Appendix B

Results of Multiple Surface Alignment

This appendix contains the numerical results from Chapter 6.

The tables in this appendix have to be read as follows. The reference molecule is given in the first column, and each row contains a single multiple alignment of the query molecules with the experimental conformer of the reference molecule. Each table entry gives the rms (root mean square) distance of the aligned query molecule to its experimental conformer.

In order to allow to quickly grasp the main information given by each table, the following colors were used for highlighting:

- green: rms distances between 1.0 and 2.0 Å.
- blue: rms distances between 2.0 and 4.0 Å.
- red: rms distances above 4.0 Å.

Furthermore, the entry "xx" denotes that the respective structure could not be aligned at all.

The relative minimum size $minSize_{\text{rel}}$ has been defined in Definition 6.2.9.

For a detailed discussion of the tables we refer the reader to Section 6.4.

B.1 Thermolysin Inhibitors

B.1.1 Experimental Conformers

Table B.1: Rms distances (in Å) of best multiple surface alignment based on pairwise surface alignments from experiment 2a (Table A.7). $minSize_{\text{rel}} = 0.4$.

	1THL	1TLP	1TMN	3TMN	5TLN	4TMN	5TMN	6TMN
1THL	–	0.53	0.26	0.27	0.93	0.42	0.64	0.89
1TLP	0.54	–	0.90	0.87	0.83	0.75	1.01	1.01
1TMN	0.23	0.97	–	0.42	0.58	0.58	0.82	0.83
3TMN	0.30	1.18	0.39	–	1.30	0.73	0.73	0.85
5TLN	0.79	0.85	0.54	1.76	–	0.71	0.55	0.69
4TMN	0.40	0.84	0.44	0.49	0.75	–	0.27	0.52
5TMN	0.52	0.93	0.56	0.55	0.85	0.41	–	0.22
6TMN	0.83	0.80	0.60	0.77	0.54	0.58	0.24	–

Table B.2: Rms distances (in Å) of best multiple atom alignment based on pairwise atom alignments from experiment 3 (Table A.11). $minSize_{\text{rel}} = 0.4$.

	1THL	1TLP	1TMN	3TMN	5TLN	4TMN	5TMN	6TMN
1THL	–	1.15	0.46	0.52	0.87	1.28	1.45	1.42
1TLP	0.71	–	1.00	0.80	0.85	1.26	1.34	1.28
1TMN	0.37	1.25	–	0.28	1.15	0.90	1.15	1.11
3TMN	0.43	1.25	0.34	–	1.13	1.46	1.02	0.95
5TLN	2.04	0.83	1.96	1.25	–	1.57	2.06	2.05
4TMN	0.55	0.94	0.36	0.68	0.76	–	0.71	0.71
5TMN	1.15	0.95	0.94	0.70	1.07	0.60	–	0.14
6TMN	1.10	0.91	0.92	0.76	1.03	0.58	0.14	–

B.1.2 Ensemble of Conformers

Table B.3: Rms distances (in Å) of best multiple surface alignment based on pairwise surface alignments from experiment 4 (Table A.12). $minSize_{\text{rel}} = 0.4$.

	1THL	1TLP	1TMN	3TMN	5TLN	4TMN	5TMN	6TMN
1THL	–	0.97	0.36	0.26	1.80	1.07	1.01	1.16
1TLP	0.85	–	0.63	xx	2.41[a]	1.53	1.20	1.01
1TMN	0.51	0.72	–	xx	2.45[a]	1.32	0.36	0.51
3TMN	xx	xx	xx	–	xx	xx	xx	xx
5TLN	1.29	0.95	0.64	xx	–	1.25	0.99	3.34[b]
4TMN	0.56	0.86	0.49	xx	2.60[a]	–	0.54	0.61
5TMN	1.98[c]	1.19	1.42	xx	0.97	0.96	–	0.48
6TMN	0.62	0.76	0.52	xx	2.72[a]	1.34	0.41	–

[a] Large rms is due to the wrong orientation of the terminating imino-hydroxyl moiety.
[b] Large rms is due to the wrong orientation of the bencyloxycarbonyl (CBZ) moiety.
[c] Large rms is due to the wrong orientation of the indole moiety.

Table B.4: Rms distances (in Å) of best multiple atom alignment based on pairwise atom alignments from experiment 5 (Table A.13). $minSize_{\text{rel}} = 0.4$.

