Szabo [16], and can provide an estimation of thermodynamic and kinetic parameters. Additionally, by performing subsequent controlled pullingrelaxing experiments on a trapped molecule, it is even possible to determine the free-energy difference (ΔG) between two conformations of the molecule [13].

2. Mechanical unfolding of oligorotaxanes

Recently, donor-acceptor oligorotaxanes were synthesized [17], at the intersection between MIMs and foldamers - synthetic molecules presenting a folded conformation. These oligorotaxanes are based on a flexible poly(ethylene oxide) (PEO) thread bearing 1,5-dioxynaphthalene (DNP) units, and encircled by several tetracationic cyclobis(paraquat-pphenylene) boxes (also known as blue boxes or CBPQT⁴⁺) (Fig. 2). The intramolecular interactions between DNP donors and 4,4'-bipyridinium (BIPY²⁺) units in the blue boxes induce a packed serpentine-like conformation, as observed by X-ray crystallography and ¹H nuclear magnetic resonance studies [17,18].



Figure 2. Chemical structure and serpentine-like conformation of an oligorotaxane, with the main PEO chain (in red) interlaced in the (blue) rings (counterions are not represented). Adapted from reference [17].

In this study in collaboration with the group of Prof. J. Fraser Stoddart, we have investigated the mechanochemical properties of those oligorotaxanes in solution and at the singlemolecule level [19,20]. The molecules were prepared with 1,2-dithiolane rings at both end for their interfacing between a gold-coated AFM tip and a gold-coated silicon substrate. The molecules were grafted using our previous strategy [11] to obtain a low-density regime that prevails the attachment of individual molecules on the tip during the force experiments.

During a force spectroscopy experiment, we first approach the AFM tip to the surface in order to create Au-S interaction between the tip and the molecule. Then, the tip is retracted in a controlled manner (i.e. at a fixed loading rate) and the restoring force is monitored by the deflection of the tip-bearing cantilever (Fig. 3a). The obtained force curve is related to the behavior of the molecule during the stretching, as well as its initial conformation.

N,N-Oligorotaxanes were stretched in dimethylformamide (DMF) and present a characteristic force-distance sawtooth profile (Fig. 3b). This reproducible pattern consists of equallyseparated rupture peaks, which we attribute to the sequential breaking of donor-acceptor intramolecular interactions (DNP-BIPY²⁺). The length increment between successive peaks (ΔL_{i}) was measured using the worm-like chain (WLC) model, an entropic elasticity model describing the behavior of a flexible polymer. Two ΔL_{a} populations were observed: the first one at $1.2 \pm$



Figure 3. AFM mechanical stretching of individual oligorotaxanes: (a) scheme of the single-molecule force spectroscopy experiment showing the rupture of one donoracceptor interaction and the characteristic length increase of 1.2 nm, (b) characteristic force-distance curve presenting a sawtooth pattern with equally-distant peaks ($\Delta L_c = 1.2$ nm), (c) force-distance curve showing the rupture of intramolecular interactions by pairs ($\Delta L_c = 2.3$ nm). Adapted from references [19,20].

0.1 nm and the second one at 2.3 ± 0.1 nm (as shown in Fig. 3b and c). Based on crystallographic data obtained previously [18], the distance between two subsequent DNP units increases from 0.7 nm in the folded state to 1.9 nm in the unfolded state (Fig. 3a). Hence, the length increment of 1.2 nm repeatedly observed in experimental force curve is in perfect agreement with the breaking of one DNP-BIPY²⁺ interaction, the second population representing the simultaneous breaking of two donor-acceptor interactions.

The most probable rupture force is about 90 pN for the stretching of the oligorotaxanes at 10^4 pN·s⁻¹. This value is consistent with the breaking of noncovalent interactions such as donor-acceptor π -interactions, hydrogen bonds or H- π interactions [21]. The last rupture peak displays a higher force (about 300 pN) that is characteristic of an S-S interaction with gold.

The stretching pattern is thus in agreement with the unfolding of the previously proposed serpentine-like (co)conformation of the oligorotaxanes in solution.

