ACS Sustainable Chemistry & Engineering

Research Article

Cite This: ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

pubs.acs.org/journal/ascecg

Do Cyclodextrins Encapsulate Volatiles in Deep Eutectic Systems?

Maria Enrica Di Pietro,*[,†] Greta Colombo Dugoni,[†] Monica Ferro,[†] Alberto Mannu,[†] Franca Castiglione,[†] Margarida Costa Gomes,[‡] Sophie Fourmentin,[§] and Andrea Mele*[,†]

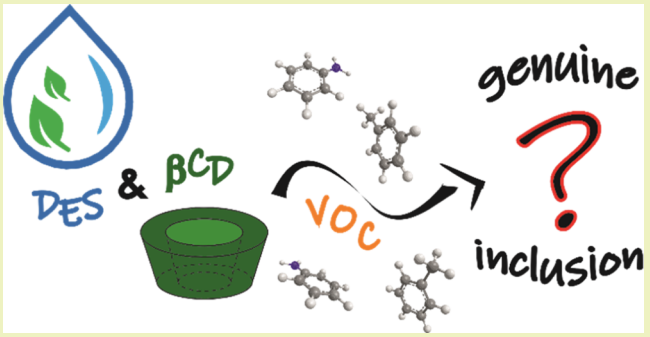
[†]Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milan, Italy

[‡]Laboratoire de Chimie, Ecole Normale Supérieure de Lyon & CNRS, 46 Allée Italie, 69364 Lyon Cedex 07, France

[§]Unité de Chimie Environnementale et Interactions sur le Vivant (UCEIV) EA 4492, SFR Condorcet FR CNRS 3417, Université du Littoral Cote d'Opale (ULCO), 145 Av. M. Schumann, 59140 Dunkerque, France

Supporting Information

ABSTRACT: Efficient renewable and nontoxic absorbents can now be designed to eliminate air pollutants such as volatile organic compounds (VOCs) from confined atmospheres. New hybrid materials result from the combination of deep eutectic systems (DESs) with well-known VOC capture agents like β-cyclodextrin (βCD). However, a question arises: does βCD retain its encapsulation ability in DESs? Multiple nuclear magnetic resonance (NMR) techniques are used here to demonstrate the formation of inclusion complexes of βCD with two VOCs, aniline and toluene, in the pure DES reline and in reline/water mixtures. Complexation-induced chemical shift changes and intermolecular host−guest nuclear Overhauser effects (NOEs) in the rotating frame give evidence of genuine encapsulation in the βCD cavity, and complementary information on the dynamics of the VOC is gathered via relaxation and diffusion experiments. This work shows how different NMR techniques can contribute to the design of task-specific sustainable materials for absorption/extraction processes.



KEYWORDS: *NADES, volatile organic compounds, host−guest complex, NMR spectroscopy, association constant, dynamics*

INTRODUCTION

Volatile organic compounds (VOCs) are among the most common air pollutants emitted from chemical and petrochemical industries, transportation vehicles, and commercial products such as solvents, paints, cleaners, and lubricants.[1−3] Nowadays, it is compulsory in many countries to limit and control VOC emissions both in terms of environment, because they affect the climate change and the growth and decay of plants, and in terms of human and animal health, because VOC exposure causes respiratory distress, eye and throat irritation, neurological toxicity, and cancer, among other effects.[1−3] In the presence of sunlight, VOCs may react with nitrogen oxides and other airborne chemicals to form ozone, leading to various environmental hazards.[4] VOC removal is hence a major concern of the society's commitment toward the ecosystem.[1]

Among the materials used as VOC capture agents, β-cyclodextrin (βCD) is one of the most attractive materials.[2,5−8] βCD is a torus-shaped cyclic oligosaccharide made up of seven α-1,4-linked D-glucopyranose units. It can form inclusion complexes by entrapping small hydrophobic molecules (guests) in the hydrophobic cavity of the macrocyclic sugar (host) through noncovalent host−guest interactions. This is especially true if the target molecules contain hydrophobic groups, such as phenyl groups that are present in many VOCs.[9] βCD-based materials have been reported to be efficient in inclusion complex formation toward several organic pollutants.[2,3,5,6,10−14]

Deep eutectic systems (DESs) have been recently suggested as innovative materials with potential in gas absorption.[15−18] Practically speaking, a DES is a result of the combination in the proper ratio of an opportune hydrogen-bond donor (HBD) and a hydrogen-bond acceptor (HBA).[19−21] Self-association of the HBD and HBA lowers the entropic difference of the phase transition, so that basically a eutectic is formed with a depressed freezing point that lies well below that of the individual components. DESs show many beneficial characteristics: among others, they can be prepared from cheap, readily available, and toxicologically well-characterized starting materials, which also accounts for their low cost. A large number of different combinations of the HBA and HBD have been reported and their use has been proposed in many fields of application.[22−25] Interestingly, studies using static headspace gas chromatography (SH-GC) on choline chloride- or tetrabutylphosphonium bromide-based DESs showed that they can be good candidates for VOC absorption processes.[15]

Received: August 4, 2019
Revised: September 18, 2019
Published: September 27, 2019

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

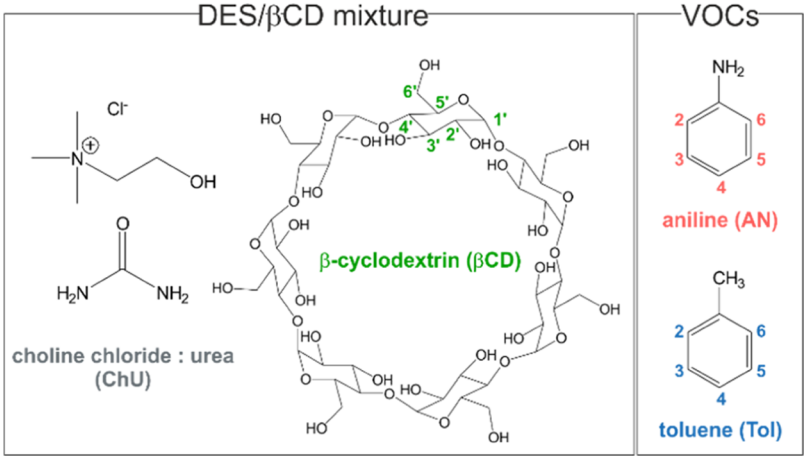


Figure 1. Structure and numbering of compounds used in this work.

