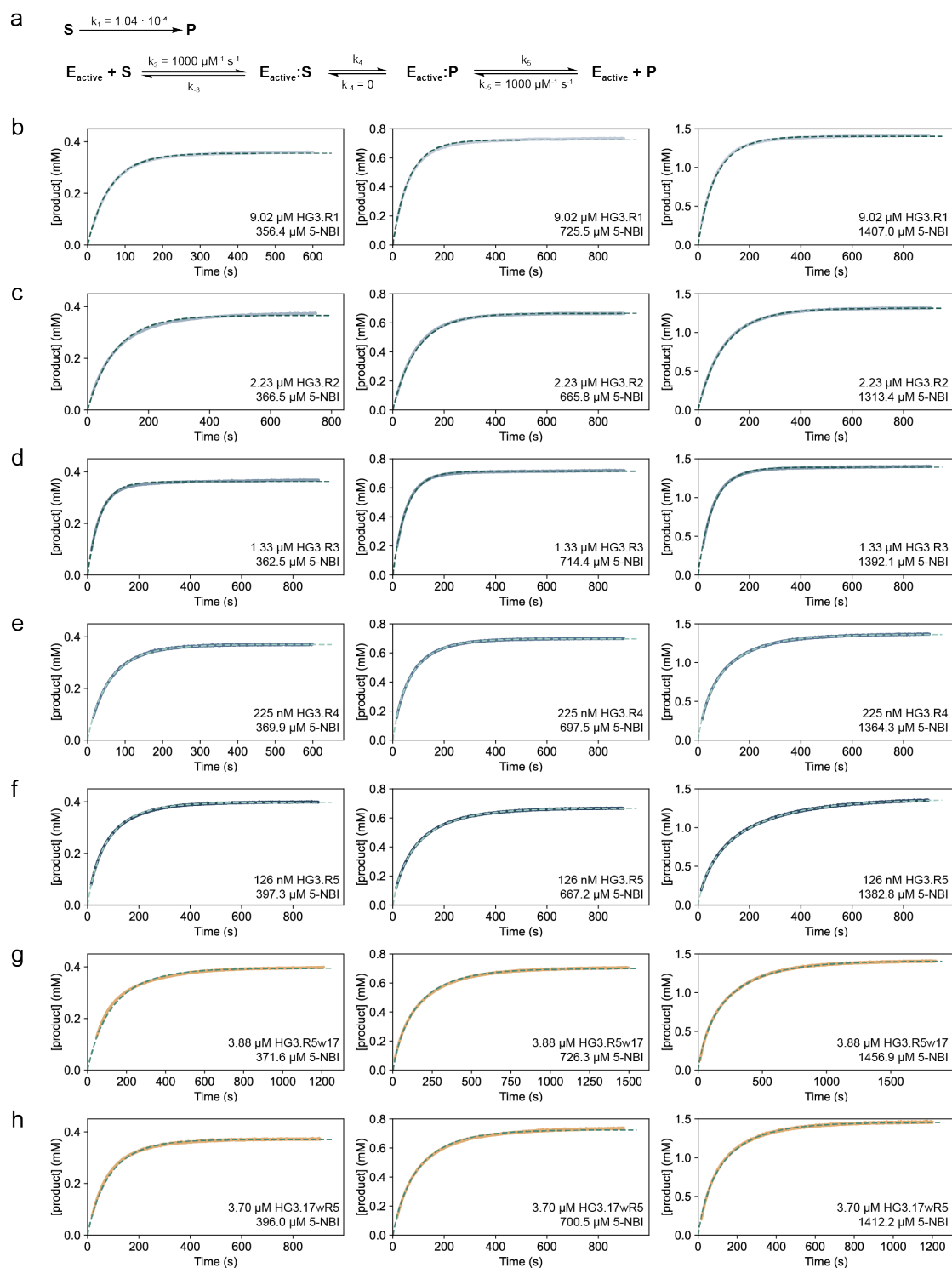


Enriching productive mutational paths accelerates enzyme evolution

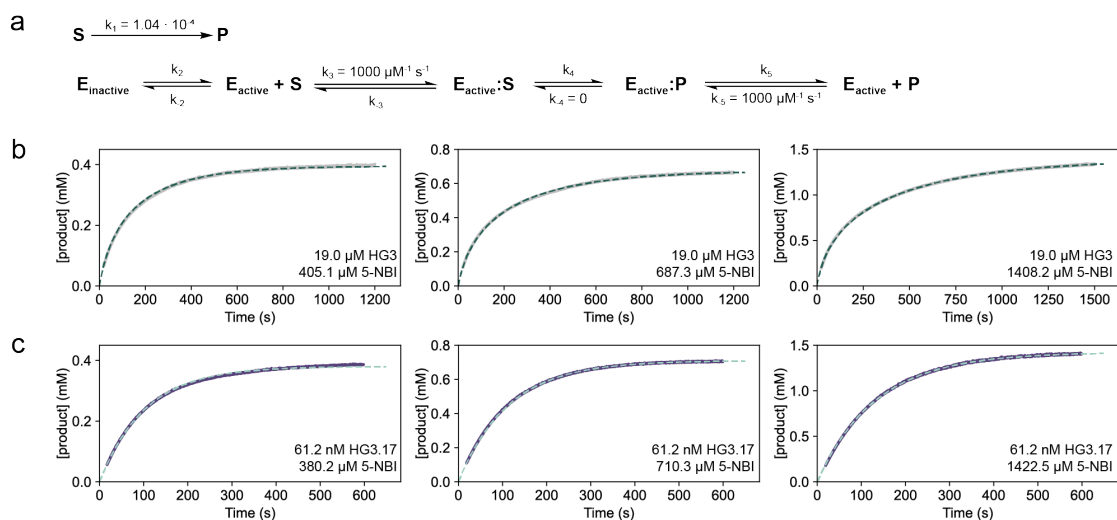
In the format provided by the
authors and unedited

Table of contents:

Supplementary Fig. S1 Progress curves of product formation.	2
Supplementary Fig. S2 Progress curves of product formation.	3
Supplementary Table S1 X-ray crystallographic data collection and refinement statistic	4
Supplementary Table S2 Energies of cluster model QM optimized structures.	5
Supplementary Table S3 Energies, entropies, and lowest frequencies of QM/MM optimized structures.....	6
Amino acid sequences of the HG3 variants	7
Nucleotide sequences of HG3 variants	9
Cartesian coordinates of cluster model QM structures calculated with PCM(H ₂ O)/M06-2X/6-31G(d)	12
Python script for $\Delta\Delta G$ predictions with PyRosetta	28
SI References	32



Supplementary Fig. S1 | Progress curves of product formation. (a) The kinetic scheme used for fitting the progress curves including the spontaneous product (5-NBI, 5-nitrobenzisoxazole) formation. Numeric fitting of the total time course data for 5-nitrobenzisoxazole conversion by variants HG3.R1 (b), HG3.R2 (c), HG3.R3 (d), HG3.R4 (e), HG3.R5 (f), HG3.R5w17 (g) and HG3.17wR5 (h). Fitting was performed as described in the Materials and Methods section and the steady-state parameters for k_{cat} and K_m were calculated according to equations E1 and E3.



Supplementary Fig. S2 | Progress curves of product formation. (a) The kinetic scheme used for fitting the progress curves including the spontaneous product (5-NBI, 5-nitrobenzisoxazole) formation. Numeric fitting of the total time course data for 5-nitrobenzisoxazole conversion by HG3 (b), HG3.17 (c). The reaction rates determining the conformational selection step (k_1 and k_{-1}) were obtained from Otten et. al.¹ (For HG3: $k_2^{\text{HG3}} = 2.32 \cdot 10^{-4} \text{ s}^{-1}$ and $k_{-2}^{\text{HG3}} = 8.12 \cdot 10^{-5} \text{ s}^{-1}$; For HG3.17: $k_2^{\text{HG3.17}} = 16.7 \cdot 10^{-4} \text{ s}^{-1}$ and $k_{-2}^{\text{HG3.17}} = 6.68 \cdot 10^{-5} \text{ s}^{-1}$). The fitting was performed as described in the Materials and Methods section and the steady-state parameters for k_{cat} and K_{m} were calculated according to equations E1 and E2

Supplementary Table S1 | X-ray crystallographic data collection and refinement statistic

Kemp variant HG3.R5	
Values in () are for highest-resolution shell	
Data collection	
Space Group	P 1
Cell dimensions:	
a, b, c (Å)	44.41, 50.07, 65.58
α, β, γ (°)	100.72, 102.70, 99.30
No. unique reflections	81699 (3878)
Resolution (Å)	48.08 – 1.50 (1.50 - 1.53)
R meas	0.079 (0.255)
R pim	0.056 (0.180)
CC1/2	0.995 (0.957)
Mean(I)/sd(I)	12.7 (6.8)
Completeness (%)	96.4 (91.9)
Redundancy	3.3 (3.3)
Wilson B-factor (Å ²)	7.1
Refinement	
Resolution (Å)	43.20 – 1.50
No. reflections all / free	81698 / 4133
Rwork / RFree	0.103 / 0.142
No. atoms	10071
Protein	9427
Ligand/ion	137
Water	507
B-factor	
Protein	7.88
Ligand/ion	17.65
Water	21.87
R.m.s deviations	
Bond lengths (Å)	0.0117
Bond angles (°)	1.65
Clashscore	3
Ramachandran favoured (%)	98.5
Ramachandran outliers	0
PDB entry	8RD5

Supplementary Table S2 | Energies of cluster model QM optimized structures.

	E_{QM} (Hartree) ^b
1 -w _e (QM)	−3534.745450
1 -w _e TS (QM)	−3534.725458
1 (QM)	−3458.339108
1 TS (QM)	−3458.318147
1 -Q50A-w _e (QM)	−3366.078240
1 -Q50A-w _e TS (QM)	−3366.056004
1 -Q50A (QM)	−3289.671991
1 -Q50A TS (QM)	−3289.648237

^a 1 Hartree = 627.51 kcal mol^{−1}

^b Calculated with PCM(H₂O)/M06-2X/6-31G(d).

Supplementary Table S3 | Energies, entropies, and lowest frequencies of QM/MM optimized structures.

	E_{ONIOM} (Hartree) ^b	$E_{\text{ONIOM}} + \text{ZPE}$ (Hartree) ^b	H (Hartree) ^b	S (cal mol ⁻¹ K ⁻¹) ^b	G (Hartree) ^b	Lowest freq. (cm ⁻¹)	# of imag. freq.
1-we (QM/MM)	-1282.034362	-1243.500511	-1241.213510	9398.5	-1245.678078	8.9	0
1-we TS (QM/MM)	-1282.022539	-1243.494585	-1241.206694	9397.5	-1245.671736	-837.4	1
1 (QM/MM)	-1205.622724	-1167.11442	-1164.829116	9387.2	-1169.289268	9.2	0
1 TS (QM/MM)	-1205.610497	-1167.10768	-1164.822647	9385.0	-1169.281770	-713.1	1

^a 1 Hartree = 627.51 kcal mol⁻¹. Thermal corrections at 298.15 K.

