

Table S1. Correlated motions found in the apo and holo form of *Tth*-MCO and corresponding bonded or non-bonded interactions.

Secondary structure	Interactions
Domain 1	
loop ($\beta 1$ - $\beta 2$)/loop ($\beta 4$ - $\beta 5$) ^a	HB:D78(sc)-S35(sc)-G37(bb), R75(sc)-Q36(sc)
loop ($\beta 3$ - $\beta 4$)/loop ($\alpha 1$ - $\beta 9$) ^a	VdW:L151(bb)-F67(sc), HB:L151(bb)-G69(bb)
$\beta 1$ /loop ($\beta 5$ - $\beta 6$) ^a	SB:K43(sc)-E85(sc), HB:E85(bb)-S45(bb)-A46(bb)
$\beta 4$ /($\alpha 1$) ^a	SB: R73(sc)-E157(sc), HB:R73(bb)-E157(bb)
$\beta 5$ / $\beta 7$ ^a	SB:R81(sc)-E121(sc), HB:W118(bb)-Leu84(bb), Y120(bb)-L82(bb), T119(bb)-T83(bb)
loop ($\beta 5$ - $\beta 6$)/ loop ($\beta 8$ - $\alpha 1$) ^a	SB:E90(sc)-R141(sc), HB:L138(bb)-T92(bb), H137(bb)-N93(bb)
$\alpha 2$ - $\alpha 3$ -helix _{D1-D2} / (loop($\beta 24$ - $\beta 25$) _{D2-D3}) ^b	VdW:L327(sc)-E168(bb), L160(sc)-L333(bb), I163(sc)-L333(bb), P164(sc)-P330(sc), HB:E165(sc)-K331(bb).
Domain 2	
$\beta 10$ / $\beta 15$ ^a	SB:E171(sc)-R221(sc), E171(sc)-R223(sc), HB:T219(bb)-E170(bb), L176(bb)-L225(bb), R221(bb)-H172(bb), R223(bb)-H172(bb), VdW:L224(sc)-L174(sc), L222(sc)-H172(bb)
$\beta 10$ / loop ($\beta 15$ - $\beta 16$) ^b	SB: D178(sc)-R231(sc), 1VdW:L176(bb)-A227(bb), HB:S228(sc)-D178(bb)
$\beta 17$ /(loop($\beta 24$ - $\beta 25$) _{D2-D3}) ^b	VdW:L329(sc)-T243(sc), L333(sc)-I245(sc)
$\beta 15$ / $\beta 20$ ^b	SB: R221(sc)-E270(sc), R223(sc)-E270(sc),VdW:L225(bb)-R268(bb), HB:L224(bb)-A269(bb), L222(bb)-V271(bb), L220(bb)-V273(bb)
$\beta 16$ / loop ($\beta 18$ - $\beta 19$) ^b	SB:R234(sc)-E260(sc)
loop ($\beta 20$ - $\beta 21$) / (loop($\beta 24$ - $\beta 25$) _{D2-D3}) ^b	VdW:P324(sc)-L275(bb), HB:E278(sc)-N323(sc)
loop ($\beta 17$ - $\beta 18$)/ $\beta 20$ ^a	SB:D248(sc)-K268(sc)
loop ($\beta 17$ - $\beta 18$)/ loop ($\beta 31$ - $\beta 32$) _{D3} ^b	SB:D248(sc)-K418(sc), HB:G249(bb)-W417(bb)
Domain 3	
$\beta 25$ / $\beta 28$ ^a	SB:R346(sc)-E381(sc), R347(sc)-E384(sc), R347(sc)-E386(sc),VdW:V349(bb)-E386(bb), L350(bb)-R387(bb), W383(bb)-Arg346(bb)
loop ($\beta 28$ - $\beta 29$)/loop ($\beta 32$ - $\beta 33$) ^a	SB:D392(sc)-K424(sc), HB:K424(bb)-G389(bb), A425(bb)-Q388(bb)
$\beta 28$ / $\beta 33$ ^a	SB:E384(sc)-R430(sc)
loop ($\beta 29$ - $\beta 30$) /loop($\beta 33$ - $\beta 34$) ^a	SB:H400(sc)-E437(sc)
$\beta 29$ / $\beta 32$ ^b	HB :L423(bb)-H393(bb)
$\beta 29$ /($\alpha 5$) ^b	Π :H393(sc)-Cu463-H450(sc)
$\beta 34$ / $\beta 35$ ^a	SB:R440(sc)-E460(sc), HB:V461(bb)-G439(sc)
$\beta 27$ / $\beta 35$ ^a	SB: K374(sc)-E460(sc), HB: L373(bb)-E460bb), G375(bb)-E460(bb)

HB, hydrogen bond; SB, salt bridge; VdW, van der Waals interactions; Π , pi interactions; sc, side-chain; bb, backbone. $\alpha 2$ - $\alpha 3$ -helix_{D1-D2} = linker between the domain 1 and 2, loop($\beta 24$ - $\beta 25$)_{D2-D3}= linker between the domain 2 and 3. Found for both systems^a, found only for holo*Tth*-MCO^b.