Table 1. Composition of Samples Used in This Work

sample	short name	DES	βCD (%)	added H_2O	guest molecule
1	ChU/βCD/AN	ChU	10		AN (1 equiv)
2	ChU/AN	ChU			AN (1 equiv)
3	ChU/βCD/Tol	ChU	10		Tol (1 equiv)
4	ChU/Tol	ChU			Tol (1 equiv)
5	ChU/βCD/H_2O/AN	ChU	10	210 equiv	AN (1 equiv)
6	ChU/H_2O/AN	ChU		210 equiv	AN (1 equiv)
7	ChU/βCD/H_2O/Tol	ChU	10	210 equiv	Tol (1 equiv)
8	ChU/H_2O/Tol	ChU		210 equiv	Tol (1 equiv)
9	ChU/βCD	ChU	10		
10	ChU/βCD/H_2O	ChU	10	210 equiv	

In this context, DES/βCD mixtures are likewise of interest as new hybrid materials because in principle their individual absorbing/sequestrating properties may be mutually reinforced. Indeed, the complexation ability of several native and substituted cyclodextrins in the DES reline (choline chloride/urea at 1:2 molar ratio, ChU) toward four VOCs [dichloromethane, toluene (Tol), *tert*-butylcyclohexane, and limonene] has been recently investigated via SH-GC.[26] The authors showed a decrease of the chromatographic peak area, which indicates higher solubilization of the VOC in the mixture. No further information on the retention mechanism—whether genuine inclusion or aggregation or other—is unfortunately accessible by means of SH-GC. Moreover, to concretely exploit reline/βCD mixtures for capturing toxic contaminants, a better characterization of the guest–host inclusion complex at the molecular level is crucial. When searching for an alternative and/or complementary technique to study interactions of small molecules with supramolecular hosts and in particular for investigating the formation of inclusion complexes, nuclear magnetic resonance (NMR) spectroscopy is probably the best option. It is possible not only to directly probe the genuine inclusion of the guest in the CD cavity but also to measure and analyze a large number of spectral parameters that give access to unique qualitative and quantitative information.[7,9,27−30] In the present work, we demonstrate that the measurement of different NMR parameters is extremely beneficial to investigate the sorption behavior of βCD toward selected VOCs in the DES reline (see Figure 1 for structures). First, complexation-induced chemical shift changes and intermolecular host–guest nuclear Overhauser effects (NOEs) in the rotating frame allow us to assess whether or not a genuine encapsulation occurs in reline (ChU)/βCD mixtures. Moreover, diffusion-ordered spectroscopy (DOSY) experiments and measurements of nonselective and selective spin–lattice relaxation times (T_1^{NS} and T_1^{SE}) are applied to glean additional insights into the dynamics of the guest molecule.

A practical limitation in ChU/βCD systems is the relatively high density and viscosity of the mixtures, which strongly reduces the resolution in NMR spectra. Luckily, DESs readily lend themselves to be added with a considerable amount of water without losing their unique properties. The effect of water on the hydrogen-bonding network of a DES is still debated, and it is generally accepted that reline keeps its nanostructure up to water concentrations of about 35 wt % and a transition from a "water-in-DES" to a "DES-in-water" regime occurs only at ca. 50 wt %.[31,32] The possibility to reduce DES viscosity while preserving its molecular interactions and its structure is an extremely advantageous feature, if considered that DESs are highly hygroscopic and latent absorbed water is unavoidable, especially in the context of industrial applications. This holds true also in the presence of βCD. Indeed, some of us have recently demonstrated that in reline/βCD/H_2O systems, βCD interacts primarily with the added water, while reline preserves a residual molecular network.[33] In this mixture, βCD benefits enough mobility to retain its encapsulation properties, as proved by selective variation of the chemical shifts and rotating-frame Overhauser spectroscopy (ROESY) host–guest intermolecular correlations in the case of a model drug, namely, the anti-inflammatory drug piroxicam.

Here, we intend to apply multiple NMR experiments to investigate more deeply the potential of reline/βCD mixtures for VOC absorption in the absence and presence of water. As

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

model compounds, we selected two major VOCs in the environment, aniline (AN) and Tol (Figure 1), which are listed as hazardous air pollutants in the Clean Air Act by the US Environmental Protection Agency (https://www3.epa.gov/ttn/atw/orig189.html). The formation of genuine inclusion complexes is evaluated, and the dynamic properties of the guest molecules are investigated.

EXPERIMENTAL SECTION

A summary of all the samples used is reported in Table 1. The DES reline (ChU) was prepared by the heating method, which consists in mixing the two components [Ch]Cl and U at a molar ratio 1:2 and then heating at 80 °C under constant stirring until a homogeneous liquid is formed. In all the samples containing βCD, 10% in weight of βCD was added to the reline under stirring at room temperature, until the formation of a homogenous liquid. In all the hydrated samples, 210 equiv of water with respect to βCD were added under stirring. As there are three hydroxyl groups for each of the seven glucose units in a single βCD molecule, this corresponds to a mole ratio βCD/added H_2O equal to 1:10. As the reline was not dried prior to utilization, also not hydrated samples contain traces of water because of the DES's hygroscopic nature. The water content of the freshly prepared solutions was determined using a Karl Fischer (KF) coulometric titrator from Mettler Toledo and was found equal to 2.1% for ChU/βCD and 0.5% for ChU. Overall, this translates into a total water content in hydrated samples between 25 and 27 wt%, which is below the expected transition to an aqueous solution. Samples **1** to **4** were prepared by adding either AN or Tol to the ChU/βCD and ChU solvents. Samples **5** to **8** were prepared by adding the same VOCs to the corresponding hydrated systems, ChU/βCD/H_2O and ChU/H_2O. All the samples containing βCD (**1**, **3**, **5**, and **7**) were prepared to have a final host/guest molar ratio of 1:1 and the same weight percentage of VOCs was also used in the samples without βCD (**2**, **4**, **6**, and **8**). Samples **9** and **10** without VOCs were used as references. The samples for NMR analysis were placed in standard 5 mm tubes and multiple NMR experiments were performed (details are given in the Supporting Information).

RESULTS AND DISCUSSION

Does βCD Form Inclusion Complexes with VOCs in Pure (Nonhydrated) Reline? It is well known that the NMR chemical shift is sensitive to changes in the electronic environment. Hence, comparing the observed chemical shifts of guest protons and of protons located in the CD cavity ($H_{3'}$ and $H_{5'}$) in the ^{1}H 1D spectra of their mixture compared to pure components give a first clue on the formation of an inclusion complex. Figure 2 shows selected regions of ^{1}H spectra corresponding to VOC's signals for the case of AN and Tol in reline with or without βCD. In the presence of βCD, it can be observed the expected downfield shift of the peaks of the guest molecule, which suggests the formation of βCD/VOC inclusion complexes (see Table S1 for complexation-induced chemical shifts).[30] Moreover, a considerable line broadening of the aromatic peaks is observed after the addition of βCD, which might indicate an exchange regime between free and encapsulated species. Overall, the variation of the chemical shifts and the line broadening are more prominent in the case of Tol than AN, which might point toward a stronger interaction of the former with βCD. Unfortunately, non-hydrated reline mixtures are highly viscous, which cause short relaxation times, broad lines, and overall poorly resolved spectra. The effect is even more relevant for βCD's signals, which also suffer from severe overlap with peaks of choline (see Figures S1 and S2). Therefore, any further analysis of ^{1}H NMR spectra is not possible. Aiming at confirming the

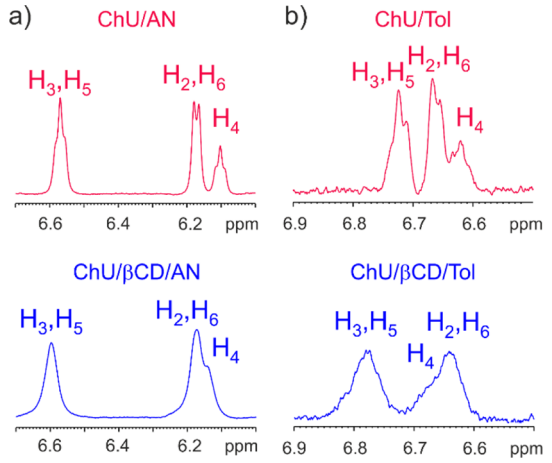


Figure 2. Selected regions of ^{1}H NMR spectra corresponding to aromatic protons of (a) AN in samples ChU/βCD/AN (bottom, in blue) and ChU/AN (top, in red) and (b) Tol in samples ChU/βCD/Tol (bottom, in blue) and ChU/Tol (top, in red).

formation of βCD/VOC inclusion complexes, we performed ROESY experiments (Figure S3). Again, the signal loss due to the short relaxation time in the highly viscous DES solutions made it impossible to distinguish any intermolecular host–guest cross peaks.

