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# CONTROLLING CRYSTAL MORPHOLOGY AND POLYMORPH SELECTION USING MOLECULAR ADDITIVES

A Dissertation

Presented to

the Faculty of the Department of Chemical and Biomolecular Engineering University of Houston

> In Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in Chemical Engineering

> > by

R John Clark

August 2019

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### Acknowledgements

I dedicate this thesis to my friends and family. They have supported me throughout the entirety of my Ph.D. research. Their patience and support as been invaluable and I will be forever grateful and appreciative of them.

I want to also acknowledge my advisor, Jeremy Palmer, for his guidance and mentorship as well as the other members of his lab group. I would also like to thank Jacinta Conrad for her support and guidance through her weekly group meetings.

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### Abstract

Crystallization is relevant to a variety of important applications ranging from chemical refinement and pharmaceutical formulation to the design of novel materials for electronics and photonics applications. In these applied settings, successful outcomes require the ability to produce the desired crystal polymorph or structure that exhibits the critical functional properties needed for a particular application. Additionally, in many scenarios, material performance is strongly affected by the size, shape, and morphology of the produced crystallites. Unfortunately, controlling polymorph selection and crystal size and shape is often very synthetically challenging, providing a significant barrier to designing materials with optimal performance characteristics for targeted applications. In this thesis, we show that computer simulation methods can be used to complement experiment and aid in the development of rational crystal design strategies based on the use of molecular additives. Specifically, we show several instances of how molecular simulation can be used to elucidate the mechanisms of molecular additives such as crystal growth modifiers and structure directing agents, which can be used to control crystal morphology and polymorph selection during synthesis, respectively. These insights provide fundamental understanding that can help with a prior identification of effective additives to achieve desired synthesis outcomes. Moreover, they suggest promising future directions in applying these computational methods to screen large libraries of compounds to identify effective molecular additives and thereby accelerate material design.

### **Table of Contents**

A	ckno	wledg	ements	v	
A	Abstract				
Ta	able (	of Con	tents	viii	
$\mathbf{L}^{\mathrm{i}}$	ist of	Figur	es	xii	
$\mathbf{L}^{\mathrm{i}}$	ist of	Table	s	xviii	
1	Inti	roduct	zion	1	
2	Coo	operati	ive Effects of Inorganic and Organic Structure-Directin	ıg	
	Age	ents in	ZSM-5 Crystallization	7	
	2.1	Intro	duction	7	
	2.2	Metho	ods	10	
		2.2.1	Materials	10	
		2.2.2	Crystallization of MFI Zeolite	10	
		2.2.3	Materials Characterization	11	
		2.2.4	Molecular Modeling	12	
	2.3	Resul	ts and Discussion	14	
		2.3.1	MFI Synthesis with Organic and Inorganic Ion Pairings	14	
		2.3.2	TPA and CTA Occlusion in MFI Pores	18	
		2.3.3	Impact of SDA Pairings on Si/Al Ratio	20	
		2.3.4	Putative Effects of SDA Pairings on MFI Nucleation	23	
		2.3.5	Generation of Mesoporosity by CTA	29	

	2.4	Concl	usions	31
	2.5	Ackno	owledgments	31
3	Ult	rathin	Mordenite Crystals Synthesized Using Cooperative Organic	C
	Str	ucture	-Directing Agents	32
	3.1	Intro	luction	32
	3.2	Metho	ods	35
		3.2.1	Materials	35
		3.2.2	Synthesis of Ultrathin Mordenite	36
		3.2.3	Synthesis of Conventional Mordenite	37
		3.2.4	Solid-State Nuclear Magnetic Resonance	37
		3.2.5	Microscopy	39
		3.2.6	X-Ray Analysis	39
		3.2.7	Molecular Dynamics Simulations	40
		3.2.8	Catalyst Preparation and Testing	41
	3.3	Resul	ts an Discussion	43
	3.4	Concl	usions	49
4	Rol	e of T	hermodynamics in the Molecular Modification of Zeolites	5
	TO	N and	LTL Crystallization	52
	4.1	Intro	luction	52
	4.2	Metho	ods	53
		4.2.1	Materials	53
		4.2.2	Zeolite Crystallization	54
		4.2.3	Materials Characterization	55
		4.2.4	Calorimetry Studies	56
		4.2.5	Molecular Modeling	56
	4.3	Resul	ts and Discussion	59

	4.4	Concl	usions	66
5	Stu	rcturi	ng of Organic Solvents at Solid Interfaces and its Ramifica	<b>ì-</b>
	tior	ns for A	Antimarlarial adsorption on Beta-Hematin Crystals	68
	5.1	Intro	luction	68
	5.2	Metho	ods	72
		5.2.1	Materials	72
		5.2.2	Hematin Crystallization	72
		5.2.3	functionalizing AFM Cantilevers	73
		5.2.4	Chemical Force Microscopy	74
		5.2.5	Contact Angle Measurements	75
		5.2.6	Molecular Modeling	75
	5.3	Resul	ts and Discussion	78
	5.4	Concl	usions	90
6	Cor	clusic	ons and future work	92
	6.1	Concl	usions	92
	6.2	Futur	e Work	94
		6.2.1	Location of aluminum sites in zeolites	94
		6.2.2	Screening for potential structure directing agents	94
		6.2.3	Screening for potential growth modifiers	95
		6.2.4	Complex crystal surfaces	95
R	efere	nces		97
A	Cha	npter 1	Supporting Information	131
	A.1	Suppl	ementary Figures	131
В	Cha	pter 2	2 Supporting Information	143
	B.1	Suppl	ementary Text	143

		B.1.1	Synchrotron X-Ray Powder Diffraction Analysis	143
		B.1.2	Minimization of Quartz Impurity	144
		B.1.3	Additional Discussion of Solid-State NMR Results	145
	B.2	Suppl	ementary Tables	149
	B.3	Suppl	ementary Figures	152
С	Cha	pter 3	Supporting Information	176
С	<b>Cha</b> C.1	a <b>pter 3</b> Suppl	Supporting Information	<b>176</b> 176
С	<b>Cha</b> C.1 C.2	o <b>pter 3</b> Suppl Suppl	Supporting Information         ementary Tables         ementary Figures	<b>176</b> 176 178
С	<b>Cha</b> C.1 C.2	o <b>pter 3</b> Suppl Suppl	Supporting Information ementary Tables	176 176 178
C D	Cha C.1 C.2 Cha	pter 3 Suppl Suppl Suppl	Supporting Information         ementary Tables         ementary Figures         Supporting Information	<ol> <li>176</li> <li>176</li> <li>178</li> <li>181</li> </ol>

## **List of Figures**

1.1	Cartoon picturing how organic molecules can template crystal growth.	1
1.2	SEM images of how structure directing agents can inhibit crystal	
	growth to alter morphology (in this case, producing elongated rods or	
	flat platelets).	2
1.3	Materials grown in the presence of modifiers ranging from ions to	
	macromolecules.	4
2.1	Molecular structures of organic structure-directing agents	9
2.2	Scanning electron micrographs of ZSM-5 crystals synthesized with	
	CTA as the OSDA in the presence of (A) potassium and (B) sodium	
	cations	15
2.3	Powder XRD patterns of solids from ZSM-5 syntheses using CTA as the	
	OSDA in the presence of (A) potassium and (B) sodium cations	16
2.4	Approximate induction times estimated by the first appearance of	
	Bragg peaks in powder XRD patterns.	17
2.5	SEM images of ZSM-5 crystals synthesized with TPA as the OSDA in	
	the presence of (A) potassium and (B) sodium	18
2.6	Energetically favorable conformations for TPA in the MFI framework	
	identified using MD.	20
2.7	Energetically favorable conformations for CTA in the MFI framework	
	identified using MD.	21
2.8	Elemental analysis of ZSM-5 samples using EDX (red) and XPS (blue)	
	to measure the Si/Al molar ratio.	22

2.9	Schematic of the straight and sinusoidal channels of MFI and ideal	
	packaing arangments for TPA (B) and CTA (C).	24
2.10	Ex situ DLS measurements of silica dissolution in Al-free solutions.	25
2.11	(A-D) SEM of amorphous precursors during the induction period. (E)	
	Average precursor size for short and long times.	27
2.12	(A) $N_2$ adsorption and desorption isotherms of calcined ZSM-5 crystals.	
	(B) SEM micrograph of a representative ZSM-5 crystal	30
3.1	The OSDA(s), corresponding zeolite structure, and representative SEM	
	images for (A) SSZ-13, (B) ZSM-5, and (C) HOU-4. (D) XRD patterns	
	of the solid precipitates.	35
3.2	TEM, AFM, and MD images of representative HOU-4 crystals (A-C,E-	
	G,I-K), XRD pattern (D), and Stabilization Energy (H).	44
3.3	Solid-state 2D NMR correlation spectrum (A), Hector spectrum (B,C),	
	and idealized depection of framework-OSDA interactions. $\ldots$	46
3.4	SEM images of conventional MOR prepared with (A) $Na^+$ , (B) 1,2-	
	pentanediol, and (C) 1,2-propanediol. (D) Stabilization energy of diols	
	and (E) Cumene conversion for H-MOR and H-HOU.	49
4.1	Crystal Structures of zeolites TON and LTL (A). SEM micrographs of	
	ZSM-22 (B, C, D) and Zeolite L (E, F, G) at varying modifier concentra-	
	tions 0 wt% (B,E), 0.2 wt% (C,F), and 1.5 wt% (D,G).	60
4.2	Aspect ratio (AR) of ZSM-22 crystals in the presence of ZGMs plotted	
	as a function of modifier hydrophobicity. $^{2,15}$	62
4.3	Calorimetry data for (A) ZSM-22 and (B) zeolite L crystals as a function	
	of aspect ratio. SEM images of (C) ZSM-22 and (D) zeolite L.	64

4.4	Calorimetry data for (A) ZSM-22 and (B) zeolite L crystals as a function $% \mathcal{A}(A)$	
	of hydrophobicity. (C) Free energy for butane diols from MD simulation	
	and favorable binding positions (D).	65
5.1	How solvent structuring dictates solute adsorption (a,b) and the differ-	
	ences between ordered and disordered substrates (c-e).	70
5.2	Hyrophilic and hyrophobic regions on the $\beta$ -Hematin surface (a,b) and	
	the hematin molecule (c).	76
5.3	Probing the interactions of functional groups with two substrates by	
	chemical force microscopy.	79
5.4	Surface structuring and octanol density near the $\beta$ -hematin and amor-	
	phous glass interfaces.	84
5.5	Orientation and density of octanol molecules near $\beta$ -hematin and glass	
	substrates.	85
5.6	Interaction of pyridine-functionalized tips (a-d) and mass density pro-	
	files for water (e,f) with $\beta$ -hematin and amorphous glass substrates	86
A.1	XRD patterns of ZSM-5 crystals at different heating times and alkali	
	content	131
A.2	$N_2$ adsorption/desorption isotherms of ZSM-5 crystals	132
A.3	TGA analysis of ZSM-5 crystals.	133
A.4	XRD patterns of solids extracted from Na growth solutions with and	
	without TMA	134
A.5	XRD patterns of solids extracted from K growth solutions with and	
	without TMA.	134
A.6	SEM images of ZSM-5 crystals prepared with various combinations of	
	alkali metals.	135
A.7	Characterization of ZSM-5 crystals synthesized using TEOS	136

A.8	Characterization of ZSM-5 crystals with TPA in the presence of Li and	
	Cs	137
A.9	Time-evolved XRD patterns of ZSM-5 crystals prepared with TPA/Na	
	and TPA/K	138
A.10	Time-evolved XRD patterns of ZSM-5 crystals prepared with TPA/Li	
	and TPA/Cs	139
A.11	Dissolution of colloidal silica in NaOH solution.	140
A.12	2 SEM images of ZSM-5 prepared with TPA and different alkali metals.	141
B.1	The MOR-type framework structure.	152
B.2	SEM of ZSM-5 crystals and X-ray powder diffraction pattern from a	
	growth mixture with molar composition C4	153
B.3	SEM of ZSM-5 crystals and X-ray powder diffraction pattern synthe-	
	sized in the presence of $D4_{1,2}$	154
B.4	SEM images of representative HOU-4 samples.	155
B.5	The OSDAs their corresponding zeolite strucutre and their composite	
	building units.	156
B.6	Quantitative Reference Intensity Ratio analysis on HOU-4.	157
B.7	Thermogravimetric analysis and weight loss as a function of ramp up	
	temperature of SSZ-13, ZSM-5, and HOU-4.	158
B.8	Synchrotron XRPD data of HOU-4 and Quartz impurity.	159
B.9	Solid-State 1D $^{13}\mathrm{C}\{^{1}\mathrm{H}\}$ CPMAS spectra of HOU-4, ZSM-5 and SSZ-13.	160
B.10	) Solid-state 2D $^{13}C{^{1}H}$ correlation spectra of as-made HOU-4	161
B.11	3-D AFM height mode image of HOU-4 and Particle size distribution of	
	HOU-4 crystals from multiple AFM samples	162
B.12	2 The refined structure of HOU-4 and possible arrangements of non-	
	framework species	163

B.13	Solid-state quantitative single-puls 1D $^{13}\mathrm{C}$ NMR spectrum of as-made	
	HOU-4	164
B.14	MD calculated stabilization energy for organics occulded in MOR	165
B.15	MD rendering of $D6_{1,2}$ and TMAda <sup>+</sup> inside the MOR channel	166
B.16	$2D^{27}Al$ triple-quantum MAS (3!MAS) spectrum of as-made HOU-4	167
B.17	1D $^{29}\mathrm{Si}$ spectra and $^{29}\mathrm{Si}\{^{1}\mathrm{H}\}$ CP MAS NMR spectrum of calcined HOU-4	.168
B.18	Solution state 1D $^{13}$ C NMR spectrum of the HOU-4 synthesis super-	
	natant solution	169
B.19	Solid-state 2d $^{29}$ Si{ $^{1}$ H} correlation spectra of HOU-4	170
B.20	SEM images of modified HOU-4 synthesis using composition C1 and	
	3.0 OSDA to SiO <sub>2</sub>	171
B.21	SEM image of modified HOU-4 synthesis using composition C1 and $0.9$	
	$SiO_2$ to 1.44 OSDA	172
B.22	SEM images of modified HOU-4 synthesis using composition C1 with a	
	25% and 40% reduction in water.	173
B.23	SEM image of solids extracted from a synthesis with molar composition	
	C2 modified with the diol $D4_{1,2}$ $\hdots$	174
B.24	SEM image of conventional mordenite crystals.	175
C.1	Comparison of zeolites LTL and TON.	178
C.2	Powder XRD patterns of PEIM modified zeolite LTL.	179
C.3	Morphology of zeolite TON modified by PDDAC	179
C.4	Linear relationship between ZGM hydrophobicity and efficacy on zeo-	
	lite LTL.	180
_		
D.1	Representative adhesion force measurements for substrate solvent sys-	
	tem	181

D.2	Quantitative comparison of the interactions between AFM tips in con-	
	tact with glass and $\beta$ -hematin	182
D.3	$\beta\text{-hematin}$ water and octanol system rendered from MD simulation	183
D.4	Renderings from MD simulations of water near $\beta$ -hematin and glass	
	substrates	184

## List of Tables

2.1	Comparison of ZSM-5 induction and crystal growth times. $^a$ Amorphous	
	products	28
A.1	t-plot analysis of ZSM-5 crystals using $\mathrm{N}_2$ adsorption/desorption data.	142
A.2	t-plot analysis of $N_2$ adsorption/desorption data for ZSM-5 crystals pre-	
	pared with CTA/Na	142
B.1	Synthesis conditions used to prepare zeolites	149
B.2	Elemental analysis and acidity of zeolite frameworks	149
B.3	Framework OSDA per unit cell based on TGA analysis of washed samples	150
B.4	Crystallographic details for the refinement of the structure of HOU-4	151
C.1	ZGMs screened for zeolite TON and size of resulted crystals	176
C.2	Parametric study of zeolite TON syntheses	177

### **Chapter 1: Introduction**

Crystallization is relevant to a variety of important applications ranging from chemical refinement and pharmaceutical formulation to the design of novel materials for electronics and photonics applications. In these applied settings, successful outcomes require the ability to produce the desired crystal polymorph or structure that exhibits the critical functional properties needed for a particular application. Additionally, in many scenarios, material performance is strongly affected by the size, shape, and morphology of the produced crystallites. Unfortunately, controlling polymorph selection and crystal size and shape is often very synthetically challenging, providing a significant barrier to designing materials with optimal performance characteristics for targeted applications.



Figure 1.1: Cartoon picturing how organic molecules can template crystal growth.

The incorporation of molecular additives during synthesis is one strategy that has been broadly applied to control crystal properties. The synthesis of crystalline materials such as zeolites, for example, which are nanoporous aluminosilicates that find widespread use in industrial catalysis and separation processes, are often carried out using structure directing agents (SDAs). SDAs are molecular compounds that direct formation of the zeolite's pore structure by acting as space fillers or "soft templates." Thus, they promote formation of specific crystal polymorphs (zeolite frameworks) with pore geometries that are commensurate with the molecular structure of the OSDA, see Figure 1.1.<sup>1</sup>



Figure 1.2: SEM images of how structure directing agents can inhibit crystal growth to alter morphology (in this case, producing elongated rods or flat platelets).

Crystal growth modifiers (CGMs), by contrast, are molecular species that selectively bind to specific crystal faces and inhibit growth along the direction normal to the surface by blocking the attachment of solute particles, see Figure 1.2.<sup>2</sup> Hence, they influence crystal size, shape, and morphology, but do not dictate the polymorph of the crystal formed during synthesis. In the context of zeolite synthesis, CGMs (or zeolite growth modifiers, ZGMs), have been used to engineer thin zeolite crystals with short channels and large accessible surfaces with exposed pore openings. These characteristics are often desirable because they help to minimize mass transport limitations that undermine material performance in a variety of applications. In catalysis, for example, poor mass transport characteristics are thought to lead to coking (i.e., catalyst poisoning) and significantly reduce catalytic lifetime. Moreover, in addition to zeolites synthesis, the use of CGMs has proven to be an effect strategy for controlling crystallization in other settings. Examples of other materials and crystallization processes that involve CGMs include the amorphous silica exoskeletons of unicellular organisms (Figure 1.3A,B), nanoporous minerals (Figure 1.3C), pathological diseases (Figure 1.3D), calcification (Figure 1.3D,F), metal oxides (Figure 1.3G), ice suppression from antifreeze proteins (Figure 1.3H), and organic crystals (Figure 1.3I).<sup>2-15</sup>

Although molecular additives such as SDAs and CGMs have shown tremendous promise in helping to gain improved control over crystallization processes, their broader application in rational crystal engineering has been impeded by an incomplete understanding of molecular-level mechanisms underlying their function. This challenge is due in part to the limited spatiotemporal resolution of existing experimental techniques, which prevent them from being able to directly characterize the molecular processes relevant to SDA and CGM function. Thus, it remains difficult to predict *a priori* how effective specific molecules will be in functioning as SDAs or CGMs based on properties such as molecular structure. As a result, promising compounds are often identified using costly and time-consuming combinatorial screening processes.

Molecular simulation methods such as molecular dynamics (MD) and Monte Carlo (MC) are well-suited for examining processes occurring on nanoscopic length and time scales.<sup>16</sup> As a result, in the context of zeolites, for example, they have played



Figure 1.3: Materials grown in the presence of modifiers ranging from ions to macromolecules.

a tremendously important role over the last several decades in complementing experimental efforts to develop fundamental understanding of molecular adsorption and transport processes in these materials.<sup>17</sup> They have also been used to examine changes in the stability of zeolite frameworks when SDAs are inserted into their pores.<sup>18</sup>Lastly, molecular simulation has been used to investigate the nucleation of zeolite precursors and early stages of crystal growth.<sup>18–21</sup>

This thesis consists of a collection of studies in which molecular simulation meth-

ods have been used in conjunction with experiment to understand SDAs and CGMs in a number of different contexts. The principal computational technique used in all of the studies is molecular dynamics (MD). Molecular dynamics is a numerical method for propagating dynamical trajectories for model systems. The model is specified by an initial set of coordinates (atomic positions and momenta) and an intermolecular potential or "force field", which is used to evaluate the total force acting on each atom in the system. The atomic positions are then propagated in time according to Newton's Second Law using a finite-difference scheme. The resulting dynamical trajectory for the model can then be analyzed to investigate processes occurring on nanoscopic time and length scales that are often inaccessible experimentally. Because MD is a well-established technique, we do not discuss it in depth in this thesis, but instead point interested readers to Frenkel and Smit,<sup>22</sup> which presents a detailed technical description of the method as well as recommendations for best practices for implementing and using the technique. Details regarding advanced variants of the method that are used in several of our studies are provided in the methods sections of the relevant chapters.

The remaining sections of this thesis are organized as follows. In Chapter 1, we present a combined experimental and computational study investigating the use of different SDAs in the synthesis of ZSM-5, a zeolite catalyst that is used in hydrocrabon isomerization and alkylation of hydrocarbons. Our simulations reveal how different SDAs help to stabilize this specific polymorph and provide detailed information on where they preferentially become occluded in the pore network during synthesis. In Chapter 2, we present an experimental and computational study investigating the mechanisms by which two different SDAs act cooperatively to stabilize a MOR structured zeolite. Examples of SDA cooperativity are rare in the literature, and to our knowledge this is the first extensive study where a specific mechanism is revealed. We show that the simulations are in remarkably good agreement with x-ray and NMR measurements, but provide much more detailed information regarding the molecular arrangement of the SDAs in the zeolite's pore network. In Chapter 3, we use advanced sampling methods to examine how CGMs bind to the surfaces of LTL and TON structured zeolites. In agreement with calorimetry measurements, the simulations show that binding strength is not significantly greater than the thermal energy, suggesting that even weak adsorption of molecular species can influence crystal growth. In Chapter 4, we use simulation to investigate solvent structuring near the surfaces of hematin crystals and how this phenomenon may influence the efficacy of antimalarial drugs that act as CGMs for hematin to prevent its crystallization. Lastly, in Chapter 5 we summarize key findings and discuss potential avenues for future research directions.

# Chapter 2: Cooperative Effects of Inorganic and Organic Structure-Directing Agents in ZSM-5 Crystallization

This chapter was published as: Chawla, A.; Li, R.; Jain, R.; Clark R.; Sutjianto, J.; Palmer, J.; Rimer, J. Cooperative Effects of Inorganic and Organic Structure-Directing Agents in ZSM-5 Crystallization. *Molecular Systems Design & Engineering* **2017**, 3(1), 159-170. R. John Clark performed the computational portion of this study.

#### **2.1 Introduction**

Zeolites are crystalline microporous aluminosilicates with unique properties, such as tunable acidity and exceptional (hydro)thermal stability, which are utilized in commercial processes ranging from ion-exchange and adsorption to catalysis and separations.<sup>23–26</sup> In this study we focus on the synthesis of ZSM-5 (MFI framework type), which is heavily used in catalytic applications that include (but are not limited to) reforming,<sup>27</sup> isomerization,<sup>28</sup> hydrocracking,<sup>29</sup> biomass conversion,<sup>30</sup> and methanol to hydrocarbon (MTH) reactions.<sup>31</sup> The MFI framework is comprised of 3-dimensional (3D) pore network consisting of intersecting straight and sinusoidal channels (ca. 5.6 Å diameter). Among the approximate 230 known zeolite structures, the vast majority are synthesized in the presence of an organic structure-directing agent (OSDA),<sup>32</sup> which is a molecule with a size and geometry similar to the channels or cages of zeolites; therefore, OSDAs facilitate pore formation, alter the kinetics of crystallization, and (in some instances) direct the incorporation of Al at specific tetrahedral sites within the crystal lattice.<sup>33</sup> It is possible to synthesize ZSM-5 in the absence of an OSDA using sodium ions.<sup>34,35</sup> as inorganic structure-directing agents;

however, the products of OSDA-free synthesis contain a significant amount of Al (i.e., Si/Al < 20). In order to achieve higher Si content, which is often desirable for catalytic applications, an OSDA must be used in the growth mixture.

The most common OSDA for zeolite MFI is tetrapropylammonium (TPA).<sup>15,36</sup> Prior literature contains examples of other OSDAs, such as triethyl butyl ammonium bromide (TEBA),<sup>37</sup> dimers and trimers of TPA,<sup>38,39</sup> amines (e.g., triethanol amime<sup>40</sup> and ethyelene diamine<sup>37</sup>), and alcohols (e.g., 1,6-hexanediol<sup>41</sup> and tetrabutyl alcohol<sup>42</sup>). Ryoo and coworkers reported the use of dual-porogenic surfactants containing mono quaternary ammonium groups to synthesize MFI nanosheets of several unit cell thickness.<sup>43</sup> Other groups have also established that under appropriate conditions the surfactant cetyltrimethylammonium (CTA) can act as an OSDA for MFI crystallization.<sup>44-46</sup> Prior studies have explored the use of CTA for alternative purposes, including its use as a crystal growth modifier to alter zeolite habit.<sup>47</sup> as a mesoporogen,<sup>48</sup> as a swelling agent in the preparation of 2-dimensional nanosheets from layered zeolites, 49-53 and in post-synthesis treatment to induce mesoporosity.<sup>54-57</sup> Few studies have explored the use of CTA strictly as an OSDA in zeolite synthesis as well as methods to optimize the physicochemical properties of ZSM-5 crystals produced by this OSDA. Examples include the work from Okubo and coworkers<sup>44</sup> that introduced CTA-directed MFI synthesis, as well as a recent paper by Hensen and coworkers<sup>46</sup> that highlighted the role of dual inorganic/organic structure-directing agents (SDAs). Interestingly, molecular analogues of CTA, such as tetramethylammonium (TMA) and its structural derivatives, do not direct the formation of MFI, but act as OSDAs for other zeolite structures (e.g., CAN, ERI, GIS, GME, LTA, LTN, MAZ, PHI, and SOD).<sup>58-63</sup> This suggests that the hydrophobic tail of CTA (Figure 2.1) is instrumental in its role as a structure-directing agent for MFI.

Alkali and alkaline earth metals are common inorganic structure-directing agents (SDAs) in zeolite synthesis<sup>64</sup> and are also found in a majority of natural ze-



Figure 2.1: Molecular structures of organic structure-directing agents.

olites.<sup>65</sup> Inorganic SDAs function as extra-framework cations and have the ability to increase the rate of crystallization. For instance, Davis and coworkers observed a seven-fold increase in the rate of MTW crystallization in the presence of alkali metals.<sup>66</sup> Prior studies have categorized the effects of inorganic SDAs on the basis of their ability to either promote or disrupt hydrogen bonding of water molecules around the cation, with subsequent displacement by (alumino)silicate species leading to the formation of nuclei.<sup>67</sup> Notably, Li and Na ions are referred to as structure formers, while K, Rb, and Cs are structure breakers owing to their large ionic radius. In general, the rate of crystallization is reduced or enhanced in the presence of structure breakers or formers, respectively;<sup>68</sup> however, it is not well understood how or why certain inorganic SDAs selectively promote the formation of a particular zeolite framework type, and how cations work in concert with organics to alter the kinetics of zeolite crystallization.