	1THL	1TLP	1TMN	3TMN	5TLN	4TMN	5TMN	6TMN
1THL	–	1.00	0.56	0.44	5.90*	1.34	1.17	1.80
1TLP	1.11	–	0.91	0.87	1.46	1.70	1.20	1.29
1TMN[b]	0.57	0.77	–	0.31	1.51	4.93[a]	1.24	1.78
3TMN	xx	xx	xx	–	xx	xx	xx	xx
5TLN	xx	1.11	3.32	xx	–	xx	1.46	3.74
4TMN[c]	0.68	0.92	0.44	1.92	xx	–	0.60	0.87
5TMN	1.02	0.84	0.94	xx	1.39	0.79	–	0.41
6TMN	1.19	0.86	0.97	0.83	1.31	0.80	0.56	–

* Miss-alignment.
[a] Large rms is due to the wrong orientation of the bencyloxycarbonyl (CBZ) moiety.
[b] Represents a good alignment, however, no alignment could be found, that positions the negatively charged binding to the zinc ion, closely to each other.
[c] Very good alignment, except for 5TLN, which could not be successfully aligned.
[d] Large rms is due to the wrong orientation of the terminating imino-hydroxyl moiety.

B.2 HIV-1 Protease Inhibitors

B.2.1 Experimental Conformers

Table B.5: Rms distances (in Å) of best multiple surface alignment based on pairwise surface alignments from experiment 7a (Table A.21). $minSize_{\text{rel}} = 0.35$.

	SQV	IDV	APV	NFV	RTV	LPV	TPV
SQV	–	0.86	0.85	0.49	1.07	0.51	0.76
IDV	1.05	–	0.66	0.58	0.98	0.61	1.40
APV	0.63	0.73	–	0.84	0.74	0.45	0.95
NFV	0.51	0.62	0.87	–	0.82	0.46	0.59
RTV	1.27	0.95	0.83	0.86	–	0.85	0.90
LPV	0.73	0.78	0.68	0.51	0.94	–	0.89
TPV	1.06	0.85	0.63	0.47	0.77	0.90	–

Table B.6: Rms distances (in Å) of best multiple atom alignment based on pairwise surface alignments from experiment 8 (Table A.26). $minSize_{\text{rel}} = 0.35$.

	SQV	IDV	APV	NFV	RTV	LPV	TPV
SQV	–	2.06	1.18	2.06	2.60	1.74	1.06
IDV	2.30	–	1.47	1.49	2.39	1.63	1.81
APV	2.09	1.99	–	1.54	2.63	1.76	xx
NFV	2.08	1.89	1.49	–	1.95	1.22	2.14
RTV	1.55	1.67	1.20	1.42	–	1.22	1.35
LPV	1.61	1.72	1.12	1.40	1.84	–	xx
TPV	2.35	1.70	3.64	1.03	3.02	5.60	–

B.2.2 Ensemble of Conformers

Table B.7: Rms distances (in Å) of best multiple surface alignment based on pairwise surface alignments from experiment 9 (Table A.27). $minSize_{\text{rel}} = 0.3$.

	SQV	IDV	APV	NFV	RTV	LPV	TPV
SQV	–	0.73	1.55	0.84	1.32	1.07	0.81
IDV	1.07	–	1.32	0.80	5.91[a]	0.84	1.11
APV	1.52	0.52	–	1.38	0.91	0.83	xx
NFV	1.27	0.49	1.23	–	1.18	0.71	4.30[b]
RTV	1.13	0.64	1.28	0.82	–	1.26	1.38
LPV	1.09	0.55	1.19	0.94	1.19	–	1.51
TPV	2.62	2.21	2.23	2.77	2.76	0.64	–

[a] One half fits very well. In the other half, there is a twist in one of the central bonds such that two moieties are interchanged.
[b] The large difference in the rmsd is mainly due to the terminating fluoric moiety, which in this alignment sticks out of the active site.

Table B.8: Rms distances (in Å) of best multiple atom alignment based on pairwise atom alignments from experiment 10 (Table A.28). $minSize_{\text{rel}} = 0.3$.

	SQV	IDV	APV	NFV	RTV	LPV	TPV
SQV	–	1.09	1.42	0.76	1.18	0.94	xx
IDV	1.20	–	1.73	0.64	1.17	0.63	xx
APV	0.91	1.21	–	1.11	1.26	2.43**	xx
NFV	0.87	0.72	1.64	–	1.20	0.94	xx
RTV	1.57	1.46	1.97	1.47	–	1.22	xx
LPV	1.02	0.65	1.60	0.95	1.46	–	xx
TPV	xx	xx	xx	xx	xx	xx	–

** Correct general orientation.