Given the poor quality of βCD signals, we focused on aromatic peaks of VOCs, which are relatively far from DES's signals and give detectable signals. Well-established NMR methods to study inclusion complexes from the guest's viewpoint are relaxation and diffusion experiments. The use of relaxation NMR spectroscopy to study aggregation and/or complexation is well known and relies mostly on the use of inversion recovery experiments for the measurement of proton nonselective and selective spin–lattice relaxation rates, R_1^{NS} and R_1^{SE}.[27,29,34] Indeed, assuming that the bound and free states interconvert quickly with respect to both the chemical shift difference and proton relaxation rate, the formation of inclusion complexes affects R_1^{NS} and R_1^{SE} at different extents. In particular, it has been shown that R_1^{SE} is more sensitive to the slower rotational tumbling of the complex than R_1^{NS}.[28,35−39] Therefore, the combination of nonselective and selective inversion recovery measurements is a rich source of information in dynamic studies. It has been used extensively to measure chemical exchange rate constants separated from the spin–lattice relaxation rates in slow exchanging systems,[40] to describe molecular conformational motion in solution,[41,42] to study interactions between small molecules with macromolecules,[28,29,37,38] and to estimate the binding affinities of ligands with proteins.[39,43,44] In the case of inclusion complexes with cyclodextrins, the application of ^{1}H nonselective, selective, and biselective spin–lattice relaxation rates can be used to address intermolecular interactions and motional dynamics of drugs encapsulated within the βCD cavity.[45] A theoretical description is provided for the interested reader in the Supporting Information. Basically, by measuring R_1^{NS} and R_1^{SE} within the initial rate approximation, it is possible to infer the molecular rotational correlation time τ_C of the encapsulated drug, which may be thought of as the average time required for the molecule to rotate by approximately 1 radian.[36,38,46] Both the R_1^{NS}/R_1^{SE} ratio and τ_C are related to the motional regime of the guest, which in turn reflects its equilibrium between the free and bound states.[28,35,45]

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

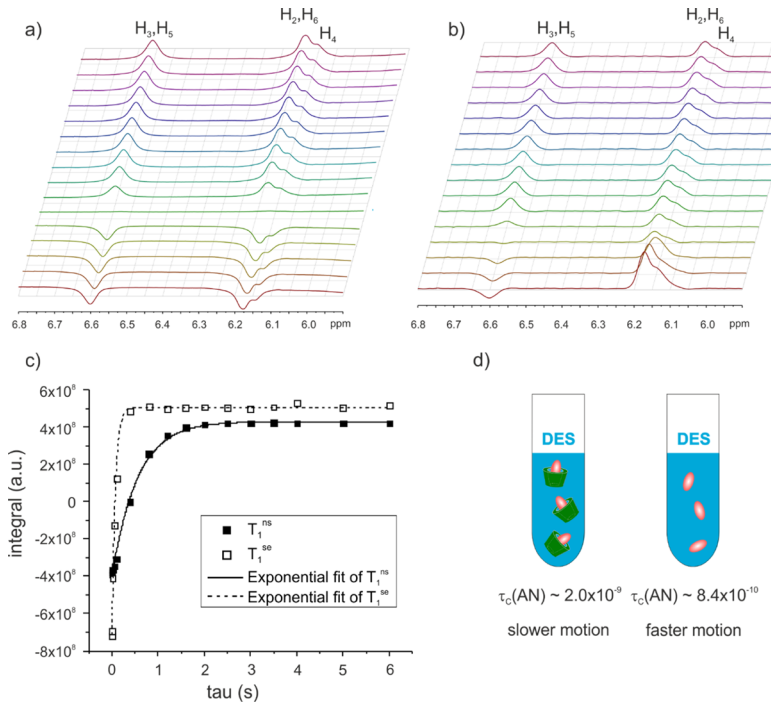


Figure 3. Stack plots of (a) nonselective and (b) selective for H_3 and H_5 protons of AN inversion recovery experiments of sample ChU/βCD/AN. (c) T_1 relaxation decays of H_3 and H_5 protons of AN measured with nonselective and selective inversion recovery experiments and corresponding mono-exponential fits. (d) Comparison of correlation times estimated for AN in the samples ChU/βCD/AN and ChU/AN. Maximum errors are estimated to be about 20%.

Table 2. R_1^{NS}/R_1^{SE} Ratio and τ_C Values Obtained for AN and Tol Dissolved in Reline Mixtures[a]

sample	short name	guest	selected proton(s)	R_1^{NS}/R_1^{SE}	τ_C (s)
1	ChU/βCD/AN	AN	H_3, H_5	0.13	2.0×10^{-9}
2	ChU/AN	AN	H_3, H_5	0.50	8.4×10^{-10}
3	ChU/βCD/Tol	Tol	CH_3	0.04	3.9×10^{-9}
4	ChU/Tol	Tol	CH_3	0.39	1.0×10^{-9}
5	ChU/βCD/H_2O/AN	AN	H_3, H_5	0.83	4.8×10^{-10}
6	ChU/H_2O/AN	AN	H_3, H_5	1.37	1.2×10^{-10}
7	ChU/βCD/H_2O/Tol	Tol	CH_3	0.74	5.7×10^{-10}
8	ChU/H_2O/Tol	Tol	CH_3	0.93	4.1×10^{-10}

[a]Maximum errors are estimated to be 10 and 20% for the hydrated and nonhydrated samples, respectively.

Here, we applied this method to get information about the dynamics of the selected VOCs in reline and on how it changes in the presence and absence of βCD. As overlapping peaks are not suitable for selective inversion, after investigation of the ^{1}H NMR spectrum, the most isolated peaks were chosen for observation, namely, protons H_3 and H_5 for AN and methyl protons for Tol (see Figures 2, S1, and S2). Figure 3 shows, as an example, the stack plots obtained with conventional nonselective pulses in the 180°-*t*-90° infrared (IR) sequence (a) and with a selective IR experiment with selective 180° centered on protons H_3 and H_5 of AN (b). In Figure 3b, the signals of unselected protons remain essentially unperturbed, but the resonance of the selected protons relaxes faster. The values of the R_1^{NS}/R_1^{SE} ratio obtained for samples **1** to **4** are summarized in Table 2.