^b Calculated with ONIOM(M06-2X/6-31+G(d):ff14SB,gaff2,TIP3P).

Amino acid sequences of the HG3 variants

>HG3

MAEAAQSVDQLIKARGKVYFGVATDQNRLTTGKNAAI IQADFGMVWPENSMKWDATEPSQGNFNFAGADYLVNWAQQNGKLIG
GGMLVWHSQLPSWVSSITDKNTLTNVMKNHITTLMTRYKGKIRAWDVVGEAFNEDGSLRQTVFLNVIGEDYIPIAFQTARAAD
PNAKLYIMDYNLDSASYPKTQAIVNRVKQWRAAGVPIDGIGSQTHLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITVFGVADPDSWRASTTPLLFDGNFNPKPAYNAIVQDLQQGSIEGRGHHHHHHH-

>HG3.R1 (K50Q, N166S, M172A)

MAEAAQSVDQLIKARGKVYFGVATDQNRLTTGKNAAI IQADFGMVWPENSMQWDATEPSQGNFNFAGADYLVNWAQQNGKLIG
GGMLVWHSQLPSWVSSITDKNTLTNVMKNHITTLMTRYKGKIRAWDVVGEAFNEDGSLRQTVFLNVIGEDYIPIAFQTARAAD
PSAKLYIADYNLDSASYPKTQAIVNRVKQWRAAGVPIDGIGSQTHLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITVFGVADPDSWRASTTPLLFDGNFNPKPAYNAIVQDLQQGSIEGRGHHHHHHH-

>HG3.R2 (K50Q, Q90H, M172A, Q207M)

MAEAAQSVDQLIKARGKVYFGVATDQNRLTTGKNAAI IQADFGMVWPENSMQWDATEPSQGNFNFAGADYLVNWAQQNGKLIG
GGMLVWHS^HLP^HSWVSSITDKNTLTNVMKNHITTLMTRYKGKIRAWDVVGEAFNEDGSLRQTVFLNVIGEDYIPIAFQTARAAD
PNAKLYIADYNLDSASYPKTQAIVNRVKQWRAAGVPIDGIGSMTHLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITVFGVADPDSWRASTTPLLFDGNFNPKPAYNAIVQDLQQGSIEGRGHHHHHHH-

>HG3.R3 (M49L, K50Q, T54I, Q90H, N102E, E131S, P154K, M172A, R190K, Q207M)

MAEAAQSVDQLIKARGKVYFGVATDQNRLTTGKNAAI IQADFGMVWPENSLQWDAIEPSQGNFNFAGADYLVNWAQQNGKLIG
GGMLVWHS^HLP^HSWVSSITDK^ETLTNVMKNHITTLMTRYKGKIRAWDVVGS^AFNEDGSLRQTVFLNVIGEDYI^KIAFQTARAAD
PNAKLYIADYNLDSASYPKTQAIVN^KVKQWRAAGVPIDGIGSMTHLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITVFGVADPDSWRASTTPLLFDGNFNPKPAYNAIVQDLQQGSIEGRGHHHHHHH-

>HG3.R4 (I10M, M49L, K50Q, T54I, L69V, Q90H, N102E, A125C, E131S, P154K, M172A,
R190K, Q207M, V266S)

MAEAAQSVDQL^MKARGKVYFGVATDQNRLTTGKNAAI IQADFGMVWPENSLQWDAIEPSQGNFNFAGADY^VVNWAQQNGKLIG
GGMLVWHS^HLP^HSWVSSITDK^ETLTNVMKNHITTLMTRYKGKIR^CWDVVG^SAFNEDGSLRQTVFLNVIGEDYI^KIAFQTARAAD
PNAKLYIADYNLDSASYPKTQAIVN^KVKQWRAAGVPIDGIGSMTHLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGIT^SFGVADPDSWRASTTPLLFDGNFNPKPAYNAIVQDLQQGSIEGRGHHHHHHH-

>HG3.R5 (I10M, M49L, K50Q, T54V, L69V, Q90H, N102E, A125V, E131S, P154K, M172A, Y174S, R190K, Q207M, H209N, V266S)
MAEAAQSVDQLMKARGKVYFGVATDQNRLTTGKNAAIIQADFGMVWPENSLQWDAVEPSQGNFNFAGADYVWNWAQQNGKLIG
GGMLVWHSHLPSWVSSITDKETLTNVNMKNHITTLMTRYKGKIRVWDVVGSAFNEDGSLRQTVFLNVIGEDYIKIAFQTARAAD
PNAKLYIADSNLDSASYPKTAIVNVKQWRAAGVPIDGIGSMNLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITSGFVADPDSWRASTTPLLFDGNFNPKNPAYNAIVQDLQQGSIEGRGHHHHHH-

>HG3.17 (V6I, Q37K, N47E, K50Q, G82A, M84C, S89N, Q90F, T105I, A125T, T208M, F267M, W275A, R276F, T279S, D300N)
MAEAAQSIDQLIKARGKVYFGVATDQNRLTTGKNAAIIKADFGMVWPEESMQWDATEPSQGNFNFAGADYLVNWAQQNGKLIG
AGCLVWHNHLPSWVSSITDKNTLINVMKNHITTLMTRYKGKIRTWDDVVGSAFNEDGSLRQNVFLNVIGEDYIPIAFQTARAAD
PNAKLYIMDYNLDSASYPKTAIVNRVKQWRAAGVPIDGIGSQMHLASAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITVMGVADPDSAFASSTPLLFDGNFNPKNPAYNAIVQNLQQGSIEGRGHHHHHH-

>HG3.17wR5 (V6I, I10M, Q37K, N47E, M49L, K50Q, T54V, L69V, G82A, M84C, S89N, Q90F, N102E, T105I, A125T, E131S, P154K, M172A, Y174S, R190K, Q207M, T208M, H209N, V266S, F267M, W275A, R276F, T279S, D300N)
MAEAAQSIDQLMKARGKVYFGVATDQNRLTTGKNAAIIKADFGMVWPEESLQWDAVEPSQGNFNFAGADYVWNWAQQNGKLIG
AGCLVWHNHLPSWVSSITDKETLINVMKNHITTLMTRYKGKIRTWDDVVGSAFNEDGSLRQNVFLNVIGEDYIKIAFQTARAAD
PNAKLYIADSNLDSASYPKTAIVNVKQWRAAGVPIDGIGSMNLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITSMGVADPDSAFASSTPLLFDGNFNPKNPAYNAIVQNLQQGSIEGRGHHHHHH-

>HG3.5w17 (V6I, I10M, Q37K, N47E, M49L, K50Q, T54V, L69V, G82A, M84C, S89N, Q90H, N102E, T105I, A125V, E131S, P154K, M172A, Y174S, R190K, Q207M, T208M, H209N, V266S, F267M, W275A, R276F, T279S, D300N)
MAEAAQSIDQLMKARGKVYFGVATDQNRLTTGKNAAIIKADFGMVWPEESLQWDAVEPSQGNFNFAGADYVWNWAQQNGKLIG
AGCLVWHNHLPSWVSSITDKETLINVMKNHITTLMTRYKGKIRVWDVVGSAFNEDGSLRQNVFLNVIGEDYIKIAFQTARAAD
PNAKLYIADSNLDSASYPKTAIVNVKQWRAAGVPIDGIGSMNLSAGQGAGVLQALPLLASAGTPEVSILMLDVAGASPTD
YVNVVNACLVQSCVGITSMGVADPDSAFASSTPLLFDGNFNPKNPAYNAIVQNLQQGSIEGRGHHHHHH-

Nucleotide sequences of HG3 variants

>HG3

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATTAAAGCACGTGGTAAAGTTTATTTTGGTGTTGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCATGAAATGGGATGCAA
CCGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATCTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCAGCTGCCGAGCTGGGTAGCAGCATTACCGATAAAAAACACCCGTACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTTCGTGCATGGGATGTTGTGGGTGAAGCCTTTAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCCCGATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAATGCAAACTGTATATCATGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATCGTGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGTCAGACCCATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCGTTTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.R1

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATTAAAGCACGTGGTAAAGTTTATTTTGGTGTTGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCATGCAGTGGGATGCAA
CCGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATCTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCAGCTGCCGAGCTGGGTAGCAGCATTACCGATAAAAAACACCCGTACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTTCGTGCATGGGATGTTGTGGGTGAAGCCTTTAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCCCGATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAGCGCAAACTGTATATCGCGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATCGTGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGTCAGACCCATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCGTTTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.R2

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATTAAAGCACGTGGTAAAGTTTATTTTGGTGTTGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCATGCAGTGGGATGCAA
CCGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATCTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCATCTGCCGAGCTGGGTAGCAGCATTACCGATAAAAAACACCCGTACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTTCGTGCATGGGATGTTGTGGGTGAAGCCTTTAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCCCGATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAACGCAAACTGTATATCGCGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATCGTGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGTATGACCCATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCGTTTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.R3

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATTAAAGCACGTGGTAAAGTTTATTTTGGTGTGGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCCTGCAGTGGGATGCAA
TTGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATCTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCATCTGCCGAGCTGGGTAGCAGCATTACCGATAAAGAAACCCCTGACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTGCATGGGATGTTGTGGGTAGCGCCTTAAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCAAAATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAACGCAAACTGTATATCGCGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATAAAGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGATTGATGGTATTGGTAGTATGACCCATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCGTTTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.R4

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATGAAAGCACGTGGTAAAGTTTATTTTGGTGTGGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCCTGCAGTGGGATGCAA
TTGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATGTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCATCTGCCGAGCTGGGTAGCAGCATTACCGATAAAGAAACCCCTGACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTTGCTGGGATGTTGTGGGTAGCGCCTTAAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCAAAATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAACGCAAACTGTATATCGCGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATAAAGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGATTGATGGTATTGGTAGTATGACCCATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACAGCTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.R5

ATGGCAGAAGCAGCACAGAGCGTTGACCAGCTGATGAAAGCACGTGGTAAAGTTTATTTTGGTGTGGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTTCAGGCAGATTTTGGTATGGTTTGGCCTGAAAATAGCCTGCAGTGGGATGCAG
TGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATGTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GGTGGTATGCTGGTTTGGCATAGCCATCTGCCGAGCTGGGTAGCAGCATTACCGATAAAGAAACCCCTGACCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTGTGTGGGATGTTGTGGGTAGCGCCTTAAATGAAGATG
GTAGCCTGCGTCAGACCGTTTTTCTGAATGTTATTGGCGAAGATTATATCAAAATTGCATTTTCAGACCGCACGTGCAGCAGAT
CCGAACGCAAACTGTATATCGCGGATAGCAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATAAAGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGATTGATGGTATTGGTAGTATGACCAACCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACAGCTTTGGTGTGGCAGATCCGGATAGCTG
GCGTGCAAGCACCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGGATCTGCAGC
AGGGTAGCATTGAAGGTGCTGGTCATCATCACCATCATCATTA

