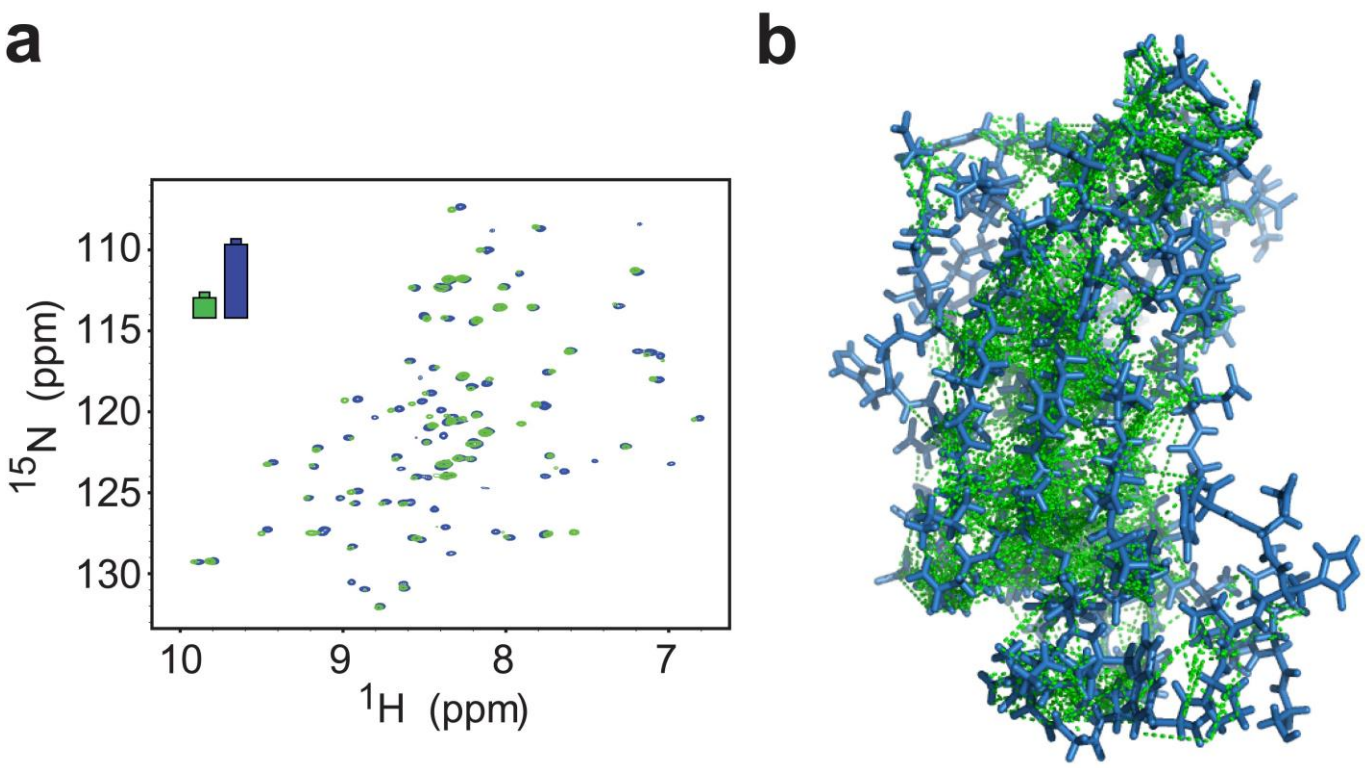