In all the four samples, the R_1^{NS}/R_1^{SE} ratio is far smaller than 1. This is symptomatic of a slow motion regime, which was expected for such viscous systems. For both AN and Tol, the R_1^{NS}/R_1^{SE} ratio decreases from the pure reline to the reline/βCD mixture. This indicates that in the presence of βCD the rotational motion of the guest gets even smaller, which is compatible with the formation of an inclusion complex. Even if it is tempting to compare the two VOCs, it should be remembered that different protons were selected for the two molecules (namely, aromatic protons for AN and methyl protons for Tol) and a direct comparison might not be fair.

From the ratio of the nonselective and selective relaxation rates, it was possible to get an estimate of the correlation times of VOCs in the ChU/βCD mixtures and to compare them with the systems without βCD. Results are reported in Table 2 and Figure 4. For both AN and Tol, τ_C in the ChU/βCD mixture is greater than the corresponding value in the pure reline. Because the correlation time is inversely proportional to the degree of molecular mobility, that is, the smaller values of τ_C correspond to higher molecular mobility,[38] this is again compatible with a slowdown in dynamics of the guest molecule because of its encapsulation in the βCD cavity.

Diffusion experiments have received attention since the mid-1990s thanks to the highly representative processing called DOSY.[39,47,48] In a DOSY map, the diffusion experiment is processed in a 2D spectrum in which one dimension is related to the chemical shift information while the other represents the

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

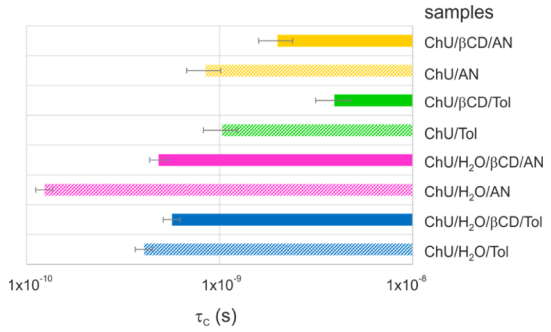


Figure 4. Summary of τ_C values obtained for AN and Tol dissolved in reline mixtures. Maximum errors are estimated to be 10 and 20% for the hydrated and nonhydrated samples, respectively.

diffusion coefficient.[49,50] Because the translational diffusion coefficients (D) of molecular species reflect their effective sizes and shapes, DOSY NMR allows both the identification and separation of the chemical entities in multicomponent systems and provides information on their intermolecular interactions and on the dynamics of the system.[49,51,52] In other words, a small molecule diffuses faster than a large one and the binding of a freely diffusing molecule to another species leads to a decrease of its translational diffusion coefficient (D). Indeed, in the fast exchange limit, the observed diffusion coefficient of the guest is the mole fraction weighted average of the diffusion coefficient of the free and bound states. This means that in the presence of a complex, the diffusion of the encapsulated molecule will be slower than that measured for the free compound. DOSY maps are well suited to study aggregation and quantify molecular interactions in chemical systems,[49,52−54] and many examples can be found in the literature where DOSY NMR has been used to investigate the structure, stoichiometry, host bound and unbound fractions to guests, association binding constant, and host−guest relative positioning in CD complexes.[34,49,55−58] DOSY maps were acquired for samples **1** to **4** (Fig. S4). Unfortunately, signals of βCD were not detectable in any samples, and VOC signals were observed only in pure reline. This indirectly suggests that in the presence of βCD, the guest (AN or Tol) is probably encapsulated, so that their lines get broader and are not visible anymore in the 2D spectra. However, no additional considerations can be drawn.

Does βCD Form Inclusion Complexes with VOCs in Hydrated Reline Mixtures? In the previous section, practical limitations to the NMR investigation of reline/βCD emerged because of the inherent viscosity of the samples. Even though both the changes in the ^{1}H pattern of the guest and the modification of its dynamic behavior suggest that the formation of βCD/VOC complexes really takes place, we do not have a direct proof of a genuine encapsulation of the VOC in the βCD cavity. To overcome this problem, we decided to add 210 equivalents of water with respect to the βCD in the mixture. The same NMR methodology was then applied to hydrated reline samples.

Figure 5 shows selected regions of ^{1}H spectra of samples **5** to **8**. Both VOC's and βCD's signals are clearly visible. In the presence of βCD, a modification of the aromatic spectral pattern of the guest molecule is observed, more relevant for Tol than for AN. As for βCD, if a guest molecule is incorporated into the CD cavity, one should observe modification of the chemical shift of protons $H_{3'}$ and $H_{5'}$,

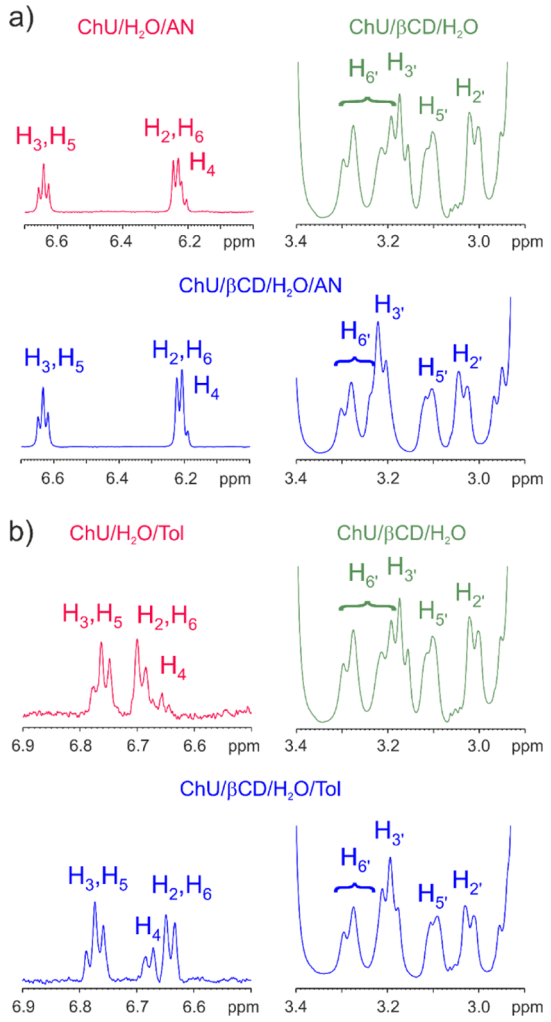


Figure 5. Comparison of ^{1}H NMR signals of the guests AN and Tol and the host macromolecule βCD in different samples: (a) ChU/βCD/H_2O/AN (bottom spectrum, in blue) vs ChU/H_2O/AN (top spectrum, left, in red) and ChU/βCD/H_2O (top spectrum, right, in green); (b) ChU/βCD/H_2O/Tol (bottom spectrum, in blue) vs ChU/H_2O/Tol (top spectrum, left, in red) and ChU/βCD/H_2O (top spectrum, right, in green).

which are located in the hydrophobic cavity of the host molecule. Here, slight changes are visible, more prominent on $H_{3'}$ than on $H_{5'}$.