>HG3.17

ATGGCAGAAGCAGCACAGAGCATTGATCAACTGATTAAAGCACGTGGCAAAGTGTATTTTGGTGTTGCAACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATCAAAGCCGATTTTGGTATGGTTTGGCCTGAAGAAAGCATGCAGTGGGATGCAA
CCGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATCTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GCCGGTTGTCTGGTTTGGCATAATTTTCTGCCGAGCTGGGTAGCAGCATTACCGATAAAAAACCCCTGATCAACGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTACCTGGGATGTTGTGGGTGAAGCCTTTAATGAAGATG
GTAGCCTGCGTCAGAATGTGTTTCTGAATGTTATTGGCGAAGATTATATCCCGATTGCATTTAGACCCGCACGTGCAGCAGAT
CCGAATGCAAACTGTATATCATGGATTATAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATCGTGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGCCAGATGCACCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCGTTATGGGTGTTGCAGATCCGGATAGCGC
CTTTGCGAGCAGCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGAATCTGCAGC
AGGGTAGCATTGAAGGTCGTGGTCATCATCACCATCATCATTA

>HG3.17wR5

ATGGCAGAAGCAGCACAGAGCATTGATCAACTGATGAAAGCACGTGGCAAAGTGTATTTTGGTGTTGCAACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATCAAAGCCGATTTTGGTATGGTTTGGCCTGAAGAAAGCCTGCAGTGGGATGCAG
TGGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATGTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GCCGGTTGTCTGGTTTGGCATAATTTTCTGCCGAGCTGGGTAGCAGCATTACCGATAAAGAAACCCCTGATCAACGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTACCTGGGATGTTGTGGGTAGCGCCTTTAATGAAGATG
GTAGCCTGCGTCAGAATGTGTTTCTGAATGTTATTGGCGAAGATTATATCAAAATTGCATTTAGACCCGCACGTGCAGCAGAT
CCGAATGCAAACTGTATATCGCGGATAGCAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATAAAGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGCATGATGAATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCAGCATGGGTGTTGCAGATCCGGATAGCGC
CTTTGCGAGCAGCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGAATCTGCAGC
AGGGTAGCATTGAAGGTCGTGGTCATCATCACCATCATCATTA

>HG3.R5w17

ATGGCAGAAGCAGCACAGAGCATTGACCAGCTGATGAAAGCACGTGGTAAAGTTTATTTTGGTGTTGGCCACCGATCAGAATCG
TCTGACCACCGGTAAAAATGCAGCAATTATTAAGCAGATTTTGGTATGGTTTGGCCTGAAGAAAGCCTGCAGTGGGATGCAG
TGGAACCGAGCCAGGGCAATTTTAACTTTGCCGGTGCAGATTATGTGGTTAATTGGGCACAGCAGAATGGTAAACTGATTGGT
GCCGGTTGTCTGGTTTGGCATAATCATCTGCCGAGCTGGGTAGCAGCATTACCGATAAAGAAACCCCTGATCAATGTGATGAA
AAACCATATCACCACACTGATGACCCGCTATAAAGGTAAAATTCGTGTGTGGGATGTTGTGGGTAGCGCCTTTAATGAAGATG
GTAGCCTGCGTCAGAATGTGTTTTCTGAATGTTATTGGCGAAGATTATATCAAAATTGCATTTAGACCCGCACGTGCAGCAGAT
CCGAACGCAAACTGTATATCGCGGATAGCAACCTGGATAGCGCAAGCTATCCGAAAACACAGGCAATTGTTAATAAAGTTAA
ACAGTGGCGTGCAGCCGGTGTTCGGATTGATGGTATTGGTAGCATGATGAATCTGAGCGCAGGTCAAGGTGCGGGTGTTCCTGC
AGGCACTGCCGCTGCTGGCAAGCGCAGGTACACCGGAAGTTAGCATTCTGATGCTGGATGTTGCAGGCGCAAGCCCGACCGAT
TATGTTAATGTTGTTAATGCATGCCTGAATGTTTCAGAGCTGTGTTGGTATTACCAGCATGGGTGTTGGCAGATCCGGATAGCGC
CTTTGCAAGCAGCACACCGCTGCTGTTTGATGGTAATTTCAATCCGAAACCGGCATATAATGCCATTGTTTCAGAATCTGCAGC
AGGGTAGCATTGAAGGTCGTGGTCATCATCACCATCATCATTA

Cartesian coordinates of cluster model QM structures calculated with PCM(H₂O)/M06-2X/6-31G(d)

1-w _e (QM)				H	4.60350000	-0.89020000	2.80030000
C	-2.27730000	-4.18000000	-1.83750000	H	5.84740000	-2.13850000	2.95770000
H	-2.38340000	-3.63470000	-2.77790000	O	6.41490000	-0.19820000	1.09940000
C	-0.84080000	-4.50710000	-1.49110000	N	5.74830000	-2.01190000	-0.06140000
C	-2.81230000	-3.34960000	-0.67690000	C	6.66510000	-1.73000000	-1.15470000
H	-2.83320000	-5.11860000	-1.91530000	H	5.17090000	-2.84110000	-0.09450000
N	0.15210000	-3.84040000	-2.11230000	C	6.28900000	-0.53940000	-2.03040000
O	-0.58630000	-5.26220000	-0.54910000	H	7.65650000	-1.50780000	-0.75250000
C	-4.26310000	-2.98620000	-0.78650000	H	6.73790000	-2.61470000	-1.78900000
H	-2.21890000	-2.42870000	-0.59390000	O	7.09160000	-0.18620000	-2.89040000
H	-2.63060000	-3.91330000	0.24530000	N	5.11600000	0.09000000	-1.80080000
C	1.51630000	-3.94740000	-1.59610000	C	4.81510000	1.38480000	-2.39350000
C	0.10210000	-3.10030000	-3.36370000	H	4.48720000	-0.22110000	-1.05580000
C	-5.34350000	-3.82430000	-0.70570000	C	4.88110000	2.53950000	-1.40390000
C	-4.76420000	-1.66400000	-0.99150000	H	5.53050000	1.56930000	-3.19700000
C	2.34400000	-3.17160000	-2.60440000	H	3.80830000	1.38760000	-2.82090000
H	1.81070000	-4.99930000	-1.52800000	O	4.52790000	3.65880000	-1.77710000
C	1.54160000	-3.29870000	-0.22610000	N	5.30900000	2.28330000	-0.16180000
C	1.52810000	-3.26860000	-3.85360000	H	5.66290000	1.36450000	0.09750000
H	-0.14250000	-2.04510000	-3.18350000	C	5.36840000	3.37500000	0.78820000
H	-0.63460000	-3.52640000	-4.04580000	H	4.45320000	3.96320000	0.68560000
N	-6.49800000	-3.08820000	-0.81080000	C	5.50650000	2.86610000	2.21870000
H	-5.38320000	-4.89420000	-0.55380000	H	6.20890000	4.03850000	0.54650000
C	-6.16720000	-1.76730000	-0.97140000	H	6.43710000	2.29850000	2.32330000
C	-4.16490000	-0.40890000	-1.16370000	C	4.36300000	1.97390000	2.65840000
H	2.42050000	-2.12730000	-2.27870000	H	5.58010000	3.73880000	2.87580000
H	3.35420000	-3.57510000	-2.69890000	H	4.36900000	1.05950000	2.05400000
O	1.28430000	-2.10570000	-0.03860000	C	2.97620000	2.53860000	2.58110000
N	1.88200000	-4.11780000	0.78600000	H	4.52800000	1.65110000	3.69530000
H	1.80130000	-2.52410000	-4.60510000	N	1.99820000	1.61550000	2.61340000
H	1.63630000	-4.26030000	-4.30640000	O	2.74740000	3.75260000	2.50160000
H	-7.43600000	-3.45750000	-0.76700000	H	1.04030000	1.90480000	2.45450000
C	-6.99180000	-0.65480000	-1.11070000	H	2.21710000	0.62500000	2.53540000
H	-3.08060000	-0.30070000	-1.17210000	H	0.12290000	-0.89640000	-0.85620000
C	-4.98810000	0.68210000	-1.29660000	O	-0.42550000	-0.12790000	-1.09650000
C	1.79320000	-3.67510000	2.16360000	H	-0.03570000	0.61510000	-0.60190000
H	1.86420000	-5.11280000	0.60200000	H	2.45370000	-0.66150000	0.27520000
H	-8.07360000	-0.74890000	-1.08720000	O	3.12410000	0.04600000	0.24410000
C	-6.37640000	0.55010000	-1.27780000	H	2.62020000	0.87430000	0.12020000
H	-4.56370000	1.67460000	-1.43050000	H	1.58510000	4.10050000	1.04660000
C	2.74530000	-2.51270000	2.43260000	N	0.89150000	4.33540000	0.33080000
H	0.78450000	-3.32330000	2.39720000	C	0.61950000	3.36770000	-0.54760000
H	2.04070000	-4.51760000	2.81220000	C	0.10640000	5.54030000	0.53220000
H	-6.96570000	1.45970000	-1.35180000	C	-0.49940000	3.59220000	-1.54320000
O	2.34600000	-1.45890000	2.91590000	O	1.24700000	2.29120000	-0.55520000
N	4.03560000	-2.73660000	2.08440000	H	-0.91600000	5.30000000	0.84670000
C	5.06270000	-1.74380000	2.30350000	H	0.06550000	6.14570000	-0.37770000
H	4.30470000	-3.68880000	1.86710000	H	0.58610000	6.12770000	1.31440000
C	5.76180000	-1.24140000	1.04510000	N	-0.61730000	2.46020000	-2.41720000

H	-0.30590000	4.51390000	-2.11040000
H	-1.43140000	3.75030000	-0.99070000
C	-1.75030000	2.23830000	-3.11800000
H	0.07150000	1.72320000	-2.31920000
C	-1.70540000	1.02920000	-4.03560000
O	-2.71060000	3.00510000	-3.07430000
H	-0.97860000	0.29070000	-3.69330000
H	-1.43690000	1.36310000	-5.04200000
H	-2.69850000	0.57750000	-4.07500000
O	-0.84820000	1.42270000	1.66450000
N	-1.69790000	2.39300000	1.10150000
C	-1.61040000	0.44070000	2.17540000
C	-2.91570000	1.98500000	1.26590000
C	-2.95390000	0.72300000	1.95200000
C	-1.17840000	-0.69500000	2.85110000
H	-3.76820000	2.59960000	0.98510000
C	-3.94000000	-0.16270000	2.37390000
C	-2.14970000	-1.57450000	3.25530000
H	-0.12260000	-0.89950000	3.00880000
H	-4.99420000	0.01140000	2.19520000
C	-3.49330000	-1.30360000	3.03410000
H	-1.87950000	-2.49020000	3.76760000
N	-4.48790000	-2.28930000	3.45860000
O	-5.65370000	-2.08940000	3.16240000
O	-4.09890000	-3.26170000	4.08340000
O	-5.42390000	3.53360000	1.34360000
C	-5.45930000	4.04170000	0.18590000
C	-4.31360000	4.94240000	-0.18720000
O	-6.34160000	3.83500000	-0.68200000
C	-4.63890000	5.84720000	-1.37320000
H	-3.45990000	4.29820000	-0.45050000
H	-4.00230000	5.51770000	0.69130000
H	-5.49080000	6.49470000	-1.14460000
H	-3.78810000	6.48340000	-1.64010000
H	-4.90830000	5.24080000	-2.23960000