3. Real-time capture of (un)folding fluctuations

In order to determine the mechanical unfolding reversibility, we performed pulling-relaxing experiments. A single oligorotaxane was trapped between the substrate and the tip, the mechanical load being subsequently increased and decreased without breaking the interaction between the molecule and the tip. Pulling-relaxing curves are shown in Fig. 4 and illustrate the stochastic behavior of the molecule under mechanical load. The subsequent breaking and reformation of a single donor-acceptor interaction can take place without (Fig. 4a) or with (Fig. 4b) hysteresis (difference between the pulling and the relaxing curves). Hysteresis indicates that the work done to break one interaction is partially dissipated and is not fully recovered for the reformation of the interaction. Fig. 4c shows the breaking of two intramolecular interactions simultaneously (one arrow in pulling curve), followed by their sequential reformation (two arrows in relaxing curve). Such force curves evidence the reversibility

of the mechanical unfolding, the molecule being able to reform the broken interaction as soon as the mechanical load is lowered.

Also, we sometimes noticed rapid fluctuations between partially folded and unfolded states both during pulling and relaxing movements (Fig. 4d and e). Such fluctuations are representative of the *hopping* of the molecule between two (co) conformations. Similar patterns have previously been observed on biomolecules and are the hallmark of an experiment performed near the thermodynamic equilibrium [22-24]. We show here the first example of small synthetic molecules undergoing such back-and-forth (un)folding transitions at high loading rates. A scrupulous analysis of the *hopping* phenomenon showed that a single oligorotaxane is able to exert a force of up to 50 pN under an external load of 60 pN in average. As a comparison, the maximum mechanical load that proteins can accommodate during such fluctuations is typically about 10 pN. At high loading rate $(10^5 \text{ pN}\cdot\text{s}^{-1})$, we observed more than 4,300 fluctuations per second between both states, about 300 times faster than calmodulin (a folding protein presenting similar fluctuations between folded and unfolded states) [23]. More importantly, the transition step occurs in less than 10 s, making the oligorotaxane the fastest folding system studied at high loading rate.

We believe that this robust behavior originates from the mechanically interlocked structure, maintaining both donor and acceptor units in a close neighborhood after being mechanically separated. Compared to larger biological specimens, the refolding of the oligorotaxane is associated with a low entropic penalty. The mechanically interlocked structure constrains the blue boxes around the DNP stations and maintains a pre-oriented conformation, facilitating the reformation of the broken interactions.

4. High performance of artificial molecules

Dynamic force spectroscopy experiments were performed on single oligorotaxanes, which were mechanically stretched at 11 different loading



Figure 4. Pulling(blue)-relaxing(red) experiments on oligorotaxanes: breaking and reformation of a single DNP-BIPY²⁺ interaction without (a) and with (b) hysteresis (pulling curve is offset for more clarity), (c) breaking of two intramolecular interactions followed by their subsequent reformation, (d) pulling and (e) relaxing curve presenting many fluctuations between locally folded and unfolded states. Adapted from references [19,20].

rates varying from 10^2 to 10^6 pN·s⁻¹ [19]. At each loading rate, the distribution of the rupture force was adjusted to provide the most probable rupture force (F). The evolution of F with the loading rate is shown in Fig. 5 (red marks). The quasi-linearity observed in this graph indicates a rate-independent rupture force in this range of loading rate, evidencing experiments performed in the near-equilibrium regime. In comparison, similar mechanical stretching of biomolecules were described by the Friddle-Noy-De Yoreo model (non-linear fit) [15] and showed the distinction between their near-equilibrium and out-of-equilibrium regimes in similar range of loading rates (Fig. 5, gray marks). The mechanical stretching of oligorotaxanes seems to be always performed in the near-equilibrium regime, at least up to 10^6 pN·s⁻¹. The kinetic (i.e. out-of-equilibrium) regime is not reached in these conditions, evidencing the high dynamics of such interlocked molecules. Furthermore, the equilibrium force (rupture force in the nearequilibrium regime) is higher than 100 pN, in comparison with the low equilibrium force (< 50 pN) experienced by biomolecules studied in similar conditions [15]. Again, the performance of those synthetic molecules surpasses the one of natural folding proteins, probably due to their specific chemical structure.