To unambiguously confirm the encapsulation, ROESY is the preferred NMR tool. ROESY studies have been extensively used to get information on inclusion complexes with βCD through analysis of intermolecular peaks between cavity protons and a part of the guest involved in complexation.[9,27,53−55,59,60] Figure 6 shows representative ROESY spectra obtained for the sample ChU/βCD/H_2O/AN and ChU/βCD/H_2O/Tol. The host−guest interactions are displayed as intermolecular correlation peaks between aromatic protons of AN and Tol and protons $H_{3'}$ and $H_{5'}$ of βCD. This unequivocally confirms the formation of the inclusion complex of the VOC in βCD. Both AN and Tol produce larger NOEs on the $H_{3'}$ proton, located in the larger diameter internal part of βCD, than they did on the other internal $H_{5'}$ proton, located nearer to the smaller diameter rim. This would indicate that they are included through the larger diameter cavity of βCD.

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

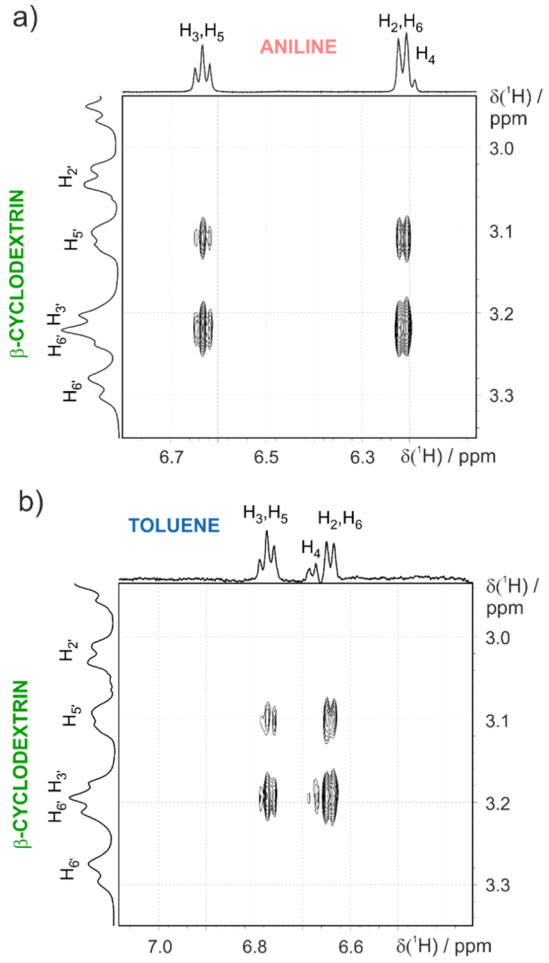


Figure 6. Selected regions of ^{1}H−^{1}H ROESY spectra showing intermolecular correlation peaks between signals corresponding to $H_{3'}$ and $H_{5'}$ protons of βCD (vertical dimension) and aromatic protons of (a) AN and (b) Tol (horizontal dimension).

Nonselective and selective relaxation experiments were performed on samples **5** to **8** to get dynamic information on the encapsulated VOC. Results are summarized in Table 2 and Figure 4. Clearly, all the R_1^{NS}/R_1^{SE} ratios and τ_C values for hydrated reline mixtures are greater than the corresponding values in nonhydrated samples. More in detail, for AN in ChU/βCD/H_2O, the R_1^{NS}/R_1^{SE} ratio is around 1.4. This value is expected when the molecule is in the extreme narrowing region ($\omega_0\tau_C \ll 1$).[38,45] For Tol in ChU/βCD/H_2O, the value of the R_1^{NS}/R_1^{SE} ratio is just close to 1, meaning that it is in the intermediate motion limit. This would indicate that in the mixture composed of reline and water, AN rotates more freely than Tol. Nevertheless, as different protons were selected for the two VOCs (aromatic protons for AN vs methyl protons for Tol) any further comparison would sound forced. When βCD is added to the mixture, the R_1^{NS}/R_1^{SE} ratio and the τ_C values for both AN and Tol get smaller. Because the correlation time is inversely proportional to the degree of molecular mobility (the smaller values of τ_C correspond to higher molecular mobility), this is compatible with a slowdown in dynamics of the guest molecule (Tol or AN) because of its encapsulation in the βCD cavity.

Finally, diffusion experiments were performed on samples **5** to **8**. DOSY maps obtained for AN and Tol in reline/water mixtures, with or without βCD, are reported in Figure 7. It can be seen that the diffusion of the VOC in the samples with βCD (left column) in both cases is slower than that in the corresponding samples without βCD (right column). This is a consequence of formation of inclusion complexes with the βCD. A graphical summary of diffusion coefficients for the different species is reported in Figure S5.

To confirm that the reduced diffusion of the guest in the presence of βCD is not due to viscosity changes caused by the addition of the macrocyclic oligosaccharide, the self-diffusion coefficient of H_2O was used as an internal reference.[61] Figure S5 and Table S2 reveal that the diffusion coefficient of water remains constant upon addition of βCD in the reline system. This means that the variations in solution viscosity are minimal and do not account for the change in diffusion of the guest molecules, Tol or AN.

Assuming a rapidly equilibrating system, the diffusion coefficients are weight-averaged NMR values between free and bound species. In this condition, diffusion coefficients measured using DOSY experiments for the guest molecule, D_G^{obs}, can be used to calculate the molar fraction of the bound guest x_G^{bound} and apparent association constants K_a of host−guest complexes (see the Supporting Information for a theoretical treatment).[50,53,55−57] In brief, the observed diffusion coefficients (D_G^{obs}) of AN and Tol measured in the equimolar host−guest mixtures (samples **5** and **7**) are the averaged values weighed by mole fractions of their bound and free molecules. The diffusion coefficients of free guests, D_G^{free}, can be measured directly in the absence of the host (samples **6** and **8**). As for the diffusion coefficients of bound guests, D_G^{bound}, it is typically assumed that when a small guest molecule binds to a large host molecule, the diffusion coefficient of the host is only insignificantly affected by complexation. Therefore, the diffusion coefficient of the complex and the observed diffusion coefficient of the CD host, D_H, are assumed to be equal. This approximation allows us to determine K_a from a single DOSY experiment. Diffusion coefficients for AN and Tol are reported together with the calculated x_G^{bound} and K_a in Table 3. Taking into account the inaccuracy in the calculations coming from the different approximations and the experimental errors both in sample preparation and in the acquisition and treatment of the experimental data, the K_a values are given with an error equal to 20% of the value. Reported values of the association constant in water are in the range 140−287 M^{-1} for βCD/Tol and about 50 M^{-1} for βCD/AN,[7] which are higher than the K_a values measured here. It has been recently observed using SH-GC that the association constant for the VOC/βCD of in reline are lower than the corresponding values in water.[26] However, it should be noted that also in reline/H_2O mixtures studied here, Tol binds more strongly to βCD than AN, which is in agreement with the data from the literature. Moreover, the K_a value found here for the βCD/Tol complex is higher than the one calculated by SH-GC (79 M^{-1} vs 11 M^{-1}). This could be ascribed to the presence of water in the systems used in this work.