1-we TS (QM)				N	5.75780000	-1.99840000	-0.05850000
C	-2.26060000	-4.18660000	-1.84150000	C	6.67500000	-1.71440000	-1.15100000
H	-2.36700000	-3.64150000	-2.78200000	H	5.18150000	-2.82820000	-0.09240000
C	-0.82360000	-4.51010000	-1.49390000	C	6.29680000	-0.52490000	-2.02710000
C	-2.79880000	-3.35740000	-0.68150000	H	7.66550000	-1.48960000	-0.74770000
H	-2.81410000	-5.12670000	-1.92010000	H	6.75070000	-2.59900000	-1.78510000
N	0.16820000	-3.84120000	-2.11430000	O	7.09950000	-0.16990000	-2.88650000
O	-0.56820000	-5.26490000	-0.55180000	N	5.12200000	0.10170000	-1.79890000
C	-4.25040000	-2.99760000	-0.79250000	C	4.81840000	1.39560000	-2.39180000
H	-2.20770000	-2.43490000	-0.59740000	H	4.49210000	-0.20940000	-1.05470000
H	-2.61730000	-3.92100000	0.24080000	C	4.88070000	2.55060000	-1.40230000
C	1.53220000	-3.94460000	-1.59670000	H	5.53380000	1.58230000	-3.19480000
C	0.11750000	-3.10120000	-3.36570000	H	3.81180000	1.39580000	-2.81960000
C	-5.32870000	-3.83840000	-0.71260000	O	4.52710000	3.66950000	-1.77690000
C	-4.75450000	-1.67670000	-0.99810000	N	5.30900000	2.29610000	-0.16030000
C	2.35890000	-3.16690000	-2.60440000	H	5.65940000	1.37660000	0.10130000
H	1.82920000	-4.99580000	-1.52860000	C	5.36390000	3.38760000	0.79020000
C	1.55450000	-3.29570000	-0.22680000	H	4.44680000	3.97280000	0.68730000
C	1.54430000	-3.26600000	-3.85430000	C	5.50200000	2.87920000	2.22090000
H	-0.13080000	-2.04690000	-3.18640000	H	6.20230000	4.05390000	0.54920000
H	-0.61750000	-3.52930000	-4.04850000	H	6.43440000	2.31460000	2.32640000
N	-6.48510000	-3.10520000	-0.81880000	C	4.36030000	1.98420000	2.65960000
H	-5.36600000	-4.90830000	-0.56060000	H	5.57240000	3.75240000	2.87760000
C	-6.15730000	-1.78350000	-0.97920000	H	4.36960000	1.07050000	2.05430000
C	-4.15820000	-0.42010000	-1.16990000	C	2.97220000	2.54550000	2.58110000
H	2.43290000	-2.12250000	-2.27860000	H	4.52670000	1.66120000	3.69630000
H	3.36990000	-3.56840000	-2.69820000	N	1.99800000	1.61830000	2.60120000
O	1.29290000	-2.10350000	-0.04120000	O	2.74310000	3.76050000	2.50970000
N	1.89650000	-4.11390000	0.78580000	H	1.03630000	1.88390000	2.40880000
H	1.81640000	-2.52100000	-4.60570000	H	2.23150000	0.63250000	2.50940000
H	1.65510000	-4.25750000	-4.30690000	H	0.08030000	-0.88570000	-0.79700000
H	-7.42230000	-3.47680000	-0.77530000	O	-0.50260000	-0.14270000	-1.03670000
C	-6.98460000	-0.67300000	-1.11950000	H	-0.29990000	0.54920000	-0.38100000
H	-3.07460000	-0.30740000	-1.17390000	H	2.45460000	-0.65130000	0.25640000
C	-4.98400000	0.66880000	-1.30370000	O	3.11860000	0.06220000	0.23120000
C	1.80500000	-3.67120000	2.16320000	H	2.60520000	0.88490000	0.10400000
H	1.88060000	-5.10890000	0.60180000	H	1.57730000	4.10580000	1.04580000
H	-8.06610000	-0.76920000	-1.09980000	N	0.88740000	4.34100000	0.32730000
C	-6.37190000	0.53340000	-1.28610000	C	0.61650000	3.36840000	-0.55020000
H	-4.54770000	1.65550000	-1.43940000	C	0.09670000	5.53980000	0.52920000
C	2.75390000	-2.50640000	2.43280000	C	-0.50230000	3.59000000	-1.54630000
H	0.79520000	-3.32080000	2.39560000	O	1.25660000	2.30350000	-0.56570000
H	2.05400000	-4.51270000	2.81250000	H	-0.90790000	5.29730000	0.89590000
H	-6.97660000	1.43190000	-1.38060000	H	0.00690000	6.11640000	-0.39610000
O	2.35500000	-1.45560000	2.92120000	H	0.60270000	6.15910000	1.26940000
N	4.04520000	-2.72690000	2.08310000	N	-0.63750000	2.42870000	-2.38160000
C	5.06960000	-1.73170000	2.30570000	H	-0.28860000	4.48490000	-2.14790000
H	4.31680000	-3.67800000	1.86440000	H	-1.42700000	3.78460000	-0.99420000
C	5.76850000	-1.22780000	1.04800000	C	-1.74840000	2.23280000	-3.12240000
H	4.60680000	-0.87960000	2.80180000	H	-0.00590000	1.65460000	-2.19750000
H	5.85440000	-2.12460000	2.96110000	C	-1.69970000	1.02360000	-4.03970000
O	6.41950000	-0.18330000	1.10240000	O	-2.68370000	3.03290000	-3.13250000

H	-1.01520000	0.26080000	-3.66460000
H	-1.36530000	1.35300000	-5.02770000
H	-2.70310000	0.60480000	-4.13580000
O	-0.79230000	1.37200000	1.66730000
N	-1.82730000	2.47580000	1.06440000
C	-1.58090000	0.44810000	2.16170000
C	-2.98000000	2.00850000	1.27690000
C	-2.95020000	0.72080000	1.95450000
C	-1.17460000	-0.69840000	2.84770000
H	-4.25020000	2.76700000	1.15010000
C	-3.93710000	-0.17300000	2.36790000
C	-2.14410000	-1.58020000	3.25100000
H	-0.12040000	-0.90760000	3.00980000
H	-4.99050000	0.00410000	2.18700000
C	-3.48820000	-1.31260000	3.02860000
H	-1.87450000	-2.49580000	3.76450000
N	-4.47390000	-2.30010000	3.44420000
O	-5.64540000	-2.10460000	3.15480000
O	-4.08810000	-3.28220000	4.06130000
O	-5.28210000	3.14060000	1.12270000
C	-5.46490000	4.02740000	0.17800000
C	-4.32110000	4.93090000	-0.19430000
O	-6.56040000	4.16760000	-0.35430000
C	-4.64750000	5.83480000	-1.38060000
H	-3.44840000	4.30050000	-0.41430000
H	-4.05000000	5.51230000	0.69570000
H	-5.50770000	6.46980000	-1.15850000
H	-3.79300000	6.47280000	-1.62240000
H	-4.89040000	5.23420000	-2.26030000

1 (QM)				N	5.74380000	-2.01430000	-0.07230000
C	-2.27920000	-4.18940000	-1.85360000	C	6.66130000	-1.73420000	-1.16520000
H	-2.38500000	-3.64680000	-2.79560000	H	5.16220000	-2.84040000	-0.10680000
C	-0.84300000	-4.51520000	-1.50480000	C	6.28590000	-0.54580000	-2.04400000
C	-2.81600000	-3.35670000	-0.69540000	H	7.65220000	-1.51060000	-0.76230000
H	-2.83550000	-5.12800000	-1.92900000	H	6.73540000	-2.62020000	-1.79760000
N	0.15080000	-3.85790000	-2.13140000	O	7.08930000	-0.19410000	-2.90400000
O	-0.59200000	-5.26410000	-0.55600000	N	5.11210000	0.08360000	-1.81720000
C	-4.26680000	-2.99410000	-0.80760000	C	4.81160000	1.37710000	-2.41300000
H	-2.22210000	-2.43710000	-0.61190000	H	4.48120000	-0.22460000	-1.07190000
H	-2.63510000	-3.91810000	0.22810000	C	4.87590000	2.53400000	-1.42590000
C	1.51420000	-3.95480000	-1.60800000	H	5.52820000	1.56070000	-3.21560000
C	0.10160000	-3.11200000	-3.37920000	H	3.80540000	1.37860000	-2.84200000
C	-5.34690000	-3.83250000	-0.72630000	O	4.53170000	3.65420000	-1.80460000
C	-4.76810000	-1.67260000	-1.01610000	N	5.29790000	2.27980000	-0.18150000
C	2.34260000	-3.18070000	-2.61700000	H	5.64760000	1.36060000	0.08170000
H	1.81240000	-5.00610000	-1.54020000	C	5.36020000	3.37450000	0.76500000
C	1.53710000	-3.30310000	-0.23950000	H	4.44640000	3.96470000	0.66090000
C	1.52830000	-3.28080000	-3.86700000	C	5.49680000	2.86880000	2.19680000
H	-0.14300000	-2.05780000	-3.19770000	H	6.20220000	4.03520000	0.52120000
H	-0.63440000	-3.53520000	-4.06400000	H	6.42760000	2.30180000	2.30350000
N	-6.50120000	-3.09700000	-0.83460000	C	4.35310000	1.97700000	2.63700000
H	-5.38630000	-4.90200000	-0.57210000	H	5.56920000	3.74280000	2.85220000
C	-6.17110000	-1.77640000	-0.99740000	H	4.36060000	1.06070000	2.03520000
C	-4.16910000	-0.41760000	-1.19030000	C	2.96630000	2.54090000	2.55680000
H	2.41950000	-2.13680000	-2.29210000	H	4.51680000	1.65730000	3.67510000
H	3.35240000	-3.58570000	-2.71090000	N	1.98890000	1.61730000	2.58160000
O	1.28310000	-2.11250000	-0.07100000	O	2.73850000	3.75580000	2.48710000
N	1.88190000	-4.12650000	0.77800000	H	1.03210000	1.90830000	2.41910000
H	1.80170000	-2.53830000	-4.62070000	H	2.20980000	0.62900000	2.48210000
H	1.63620000	-4.27360000	-4.31750000	H	2.42690000	-0.66060000	0.20820000
H	-7.43930000	-3.46640000	-0.79110000	O	3.10450000	0.04240000	0.21390000
C	-6.99600000	-0.66450000	-1.14020000	H	2.60860000	0.87310000	0.07260000
H	-3.08640000	-0.30890000	-1.19690000	H	1.57760000	4.10190000	1.01890000
C	-4.99270000	0.67280000	-1.32660000	N	0.87050000	4.32610000	0.31460000
C	1.78620000	-3.67420000	2.15150000	C	0.61340000	3.36250000	-0.57700000
H	1.81300000	-5.12090000	0.60290000	C	0.09750000	5.53700000	0.49790000
H	-8.07780000	-0.75900000	-1.11720000	C	-0.50490000	3.58400000	-1.57370000
C	-6.38090000	0.54030000	-1.30920000	O	1.27690000	2.31520000	-0.62220000
H	-4.56970000	1.66590000	-1.45960000	H	-0.93180000	5.31320000	0.80310000
C	2.73740000	-2.51080000	2.41900000	H	0.07280000	6.13830000	-0.41590000
H	0.77760000	-3.31950000	2.38320000	H	0.57290000	6.12620000	1.28170000
H	2.03260000	-4.51110000	2.80820000	N	-0.64600000	2.42450000	-2.40390000
H	-6.96890000	1.45050000	-1.38310000	H	-0.29280000	4.48240000	-2.17150000
O	2.34060000	-1.46000000	2.91150000	H	-1.43520000	3.77600000	-1.02980000
N	4.02770000	-2.73320000	2.06940000	C	-1.75330000	2.22630000	-3.14750000
C	5.05480000	-1.74110000	2.29090000	H	0.11870000	1.76150000	-2.38240000
H	4.29340000	-3.68320000	1.83910000	C	-1.70670000	1.01520000	-4.06230000
C	5.75520000	-1.24120000	1.03250000	O	-2.71440000	2.99180000	-3.11550000
H	4.59370000	-0.88720000	2.78530000	H	-0.78600000	0.43910000	-3.95970000
H	5.83860000	-2.13490000	2.94700000	H	-1.79990000	1.36020000	-5.09510000
O	6.40860000	-0.19790000	1.08480000	H	-2.56500000	0.37320000	-3.84570000