Herein, we investigate the effects of dual inorganic and organic SDAs on the synthesis of ZSM-5 through integrated experimental and molecular modeling studies. Comparisons are made using CTA and TPA as organic SDAs in combination with various alkali metals as the inorganic SDAs. Our findings reveal that the selection of specific organic/inorganic SDA combinations has a direct impact on the kinetics of MFI crystallization. Moreover, our findings indicate that SDA combinations influence the physicochemical properties of ZSM-5, which includes crystal size, morphology, and the number and/or spatial distribution of aluminum in the MFI framework. Time-resolved analysis of zeolite nucleation and crystal growth indicate a synergistic effect of organic and inorganic cations on MFI formation.

#### 2.2 Methods

#### 2.2.1 Materials

The following chemicals were purchased from Sigma-Aldrich (St. Louis, MO): LUDOX AS-30 (30 wt% suspension in water), LUDOX AS-40 (40 wt% suspension in water), tetraethylorthosilicate (TEOS, 98%), potassium hydroxide (85% pellets), aluminum sulfate hydrate (98%, 14-18 H<sub>2</sub>O, calculated as 18 H<sub>2</sub>O), hexadecyltrimethylammonium bromide (CTAB, BioXtra,  $\geq$  99%), tetrapropylammonium bromide (TPABr, 98%), and tetramethylammonium bromide (TMABr, 98%). Additional reagents used for the synthesis of ZSM-5 include sodium hydroxide (98% pellets, MACRON Fine Chemicals), lithium hydroxide (anhydrous 98 Alfa Aesar), and cesium hydroxide (50% w/w aq. soln., Alfa Aesar). Deionized (DI) water used in all experiments was purified with an Aqua Solutions RODI-C-12A purification system (18.2 MΩ). All reagents were used as received without further purification.

#### 2.2.2 Crystallization of MFI Zeolite

ZSM-5 crystals were synthesized from a growth mixture with a molar composition of 2 OSDA: 11.9  $M_2O$ :  $Al_2O_3$ : 90 SiO<sub>2</sub>: 3588  $H_2O$  (OSDA = CTAB or TPABr; M = K and/or Na). Aqueous solutions of potassium hydroxide (0.33 g in 1.44 g of DI water) and aluminum sulfate (0.14 g in 1.44 g of DI water) were mixed with 5.76 g of water, and LUDOX AS-30 solution (3.76 g in 2.13 g of DI water) was added under vigorous stirring. AS-30 was used as the nominal silicon source unless otherwise stated. The resulting mixture was stirred for ca. 20 h at room temperature (referred to as aging). After aging, the OSDA (e.g., 0.1515 g CTAB) was added and the solution was left to stir for another 2 h at room temperature. The growth mixture (ca. 10 g) was then placed in a Teflon lined stainless steel acid digestion bomb (Parr Instruments) and was heated under rotation (30 rpm) and autogenous pressure in a Thermo Fisher Precision Premium 3050 Series gravity oven. The nominal time and temperature for ZSM-5 synthesis was 3 days at 160 °C. For X-ray and microscopy analyses, the particulates in the growth mixture (amorphous and/or crystalline) were isolated as a white powder by centrifugation (Beckman Coulter Avanti<sup>®</sup> J-E series high-speed centrifuge) at 13 000 rpm for 45 min. The solid was washed with DI water to remove the supernatant and the centrifuge/washing step was repeated a second time. The resulting solid was dried at ambient conditions. During the preparation of microscopy samples, the solid was dispersed in DI water and an aliquot of the suspension was placed on a glass slide and dried overnight. Crystals on the glass slide were transferred to SEM sample holders (Ted Pella) by gently pressing the glass slide on the carbon tape.

#### 2.2.3 Materials Characterization

Powder X-ray diffraction (XRD) patterns of as made samples were collected on a Siemens D5000 X-ray diffractometer using a Cu K $\alpha$  source (40 kV, 30 mA). Scanning electron microscopy (SEM) images were obtained with a LEO 1525 FEG system operated at 15 kV and a 5 mm working distance. All SEM samples were coated with a thin carbon layer (ca. 30 nm) prior to imaging. Textural analysis was performed with a Micromeritics ASAP 2020 instrument using N<sub>2</sub> as a probe gas for physisorption at an incremental dosing rate of  $3 \text{ m}^3 \text{ g}^{-1}$  STP and an analysis bath temperature of 77 K. Prior to analysis, samples were calcined at 550 °C for 6 h under flow of compressed air at 100 cm<sup>3</sup> min<sup>-1</sup>. The surface area was calculated from BET analysis selecting the initial low pressure points with a correlation coefficient greater than 0.999. The weight percentage of occluded organics in ZSM-5 samples were assessed

by thermogravimetric analysis (TGA) using a TA instruments Q50 model and  $N_2$ as the carrier gas at a flow rate of  $100 \,\mathrm{mLmin^{-1}}$ . The temperature was ramped up to 800 °C at the rate of 1 °Cmin<sup>-1</sup> with an isothermal dwell time of 10 min. Xray photoelectron spectroscopy (XPS) data were collected by a Physical Electronics Model 5700 XPS instrument. A monochromatic Al K $\alpha$  X-ray source (1486.6 eV) was used with the power of 350 W. All spectra were obtained once reaching a vacuum of  $5 \times 10^{-9}$  torr or better. Elemental analysis of samples was conducted by energy dispersive X-ray (EDX) spectroscopy using a JEOL SM-31010/METEK EDAX system at 15 kV and 15 mm working distance. Dynamic light scattering (DLS) measurements were performed on a Brookhaven Instruments BI-200SM machine equipped with a TurboCorr Digital Correlator, a red HeNe laser diode (30 mW, 637 nm), and a decalin bath that was filtered to remove dust. The liquid sample cell was regulated at 25 °C with a Polyscience digital temperature controller. Samples were prepared by diluting zeolite growth mixtures in pre-filtered DI water (0.45 µm nylon syringe filter, Pall Life Sciences) to achieve reasonable scattering counts (>20000 count/s). At least three measurements were performed per sample. Autocorrelation functions were collected over a 2 min timeframe and the hydrodynamic diameter DH was analyzed by the method of cumulants to assess particle size distribution. Silica dissolution experiments were performed by adding colloidal silica to metal hydroxide solutions (pH = 12) in the absence of aluminum. Solutions were separated into different vials and heated at specified temperatures in a Julabo ED-5M/B water bath. Vials were removed at periodic times and immersed in ice to cool down to room temperature before performing DLS analysis.

#### 2.2.4 Molecular Modeling

Molecular dynamics (MD) simulations were performed with GROMACS 4.6.7<sup>69</sup> to identify energetically favorable conformations of the OSDA molecules (i.e., CTA and TPA) within the MFI framework. The structure of MFI was modeled using the

atomic positions and lattice parameters from the IZA database. Interactions between zeolite framework atoms (Si and O) were described the ClayFF potential,<sup>70</sup> whereas TPA and CTA were modeled using the generalized AMBER force field.<sup>71</sup> Standard Lorentz-Berthelot combining rules were employed to determine the potential parameters for modeling van der Waals interactions between the SDAs and zeolite framework.<sup>22</sup> Van der Waals and real-space Coulombic interactions were truncated using a cutoff of 0.9 nm, and the particle mesh Ewald method<sup>22</sup> was used to treat longrange electrostatics. Parameters for the Ewald summation were chosen to ensure a relative error of less than  $1 \times 10^{-5}$  in the calculated energy. The equations of motion were integrated using a velocity-Verlet scheme with a 2 fs time step.<sup>22</sup> A Bussi-Parrinello velocity-rescaling thermostat<sup>72</sup> was used to maintain temperature, and constant pressure conditions were imposed using a Parrinello-Rahman barostat.<sup>73</sup> A relaxation time constant of 2 ps was used for the both the thermostat and barostat.

Energetically favorable conformations for the OSDAs were sampled using a threestep procedure. In the first step, OSDA molecules were inserted into the zeolite framework. To avoid trapping the systems in high-energy conformations, the insertions were performed gradually using an alchemical transformation procedure<sup>74</sup> in which the OSDAs were converted from an ideal gas to fully interacting molecules over the course of a 500 ps canonical ensemble MD simulation at 300 K. The details of this procedure follow those described by Kim et al.<sup>75</sup> In the second step, the configurational energy of the system (OSDAs + zeolite framework) was minimized using the conjugate gradient algorithm. Minimization was stopped when the maximum pairwise force fell below a threshold of  $5 \text{ kJ mol}^{-1} \text{ nm}^{-1}$ . Finally, in the third step, the energy-minimized configuration was used to initialize a ns-long isothermal-isobaric ensemble MD simulation at 300 K and 0 bar. The last half of each MD trajectory was used to evaluate the average energy for the system  $\langle U_{sys} \rangle$  and the stabilization energy<sup>76,77</sup>  $E_s \equiv \langle U_{sys} \rangle - \langle U_{zeo} \rangle - n \langle U_{SDA} \rangle$ , where n is the number of SDA molecules in the system, and  $\langle U_{SDA} \rangle$  and  $\langle U_{zeo} \rangle$  are average energies computed for a single SDA molecule and the empty zeolite framework, respectively. Previous computational investigations have shown that  $E_s$  computed a similar manner is a good descriptor for identifying novel OSDAs to stabilize otherwise thermodynamically unstable zeolite polymorphs.<sup>76,77</sup> For the purpose of this study,  $E_s$  was used to identify energetically favorable arrangements of OSDAs that enhance the MFI framework stability. The three steps above were repeated to evaluate  $E_s$  for ~ 10<sup>3</sup> different conformations for each OSDA; favorable conformations with  $E_s < 0$  were kept for further analysis.

#### 2.3 Results and Discussion

#### 2.3.1 MFI Synthesis with Organic and Inorganic Ion Pairings

Here we investigate various combinations of inorganic and organic ions in ZSM-5 synthesis using two commonly reported SDAs for MFI - tetrapropylammonium (TPA) and Na - and two less commonly reported SDAs - cetyltrimethylammonium (CTA) and K. Beginning with studies of CTA, scanning electron micrographs reveal the formation of ca. 1.3 µm ZSM-5 crystals in the presence of K (Figure 1A). In the presence of Na we observe ca. 650 nm crystals (Figure 1B), which is a factor of 3 less than those reported in prior studies of CTA-directed MFI crystallization.<sup>44</sup> The ability to produce small ZSM-5 crystals is associated, in part, to the SDA pairings. In addition, our findings indicate that crystal size is attributed to the use of colloidal silica compared to alternative silicon sources, such as tetraethylorthosilicate (TEOS). For instance, we prepared a ZSM-5 growth mixture with the same composition and switched from colloidal silica to TEOS. The resulting crystals (shown in Figure 2.2) were approximately three times larger, which highlights the importance of Si source selection in MFI synthesis.

Meng et al. reported that combinations of CTA and K resulted in the formation of MFI, whereas solutions of CTA and Na did not produce crystals under the conditions



Figure 2.2: Scanning electron micrographs of ZSM-5 crystals synthesized with CTA as the OSDA in the presence of (A) potassium and (B) sodium cations.

tested.<sup>46</sup> Here, we report that both SDA combinations result in MFI formation, with shorter crystallization times for solutions containing K. Notably, time-resolved powder X-ray diffraction (XRD) analysis of samples containing both CTA and K reveal that crystallization is complete within 17 h of hydrothermal treatment (Figure 2.3A). We observed that the combination of CTA and Na results in MFI crystals after longer heating time (ca. 60 h), as shown in Figure 2.3B. It should be noted that our experiments were performed at 160 °C compared to 140 °C in the study by Meng et al., which seems to indicate that crystals will form if given sufficient time to nucleate and grow.<sup>46</sup> If true, this suggests that MFI crystallization potentially occurs in solutions containing CTA/Na at lower temperature with adequate heating time (i.e., > 10

days at 140 °C).



Figure 2.3: Powder XRD patterns of solids from ZSM-5 syntheses using CTA as the OSDA in the presence of (A) potassium and (B) sodium cations.

The synergy observed in the combination of CTA and K is quite unexpected given that K is reported in literature to either slow MFI crystallization or suppress its formation.<sup>68</sup> For instance, organic-free syntheses of ZSM-5 are possible using Na as an inorganic structure-directing agent (SDA),<sup>35</sup> but to our knowledge MFI cannot form in the presence of K as the only SDA. Conversely, K is known to direct the formation of many other zeolite frameworks (e.g., LTL, TON, and MER, among others).<sup>2,78–80</sup> As shown in Figure 2.4, a systematic analysis of MFI growth mixture containing CTA and varying ratios of K and Na reveal that there is a three-fold reduction in the induction time when switching from mixtures of CTA with Na to those with K. The x-axis of Figure 2.4 indicates the inorganic SDA content as the molar ratio of potassium relative to the total alkali metal content in each ZSM-5 growth mixture. The corresponding time-elapsed XRD patterns are shown in Figure A.1 of the Supporting Information. It should be noted that the reported induction times are an overestimation given that we use the first appearance of Bragg peaks in powder XRD patterns of extracted solids to estimate the onset of nucleation (i.e., peaks in XRD patterns appear once there is ca. 3% crystalline material in the sample).<sup>81</sup>



Figure 2.4: Approximate induction times estimated by the first appearance of Bragg peaks in powder XRD patterns.

By comparison we tested ZSM-5 synthesis using combinations of TPA and alkali metals and observed an opposite trend. Crystallization of ZSM-5 in the presence of Na is complete within ca. 24 h of hydrothermal treatment (Figure A.9), whereas the combination of TPA and K yields a partially amorphous product (Figure 2.5). Scanning electron micrographs of products extracted after 24 h of heating also reveal dramatic differences in crystal morphology (Figure 2.5), which was not observed in samples prepared with CTA. For instance, growth mixtures containing TPA and K result in the formation of hexagonal crystals (ca. 6 µm) with residual amorphous precursors (Figure 2.5A, arrow) clearly visible. SEM images of crystals prepared with TPA and Na reveal an ellipsoidal morphology (Figure 2.5B) with smaller size (ca. 3 µm). The increased crystallization time for solutions containing K is qualitatively consistent with reports of MFI synthesis in literature. The ability of K to reduce crystallization time is only observed with CTA; therefore, our findings indicate that organic/inorganic SDA pairings do not follow identical trends, but are dependent upon the selected combination. The molecular mechanism(s) governing the cooperative effects of inorganic/organic SDA combinations is not well understood.



Figure 2.5: SEM images of ZSM-5 crystals synthesized with TPA as the OSDA in the presence of (A) potassium and (B) sodium

#### 2.3.2 TPA and CTA Occlusion in MFI Pores

We also used MD to locate regions within the MFI framework where the OSDAs (TPA and CTA) become preferentially occluded during synthesis. Favorable conformations were identified by computing the stabilization energy  $E_s$  for each OSDA in an MFI framework consisting of 36 unit cells ( $3 \times 3 \times 4$ ) (see Methods). Modeling such a large system was necessary to avoid spurious self-interactions when inserting CTA,
which is more than 2 nm in length in its fully extended conformation. To minimize the computational cost of the simulations, conformational sampling was performed using only a single OSDA molecule. The results from these simulations, however, were found to be qualitatively consistent with limited sets of calculations performed using higher OSDA loadings (i.e., 1 and 2 OSDAs per unit cell). The simulations predict that TPA preferentially occupies MFI's large pores located at the junctions where the straight and sinusoidal channels in the framework intersect (Figure 2.6A). These pores are ~ 0.7 nm in diameter, which is similar to the size of TPA (min/max dimensions:  $\sim 0.65/0.91$  nm). TPA adopts conformations inside these pores in which its N center sits near pore's middle and its bulky propyl groups extend into the adjoining channels (Figure 2.6B). These favorable conformations significantly enhance the stability of the MFI framework ( $E_s \sim -530 \, \text{kJ} \, \text{mol}^{-1}$ ). Further, they are in excellent agreement with the TPA conformations deduced from nuclear magnetic resonance and X-ray diffraction measurements and predicted in other computational studies of MFI.<sup>82-85</sup> By contrast, conformations in which the N center of TPA is located inside the straight or sinusoidal channels result in unfavorable steric interactions that destabilize the MFI framework (i.e.,  $E_s > 0$ ). Hence, the simulations suggest that TPA is too large to become occluded in other regions within the framework.

Whereas TPA molecules can only be accommodated in MFI's large pores, there are at least two distinct conformations accessible to CTA, which has a chain-like structure (min/max dimensions: ~ 0.3/2.3 nm nm). In the first conformation, CTA occupies a straight channel with its trimethylammonium head group extending into one of MFI's large pores (Figure 2.7). In the second conformation, CTA's backbone bends to allow it to occupy a sinusoidal channel (Figure 2.7). While both conformations are favorable ( $E_s \sim -575$  and -500 kJ mol<sup>-1</sup>, respectively), the former leads to greater framework stability and thus will be energetically preferred. Nevertheless, the similar magnitude of the stabilization energies suggest that CTA may be occluded



Figure 2.6: Energetically favorable conformations for TPA in the MFI framework identified using MD.

in both conformations during zeolite synthesis. Although, to our knowledge, no prior computational studies have been performed to examine CTA occlusion in MFI. The first conformation is remarkably similar to those that have been previously posited on the basis of steric considerations.<sup>44,45</sup> The second conformation, however, has not been previously hypothesized, which is likely due to the fact that it involves a complex rearrangement of CTA's backbone structure.

#### 2.3.3 Impact of SDA Pairings on Si/Al Ratio

The inorganic and organic SDAs in this study are both capable of becoming extraframework cations to counterbalance negatively-charged framework Al sites. The occlusion of TPA cations in MFI can direct Al siting at channel intersections, whereas Na has the capability of directing Al siting in straight and sinusoidal channels.<sup>86</sup> It is postulated that Al siting in MFI<sup>87</sup> and other frameworks<sup>33,88</sup> is biased to particular tetrahedral sites, wherein the choice of organic and/or inorganic cations can alter Al



Figure 2.7: Energetically favorable conformations for CTA in the MFI framework identified using MD.

distributions.<sup>89</sup> Motivated by past studies of Al distribution, we examined the molar Si/Al ratio (SAR) of ZSM-5 crystals prepared with various SDA pairings (Figure 2.8). To study the spatial distribution of Al, we used a combination of electron dispersive X-ray (EDX) spectroscopy and X-ray photoelectron spectroscopy (XPS). The former probes greater depths of particles, thereby assessing the bulk SAR, whereas XPS is a surface-sensitive technique with a shorter penetration depth that assesses the outer rim of zeolite crystals. Numerous studies have reported aluminum zoning in ZSM-5 crystals, which refers to a gradient in SAR (high to low Al content) from the outer rim of the crystal to its interior.<sup>90–92</sup> The presence of an Al-rich rim has been observed for ZSM-5 crystals synthesized in the presence of TPA, whereas it is postulated that OSDA-free syntheses lead to a more homogenous Al distribution. This is seemingly true for ZSM-5 crystals prepared with a combination of TPA and K, which is aluminum zoned (Figure 2.8). Interestingly, synthesis mixtures containing TPA and Na resulted in the opposite trend: crystals with a Si-rich exterior and a more aluminous interior. Combinations of CTA and alkali metals resulted in more homogenous Al distributions (i.e., similar SAR measurements by XPS and EDX), with a small degree of silicon zoning. It is evident from this study that the judicious selection of SDA combinations has a marked influence on the spatial distribution of Al sites in the MFI framework.



Figure 2.8: Elemental analysis of ZSM-5 samples using EDX (red) and XPS (blue) to measure the Si/Al molar ratio.

As shown in Figure 2.8, EDX analysis reveals that the SAR of TPA-MFI crystals is approximately two-times higher than CTA-MFI crystals. This indicates that specific SDA combinations are capable of altering the degree of Al incorporation in framework sites; however, measurements of occluded organic by TGA reveal a relatively constant number of molecules per unit cell (labelled Z) for all SDA combinations: Z = 2.4, 2.2, 2.9, and 2.5 for CTA/K, CTA/Na, TPA/K, and TPA/Na, respectively. The inorganic and organic SDAs compensate the negative charge of framework Al, although it is not evident from our studies how Al is distributed within the straight and sinusoidal pores of the crystal structure (Figure 2.9 A). Moreover, it is understood that SDAs can stabilize defect sites (i.e., deprotonated siloxy groups), which is not explicitly considered in this discussion. Schematics of SDA occlusion in the pores of MFI are depicted in Figure 2.9 B and C. In the idealized rending of SDA occupancy, we postulate that TPA places a single Al site at the intersection of straight and sinusoidal channels (i.e., "A" site in Figure 2.9 B). It could be argued on the basis of steric constraints that the propyl groups of TPA extending into adjoining channels reduce the likelihood of alkali metals occupying Al sites in close proximity of the organic. Conversely, molecular modeling of CTA occlusion in MFI (Figure 2.7) revealed an energetic preference for its alignment with the straight channel (analogous to assumptions in prior literature<sup>46</sup>). This allows for Al siting at channel intersections near the tetraalkylammonium (head) group of CTA (i.e., "A" site in Figure 2.9 C). We postulate that the short methyl groups of CTA are less prohibitive for alkali metals to direct Al siting in vacancies or in close proximity of the head groups (sites "B" in Figure 2.9 C). CTA may also direct Al siting within the channels (e.g., illustrated as site "C" for a sinusoidal channel in Figure 2.9 C). It should be emphasized that the scenarios illustrated in Figure 2.9 are merely suggestive, and do not reflect direct evidence of Al siting; however, the hypothesized sequence of Al positions is qualitatively consistent with the nearly two-fold difference in SAR of CTA- and TPA-MFI samples.

#### 2.3.4 Putative Effects of SDA Pairings on MFI Nucleation

Meng et al.<sup>46</sup> reported a relatively short timeframe of MFI crystallization in the presence of CTA and K, which they attributed to the kinetics of silica dissolution. This is consistent with studies in literature showing that silica dissolves more rapidly



Figure 2.9: Schematic of the straight and sinusoidal channels of MFI and ideal packaing arangments for TPA (B) and CTA (C).

in alkaline solutions of K compared to those of Na.<sup>93</sup> Here, we confirmed this phenomenon using solutions similar to those of ZSM-5 synthesis, but in the absence of alumina. Alkaline solutions were prepared with colloidal silica (LUDOX AS-40) using the molar composition 20 SiO<sub>2</sub>: 0.2 MOH: 1030 H<sub>2</sub>O (with M = K and Na). The temporal reduction in the hydrodynamic diameter of silica particles was measured ex situ by dynamic light scattering (DLS) using a previously reported protocol.<sup>94</sup> The results for KOH and NaOH are shown in Figures 2.10 A and S11, respectively. The hydrodynamic diameter of colloidal silica decreases linearly with time. A monotonic increase in the slope, or rate of dissolution, is observed with an increase in temperature. It was noted that once the silica particles reach ca. 91% of their original size, dissolution ceases and the particle size remains constant (dashed line in Figure 2.10A). This indicates that the solution is saturated (i.e., silica solubility).

In synthesis mixtures the presence of alumina forms a shell surrounding silica particles that reduces the rate of dissolution.<sup>95</sup> It is also expected that the adsorption of OSDAs would impact precursor dissolution; however, the kinetic data in Figure 2.10 indicates that the rate of silica dissolution at the actual synthesis temperature should be 500 - 1000 times faster (i.e., on the order of seconds). Given that the



Figure 2.10: Ex situ DLS measurements of silica dissolution in Al-free solutions.

timescale of zeolite nucleation is on the order of hours, it is reasonable to argue that dissolution is not the rate determining step in MFI crystallization.

An Arrhenius plot in Figure 2.10 B confirms that silica dissolves more rapidly in KOH compared to NaOH, but the apparent activation energy of dissolution is approximately equal for both alkali metals. We propose that differences in dissolution cannot account for the relatively short time of MFI crystallization by CTA/K. Indeed, if a short induction time was attributed to faster silica dissolution, we would anticipate similar outcomes for growth mixtures containing TPA/K, which we did not observe. The cooperative interactions between organic and inorganic SDAs that lead to significant differences in crystal nucleation and growth times, as well as the final crystal size and morphology, are not well understood. SDA combinations could potentially impact MFI growth by influencing the formation of composite building units, altering the solvation of (alumino)silicate species in solution and/or at crystal interfaces, which can subsequently influence monomer or oligomer addition to growing crystals, or display favorable packing configurations within the pores of MFI crystals. Elucidating the nature of cooperative SDA interactions is a topic that requires further analysis by concerted modeling and experimental efforts to identify their mechanism(s) of action.

A common characteristic of zeolite growth mixtures is the presence of amorphous precursors, which can range in size from small nanoparticles<sup>96,97</sup> to micron-sized agglomerates that are often referred to as worm-like particles (WLPs).<sup>47,78,98</sup> During hydrothermal treatment, precursors evolve in size, composition, and/or microstructure, eventually reaching a steady state at a time that generally coincides with the end of the induction period. During crystal growth the population of precursors gradually reduces, and in many instances precursors are implicated in nonclassical pathways of growth, referred to as crystallization by particle attachment (or CPA).<sup>99</sup> Prior studies of zeolites, such as zeolite L (LTL), revealed an apparent correlation between the final size of evolved precursors and crystallization time. Notably, the slower the rate of crystallization, the larger the average size of evolved precursors.<sup>78</sup> In this study of ZSM-5 we observe similar trends. In Figure 2.11 we report the size of precursors at early and later stages of crystallization for all four SDA combinations. When evaluating the differences in precursor size (from smallest to largest), we obtain the following order: TPA/Na < CTA/K < TPA/K < CTA/Na. This sequence matches the order of crystallization time, which is 15, 17, 48, and 60 h, respectively, which indicates that SDA combinations leading to faster crystallization (i.e., TPA/Na and CTA/K) provide less time for precursors to evolve. Similar observations for zeolite LTL have been reported when using modifiers (e.g., peptoids) that inhibit nucleation and allow more time for precursors to evolve.<sup>100</sup>



Figure 2.11: (A-D) SEM of amorphous precursors during the induction period. (E) Average precursor size for short and long times.

A comparison of ZSM-5 induction and crystal growth times are provided in Table 2.1 for various combinations of inorganic and organic SDAs with the addition of two alkali metals, Li and Cs. The induction time is estimated as the onset of Bragg peaks in powder XRD patterns (Figures 2.3, S9, and S10) where it is recognize that nucleation begins slightly before this point and may continue beyond it based on prior observations in literature.<sup>41,78</sup> For estimates of crystal growth times we use a combination of powder XRD patterns and SEM images (Figure A.12) to confirm that all amorphous precursors have been consumed (which is difficult to determine from XRD alone). Comparison of natural zeolites and prior literature of OSDA-free zeolite synthesis reveals that Li can direct structures such as EDI, ABW, EMT, FAU, and ANA,<sup>101</sup> whereas Cs can direct the formation of TON, RHO, CHA, LTA, and ANA.<sup>101,102</sup> In this study we found that combinations of CTA with either Li or Cs results in amorphous products. Conversely, MFI crystallization occurs in the presence of TPA with each alkali metal tested. The induction times for syntheses with Li and Cs are ca. 12 h, which is longer than those of Na and K; however, there is a substantial difference in the crystal growth times. Specifically, K and Cs have much longer growth times as compared to Li and Na, which is qualitatively consistent with the structure forming and structure breaking effects observed for different cations reported in literature.<sup>67,68</sup>

	Inudction time (h)		Crystal Growth (h)	
Alkali metal	TPA	CTA	TPA	CTA
Li	9-12	a	<12	a
Κ	3-6	15 - 17	>21	<2
Na	3-6	54-60	<21	<6
$\mathbf{Cs}$	9-12	a	>60	a

Table 2.1: Comparison of ZSM-5 induction and crystal growth times. <sup>a</sup>Amorphous products.