Figure 5. Dynamic force spectrum of the mechanical unfolding of single oligorotaxanes in DMF at 11 loading rates (in red) superimposed with force spectra of 10 data sets (gray scale) taken from the literature and fit by the Friddle-Noy-De Yoreo model (reference [15]). The near-equilibrium regime is maintained for the oligorotaxane, even at high loading rates, evidencing the high dynamics of this artificial interlocked molecule compared to biomolecules. Adapted from reference [19].

In an attempt to evaluate the energy required to break one DNP-BIPY²⁺ interaction, we designed pulling-relaxing experiments probing only one donor-acceptor interaction. We compared the distribution of work (area under the force curve) done to break this interaction with the distribution of work performed by the molecule to reform it at 10³ pN·s⁻¹. Using the Crooks fluctuation theorem (CFT) [25] relating the free-energy difference between two conformations with the forward and reverse works measured during pulling-relaxing experiments, we determined a ΔG (DNP-BIPY²⁺) of 6 ± 1 kcal·mol⁻¹. This value is close to the one obtained previously by calculations [3] and is in agreement with the breaking of one interaction inside the oligorotaxane in a serpentine-like folded (co) conformation.

5. Conclusions and perspectives

In summary, we reported here the singlemolecule investigation of oligorotaxanes using AFM-based force spectroscopy. Standard pulling experiments evidenced the sequential mechanical breaking of intramolecular donoracceptor interactions supporting the serpentinelike folded structure. For the first time, we were able to capture real-time fluctuations of a single synthetic molecule between different (co) conformations. The transitions between partially folded states are at least as fast as that observed in proteins but remarkably more robust. Pullingrelaxing experiments showed the reversibility of the mechanical unfolding and revealed the stochastic nature of the process. Finally, dynamic force spectroscopy performed on these molecules illustrated their high dynamics compared to folding proteins, probably due to the specific nature and superstructure of the oligorotaxanes.

Taking inspiration from nature's molecular machines, chemists are now able to design artificial molecules with well-defined and stable folded architecture. Our results show that such synthetic molecules could eventually surpass the performance of their natural counterparts.

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Arnaud BOREUX

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Synthèse et Réactivité d'Allènes en Présence de Catalyseurs de Cuivre et d'Or

Parmi les groupements fonctionnels présentés en cours de chimie organique, les liaisons multiples formées entre atomes de carbone restent les motifs les plus simples et les premiers à être étudiés. Les alcènes et les alcynes, représentant respectivement les doubles et les triples liaisons dans un squelette carboné, sont en général bien connus tant au point de vue de leur structure que de leur réactivité. En revanche, les allènes (ou 1,2-diènes) font souvent figure de fonction



chimique exotique pour le public moins spécialisé. Ces deux insaturations adjacentes consituent pourtant un motif stable dans un grand nombre de composés [1]. Avec son carbone central linéaire d'hybridation sp entouré de deux carbones sp², l'allène se présente comme un intermédiaire entre les alcènes trigonaux et les alcynes linéaires (Schéma 1A). Bien que la fonction allène soit composée exclusivement de carbone, deux insaturations adjacentes peuvent également incorporer l'un ou plusieurs hétéroatomes. Cela donne naissance à toute une gamme de fonctions chimiques comme les cétènes, les céténimines ou les isocyanates, mais également au célèbre dioxyde de carbone (Schéma 1B). Enfin, un aspect structural intéressant des allènes réside dans leur chiralité axiale. Bien que ceux-ci ne possèdent pas de centre asymétrique, la disposition des groupements autour de l'axe de la fonction allène rend ces composés non superposables à leur image miroir (Schéma 1C). Tous ces aspects font des allènes des composés de choix pour le développement de méthodes de synthèse de structures plus ou moins complexes. Durant cette thèse, nous nous sommes intéressés d'une part à la préparation d'allènes contenant des groupements fluorés (Schéma 1D). Pour ce faire, une réaction de catalyse à l'or a été mise au point et fera l'objet du premier paragraphe de cet article. Par la suite, nous avons également étudié la réactivité d'allènes dans un processus impliquant un catalyseur de cuivre. Le second paragraphe donnera quelques éléments sur le mise au point de cette seconde méthode.