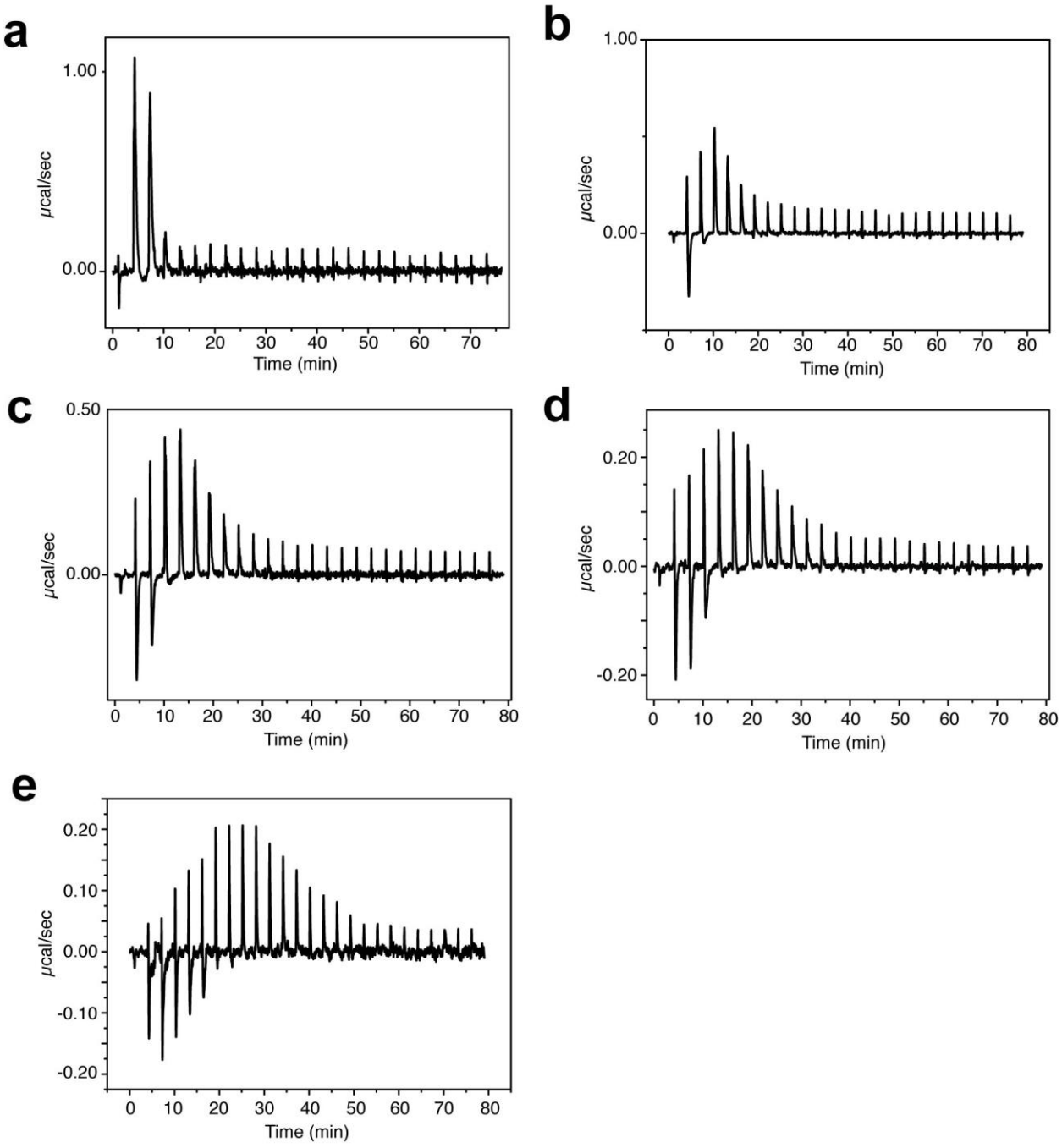


