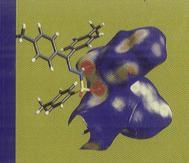
## ORGANIC CRYSTAL ENGINEERING

FRONTIERS IN CRYSTAL ENGINEERING







## **Contents**

	List of Contributors Preface					
1.	The Role of the Cambridge Structural Database in Crystal Engineering Andrew D. Bond					
	1.1	Introduction	1			
	1.2	Organisation and Management of Crystallographic Information	2			
		1.2.1 Validation of New Crystal Structures: Mogul	3			
		1.2.2 Validation of Structural Discoveries: What is New and What is Not?	5			
	1.3	Organisation of Crystallographic Information for Crystal Engineering	6			
		1.3.1 IsoStar	6			
		1.3.2 CSDContact	8			
		1.3.3 CSDSymmetry	10			
	1.4	New Tools for Database Research	13			
		1.4.1 A General Tool for 3-D Searches of the CSD: 3DSEARCH	13			
		1.4.2 Ad hoc Software	17			
	1.5	Search for Functional Group Exchanges: GRX				
	1.6	Search for Solvated and Unsolvated Structures: Solvates	20			
		1.6.1 Tools to Examine Structural Similarity	22			
	1.7	Clustering and Classifying CSD Search Results: dSNAP				
	1.8 The PXRD Profile as a Structural Descriptor		25			
		1.8.1 IsoQuest	26			
		1.8.2 Self-organising maps	28			
		1.8.3 Discrimination of polymorphs and redeterminations	30			
	1.9	Identifying Supramolecular Constructs: XPac	32			
	1.10	· S ·············				
	References					
2.		putational Crystal Structure Prediction: Towards In Silico Solid				
		n Screening me M. Day	43			
	2.1	Introduction	43			
	2.2	Methods used to Predict Crystal Structures	45			
		2.2.1 Search Methods	46			

		2.2.2	Evaluating the Computer-generated Crystal Structures	47			
	2.3	Curren	t Capabilities of Crystal Structure Prediction	48			
		2.3.1	The Blind Tests	48			
		2.3.2	Further Assessments of Crystal Structure Prediction	52			
		2.3.3	Flexible Molecules	57			
	2.4	Explor	ation of Crystal Forms. A Case Study: Carbamazepine	58			
		2.4.1	Polymorphism and the Influence of Small Molecular Changes on Packing	59			
		2.4.2	Solvate and Co-crystal Formation	61			
		2.4.3	Computational Solid Form Screening?	63			
	2.5	Summa	ary	64			
	Ackn	owledge	ments	64			
	Refer	ences		64			
3.	Multi-component Pharmaceutical Crystalline Phases: Engineering for Performance						
	Matthew L. Peterson, Edwin A. Collier, Magali B. Hickey, Hector Guzman						
		Ögn Alma	ursson				
	3.1	Introdu		67			
	3.2	-	ing Crystal Form Diversity	68			
	3.3		hroughput Experimentation	72			
	3.4	_	les of 'Form and Formulation'	75			
		3.4.1 3.4.2	Indinavir sulfate ethanolate – a case of a salt hydrate/solvate Norfloxacin – polymorphs, solvates, salts, complexes and	75			
	~ ~		co-crystals	77			
	3.5	AMG5 3.5.1	17 and Celecoxib – 'Spring and Parachute' Approach β-Lactam antibiotics and hydrates – the importance of	78			
	2 -	~ .	crystallinity	82			
	3.6	Carban	nazepine – Stabilization Against a Hydrate	83			
	3.7		nylline:Phenobarbital – Two is Better Than One	87			
	3.8		ridine Mesylate - Material Misbehaviour	90			
	3.9		ary and Outlook	91			
	Keier	ences		93			
4.		-	mation of Surfactants with Aromatic Compounds and	101			
	their Pharmaceutical Applications Yuji Ohashi, Keiju Sawada and Nahoko Iimura						
	4.1	Introdu		101			
	4.2		ires of the Complexes Formed Between Surfactants and				
			tic Compounds	103			
		4.2.1	Crystal structure of I (CTAB-p-hydroxybenzoic acid)	103			
		4.2.2	Crystal structure of II (CTAB-m-cyanophenol)	105			
		4.2.3	Crystal structure of III (CTAB-p-cresol)	105			
		4.2.4	Crystal structure of IV (CTAB-hydroquinone)	106			
		4.2.5	Crystal structure of V (CTAB-o-iodophenol)	107			