1. Préparation d'allènes-CF₃ par catalyse à l'or [2, 3]

Une application importante de la synthèse organique est la préparation de nouveaux composés bioactifs. Durant les dernières décennies, près de 25% des médicaments mis sur le marché contenaient au moins un atome de fluor dans leur structure. De par l'absence d'atome de fluor dans la plupart des produits naturels, l'incorporation de cet élément dans les composés organiques fait donc l'objet d'une attention particu-



lière pour les chimistes de synthèse. L'une des stratégies possibles consiste à transformer des sources de fluors simples et bon marché (Schéma 2A) en composés d'intérêt (Schéma 2C) par transformations successives. Deux exemples de structures complexes sont présentés ici, l'Efavirenz et le Celecoxib, mais ne sont qu'un échantillon très restreint des composés fluorés présents dans nos médicaments [4]. Pour ce faire,



Schéma 3. Stratégie pour la préaparation d'allènes-CF₃ au départ de trifluoroacétate d'éthyle

des fonctions chimiques de complexité intermédiaire sont généralement impliquées dans ce processus (Schéma 2B). Ces motifs, ou intermédiaires synthétiques, se caractérisent d'une part par leur stabilité, ce qui les rend manipulables, et d'autre part par leur réactivité potentielle, ce qui permet de les fonctionnaliser. Parmi ceux-ci, nous pouvons citer les allènes, les énones, les alcynes ou les alcènes possédant le groupement trifluorométhyle (ou CF_3). La synthèse de ces intermédiaires, en partant de blocs de construction simples et disponibles, représente donc un domaine de recherche vaste et nécessaire à la création de nouvelles voies vers la préparation de nouveaux composés bioactifs.

Pour toutes les raisons évoquées ci-dessus, la

fonction allène représente un intérêt synthétique évident, de même que son analogue trifluorométhylé. Durant cette thèse, nous nous sommes intéressés à la préparation d'allènes-CF, par un réarrangement catalysé à l'or (Schéma 3). L'un des avantages de cette méthode réside dans l'utilisation du trifluoroacétate d'éthyle comme source de fluor organique. En plus d'être stable et liquide à température ambiante, ce qui rend son usage en laboratoire aisé, ce composé est une des sources de CF₃ les moins chères. La conversion du trifluoroacétate d'éthyle en divers substrats s'opère au moyen de méthodes standards de synthèse organique. Le développement de l'étape finale catalysée à l'or fait donc l'objet d'un chapitre de cette thèse. Cette transforma-



Schéma 4. Catalyseurs d'or employés pour la synthèse d'allènes étudiée

tion se base sur des travaux antérieurs du groupe du Professeur Gagosz, dans lesquels la synthèse d'allènes a été décrite [5]. Cette méthode s'est révélée très générale et applicable à un grand nombre de produits mais présentait une certaine limitation quand des allènes- CF_3 étaient impliquées.

En revisitant les conditions réactionnelles de cette transformation, il a été possible d'optimiser cette dernière en jouant sur un paramètre essentiel : la nature du ligand contenu dans le complexe d'or (Schéma 4). En effet, les substrats employés étant relativement pauvres en électrons de par la présence des atomes de fluor électronégatifs, il était nécessaire d'employer un catalyseur particulièrement réactif. Le passage d'un ligand phosphine (**A**) à un ligand phosphonite (**B**) ou un ligand phosphite (**C**) a permis d'obtenir l'allène-CF₃ désiré de manière plus efficace. Etant donné la meilleure stabilité du ligand phosphonite **B** dans les conditions réactionnelles par rapport au phosphite **C**, celui-ci a été sélectionné pour la suite du projet. L'ajustement d'autres paramètres, comme le solvant ou la température, a terminé cette étape d'optimisation des conditions réactionnelles.