Supplementary Figure 1

The structure of the misfolded monomeric conformation of TTR is well defined.

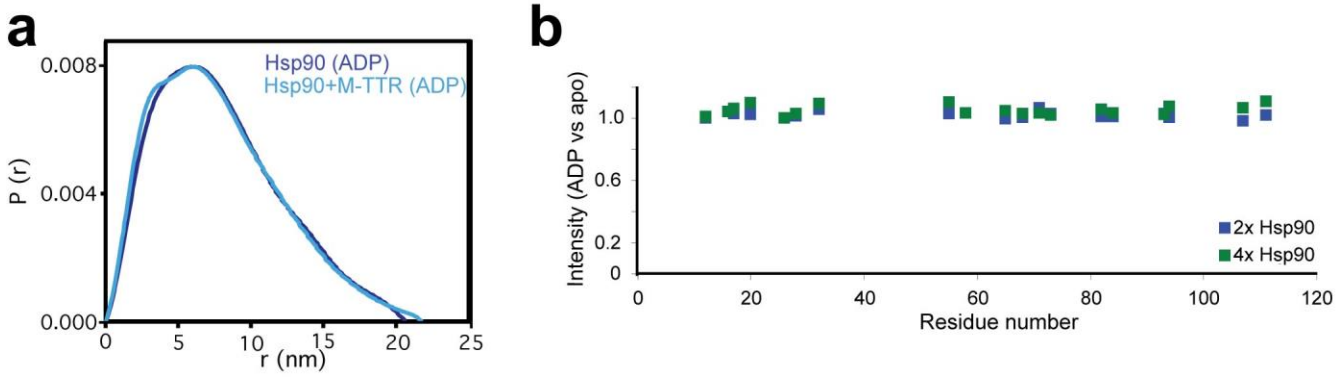
(**a**) Comparison of ^{1}H-^{15}N NMR spectra of M-TTR at ambient pressure (green) and 500 bar (blue). Working at 500 bar improves the spectral quality. (**b**) Experimentally observed NOEs (green dotted lines) are visualized on the 3D structure of M-TTR (blue).



Supplementary Figure 2

Reproducibility in calorimetric titrations of Hsp90 with M-TTR.

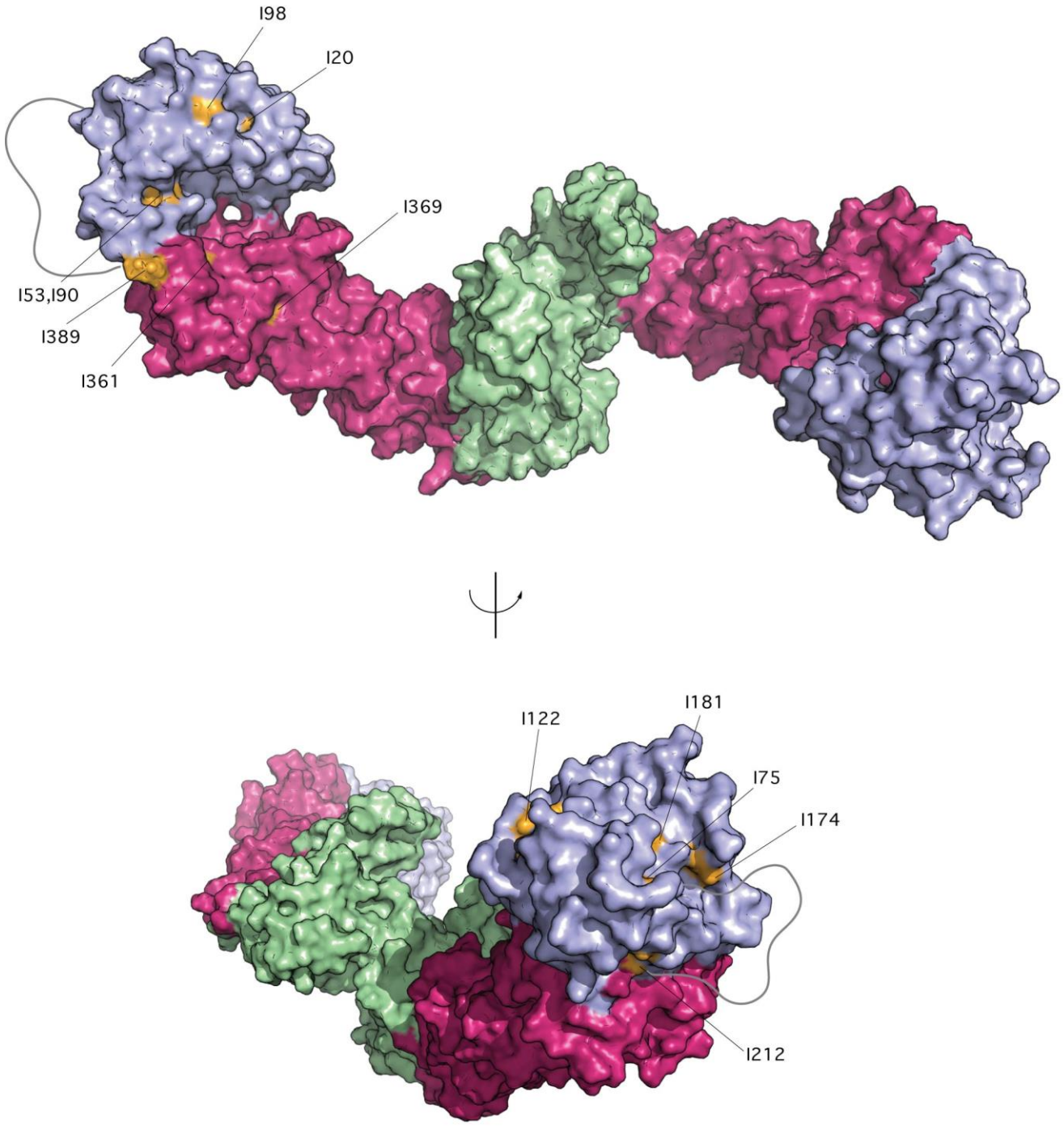
From left to right and top to bottom, raw data resulting from the titration of 25x1.5 µl aliquots of 1671 µM of M-TTR into 25 µM of Hsp90 (**a**), 783 µM of M-TTR into 30 µM of Hsp90 (**b**), 520 µM of M-TTR into 30 µM of Hsp90 (**c**), 313 µM of M-TTR into 25,5 µM of Hsp90 (**d**) and 166 µM of M-TTR into 22,75 µM of Hsp90 (**e**) are shown. The biphasic thermodynamic behavior was present in all tested conditions.