O	-0.86660000	1.46220000	1.70330000
N	-1.71840000	2.44280000	1.16380000
C	-1.62290000	0.46010000	2.18310000
C	-2.93410000	2.01990000	1.30500000
C	-2.96660000	0.73790000	1.95330000
C	-1.18740000	-0.69380000	2.82880000
H	-3.78900000	2.63810000	1.03640000
C	-3.94870000	-0.16370000	2.34700000
C	-2.15890000	-1.57270000	3.23370000
H	-0.13130000	-0.89870000	2.98400000
H	-5.00250000	0.00460000	2.16030000
C	-3.50230000	-1.30280000	3.01030000
H	-1.88810000	-2.49250000	3.73840000
N	-4.49580000	-2.29320000	3.42630000
O	-5.66100000	-2.09620000	3.12540000
O	-4.10700000	-3.26570000	4.05110000
O	-5.45260000	3.55680000	1.31870000
C	-5.46700000	4.03540000	0.14810000
C	-4.32130000	4.93580000	-0.22580000
O	-6.32950000	3.80030000	-0.73250000
C	-4.64540000	5.83780000	-1.41400000
H	-3.46820000	4.28980000	-0.48680000
H	-4.01060000	5.51310000	0.65160000
H	-5.49470000	6.48930000	-1.18610000
H	-3.79310000	6.47050000	-1.68410000
H	-4.91840000	5.22930000	-2.27770000

1 TS (QM)				N	5.75290000	-1.99980000	-0.06410000
C	-2.26120000	-4.20180000	-1.85170000	C	6.67120000	-1.71930000	-1.15630000
H	-2.36720000	-3.66150000	-2.79500000	H	5.17230000	-2.82650000	-0.09840000
C	-0.82450000	-4.52270000	-1.50020000	C	6.29350000	-0.53380000	-2.03800000
C	-2.80200000	-3.36830000	-0.69600000	H	7.66080000	-1.49180000	-0.75230000
H	-2.81460000	-5.14220000	-1.92600000	H	6.74900000	-2.60650000	-1.78660000
N	0.16820000	-3.86390000	-2.12690000	O	7.09740000	-0.18150000	-2.89740000
O	-0.57270000	-5.26930000	-0.54980000	N	5.11760000	0.09250000	-1.81440000
C	-4.25370000	-3.01010000	-0.81090000	C	4.81420000	1.38400000	-2.41310000
H	-2.21080000	-2.44690000	-0.61270000	H	4.48560000	-0.21600000	-1.07020000
H	-2.62120000	-3.92730000	0.22900000	C	4.87380000	2.54310000	-1.42830000
C	1.53100000	-3.95570000	-1.60140000	H	5.53140000	1.56820000	-3.21510000
C	0.11860000	-3.12080000	-3.37630000	H	3.80870000	1.38160000	-2.84350000
C	-5.33150000	-3.85150000	-0.72930000	O	4.52840000	3.66190000	-1.81050000
C	-4.75850000	-1.69060000	-1.02290000	N	5.29480000	2.29290000	-0.18300000
C	2.35880000	-3.18140000	-2.61090000	H	5.64340000	1.37430000	0.08360000
H	1.83210000	-5.00600000	-1.53110000	C	5.35270000	3.38960000	0.76140000
C	1.55050000	-3.30100000	-0.23420000	H	4.43710000	3.97670000	0.65560000
C	1.54640000	-3.28650000	-3.86180000	C	5.48870000	2.88730000	2.19440000
H	-0.12930000	-2.06690000	-3.19750000	H	6.19290000	4.05230000	0.51700000
H	-0.61520000	-3.54760000	-4.06130000	H	6.42160000	2.32400000	2.30370000
N	-6.48790000	-3.11960000	-0.84100000	C	4.34710000	1.99310000	2.63490000
H	-5.36810000	-4.92080000	-0.57310000	H	5.55730000	3.76320000	2.84780000
C	-6.16130000	-1.79840000	-1.00590000	H	4.35840000	1.07620000	2.03450000
C	-4.16300000	-0.43420000	-1.19890000	C	2.95860000	2.55290000	2.55180000
H	2.43220000	-2.13670000	-2.28790000	H	4.51190000	1.67560000	3.67360000
H	3.36980000	-3.58390000	-2.70250000	N	1.98770000	1.62400000	2.57070000
O	1.29300000	-2.11100000	-0.06870000	O	2.72880000	3.76830000	2.48050000
N	1.89650000	-4.12170000	0.78550000	H	1.02130000	1.88470000	2.39270000
H	1.81860000	-2.54460000	-4.61660000	H	2.22400000	0.63830000	2.48280000
H	1.65800000	-4.27980000	-4.31010000	H	2.42990000	-0.65240000	0.21020000
H	-7.42490000	-3.49160000	-0.79730000	O	3.10730000	0.05070000	0.20820000
C	-6.98920000	-0.68920000	-1.15220000	H	2.60880000	0.88180000	0.07730000
H	-3.08130000	-0.31980000	-1.20060000	H	1.56000000	4.10050000	1.01550000
C	-4.98940000	0.65350000	-1.33860000	N	0.85680000	4.32420000	0.30700000
C	1.79720000	-3.66650000	2.15780000	C	0.60740000	3.36070000	-0.58680000
H	1.82800000	-5.11650000	0.61240000	C	0.08420000	5.53630000	0.48260000
H	-8.07060000	-0.78620000	-1.13390000	C	-0.50960000	3.57750000	-1.58590000
C	-6.37730000	0.51700000	-1.32280000	O	1.28210000	2.32090000	-0.63820000
H	-4.55380000	1.64010000	-1.47890000	H	-0.94940000	5.31140000	0.77200000
C	2.74470000	-2.49970000	2.42420000	H	0.07470000	6.14150000	-0.42920000
H	0.78720000	-3.31310000	2.38700000	H	0.54910000	6.12150000	1.27580000
H	2.04520000	-4.50090000	2.81700000	N	-0.63320000	2.43190000	-2.43780000
H	-6.98130000	1.41510000	-1.42230000	H	-0.31310000	4.49030000	-2.16680000
O	2.34760000	-1.45120000	2.91960000	H	-1.44230000	3.74010000	-1.03640000
N	4.03610000	-2.71880000	2.07400000	C	-1.75210000	2.21260000	-3.15830000
C	5.06000000	-1.72370000	2.29780000	H	0.13610000	1.77400000	-2.41910000
H	4.30480000	-3.66790000	1.84380000	C	-1.70080000	0.99970000	-4.07060000
C	5.76060000	-1.22430000	1.03920000	O	-2.72850000	2.95800000	-3.10460000
H	4.59510000	-0.87030000	2.78960000	H	-0.76320000	0.44770000	-3.99200000
H	5.84370000	-2.11420000	2.95590000	H	-1.83290000	1.33680000	-5.10170000
O	6.41190000	-0.17960000	1.08990000	H	-2.53590000	0.33720000	-3.82640000

O	-0.81410000	1.44200000	1.76190000
N	-1.87240000	2.56610000	1.17400000
C	-1.59340000	0.48640000	2.18790000
C	-3.01000000	2.05630000	1.33950000
C	-2.96780000	0.74330000	1.96370000
C	-1.18600000	-0.69320000	2.82480000
H	-4.29700000	2.82060000	1.19600000
C	-3.94810000	-0.17220000	2.33820000
C	-2.15540000	-1.57420000	3.23020000
H	-0.13170000	-0.90270000	2.98550000
H	-5.00080000	-0.00410000	2.14500000
C	-3.49930000	-1.30870000	3.00440000
H	-1.88460000	-2.49580000	3.73240000
N	-4.48240000	-2.30110000	3.40870000
O	-5.65370000	-2.11090000	3.11250000
O	-4.09740000	-3.28340000	4.02730000
O	-5.31900000	3.18020000	1.12420000
C	-5.47560000	4.01790000	0.12840000
C	-4.33200000	4.92070000	-0.24580000
O	-6.55200000	4.11250000	-0.44930000
C	-4.65710000	5.81940000	-1.43640000
H	-3.46060000	4.28690000	-0.46240000
H	-4.05960000	5.50470000	0.64190000
H	-5.51800000	6.45510000	-1.21850000
H	-3.80230000	6.45690000	-1.67830000
H	-4.89790000	5.21510000	-2.31400000