CONCLUSIONS

DES/βCD mixtures are interesting candidates as new hybrid materials for VOC removal. To design the best-performing DES-based absorbents, it is imperative to probe the formation of inclusion complexes and to have access to the dynamics of the system at the molecular level. Here, we have illustrated the complementarity of the structural and dynamic information obtained from the 1D ^{1}H and ROESY spectra with diffusion

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

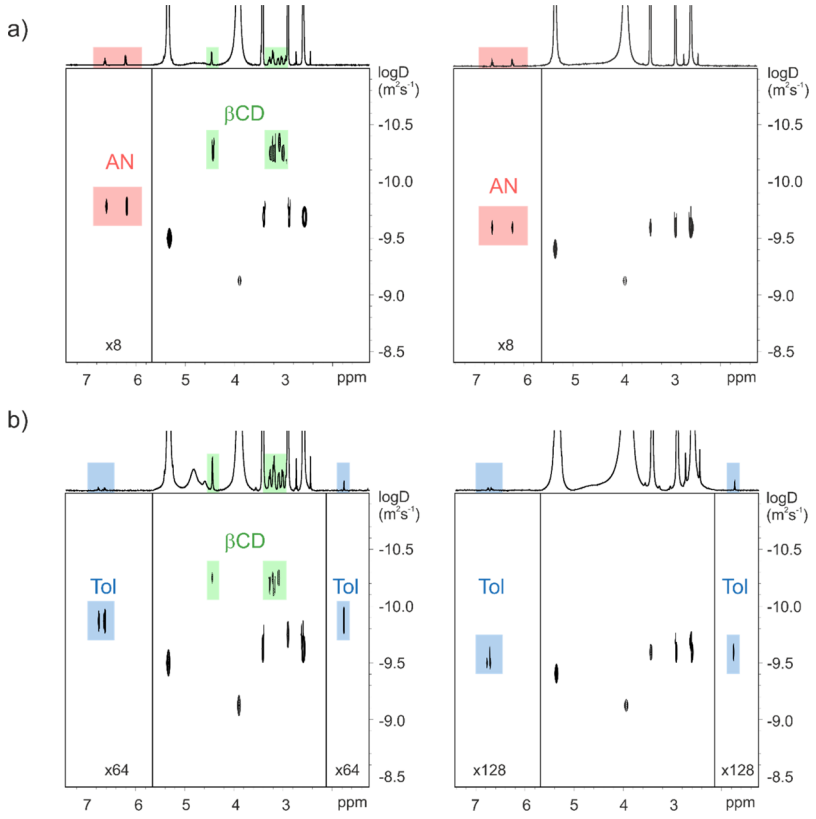


Figure 7. DOSY maps acquired for hydrated reline mixtures with (left column) and without (right column) βCD for (a) AN and (b) Tol.

Table 3. Diffusion Coefficients Measured in Hydrated Reline Mixtures and Corresponding Molar Fraction of the Bound Guest x_G^{bound} and Apparent Association Constant K_a Estimated for AN and Tol

guest	D_G^{obs} (m^2 s^{-1})	D_G^{free} (m^2 s^{-1})	D_H (m^2 s^{-1})	x_G^{bound}	K_a (M^{-1})
AN	$1.7 \times 10^{-10} \pm 0.1 \times 10^{-10}$	$2.6 \times 10^{-10} \pm 0.1 \times 10^{-10}$	$5.6 \times 10^{-11} \pm 0.6 \times 10^{-11}$	0.46 ± 0.05	19 ± 4
Tol	$1.4 \times 10^{-10} \pm 0.1 \times 10^{-10}$	$3.2 \times 10^{-10} \pm 0.2 \times 10^{-10}$	$5.6 \times 10^{-11} \pm 0.6 \times 10^{-11}$	0.70 ± 0.07	79 ± 16

and relaxation NMR experiments and shown that their combination provides unique information to understand the formation of inclusion complexes with βCD in complex media such as DESs.

Interestingly, we have proved that a certain amount of water is beneficial in reline systems because the viscosity of the medium is reduced while preserving both the DES network and the complexing ability of βCD. In nonhydrated systems, NMR results suggest the formation of inclusion complexes but given the impossibility to obtain correlation peaks in the ROESY spectra, a direct evidence is not available. When water is added to the mixture, intermolecular peaks are clearly visible in the ROESY spectra, confirming unequivocally the inclusion of the VOC.

In both hydrated and nonhydrated samples, selective T_1 measurements turned out to be very sensitive and convenient for the investigation of the complexation of VOCs into the βCD, allowing the calculation of the correlation times. The R_1^{NS}/R_1^{SE} ratio is a marker for the transition between dynamic states of solutes in DESs: the border value 1.5 for molecules in the extreme narrowing limit can be exploited to monitor the transition between fast and slow tumbling solutes. The data of Table 2 related to samples **5** and **6** clearly point out that the formation of an inclusion complex between βCD and AN causes the transition between a fast and slow regime, not observed in the other examples of Table 2. Additionally, DOSY experiments allowed a rough but simple estimate of the molar fraction of the bound guest and the association constant of the complex in reline/water mixtures.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.9b04526.

Experimental details, table of complexation-induced chemical shift, additional NMR spectra, graphical summary of diffusion coefficients, and theoretical background for the treatment of relaxation and diffusion data (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: mariaenrica.dipietro@polimi.it. Phone +39 02 2399 3045 (M.E.D.P.).

*E-mail: andrea.mele@polimi.it. Phone +39 02 2399 3006 (A.M.).

ORCID

Maria Enrica Di Pietro: 0000-0002-2370-1948

Margarida Costa Gomes: 0000-0001-8637-6057

Sophie Fourmentin: 0000-0002-4334-0051

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

Andrea Mele: 0000-0002-0351-0538

Author Contributions

The manuscript was written through contributions of all the authors. All the authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The work has been carried out within the frame of the bilateral France−Italy Galileo Programme (grant G18-392 and 39467XJ). G.C.D. thanks Politecnico di Milano for her Interdepartment PhD scholarship. The authors acknowledge Tarek Moufawad for helpful discussion.