		4.2.6	Crystal structure of VI (MTAB-o-iodophenol)	107			
		4.2.7	Crystal structures of VII (LTAB-o-iodophenol) and VIII				
			(DTAB-o-iodophenol)	107			
		4.2.8	Crystal structure of IX (DTAB-p-hydroxybenzoic acid)	108			
	4.3		ex Formation of Aromatic Compounds Containing an Hetero				
		Ring		109			
		4.3.1	Crystal structures of X (CTAB-acridine), XI (CTAB-				
			phenoxazine) and XII (CTAB-phenothiazine)	109			
		4.3.2	Crystal structures of XIII (CTAB-dibenzofuran) and XIV				
			(CTAB-carbazole)	109			
	4.4		ex Formation of Biphenyl with Cationic Surfactants	110			
	4.5		ex Formation of Odd-Number Surfactants with Biphenyl	112			
	4.6		on Packing Mode in the Complexes	114			
	4.7		ex Formation by Grinding in a Mortar	117			
	4.8		$\pi$ interactions	122			
	4.9		ex Formation of Anionic Surfactants with Aromatic Compounds	125			
	4.10		ed Solubility of Insoluble Drugs	127			
	4.11		ced Thermal Stability of Perfumes	130			
	4.12		ex Formation with Surfactants other than Quaternary Alkylam-				
	1.10	moniur		134			
	4.13	-	quinone Complexes	136			
	4.14		ation to Whitening Agents	142			
	Refere	owledge:	ments	147			
	Kelen	ences		147			
5.	Hydrogen Bonding and Molecular Packing in Multi-functional Crystal						
	Structures						
	Ashwi	ini Nang	ria	151			
	5.1	Introdu	uction	151			
	5.2		gen Bonding in Ureas and Amides	154			
	5.3		Ureas and Amides	156			
	5.4		nenyl Ureas and Amides	160			
	5.5		ılar Conformation and Hydrogen Bonding	166			
	5.6		nolecular HSAB Interactions	182			
	5.7	gem-Al		184			
	5.8	Conclu		186			
	Ackno	owledge	ments	187			
		References 1					
6.	Persis	Persistence of N-HS Hydrogen Bonding in Thiocarbamide Structures 1					
		Persistence of N-HS Hydrogen Bonding in Thiocarbamide Structures 19 Edward R. T. Tiekink					
	6.1	Introdu	ection	191			
	6.2		polecular Aggregation Patterns in the Thiocarbamides	194			
		6.2.1	Cyclic thiocarbamides – five-membered rings	194			
		V.=.1	Cyone unocuroumaco inve memberea imas	エンコ			
		6.2.2	Cyclic thiocarbamides – six-membered rings	196			

	_	
v	- f ∩r	itents

		6.2.3	Acyclic thiocarbamides – E configuration	196	
		6.2.4	Acyclic thiocarbamides – Z configuration	201	
		6.2.5	Co-crystals containing thiocarbamides	206	
	6.3	Conclu	sions	206,	
	Refer	ences		211	
7.	Cryst	tal Engi	neering with Molecules Containing Amide and Pyridine		
		tionaliti		215	
	Kumo	ır Biradl	na and Lalit Rajput		
	7.1	Introdu	action	215	
	7.2	Primar	y Amides Containing a Pyridine Moiety	217	
		7.2.1	Amides directly linked to a pyridine moiety	218	
		7.2.2	Primary amide and pyridine linked by spacer units	220	
	7.3	Co-cry	stals with Primary Amidopyridines	220	
		7.3.1	Combination of amides for co-crystallization	223	
	7.4	Second	lary Amides Containing a Pyridine Moiety	224	
		<b>7.4.</b> 1	Monoamide and monopyridine derivatives	224	
	7.5	Bis-An	nidopyridine Derivatives	225	
		7.5.1	C-Terminal bis-amidopyridines	227	
		7.5.2	N-Terminal bis-amidopyridines (reverse amides)	229	
	7.6	Two-co	omponent Structures Containing Secondary Amides and Pyridine		
		Deriva	tives	231	
	7.7	Triami	dopyridine Derivatives	232	
		7.7.1	2-Pyridyl based systems	232	
		7.7.2	3-Pyridyl and 4-pyridyl based systems	233	
	7.8	Conclu	sions	234	
	Ackn	owledge	ments	236 236	
	References				
8.	Urea	/Thioure	ea-Anion Host Lattices, Stabilization of Labile Species, and		
	Desig	ned Co	nstruction of Rosette Ribbon and Layers	239	
	Thom	as C. W	. Mak, Chi-Keung Lam, Jie Han, Qi Li and Feng Xue		
	8.1	Introdu	action	239	
	8.2	Inclusi	on Compounds with Urea/Thiourea-Anion Host Lattices	241	
		8.2.1	Isostructurality Based on Interchangeability of Supramolecu-		
			lar Synthons	241	
		8.2.2	Carbonate and Oxalate as Prolific Hydrogen-Bond Acceptors	243	
		8.2.3	Hydrogen-Bonded Networks Constructed with		
			5-Nitrobarbiturate	247	
		8.2.4	Generation and Trapping of Labile Anions	257	
	8.3	zation of Cyclic Oxocarbon Dianions by Hydrogen Bonding with			
		Urea/Thiourea			
		8.3.1	Cyclic Oxocarbon Acids	265	
		8.3.2	Trapping Cyclic Oxocarbon Dianions in the Crystalline State	265	

				Contents	ΧI
		8.3.3	Charge-localized and -delocalized Valence Tautomeric	Forms	
			of Cyclic Oxocarbon Dianions		278
8	3.4	Suprar	nolecular Assembly Based on the Rosette Motif		289
		8.4.1	Anionic Rosette Ribbon Built of Guanidinium and Hy	drogen	
			Carbonate Dimer	Ü	289
		8.4.2	Anionic Rosette Networks Assembled with Guanidiniu	ım and	
			C <sub>3</sub> -symmetric Oxo-anion Building Blocks		293
		8.4.3	Anionic Rosette Layers Formed by Guanidinium and N	$Von-C_3$	
			Molecular Building Blocks		301
8	3.5	Conclu	sion and Outlook		306
A	Ackn	owledge	ements		307
I	References				307
Index	x				313