1-Q50A-w _e (QM)				N	5.91460000	-1.69550000	0.06280000
C	-1.98450000	-4.00800000	-2.06010000	C	6.84530000	-1.30430000	-0.98340000
H	-2.08930000	-3.40100000	-2.96190000	H	5.36900000	-2.53950000	-0.04360000
C	-0.54510000	-4.30900000	-1.70190000	C	6.44600000	-0.06820000	-1.78220000
C	-2.57530000	-3.28150000	-0.85760000	H	7.81750000	-1.07440000	-0.54050000
H	-2.50390000	-4.95760000	-2.21760000	H	6.96760000	-2.13820000	-1.67630000
N	0.43630000	-3.56480000	-2.24880000	O	7.25780000	0.37550000	-2.59100000
O	-0.28490000	-5.12160000	-0.81080000	N	5.24590000	0.50130000	-1.54180000
C	-4.03550000	-2.96170000	-0.97760000	C	4.91160000	1.82480000	-2.04570000
H	-2.01710000	-2.34900000	-0.69650000	H	4.60410000	0.11070000	-0.84680000
H	-2.39370000	-3.90250000	0.02710000	C	4.91330000	2.90760000	-0.97590000
C	1.79170000	-3.66190000	-1.70820000	H	5.63690000	2.09300000	-2.81620000
C	0.38780000	-2.74050000	-3.44660000	H	3.91490000	1.82340000	-2.49620000
C	-5.08620000	-3.84040000	-0.98300000	O	4.52000000	4.03560000	-1.27800000
C	-4.57950000	-1.64650000	-1.10150000	N	5.33880000	2.58450000	0.25060000
C	2.61320000	-2.78800000	-2.63840000	H	5.69010000	1.65310000	0.46520000
H	2.12240000	-4.70530000	-1.70690000	C	5.32060000	3.60130000	1.28100000
C	1.76260000	-3.11190000	-0.29580000	H	4.37870000	4.15410000	1.18800000
C	1.82960000	-2.82400000	-3.91130000	C	5.44490000	2.99690000	2.67520000
H	0.09930000	-1.71000000	-3.20080000	H	6.12760000	4.32480000	1.10800000
H	-0.31630000	-3.14390000	-4.17560000	H	6.40630000	2.47240000	2.74430000
N	-6.26410000	-3.13920000	-1.06490000	C	4.32510000	2.03640000	3.02220000
H	-5.09030000	-4.91910000	-0.90770000	H	5.48350000	3.82070000	3.39610000
C	-5.97800000	-1.79950000	-1.12370000	H	4.24110000	1.23890000	2.27910000
C	-4.02260000	-0.36220000	-1.16990000	H	4.48850000	1.58040000	4.00390000
H	2.64400000	-1.76750000	-2.23780000	H	3.35960000	2.55640000	3.05430000
H	3.63920000	-3.14840000	-2.73550000	H	0.31890000	-0.72780000	-0.84000000
O	1.45380000	-1.94690000	-0.03090000	O	-0.24560000	0.03580000	-1.06010000
N	2.10990000	-3.99010000	0.66390000	H	0.06160000	0.74330000	-0.46630000
H	2.09200000	-2.01870000	-4.60160000	H	2.55830000	-0.48320000	0.48070000
H	1.98390000	-3.77650000	-4.43010000	O	3.19840000	0.24300000	0.37630000
H	-7.18880000	-3.54310000	-1.06990000	H	2.66920000	1.06190000	0.35260000
C	-6.83920000	-0.70920000	-1.20500000	O	1.27240000	2.47810000	-0.23370000
H	-2.94320000	-0.21660000	-1.14110000	C	0.60650000	3.52440000	-0.17050000
C	-4.88180000	0.70620000	-1.24620000	N	0.83830000	4.45280000	0.76410000
C	1.97410000	-3.64870000	2.06710000	C	-0.49730000	3.78050000	-1.17490000
H	2.13190000	-4.96920000	0.40860000	H	1.53210000	4.18860000	1.45270000
H	-7.91710000	-0.84220000	-1.21580000	C	-0.00970000	5.59560000	1.04680000
C	-6.26440000	0.52520000	-1.27140000	N	-0.55690000	2.70670000	-2.12450000
H	-4.49200000	1.72040000	-1.29550000	H	-0.31840000	4.74280000	-1.67530000
C	2.87690000	-2.47610000	2.44090000	H	-1.44720000	3.87260000	-0.63860000
H	0.94810000	-3.34850000	2.29830000	H	-0.98680000	5.27920000	1.42890000
H	2.23690000	-4.52510000	2.66240000	H	-0.15600000	6.20090000	0.14860000
H	-6.88390000	1.41730000	-1.29620000	H	0.48350000	6.21250000	1.79640000
O	2.43700000	-1.49100000	3.01490000	C	-1.66260000	2.49940000	-2.87200000
N	4.18270000	-2.62610000	2.09590000	H	0.15920000	1.99150000	-2.07070000
C	5.16730000	-1.61990000	2.42400000	C	-1.55310000	1.36120000	-3.87120000
H	4.48930000	-3.54780000	1.80910000	O	-2.65040000	3.22790000	-2.80100000
C	5.87570000	-1.00530000	1.22220000	H	-0.76100000	0.66030000	-3.60420000
H	4.66160000	-0.81730000	2.95990000	H	-1.34930000	1.78400000	-4.85910000
H	5.94830000	-2.03260000	3.07180000	H	-2.50950000	0.83580000	-3.91380000
O	6.49280000	0.05140000	1.36240000	H	-3.50540000	4.30400000	-0.11030000

C	-4.38770000	4.89740000	0.17670000
C	-5.50800000	3.93340000	0.45700000
C	-4.71890000	5.87270000	-0.95020000
H	-4.11670000	5.41920000	1.10080000
O	-5.48450000	3.35290000	1.58000000
O	-6.35590000	3.75060000	-0.45050000
H	-5.59470000	6.47680000	-0.69430000
H	-3.88400000	6.55160000	-1.15490000
H	-4.95450000	5.32140000	-1.86150000
H	-3.77160000	2.49890000	1.18490000
C	-2.90840000	1.89260000	1.44760000
N	-1.69870000	2.34510000	1.34110000
C	-2.92230000	0.58670000	2.04640000
O	-0.83100000	1.37060000	1.85890000
C	-1.57330000	0.33610000	2.28230000
C	-3.88640000	-0.36120000	2.38070000
C	-1.11850000	-0.82990000	2.88820000
H	-4.94180000	-0.21140000	2.18790000
C	-3.41340000	-1.52980000	2.97000000
C	-2.06610000	-1.76900000	3.20510000
H	-0.05940000	-1.00650000	3.05630000
N	-4.38090000	-2.57640000	3.30000000
H	-1.77420000	-2.70880000	3.65860000
O	-5.54790000	-2.39390000	2.99630000
O	-3.97030000	-3.57990000	3.85840000

1-Q50A-w_e TS (QM)

C	-1.96700000	-4.01120000	-2.06680000
H	-2.07230000	-3.40350000	-2.96830000
C	-0.52730000	-4.30900000	-1.70760000
C	-2.56040000	-3.28680000	-0.86440000
H	-2.48390000	-4.96190000	-2.22600000
N	0.45300000	-3.56300000	-2.25400000
O	-0.26580000	-5.12170000	-0.81690000
C	-4.02130000	-2.97030000	-0.98520000
H	-2.00510000	-2.35240000	-0.70290000
H	-2.37850000	-3.90790000	0.02020000
C	1.80820000	-3.65650000	-1.71180000
C	0.40340000	-2.73730000	-3.45070000
C	-5.07000000	-3.85140000	-0.99200000
C	-4.56830000	-1.65630000	-1.10870000
C	2.62820000	-2.78000000	-2.64080000
H	2.14150000	-4.69900000	-1.71120000
C	1.77650000	-3.10740000	-0.29900000
C	1.84570000	-2.81710000	-3.91430000
H	0.11270000	-1.70770000	-3.20390000
H	-0.29970000	-3.14060000	-4.18060000
N	-6.24960000	-3.15290000	-1.07450000
H	-5.07180000	-4.93020000	-0.91750000
C	-5.96640000	-1.81250000	-1.13210000
C	-4.01430000	-0.37070000	-1.17580000
H	2.65740000	-1.76010000	-2.23920000
H	3.65490000	-3.13880000	-2.73790000
O	1.46320000	-1.94330000	-0.03590000
N	2.12540000	-3.98540000	0.66040000
H	2.10690000	-2.01100000	-4.60410000
H	2.00230000	-3.76910000	-4.43340000
H	-7.17340000	-3.55910000	-1.08000000
C	-6.83010000	-0.72410000	-1.21340000
H	-2.93570000	-0.22110000	-1.13910000
C	-4.87590000	0.69580000	-1.25210000
C	1.98750000	-3.64530000	2.06370000
H	2.14990000	-4.96400000	0.40410000
H	-7.90760000	-0.85860000	-1.22770000
C	-6.25800000	0.51160000	-1.27850000
H	-4.47400000	1.70500000	-1.30040000
C	2.88730000	-2.47080000	2.43890000
H	0.96060000	-3.34660000	2.29410000
H	2.25210000	-4.52110000	2.65900000
H	-6.89340000	1.39250000	-1.32390000
O	2.44850000	-1.49170000	3.02250000
N	4.19350000	-2.61630000	2.09100000
C	5.17570000	-1.60940000	2.42450000
H	4.50220000	-3.53620000	1.80060000
C	5.88360000	-0.99230000	1.22350000
H	4.66740000	-0.80860000	2.96050000
H	5.95670000	-2.02170000	3.07250000
O	6.49840000	0.06570000	1.36450000

N	5.92480000	-1.68160000	0.06360000
C	6.85560000	-1.28770000	-0.98150000
H	5.37990000	-2.52570000	-0.04450000
C	6.45410000	-0.05200000	-1.77980000
H	7.82680000	-1.05590000	-0.53750000
H	6.98040000	-2.12080000	-1.67480000
O	7.26530000	0.39360000	-2.58830000
N	5.25270000	0.51490000	-1.53950000
C	4.91550000	1.83760000	-2.04330000
H	4.61010000	0.12520000	-0.84450000
C	4.91390000	2.91980000	-0.97280000
H	5.64040000	2.10820000	-2.81330000
H	3.91880000	1.83390000	-2.49390000
O	4.51960000	4.04750000	-1.27490000
N	5.34130000	2.59770000	0.25320000
H	5.68900000	1.66530000	0.46900000
C	5.31780000	3.61290000	1.28490000
H	4.37390000	4.16250000	1.19130000
C	5.44240000	3.00790000	2.67880000
H	6.12230000	4.33970000	1.11390000
H	6.40500000	2.48560000	2.74780000
C	4.32450000	2.04460000	3.02430000
H	5.47900000	3.83120000	3.40040000
H	4.23560000	1.25320000	2.27500000
H	4.49310000	1.58100000	4.00160000
H	3.35930000	2.56430000	3.06550000
H	0.23320000	-0.71830000	-0.73260000
O	-0.39490000	0.00250000	-0.92210000
H	-0.30150000	0.61340000	-0.16790000
H	2.55090000	-0.46300000	0.43890000
O	3.18570000	0.27090000	0.36010000
H	2.64380000	1.08150000	0.31430000
O	1.29060000	2.49800000	-0.24680000
C	0.60490000	3.52610000	-0.17020000
N	0.83120000	4.45500000	0.76910000
C	-0.49890000	3.78010000	-1.17550000
H	1.53110000	4.19620000	1.45300000
C	-0.01700000	5.59500000	1.04790000
N	-0.59330000	2.65330000	-2.06290000
H	-0.28040000	4.70170000	-1.73360000
H	-1.43790000	3.93910000	-0.63720000
H	-0.99130000	5.28040000	1.43910000
H	-0.17180000	6.19250000	0.14540000
H	0.47850000	6.22180000	1.78800000
C	-1.65960000	2.49770000	-2.87440000
H	0.03490000	1.87260000	-1.89090000
C	-1.54680000	1.36010000	-3.87400000
O	-2.60010000	3.29220000	-2.88570000
H	-0.89940000	0.56270000	-3.50420000
H	-1.12880000	1.75990000	-4.80250000
H	-2.54160000	0.96320000	-4.08310000
H	-3.49080000	4.30660000	-0.06560000