■ REFERENCES

(1) Khan, F. I.; Ghoshal, A. K. Removal of volatile organic compounds from polluted air. *J. Loss Prev. Process Ind.* **2000**, *13*, 527−545.
(2) Alzate-Sánchez, D. M.; Smith, B. J.; Alsbaiee, A.; Hinestroza, J. P.; Dichtel, W. R. Cotton Fabric Functionalized with a β-Cyclodextrin Polymer Captures Organic Pollutants from Contaminated Air and Water. *Chem. Mater.* **2016**, *28*, 8340−8346.
(3) Celebioglu, A.; Sen, H. S.; Durgun, E.; Uyar, T. Molecular entrapment of volatile organic compounds (VOCs) by electrospun cyclodextrin nanofibers. *Chemosphere* **2016**, *144*, 736−744.
(4) Finlayson-Pitts, B. J. Tropospheric Air Pollution: Ozone, Airborne Toxics, Polycyclic Aromatic Hydrocarbons, and Particles. *Science* **1997**, *276*, 1045−1051.
(5) Celebioglu, A.; Ipek, S.; Durgun, E.; Uyar, T. Selective and Efficient Removal of Volatile Organic Compounds by Channel-type Gamma-Cyclodextrin Assembly through Inclusion Complexation. *Ind. Eng. Chem. Res.* **2017**, *56*, 7345−7354.
(6) Landy, D.; Mallard, I.; Ponchel, A.; Monflier, E.; Fourmentin, S. Remediation technologies using cyclodextrins: An overview. *Environ. Chem. Lett.* **2012**, *10*, 225−237.
(7) Kfoury, M.; Landy, D.; Fourmentin, S. Characterization of cyclodextrin/volatile inclusion complexes: A review. *Molecules* **2018**, *23*, 1204−23.
(8) Blach, P.; Fourmentin, S.; Landy, D.; Cazier, F.; Surpateanu, G. Cyclodextrins: A new efficient absorbent to treat waste gas streams. *Chemosphere* **2008**, *70*, 374−380.
(9) Srinivasan, K.; Stalin, T. Study of inclusion complex between 2,6-dinitrobenzoic acid and β-cyclodextrin by ^{1}H NMR, 2D ^{1}H NMR (ROESY), FT-IR, XRD, SEM and photophysical methods. *Spectrochim. Acta, Part A* **2014**, *130*, 105−115.
(10) Alsbaiee, A.; Smith, B. J.; Xiao, L.; Ling, Y.; Helbling, D. E.; Dichtel, W. R. Rapid removal of organic micropollutants from water by a porous β-cyclodextrin polymer. *Nature* **2016**, *529*, 190−194.
(11) Wang, L.; Kang, Y.; Xing, C.-Y.; et al. β-Cyclodextrin based air filter for high-efficiency filtration of pollution sources. *J. Hazard. Mater.* **2019**, *373*, 197−203.
(12) Szaniszló, N.; Fenyvesi, É.; Balla, J. Structure-stability study of cyclodextrin complexes with selected volatile hydrocarbon contaminants of soils. *J. Inclusion Phenom. Macrocyclic Chem.* **2005**, *53*, 241−248.
(13) Morin-Crini, N.; Crini, G. Environmental applications of water-insoluble β-cyclodextrin-epichlorohydrin polymers. *Prog. Polym. Sci.* **2013**, *38*, 344−368.
(14) Mauri-Aucejo, A. R.; Llobat-Estellés, M.; Egea, M. G.; Guillem, C.; Amorós, P. Samplers for VOCs in air based on cyclodextrin-silica hybrid microporous solid phases. *Analyst* **2012**, *137*, 1275−1283.
(15) Moura, L.; Moufawad, T.; Ferreira, M.; et al. Deep eutectic solvents as green absorbents of volatile organic pollutants. *Environ. Chem. Lett.* **2017**, *15*, 747−753.
(16) Sze, L. L.; Pandey, S.; Ravula, S.; et al. Ternary deep eutectic solvents tasked for carbon dioxide capture. *ACS Sustainable Chem. Eng.* **2014**, *2*, 2117−2123.
(17) Li, Z.; Wang, L.; Li, C.; et al. Absorption of Carbon Dioxide Using Ethanolamine-Based Deep Eutectic Solvents. *ACS Sustainable Chem. Eng.* **2019**, *7*, 10403−10414.
(18) Zhong, F.-Y.; Peng, H.-L.; Tao, D.-J.; Wu, P.-K.; Fan, J.-P.; Huang, K. Phenol-Based Ternary Deep Eutectic Solvents for Highly Efficient and Reversible Absorption of NH3. *ACS Sustainable Chem. Eng.* **2019**, *7*, 3258−3266.
(19) Francisco, M.; van den Bruinhorst, A.; Kroon, M. C. Low-transition-temperature mixtures (LTTMs): A new generation of designer solvents. *Angew. Chem., Int. Ed.* **2013**, *52*, 3074−3085.
(20) Abbott, A. P.; Capper, G.; Davies, D. L.; Rasheed, R. K.; Tambyrajah, V. Novel solvent properties of choline chloride/urea mixtures. *Chem. Commun.* **2003**, 70−71.
(21) Ruß, C.; König, B. Low melting mixtures in organic synthesis - An alternative to ionic liquids? *Green Chem.* **2012**, *14*, 2969−2982.
(22) Zhang, Q.; De Oliveira Vigier, K.; Royer, S.; Jérôme, F. Deep eutectic solvents: syntheses, properties and applications. *Chem. Soc. Rev.* **2012**, *41*, 7108−7146.
(23) Liu, Y.; Friesen, J. B.; McAlpine, J. B.; Lankin, D. C.; Chen, S.-N.; Pauli, G. F. Natural Deep Eutectic Solvents: Properties, Applications, and Perspectives. *J. Nat. Prod.* **2018**, *81*, 679−690.
(24) Pena-Pereira, F.; Namieśnik, J. Ionic liquids and deep eutectic mixtures: Sustainable solvents for extraction processes. *ChemSusChem* **2014**, *7*, 1784−1800.
(25) Cruz, H.; Jordão, N.; Branco, L. C. Deep eutectic solvents (DESs) as low-cost and green electrolytes for electrochromic devices. *Green Chem.* **2017**, *19*, 1653−1658.
(26) Moufawad, T.; Moura, L.; Ferreira, M.; et al. First Evidence of Cyclodextrin Inclusion Complexes in a Deep Eutectic Solvent. *ACS Sustainable Chem. Eng.* **2019**, *7*, 6345−6351.
(27) Schneider, H.-J.; Hacket, F.; Rüdiger, V.; Ikeda, H. NMR Studies of Cyclodextrins and Cyclodextrin Complexes. *Chem. Rev.* **1998**, *98*, 1755−1786.
(28) Li, Y.; Yin, G.; Wei, W.; et al. Interactions of Lycopodium alkaloids with acetylcholinesterase investigated by 1H NMR relaxation rate. *Biophys. Chem.* **2007**, *129*, 212−217.
(29) Reddy, R. R.; Phani Kumar, B. V. N.; Shanmugam, G.; Madhan, B.; Mandal, A. B. Molecular Level Insights on Collagen-Polyphenols Interaction Using Spin-Relaxation and Saturation Transfer Difference NMR. *J. Phys. Chem. B* **2015**, *119*, 14076−14085.
(30) Marques, H. M. C. A review on cyclodextrin encapsulation of essential oils and volatiles. *Flavour Fragrance J.* **2010**, *25*, 313−326.
(31) Posada, E.; López-Salas, N.; Jiménez Riobóo, R. J.; Ferrer, M. L.; Gutiérrez, M. C.; Del Monte, F. Reline aqueous solutions behaving as liquid mixtures of H-bonded co-solvents: microphase segregation and formation of co-continuous structures as indicated by Brillouin and ^{1}H NMR spectroscopies. *Phys. Chem. Chem. Phys.* **2017**, *19*, 17103−17110.
(32) Hammond, O. S.; Bowron, D. T.; Edler, K. J. The Effect of Water upon Deep Eutectic Solvent Nanostructure: An Unusual Transition from Ionic Mixture to Aqueous Solution. *Angew. Chem., Int. Ed.* **2017**, *56*, 9782−9785.
(33) Colombo Dugoni, G.; Di Pietro, M. E.; Ferro, M.; et al. Effect of Water on Deep Eutectic Solvent/β-Cyclodextrin Systems. *ACS Sustainable Chem. Eng.* **2019**, *7*, 7277−7285.
(34) Tošner, Z.; Aski, S. N.; Kowalewski, J. Rotational dynamics of adamantanecarboxylic acid in complex with β-cyclodextrin. *J. Inclusion Phenom. Macrocyclic Chem.* **2006**, *55*, 59−70.
(35) Freeman, R.; Hill, H. D. W.; Tomlinson, B. L.; Hall, L. D. Dipolar contribution to NMR spin-lattice relaxation of protons. *J. Chem. Phys.* **1974**, *61*, 4466−4473.
(36) Hall, L. D.; Hill, H. D. W. Spin-Lattice Relaxation of Protons. A General, Quantitative Evaluation of Contributions from the Intramolecular Dipole-Dipole Mechanism. *J. Am. Chem. Soc.* **1976**, *98*, 1269−1270.

