STRUCTURAL SCIENCE
CRYSTAL ENGINEERING
MATERIALS

Volume 73 (2017)

Supporting information for article:

Solid-state structure of cyclic dipeptides: an X-ray and computational study of *cis*- and *trans*-diketopiperazines of N-Methyl-Phenylalanine with the thia-pipecolic acids and thia-prolines

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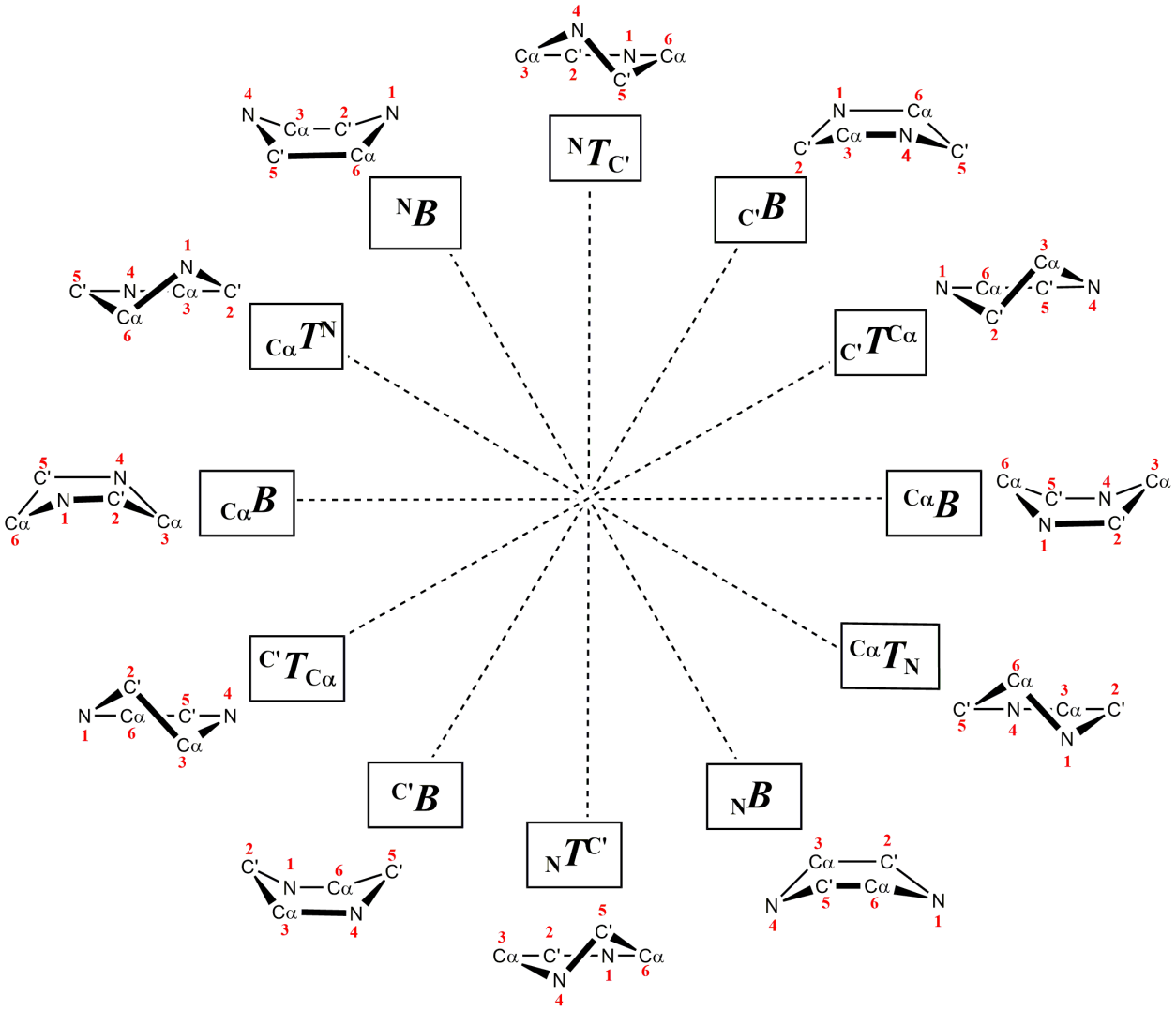

Figure S1

Scheme of pseudorotation pathway of diketopiperazine ring showing twist and boat conformations. Numbers (in red) correspond to the numbering of title compounds used in paper and shown in Figure 2.