C	-4.39260000	4.88710000	0.17300000
C	-5.51000000	3.92000000	0.45360000
C	-4.72530000	5.86270000	-0.95250000
H	-4.16530000	5.41240000	1.10910000
O	-5.31540000	2.97160000	1.33720000
O	-6.60080000	4.06270000	-0.08490000
H	-5.61140000	6.45110000	-0.70560000
H	-3.88840000	6.54430000	-1.12760000
H	-4.92900000	5.32010000	-1.87880000
H	-4.28610000	2.63500000	1.35040000
C	-2.97390000	1.89800000	1.43050000
N	-1.84240000	2.41740000	1.25640000
C	-2.91610000	0.57720000	2.03760000
O	-0.76040000	1.29780000	1.82960000
C	-1.53670000	0.33960000	2.25400000
C	-3.88120000	-0.37210000	2.37400000
C	-1.11280000	-0.83350000	2.88430000
H	-4.93600000	-0.21840000	2.18140000
C	-3.40540000	-1.53930000	2.96400000
C	-2.05780000	-1.77590000	3.20000000
H	-0.05570000	-1.01720000	3.05660000
N	-4.36350000	-2.58410000	3.28830000
H	-1.76700000	-2.71430000	3.65780000
O	-5.53730000	-2.40580000	2.99460000
O	-3.95580000	-3.59800000	3.83780000

1-Q50A (QM)

C	-1.98370000	-4.01590000	-2.07330000
H	-2.08860000	-3.41230000	-2.97760000
C	-0.54460000	-4.31530000	-1.71280000
C	-2.57590000	-3.28620000	-0.87350000
H	-2.50350000	-4.96580000	-2.22740000
N	0.43810000	-3.58120000	-2.26740000
O	-0.28780000	-5.12120000	-0.81370000
C	-4.03620000	-2.96730000	-0.99580000
H	-2.01800000	-2.35460000	-0.71160000
H	-2.39510000	-3.90480000	0.01280000
C	1.79210000	-3.66730000	-1.71880000
C	0.38940000	-2.75150000	-3.46120000
C	-5.08650000	-3.84640000	-0.99970000
C	-4.58060000	-1.65260000	-1.12400000
C	2.61410000	-2.79580000	-2.65070000
H	2.12690000	-4.70980000	-1.71700000
C	1.76140000	-3.11340000	-0.30790000
C	1.83170000	-2.83580000	-3.92430000
H	0.10270000	-1.72170000	-3.21310000
H	-0.31500000	-3.15070000	-4.19220000
N	-6.26430000	-3.14570000	-1.08480000
H	-5.09030000	-4.92480000	-0.92130000
C	-5.97890000	-1.80620000	-1.14710000
C	-4.02400000	-0.36830000	-1.19560000
H	2.64610000	-1.77550000	-2.25160000
H	3.63970000	-3.15820000	-2.74770000
O	1.45360000	-1.94930000	-0.06340000
N	2.11300000	-3.99520000	0.65730000
H	2.09410000	-2.03290000	-4.61760000
H	1.98570000	-3.79000000	-4.44010000
H	-7.18890000	-3.54980000	-1.08970000
C	-6.84050000	-0.71640000	-1.23240000
H	-2.94610000	-0.22180000	-1.16700000
C	-4.88350000	0.69960000	-1.27580000
C	1.97070000	-3.64330000	2.05660000
H	2.08510000	-4.97620000	0.40980000
H	-7.91830000	-0.84980000	-1.24400000
C	-6.26600000	0.51800000	-1.30180000
H	-4.49540000	1.71440000	-1.32550000
C	2.87280000	-2.46920000	2.42780000
H	0.94470000	-3.34040000	2.28650000
H	2.23330000	-4.51390000	2.66090000
H	-6.88440000	1.41040000	-1.33030000
O	2.43610000	-1.49230000	3.01820000
N	4.17770000	-2.61630000	2.07880000
C	5.16290000	-1.61230000	2.41090000
H	4.48060000	-3.53420000	1.77670000
C	5.87220000	-1.00080000	1.20780000
H	4.65590000	-0.80870000	2.94400000
H	5.94260000	-2.02500000	3.06020000
O	6.49000000	0.05610000	1.34510000

N	5.91310000	-1.69470000	0.05060000
C	6.84400000	-1.30590000	-0.99590000
H	5.36070000	-2.53380000	-0.05800000
C	6.44510000	-0.07220000	-1.79860000
H	7.81570000	-1.07450000	-0.55270000
H	6.96740000	-2.14150000	-1.68650000
O	7.25720000	0.36870000	-2.60890000
N	5.24490000	0.49800000	-1.56030000
C	4.91020000	1.81940000	-2.06910000
H	4.60170000	0.11320000	-0.86200000
C	4.91060000	2.90540000	-1.00240000
H	5.63560000	2.08620000	-2.83990000
H	3.91370000	1.81610000	-2.52010000
O	4.52110000	4.03350000	-1.30900000
N	5.33350000	2.58560000	0.22580000
H	5.68320000	1.65440000	0.44400000
C	5.31530000	3.60570000	1.25290000
H	4.37370000	4.15870000	1.15780000
C	5.43850000	3.00540000	2.64900000
H	6.12280000	4.32830000	1.07810000
H	6.40000000	2.48120000	2.72000000
C	4.31870000	2.04550000	2.99760000
H	5.47660000	3.83100000	3.36770000
H	4.23220000	1.24900000	2.25340000
H	4.48430000	1.58780000	3.97830000
H	3.35380000	2.56610000	3.03280000
H	2.53580000	-0.48620000	0.36140000
O	3.18820000	0.23830000	0.34260000
H	2.66250000	1.05840000	0.28860000
O	1.30110000	2.50620000	-0.29680000
C	0.60260000	3.52310000	-0.20280000
N	0.82370000	4.44940000	0.73940000
C	-0.50030000	3.77550000	-1.20910000
H	1.53650000	4.20140000	1.41370000
C	-0.01540000	5.59720000	1.00780000
N	-0.59000000	2.66040000	-2.10520000
H	-0.29450000	4.71020000	-1.75070000
H	-1.44770000	3.91420000	-0.67880000
H	-0.99420000	5.29420000	1.39710000
H	-0.16100000	6.19280000	0.10240000
H	0.48160000	6.22280000	1.74790000
C	-1.66340000	2.48940000	-2.90380000
H	0.19500000	2.02140000	-2.10970000
C	-1.55260000	1.34820000	-3.89940000
O	-2.64270000	3.23020000	-2.85800000
H	-0.63900000	0.76450000	-3.77830000
H	-1.57720000	1.76880000	-4.90780000
H	-2.42140000	0.69420000	-3.78780000
H	-3.51050000	4.29960000	-0.14870000
C	-4.39230000	4.89510000	0.13550000
C	-5.51260000	3.93140000	0.41750000
C	-4.72280000	5.86690000	-0.99460000

H	-4.12210000	5.41990000	1.05810000
O	-5.51190000	3.38040000	1.55530000
O	-6.33980000	3.72130000	-0.50320000
H	-5.59850000	6.47230000	-0.74070000
H	-3.88780000	6.54500000	-1.20100000
H	-4.95820000	5.31260000	-1.90410000
H	-3.78960000	2.53960000	1.24370000
C	-2.92430000	1.93000000	1.49390000
N	-1.71740000	2.39670000	1.41540000
C	-2.93200000	0.60540000	2.05080000
O	-0.84730000	1.41340000	1.90910000
C	-1.58290000	0.35950000	2.29410000
C	-3.89110000	-0.35700000	2.35520000
C	-1.12370000	-0.82320000	2.86660000
H	-4.94570000	-0.21260000	2.15380000
C	-3.41840000	-1.52380000	2.94820000
C	-2.07130000	-1.76180000	3.18530000
H	-0.06410000	-1.00070000	3.03070000
N	-4.38410000	-2.57470000	3.26890000
H	-1.77810000	-2.70530000	3.63040000
O	-5.54960000	-2.39670000	2.95670000
O	-3.97410000	-3.57680000	3.83050000

1-Q50A TS (QM)				N	5.92150000	-1.68010000	0.05980000
C	-1.96540000	-4.02910000	-2.06960000	C	6.85320000	-1.29160000	-0.98620000
H	-2.07040000	-3.42820000	-2.97560000	H	5.37020000	-2.52010000	-0.04780000
C	-0.52600000	-4.32350000	-1.70610000	C	6.45200000	-0.06130000	-1.79300000
C	-2.56150000	-3.29770000	-0.87270000	H	7.82330000	-1.05610000	-0.54190000
H	-2.48230000	-4.98080000	-2.22200000	H	6.98030000	-2.12890000	-1.67410000
N	0.45540000	-3.58810000	-2.26120000	O	7.26410000	0.37950000	-2.60330000
O	-0.26830000	-5.12660000	-0.80470000	N	5.24990000	0.50610000	-1.55800000
C	-4.02240000	-2.98320000	-0.99810000	C	4.91240000	1.82540000	-2.07080000
H	-2.00650000	-2.36420000	-0.71180000	H	4.60590000	0.12110000	-0.86060000
H	-2.38080000	-3.91340000	0.01570000	C	4.90800000	2.91420000	-1.00720000
C	1.80870000	-3.66890000	-1.71040000	H	5.63840000	2.09200000	-2.84110000
C	0.40640000	-2.76200000	-3.45740000	H	3.91660000	1.81800000	-2.52340000
C	-5.07030000	-3.86520000	-1.00120000	O	4.51720000	4.04080000	-1.31780000
C	-4.57020000	-1.67040000	-1.13070000	N	5.33030000	2.59910000	0.22250000
C	2.62990000	-2.79780000	-2.64340000	H	5.67950000	1.66860000	0.44440000
H	2.14630000	-4.71050000	-1.70540000	C	5.30740000	3.62170000	1.24680000
C	1.77460000	-3.11150000	-0.30100000	H	4.36430000	4.17160000	1.14880000
C	1.84960000	-2.84350000	-3.91800000	C	5.43020000	3.02560000	2.64470000
H	0.11610000	-1.73240000	-3.21270000	H	6.11310000	4.34630000	1.07130000
H	-0.29570000	-3.16540000	-4.18840000	H	6.39300000	2.50420000	2.71830000
N	-6.25000000	-3.16800000	-1.09020000	C	4.31250000	2.06350000	2.99430000
H	-5.07130000	-4.94340000	-0.91990000	H	5.46520000	3.85320000	3.36130000
C	-5.96810000	-1.82790000	-1.15550000	H	4.22670000	1.26660000	2.25050000
C	-4.01710000	-0.38480000	-1.20490000	H	4.47940000	1.60680000	3.97510000
H	2.65840000	-1.77630000	-2.24690000	H	3.34660000	2.58230000	3.02970000
H	3.65660000	-3.15770000	-2.73770000	H	2.53310000	-0.46970000	0.36890000
O	1.46490000	-1.94740000	-0.06020000	O	3.18410000	0.25550000	0.33760000
N	2.12750000	-3.99010000	0.66720000	H	2.65640000	1.07440000	0.28040000
H	2.11080000	-2.04180000	-4.61320000	O	1.31040000	2.51630000	-0.31910000
H	2.00700000	-3.79870000	-4.43090000	C	0.59700000	3.52200000	-0.21570000
H	-7.17350000	-3.57480000	-1.09480000	N	0.80690000	4.44500000	0.73160000
C	-6.83250000	-0.74070000	-1.24500000	C	-0.50460000	3.76910000	-1.22460000
H	-2.94070000	-0.23310000	-1.17020000	H	1.52220000	4.20220000	1.40480000
C	-4.87940000	0.68050000	-1.28930000	C	-0.02840000	5.59790000	0.98820000
C	1.98170000	-3.63420000	2.06520000	N	-0.57440000	2.67130000	-2.14340000
H	2.09880000	-4.97180000	0.42260000	H	-0.31630000	4.71820000	-1.74680000
H	-7.90990000	-0.87620000	-1.26000000	H	-1.45460000	3.87520000	-0.69160000
C	-6.26140000	0.49500000	-1.31700000	H	-1.02230000	5.29620000	1.33790000
H	-4.47790000	1.68940000	-1.34890000	H	-0.13610000	6.21050000	0.08860000
C	2.88000000	-2.45660000	2.43470000	H	0.44820000	6.20510000	1.75650000
H	0.95450000	-3.33200000	2.29220000	C	-1.66190000	2.47460000	-2.91720000
H	2.24540000	-4.50210000	2.67280000	H	0.21660000	2.03970000	-2.15290000
H	-6.89590000	1.37620000	-1.36690000	C	-1.54630000	1.33120000	-3.90970000
O	2.44320000	-1.48060000	3.02540000	O	-2.65860000	3.19070000	-2.84720000
N	4.18600000	-2.60090000	2.08610000	H	-0.59750000	0.79800000	-3.83560000
C	5.16760000	-1.59350000	2.41880000	H	-1.65140000	1.73780000	-4.91860000
H	4.49190000	-3.51830000	1.78580000	H	-2.37130000	0.63310000	-3.74310000
C	5.87710000	-0.98330000	1.21520000	H	-3.50340000	4.29500000	-0.12580000
H	4.65730000	-0.79020000	2.94910000	C	-4.40210000	4.88120000	0.11100000
H	5.94750000	-2.00240000	3.07040000	C	-5.51980000	3.91570000	0.39480000
O	6.49230000	0.07540000	1.35040000	C	-4.73350000	5.84900000	-1.02210000