Supplementary Figure 3

Nucleotide binding does not promote allosteric changes in the Hsp90–M-TTR complex.

(**a**) As observed from the P(r) distribution obtained from SAXS scattering data, ADP binding does not change the global extended conformation of the Hsp90/M-TTR complex. While Hsp90 shows R_g= 6.34 ± 0.16 nm and D_{MAX}= 20.94 ± 0.52 nm, the Hsp90+M-TTR complex has R_g= 6.58 ± 0.44 nm and D_{MAX}= 21.77 ± 0.71 nm. (**b**) Comparison of NMR signal intensities of the methyl signals of M-TTR/Hsp90 in the absence and presence of 2 mM ADP. Samples contained 0.07 mM ^{13}C-labeled and methyl-protonated M-TTR in 50 mM MES, pH 7, 100 mM NaCl, 5 mM DTT, 1 mM $MgSO_4$, 0.1 mM DSS, and a 2-fold (blue) or 4-fold (green) molar excess of Hsp90.



Supplementary Figure 4

Hsp90 uses several binding interfaces to bind M-TTR.

Residues in the N- and M-domain of Hsp90, which show the strongest PCSs in the presence of M-TTR, are highlighted in orange in the 3D structure. Hsp90's N-domain is colored in light blue, M-domain in red and C-terminal domain in light green. The charged linker, which connects Hsp90's N and M domain, is represented by a grey line.

Supplementary Table 1. Binding properties of M-TTR and Hsp90 obtained by ITC.

	First phase	Second phase
Kd (μM)	0.3 (± 0.7)	47.3 (± 4.9)
ΔH (kcal mol^{-1})	-7.99 (± 0.36)	19.10 (± 0.99)
$T\Delta S$ (kcal mol^{-1})	0.19	2.26