One notable difference between TPA and CTA is the amphiphilic nature of the latter that can lead to micelle formation at sufficiently high concentration. CTA is one of the most extensively studied surfactants, and in the presence of alkali metals it has been reported<sup>103</sup> that when introducing Na salts to an aqueous CTAB solution (0.1 M CTAB), the dissociation enthalpy of the salts is an order of magnitude higher than that measured in water. Similar studies for K salts reveal that the relative increase in enthalpy (from water to a CTAB solution) is much less,<sup>103</sup> which is inconsistent with the Hofmeister series that is used to explain differences in alkali

salt dissociation in water and the potential influence of alkali metals on the critical micelle concentration of surfactants.<sup>103</sup> To this end, we performed DLS measurements of CTA dissolved in KOH and NaOH solutions at room temperature (using the exact concentration of MFI synthesis, but without the addition of silica and alumina sources) to test the effect of alkali metals on CTA micellization. The scattering counts of the NaOH mixture was 1.5-times higher than that of KOH at 25 °C, indicating a higher concentration of CTA micelles in the former; however, the counts were insufficient to obtain reliable hydrodynamic diameters. It is also expected that the critical micelle concentration at 160 °C (i.e., the actual synthesis condition) will be different.<sup>104</sup> Nevertheless, Na is a more effective promoter of CTA micellization than K, which may offer some insight into the latter's ability to increase the rate of MFI crystallization. If the interaction between organic and inorganic cations is indeed critical, this would also suggest that the effective TPA/Na combination is due to less favorable interactions between TPA and Na ions (relative to the interactions of TPA with other alkali metals).

## 2.3.5 Generation of Mesoporosity by CTA

The most common uses of CTA in zeolite synthesis are associated with its role as a mesoporogen,<sup>48,105</sup> as a post-synthesis agent to generate mesoporosity,<sup>106</sup> or a swelling agent to generate 2-dimensional zeolites from layered structures.<sup>49</sup> To this end, we performed textural analysis of MFI samples prepared with CTA and observed a type IV isotherm (Figure 2.12 A, i) that indicates the presence of mesoporosity. The t-plot external surface area contribution to the total surface area is 31% (or  $139 \text{ m}^2 \text{ g}^{-1}$ ) of the measured surface area of crystals. The shape of the adsorption/desorption curve suggests that mesopores are likely formed by nanocrystal aggregation, which is qualitatively consistent with SEM images in Figure 2.2. Interestingly, when we switch silicon sources from LUDOX AS-30, which was used for all previous syntheses, to tetraethylorthosilicate (TEOS), we observed several notable differences in the crystalline product. Crystals prepared using TEOS exhibit a type 1 isotherm (Figure 2.12 A, ii) which is a characteristic of microporous materials without evidence of mesoporosity. Nitrogen adsorption measurements reveal that crystals prepared with TEOS have lower surface area (Table A.2). TEOS also leads to a 3-fold increase in crystal size (ca. 3 µm), as shown in Figure 2.12. Moreover, elemental analysis reveals that crystals prepared with TEOS have much higher silicon content (i.e., the SAR increases from 17 to 53). Overall, our parametric examination of MFI crystallization reveals that the physicochemical properties of ZSM-5 crystals can be tailored through the judicious selection of SDA combinations, synthesis conditions, and reagent sources.



Figure 2.12: (A) N<sub>2</sub> adsorption and desorption isotherms of calcined ZSM-5 crystals. (B) SEM micrograph of a representative ZSM-5 crystal.

# 2.4 Conclusions

In summary, we have shown that CTA can be an effective SDA for ZSM-5 crystallization based on its ability to generate sub-micron particles in a period of time that is equivalent to more conventional SDAs, such as TPA. We have shown that CTAdirected growth of MFI crystals leads to a more uniform distribution of aluminium throughout the particle, which may be explained by computational simulations showing that CTA can access both straight and sinusoidal channels, unlike TPA that resides strictly at the intersection of the channels. Investigation of organic and inorganic SDA combinations reveals a cooperative effect between two positively-charge species that act as both structure-directing agents and extraframework cations. We observe that pairings of CTA/K and TPA/Na result in the fastest crystallization times, suggesting these combinations have a synergistic effect on ZSM-5 growth that is unique to the selection of SDAs. The ability of dual SDAs to alter the physicochemical properties of zeolite crystallization is a potentially useful approach to rational design. Moreover, the relatively low cost and high market availability of CTA makes it a promising candidate for commercial production of ZSM-5.

## 2.5 Acknowledgments

J.D.R. and J.C.P acknowledge financial support from the National Science Foundation (DMREF Award 1629398) and from the Welch Foundation (Awards E-1794 and E-1882, respectively).

# Chapter 3: Ultrathin Mordenite Crystals Synthesized Using Cooperative Organic Structure-Directing Agents

This chapter is a manuscript in the process of being published: Kumar, M.; Berkson, Z.; Clark, R.; Shen, Y.; Prisco, N.; Zeng, Z.; Zheng, H.; McCusker, L.; Palmer, J.; Chmelka, B.; and Rimer, J., Ultrathin mordenite crystals synthesized using cooperative organic structure-directing agents. R. John Clark performed the computational portion of this study.

# **3.1 Introduction**

The demand for more efficient zeolite catalysts creates a need to develop new synthesis approaches capable of tailoring crystal properties for optimal performance. Among many physicochemical properties of zeolites, crystal size plays a significant role in mediating internal mass transport<sup>107,108</sup> wherein diffusion pathlengths of less than 100 nm can markedly improve catalyst lifetime and alter product selectivity.<sup>109</sup> Various approaches have been explored to tune the anisotropic growth of zeolite crystals precisely, including the modification of synthesis conditions, introduction of growth modifiers,<sup>5</sup> design of new organic structure-directing agents (OSDAs),<sup>110–114</sup> and the use of crystalline seeds.<sup>115</sup> Achieving materials with well-controlled properties is often challenging, because the mechanisms of zeolite crystallization<sup>99,116–118</sup> are complex and poorly understood. Here, we combine state-of-the-art X-ray powder diffraction (XRPD) and NMR characterization techniques with computer modeling to examine the role of OSDAs in the formation of mordenite (MOR), which is difficult to prepare with sub-micron dimensions.<sup>119</sup>

Mordenite is a large-pore zeolite (pore diameter ca. 0.7 nm) with unidirectional channels aligned along the c-axis that is used as a commercial catalyst in reactions such as dehydration of alcohols to olefins,<sup>120</sup> oxidation of methane to methanol,<sup>121</sup> (hydro)isomerization,<sup>122</sup> cracking,<sup>123</sup> alkylation,<sup>124</sup> and carbonylation.<sup>125</sup> Prior studies have attributed the catalytic activity of mordenite to the intersection of 12-ring channels with 8-ring side-pockets (Figure B.1) that facilitate shape-selective reactions; however, mordenite is highly susceptible to deactivation owing to mass transport limitations imposed by its 1-dimensional pores and large channels that facilitate the formation of polyaromatics (i.e., coke precursors). Reported syntheses of mordenite typically yield large crystallites with sizes that range from 5 to 20 µm and with stacking faults that alter the placement of 8-ring pockets within the channels.<sup>126,127</sup> Post-synthesis modification to introduce mesoporosity is one way of mitigating internal diffusion limitations.<sup>128</sup> Alternatively, the synthesis of crystallites with sub-micron dimensions of the [001] facet can extend catalyst lifetime. Suib and coworkers have reported sizes as small as 40 - 60 nm using complicated synthesis protocols that include the use of crystalline seeds, <sup>129</sup> alcohol additives, and/or microwave heating.<sup>130</sup> Mordenite nanorods (ca.  $10 \times 100$  nm) have been synthesized using seeds or cationic gemini surfactants by Xiao<sup>131</sup> and Ryoo<sup>43</sup> and their coworkers, respectively. These syntheses have resulted in nanometer-sized domains within larger aggregates, which similarly involve limitations in internal mass transport.

A combination of inorganic and organic structure-directing agents are often used in zeolite syntheses to regulate the kinetics of crystallization.<sup>132</sup> The synthesis of most zeolites requires the use of OSDA molecules with sizes and shapes that are commensurate with the cages/channels of the target zeolite, thereby facilitating the generation of the desired porous structure.<sup>112</sup> OSDAs are occluded within the framework and are typically removed by post-synthesis calcination. It is common practice to use a single OSDA. In select cases, OSDAs can form clusters (e.g., dimers or aggregates) to stabilize the framework.<sup>1</sup> Few syntheses employ two or more different OSDAs. Examples often involve scenarios where only one organic functions as the OSDA and the other alters properties such as crystal size or habit, but is a by-stander for structure direction.<sup>133</sup> Combinations of OSDAs have also been used to prevent polymorphism in order to improve product purity.<sup>134</sup> Wright and coworkers have demonstrated for zeotypes, such as STA-20, that two organics may be necessary to achieve a desired crystalline phase.<sup>135</sup> In such cases, the OSDAs act cooperatively to produce a product that could not be achieved with either one alone.

Here, we show that a combination of two OSDAs, N,N,N-trimethyl-1-1adamantammonium (TMAda<sup>+</sup>) and 1,2-hexanediol (D6<sub>1,2</sub>), work cooperatively to yield mordenite. TMAda<sup>+</sup> is a well-documented OSDA for commercial SSZ-13 (CHA) (Figure 3.1A). The same synthesis using only D6<sub>1,2</sub> results in ZSM-5 (MFI) (Figure 3.1B), whereas an organic-free synthesis with Na<sup>+</sup> as an inorganic structuredirecting agent also yields ZSM-5 (Figures B.2 and B.3). Interestingly, the combination of D6<sub>1,2</sub> and TMAda<sup>+</sup> produces mordenite (Figure 3.1C and Figure B.4), referred to hereafter as HOU-4. We observe that individual OSDAs and their binary combination generate three different zeolites (Figure 3.1D): ZSM-5 is a 3-dimensional medium-pore zeolite; SSZ-13 is a 3-dimensional small-pore zeolite; and mordenite is a 1-dimensional large-pore zeolite. The composite building units (CBUs) of these three structures are vastly different, with the exception of mor being shared by both MFI and MOR framework types (Figure B.5). The three zeolites have similar elemental compositions (Table B.2), but differ with respect to crystal habit and quantity of occluded OSDA (Figure B.7 and Table B.3).



Figure 3.1: The OSDA(s), corresponding zeolite structure, and representative SEM images for (A) SSZ-13, (B) ZSM-5, and (C) HOU-4. (D) XRD patterns of the solid precipitates.

# **3.2 Methods**

#### 3.2.1 Materials

The following chemicals were used as reagents: Cab-O-Sil (M-5, Spectrum Chemical), silica gel (91%, Sigma-Aldrich), sodium hydroxide (98% pellets, MACRON Fine Chemicals), N,N,N-trimethyl-1-1-adamantammonium hydroxide (25 wt% in water, SACHEM Inc.), 1,2-hexanediol (D6<sub>1,2</sub>, 98%), 1,2-pentanediol (D5<sub>1,2</sub>, 96% Aldrich), 1,2-butanediol (D4<sub>1,2</sub>,  $\geq$ 98%,Sigma-Aldrich), 1,2-propanediol (D3<sub>1,2</sub>,  $\geq$ 99.5%,Sigma-Aldrich), and aluminum hydroxide (80.3 wt% Al(OH)<sub>3</sub>, SPI0250 hydrogel). Ion exchange was performed using ammonium nitrate (ACS reagent  $\geq$ 98%, Sigma-Aldrich. Deionized (DI) water used in all experiments was purified with an Aqua Solutions RODI-C-12A purification system (18.2 M $\Omega$ ). All reagents were used as received without further purification.

## 3.2.2 Synthesis of Ultrathin Mordenite

Mordenite (HOU-4) was synthesized with the OSDA N,N,N-trimethyl-1-1adamantammonium hydroxide (TMAda-OH) and 1,2-hexanediol (D61,2) using solutions with a molar composition of 0.052 Al(OH)3:1.0 SiO<sub>2</sub>:0.2 NaOH:44 H<sub>2</sub>O:0.1 TMAda-OH:1.6 1,2-hexanediol. Sodium hydroxide (0.09 g, 0.0022 mol) was first dissolved in water (8.21 g, 0.4959 mol), followed by the addition of TMAda-OH (0.95 g, 0.0011 mol) and 1,2-hexanediol (2.17 g, 0.018 mol). This solution was stirred until clear (ca. 15 min). Aluminum hydroxide (0.06 g, 0.0005 mol) was added to the solution and left to stir for another 15 min at room temperature. To this clear solution was added the silica source (0.67 g, 0.0112 mol), and the resulting mixture was first manually stirred with a plastic rod for ca. 15 min, followed by continuous stirring using a stir bar (400 rpm) for 4 h at 80 °C in a mineral oil bath. Approximately 10 g of growth solution after 4 h of heated stirring was placed in a Teflon-lined stainless steel acid digestion bomb (Parr Instruments) and was heated under rotation (~30 rpm) and autogenous pressure in a Thermo-Fisher Precision Premium 3050 Series gravity oven. The nominal time and temperature for HOU-4 synthesis was 6 days at 180 °C. The products of all syntheses were isolated as white powder (ca. 600 mg) by centrifuging the mother liquor (13,000 rpm for 45 min) for three cycles with DI water washes. Samples for microscopy were prepared by first redispersing a small amount of powder (ca. 5 mg) in DI water. An aliquot of this solution was placed on a glass slide and dried overnight. Crystals were transferred to metal sample disks for microscopy studies by contacting the glass slide with carbon tape for SEM.

#### 3.2.3 Synthesis of Conventional Mordenite

Conventional mordenite was synthesized using a growth solution with a molar composition of  $1 \text{ Al}_2\text{O}_3$ : 30 SiO<sub>2</sub>:5 Na<sub>2</sub>O:780 H<sub>2</sub>O.<sup>129,136</sup> Sodium hydroxide (0.25 g, 0.0061 mol) was first dissolved in water (8.437 g, 0.468 mol), followed by the addition of sodium aluminate (0.1003 g, 0.00061 mol). The solution was stirred until clear (ca. 15 min) followed by the addition of silica gel (1.212 g, 0.0183 mol), and the resulting mixture was stirred at 400 rpm for 4 h. Approximately 10 g of the growth mixture was placed in a Teflon-lined stainless steel acid digestion bomb and was heated under static and autogenous pressure. The nominal time and temperature for synthesis was 4 days and 170 °C, respectively. The products of all syntheses were isolated from mother liquor using vacuum filtration and 0.45 µm membrane filter with copious amount of DI water washes. Samples for microscopy were prepared as described above.

## 3.2.4 Solid-State Nuclear Magnetic Resonance

Solid-state 1D and 2D <sup>1</sup>H, <sup>13</sup>C, <sup>27</sup>Al, and <sup>29</sup>Si MAS NMR spectroscopy was used to analyze the <sup>1</sup>H, <sup>13</sup>C, <sup>27</sup>Al, and <sup>29</sup>Si environments in as-made ultrathin HOU-4 crystallites. The 2D <sup>27</sup>Al<sup>29</sup>Si J-mediated NMR correlation spectrum (Figure 3.3A) was acquired on a Bruker ASCEND 400 MHz (9.4 T) DNP NMR spectrometer operating at Larmor frequencies of 400.203, 104.283, and 79.501 MHz for <sup>1</sup>H, <sup>27</sup>Al, and <sup>29</sup>Si nuclei, respectively. This instrument is equipped with a 3.2 mm triple-resonance HXY low-temperature MAS probehead. Low-temperature measurement conditions of 95 K were used for improved signal sensitivity. The spectrum was acquired using a 2D Heteronuclear Multiple Quantum Correlation (HMQC) pulse sequence <sup>137,138</sup> with an experimentally-optimized half-echo tau delay of 20 ms used to refocus the weak (ca.  $1/(4\tau) = 12.5$  Hz) through-bond <sup>27</sup>Al-O-<sup>29</sup>Si J-couplings. The signal sensitivity was enhanced by applying a 1 ms <sup>27</sup>Al adiabatic double-frequency sweep pulse during the preparation period to invert the <sup>27</sup>Al satellite transitions.<sup>139</sup> During the rotor-synchronized tau delay periods, 100 kHz of continuous wave 1H decoupling was applied. A recycle delay time of 1 s was used with a rotor-synchronized  $t_1$  increment step size of  $100 \,\mu\text{s}$ , 96  $t_1$  increments, and 256 transients for a total acquisition time of 7 h. The 2D  $^{29}$ Si<sup>1</sup>H and  $^{13}C^{1}$ H spectra were acquired on a Bruker AVANCE 500 MHz (11.7 T) wide-bore spectrometer operating at Larmor frequencies of 500.222, 125.789, and 99.369 MHz for <sup>1</sup>H, <sup>13</sup>C, and <sup>29</sup>Si, respectively. Recycle delay times of 0.75 s were used with t1 increment step sizes of 128 µs. The 2D <sup>29</sup>Si<sup>1</sup>H HETCOR spectrum acquired at a short contact time (0.5 ms, Figure 3.3B) was acquired with 196  $t_1$  increments and 256 transients for a total acquisition time of 10.5 h. The 2D <sup>29</sup>Si<sup>1</sup>H HETCOR spectrum acquired at a longer contact time (5 ms, Figure B.18) was acquired with 256  $t_1$  increments and 64 transients for a total acquisition time of 3.5 h. The 2D <sup>13</sup>C<sup>1</sup>H HETCOR spectra acquired with contact times of 0.5 and 5 ms (Figure B.10) were acquired respectively with 250 and 430  $t_1$  increments and 512 and 128 transients for total acquisition times of 27 h and 11.5 h. The 2D <sup>27</sup>Al<sup>1</sup>H HETCOR spectrum (Figure 3.3C) was acquired on a Bruker AVANCE-III Ultrashield Plus 800 MHz (18.8 T) narrow-bore spectrometer operating at Larmor frequencies of 208.527 and 800.242 MHz for <sup>27</sup>Al and <sup>1</sup>H, respectively, and a Bruker 3.2 mm broadband double-resonance HX probehead was used. The 2D <sup>27</sup>Al<sup>1</sup>H HETCOR spectrum was acquired with a repetition time of 1 s, 50  $t_1$  increments and 512 transients for a total acquisition time of 7 h. All of the 2D HETCOR spectra were acquired using homonuclear  ${}^{1}\text{H}{}^{-1}\text{H}$  eDUMBO-1<sub>2</sub>2 decoupling  ${}^{140}$  during the  ${}^{1}\text{H}$  evolution periods to improve resolution in the <sup>1</sup>H dimensions. For the 2D <sup>29</sup>Si<sup>1</sup>H, <sup>13</sup>C<sup>1</sup>H, and <sup>27</sup>Al<sup>1</sup>H HECTOR experiments, a variable-temperature chiller unit was to cool the sample temperature to approximately 263 K to reduce the mobility of the OSDA species and improve crosspolarization signal sensitivity. All of the 1D and 2D spectra were acquired with 100 kHz heteronuclear SPINAL-64<sup>141</sup> <sup>1</sup>H decoupling during the acquisition period.

#### 3.2.5 Microscopy

Atomic force microscopy (AFM) measurements were performed in air using an Asylum Research MFP-3D-SA instrument (Santa Barbara, CA). An aliquot of HOU-4 dispersed in water was placed on silicon wafer and was allowed to dry at room temperature. The silicon wafer was calcined at 500 °C for 5 h, followed by cleaning under inert Ar gas flow to remove loosely-bound crystals. AFM images were collected using a Cr/Au-coated silicon nitride cantilever (Olympus RC800PB with a spring constant of 0.82 N/m) in contact mode at a scan rate of 1.2 Hz and 256 lines/scan.

Scanning electron microscopy (SEM) was performed with a FEI 235 dual-beam (focused ion-beam) system operated at 15 kV and a 5 mm working distance. All SEM samples were coated with a thin carbon layer (ca. 20 nm) prior to imaging. Transmission electron microscopy (TEM) was carried out for structural and morphology characterization using a Thermo Fischer (formerly FEI) 200 kV TitanX transmission electron microscope equipped with the windowless SDD Bruker EDS detector with fast processor.

## 3.2.6 X-Ray Analysis

Energy-dispersive X-ray spectroscopy (EDX) was performed using a JEOL JSM 6330F field emission SEM at working distance of 15 mm and voltage of 15 kV and 12 mA. X-ray powder diffraction (XRPD) patterns of as-made zeolite samples were collected on a Siemens D5000 X-ray diffractometer using a Cu KÎś1 source (40 kV, 30 mA). For reference intensity ratio (RIR) analysis using mordenite-quartz mixtures, a Rigaku SmartLab diffractometer (40 kV, 44 mA) was used. The MOR-type framework was confirmed using a reference pattern provided by the International Zeolite Association Structure Database. Synchrotron powder diffraction data were collected on an unwashed sample of HOU-4 in a 0.5 mm glass capillary on the Materials Science Beamline at the Swiss Light Source (SLS) in Villigen, Switzerland.<sup>142</sup>

The wavelength was determined from a Si standard to be 0.7087 Å.

## 3.2.7 Molecular Dynamics Simulations

MD simulations were performed with GROMACS 4.6.7.69 The MOR zeolite framework was modeled as an all silica structure using the ClayFF potential,<sup>70</sup> whereas the OSDAs (TMAda<sup>+</sup>, 1,2-pentanediol, 1,2-butanediol, 1-2-hexanediol, and 1-2-heptanediol) were described using the generalized AMBER force field.<sup>71</sup> Atomic positions and lattice parameters for the MOR framework were taken from the International Zeolite Database.<sup>143</sup> Na<sup>+</sup> ions were inserted into the 8-ring pockets, in the positions suggested by XRPD analysis (Figure B.12). Although Na<sup>+</sup> ions stabilize Al in the framework, the positions of the Al sites are not precisely known. Consequently, Al was implicitly modeled by smearing a negative charge over the oxygens in the 8-ring pockets to counterbalance the Na<sup>+</sup> ions and ensure electroneutrality. Potential parameters for describing van der Waals interactions between the OSDAs and zeolite framework atoms were evaluated using standard Lorentz-Berthelot combining rules.<sup>22</sup> Van der Waals and real-space Coulombic interactions were truncated using a cutoff of 0.9 nm, and the particle mesh Ewald method<sup>22</sup> was used to treat long-range electrostatics, with parameters chosen to ensure a relative error of less than  $10^{-4}$  in the calculated energy. The equations of motion were propagated using a leapfrog integration scheme with a 2 fs time step.<sup>22</sup> The temperature and pressure of the system were maintained using a Bussi-Parrinello velocity-rescaling thermostat<sup>72</sup> and a Parrinello-Rahman barostat, <sup>73</sup> respectively. The relaxation time constants for both the thermostat and barostat were set to 2 ps.

Following our recent study of surfactant occlusion in MFI structured zeolites,<sup>144</sup> energetically favorable conformations for the OSDAs in mordenite were sampled using a three-step procedure. First, the OSDAs were gradually inserted into the zeolite framework using the alchemical transformation procedure described by Kim et al.,<sup>75</sup> whereby the OSDAs were converted from an ideal gas to fully interacting molecules

over the course of a short MD simulation (500 ps) at ambient temperature. This gradual insertion step ensured that the system did not become trapped in unphysical, high-energy conformations. Next, the conjugate gradient algorithm was used to minimize the configurational energy of the system. Finally, the configuration from the energy minimization step was use to initialize a ns-long MD simulation at 300 K and 0 bar. Data from the last half of the MD trajectory were to evaluate the stabilization energy<sup>76,77</sup>  $E_s \equiv \langle U_{sys} \rangle - \langle U_{zeo} \rangle - \sum_i n_i \langle U_{SDA,i} \rangle$ , where  $\langle U_{sys} \rangle$  the average energy of the system,  $\langle U_{zeo} \rangle$  is the average energy of the empty zeolite framework,  $n_i$  is the number of inserted OSDA molecules of type i, and  $\langle U_{SDA,i} \rangle$  is the average energy computed for a single OSDA molecule in vacuum. The steps above were repeated to evaluate  $E_s$  for ~ 10<sup>3</sup> different conformations at each OSDA loading considered in the study. Conformations with low  $E_s$  values (lowest 10%) were saved for subsequent analysis.

#### 3.2.8 Catalyst Preparation and Testing

Samples for catalysis were calcined in a Thermo Fisher Lindberg Blue furnace under constant flow of 100 sccm dried air (Matheson Tri-Gas) at 550 °C for 5 h with a temperature ramping/cooling rate of 1 °C/min. These samples were converted to an acid form (Brønsted acids) by ion exchange wherein calcined zeolite was mixed with 1.0 M ammonium nitrate solution to obtain a 2 wt% suspension. This mixture was heated to 80 °C for 2 h to allow the exchange of Na<sup>+</sup> with  $NH_4^+$ . This process was performed three times with centrifugation/washing between each ion exchange cycle. The final  $NH_4$ -zeolite samples were washed three times with DI water before they were calcined once again with the same conditions stated above, thus becoming H-form zeolite.

Cumene cracking over H-form catalysts was carried out in a 1/4 inch stainless steel tube installed in a Thermo Scientific Lindberg Blue M furnace. The catalyst bed was supported between two plugs of quartz wool, and a K-type thermocouple (Omega Engineering) was inserted into the stainless tube to measure the temperature of the catalyst bed. Prior to the reaction, the catalyst bed was pretreated *in situ* at 550 °C for 3 h under flow of dried air (6 cm<sup>3</sup>/min of O<sub>2</sub>, 24 cm<sup>3</sup>/min of N<sub>2</sub>). After this pretreatment, the catalyst bed was cooled down to the reaction temperature, i.e.  $450 \,^{\circ}$ C. Cumene (98%, Sigma Aldrich) was fed by a syringe pump (Harvard Apparatus) at 2 µL/min into a heated inert gas stream of Ar (50 cm<sup>3</sup>/min), which resulted in a reactant flow with a weight hourly space velocity (WHSV) of 2 h-1. The cumene conversion is defined as the percentage of cumene reacted at the effluent of catalyst bed. To compare the deactivation rate between different catalyst samples, the turnover number (TON) is calculated for a selected span of time-on-stream (TOS) using a modified form of the equation reported by Bhan and coworkers, <sup>145</sup>

$$TON(t) = \frac{1}{[H^+]_0} \int_{t_1}^{t_2} F(\tau) d\tau,$$

where  $[H^+]_0$  is the total number of Brønsted acid sites (obtained from the NH3-TPD data in Table B.3),  $F(\tau)$  is the molar flow rate of converted carbon (reacted cumene), and t is TOS selected between times  $t_1$  and  $t_2$  corresponding to 85 and 70% cumene conversion (i.e., regions of nearly linear deactivation in Figure 3.4E).

Temperature-programmed desorption of ammonia was performed by the Bhan Group (University of Minnesota) on a Micromeritics Autochem II 2920 equipped with a TCD detector. Prior to TPD, ca. 100 mg of catalyst was first out gassed in He for 1 h at 600 °C with a heating ramp of 10 °C/min. Ammonia was adsorbed at 100°Cuntil saturated, followed by flushing with He for 120 min at 100°C. The ammonia desorption was monitored using the TCD detector until 600°Cwith a ramp of 10 °C/min, using a flow of 25 mL min<sup>-1</sup>.