L'étape suivante de ce projet était de tester nos nouvelles conditions réactionnelles à divers substrats afin de définir les limites de notre méthode. Dans ces conditions, une bibliothèque d'allènes-CF₃ a pu être préparée avec de bons rendements. Quelques exemples représentatifs sont détaillés sur le Schéma 5. Parmi les fonctions chimiques tolérées, nous pouvons citer les chaines alkyles, les cycles aromatiques fonctionnalisés, les hétéroatomes portant un groupement protecteur (oxygène, azote). La réaction s'étend à d'autres groupements fluorés que le



Schéma 5. Etude du scope de la réaction : exemples représentatifs



Schéma 6. Etude du transfert de chiralité de la transformation

trifluorométhyle, tels que le difluorométhyle (CF_2H) et le pentafluoroéthyle (CF_2CF_3) , qui sont également deux motifs d'intérêt dans la préparation de molécules bioactives.

Pour tous ces exemples, le substrat de départ et le produit d'arrivée sont tous deux des composés chiraux. Comme mentionné précédemment, les allènes présentent une chiralité axiale, ce qui les rend présents sous la forme de deux énantiomères. Les substrats présentent quant à eux une chiralité centrale plus classique, due à la présence d'un carbone asymétrique au pied du groupement CF₃. Durant toute l'étude de la réaction, nous avons employé des mélanges racémiques de substrat, et avons donc obtenu assez logiquement des mélanges racémiques de l'allène-CF₃ correspondant. Connaissant l'intérêt croissant des chimistes organiciens et médicinaux pour la préparation de composés énantioenrichis, nous nous sommes donc interrogés sur le transfert potentiel de l'information chirale de notre transformation (Schéma 6). Pour répondre à cette question, un substrat standard a été préparé sous forme énantioenrichie (ratio 98.5 / 1.5, ou excès énantiomérique (ee) = 97%). Quand ce composé a été soumis aux conditions de catalyse à l'or, l'allène-CF₃ correspondant a été isolé avec un excès énantiomérique quasi intact (ee = 94%). Cette expérience a permis de montrer que la transformation procède avec un transfert de chiralité centrale-axiale, et qu'il est donc a priori possible de préparer des allènes-CF₃ chiraux au départ d'alcools propargyliques- CF_3 chiraux. Sachant que ces derniers peuvent être obtenus aisément à l'aide de méthodes connues [6], notre méthode offre un accès simple et efficace aux allènes- CF_3 énantioenrichis.

Enfin, la fonctionnalisation des allènes- CF_3 préparés a été brièvement étudiée. En utilisant des substrats adéquats ou des conditions réactionnelles choisies, un accès vers divers motifs tels que les dihydrofuranes- CF_3 , les indènes- CF_3 ou des composés vinylborés- CF_3 a été élaboré. Ces résultats sortent du cadre de cet article, mais sont repris avec plus de détail dans la publication citée précédemment.

2. Boroacylation d'allènes par catalyse au cuivre [7, 8]

Comme mentionné ci-dessus, l'une des applications directes de la chimie organique est la synthèse de composés bioactifs dans le contexte de la chimie médicinale. Pour ce faire, la préparation de petits fragments moléculaires susceptibles d'être facilement couplés à d'autres constitue un point de recherche important à l'heure actuelle. Parmi les fragments envisageables, les esters boroniques constituent une famille d'intérêt important de par leur diversification aisée via des réactions de couplages. Par exemple, les composés vinylborés soumis à ces réactions permettent d'accéder à des oléfines fonctionnalisées (Schéma 7, couplage de Suzuki), ainsi qu'à des



Schéma 7. Exemples d'applications des motifs vinylbores par réactions de couplages

fonctions contenant un hétéroatome comme les énamines ou les éthers d'énol (Schéma 7, couplage de Chan-Lam-Evans).

Une des façons d'obtenir ce motif vinylbore consiste à incorporer le groupement ester boronique (BPin) sur une insaturation multiple, comme un alcyne ou un allène, par catalyse au cuivre. Si cette stratégie est déjà bien connue dans le cas des alcynes [9], elle est beaucoup plus récente pour la fonction allène (Schéma 8) [10]. Les premiers développements remontent à 2011, quand le groupe de Santos a décrit l'hydroboration d'allènes activés catalysée par le cuivre en présence de bisboronate et de méthanol [11]. L'extension de cette méthode aux allènes non activés a été étudiée par les groupes de Ma [12], Tsuji [13] et Hoveyda [14]. Par la suite, l'emploi d'un autre électrophile qu'un proton a été rapporté par différents groupes de recherche. Ainsi, l'utilisation d'aldéhydes [15],



Schéma 8. Précédents développements de boration d'allènes catalysée au cuivre



Schéma 9. Développement d'une réaction de boroacylation d'allènes

de cétones [15], d'imines [16], d'électrophiles allyliques [17] et aryles [18] a été décrite dans le cadre de cette réaction.