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405

(37) Gaggelli, E.; Gaggelli, N.; Maccotta, A.; Valensin, G. 1H Relaxation Investigation of the Interaction of Vinblastine with Tubulin. *J. Magn. Reson.* **1994**, *104*, 89−94.
(38) Tinoco, L. W.; Figueroa-Villar, J. D. Determination of Correlation Times from Selective and Non-Selective Spin-Lattice Relaxation Rates and their Use in Drug-Drug and Drug-Albumin Interaction Studies. *J. Braz. Chem. Soc.* **1999**, *10*, 281−286.
(39) Fielding, L. NMR methods for the determination of protein-ligand dissociation constants. *Prog. Nucl. Magn. Reson. Spectrosc.* **2007**, *51*, 219−242.
(40) Bain, A. D. Chemical exchange in NMR. *Prog. Nucl. Magn. Reson. Spectrosc.* **2003**, *43*, 63−103.
(41) Rossi, C.; Pogliani, L.; Laschi, F.; Niccolai, N. Proton magnetic relaxation mechanisms and solution dynamics of L-histidine. *J. Chem. Soc., Faraday Trans. 1* **1983**, *79*, 2955−2959.
(42) Sai, T.; Takao, N.; Sugiurat, M. Application of ^{1}H NMR selective and biselective relaxation times. III—conformational analysis of quinidine in solution. *Magn. Reson. Chem.* **1992**, *30*, 1041−1046.
(43) Rossi, C.; Bonechi, C.; Martini, S.; et al. Ligand-macromolecule complexes: Affinity index determination by selective nuclear relaxation analysis. *Magn. Reson. Chem.* **2001**, *39*, 457−462.
(44) Bonechi, C.; Martini, S.; Brizzi, V.; et al. Nuclear magnetic resonance for studying recognition processes between anandamide and cannabinoid receptors. *Eur. J. Med. Chem.* **2006**, *41*, 1117−1123.
(45) Kumar, D.; Krishnan, Y.; Paranjothy, M.; Pal, S. Analysis of Molecular Interaction of Drugs within *β*-Cyclodextrin Cavity by Solution-State NMR Relaxation. *J. Phys. Chem. B* **2017**, *121*, 2864−2872.
(46) Campbell, I. D.; Freeman, R. Influence of Cross-Relaxation on NMR Spin-Lattice Relaxation Times. *J. Magn. Reson.* **1973**, *11*, 143−162.
(47) Morris, K. F.; Johnson, C. S. Diffusion-Ordered Two-Dimensional Nuclear Magnetic Resonance Spectroscopy. *J. Am. Chem. Soc.* **1992**, *114*, 3139−3141.
(48) Stilbs, P. Fourier transform pulsed-gradient spin-echo studies of molecular diffusion. *Prog. Nucl. Magn. Reson. Spectrosc.* **1987**, *19*, 1−45.
(49) Pagès, G.; Gilard, V.; Martino, R.; Malet-Martino, M. Pulsed-field gradient nuclear magnetic resonance measurements (PFG NMR) for diffusion ordered spectroscopy (DOSY) mapping. *Analyst* **2017**, *142*, 3771−3796.
(50) Brand, T.; Cabrita, E. J.; Berger, S. Intermolecular interaction as investigated by NOE and diffusion studies. *Prog. Nucl. Magn. Reson. Spectrosc.* **2005**, *46*, 159−196.
(51) Senra, T. D. A.; Khoukh, A.; Desbrières, J. Interactions between quaternized chitosan and surfactant studied by diffusion NMR and conductivity. *Carbohydr. Polym.* **2017**, *156*, 182−192.
(52) Barhoum, S.; Palit, S.; Yethiraj, A. Diffusion NMR studies of macromolecular complex formation, crowding and confinement in soft materials. *Prog. Nucl. Magn. Reson. Spectrosc.* **2016**, *94*−*95*, 1−10.
(53) Fernandes, S. A.; Cabeça, L. F.; Marsaioli, A. J.; De Paula, E. Investigation of tetracaine complexation with beta-cyclodextrins and p-sulphonic acid calix[6]arenes by nOe and PGSE NMR. *J. Inclusion Phenom. Macrocyclic Chem.* **2007**, *57*, 395−401.
(54) Simova, S.; Berger, S. Diffusion measurements vs. chemical shift titration for determination of association constants on the example of camphor-cyclodextrin complexes. *J. Inclusion Phenom. Macrocyclic Chem.* **2005**, *53*, 163−170.
(55) Lis-Cieplak, A.; Sitkowski, J.; Kolodziejski, W. Comparative proton nuclear magnetic resonance studies of amantadine complexes formed in aqueous solutions with three major cyclodextrins. *J. Pharm. Sci.* **2014**, *103*, 274−282.
(56) Martins, L.; Arrais, M.; De Souza, A.; Marsaioli, A. ^{1}H NMR studies of binary and ternary dapsone supramolecular complexes with different drug carriers: EPC liposome, SBE-*β*-CD and*β*-CD. *Magn. Reson. Chem.* **2014**, *52*, 665−672.
(57) Uccello-Barretta, G.; Balzano, F.; Paolino, D.; Ciaccio, R.; Guccione, S. Combined NMR-crystallographic and modelling investigation of the inclusion of molsidomine into *α*-, *β*- and *γ*-cyclodextrins. *Bioorg. Med. Chem.* **2005**, *13*, 6502−6512.
(58) Kfoury, M.; Landy, D.; Ruellan, S.; Auezova, L.; Greige-Gerges, H.; Fourmentin, S. Determination of formation constants and structural characterization of cyclodextrin inclusion complexes with two phenolic isomers: Carvacrol and thymol. *Beilstein J. Org. Chem.* **2016**, *12*, 29−42.
(59) Ali, S. M.; Fatma, K.; Dhokale, S. Structure elucidation of *β*-cyclodextrin-xylazine complex by a combination of quantitative ^{1}H-^{1}H ROESY and molecular dynamics studies. *Beilstein J. Org. Chem.* **2013**, *9*, 1917−1924.
(60) Ali, S. M.; Shamim, S. Analysis of computational models of *β*-cyclodextrin complexes: structural studies of morniflumate hydrochloride and *β*-cyclodextrin complex in aqueous solution by quantitative ROESY analysis. *J. Inclusion Phenom. Macrocyclic Chem.* **2015**, *83*, 19−26.
(61) Silva, M.; Figueiredo, A. M.; Cabrita, E. J. Epitope mapping of imidazolium cations in ionic liquid-protein interactions unveils the balance between hydrophobicity and electrostatics towards protein destabilisation. *Phys. Chem. Chem. Phys.* **2014**, *16*, 23394−23403.

DOI: 10.1021/acssuschemeng.9b04526
ACS Sustainable Chem. Eng. 2019, 7, 17397−17405