## **3.3 Results an Discussion**

SSZ-13 crystals have a spheroidal morphology with sizes of  $1 - 2 \mu m$  and 10 wt% organic (ca. 1.3 TMAda<sup>+</sup> per unit cell). ZSM-5 crystals exhibit an indistinct morphology with sub-micron dimensions, and contain 5 wt% organic (ca. 2.7 D6<sub>1,2</sub> per unit cell). By comparison, HOU-4 crystallizes as thin plate-like particles that retain ca. 2 D6<sub>1,2</sub> and 2 TMAda<sup>+</sup> molecules per unit cell, as determined by synchrotron XRPD discussed below (Figure B.8). All of the D6<sub>1,2</sub> molecules are removed by post-synthetic washing with water (Figures B.9 and B.10), which establishes that D6<sub>1,2</sub> molecules are able to diffuse without appreciable restrictions out of the mordenite nanochannels. The mobility of D6<sub>1,2</sub> within the large pore channels of mordenite was corroborated by molecular dynamics (MD) simulations (not shown). Facile extraction of the diol molecules from zeolite frameworks without the need for post-synthesis calcination is uncommon; therefore, the synthesis of HOU-4 offers a unique route to recover and potentially recycle the OSDAs.

Transmission electron micrographs (Figure 3.2A) show that the width of the HOU-4 crystallites in the [100] direction can reach 1 µm with an average length-towidth (or [010]/[100]) aspect ratio of  $4.0 \pm 0.7$ . Selected-area electron diffraction (Figure 3.2B) confirms that the basal surface is the (001) face. Atomic force microscopy (AFM) topographical images of HOU-4 crystals (Figure 3.2C) reveal an ultrathin habit wherein the analysis of multiple crystals shows a distribution of thicknesses in the [001] direction around 80 nm (Figure B.11). The cooperativity of OSDAs leads to this unique morphology; however, to ascertain the spatial arrangement of OSDAs within zeolite channels, we analyzed an unwashed HOU-4 sample using synchrotron XRPD (Figure 3.2D) and confirmed that TMAda<sup>+</sup> resides within the 12-ring channels (Figure 3.2E and G), Na<sup>+</sup> in the oval 8-ring channels, and D6<sub>1,2</sub> in the 8-ring side pockets (Figure 3.2F). Rietveld refinement of the framework structure with occluded structure-directing agents indicates that there are 2 Na<sup>+</sup>, 2 TMAda<sup>+</sup>, 2 D6<sub>1,2</sub> and 2 water molecules per unit cell. No evidence of crystallite shape anisotropy or stacking faults was apparent in the peak-shape profiles or in the structure refinement. Quantitative solid-state one-dimensional (1D) single-pulse <sup>13</sup>C and <sup>1</sup>H magic-angle-spinning (MAS) NMR analyses (Figure B.13) yield a larger estimated quantity of  $D6_{1,2}$  (6 - 13  $D6_{1,2}$ /TMAda<sup>+</sup>). This suggests that unwashed samples probably retain significant quantities of diol molecules on the particle surfaces, and this is in agreement with thermogravimetric analysis of unwashed HOU-4 showing 37 wt% mass loss, consistent with the desorption of surface-adsorbed diol molecules (Figure B.7C).



Figure 3.2: TEM, AFM, and MD images of representative HOU-4 crystals (A-C,E-G,I-K), XRD pattern (D), and Stabilization Energy (H).

To further understand the role of occluded organics in the ultrathin mordenite, we performed MD simulations of both OSDAs in mordenite. Models placing an increasing amount of alcohol within a single MOR unit cell at fixed TMAda+ loading (Figure 3.2H) show that alcohols stabilize the structure, leading to a minimum in the energy profile around  $1.5 - 2.0 \text{ D6}_{1,2}$  molecule per unit cell. As the quantity of TMAda<sup>+</sup> per unit cell is increased, less alcohol is required to minimize the energy (Figure B.14). MD simulations corroborate that TMAda<sup>+</sup> is located within 12-ring channels (Figure 3.2I and K) with the amine groups oriented in close proximity to the 8-ring pockets. At high TMAda<sup>+</sup> loading (2 per unit cell), D6<sub>1,2</sub> molecules are oriented within the 8-ring pockets (Figure 3.2J), consistent with XRPD refinement. At lower TMAda<sup>+</sup> loadings, D6<sub>1,2</sub> molecules are also observed to reside within the 12-ring channels between adjacent TMAda<sup>+</sup> molecules (Figure B.15).

The site-specific interactions of the different framework <sup>27</sup>Al species with OSDA molecules are established by solid-state two-dimensional (2D) HETeronuclear CORrelation (HETCOR) NMR spectra of HOU-4 (Figure 3.3). The 2D NMR correlation spectra exploit internuclear dipole-dipole (through-space) or J (through-covalentbond) couplings and are plotted as 2D contour plots where correlated signal intensities manifest the mutual proximities or covalent connectivities of the corresponding <sup>1</sup>H, <sup>13</sup>C, <sup>27</sup>Al, or <sup>29</sup>Si species.<sup>146,147</sup> For example, covalent <sup>27</sup>Al-O-<sup>29</sup>Si bonds within the HOU-4 frameworks are unambiguously established by the 2D <sup>27</sup>Al<sup>29</sup>Si J-mediated NMR correlation spectrum (Figure 3.3A), which shows a distribution of correlated signal intensity at 54 ppm in the <sup>27</sup>Al dimension and -109 to -99 ppm in the <sup>29</sup>Si dimension arising from framework aluminum atoms bonded to fullyor partially-crosslinked <sup>29</sup>Si atoms. Previously, such 2D <sup>27</sup>Al<sup>29</sup>Si through-bondmediated correlation spectra of aluminosilicate zeolites have been limited due in part to the low natural isotopic abundance of <sup>29</sup>Si (4.7%) and weak <sup>27</sup>Al-O-<sup>29</sup>Si J couplings (<20 Hz), but are enabled here by the improved sensitivity of low-temperature measurement conditions. The <sup>27</sup>Al signals exhibit Czjzek lineshapes<sup>148</sup> that reflect a random distribution of <sup>27</sup>Al heteroatom environments within the mordenite framework and among the four distinct tetrahedral (T) sites, corroborated by complementary <sup>27</sup>Al triple-quantum MAS NMR analyses (Figure B.16). The relatively small

percentage of partially-crosslinked <sup>29</sup>Si species (ca. 2%, Figure B.17) are likely associated with defect sites at the exterior of the particle surfaces. The Si/Al ratio of HOU-4 estimated by quantitative <sup>29</sup>Si MAS NMR is ca. 10 (Figure B.17), which is consistent with values of ca. 10 and 13 measured by energy-dispersive X-ray spectroscopy (Table B.2) and estimated from synchrotron XRPD refinement, respectively.



Figure 3.3: Solid-state 2D NMR correlation spectrum (A), Hector spectrum (B,C), and idealized depection of framework-OSDA interactions.

Different types of framework aluminum sites in HOU-4 are distinguished on the basis of their site-specific interactions with different OSDA molecules, which are established by the 2D  $^{27}$ Al<sup>1</sup>H (Figure 3.3B) and  $^{13}$ C<sup>1</sup>H HETCOR (Figure 3.3C) NMR

spectra. The HETCOR spectra yield correlated <sup>13</sup>C- or <sup>27</sup>Al-<sup>1</sup>H signal intensities from <sup>13</sup>C-<sup>1</sup>H or <sup>27</sup>Al-<sup>1</sup>H nuclear spin pairs that are dipole-dipole-coupled through space over sub-nanometer distances. The different <sup>1</sup>H and <sup>13</sup>C signals are assigned to  ${}^{1}H$  and  ${}^{13}C$  moieties on  $D6_{1,2}$  (green shaded regions) or TMAda<sup>+</sup> (red shaded regions) molecules by analyses of complementary solid-state 1D and 2D <sup>13</sup>C<sup>1</sup>H NMR spectra (Figure B.10) and solution state 1D <sup>13</sup>C NMR spectra of the zeolite synthesis effluent (Figure B.18). The 2D <sup>27</sup>Al<sup>1</sup>H HETCOR spectrum (Figure 3.3B) resolves two <sup>27</sup>Al signals: one at 55 ppm, which is correlated to 1H signals at 2.2 to 3.6 ppm from TMAda<sup>+</sup> and D6<sub>1.2</sub> <sup>1</sup>H moieties, and one at 53 ppm, which is correlated only to the <sup>1</sup>H signal at 3.6 ppm from  $D6_{1,2}$  alcohol headgroups coordinated to Na<sup>+</sup> cations.<sup>149</sup> These correlated signals evidence two different types of framework <sup>27</sup>Al species with either TMAda<sup>+</sup> or Na<sup>+</sup> cations charge-balancing the associated framework negative charges. As the TMAda<sup>+</sup> molecules are sterically hindered from entering the 8-ring mordenite channels, the framework <sup>27</sup>Al species proximate to TMAda<sup>+</sup> cations must be within the 12-rings, while those associated with charge-balancing Na<sup>+</sup> cations may be located within the 8-ring pockets, as corroborated by the synchrotron XRPD analysis (Figure B.8). Furthermore, the different OSDA molecules are in close mutual proximities within the mordenite channels, as established by the 2D <sup>13</sup>C<sup>1</sup>H HET-COR spectrum of HOU-4 (Figure 3.3C). This spectrum shows correlated signals at 2.2-3.1 ppm in the <sup>1</sup>H dimension and at  $^{13}$ C shifts of 15, 24, 26, 34, 67, and 73 ppm (purple shaded regions) that arise from intermolecular interactions of <sup>1</sup>H environments in TMAda<sup>+</sup> molecules and the different <sup>13</sup>C environments in proximate (<1 nm) D6<sub>1.2</sub> molecules. Based on complementary 2D <sup>29</sup>Si<sup>1</sup>H HETCOR spectra (Figure B.19), we conclude that the different OSDA molecules are intimately commingled within the zeolite pores and act cooperatively (as idealized in Figure 3.3D) during the hydrothermal syntheses of HOU-4 to direct the formation of the linear 12-ring channels and the distribution of Al heteroatoms within the framework.

Parametric studies of HOU-4 synthesis reveal a sensitivity to growth mixture composition (Figures B.20 - B.23). Attempts to prepare HOU-4 in growth mixtures more commonly reported for mordenite at higher aluminum content result in much larger crystals (Figure 3.4A). Mordenite is typically synthesized using Na<sup>+</sup> ions as the sole structure-directing agent. Introduction of D6<sub>1,2</sub> and/or TMAda<sup>+</sup> to conventional synthesis mixtures does not markedly reduce crystal size. Indeed, the growth mixture that generates HOU-4 is adopted from a SSZ-13 synthesis<sup>47</sup> where we have reported D6<sub>1,2</sub> to be an effective modifier of SSZ-13 crystallization at low concentration (i.e., molar ratios less than 1.0 D6<sub>1,2</sub>: 1.0 SiO<sub>2</sub>). Under such conditions, the diol reduces the size of SSZ-13 crystals by an order of magnitude; however, increased diol content (i.e., molar ratios in excess of 1.6 D6<sub>1,2</sub>: 1.0 SiO<sub>2</sub>) shifts its role from that of crystal growth modifier to an OSDA that operates synergistically with TMAda<sup>+</sup> to direct the formation of ultrathin mordenite crystals. This reveals that HOU-4 requires a threshold amount of diol and growth mixtures with much higher silicon content than is typically required for conventional mordenite synthesis.

The formation of HOU-4 and its purity are sensitive to the carbon length of the diol. For example, combinations of TMAda<sup>+</sup> with either 1,2-pentanediol (Figure 3.4B) or 1,2-butanediol (Figure B.23) lead to SSZ-13 impurity, whereas 1,2-propanediol (Figure 3.4C) results in pure SSZ-13. Experiments with carbon lengths in excess of six were not tested owing to their immiscibility in water. The results of diol substitution are consistent with MD simulations of mordenite with TMAda<sup>+</sup> and diols of varying carbon length. At fixed TMAda<sup>+</sup> content and varying diol quantity, the minimum in the stabilization energy (Figure 3.4D) for D6<sub>1,2</sub> indicates the combination of this diol with TMAda<sup>+</sup> is an energetically favorable pairing for HOU-4 synthesis, consistent with experimental observations. Experiment and simulation thus suggest that D6<sub>1,2</sub> is optimal in size to span the 8-ring pockets and direct their growth.



Figure 3.4: SEM images of conventional MOR prepared with (A) Na<sup>+</sup>, (B) 1,2pentanediol, and (C) 1,2-propanediol. (D) Stabilization energy of diols and (E) Cumene conversion for H-MOR and H-HOU.

# 3.4 Conclusions

It is not fully understood how the ultrathin plate-like morphology of HOU-4 crystals is derived from the combined structure-directing influences of TMAda<sup>+</sup> and D6<sub>1,2</sub> molecules. Their role in zeolite crystallization is seemingly unrelated to that of a growth modifier that alters the crystal morphology in conventional mordenite synthesis, as neither organic produces solely thin crystals. In fact, the presence of D6<sub>1,2</sub> has the opposite effect in conventional mordenite syntheses, where it increases the thickness of the crystals in the [001] direction in the absence of TMAda<sup>+</sup> (Figure B.24). The ability to prepare nanosized crystals has significant implications for catalytic applications. Zeolite catalysts with restricted mass transport, such as mordenite and other one-dimensional framework types, are the most susceptible to rapid deactivation by coking; thus, a reduction in crystal dimension along the c-direction of mordenite (parallel to the large-pore channels) can have a substantial impact on catalyst performance. To illustrate this point, we prepared H-HOU-4 and H-MOR (i.e., acid forms of each sample) and compared their catalytic performance. The substantial difference in [001] facet thickness of H-HOU-4 (ca. 100 nm) and H-MOR (ca. 5 µm) imposes disparate limitations on internal diffusion. To quantify catalyst performance, we selected cumene cracking as a model reaction to evaluate time-onstream lifetime. Tests in a packed bed reactor at 450 °C reveal that the turnover number (evaluated in the shaded regions of Figure 3.4E) is much larger for H-HOU-4 (38.7 mol cumene/mol H<sup>+</sup>) compared to conventional mordenite (10.3 mol cumene/mol H<sup>+</sup>) owing to the faster rate of H-MOR deactivation. These results are qualitatively consistent with studies of nanosized zeolite catalysts in literature<sup>43,108</sup> that generally report much longer lifetime owing to reduced mass transport limitations.

The generation of ultrathin HOU-4 crystallites using a combination of two organics is one of only a few reported cases where multiple OSDAs work cooperatively to direct zeolite crystallization and structure. Furthermore, syntheses of sub-micron mordenite crystals have been a significant challenge with implications for improving the design of commercial catalysts. Here we show that the generation of ultrathin mordenite crystals with reduced stacking faults improves catalyst lifetime fourfold relative to micron-sized materials prepared by conventional methods. Using a combination of high resolution characterization techniques and molecular modeling, we are able to resolve the location of both OSDAs in the pores of HOU-4. One challenge in zeolite synthesis is determining how multiple organic and inorganic structuredirecting species function in a concerted manner to influence the physicochemical properties of zeolites, and control crystal polymorphism a priori. A unique aspect of HOU-4 crystallization is the role of non-ionic alcohols, which interact relatively weakly with crystalizing zeolite frameworks, and are rarely employed as OSDAs in zeolite syntheses. Here, diol molecules work in tandem with cationic Na+ and TMAda+ species to stabilize the different linear nanopore networks in mordenite. Collectively, the findings in this study suggest that further exploration into the use of cooperative organics in zeolite syntheses holds considerable promise for engineering and optimization of microporous materials.

# Chapter 4: Role of Thermodynamics in the Molecular Modification of Zeolites TON and LTL Crystallization

This chapter is a manuscript in the process of being published: Li, R.; Elliott W.; Clark, R.; Sutjianto, J; Palmer, J.; Rioux, R.; Rimer, J. Role of Thermodynamics in the Molecular Modification of Zeolites TON and LTL Crystallization. R. John Clark performed the computational portion of this study.

## 4.1 Introduction

Designing crystalline materials with tailored physicochemical properties is critical to industries spanning chemicals and petroleum to pharmaceuticals and electronics. A technique that is utilized in both natural and synthetic crystallization to control crystal properties is the use of modifiers, which are molecular additives that possess an affinity for adsorbing on specific crystal (or precursor) interfaces and altering the anisotropic rate(s) of growth and assembly.<sup>150,151</sup> This technique has proven to be an effective and integral component of diverse processes such as biomineralization, catalyst and drug design, and scaling in oil and gas pipelines. Examples include the amorphous silica exoskeletons of unicellular organisms,<sup>3,4</sup> nanoporous minerals,<sup>5</sup> pathological diseases,<sup>6</sup> calcification,<sup>7,8</sup> metal oxides,<sup>9</sup> ice suppression from antifreeze proteins,<sup>10</sup> and organic crystals.<sup>14</sup> One of the most challenging aspects regarding tailoring the physicochemical properties of crystalline materials by the use of molecular modifiers, irrespective of the material and application, is the incomplete understanding of the interactions and thermodynamic driving forces that govern the adsorption and binding specificity of modifiers to different crystal surfaces.

Here we examine the effects of modifiers in zeolite synthesis using a combination of bulk crystallization assays, calorimetry measurements, and molecular modeling to characterize the thermodynamics of modifier adsorption on zeolites, and to quantify its impact on crystal habit. We previously demonstrated that modifiers can significantly alter zeolite crystal size and shape, thus providing a facile and highly versatile method to tailor crystal properties and optimize their performance in commercial applications.<sup>2,15</sup> The study of zeolite growth modification falls within the broader scope of understanding sorbate-sorbent interactions and their role in catalysis, ion exchange, adsorption, and selective separations, among other applications. Thermodynamic analyses of small molecule adsorption on zeolites in gas<sup>152</sup> and solution<sup>153</sup> phases have examined the partitioning of species between the continuous phase and sorbent, selecting molecules with relevance to catalysis (e.g., alkanes and amines) and separations (e.g., alcohols); however, to our knowledge, no prior study has attempted to elucidate the relationship between the strength of modifier adsorption and their effectiveness in tailoring crystal size and/or morphology. Interestingly, we find in this study that there is no direct correlation between the adsorption strength inferred from calorimetry measurements and the effects of modifiers on zeolite crystal habit. This finding underscores the importance of understanding the kinetic factors governing a modifier's mode of action.

# 4.2 Methods

#### 4.2.1 Materials

The following chemicals for zeolite synthesis were purchased from Sigma Aldrich (St. Louis, MO): LUDOX AS-30 (30 wt% suspension in water), LUDOX AS-40 (40 wt% suspension in water), potassium hydroxide (85% pellets), aluminum sulfate hydrate (98%, 14-18 H<sub>2</sub>O, calculated as  $18H_2O$ ), 1,8-diamonooctane (98%), 1-butanol (99.4%), 1,2-hexanediol (98%), (±)-1,3-butanediol (99%), 1,2,6-

hexanetriol (96%), glycerol (99%), ethanol (200 proof), 1,6-hexanediol (99%), 1,2butanediol (98%), 1,3-propanediol (98%), 1,4-butanediol (99%), spermine (97%), tris(hydroxymethyl)aminomethane (99.7%), L-threonine (98%), L-lysine (97%), 1,2propanediol (99.5%), ethlyene glycol (98%), poly(diallyldimethylammonium chloride) (20%), poly(ethyleneimine) (50%), and triethylenetetramine (98%). Deionized (DI) water used in all experiments was purified with an Aqua Solutions RODI-C-12A purification system (18.2 M $\Omega$ ). All reagents were used as received without further purification.

#### 4.2.2 Zeolite Crystallization

TON zeolites were synthesized with 1,8-diamonooctane (C8DN) as an organic structure-directing agent (OSDA). Growth solutions were prepared with a molar composition of 1 Al2O3: 90 SiO<sub>2</sub>:11.9 K<sub>2</sub>O: 27.3 C<sub>8</sub>DN: 3588 H<sub>2</sub>O.<sup>154</sup> In a typical synthesis, solutions of each component were prepared separately: KOH solution was prepared by dissolving potassium hydroxide (0.21 g) in DI water (0.91 g); aluminium solution was made by dissolving aluminium sulfate (0.089 g) in DI water (0.91 g);  $C_8DN$  (0.53 g) was dissolved in DI water (3.64 g); and LUDOX AS-30 (2.37 g) mixed with DI water (1.35 g) was introduced as a colloidal suspension. The KOH, OSDA and  $Al_2(SO_4)^3$  solutions were first mixed together and stirred for ca. 5 min to generate a uniform mixture. The silica suspension was then added dropwise under constant stirring. The resulting mixture was left to stir overnight (ca. 21 h) at room temperature (referred to herein as the "aging" period). After aging was complete, the growth mixture (ca. 10g) was placed in a Teflon-lined stainless steel acid digestion bomb (Parr Instruments) and was heated under rotation at 34 rpm in a ThermoFisher Precision Premium 3050 Series gravity oven at 160 °C and autogenous pressure. TON growth mixtures and the resulting crystals prepared by this procedure are referred to herein as the control.

LTL zeolites were synthesized in the absence of an organic using K+ as an inor-
ganic structure-directing agent (SDA). Growth mixtures were prepared with a molar ratio of 0.5 Al<sub>2</sub>O<sub>3</sub>:20 SiO<sub>2</sub>:10.2 K<sub>2</sub>O:1030 H<sub>2</sub>O according to a reported protocol.<sup>25</sup> Potassium hydroxide (0.64 g) was first dissolved in DI water (7.78 g), followed by the addition of aluminium sulfate (0.17 g). This mixture was stirred until clear (ca. 5 min). LUDOX AS-40 (1.42 g) was added and the resulting mixture was aged overnight (ca. 21 h) with constant stirring. The aged growth mixture (ca. 10 g) was placed in a Teflon-lined stainless steel acid digestion bomb and was heated under static conditions at 180 °C and autogenous pressure. LTL growth mixtures and the resulting crystals prepared by this procedure are referred to herein as the control.

In select cases, a zeolite growth modifier (ZGM) was added 2 h prior to the finish of the aging period (ca. 19 h). Alcohols were added in a molar ratio of 1.5 ZGM:1.0 SiO<sub>2</sub> while amines, amino acids, and polymers were employed as 1 wt% of the entire growth mixture (unless otherwise stated). The pH of the growth mixture was measured with a Thermo Scientific Orion 3 Star meter. The ionic conductivity of the solution was measured with a VWR international EC meter (Model 2052). For Xray and microscopy analyses, solids in the growth mixture were isolated as a white powder (ca. 1 g) by centrifugation at 13,000 rpm for 45 min. The solid was washed with DI water to remove the supernatant. The centrifuge-wash cycle was repeated for a second time and the resulting gel was dried at ambient conditions. During the preparation of microscopy samples, an aliquot of the sample suspension was placed on a glass slide and dried overnight. Crystals on the glass slide were transferred to SEM sample holders (Ted Pella) by gently pressing the glass slide on carbon tape.

#### 4.2.3 Materials Characterization

Solids extracted from a zeolite growth mixture were characterized by powder Xray diffraction (XRD) using a Rigaku SmartLab Diffractometer with Cu-K $\alpha$  radiation (40 kV, 44 mA, 1.54 Å). Scanning electron microscopy (SEM) was performed with a FEI 235 Dual-Beam (Focused Ion-beam) or a LEO 1525 FEG system operated at 15 kV and a 5-mm working distance. All SEM samples were coated with a thin layer of carbon (ca. 30 nm) prior to imaging. The average size and size distribution of crystals in each batch were obtained from at least 100 measurements performed on SEM images.

#### 4.2.4 Calorimetry Studies

Calorimetry measurements were made on a semi-adiabatic solution calorimeter (TAMIII Precision Solution Calorimeter, TA Instruments) maintained at (25.0000  $\pm$  0.0001) °C. The zeolite was dried under flow of helium at 400 °C for 4 hours with a ramp rate of 2 °C/min. The zeolite was stored under nitrogen to prevent uptake of atmospheric moisture. Zeolite (20 mg) was placed in a 1 mL glass ampoule and sealed with a silicone rubber stopper and beeswax. The ampoule was submerged in a 25 mL reaction vessel containing the wetting solution. The ampoule was broken while stirring at 600 rpm and the change in temperature associated with the wetting event was measured. The heat capacity of the system was determined by injecting a pulse of 3 J before and after breaking the ampoule. The temperature change was converted to enthalpy change using the average of the heat capacities. An empty ampoule was broken in each solution to determine the heat associated with the breaking of the ampoule. This was used to correct the raw heat for the true heat of wetting. SolCal software (v1.2, TA Instruments) was used to analyze the experimental data.

#### 4.2.5 Molecular Modeling

Molecular dynamics (MD) simulations were performed using GROMACS 4.6.7 to study the adsorption of selected ZGMs (1,2-butanediol (D4<sub>1</sub>,2), 1,3-butanediol (D4<sub>1</sub>,3), and 1,4-butanediol (D4<sub>1</sub>,4)) on the crystallographic surfaces of all-silica TON and LTL structured zeolites. The ZGMs were modeled using the generalized AMBER force field,<sup>71</sup> whereas the zeolite frameworks were described with the ClayFF potential.<sup>70</sup> Force field parameters for modeling van der Waals interactions between the ZGMs and zeolite frameworks were determined using standard Lorentz-Berthelot combining rules.<sup>22</sup> Real-space van der Waals and Coulombic interactions were truncated using a cutoff of 0.9 nm. Long-range contributions to the electrostatic interactions were treated using the particle mesh Ewald method,<sup>22</sup> with parameters chosen to ensure a relative error of less than  $10^{-4}$  in the calculated energy. In all simulations, the equations of motion were integrated using a velocity-Verlet scheme with a 2 fs time step,<sup>22</sup> and temperature was maintained using a Bussi-Parrinello velocity-rescaling thermostat<sup>73</sup> with a 2 ps relaxation time constant.

Models for TON and LTL were constructed from unit cell data (lattice parameters and atomic positions) reported in the International Zeolite Association's Database of Zeolite Structures.<sup>143</sup> The  $1 \times 1 \times 1$  unit cells from the database were replicated to generate  $3 \times 2 \times 7$  and  $3 \times 2 \times 5$  supercells for TON and LTL, respectively. Model surfaces were created from the supercells by disrupting their periodicity along the axes perpendicular to the crystallographic planes of interest. In each case, the position at which the periodicity was disrupted was chosen to minimize the number of broken Si-O bonds and hence the surface energy. Approximately 80% of the undercoordinated oxygens were protonated on each surface to mimic the neutral pH conditions of the calorimetry experiments. Following Kroutil et al.,<sup>155</sup> the charges assigned to non-surface oxygens within the zeolite framework were adjusted slightly (<0.1%) to compensate for excess surface charge and ensure electroneutrality.

The MD simulations of each zeolite surface were performed using an infinite slab geometry. The infinite slabs were generated by placing each model zeolite surface in an elongated rectangular (TON) or triclinic (LTL) simulation cell with its surface normal aligned parallel to the cell's major axis (z-axis). The dimensions of the simulation along the minor axes (x- and y-axes) were chosen to be commensurate with the periodicity of the zeolite structure, whereas the length of major axis was chosen to be at least three times larger than the thickness of the zeolite slab. A single ZGM molecule was placed in the empty region above the slab's upper surface and the system was solvated with approximately  $\sim$ 5,000 SPC/E<sup>156</sup> water molecules to create two solid-liquid interfaces. The solvated system was then equilibrated for 10 ns in the isothermal-isobaric ensemble at 300 K and 1 bar using an anisotropic Parrinello-Rahman barostat<sup>73</sup> with a 2 ps relaxation time constant to impose constant pressure (isostress) conditions along the z-axis of the simulation cell.