Dans ce contexte, nous avons contribué au développement de cette méthode en envisageant un nouvel électrophile peu commun en catalyse au cuivre : un fluorure d'acyle (Schéma 9). Tels leurs analogues anhydrides ou chlorures d'acyle, les fluorures d'acyle sont des agents acylants et se sont révélés être les plus efficaces dans notre optimisation. Plusieurs autres paramètres, tels la nature du catalyseur et du solvant, ainsi que l'ajout d'un additif ont été testés afin d'arriver à des conditions optimales.

Le catalyseur sélectionné était formé par mélange d'acétate de cuivre(II) avec la 1,1'ferrocènediyl-bis(diphénylphosphine) (dppf) comme ligand. La réaction s'est révélée être efficace dans le THF, et nécessitait l'ajout de TMSONa comme base de Lewis pour avoir lieu. Une fois les conditions réactionnelles fixées, nous avons commencé l'étude du scope de la réaction et quelques exemples représentatifs sont indiqués sur le Schéma 10. Divers motifs structuraux ont été tolérés tant au niveau de l'allène que du fluorure d'acide employés. Des allènes monosubstitués ou 1.1-disubstitués ont mené à des conversions efficaces en produits de boroacylation désirés. La présence de groupements aromatiques, aliphatiques, hétéroatomiques était en général tolérée, avec des rendements relativement bons. Le choix du fluorure d'acide s'est révélé plus critique : alors que les fluorures d'acides aromatiques étaient en général tolérés par la réaction, l'emploi de fluorures d'acides aliphatiques a mené a de faibles rendements du produit désiré et à la formation de produits secondaires indésirables. Enfin, l'emploi d'allènes tri-substitués, en général peu employés dans les travaux précédents de la littérature, a mené à de faibles rendements, mais avec une sélectivité parfaite pour l'oléfine (E), ce qui a permis d'élucider certains points mécanistiques de cette transformation.

Au cours de ce projet, l'initiation d'une nouvelle méthode de boroacylation d'allènes a donc été mise en place. L'optimisation des conditions a conduit à l'obtention d'une librairie de produits de type vinylbore. De plus amples détails sur les substrats, ainsi que quelques essais de postfonctionnalisation des produits peuvent être trouvés dans la publication susmentionnée [7].

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Schéma 10. Exemples représentatifs de boroacylation d'allènes catalysée au cuivre

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2018 SRC Scientific Day

CHEMISTRY OF BIO-SOURCED MOLECULES AND MATERIALS

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08.30-09.00	Welcome
09.00-09.15	Introduction: Prof. Pascal Gerbaux (President of the Mons Section of SRC) and Prof. Claudine Buess-Herman (General Secretary of SRC)
09.15-10.05	Prof. Pierre Duez (UMONS) Pharmacology and chemistry of phytomedicines: a clue for the rational design of innovative drugs?
10.05-10.20	Oral communication of best master thesis (UNamur)
10.20-10.35	Oral communication of best master thesis (ULB)
10.35-11.05	Coffee break
11.05-11.20	Oral communication of best master thesis (UMONS)
11.20-12.10	Prof. Florent Allais (AgroParisTech) Transforming biomass and by-products into renewable molecules and polymers through the combination of white biotechnologies, green chemistry and downstream processing
12.10-14.15	Lunch and posters session
14.15-15.05	Prof. Serge Bourbigot (Lille 1) To be announced
15.05-15.20	Oral communication of best master thesis (ULg)
15.20-15.35	Oral communication of best master thesis (UCL)
15.35-16.05	Coffee break
16.05-16.45	« C.G.BC.B.B. Incentive awards 2018 »
16.45-17.15	SRC, Solvay, and 2017 SRC triennial award

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