H	-4.17120000	5.41090000	1.04330000	C	-3.88980000	-0.36340000	2.34630000
O	-5.35980000	3.02700000	1.34860000	C	-1.12180000	-0.82040000	2.86280000
O	-6.58160000	4.00040000	-0.20820000	H	-4.94310000	-0.21830000	2.13920000
H	-5.62140000	6.43790000	-0.78190000	C	-3.41460000	-1.52730000	2.94280000
H	-3.89720000	6.53110000	-1.19790000	C	-2.06720000	-1.76100000	3.18270000
H	-4.93280000	5.30010000	-1.94530000	H	-0.06450000	-1.00560000	3.03120000
H	-4.33930000	2.70480000	1.42220000	N	-4.36830000	-2.57740000	3.25190000
C	-3.00800000	1.96120000	1.52860000	H	-1.77400000	-2.70600000	3.62530000
N	-1.89690000	2.52960000	1.42210000	O	-5.54040000	-2.40860000	2.94240000
C	-2.93400000	0.61020000	2.06080000	O	-3.96280000	-3.58880000	3.80930000
O	-0.78500000	1.38450000	1.97020000				
C	-1.54850000	0.39140000	2.29890000				

Python script for $\Delta\Delta G$ predictions with PyRosetta

```
def mutate_repack_func4(pose, target_position, mutant, repack_radius, sfxn, ddg_bbnbrs=1,
verbose=False, cartesian=True, max_iter=None):
    import time
    from pyrosetta.rosetta.core.pack.task import operation

    #logger.warning("Interface mode not implemented (should be added!)")

    if cartesian:

sfxn.set_weight(pyrosetta.rosetta.core.scoring.ScoreTypeManager.score_type_from_name('cart_bonded'), 0.5)
        #sfxn.set_weight(atom_pair_constraint, 1)#0.5

sfxn.set_weight(pyrosetta.rosetta.core.scoring.ScoreTypeManager.score_type_from_name('pro_close'), 0)

#logger.warning(pyrosetta.rosetta.basic.options.get_boolean_option('ex1'))#set_boolean_option(
'-ex1', True )
        #pyrosetta.rosetta.basic.options.set_boolean_option( 'ex2', True )

    #Cloning of the pose including all settings
    working_pose = pose.clone()

    #Select mutant residue
    mutant_selector =
pyrosetta.rosetta.core.select.residue_selector.ResidueIndexSelector(target_position)

    #Select all except mutant
    all_nand_mutant_selector =
pyrosetta.rosetta.core.select.residue_selector.NotResidueSelector()
    all_nand_mutant_selector.set_residue_selector(mutant_selector)

    #Select neighbors with mutant
    nbr_or_mutant_selector =
pyrosetta.rosetta.core.select.residue_selector.NeighborhoodResidueSelector()
    nbr_or_mutant_selector.set_focus(str(target_position))
    nbr_or_mutant_selector.set_distance(repack_radius)
    nbr_or_mutant_selector.set_include_focus_in_subset(True)

    #Select mutant and it's sequence neighbors
    seq_nbr_or_mutant_selector =
pyrosetta.rosetta.core.select.residue_selector.PrimarySequenceNeighborhoodSelector(ddg_bbnbrs,
ddg_bbnbrs, mutant_selector, False)

    #Select mutant, it's seq neighbors and it's surrounding neighbors
    seq_nbr_or_nbr_or_mutant_selector =
pyrosetta.rosetta.core.select.residue_selector.OrResidueSelector()
    seq_nbr_or_nbr_or_mutant_selector.add_residue_selector(seq_nbr_or_mutant_selector)
    seq_nbr_or_nbr_or_mutant_selector.add_residue_selector(nbr_or_mutant_selector)

    if verbose:
        print(f'mutant_selector:
{pyrosetta.rosetta.core.select.residue_selector.selection_positions(mutant_selector.apply(working_pose))}')
    }
```

```

        print(f'all_nand_mutant_selector:
{pyrosetta.rosetta.core.select.residue_selector.selection_positions(all_nand_mutant_selector.a
pply(working_pose))}')
        print(f'nbr_or_mutant_selector:
{pyrosetta.rosetta.core.select.residue_selector.selection_positions(nbr_or_mutant_selector.app
ly(working_pose))}')
        print(f'seq_nbr_or_mutant_selector:
{pyrosetta.rosetta.core.select.residue_selector.selection_positions(seq_nbr_or_mutant_selector
.apply(working_pose))}')
        print(f'seq_nbr_or_nbr_or_mutant_selector:
{pyrosetta.rosetta.core.select.residue_selector.selection_positions(seq_nbr_or_nbr_or_mutant_s
elector.apply(working_pose))}')

#Mutate residue and pack rotamers before relax
#if list(pose.sequence())[target_position-1] != mutant:
    #generate packer task
    tf = TaskFactory()
    tf.push_back(operation.InitializeFromCommandline())
    tf.push_back(operation.IncludeCurrent())

    #Set all residues except mutant to false for design and repacking
    prevent_repacking_rlt = operation.PreventRepackingRLT()
    prevent_subset_repacking = operation.OperateOnResidueSubset(prevent_repacking_rlt,
all_nand_mutant_selector, False)
    tf.push_back(prevent_subset_repacking)

    #Assign mutant residue to be designed and repacked
    resfile_comm =
pyrosetta.rosetta.protocols.task_operations.ResfileCommandOperation(mutant_selector, f"PIKAA
{mutant}")
    resfile_comm.set_command(f"PIKAA {mutant}")
    tf.push_back(resfile_comm)

    #Apply packing of rotamers of mutant
    packer = pyrosetta.rosetta.protocols.minimization_packing.PackRotamersMover()
    packer.score_function(sfxn)
    packer.task_factory(tf)
    if verbose:
        logger.warning(tf.create_task_and_apply_taskoperations(working_pose))
    packer.apply(working_pose)

    #allow the movement for bb for the mutant + seq. neighbors, and sc for neighbor in range,
seq. neighbor and mutant
    movemap = pyrosetta.rosetta.core.select.movemap.MoveMapFactory()
    movemap.all_jumps(False)
    movemap.add_bb_action(pyrosetta.rosetta.core.select.movemap.mm_enable,
seq_nbr_or_mutant_selector)
    movemap.add_chi_action(pyrosetta.rosetta.core.select.movemap.mm_enable,
seq_nbr_or_nbr_or_mutant_selector)

    #for checking if all has been selected correctly
    #if verbose:
    mm = movemap.create_movemap_from_pose(working_pose)

    logger.info(mm)

    #Generate a TaskFactory

```

```

tf = TaskFactory()
tf.push_back(operation.InitializeFromCommandline())
tf.push_back(operation.IncludeCurrent())
#tf.push_back(operation.NoRepackDisulfides())

#prevent all residues except selected from design and repacking
prevent_repacking_rlt = operation.PreventRepackingRLT()
prevent_subset_repacking = operation.OperateOnResidueSubset(prevent_repacking_rlt,
seq_nbr_or_nbr_or_mutant_selector, True)
tf.push_back(prevent_subset_repacking)

# allow selected residues only repacking (=switch off design)
restrict_repacking_rlt = operation.RestrictToRepackingRLT()
restrict_subset_repacking = operation.OperateOnResidueSubset(restrict_repacking_rlt ,
seq_nbr_or_nbr_or_mutant_selector, False)
tf.push_back(restrict_subset_repacking)

#Perform a FastRelax
fastrelax = pyrosetta.rosetta.protocols.relax.FastRelax()
fastrelax.set_scorefxn(sfxn)

if cartesian:
    fastrelax.cartesian(True)
if max_iter:
    fastrelax.max_iter(max_iter)

fastrelax.set_task_factory(tf)
fastrelax.set_movemap_factory(movemap)
fastrelax.set_movemap_disables_packing_of_fixed_chi_positions(True)

if verbose:
    logger.info(tf.create_task_and_apply_taskoperations(working_pose))
fastrelax.apply(working_pose)
return working_pose

def cart_ddg(site,res):

    newpose = pose.clone()
    scores = []

    for i in range(3): #ONLY RUNS ONCE!!!!
        scorefxn = create_score_function("ref2015_cart")
        newpose = mutate_repack_func4(newpose,site, res, 6, scorefxn,verbose = False, cartesian
= True)
        news = scorefxn(newpose)
        scores.append(news)
    return scores

all_as = sorted(list(set(pose.sequence())))
sites = np.arange(1,len(pose.sequence()) + 1)

assert len(all_as) == 20

inputs_ = [[site,res] for site in sites for res in all_as]
print(len(inputs_))
cores = 60 # os.cpu_count()
print(cores)

```

```
with multiprocessing.Pool(processes=cores) as pool:
    results = pool.starmap(cart_ddg, inputs_)

import pickle
with open('hg34_base.pkl', 'wb') as f:
    pickle.dump(results, f)
```

SI References

1. Otten, R. *et al.* How directed evolution reshapes the energy landscape in an enzyme to boost catalysis. *Science* **370**, 1442–1446 (2020).