Modifier adsorption on TON and LTL was characterized by computing the potential of mean force (PMF)  $W(d_{com}) = -k_B T \ln[P(d_{com})]$ , where  $d_{com}$  is the separation distance along the z-axis of the simulation cell between the ZGM's center of mass and the zeolite surface,  $k_B$  is the Boltzmann constant, T is the temperature, and  $P(d_{com})$ is the equilibrium distribution associated with  $d_{com}$ . The bidning free energy from solution was estimated from the PMF using  $\Delta G_b \approx W(d_b) - W(d_u)$ , where  $d_b$  and  $d_u$  correspond to the characteristic separation distances for the bound and unbound states of the ZGM, respectively. Accurate estimates of  $P(d_{com})$  were obtained for each ZGM by performing windowed umbrella sampling MD (USMD) simulations using the PLUMED 2.1.1 plugin for GROMACS. The USMD simulations were carried out in the canonical ensemble at 300 K, with the z-dimension of the simulation box fixed to the average value computed from the isothermal-isobaric simulations described above. Independent USMD simulations were run in each sampling window using a harmonic bias potential with a spring constant  $k=750 \text{ kJmol}^{-1} \text{ nm}^{-2}$  to restrict sampling to the targeted region along  $d_{com}$ . A window spacing of 0.05 nm was chosen to ensure sufficient statistical overlap between the sampled distributions in adjacent regions. Each simulation was equilibrated for 1 ns, followed by a production period of at least 10 ns. Data from the production period of each USMD simulation were combined using BayesWHAM<sup>157</sup> to obtain an unbiased global estimate of the PMF.

## 4.3 **Results and Discussion**

We first performed bulk crystallization assays to screen a library of zeolite growth modifiers (ZGMs) for two structures: ZSM-22 (TON) and zeolite L (LTL). These materials were selected on the basis of their commercial relevance as catalysts<sup>25,80,154,158–167</sup> and their promise in photonics<sup>168</sup> and drug delivery<sup>169</sup> applications. The TON and LTL frameworks both consist of one-dimensional straight channels (Figure 1A) with slight differences in their average pore diameters (roughly 0.5 and 0.7nm, respectively). ZSM-22 crystals are more siliceous  $(Si/Al = 30 - 50)^{80,170}$ compared to zeolite L (Si/Al = 2.6 - 3.3),<sup>2</sup> which is reflected in a ternary (kinetic) phase diagram (Figure C.1) for the two structures revealing that ZSM-22 forms in Si-rich mixtures and over a wider compositional space than zeolite L. Previous studies<sup>78</sup> have demonstrated that changes in synthesis parameters, such as water content or temperature, are capable of altering the aspect ratio of LTL crystals. It has also been reported that the morphology of ZSM-22 can be subtly switched from needle-shaped to rod-like crystals.<sup>171</sup> Parametric studies of ZSM-22 synthesis over a broad range of conditions (Table C.2) seems to indicate that the modification of crystal size and shape is more restricted for ZSM-22 than zeolite L. Moreover, ZSM-22 is more sensitive to changes in synthesis parameters. For instance, minor reductions in water content (ca. 20%) promote the formation of the common impurity ZSM-11 (MEL).<sup>172</sup>

The synthesis conditions for ZSM-22 and zeolite L were selected based on reported protocols (for details see the Supporting Information, SI), yielding assynthesized samples with Si/Al ratios of 34 and 3, respectively. The library of ZGMs selected for this study (Table C.1) was based on molecules previously tested for zeolite  $L^2$  and other framework types. In the absence of modifiers, ZSM-22 (Figure 4.1B) and zeolite L (Figure 4.1E) crystals have an elongated needle and cylinder morphology, respectively. Zeolite L crystals are relatively monodisperse with an average ax-



Figure 4.1: Crystal Structures of zeolites TON and LTL (A). SEM micrographs of ZSM-22 (B, C, D) and Zeolite L (E, F, G) at varying modifier concentrations 0 wt% (B,E), 0.2 wt% (C,F), and 1.5 wt% (D,G).

ial [001] dimension of 3 µm whereas ZSM-22 crystals exhibit a broader range of sizes and a minor fraction of spheroidal particles (Figure 4.1E, white arrow). Herein, we refer to changes in crystal morphology on the basis of aspect ratio (AR), which is measured as the length of the longest dimension (c-direction for both zeolites) to that of the diameter. Our findings are consistent with prior literature showing that ZSM-22 crystals are more anisotropic (AR =  $5 \cdot 20$ )<sup>173,174</sup> compared to zeolite L (AR  $\approx$ 2).<sup>2</sup> Prior studies of zeolite L<sup>2</sup> and other crystalline materials<sup>175</sup> report that macromolecules are effective modifiers of crystal growth owing to their proximal functional groups that promote modifier binding to crystal surfaces. Indeed, the positivelycharged polymer poly(diallyldimethylammonium chloride), or PDDAC, increases the AR of zeolite L crystals<sup>2</sup> and has been shown to increase the size of other zeolites, such as SSZ-13 (CHA).<sup>47</sup> Here we show that 0.2 wt% PDDAC increases the AR of both ZSM-22 (Figure 4.1C) and zeolite L (Figure 4.1F) crystals by factors of 2 and 4, respectively. At higher modifier content (0.5 wt% PDDAC), we observe a distribution of ZSM-22 crystal sizes with AR values as high as 40 (Figure C.3). In contrast, syntheses in the presence of polyethylenimine, or PEIM, reveal that the AR of ZSM-22 crystals is slightly reduced (Figure 4.1D), whereas there is little change in zeolite L morphology (Figure 4.1G). The impact of PEIM was more significant in a prior study of SSZ-13 where we observed an order of magnitude reduction in crystal size.<sup>47</sup> Collectively, these observations indicate that ZGMs have disparate effects on zeolites; and that predicting these effects a priori or identifying heuristic guidelines among structures of incongruent topology is nontrivial.

The complete library of ZGMs (Table C.1) was assessed in bulk assays to elucidate their effect on the AR of ZSM-22 (Figure 2) and zeolite L Figure C.4. For brevity, we establish a nomenclature for modifiers where alcohols are referenced as  $LN_{i,j,k}$ where L = P for primary alcohols, D for diols, and T for triols; and N refers to the total number of carbons in the alkyl backbone with subscripts i,j,k referring to the location of the alcohol groups along the alkyl backbone. Amines, amino acids, and polymers are referred to by their names or common abbreviations. We previously proposed that the hydrophobicity of ZGMs is one parameter that influences ZGM specificity for zeolite L crystal surfaces.<sup>2</sup> For select ZGMs, it was observed that the AR of zeolite L crystals decreases with increased molecule hydrophobicity Figure C.4. This trend was evident among homologous alcohols (e.g., primary alcohols or diols), but it was not observed over the entire library of ZGMs, suggesting that hydrophobicity cannot be used as a universal indicator of modifier efficacy. We have performed a similar comparison of crystal AR as a function on ZGM hydrophobicity for ZSM-22 (Figure 4.2). The latter is quantified using the logarithm of the octanol-water partition coefficient (log P) where values less or greater than zero indicate hydrophilic or hydrophobic molecules, respectively. The AR values for ZSM-22 are seemingly a random distribution scattered around the shaded gray region, which is the average AR of crystals prepared in the absence of ZGMs. The large error bars reflect the polydisperse size distribution of ZSM-22 crystals. Within the confidence intervals of these measurements, there are no ZGMs that markedly reduce the AR of ZSM-22 crystals; however, there are several modifiers that lead to notable increases in AR.



Figure 4.2: Aspect ratio (AR) of ZSM-22 crystals in the presence of ZGMs plotted as a function of modifier hydrophobicity.<sup>2,15</sup>

We generally observe that alcohols increase the AR of ZSM-22 crystals, whereas amines have the opposite effect (in contrast to zeolite L where only minor differences were observed between alcohols and amines<sup>2</sup>). When evaluating the effects of various diols and triols, the positioning of alcohols along the carbon backbone is seemingly more impactful than the length of the carbon chain. This is evident when comparing the net change in AR with increasing chain length where the alcohol positions are fixed (i.e,  $D2_{1,2} < D3_{1,2} < D4_{1,2} < D6_{1,2}$ ) to trends where the chain length is fixed and the alcohol position varies (i.e.,  $D4_{1,2} < D4_{1,4} < D41,3 \approx D6_{1,2} < D6_{1,6}$ ). A comparison of AR values for diols reveals that the 1-3 and 1-4 positions of alcohols are more effective than the 1-2 position, which is true for both ZSM-22 and zeolite L, as well as other minerals (e.g., 1-3 diol adsorption on aluminates).<sup>2,176</sup> A hypothesis for such differences is discussed later in the analysis of modifier-zeolite interactions by molecular modeling.

In order to quantify the strength of ZGM binding to zeolite crystals, we performed calorimetry experiments (Figure 4.3 to assess the heat generated by placing calcined

zeolite powders in contact with KOH solution containing a fixed quantity of each modifier. The heat generated is a culmination of several phenomena that include solvation, dissociation of silanol groups in the presence of hydroxide ions, and the adsorption of K+ ions (or ion exchange) at negatively-charged sites within the zeolite framework. In the presence of ZGMs, there is an additional heat of adsorption related to modifier interactions with the exterior or interior surfaces of zeolite crystals. Plots of heat generation as a function of modifier hydrophobicity for ZSM-22 (Figure 4.3A) and zeolite L (Figure 4.3B) reveal exothermic values spanning - 46 to - 87 J/g. The heats of immersion are larger for zeolite L, which may be attributed to differences in composition (i.e., the Al content in LTL is significantly larger). Comparison of zeolite crystal AR and the heats of immersion show no apparent trends for the alcohols selected for calorimetric analysis. Indeed, it was anticipated that large changes in crystal morphology would be associated with higher heats of ZGM adsorption on crystal surfaces; however, this lack of complementary seems to indicate that kinetic factors are more responsible for changes in crystal habit. These effects are not entirely obvious and can be quite different for both zeolites in this study. For instance, the effect of diols (e.g.,  $D4_{1,3}$ ) has opposite effects on habit modification, leading to a highly anisotropic rod-like crystals with increased AR for ZSM-22 (Figure 4.3C) and thin disks with reduced AR for zeolite L (Figure 4.3D).

We have also examined the heats of immersion from calorimetry measurements of ZSM-22 and zeolite L as a function of modifier hydrophobicity (Figure 4.4). An identical measurement was performed for each zeolite in the absence of modifiers (using only KOH solution), which is depicted by the shaded grey regions. Interestingly, there is little difference in the magnitude of heat generation in the absence or presence of modifiers, indicating that the adsorption of ZGMs on zeolite surfaces is weak (i.e. 1 - 4 J/g).<sup>177–179</sup> This suggests a significant energetic penalty for displacing solvent from zeolite surfaces by modifiers. For several ZSM-22 samples (e.g.,



Figure 4.3: Calorimetry data for (A) ZSM-22 and (B) zeolite L crystals as a function of aspect ratio. SEM images of (C) ZSM-22 and (D) zeolite L.

 $T3_{1,2,3}$ ), we observe endothermic heats of immersion. At high temperatures of zeolite synthesis, it is likely that modifier adsorption and desorption on crystals (or amorphous precursors) dhappens rapidly and reversibly, leading to dynamic coverages of modifiers, solute, and ions during crystallization.

To characterize the molecular interactions with the ZSM-22 surfaces, we performed molecular dynamics (MD) simulations using a set of ZGMs with clear trends in their calorimetric heats of interaction: butane diols (D4<sub>1,2</sub>, D4<sub>1,3</sub>, and D4<sub>1,4</sub>). Using umbrella sampling MD (see SI for details), we calculated the free energy as a function of the ZGM's center-of-mass-distance from the (010) surface of ZSM-22 (Figure 4.4C). The (010) surface was selected as a representative termination of rodlike crystals along their largest surface area, which is a preferential binding site for ZGM adsorption (based on observations of increased AR, which would indicate slower growth in both the a- and b-directions). The small binding free energies from MD simulations ( $\Delta G_b \approx -2to - 4$  kJ/mol) reveal that the ZGM-(010) surface interactions are relatively weak, similar to those calculated for other surfaces of ZSM-22. Moreover, whereas D4<sub>1,2</sub> and D4<sub>1,3</sub> have similar binding energies (ca. -2 kJ/mol), D4<sub>1,4</sub> has slightly stronger interactions ( $\delta G_b \approx -4$  kJ/mol), consistent with the calorimetry measurements (Figure 4.4A). Binding configurations (Figure 4.4D) show that the two alcohol ( $\equiv$  OH) groups on each diol form a hydrogen bond with exposed surface silanols ( $\equiv$  SiOH/SiO-). The proximal spacing of these groups on D4<sub>1,2</sub> and D4<sub>1,3</sub> promotes binding atop of truncated 6-member ring (6-MR) features (S1). The larger spacing of these groups on D4<sub>1,4</sub>, by contrast, leads to a more energetically favorable binding position in which the molecule forms hydrogen bonds with two adjacent 6-MRs and its center sits inside exposed channels formed from truncated 10-MRs (S2).



Figure 4.4: Calorimetry data for (A) ZSM-22 and (B) zeolite L crystals as a function of hydrophobicity. (C) Free energy for butane diols from MD simulation and favorable binding positions (D).

The lack of distinct trends among ZGMs tested for ZSM-22 may be reflected in the

inherently complex processes of zeolite crystallization.<sup>78,99</sup> The mechanism of ZGM action is not well understood.<sup>117</sup> For organic<sup>180</sup> or inorganic<sup>181</sup> crystals that grow predominantly by classical mechanisms (i.e., monomer by monomer addition), modifiers bind to surface sites (kinks, step edges, and/or terraces)<sup>180,182,183</sup> and inhibit solute attachment by modes that include kink blocking<sup>184,185</sup> or step pinning.<sup>186,187</sup> Zeolites grow by a combination of classical pathways and nonclassical mechanisms involving particle attachment wherein ZGMs may interact with a range of species: soluble (alumino)silicates, amorphous precursors, or zeolite crystal surfaces.<sup>36,100</sup> ZGMs with multivalent charge have been reported to bridge negatively charged precursors.<sup>36</sup> Moreover, macromolecular ZGMs, such as PEIM and PDDAC, have been shown to inhibit and promote precursor aggregation, respectively, thereby reducing or increasing the size of SSZ-13 (CHA) crystals by several orders of magnitude.<sup>47</sup> There is evidence suggesting ZGMs tailor crystal growth through surface attachment, although it is difficult to elucidate modifier adsorption on zeolite surfaces owing to nonclassical pathways that lead to roughened (3D) growth.<sup>96</sup> With many potential modes of ZGM action, its efficacy may not necessarily derive from strong interactions with crystal surfaces. Multiple modifier-crystal interactions have been reported, such as van der Waals, electrostatic, hydrogen bonding, and  $\pi - \pi$  stacking, where steric constraints, solvent ionic strength<sup>188</sup> and solvent displacement<sup>189,190</sup> are factors that contribute to modifier efficacy. It is likely that ZGMs act by more than one mechanism. In order to assess modifier-crystal interactions, we performed liquid-phase calorimetry measurements to quantify the heats of modifier adsorption on TON and LTL crystals.

## 4.4 Conclusions

In summary, we have used a combination of bulk crystallization and calorimetry measurements to screen a library of ZGMs for two different 1D zeolite frameworks (LTL and TON). We addressed working hypotheses regarding the efficacy and specificity of modifiers, which were derived from prior studies of zeolite L, and were expanded in this study to include ZSM-22. In certain cases we find that zeolite composition (e.g., Si content) and the molecular structure of ZGMs have predictable effects on modifier efficacy; however, there is no obvious correlation between modifier hydrophobicity and its propensity to bind to zeolite surfaces. To this end, the complexity of growth mixtures, which contain soluble species, amorphous precursors, and possibly small crystallites, render the identification of ZGM mode(s) of action a challenging task. Indeed, the role of modifiers in systems that exhibit nonclassical crystallization is not well understood and remains an elusive goal for future studies and the a priori identification of effective ZGMs for any given zeolite structure.

# Chapter 5: Sturcturing of Organic Solvents at Solid Interfaces and its Ramifications for Antimarlarial adsorption on Beta-Hematin Crystals

This chapter was published as: Olafson, K.; Clark, R.; Vekilov, P.; Palmer, J.; Rimer, J. Structuring of Organic Solvents at Solid Interfaces and Ramifications for Antimalarial Adsorption on  $\beta$ -Hematin Crystals. *American Chemical Society Applied Materials and Interfaces* **2018**, *10*(35), 29288-29298. R. John Clark performed the computational portion of this study.

# 5.1 Introduction

Solution crystallization is ubiquitous and underlies a variety of natural and synthetic processes that include synthesis of new drugs,<sup>191</sup> manufacture of electronic detectors,<sup>192,193</sup> biomineralization,<sup>194,195</sup> pathological condensation,<sup>182,183</sup> and rational design of catalysts.<sup>196</sup> Solute incorporation into a crystal lattice occurs through its interaction with specific sites on growing interfaces, which are defined as kinks, steps, and terraces.<sup>197</sup> In addition to solute, foreign species acting as growth modifiers may adsorb at these sites and inhibit or promote the anisotropic rates of crystallization.<sup>10,198</sup>

Solvent molecules in contact with either ordered or disordered surfaces may align into structures that are distinct from the disorder that is typical of bulk liquids. The degree of structuring at an interface is correlated with the interactions between solid and solvent.<sup>199</sup> Localized surface charge, hydrophilicity or hydrophobicity, and other physicochemical surface properties can induce ordered or disordered solvent layers at the solid-solution interface.<sup>200</sup> For instance, water and organic compounds may respond disparately to surface forces, creating different structured patterns.<sup>201</sup> Solvent ordering dissipates with increased distance from a substrate, such that the solvent reaches bulk properties within 1-2 nm from a solid surface.<sup>202</sup> In aqueous solutions, water aligns into layers that affect the Brownian trajectories of the solute molecules toward the surface.<sup>203</sup> Additional complexity arises with the addition of foreign species. Ions and macromolecules, such as, proteins and collagen, partake in hydrophobic,  $\pi$ -stacking, and electrostatic interactions, which can modify solvent structuring at the substrate surface.<sup>204</sup>

Solvent structuring at the interface between a supersaturated solution and a growing crystal is a dominant factor in the energy landscape and dictates the selection of kinetic pathways and their rates.<sup>205</sup> For crystals in contact with aqueous solvents, structuring of the latter is governed by a fundamental property of water to form a three-dimensional network of hydrogen bonds, molded around solute molecules and along the crystal-solution interface. The incipient layered patterns have been identified as a major factor that determines the thermodynamic and kinetic control parameters of solute incorporation into growth sites 185,205-207 and, correspondingly, the pathways and rates of crystallization from aqueous solvents.<sup>205,208,209</sup> Two pathways by which a solute molecule arrives at an incorporation site from bulk solution have been proposed (Figure 5.1A): direct incorporation or via adsorption on the terraces followed by two-dimensional diffusion toward the steps.<sup>197</sup> Along both pathways, as solute adsorbs, diffuses, and attaches to kinks, it displaces solvent molecules. The degree of solvent structuring at the surface sites determines the contributions of each stage to the total crystallization enthalpy and entropy. Identifying localized solvent structuring in the vicinity of growth sites (Figure 5.1B), the correlation between surface motifs (Figure 5.1C-E), and solvent structure patterns (Figure 5.1B) and estimating the energy barriers for displacing solvent during solute attachment is essential for predicting crystal growth. Furthermore,

in several prominent instances, the activity of crystal growth modifiers has been attributed to the molecule's ability to alter solvent structuring near the sites of solute incorporation.<sup>12,14,184</sup>



Figure 5.1: How solvent structuring dictates solute adsorption (a,b) and the differences between ordered and disordered substrates (c-e).

In recent years, organic and mixed inorganic-aqueous liquids have received greater attention as alternative solvents for preparation of crystalline materials and for applications of separation and purification by crystallization,<sup>210</sup> in particular for high-value materials such as pharmaceuticals and fine chemicals. In contrast to crystallization from purely aqueous solvents, the level of understanding of the fundamental processes of crystal growth from such liquids is severely limited. The lack of insight into the relevant fundamental mechanisms, in particular on the interfacial structuring of the solvents, has emerged as a major obstacle to a rational approach to optimize and control crystallization in organic and mixed solvents.<sup>211</sup>

Here, we examine the consequences of structuring of a multicomponent solvent on molecular interactions at the surfaces of  $\beta$ -hematin crystals, which form as the byproduct of heme detoxification in malaria parasites.<sup>212,213</sup> The crystal surface is composed of rows of alternating hydrophobic and hydrophilic regions,<sup>214</sup> similar to the pattern in Figure 5.1C, which differs from other ordered substrates where specific functional moieties are dispersed homogeneously, as depicted in Figure 5.1D. Prior studies indicate that  $\beta$ -hematin grows in a complex medium consisting of organic lipids (e.g., monoglycerides such as monostearoylglycerol) in contact with an aqueous solution.<sup>215,216</sup> In vitro assays used to model this system employ n-octanol as a lipid surrogate and saturate the solution with a citrate buffer to match the acidic medium in contact with the lipid phase.<sup>183,217</sup> We characterize the interactions of the crystal surface with chemical moieties matching known antimalarial drugs and with groups that mimic the hydrophilic and hydrophobic domains of hematin as well as the organic solvent. As a benchmark, we employ amorphous glass to highlight how solvent structuring responds to a disordered substrate and to quantify the effects of ordering on interactions of the tested moieties with the substrate. The structure of glass surfaces is akin to the pattern depicted in Figure 5.1E, wherein hydrophilic silanol (SiOH) groups are irregularly distributed on the substrate interface.

Prior studies of solvent structuring at interfaces have employed several techniques. For example, quantification of the variations in fluid pressure as two surfaces are brought together has provided the first indication of the presence of solvent layers.<sup>218</sup> Surface X-ray diffraction has been used to examine ordered water layers on crystal surfaces.<sup>219,220</sup> Moreover, Brewster angle measurements and scanning probe microscopy have directly revealed the presence of ordered layers across a variety of interfaces,<sup>221</sup> which include (but are not limited to) air-water,<sup>222</sup> liquid-liquid,<sup>223</sup> solid-liquid (e.g., water-graphene),<sup>224</sup> and lipid bilayers. In this study, we use chemical force microscopy (CFM) to probe molecule-substrate interactions. CFM measures the rupture force between a substrate in contact with an atomic force microscope (AFM) tip decorated with the tested functional groups.<sup>225</sup> To understand the role of solvent structuring near  $\beta$ -hematin (100) and amorphous glass surfaces, we use a combination of CFM measurements with complementary molecular dynamics (MD) simulations.

### 5.2 Methods

#### 5.2.1 Materials

The following materials were purchased from Sigma-Aldrich (St. Louis, MO): citric acid (anhydrous,  $\geq$  99.5%), porcine hematin (> 95%), n-octanol (anhydrous, 99%), thiophenol (97%), 4-mercaptopyridine (95%), 1-butanethiol (99%), 3-mercapto-1-propanol (95%), 200-proof ethanol (anhydrous,  $\geq$  99.5%), and sodium hydroxide (anhydrous reagent-grade pellets,  $\geq$  98%). All reagents were used as received without further purification. Deionized (DI) water was produced by a Millipore reverse osmosis-ion exchange system (RiOs-8 Proguard 2-Milli-Q Q-guard).

#### 5.2.2 Hematin Crystallization

Prior to solution preparation, all glassware was thoroughly cleaned with 0.1 M NaOH to remove residual hematin. Citric buffer at pH 4.8 was prepared by dissolving 50 mM of citric acid in DI water, which was titrated with 0.10 M NaOH during continuous stirring to achieve the desired pH. Prior to each experiment, the buffer pH was verified. To prepare citric-buffer-saturated octanol (CBSO), 5 mL of citric buffer stock solution was placed in a 40 mL glass vial to which 20 mL of n-octanol was added. The resulting two-phase solution was sealed with a poly(tetrafluoroethylene) (PTFE) storage cap and allowed to equilibrate without stirring at 23 °C for 30 min. The denser citric buffer occupied the bottom layer, and the n-octanol formed an orthogonal upper layer. The latter was carefully removed with a pipet far from the interface in order to avoid resuspension of the two phases. Fresh CBSO solutions

were prepared for each bulk crystallization assay and for in situ AFM experiments.

We dissolved known masses of commercial hematin into CBSO to obtain hematin crystals for single-crystal studies. Supersaturated hematin solutions were prepared by placing 5 mL of CBSO in a 20 mL glass vial along with an amount of hematin powder sufficient for a 2 mM solution. As previously described by Olafson et al.,<sup>226</sup> the hematin in this mixture is amorphous. The unsealed vial was kept at  $39.5 \pm 0.2$  °C in the absence of direct light. Previous measurements of hematin solubility in CBSO at this temperature yielded 0.32 mM.<sup>183</sup> Aliquots periodically extracted from these solutions by pipet were filtered through a 0.22 mm poly(vinylidene difluoride) (PVDF) membrane, and the hematin concentration was measured spectrophotometrically by use of the previously determined extinction coefficient,  $\epsilon = 3.1 \pm 0.3 \,\mathrm{cm}^{-1} \,\mathrm{mM}^{-1}$ , measured at  $\gamma = 594$  nm.<sup>217</sup> The concentration of the working solutions was adjusted to 0.1-0.3 mM by addition of CBSO. From this solution,  $\beta$ -hematin crystals of size 10-30 µm were grown.<sup>226</sup> The vial was sealed with a PTFE storage cap and incubated at 22.6  $\pm 0.2$  °C for 48 h to achieve crystals of size 10-50 µm. For CFM measurements,  $\beta$ -hematin crystals were grown on 12 mm round glass coverslips (Ted Pella, Redding, CA). Prior to being placed into a supersaturated hematin CBSO solution, the coverslip was scratched near the center with a diamond cutter and placed in the vial. The coverslip was removed from the growth solution, rinsed with DI water and ethanol, and dried under a gentle flow of air. All crystals were used immediately upon drying. Crystals grown for AFM studies were removed from the glass coverslips and washed with ethanol to remove the supernatant. By powder X-ray diffraction (PXRD), we confirmed the structure as  $\beta$ -hematin from the Cambridge Structural Database, as previously reported.<sup>226</sup>

#### 5.2.3 functionalizing AFM Cantilevers

All CFM measurements were performed with Olympus RC800PSA cantilevers (silicon nitrite-coated with Cr/Au = 5/40), which have a spring constant k of

 $0.42 \,\mathrm{N\,m^{-1}}$  and a 15 nm radius of curvature. Gold-coated AFM cantilevers were functionalized according to previous gold-thiol coupling protocols<sup>227</sup> with the following thiol compounds: thiophenol, 4-mercaptopyridine, 1-butanethiol, and 3-mercapto-1propanol. A new AFM cantilever was placed in a glass Petri dish with 5 mM thiol in 200-proof EtOH. The dish was sealed with Parafilm and left overnight. The solution was decanted and replaced with 200-proof EtOH in triplicate to remove unbound material. The cantilever was then removed and dried under nitrogen. All cantilevers were prepared within 15 min of being used for in situ AFM experiments. To avoid potential contamination, each experiment was performed with a freshly prepared AFM cantilever.