Table S1

List of Ciarkowski's parameters *z*, *l*, *t* obtained from X-ray structures (in black) and from theoretical gas-phase geometries, as calculated with DFT (see computational details).

No.	Compound	Mol. No.	*z*	*l*	*t*
2A	**c(L-Pip-L-(NMe)Phe)**	1	-3.736	15.618	-10.561
		2	-3.300	16.405	-12.220
			-2.278	12.541	-4.269
2B	**c(D-Pip-L-(NMe)Phe)**		-3.900	20.013	-4.093
			-3.018	18.293	-6.974
4A	**c(L-(β-S)Pip-L-(NMe)-Phe)**	1	5.846	16.254	-5.702
		2	7.025	17.785	-8.571
			4.200	17.656	-7.290
4B	**c(D-(β-S)Pip-L-(NMe)-Phe)**		-15.768	-0.763	2.120
			-13.043	-1.187	2.083
6A	**c(L-(γ-S)Pip-L-(NMe)-Phe)**	1	-4.732	15.783	-10.223
		2	-3.168	16.993	-8.984
			-1.711	14.977	-5.539
6B	**c(L-(γ-S)Pip-D-(NMe)-Phe)**	1	3.796	-22.145	12.083
		2	7.093	-23.561	6.564
			5.432	-16.073	6.011
8A	**c(L-(δ-S)Pip-L-(NMe)-Phe)**	1	-1.139	19.334	-13.261
		2	-1.082	19.184	-12.819
			0.225	17.460	-6.797
8B	**c(D-(δ-S)Pip-L-(NMe)-Phe)**		-9.190	14.145	0.854
			-8.332	9.163	-3.852
10A	**c(L-Pro-L-(NMe)Phe)**		-9.097	9.221	-8.214
			-7.382	0.772	-6.524
10B	**c(L-Pro-D-(NMe)Phe)**		0.350	-30.439	-2.544
			-2.918	-31.385	-0.345
12A	**c(L-(β-S)Pro-L-(NMe)Phe)**		-4.254	12.929	-8.994
			-0.243	7.804	-8.641
12B	**c(D-(β-S)Pro-L-(NMe)Phe)**		-5.121	24.857	2.873
			-0.107	29.03	2.270
14A	**c(L-(γ-S)Pro-L-(NMe)-Phe)**		-6.036	10.732	-10.782
			1.025	15.773	-11.979
14B	**c(L-(γ-S)Pro-D-(NMe)-Phe)**	1	4.282	-19.487	4.275
		2	3.679	-21.401	2.250
		3	-2.050	-29.781	1.007
			-1.511	-28.995	2.335

Table S2

Deformation energies (see Computational details) of the solid state conformations of *cis* and *trans* N-methylated diketopiperazines in kcal/mol relative to the gas-phase fully optimized structures, providing a lower bound on estimated lattice energies (as suggested by a referee).

Compound	Molecule	E (gas) [Hartree]	E (solid) [Hartree]	E = (solid) – (gas) [kcal/mol]
2A	1	-881.96523838	-881.96498343	0.160
	2	-881.96523838	-881.96487176	0.230
4A	1	-1240.84474060	-1240.84471526	0.016
	2	-1240.84474060	-1240.84431297	0.268
6A	1	-1240.85158796	-1240.85136894	0.137
	2	-1240.85158796	-1240.85146960	0.074
8A	1	-1240.85016306	-1240.84984586	0.199
	2	-1240.85016306	-1240.84987777	0.179
2B		-881.96500061	-881.96496290	0.024
4B		-1240.84523200	-1240.84512694	0.659
6B	1	-1240.85041156	-1240.85014023	0.170
	2	-1240.85041156	-1240.84992034	0.308
8B		-1240.84915242	-1240.84864805	0.316
10A		-842.63233244	-842.63188558	0.280
12A		-1201.51649318	-1201.51604599	0.281
14A		-1201.52008341	-1201.51980500	0.175
10B		-842.63669449	-842.63662412	0.044
12B		-1201.51843200	-1201.51829709	0.847
14B	1	-1201.52150185	-1201.52095321	0.344
	2	-1201.52150185	-1201.52122754	0.172
	3	-1201.52150185	-1201.52139720	0.066