#### 5.2.4 Chemical Force Microscopy

All CFM measurements were performed on a MFP-3D atomic force microscope from Asylum Research (Santa Barbara, CA). The tip-substrate rupture force was measured between functionalized AFM tips and two substrates: hematin 100 crystal surfaces and glass. The glass slides were uncoated water white Schotts D263 M borosilicate glass that has a very low iron content, with dimensions of 12 mm diameter and 0.13-0.17 mm thick (Ted Pella). Samples were loaded into a liquid cell. Prior to collection of data, the topography of each substrate was imaged in tapping mode (ca. 64 kHz frequency) to locate regions for CFM analysis. The liquid cell was then closed and flooded with the solvent. All measurements were done under static conditions (i.e., liquid was not continuously supplied to the sample cell). After the solution was introduced, the system was allowed to reach thermal equilibration for ca. 2 h prior to measuring the spring constant (k = 318-515 pN/nm). CFM measurements were collected in contact mode with a trigger point of 2.0 nN. In order to sample various loading rates, the approach velocity was varied between 50 and 1000 nm/s. For each velocity, we collected more than 1000 data points at a minimum of 20 sites on each substrate. For hematin crystals, data were collected on relatively flat terraces with a minimal number of steps and/or defects. Histograms of the collected data were plotted with Gaussian fits in order to obtain the average tip-substrate rupture force as a function of the approach velocity. The loading rates (piconewtons per second) were calculated by multiplying the measured spring constant k (piconewtons per nanometer) by the approach velocity (nanometers per second).

#### 5.2.5 Contact Angle Measurements

Static contact angle measurements were performed on glass slides obtained from Ted Pella (i.e., same substrates used for hematin crystallization and CFM measurements). Contact angles were measured independently for each solvent by use of new glass slides and an OCA 15EC video-based optical contact angle measuring instrument (DataPhysics). Data were recorded at ambient temperature and pressure by SCA 20 software. Each deposited solvent droplet was approximately 1 mL.<sup>228</sup> The solvents measured were prepared in the same manner as previously described.

#### 5.2.6 Molecular Modeling

MD simulations were performed with GROMACS 4.6.7<sup>69</sup> to investigate solvent structuring near model  $\beta$ -hematin (100) and glass (amorphous silica) surfaces (Figure 5.2). The surfaces were modeled as infinite slabs by use of an elongated rectangular simulation cell with periodic boundary conditions in all directions. The slabs were oriented with their surface normal parallel to the major axis of the simulation cell (z-axis). The dimensions along the minor axes (x- and y-axes) were chosen to be commensurate with the surface structure and thus create infinite slabs in the x-y plane. The slabs were placed into contact with solvent by inserting ~460 n-octanol molecules into the simulation cell; water molecules were also added to mimic experimental solvent conditions. Solvent insertion was followed by steepest-descent minimization to remove large (>1000 kJ mol<sup>-1</sup> nm<sup>-1</sup>), unphysical forces between atoms.

The solvated systems were equilibrated for 10 ns in the NpzT ensemble at 325 K



Figure 5.2: Hyrophilic and hyrophobic regions on the  $\beta$ -Hematin surface (a,b) and the hematin molecule (c).

and 1 bar. The temperature was maintained by applying separate Bussi-Parrinello velocity-rescaling thermostats<sup>72</sup> to mobile atoms in the surface slabs and to solvent molecules, respectively. Constant pressure (isostress) conditions were imposed along the z-axis of the simulation cell by use of a semi-isotropic Parrinello-Rahman barostat;<sup>73</sup> no pressure coupling was applied along the x- and y-axes. Relaxation time constants of 2 ps were used for the barostat and both thermostats. The NpzT simulations were followed by longer runs in the NVT ensemble ( $\geq 100$  ns) in which the barostat was turned off. Configurations from the equilibrated portions of the NVT simulations were saved every 2 ps for subsequent analysis. In all simulations, the equations of motion were integrated by use of a velocity-Verlet scheme with a 2 fs time step.<sup>22</sup> Bond and angle constraints were handled by the LINCS algorithm.<sup>229</sup> Real-space Coulombic and van der Waals interactions were truncated at 1.2 nm, and the particle mesh Ewald method<sup>22</sup> was used to treat long-range electrostatics.

The  $\beta$ -hematin surface was modeled by use of AMBER-compatible (FF99SB-ILDN) force field parameters derived from heme.<sup>230</sup> These parameters were sup-

plemented with those from the AMBER FF99SB-ILDN release<sup>231</sup> distributed with GROMACS to model protonated carboxylic groups on hematin. A model for the basal (100) surface was constructed by use of the atomic positions and unit cell parameters for  $\beta$ -hematin crystal from X-ray diffraction measurements [(a, b, c) = (1.2196, 1.4684, 0.8040) nm;  $(\alpha, \beta, \gamma) = (99.22, 96.80, 97.92)^{\circ}]^{.214}$  Similar unit cell parameters  $[(a, b, c) = (1.2618, 1.4840, 0.8350) \text{ nm}; (\alpha, \beta, \gamma) = (83.68, 95.46, 100.8)^{\circ}]$  were obtained upon relaxing the crystal with MD at 300 K and 1 bar by use of an anisotropic Parrinello-Rahman barostat.<sup>73</sup> This good agreement indicates that the chosen force field provides a reasonably accurate description of the interactions between hematin molecules in the crystal environment. The model  $\beta$ -hematin surface was created by replicating the relaxed crystal structure, mapping the molecule positions onto an orthorhombic cell, and adjusting the dimension of the simulation box along the z-axis to expose the basal (100) plane. Hence, the final crystal slab used in the MD simulations had dimensions of ~4.4 x 3.2 x 3.7 nm. The solvent was modeled with TIP3P water<sup>232</sup> and an all-atom description of n-octanol from the general AMBER force field (GAFF).<sup>71</sup>

The silica (SiO<sub>2</sub>) glass surface was constructed by a reported procedure.<sup>233</sup> Briefly, NVT MD was used to simulate a large cristobalite crystal (4.1 x 4.1 x 4.1 nm) with the ionic silica potential of Tsuneyuki et al.<sup>234</sup> The thermostat temperature was raised from 300 to 4000 K to melt the cristobalite crystal. The molten silica was subsequently cooled back down to 300 at  $10 \text{ Kps}^{-1}$  to form an amorphous glass with a bulk density of  $2.2 \text{ gcm}^{-3}$ . The length of the simulation cell was then increased along the z-axis to create a slab with exposed surfaces in the x-y plane. Finally, to mimic the slightly acidic conditions (pH  $\approx$  4.8) in experiment, unsaturated oxygen and silicon atoms were capped by adding H or OH groups, respectively.<sup>235</sup> In simulations with solvent, ClayFF,<sup>70</sup> GAFF,<sup>71</sup> and SPC/E<sup>156</sup> potentials were used to model silica atoms, n-octanol, and water, respectively. Standard Lorentz-Berthelot

combining rules were employed to determine the potential parameters for modeling interactions between unlike components in the system (e.g., octanol-silica interactions).

## 5.3 **Results and Discussion**

The heterogeneous landscape of chemical moieties on  $\beta$ -hematin crystal surfaces represents a suitable system to examine fundamental molecule-substrate interactions that are relevant to crystal growth and its inhibition by modifiers. The basal (100) surface of the triclinic ( $P\bar{1}$ )  $\beta$ -hematin crystals (Figure 5.2A,B) is terminated with head-to-tail dimers of hematin (Figure 5.2C), wherein the metal centers are ligated to carboxyl groups (Figure 5.2A, inset). The alignment of hematin molecules in the lattice renders the surface of (100) faces predominantly hydrophobic, interspersed with rows of hydrophilic groups (gold regions in Figure 5.2A), separated by ca. 1.5 nm.

In this study, we assess the interactions between molecular adsorbates and two substrates: the (100)  $\beta$ -hematin crystal face and an amorphous glass surface. We employ CFM to measure the rupture force between molecules tethered to an AFM cantilever and the substrate (Figure 5.3A). This technique monitors changes in tip deflection during vertical approach and retraction of an AFM cantilever (Figure 5.3B). CFM yields the tip-substrate rupture force as a function of loading rate (2-50 pN/s). The latter is the product of the cantilever spring constant k (ca. 450 pN/nm) and the approach velocity v, which is systematically varied from 50 to 1000 nm/s (Figure 5.3C). CFM has been used to detail binding conformations and strengths, including ligand-protein binding,<sup>236,237</sup> cell adhesion to a variety of surfaces,<sup>238</sup> and measurements of surface hydrophilicity.<sup>239</sup> Molecules with long linkers or flexible tethers produce force profiles compatible with a semiharmonic probe potential.<sup>240</sup> Macromolecules, such as proteins, attached to a cantilever tip exhibit a variety of inter- and intramolecular binding/unbinding events upon approach and retraction

of the tip to the substrate. Conversely, experiments employing small molecules attached to the AFM cantilever exhibit more simplistic single pull-off curves as they probe the physicochemical interactions that arise between chemical moieties at the molecule terminus and the substrate.<sup>241</sup>



Figure 5.3: Probing the interactions of functional groups with two substrates by chemical force microscopy.

Rupture force measurements in CFM enable quantification of the attractive force between a functional group attached to an AFM tip (Figure 5.3A) and a substrate. A typical approach-retraction profile (Figure D.1) consists of a positive tip deflection  $\Delta z$ , which results as the cantilever is pushed into the substrate, and a negative tip deflection due to tip-substrate attraction that is measured as the tip is withdrawn from the surface (Figure 5.3B). The attractive force between the surface and the functional group decorating the tip is evaluated from the deflection  $\Delta z$  at the minimum in the force curve, or the rupture point, as  $f = k\Delta z$ . The separation between the functional moieties attached to an AFM tip is much less than the average radius of curvature (ca. 15 nm) of tips used in CFM measurements. Thus, the rupture force from tip-substrate contact derives from the binding of multiple functional groups on the tip with multiple groups on the substrate within an approximate  $10 \ge 10 \text{ nm}^2$  surface area.

At fast retraction velocities v, physical bonds between the AFM tip and substrate formed upon approach do not have adequate time to reform, leading to a greater rupture force.<sup>241</sup> Under these nonequilibrium conditions, the rupture force monotonically increases with loading rate, as shown in Figure 5.3C. This is referred to as the kinetic regime. By contrast, low loading rates permit tip-substrate bonds to fluctuate between unbound and bound states at near-equilibrium, which is observed as a plateau in Figure 5.3C at low loading rate. The characteristic time of the transition to the equilibrium regime is viewed as the bond's natural lifetime,<sup>242</sup> and the low v range is referred to as the thermodynamic binding regime.

Using CFM, we tested the interaction between  $\beta$ -hematin surfaces and AFM tips decorated with two types of functional moieties: (1) hydrophobic and hydrophilic groups that probe the amphiphilic nature of the crystal substrate and the organic solvent and (2) functional groups known to interact with  $\beta$ -hematin surfaces. Inspiration for the latter was derived from prior studies of antimalarial drugs showing that several quinoline molecules and their analogues selectively bind to surface sites on  $\beta$ -hematin crystals and impact the kinetics of crystallization.<sup>243</sup> The three antimalarial compounds considered here are chloroquine (CQ), quinine (QN), and amodiaquine (AQ) (Figure 5.3D). The functional moieties shared among these drugs include aromatic groups (i and iv), hydrophobic groups (ii and v), and hydrophilic groups (iii). As representatives of these groups, we selected four moieties, depicted in Figure 5.3E-H: benzene (I), pyridine (II), a saturated carbon chain (III), and a hydroxyl group (IV). Interestingly, compounds III and IV mimic the hydrophobic and hydrophilic segments of octanol, respectively. To minimize the flexibility of functional groups on AFM tips, we selected short aliphatic linkers  $C_n H_2 n$  with n < 3. Each linker is terminated with a thiol group that attaches to gold-coated AFM tips via a strong gold-thiol bond,<sup>227</sup> as illustrated in Figure 5.3E-H.

We carried out CFM measurements in CBSO on disordered glass (Figure 5.3I) and ordered  $\beta$ -hematin (Figure 5.3J) substrates. We compared the rupture forces of modified tips I, III, and IV to that of a bare Au-coated AFM tip (the results for tip **II** will be discussed separately). Correlations of rupture force with loading rate (Figure D.2) for all modified tips reveal that CFM measurements probe the thermodynamic regime (i.e., slopes of m = 0). As expected, the nonfunctionalized tip exhibits the lowest rupture forces. For the functionalized tips, the rank order of rupture forces is identical for both substrates, III > IV > I, with benzene exhibiting the lowest rupture force and the alkyl group exhibiting the highest force. Interestingly, there is an approximate 3-fold increase in rupture forces measured on the glass substrate compared to those on the crystal. Identical trends among the modified tips, irrespective of the differences in substrate composition and topology, suggest that the dominant factor contributing to the rupture force is tip interactions with solvent lining the substrate rather than with the underlying substrate. To this end, the large disparity between rupture forces on the two substrates is likely due to differences in solvent structuring, which was elucidated by molecular modeling (as will be discussed in greater detail).

Glass substrates are terminated with silanol groups, which are expected to be fully protonated in CBSO. CFM measurements on this substrate were carried out in the thermodynamic regime affording ample time for the formation of hydrogen bonds between tip-bound -OH and SiOH groups on the glass surface. Such bonds would induce strong attraction between the tip and substrate that requires a high rupture force. Hence, it was surprising to observe stronger attraction between glass and the hydrophobic alkyl chain (**III**) than between the hydrophilic hydroxyl group (**IV**) and the same substrate, as indicated by the rupture force measurements in Figure 5.3i. This seems to suggest that SiOH groups are saturated by hydrogen bonds with the -OH groups of octanol. Correspondingly, this would imply that the rupture force reflects the interaction of functional moieties with the layer of associated solvent and not with the substrate. The affinity of octanol in CBSO to glass is supported by determinations of the contact angles of droplets of water and CBSO deposited on glass (74° and 25°, respectively). The lower contact angle of the CBSO droplet indicates that this solvent wets the glass surface owing to favorable interactions.

The trend of the interactions of tips III and IV with the  $\beta$ -hematin crystal surface is similar to that with glass. The stronger attraction to the substrate of the hydrophobic alkyl chain III suggests that the polar stripes on the  $\beta$ -hematin crystal surface (Figure 5.2A) are masked owing to octanol associated with the crystal surface. The weaker surface binding to both glass and  $\beta$ -hematin of tip I (phenyl group) than the alkane chain attached to tip III is consistent with a structure of the octanol composed of aligned aliphatic residues shared among both substrates. The bulky phenyl disrupts this alignment, which weakens the attraction between the substrate and the tip.

To understand why the attraction between tips I, III, and IV and the hematin surface is dramatically weaker than that with glass, we invoke the two notions formulated above: (1) interactions of the respective functional groups and the two substrates are dominated by octanol molecules associated with the respective surfaces and (2) octanol forms a structured layer consisting of aligned aliphatic chains. The stronger attraction to glass suggests that the octanol chains are ordered in the direction of tip retraction, that is, perpendicular to the substrate plane, forming a lamellar layer of octanol molecules bound to the glass with their hydroxyl groups oriented toward the glass surface. Contrastingly, octanol in contact with the hematin surface is likely oriented parallel to the surface. Remarkably, nonfunctionalized Au-coated tips are attracted to hematin more strongly than to glass (Figure 5.3I,J), contrary to the trends recorded with the functionalized tips I, III, and IV. This observation is consistent with the conclusion that the interaction between functional groups and solvent structured at the surfaces of the two substrates dominates tip-substrate rupture forces.

To test the feasibility of the solvent structures suggested by CFM measurements, we carried out MD simulations of the mixed n-octanol-water solvent in contact with  $\beta$ -hematin and glass surfaces. As will be discussed, simulations of a 5% water CBSO solution revealed the presence of water nanodroplets dispersed in the solvent phase (Figure D.3), consistent with previous dynamic light scattering measurements.<sup>217</sup> In some simulations, these droplets were observed to adsorb and wet portions of the  $\beta$ -hematin and glass surfaces. Thus, to account for this behavior and study solvent structuring away from the immediate vicinity of adsorbed nanodroplets, we performed simulations of CBSO solutions with reduced water content (ca. 1%). The results reveal distinct solvent structures at crystalline and amorphous interfaces. At the crystal surface, the octanol aligns into ordered regions (Figure 5.4A) that correspond to the repeating hydrophobic and hydrophilic stripes on a  $\beta$ -hematin crystal surface depicted in Figure 5.1C and Figure 5.2A. By contrast, the octanol at an amorphous glass interface is significantly less ordered (Figure 5.4D), analogous to the disordered motif depicted in Figure 5.1E. Comparison between effects of the two substrates reveals that solvent structuring in organic media is a function of ordering at a solid interface and that the arrangement of hydrophilic groups on the surface guides the ordering of solvent molecules.

The ordering of octanol near the (100) surface of  $\beta$ -hematin arises from its amphiphilic nature. Octanol's hydroxyl headgroup forms hydrogen bonds with the exposed carboxylic groups located in the hydrophilic stripes on the  $\beta$ -hematin crystal (Figure 5.5B,C). Similarly, octanol's alkyl tail interacts with hydrophobic patches on  $\beta$ -hematin, such that molecules in the first solvent layer lie parallel to the surface (Figure 5.5A,B). This preferred parallel orientation results in pronounced ordering



Figure 5.4: Surface structuring and octanol density near the  $\beta$ -hematin and amorphous glass interfaces.

near the solvent-crystal interface and the formation of compact layers (Figure 5.5B). The solvent density profile (Figure 5.5C) reveals that octanol's parallel orientation near the surface induces strong ordering and the formation of ~5 distinct solvent layers. In each of these layers, octanol preferentially aligns with its major axis parallel to the surface (Figure 5.5B). The compact structure of the first layer therefore induces similar order in the solvent at distances further away from the surfaces. Alignment of the octanol molecules in layers of parallel molecules explains the strong attraction of the alkyl-coated tips to the  $\beta$ -hematin crystal surface (tip **III** in Figure 5.3j). This octanol layer prevents the formation of hydrogen bonds between the crystal and the hydroxyl functional group on tip **IV** and is disrupted by the phenyl group on tip **I**, leading to weaker attraction with these two tips.

The amorphous structure of silica glass, by contrast, frustrates compact solvent ordering near the interface (Figure 5.4D). Octanol forms hydrogen bonds with the silanol groups on the glass surface (Figure 5.4E,F). Because of the dense and uniform distribution of surface silanol groups, however, octanol preferentially orients with its major axis perpendicular to the surface (Figure 5.5A,D). This preferred orientation



Figure 5.5: Orientation and density of octanol molecules near  $\beta$ -hematin and glass substrates.

results in two diffuse layers near the interface (Figure 5.5D,E). In the first layer, octanol's alkyl tail points away from the surface to allow its hydroxyl head to form a hydrogen bond with surface silanols (Figure 5.5D). Conversely, octanol preferentially adopts the opposite orientation in the second layer to bring the hydrophobic alkyl tail groups of molecules in the first two layers into contact (Figure 5.5D). This lamellarlike structuring is diffuse and decays rapidly away from the surface (Figure 5.5E). The parallel alignment of the octanol molecules in contact with glass is consistent with the ranking of attractive force between tips in Figure 5.3I: **III** > **IV** > **I**. Similar to the interaction of the respective functional groups with hematin, the alkyl chains on tip **III** are attracted more strongly to the octanol layer than the hydroxylfunctionalized tip **IV** or the phenyl-coated tip **I**, both of which disrupt the ordered octanol layer. The perpendicular orientation of the octanol molecules relative to the substrate has one additional important consequence: it induces stronger attraction with tips **I**, **III**, and **IV** than with the octanol layers oriented parallel to  $\beta$ -hematin, thus confirming the impact of solvent structuring on sorbate-solid interactions. The correlations of the rupture force f to the loading rate for AFM tips modified with pyridine (II) suggest even more elaborate solvent structuring beyond those proposed above. With both substrates, f monotonically increases with increasing loading rates (Figure 5.6A), in agreement with the relationship  $f \approx 0.5 * (ln(kv))$ .<sup>242</sup> The probed loading rates are relatively low, below 106 pN s<sup>-1</sup>, identical to the loading rates used during tests with tips I, III, and IV (Figure D.2). Thus, the observed dynamic behavior of the rupture force is not equivalent to the kinetic regime in Figure 5.3C but represents a new phenomenon that, to our knowledge, has not been previously reported.



Figure 5.6: Interaction of pyridine-functionalized tips (a-d) and mass density profiles for water (e,f) with  $\beta$ -hematin and amorphous glass substrates.

The hypothesis of complex solvent structuring is supported by the correlations of rupture force to loading rate with tip **II** and glass in three different solvents. The

selected solvents represent the individual components of CBSO: deionized water, citrate buffer (pH 4.8), and anhydrous octanol (Figure 5.6B). With all three solvents, the rupture force is reduced 6-fold and is independent of the loading rate. The dramatic switch to a thermodynamic binding regime in anhydrous octanol indicates that the alignment of octanol alkyl chains is insufficient to describe the dynamic tip-substrate interaction in CBSO. We propose that the unique dynamic behavior observed in Figure 5.6A could be attributed to (i) the ability of pyridine to disrupt solvent ordering on the substrate and/or (ii) the accumulation of positive charge on the tip that induces a repulsive interaction with the substrate. Indeed, one differentiating aspect of pyridine relative to the other tested functional moieties is its affinity to protons, which are available either from H<sub>3</sub>O<sup>+</sup> in citrate buffer or from any of the three carboxylic groups of citric acid. During preparation of CBSO, octanol is placed in contact with 50 mM citrate buffer at pH 4.8. It is uncertain what fraction of the acid transfers to the organic phase. Previous studies of acids in nonpolar solvents indicate that citric acid should be predominantly fully protonated;<sup>244</sup> however, it may dissociate in pockets of water suspended in CBSO. Citric acid is polyprotic and can have as many as two deprotonated carboxyl groups (pKa = 3.1 and 4.8)<sup>245</sup> at this pH. The disparity of dissociation constants between pyridine  $(pKa = 5.2)^{246}$  and citrate indicates the latter has stronger proton affinity.

Thus, the transfer of protons to the pyridine residues is favored in an aqueous phase, such as the water nanodroplets in CBSO.<sup>217</sup> The exact pH of these droplets is unknown; however, the water droplets may coalesce on the substrate surface into an aqueous layer enriched with citrate and hydronium proton donors, as depicted in Figure 5.6C. Similarly, water would be expected to accumulate along the hydrophilic stripes of  $\beta$ -hematin surfaces, as illustrated in Figure 5.6D (see also Figure D.4). During the penetration of the tip though this layer, protons can presumably transfer to the pyridine nitrogen atoms and charge the tip. The accumulation of positive

charge induces repulsion between tip and substrate. This effect is stronger at longer residence times of the tip in the aqueous layer in the vicinity of the substrate that correspond to reduced loading rates. Stronger repulsion lowers the rupture force at slow loading rates, leading to the dynamic behavior observed in Figure 5.6A with a time constant of milliseconds, as estimated from the slope of the curves in Figure 5.6A. This is much longer than the time scale of bond breakage/formation that is associated with the kinetic regime in Figure 5.3C.

According to this scenario, the rate of accumulation of charge on pyridine-coated tips dictates the increase in repulsion and the reduction in rupture force with decreasing loading rate. Charge accumulation due to proton transfer is likely delayed by the low concentration of citrate and hydronium ions in the aqueous subphase of CBSO, and the spatial hindrance to diffusion is due to structured octanol in the aqueous layer. The slow proton transfer delays the dynamics of tip-substrate interactions and extends the characteristic time scales to the range probed by CFM measurements. Furthermore, the rate of proton accumulation is determined by the bulk properties of the interfacial aqueous layer but is apparently independent of the substrate; that is, there is a similar rate of increase of the rupture force with loading rate for  $\beta$ -hematin and glass that reflects the identical properties of interfacial solvent layers on these two substrates. The significantly weaker attraction between pyridine-coated tips and  $\beta$ -hematin surfaces is consistent with the observed trends of other tip-functionalized moieties. CFM measurements with AFM tips I, III, and **IV** (Figure 5.3i,j) did not show any evidence that the solvent structure on either substrate is perturbed by changes in loading rate. The weaker attraction between tip **II** and glass in anhydrous octanol than in CBSO is consistent with the stabilization of ordered octanol by the water layer. Moreover, the presence of water is critical to hematin crystallization since the incorporation of hematin molecules into the crystal lattice requires the formation of hydrogen bonds between carboxyl groups belonging to adjacent hematin and coordination bonds between a carboxyl residue and a Fe<sup>3+</sup> ion from another molecule. The former bonds are possible only between protonated COOH groups, whereas the latter demand deprotonated COO<sup>-</sup>. Precise control of the protonation state implies exchange of H<sup>+</sup> ions between the solvent and the incoming hematin molecules, which is possible only in aqueous solvents, consistent with water in CBSO being in close proximity to  $\beta$ -hematin surfaces.

The tendency for water nanodroplets to adsorb and wet the glass surface was directly observed in MD simulations where a ca. 5% water CBSO solution was used to mimic experimental conditions. A clear peak near the glass surface is observed in the mass density profile for water, demonstrating that it can adsorb and wet portions of the interface by forming hydrogen bonds with the exposed surface silanol groups (Figure 5.6E and Figure D.4). Congregation of the hydroxyl groups along the glass surface promotes the formation of an aqueous layer at the substrate, which attenuates the repulsion between the charged pyridine-coated tips **II**, leading to higher rupture force of this tip with the glass substrate (Figure 5.6A); however, to model the dynamic behavior of the pyridine-coated tip **II** would require running MD simulations for times comparable to the characteristic times of tip-substrate interactions. The tip is attracted to the substrate over separations of ca. 10 nm. With the fastest rate of retraction that we apply,  $1000 \text{ nm s}^{-1}$ , the shortest time of attraction between tip and substrate is ca. 10 ms, which is ca.  $10^5$  longer than the typical times (~100 ns) probed in MD simulations.

Molecular dynamics simulations also predict that water from the 5% CBSO solution adsorbs on the  $\beta$ -hematin crystal, as indicated by the pronounced peak in the mass density profile for water near the interface (Figure 5.6F). Adsorption of water is promoted by the hydrophilic stripes on the  $\beta$ -hematin surfaces containing exposed carboxylic groups and the hydroxyl groups of aligned octanol molecules, both of which are available for hydrogen bonding. The lower density of hydrophilic adsorption sites on  $\beta$ -hematin, however, results in less water accumulation at the crystal surface than observed on the disordered glass substrate. Consequently, an appreciable fraction of the water remains dispersed in small clusters throughout the CBSO phase. The arrangement of hydrophilic surface groups also has a profound influence on the structure of the adsorbed water. In contrast to the disordered arrangement of silanol groups on the glass surface that facilitates the formation of a uniform hydration layer near the surface (Figure D.4, left), the patterning of  $\beta$ -hematin surfaces promotes the formation of clusters (or nanodroplets) of water at the surface that frequently become large enough to bridge the  $\sim 1.5$  nm gap between carboxyl groups on adjacent hydrophilic stripes (Figure D.4, right). The presence of aqueous nanophases at  $\beta$ -hematin interfaces may have significant implications for understanding hematin crystallization from mixed organic-aqueous solvents, as has been suggested for crystallization in vivo.<sup>212,216</sup> Precise control of the protonation state implies an ability to exchange H<sup>+</sup> ions between the solvent and hematin molecules incorporating into the crystal surface. Such processes are likely enhanced by aqueous nanodroplets, which can facilitate proton exchange.

## 5.4 Conclusions

In summary, the combination of experiments and modeling reveals that the distinct solvent structures at ordered and disordered solid-liquid interfaces have an influence on molecule adsorption. These findings have implications for understanding processes that underlie the interactions governing crystal growth modification and the kinetics of solute incorporation in crystal surfaces. Notably, the presence of structured amphiphilic solvent layers at  $\beta$ -hematin interfaces may play an important role in hematin crystallization from mixed organic-aqueous solvents that mimic in vivo environments. In close proximity to the crystal surface, parallel layers of octanol, which mimic neutral lipids in parasite digestive vacuoles, can influence the adsorption and diffusion of antimalarial drugs at surface sites critical for hematin
crystallization, thereby hindering growth (i.e., heme detoxification). Moreover, the presence of aqueous phases at  $\beta$ -hematin crystal surfaces may play a role in crystal growth and the impact of modifiers.

Future challenges in understanding the role(s) of solvent in crystallization include the identification of model systems for a particular crystalline substrate wherein the solvent can be systematically altered to yield various structured patterns at the liquid-solid interface. These systems can serve as a platform for assessing the effects of solvent ordering on crystal growth and/or growth modification, which may prove to be relevant for natural or synthetic crystallization from organic or multicomponent solvents. For example, the organic medium for hematin crystallization in malaria parasites is composed of around eight different neutral lipids. It remains to be determined if each lipid, or combinations thereof, exhibits unique structured patterns on the surfaces of  $\beta$ -hematin crystals, and to what extent this will impact heme detoxification and the modes of antimalarial action in these complex growth environments.

# **Chapter 6: Conclusions and future work**

This research focused on understanding how molecular additives and solvent structuring affect crystallization processes. Through this work we have investigated two types of molecular additives, crystsal growth modifiers and organic structure directing agents. Many different crystal systems have been studied in this work from various zeolite systems to  $\beta$ -hematin. Molecular dynamic simulations allow us to study these systems on a level unobtainable in experiment. These simulations allow us to gain insight into these systems and elucidate various mechanisms that affect crystal growth.

## 6.1 Conclusions

Through our work with CTA and TPA in ZSM-5 crystallization, we determined the probable locations for both molecules within the zeolite framework. CTA, a more linear molecule, can access both the straight and sinusoidal channels within ZSM-5 (Chapter 2). Conversly TPA is restricted to the intersection of the channels. From experiment we are able to observe a more uniform distribution of aluminum throughout the pore structure when CTA is used as a structure directing agent. From simulation we have shown CTA has a greater access to the pore network of the zeolite, and we hypothesize that this ability allows it to counterbalance aluminum sites more uniformly throughout the zeolite framework.

The cooperative effects of structure directing agents and diol molecules was observed by the Rimer group MOR structured zeolites (Chapter 3). In experiment, they showed that by changing the quantities of TMADA<sup>+</sup> and various diols in the same growth solution, three different zeolite frameworks or amorphous material can be produced. Through simulation work we investigated the optimal packing of OSDA and diols inside the frameworks. In MOR zeolite our simulations revealed how the diols fit inside the pores along side TMADA<sup>+</sup> and identify energetically favorable configurations, thereby elucidating how the two SDAs act cooperatively to stabilize the framework.

A relationship between zeolite growth modifier efficacy and the hydrophobicity of the modifierhas been observed in synthesis experiments performed by the the Rimer group (Chapter 4). Conventional understanding of these systems suggests that hydrophobic interactions may cause certain molecules to bind more strongly to zeolite surfaces and thus exhibit greater efficacy in inhibiting crystal growth. Our simulations results, by contrast, showed no clear correlation between modifier adsorption strength and efficacy. In agreement with calorimitry experiment by the Rioux group, we observed that even effective modifiers bind relatively weakly to the surface. Moreover, the calorimitry experiment reveal that modifer binding strength is not strongly correlated with measures of hydrophobicity. While the full implications of these findings are not completely understood, they suggest that, in contrast to conventional understanding of crystal growth modifiers, the strength of binding may not be a good descriptor for characterizing modifiers for zeolites.

The effects of solvent structuring at ordered and disordered solid-liquid interfaces have an influence on molecule adsorption. Molecular dynamics allows us to visualize and quantify the solvent structuring at these interfaces. These findings have implications for understanding processes that underlie the interactions governing crystal growth modifications and the kinetics of solute incorporation in crystal surfaces. The presence of structured amphiphilic solvent layers at the  $\beta$ -hematin interfaces observed in our study (Chapter 5) led to the hypothesis that these interfaces may plan an important role in hematin crystallization in vivo and in determining the efficacy of different antimalarial compounds.

### 6.2 Future Work

Although this work allows us to gain insight into the mechanisms behind crystal growth, the findings also raise many questions that should be the focus of future studies. Some potential directions for future research are detailed below.

#### 6.2.1 Location of aluminum sites in zeolites

Our research has been able to predict optimal locations for structure directing agents inside zeolite frameworks. All of our research has investigated siliceous zeolite frameworks, predominately because the location of substituent atoms in the framework is unknown. There is a lack of understanding on where substituent atoms, specifically aluminum, will be likely to populate inside the framework and furthermore it has been shown changing the structure directing agent can lead to changes in aluminum concentration and potentially alter the location of the aluminum sites. <sup>144,247,248</sup> Monte Carlo simulation methods in combination with molecular dynamics can allow us to explore these energy landscapes and predict likely acid sites. After validating the method against known structure directing agents and silica alumina ratios (SAR), this method could be used to to predict the effects of structure directing agents on SAR and aluminum site locaiton, thereby allowing material scientists to engineer acid sites into their catalysts in a precise and controlled manner.

#### 6.2.2 Screening for potential structure directing agents

Using the slow insertion method we can predict stabilization energies related to molecules occluded in the zeolite framework. These stabilization energies can be tied to the efficacy of a structure directing agent. Typically OSDAs can be expensive in a manufacturing enviornment , and there is a need to find cheap alternatives without sacrificing the quality of the final product.<sup>249–251</sup> The utilization of molecular dynamics can allow us to quickly screen through hundreds of OSDAs to then be

tested experimentally, thereby reducing the time and cost associated with OSDA discovery.

#### 6.2.3 Screening for potential growth modifiers

Similarly we can also investigate high throughput screening of zeolite growth modifiers. Although our studies suggests the that adsorption energy to specific crystal planes is not the only variable influencing the effectiveness of a given growth modifier, it still may be a useful high-level descriptor for computational screening. The the computational cost of computing binding energies is typically high, however, due to the explicit solvent in the system. From our LTL/TON work we have also seen a relation between our free energy of adsorption onto the surface in vacuum and in solution. This obesrvation suggests that one could perform high throughput screening of growth modifiers in vacuum and then perform more rigorous calculations in solution before running experiments. The cost of computing is continuously decreasing as technology advances, and with these advancements we can aid experimental results in a cost effective and timely manner.

#### 6.2.4 Complex crystal surfaces

Throughout our work we have looked at periodic crystal systems as well as solidliquid interfaces along specific crystallographic planes. Although these results can be informative, the surfaces of crystals growing in solution may not be this ideal. Indeed, the evolution of step and kink sites can be observed in AFM images during crystal growth experiments. These more complex surface features could also be the favored locations for growth modifier adsorption. Because of this we might not be capturing all of the physics of growth modifier attachment to specific surfaces. Furthering the complexity of our simulations will allow greater insight into the mechanisms behind crystal growth and inhibition.

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# **Appendix A:** Chapter 1 Supporting Information

### A.1 Supplementary Figures



Figure A.1: XRD patterns of ZSM-5 crystals at different heating times and alkali content.

Figure A.1 shows time-elapsed powder X-ray diffraction patterns of solids extracted from ZSM-5 growth solutions containing CTA as the organic SDA and the following ratios of inorganic SDAs (listed as molar fractions of K:Na): (A) 1:0, (B) 0.75:0.25, (C) 0.5:0.5, and (D) 0:1.



Figure A.2:  $N_2$  adsorption/desorption isotherms of ZSM-5 crystals.

Figure A.2 shows  $N_2$  adsorption (solid line) and desorption (dashed line) isotherms of ZSM-5 crystals synthesized in the presence of (A) potassium and (B) sodium. Isotherms of samples prepared with CTA (i) are type IV, which indicates the presence of mesopores. Isotherms of samples prepared with TPA (ii) are type I, which is characteristic of microporous materials.



Figure A.3: TGA analysis of ZSM-5 crystals.

Figure A.3 shows thermogravimetric analysis (TGA) of ZSM-5 crystals prepared in the presence of (A) CTA and (B) TPA. Blue and orange lines denote samples prepared with potassium and sodium, respectively. TGA data were obtained using a 1 °C/min temperature ramp rate under the constant flow of  $N_2$  gas.



Figure A.4: XRD patterns of solids extracted from Na growth solutions with and without TMA

Figure A.4 shows powder X-ray diffraction patterns of solids extracted from growth mixtures after 72 h of hydrothermal treatment. The inorganic SDA in both samples is sodium. Here we compare a sample prepared with (i) tetramethylammonium (TMA) as the organic SDA to (ii) a sample prepared from an organic-free growth mixture.



Figure A.5: XRD patterns of solids extracted from K growth solutions with and without TMA.

Figure A.5 shows powder X-ray diffraction patterns of solids extracted from growth solutions after 72 h of hydrothermal treatment. The inorganic SDA in both samples is potassium. Here we compare a sample prepared with (i) tetramethylammonium (TMA) as the organic SDA to (ii) a sample prepared from an organic-free growth mixture.



Figure A.6: SEM images of ZSM-5 crystals prepared with various combinations of alkali metals.

Figure A.6 shows scanning electron micrographs of ZSM-5 samples prepared with CTA as the organic SDA in the presence of the following molar percentages of potassium relative to the total alkali content (K + Na): (A) 0%, (B) 50%, (C) 75%, and (D) 100%. Scale bars equal 1 µm



Figure A.7: Characterization of ZSM-5 crystals synthesized using TEOS.

Figure A.7 shows ZSM-5 crystals synthesized with TEOS as an alternative silica source. (A) Scanning electron micrograph revealing crystals grown from TEOS are larger than those from colloidal silica. (B) Powder X-ray diffraction pattern of solids extracted from a growth mixture prepared with TEOS reveals that crystallization is complete within 48 h of hydrothermal treatment



Figure A.8: Characterization of ZSM-5 crystals with TPA in the presence of Li and Cs.

Figure A.8 shows characterization of ZSM-5 crystals synthesized using TPA as the organic SDA. (A and B) Scanning electron micrographs of ZSM-5 crystals after 72 h of hydrothermal treatment. Growth mixtures were prepared with (A) lithium and (B) cesium. (C and D) Powder X-ray diffraction patterns of solids extracted from ZSM-5 syntheses after listed times of hydrothermal treatment corresponding to growth mixtures prepared with (C) lithium and (D) cesium.



Figure A.9: Time-evolved XRD patterns of ZSM-5 crystals prepared with TPA/Na and TPA/K.

Figure A.9 shows comparison of powder X-ray diffraction patterns of solids extracted from ZSM-5 growth mixtures after specified heating times. Growth mixtures were prepared with TPA as the organic SDA and the following inorganic SDAs: (A) sodium and (B) potassium.



Figure A.10: Time-evolved XRD patterns of ZSM-5 crystals prepared with TPA/Li and TPA/Cs.

Figure A.10 shows comparison of powder X-ray diffraction patterns of solids extracted from ZSM-5 growth mixtures after specified heating times. Growth mixtures were prepared with TPA as the organic SDA and the following inorganic SDAs: (A) lithium and (B) cesium.



Figure A.11: Dissolution of colloidal silica in NaOH solution.

Figure A.11 shows dissolution of colloidal silica (LUDOX AS-40) in NaOH solution (pH 12) with a molar composition of 20 SiO<sub>2</sub>: 0.2 NaOH: 1030 H<sub>2</sub>O at temperatures between 25 and 50 °C. The average hydrodynamic diameter of silica particles DH scaled by the initial size DH(t=0) (measured at t = 0 min) is plotted as a function of time. Solid lines are linear regression with slopes equaling the kinetic rate of dissolution. The experiment details are consistent with what is reported in the manuscript (Figure 2.9).



Figure A.12: SEM images of ZSM-5 prepared with TPA and different alkali metals.

Figure A.12 shows scanning electron micrographs of ZSM-5 samples prepared with TPA as the organic SDA after specified heating times in the presence of (A) lithium, (B) sodium, (C) potassium, and (D) cesium cations. An arrow indicates the presence of residual amorphous precursors in TPA/K-MFI and TPA/Cs-MFI samples. Note that the times account for both induction (nucleation) and crystal growth.

SDA Combinations	Total surface area (m <sup>2</sup> /g)	Micropore surface area (m <sup>2</sup> /g)	External surface area (m <sup>2</sup> /g)
CTA/Na	443	305	139
TPA/Na	398	311	87
CTA/K	450	316	134
TPA/K	423	346	77

Table A.1: t-plot analysis of ZSM-5 crystals using  $N_{\rm 2}$  adsorption/desorption data.

Table A.2: t-plot analysis of  $N_2$  adsorption/desorption data for ZSM-5 crystals prepared with CTA/Na.

	Total	Micropore	External
SDA Combinations	surface area	surface area	surface area
	$(m^2/g)$	(m <sup>2</sup> /g)	$(m^2/g)$
LUDOX	443	305	139
TEOS	409	319	90

## **Appendix B:** Chapter 2 Supporting Information

### **B.1** Supplementary Text

#### **B.1.1 Synchrotron X-Ray Powder Diffraction Analysis**

In the hope that the arrangement of the sodium and organic species within the pores of the mordenite framework structure could be discerned experimentally, synchrotron powder diffraction data were collected. Analysis of the data revealed the presence of a quartz impurity, so a 2-phase refinement using the program Topas (A.A. Coelho, TOPAS-ACADEMIC v5.0; 2012) was undertaken. Idealized structures for the two OSDA species were generated using the program Avogadro (version 1.2.0).<sup>252</sup>

For the quartz phase, the published structure<sup>253</sup> was used and only the peakshape parameters and scale factor were refined. For the mordenite phase, structure analysis was initiated using the known MOR-type framework structure<sup>254</sup> in the highest symmetry space group (Cmcm). A drawing of the MOR-type framework structure and its main features is shown in Figure B.1. The pattern was scaled using only the high-angle data and then a difference electron density (DED) map was generated using the complete pattern. This showed a significant column of electron density in the middle of the 12-ring channel. As the width of this column had a diameter consistent with that of the TMAda<sup>+</sup> molecule, a simulated annealing (SA) global optimization procedure for locating organic species in zeolites<sup>255</sup> was applied to find the best location and orientation of a rigid TMAda<sup>+</sup> molecule within this electron density. A second DED map revealed the positions of the Na<sup>+</sup> ions in the center of the oval 8-ring channels, where they coordinate to six framework oxygen atoms. The next DED map showed electron density in the 8-ring side pocket of the 12-ring channel, so the SA procedure was applied once again, this time searching for the best position of the head group ( $C_2O_2$ ) of the  $D6_{1,2}$  molecule. The final DED map showed a peak distinct from the diol O atom that was within bonding distance of the Na<sup>+</sup> ion, so this was interpreted as a water molecule.

This approximate model was then refined to yield the structure shown in figure B.12 and the profile fit shown in Figure B.8. Because NMR results showed that ca. 1/3 of the TMAda<sup>+</sup> cations were in fact neutral dimethyladamantine (DMAda) molecules, the occupancy parameters of the methyl groups were adjusted accordingly. Geometric restraints were applied to the zeolite framework structure and the  $D_{1,2}$  head group for structure refinement. The TMAda<sup>+</sup>/DMAda species were treated as a rigid body and only the occupancy, position, orientation and the torsion angle around the N1-C4 bond were refined. Refinement including the quartz phase converged with the R-values given in Table B.4.

The TMAda<sup>+</sup>/DMAda species are centered in the 12-ring channel and tilted with respect to the crystallographic c axis by approximately 20 °C. There are two entities per unit cell (one per 12-ring channel). The two Na+ ions per unit cell are located at the center of the tilted 8-rings that form the oval 8-ring channel. Each is coordinated to six framework O atoms, one  $D_{1,2}$  O atom and one water molecule. Only the  $C_2O_2$ head group of the  $D6_{1,2}$  molecule could be located. This probably reflects the fact that the tail is extremely flexible and probably disordered over many different sites. Because the O atom of the terminal OH group interacts with Na<sup>+</sup> ions and the second OH group can form a hydrogen bond with framework O atoms, their positions are better defined and therefore visible in the DED map. The disordered tail appears to go through the 8-ring side pocket towards the 12-ring channel.

#### **B.1.2 Minimization of Quartz Impurity**

Excess silica in the HOU-4 reaction mixture results in the formation of a dense and inert quartz phase and a minor unidentified aluminosilicate phase as detected by synchrotron XRPD (Figure 3.1D and Figure B.8). The quartz byproduct identified in HOU-4 is a commonly reported impurity in zeolite synthesis.<sup>256,257</sup> The formation of quartz from growth solution C1 is attributed to a higher silica concentration that is more common for syntheses of SSZ-13 and ZSM-5, compared to less siliceous growth mixtures used to prepare conventional mordenite (e.g. growth solution C5 in Table B.1). In order to reduce the quartz content in HOU-4, the composition of the growth mixture was varied by first increasing the D6<sub>1,2</sub> concentration and then decreasing the quantity of silica (Figures S19 and S20). Additional modifications, such as the reduction of water content (Figure B.21), had a negligible impact on product purity. Collectively, the changes made to the growth mixture improved the purity of HOU-4, but they were unable to remove the quartz phase completely. It should be noted that the presence of quartz in the H-HOU-4 catalyst used for cumene cracking (Figure 3.4E) is accounted for in the calculation of TON through NH<sub>3</sub> TPD measurements of total acid density.

#### **B.1.3 Additional Discussion of Solid-State NMR Results**

Molecular-level insights into the Al heteroatom distribution and framework-OSDA interactions in HOU-4 are provided by solid-state two-dimensional (2D) heteronuclear correlation MAS NMR spectra. Solid-state 2D NMR correlation spectra exploit internuclear dipole-dipole (through-space) or J (through-covalent-bond) couplings and are plotted as 2D contour plots, where correlated signal intensities indicate the mutual proximities or covalent connectivities of the corresponding <sup>1</sup>H, <sup>13</sup>C, <sup>27</sup>Al, or <sup>29</sup>Si species. <sup>118,136</sup> The covalently bonded <sup>27</sup>Al-O-<sup>29</sup>Si framework moieties in HOU-4 are unambiguously established by the 2D <sup>27</sup>Al<sup>29</sup>Si J-mediated NMR correlation spectrum (Figure 3.3A), which selectively detects <sup>27</sup>Al-<sup>29</sup>Si nuclear spin pairs that are J coupled through covalent <sup>27</sup>Al-O-<sup>29</sup>Si bonds. The 2D spectrum shows a single <sup>27</sup>Al signal at 54 ppm from tetrahedral framework aluminum sites, which is correlated to <sup>29</sup>Si signals at -109 to -102 ppm from fully crosslinked  $Q^4(1Al)$  <sup>29</sup>Si species and at -99 ppm from partially crosslinked  $Q^3(1Al)$  <sup>29</sup>Si species. ( $Q^m(nAl)$  denotes a tetrahedral Si atom that is bonded through bridging oxygen atoms to m Si or Al atoms, of which n are Al.) Previously, such 2D <sup>27</sup>Al<sup>29</sup>Si through-bond J-mediated correlation spectra of aluminosilicate zeolites have been challenging to obtain due in part to the low natural isotopic abundance of <sup>29</sup>Si (4.7%) and the weak <sup>27</sup>Al-O-<sup>29</sup>Si J couplings (<20 Hz), but are enabled here by the improved sensitivity provided by low-temperature (95 K) measurement conditions. The <sup>27</sup>Al signals exhibit Czjzek lineshapes<sup>148</sup> that reflect a random distribution of <sup>27</sup>Al heteroatom environments within the mordenite framework and among the four distinct tetrahedral (T) sites. This is corroborated by complementary <sup>27</sup>Al triple-quantum MAS NMR analyses of the same HOU-4 sample (Figure B.16). The relatively small percentage of partiallycrosslinked  $Q^3$  species (ca. 2%, Figure B.17) are likely associated with defect sites at the exterior particle surfaces of the ultrathin HOU-4 crystallites.

The site-specific interactions of the different framework <sup>27</sup>Al species with OSDA molecules are established by 2D <sup>27</sup>Al<sup>1</sup>H and <sup>13</sup>C<sup>1</sup>H dipolar-mediated HETeronuclear CORrelation (HETCOR) NMR spectra (Figure 3.3B and C). The 2D HETCOR spectra yield correlated <sup>13</sup>C- or <sup>27</sup>Al-<sup>1</sup>H signal intensities from <sup>13</sup>C-<sup>1</sup>H or <sup>27</sup>Al-<sup>1</sup>H nuclear spin pairs that are dipole-dipole coupled through space over distances of <1 nm. The different <sup>1</sup>H signals are assigned to the different <sup>1</sup>H moieties on D6<sub>1,2</sub> (green shaded regions) or TMAda<sup>+</sup> (red shaded regions) OSDA molecules on the basis of the 2D <sup>13</sup>C<sup>1</sup>H HETCOR NMR spectrum of HOU-4 acquired with a very short contact time (0.5 ms, Figure B.10).

Different types of tetrahedrally-coordinated framework aluminum sites within the mordenite zeolite framework are distinguished on the basis of their interactions with the different OSDA molecules, as manifested by the 2D  $^{27}$ Al<sup>1</sup>H HETCOR spectrum in Figure 3.3B. Specifically, the  $^{27}$ Al signal at 55 ppm from tetrahedrallycoordinated  $^{27}$ Al is correlated with <sup>1</sup>H signals at 2.2 ppm and 2.6-3.1 ppm from alkyl D6<sub>1.2</sub> and TMAda<sup>+</sup> moieties, respectively, indicating the mutual nanoscale proximities of the corresponding <sup>27</sup>Al species to both types of OSDA molecules. These correlated intensities are consistent with the TMAda<sup>+</sup> molecules acting as chargebalancing cations for the negative charges associated with the framework <sup>27</sup>Al heteroatom sites. As the TMAda<sup>+</sup> molecules are too large to occupy the 8-membered ring channels in the mordenite zeolite structure and must be situated within the 12membered ring channels, the <sup>27</sup>Al signal at 55 ppm corresponds to <sup>27</sup>Al heteroatom sites within the 12-membered ring channels. Interestingly, <sup>27</sup>Al signals at 53 and 55 ppm are both also correlated with an additional <sup>1</sup>H signal at 3.4 ppm, which arises from the -OH moieties on the  $D6_{1,2}$  molecules (Figure B.10). The 3.4 ppm <sup>1</sup>H chemical shift of the  $D6_{1,2}$  -OH moieties is characteristic of the coordination of the alcohol -OH moieties to Na+ cations that balance the negative framework charges, <sup>149</sup> as depicted schematically in Figure 3.3D. Within the detection limits of the NMR measurements, the <sup>27</sup>Al signal at 53 ppm is not correlated to <sup>1</sup>H signals from TMAda<sup>+</sup> molecules, indicating that the corresponding <sup>27</sup>Al species are not proximate (within ~0.5 nm for the short contact time used for the 2D  $^{27}$ Al<sup>1</sup>H HETCOR spectrum) to TMAda<sup>+</sup> molecules. On the basis of the synchrotron XRPD analysis, the Na<sup>+</sup> cations are sited primarily within the 8-membered ring channels. The 2D <sup>27</sup>Al<sup>1</sup>H HETCOR spectrum thus establishes the presence of two different types of <sup>27</sup>Al species: those charge-balanced by TMAda<sup>+</sup> headgroups within the 12-membered ring channels and those charge-balanced by Na<sup>+</sup> cations complexed with D6<sub>1.2</sub> -OH moieties, which are within the 8-membered ring channels. Complementary 2D <sup>29</sup>Si<sup>1</sup>H HETCOR analyses of HOU-4 support these conclusions and additionally show that the hydrophobic regions of the TMAda<sup>+</sup> and D6<sub>1,2</sub> OSDA molecules interact with siliceous  $Q^4(0Al)$ and  $Q^4(1Al)$  <sup>29</sup>Si species within the zeolite framework (Figure B.19).

The different TMAda<sup>+</sup> and  $D6_{1,2}$  OSDA molecules are intimately commingled and interact with each other within the mordenite zeolite framework, as determined by analysis of the 2D <sup>13</sup>C<sup>1</sup>H HETCOR spectrum of HOU-4 in Figure 3.3C. The 2D  $^{13}$ C<sup>1</sup>H HETCOR spectrum shows correlated signal intensities from intramolecular interactions of <sup>1</sup>H and <sup>13</sup>C moieties on the D6<sub>1,2</sub>, molecules (green shaded regions) and on the TMAda<sup>+</sup> molecules (red shaded regions). Additionally, the <sup>13</sup>C signals at 15, 24, 28, 34, 67, and 73 ppm from the six different <sup>13</sup>C atoms on the D6<sub>1,2</sub> molecules are each correlated with <sup>1</sup>H signals in the 2.6-3.3 ppm range, which arise from <sup>1</sup>H moieties on the TMAda<sup>+</sup> molecules (purple shaded regions). These correlated signal intensities establish unambiguously that D6<sub>1,2</sub> and TMAda<sup>+</sup> OSDA molecules interact with each other over nanoscale distances (<1 nm) within the mordenite zeolite nanochannels. We conclude that the different types of OSDA molecules are aggregated within the zeolite nanopores and likely act in tandem during the hydrothermal crystallization of the zeolite framework to direct the formation and stabilization of the large linear 12-membered rings that comprise the mordenite nanochannel system.

N,N-dimethyladamantamine (DMAda) forms from partial decomposition of TMAda<sup>+</sup> and is occluded within HOU-4. This is evidenced by the solid-state 1D <sup>13</sup>C MAS NMR spectrum of HOU-4 in Figure B.13, which shows <sup>13</sup>C signals at 15, 23, 29, 34, 67, and 73 ppm from 1,2-hexanediol as well as 31, 49, and 78 ppm from TMAda<sup>+</sup>. Additional weak <sup>13</sup>C signals at 46 and 58 ppm are assigned to <sup>13</sup>C species in DMAda,<sup>258</sup> consistent with the hydrothermal degradation of TMAda<sup>+</sup> via Hofmann elimination.<sup>259</sup> The quantitative <sup>13</sup>C NMR analysis indicates an approximate molar ratio of 1 DMAda : 2 TMAda<sup>+</sup> in HOU-4. DMAda is also present in the HOU-4 synthesis mixture, as established by the <sup>13</sup>C signals at 54, 44, 35, and 31 ppm in the solution-state 1D <sup>13</sup>C NMR spectrum of the synthesis mixture effluent in Figure B.18. While DMAda and TMAda<sup>+</sup> cannot be distinguished in the synchrotron XRPD analyses because of their similar molecular architectures, it is likely that DMAda and TMAda<sup>+</sup> occupy the same positions within the linear 12-ring mordenite channels in HOU-4. The removal of a methyl group on TMAda<sup>+</sup> would allow more easily

for accommodation of the alkyl tail of hexanediol, which may protrude into the 12ring channels.

### **B.2** Supplementary Tables

Samuela	Mo	olar Coi	mposition	n of Gr	owth Mixture	9	Т	Time	Zeolite
Sample	$Al(OH)_3$	$\mathrm{SiO}_2$	NaOH	$H_2$	TMAdaOH	$D6_{1}, 2$	(°C)	(d)	Structure
C1	0.052	1.0	0.2	44	0.1	1.6	180	6	$HOU-4^{(a)}$
C2	0.052	1.0	0.2	44	0.1	0.0	180	6	SSZ-13
C3	0.052	1.0	0.2	44	0.0	1.6	180	6	ZSM-5
C4	0.052	1.0	0.2	44	0.0	0.0	180	6	ZSM-5
C5	2.0	30	12	775	0.0	0.0	170	4	MOR
								_	

Table B.1: Synthesis conditions used to prepare zeolites

(a) Contains quartz impurity (see Figure B.6)

Table B.2: Elemental analysis and acidity of zeolite frameworks

Sampla	Si/Al	Si/Al	$\rm NH_3$ -TPD
Sample	(EDX)	(ICP)	( $\mu$ mol/g)
HOU-4	9.5	$16.0^{(a)}$	345
MOR	8.0	7.7	974
SSZ-13	11.6	<b>_</b>	— <b>-</b>
ZSM-5	11.7	— <b>-</b>	— <b>-</b>

(a) Contains quartz impurity (see Figure B.6)

Sample	Framework	Unit Cell	Molecular Wt/ Unit Cell	% Weight Loss	SDA/Unit Cell
SSZ-13	CHA	$\mathrm{NA}_3\mathrm{Al}_3\mathrm{Si}_{33}\mathrm{O}_{72}$	2228.52	10	$1.3~{ m TMAda^+}$
ZSM-5	MFI	$Na_8Al_8Si_{88}O_{192}$	5942.72	5	$2.7 \ \mathrm{D6_{1,2}}$
HOU-4	MOR	$\mathrm{Na_5Al_5Si_{43}O_{96}}$	2993.24	3.5	$0.6 \text{ TMAda}^{+(a)}$
				37	(b)

Table B.3: Framework OSDA per unit cell based on TGA analysis of washed samples

(a) Analysis of unwashed samples by <sup>13</sup>C NMR analysis reveals 1.1 - 1.5 TMAda<sup>+</sup> and 0.6 - 0.8 DMAda per unit cell (total of 1.7 - 2.3 TMAda<sup>+</sup>/DMAda per unit cell). PXRD analysis estimates 2 TMAda<sup>+</sup> per unit cell, but cannot distinguish between TMAda<sup>+</sup> and DMAda. (b) Thermogravimetric analysis of unwashed sample contains organics within zeolite pores and on exterior surfaces, rendering the determination of SDA/per unit cell difficult [This work was supported, in part, by the State of Texas through the Texas Center for Superconductivity at the University of Houston]

Sample	HOU-4		
<b>Chemical Composition</b>	$ Na_2(C_{13}H_{24}N)_{1.2}(C_{12}H_{21}N)_{0.6}(C_6H_{14}O_2)_{1.9}(H_2O)_2 [Al_{3.2}Si_{44.8}O_{96}] $		
Space Group	Cmcm		
a (Å)	17.9875(2)		
b (Å)	20.4609(3)		
c (Å)	7.4826(1)		
V (Å <sup>3</sup> )	2754		
λ (Å)	0.70847(1)		
2 heta range (°)	2.7-39.8		
HOU-4 : Quartz (wt %)	62.5:37.5		
<b>HOU-4</b> $R_I$	0.097		
Quartz $R_I$	0.050		
$R_{wp}$	0.235		
$R_{exp}$	0.009		
Observations	10298		
<b>Reflections (HOU-4)</b>	763		
Parameters	31 (framework)		
	13 (D <sub>1,2</sub> , water)		
	8 (TMAda <sup>+</sup> /DMAda)		
	13 (profile)		
	7 (quartz)		
<b>Geometric Restraints</b>	44(framework)		
	6 (D <sub>1.2</sub> )		

Table B.4: Crystallographic details for the refinement of the structure of HOU-4.

## **B.3** Supplementary Figures



Figure B.1: The MOR-type framework structure.

Figure B.1 shows the arrangement of the 12-ring channels, their 8-ring side pockets, and the parallel oval 8-ring channels in the MOR-type framework structure.



Figure B.2: SEM of ZSM-5 crystals and X-ray powder diffraction pattern from a growth mixture with molar composition C4.

Figure B.2 shows (A) Electron micrograph of ZSM-5 crystals obtained from a growth mixture with molar composition C4 (table B.1). (B) X-ray powder diffraction pattern of as-made ZSM-5 crystals (red marked) synthesized without organic (i.e., sodium was used as an inorganic structure-directing agent).



Figure B.3: SEM of ZSM-5 crystals and X-ray powder diffraction pattern synthesized in the presence of  $D4_{1,2}$ 

Figure B.3 shows (A) Electron micrograph of ZSM-5 crystals synthesized in the presence of 1.6 D41,2 : 1.0 SiO2. (B) Powder X-ray diffraction patterns of as-made products without alcohols (control: black, solution C4) and those in the presence of D6<sub>1,2</sub> (green, solution C3) and D4<sub>1,2</sub> (red, modified solution C3).



Figure B.4: SEM images of representative HOU-4 samples.

Figure B.4 shows (A - D) Representative low-resolution scanning electron micrographs of HOU-4 samples prepared from four separate batches using growth solution C1. The scale bars are equal to  $5 \,\mu$ m.



Figure B.5: The OSDAs their corresponding zeolite strucutre and their composite building units.

Figure B.5 shows the OSDA(s) (left column), corresponding zeolite structure (middle column), and composite building units (right column)<sup>143</sup> for (A) SSZ-13 (CHA), (B) ZSM-5 (MFI), and (C) HOU-4 (MOR).



Figure B.6: Quantitative Reference Intensity Ratio analysis on HOU-4.

Figure B.6 shows quantitative Reference Intensity Ratio (RIR) analysis was performed using (A) a series of XRPD patterns of physically mixed mordenite-quartz reference mixtures of increasing quartz weight %, followed by (B) interpolation of the sample (HOU-4, indicated in red) on the corresponding calibration curve. Analysis performed using the Integrated Powder X-ray Diffraction Software PDXL 2.2 (Rigaku Corporation), using mordenite (Zeolyst Int., CBV 10A) and ground white quartz sand (Sigma Aldrich) as reference materials. Mordenite (ICDD 01-081-8072, RIR = 0.65) and quartz (ICDD 01-085-0930, RIR = 3.15) were used as reference patterns. For the HOU-4 sample, the estimated weight percentage of quartz by the RIR method is 22 wt% (interpolated: 23 wt%).



Figure B.7: Thermogravimetric analysis and weight loss as a function of ramp up temperature of SSZ-13, ZSM-5, and HOU-4.

Figure B.7 shows (A) Thermogravimetric analysis (TGA) of washed SSZ-13 (blue), ZSM-5 (green), and HOU-4 (red) samples. (B) Derivative weight loss as function of ramp up temperature in TGA. The graphs correspond to the following samples synthesized using the compositions listed in table B.1: (black) SSZ-13 prepared with solution C2; (green) ZSM-5 prepared with solution C3; and (red) HOU-4 prepared with solution C1. (C) TGA of an unwashed HOU-4 sample.



Figure B.8: Synchrotron XRPD data of HOU-4 and Quartz impurity.

Figure B.8 shows (A) Synchrotron XRPD data displayed as the measured (blue), calculated (red), and difference profiles (gray) for the Rietveld refinement of the structure of HOU-4 with the quartz impurity included as a second phase. The contribution from HOU-4 is highlighted in blue in (B) and that from quartz in black in (C).



Figure B.9: Solid-State 1D <sup>13</sup>C{<sup>1</sup>H} CPMAS spectra of HOU-4, ZSM-5 and SSZ-13.

Figure B.9 shows solid-state 1D  ${}^{13}C^{1}H$  CPMAS spectra of (A) washed as-made HOU-4 synthesized with TMAda<sup>+</sup> and D6<sub>1,2</sub> as dual OSDAs, (B) washed ZSM-5 synthesized with D6<sub>1,2</sub> as the OSDA, and (C) washed SSZ-13 synthesized with TMAda<sup>+</sup> as the OSDA. The spectra were acquired at 11.7 T, 10 kHz MAS, 298 K, and with contact times of 2 ms. The spectrum in (A) shows only signals from TMAda<sup>+</sup> molecules, consistent with the removal of D6<sub>1,2</sub> molecules by the post-synthesis washing.



Figure B.10: Solid-state 2D <sup>13</sup>C{<sup>1</sup>H} correlation spectra of as-made HOU-4.

Figure B.10 shows solid-state 2D  ${}^{13}C^{1}H$  correlation spectra of as-made HOU-4 (same sample as Figure 3.3) acquired at 263 K, 11.7 T, 12.5 kHz MAS, and with  ${}^{13}C{}^{1}H$  contact time of (A) 0.5 ms and (B) 5 ms. All of the  ${}^{13}C$  signals are assigned to  ${}^{13}C$  moieties on the TMAda<sup>+</sup> and D6<sub>1,2</sub> molecules as indicated on the molecular structures in the inset. 1D  ${}^{13}C{}^{1}H$  CP-MAS or  ${}^{1}H$  spin-echo spectra acquired under the same conditions as the 2D spectra are shown along the corresponding  ${}^{13}C$  or 1H axes for comparison with the 1D projections of the 2D spectra. Correlated  ${}^{13}C{}^{1}H$  signal intensities that arise from the TMAda<sup>+</sup> molecules, D6<sub>1,2</sub> tail moieties, or D6<sub>1,2</sub> headgroup moieties are indicated with red, green, and blue boxes, respectively, while correlated signals arising from intermolecular interactions among the different OSDA molecules are indicated by purple boxes. The presence of correlated signals from intermolecular interactions establishes the mutual nanoscale proximities (<1 nm) of the D6<sub>1,2</sub> and TMAda<sup>+</sup> molecules.



Figure B.11: 3-D AFM height mode image of HOU-4 and Particle size distribution of HOU-4 crystals from multiple AFM samples.

Figure B.11 shows (A) 3-D AFM height mode image of a HOU-4 crystal that was extracted from a growth solution (after washing with DI water) and dried on a silicon wafer. (B) Particle size distribution of HOU-4 crystals from multiple AFM samples prepared from a single zeolite synthesis batch. The thickness measured along the [001] direction of ultrathin mordenite crystals was measured ex situ (in air) by AFM.


Figure B.12: The refined structure of HOU-4 and possible arrangements of nonframework species.

Figure B.12 shows the refined structure of HOU-4 showing (A) a possible arrangement of the non-framework species in the channels and cavities, (B) the TMAda<sup>+</sup>/DMAda species in the 12-ring channel, and (C) the Na+ ion in the oval 8-ring channel coordinated to 6 framework O atoms, one water molecule, and an O atom of  $D_{1,2}$ . The second O atom of  $D_{1,2}$  is within hydrogen bonding distance of two framework O atoms. For clarity, only the framework O atoms interacting with the non-framework species are shown.



Figure B.13: Solid-state quantitative single-puls 1D  $^{13}\mathrm{C}$  NMR spectrum of as-made HOU-4.

Figure B.13 shows solid-state quantitative single-pulse 1D  $^{13}$ C NMR spectrum of as-made HOU-4 (same sample as Figure 3.3 and Figure B.10), acquired at 11.7 T, 298 K, and 12.5 kHz MAS. The fit deconvolution is offset below the 1D spectrum. The relative integrated intensities of the different  $^{13}$ C NMR signals indicates a relative mole fraction of OSDA species to be 1 TMAda<sup>+</sup> : 6-13 D6<sub>1,2</sub>. The signal at 3.5 ppm arises from TKS, which was added as an internal spin counting reference to determine the absolute quantities of occluded OSDA molecules in HOU-4.



Figure B.14: MD calculated stabilization energy for organics occulded in MOR.

Figure B.14 shows MD calculations of the stabilization energy for organics occluded in mordenite as a function of  $D6_{1,2}$  loading at fixed TMAda<sup>+</sup> loadings of 1.0 (orange), 1.5 (blue), and 2.0 (grey) per unit cell. Solid lines are guides for the eye.



Figure B.15: MD rendering of  $D6_{1,2}$  and TMAda<sup>+</sup> inside the MOR channel.

Figure B.15 shows a rendering of a configuration from an MD simulation showing  $D6_{1,2}$  in the 12-ring channel of mordenite between adjacent TMAda<sup>+</sup> molecules (c-direction oriented to the right). The loadings for  $D6_{1,2}$  and TMAda<sup>+</sup> are both 1.5 per unit cell. Atoms are color coded as grey (carbon), red (oxygen), blue (nitrogen), white (hydrogen), and yellow (T-sites occupied by silicon/aluminum).



Figure B.16: 2D<sup>27</sup>Al triple-quantum MAS (3!MAS) spectrum of as-made HOU-4.

Figure B.16 shows (A) 2D <sup>27</sup>Al triple-quantum MAS (3QMAS) spectrum of asmade HOU-4 (same sample as Fig. 3 and figs. S10 and S13) acquired at 18.8 T, 298 K, and 20 kHz MAS. The inhomogeneously-broadened <sup>27</sup>Al spectrum exhibits a Czjzek lineshape, as corroborated in (B) by comparing a single-quantum (SQ) slice of the 2D 3QMAS spectrum extracted at a triple-quantum (TQ) shift of 57 ppm (black) to a simulated <sup>27</sup>Al Czjzek lineshape (dotted red). The simulated <sup>27</sup>Al spectrum is shown offset below in red. The fitted Czjzek parameters were a 1.4 ppm chemical shift FWHM and a maximum nuclear quadrupolar coupling constant (C<sub>Q</sub>) value of 1600 kHz. The simulation was performed using dmfit software.<sup>260</sup>



Figure B.17: 1D  $^{29}{\rm Si}$  spectra and  $^{29}{\rm Si}\{^{1}{\rm H}\}$  CP MAS NMR spectrum of calcined HOU- 4.

Figure B.17 shows 1D <sup>29</sup>Si spectra of calcined HOU-4 acquired at 11.7 T and 298 K: (A) quantitative single-pulse <sup>29</sup>Si NMR spectrum, acquired at 10 kHz MAS and with a recycle delay of 120 s for full spin-lattice relaxation of the <sup>29</sup>Si nuclei within the zeolite, and (B) <sup>29</sup>Si{<sup>1</sup>H} CP MAS NMR spectrum, acquired with a contact time of 5 ms, a recycle delay of 1 s, and at 5 kHz MAS. The <sup>29</sup>Si signal at -99 ppm arises from dilute partially-crosslinked  $Q^3$ (1Al) moieties that are likely associated with defect sites at the HOU-4 crystal surfaces.



Figure B.18: Solution state 1D  $^{13}\mathrm{C}$  NMR spectrum of the HOU-4 synthesis supernatant solution.

Figure B.18 shows solution state 1D  $^{13}$ C NMR spectrum of the HOU-4 synthesis supernatant solution, diluted with 10% D2O by volume. The  $^{13}$ C signals assigned to  $^{13}$ C moieties on the TMAda<sup>+</sup> and D6<sub>1,2</sub> molecules are labeled with red numbers and green Roman numerals, respectively, as indicated on the molecular structures in the inset. Signals assigned to decomposition products of TMAda<sup>+</sup> are indicated with asterisks. Based on their  $^{13}$ C shifts, all of the  $^{13}$ C signals from TMAda<sup>+</sup> decomposition products are assigned to dimethyladamantamine, DMAda. <sup>258</sup> From the relative integrated intensities of the  $^{13}$ C NMR signals, the supernatant solution contains TMAda<sup>+</sup>, adamantanol, and D6<sub>1,2</sub> at approximate molar ratios of 1 TMAda<sup>+</sup> : 2 DMAda : 50 D6<sub>1,2</sub>.



Figure B.19: Solid-state 2d  $^{29}$ Si $^{1}$ H} correlation spectra of HOU-4.

Figure B.19 shows solid-state 2D  $^{29}$ Si{<sup>1</sup>H} correlation spectra of HOU-4 (same sample as Figure 3.3 and Figures B.10, B.13, and B.16) acquired at 263 K, 11.7 T, 12.5 kHz MAS, and with  $^{29}$ Si{<sup>1</sup>H} contact times of (A) 0.2 ms and (B) 5 ms. 1D  $^{29}$ Si{<sup>1</sup>H} CP-MAS and <sup>1</sup>H spin-echo spectra acquired under the same conditions as the 2D spectra are shown along the horizontal and vertical axes, respectively, for comparison with the 1D  $^{29}$ Si and 1H projections of the 2D spectrum. Correlated  $^{29}$ Si{<sup>1</sup>H} signal intensities that arise from interactions with the TMAda<sup>+</sup> and D61,2 molecules are indicated with red and green boxes, respectively. All of the  $^{29}$ Si signals are correlated with all of the 1H signals from the different OSDA moieties, consistent with the mutual proximities (<1 nm) of the OSDA molecules within the nanopores of HOU-4.



Figure B.20: SEM images of modified HOU-4 synthesis using composition C1 and 3.0 OSDA to  $SiO_2$ .

Figure B.20 shows (A and B) Scanning electron micrographs of a modified HOU-4 synthesis using composition C1 (Table B.1) with an alteration in the quantity of OSDA (i.e., using a molar ratio of  $3.0 \text{ D6}_{1,2}$ :1.0 SiO<sub>2</sub>). (C) Corresponding XRPD pattern of as-made MOR product.



Figure B.21: SEM image of modified HOU-4 synthesis using composition C1 and 0.9  $\rm SiO_2$  to 1.44 OSDA

Figure B.21 shows (A and B) Scanning electron micrographs of a modified HOU-4 synthesis using composition C1 (Table B.1) with an alteration in the quantity of silica (i.e., using a molar ratio of 0.9 SiO<sub>2</sub>: 1.44 D6<sub>1,2</sub>). (C) Corresponding XRPD pattern of as-made mordenite (MOR) product.



Figure B.22: SEM images of modified HOU-4 synthesis using composition C1 with a 25% and 40% reduction in water.

Figure B.22 shows scanning electron micrographs of a modified HOU-4 synthesis using composition C1 (Table B.1) with an alteration in the quantity of water: (A) 25% reduction using a molar ratio of 33 H<sub>2</sub>O:1.0 SiO<sub>2</sub>; (B) 40% reduction using a molar ratio of 26.4 H<sub>2</sub>O:1.0 SiO<sub>2</sub>. (C) Corresponding XRPD pattern of as-made MOR products at lower water content.

![](_page_191_Figure_0.jpeg)

Figure B.23: SEM image of solids extracted from a synthesis with molar composition C2 modified with the diol  $D4_{1,2}$ 

Figure B.23 shows A) Scanning electron micrograph of solids extracted from a synthesis with molar composition C2 modified with the diol  $D4_{1,2}$  (Table B.1). (B) Corresponding XRPD pattern of the mordenite product which shows two impurities: SSZ-13 and quartz.

![](_page_192_Figure_0.jpeg)

Figure B.24: SEM image of conventional mordenite crystals.

Figure B.24 shows (A) Scanning electron micrograph of conventional mordenite crystals obtained using composition C5 with a molar ratio of 6 Na<sub>2</sub>O: 1 Al<sub>2</sub>O<sub>3</sub>: 30 SiO<sub>2</sub>: 780 H<sub>2</sub>O. (B) SEM image of mordenite crystals obtained using composition C5 with 1.6 D6<sub>1,2</sub>:1.0 SiO<sub>2</sub>. (C) XRPD pattern for conventional mordenite synthesis (bottom) compared to the same synthesis with the addition of D6<sub>1,2</sub> (top).

# **Appendix C:** Chapter 3 Supporting Information

# C.1 Supplementary Tables

	ZGM Name	<b>Fomula</b>	MW(gmol <sup>-1</sup> )	Structure	Average width/nm	Aspect ratio (L/D)
	Control				105.73	5.47
Alcohols	Ethanol	C <sub>2</sub> H <sub>6</sub> O	46.07	OH	178.64	7.35
	Ethylene glycol	$C_2H_6O_2$	62.07	HOHO	132.04	4.31
	1,2-Propanediol	$C_3H_8O_2$	76.09	OH	188.59	5.83
	1,3-Propanediol	$C_3H_8O_2$	76.09	но он	112.39	6.17
	1-Butanol	$C_4H_{10}O$	74.12	он он	132.85	8.00
	1,2-Butanediol	$C_4H_{10}O_2$	90.12	ОН	131.89	5.90
	1,4-Butanediol	$C_4H_{10}O_2$	90.12	ОН	128.72	8.43
	1,3-Butanediol	$C_4H_{10}O_2$	90.12	Стон	135.40	10.02
	1,6-Hexanediol	$C_6H_{14}O_2$	118.17	HO	130.51	7.85
	1,2-Hexanediol	$C_6H_{14}O_2$	118.17	H <sub>3</sub> C OH	125.23	6.44
	Glycerol	$C_3H_8O_3$	92.09		97.90	8.39
	1,2,6-Hexanetriol	C <sub>6</sub> H <sub>14</sub> O <sub>3</sub>	134.17	HOOH OH	127.12	7.76
Amines	TETA	C6H18N4	146.23	$H_{2N}$ $N_{N}$ $N_{N}$ $N_{N}$ $N_{N}$	154.24	4.92
	L-Lysine	C <sub>6</sub> H <sub>14</sub> N <sub>2</sub> O 2	146.19	H <sub>2</sub> N NH <sub>2</sub> OH	143.48	8.47
	L-Threonine	C4H9NO3	119.12		134.71	7.29
	Spermine	$C_{10}H_{26}N_4$	202.34	H <sub>2</sub> N N N	157.94	4.40
	THAM	$C_4H_{11}NO_3$	121.14		119.63	5.02
Polymers	PEIM			$H_2N \left( \begin{array}{c} & & & \\$	<sup>NH2</sup> 94.50	5.24
	PDDAC				175.95	9.95

### Table C.1: ZGMs screened for zeolite TON and size of resulted crystals

Sampla	DAO:	K <sub>2</sub> O:	$H_2O:$	Synthesis	Т	Time	Zaalita
Sample	$SiO_2$	$\mathrm{SiO}_2$	$SiO_2$	Synthesis	(°C)	(d)	Zeome
N-1	0.3	0.13	40	Rotation	160	3	TON
N-2	0.3	0.13	40	Rotation	160	14	TON
N-3	0.3	0.17	40	Rotation	160	3	MEL
N-4	0.3	0.13	40	Static	180	3	MEL
N-5	0.3	0.04	40	Static	160	3	Amorphous
N-6	0.3	0.04	40	Static	160	14	MEL
N-7	0.3	0.04	40	Static	160	31	MEL
N-8	0.3	0.03	40	Static	160	7	Amorphous
N-9	0.3	0.03	40	Static	160	14	MEL
N-10	0.3	0.03	40	Static	160	31	MEL
N-11	0.3	0.13	11	Rotation	160	3	MEL + TON
$N-12^{[a]}$	0.3	0.13	40	Rotation	160	1	Amorphous
$N-13^{[a]}$	0.3	0.13	40	Rotation	160	3	MEL
$N-14^{[b]}$	0.3	0.13	40	Rotation	160	3	Amorphous
$N-15^{[c]}$	0.3	0.13	40	Rotation	160	3	TON
$N-16^{[d]}$	0.3	0.13	40	Static	160	3	TON + MEL
$N-17^{[e]}$	0.3	0.13	40	Rotation	160	3	TON
N-18 <sup>[<math>d,e</math>]</sup>	0.3	0.13	40	Static	160	3	MEL

Table C.2: Parametric study of zeolite TON syntheses.

<sup>[a]</sup> synthesized with alternative Si source Ludox SM-30; <sup>[b]</sup> synthesized with alternative Si source potassium silicate; <sup>[c]</sup> rotation until the end of induction time (i.e., 17h) then static to 3d; <sup>[d]</sup> static for 17h then rotation to 3 d; <sup>[e]</sup> synthesized with alternative Si source Syton HT-50

#### C.2 Supplementary Figures

![](_page_195_Figure_1.jpeg)

Figure C.1: Comparison of zeolites LTL and TON.

Figure C.1 shows electron micrographs show the size and morphology of (A) TON and (B) LTL control crystals. TON crystals exhibit high length-to-width aspect ratio (AR) and broad size distribution with small spheroidal crystals (orange arrow) and high AR rods (white arrow). (C) Both zeolites exhibit one-dimensional channels along the c axis. (D) Summary of synthesis recipes of TON (red) and LTL (yellow) type crystals from literature (see Table S2 for a listing of references and corresponding synthesis conditions). Note that this is a truncated ternary phase diagram (i.e., only the top portion is demonstrated) that omits additional synthesis parameters (e.g., water content, temperature, OSDA, etc.).

![](_page_196_Figure_0.jpeg)

Figure C.2: Powder XRD patterns of PEIM modified zeolite LTL.

Figure C.2 shows reference patterns for zeolite LTL (International Zeolite Association) and impurity potassium aluminum silicate (KAlSi3O8, ICSD) are provided.

![](_page_196_Figure_3.jpeg)

Figure C.3: Morphology of zeolite TON modified by PDDAC

Figure C.3 shows (A) 0.2 wt%; (B) 0.5 wt%. Increased PDDAC concentration significantly altered zeolite crystal sizes and distributions.

![](_page_197_Figure_0.jpeg)

Figure C.4 shows the relationship between hydrophobicity and the aspect ratio of the zeolite LTL using different zeolite growth modifiers.

## **Appendix D:** Chapter 4 Supporting Information

### **D.1** Supplementary Figures

![](_page_198_Figure_2.jpeg)

Figure D.1: Representative adhesion force measurements for substrate solvent system

Figure D.1a shows representative approach-retraction profiles for adhesion force measurements. Figure D.1b shows a representative distribution of force measurements taken for a single loading rate, revealing a narrow distribution of force measurements. The data were fit with a Gaussian distribution.

![](_page_199_Figure_0.jpeg)

Figure D.2: Quantitative comparison of the interactions between AFM tips in contact with glass and  $\beta$ -hematin.

Figure D.2 shows quantitative comparison of the interactions between AFM tips, bare and modified, in contact with glass (open symbols) and  $\beta$ -hematin (closed symbols) in citric buffer-saturated octanol (CBSO). We observe a thermodynamic binding regime where the rupture force remains independent of the loading rate for Figure D.2a bare tips, Figure D.2b thiophenol I, Figure D.2c 1-butanethiol III, and Figure D.2d 3-mercapto-1-propanol IV.

![](_page_200_Figure_0.jpeg)

Figure D.3:  $\beta$ -hematin water and octanol system rendered from MD simulation.

Figure D.3 shows a rendering from molecular dynamics trajectories illustrating the presence of water nanodroplets in a 5% water/CBSO solution over the surface of  $\beta$ -hematin. Similar nanodroplets form over the glass surface. In some simulations, the nanodroplets adsorb and partially wet regions of the substrates (see Figure D.4).

![](_page_201_Picture_0.jpeg)

Figure D.4: Renderings from MD simulations of water near  $\beta$ -hematin and glass substrates.

Figure D.4 shows renderings from molecular dynamics trajectories highlighting the behavior of water in a ca. 5% water/CBSO solution near the solid substrates. (left) Water preferentially adsorbs in a uniform layer on the glass surface to form hydrogen bonds with exposed silanol groups. (right) Water forms small nanodroplets on the  $\beta$ -hematin surface that are large enough to span the ~1.5 nm gap between carboxyl groups on adjacent hydrophilic stripes. Octanol molecules have been omitted from the renderings for clarity.