Gas-Phase Salt Bridge Interactions between Glutamic Acid and Arginine

Sander Jaeqx[1], *Jos Oomens*[1,2], *Anouk M. Rijs*[1,*]

[1]Radboud University Nijmegen, Institute for Molecules and Materials, FELIX facility, Toernooiveld 7, 6525 ED Nijmegen, The Netherlands

[2]Van't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands

* corresponding author: a.rijs@science.ru.nl

Supporting Information

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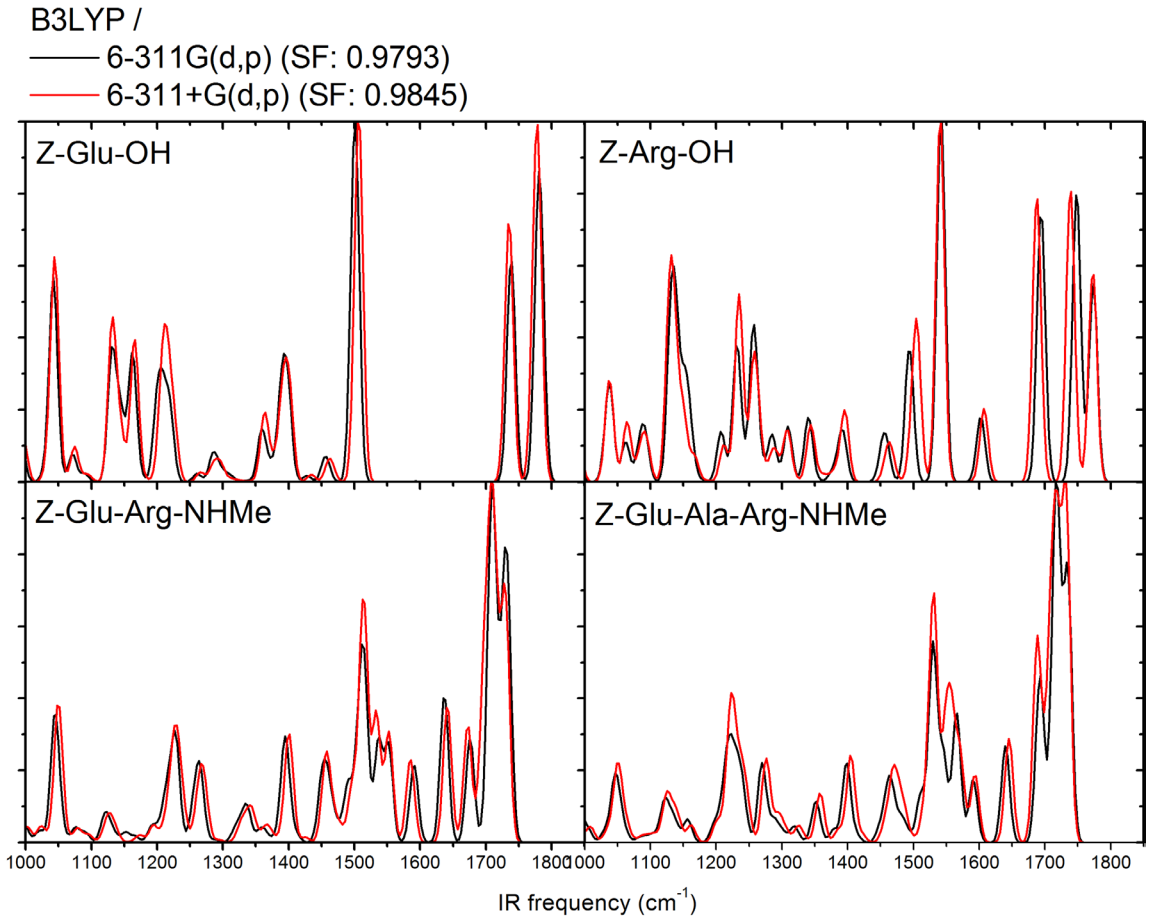

Figure SI-1. Influence of diffuse functions on the calculated spectra of the systems investigated in this study. The black trace is without diffuse functions added to the basis set, the red trace is with diffuse functions added to the basis set.

Table SI-1. ZPE-corrected energies (ZPE), Gibbs free energies at 300K (ΔG) and intramolecular interactions for the optimized structures of Z-Glu-Arg-NHMe. The employed basis set for the M05-2X and B3LYP functionals is 6-311+G(d,p).

	M05-2X		B3LYP		Interactions			
	ZPE	Gibbs	ZPE	Gibbs	SC - SC	Disp. Int.	BB - BB	BB - SC
ER_Z1	0.00	0.00	4.06	5.79	A	NH_2	C10(O0-N3)	N1-O
ER_Z2	3.76	3.24	5.89	5.01	C	N2	C10(O0-N3)	N1-O + O1-H_2N
ER_C1	3.81	2.00	5.41	5.03	OH - NH	NH_2	C10(O0-N3)	N1-O
ER_Z3	4.08	4.06	5.82	8.22	A	2 x NH_2	C10(O0-N3)	N1-O^1 + N2-O^2 + O2-H_2N
ER_Z4	4.28	0.54	0.00	0.00	A		C5(N1-O1) + C7(O1-N3)	N2-O + O2-H_2N
ER_Z5	4.37	3.60	6.60	7.20	B		C5(N1-O1)	N2-O^1 + N3-O^2 + O0-(Hε+H_2N)
ER_Z6	4.46	2.71	5.14	6.34	B	Hε + NH_2	C7(O1-N3)	N1-O
ER_Z7	4.56	2.57	6.55	6.89	A	NH_2	C5(N1-O1)	N2-O + O0-H_2N
ER_Z8	4.85	4.27	11.21	11.97	C		C5(N1-O1) + C7(O1-N3)	N3-O + O0-H_2N + O2-Hε
ER_Z9	5.54	3.51	2.60	1.35	A		-	
ER_C2	6.59	4.41	5.88	3.74	OH - NH	NH_2	C7(O1-N3)	N1-O
ER_Z10	7.84	5.23	4.64	3.82	A		C5(N1-O1)	N2-O^1 +N3-O^2
ER_Z11	8.80	5.28	5.44	5.75	A		C7(O1-N3)	N2-O + O2-N
ER_Z12	9.08	8.07	10.02	9.55	A		C10(O0-N3)	N2-O
ER_C3	9.75	6.06	8.37	7.56	OH - NH	N2	C10(O0-N3)	N1-O
ER_T1	9.98	7.92	10.83	10.76	NH_2-OH	NH_2	C5(N1-O1)	N1-O + O3-HO + N2-Nε
ER_Z13	10.13	5.68	7.00	6.18	C		-	N1-O + O1-H_2N
ER_Z14	10.13	6.30	8.30	9.48	B	Hε + NH_2	-	N1-O + O2-Hε
ER_Z15	10.30	6.96	9.17	9.15	C		C5(N1-O1)	N2-O^1 + N3-O^1 + O0-H_2N
ER_T2	11.12	8.16	7.66	7.29	O-(H_2N)$_2$		C7(O1-N3	N2-Nε + N3-Nε + O0-HO
ER_C4	11.41	9.52	9.76	9.41			C5(N1-O1) + C7(O1-N3)	O0-HO
ER_T3	12.80	10.21	11.96	10.69			C10(O0-N3)	N1-O + N3-Nε + O2-HO
ER_C5	12.90	9.87	10.48	9.84	OH - NH		C5(N1-O1) + C7(O1-N3)	N2-O
ER_T4	13.40	9.78	13.19	12.70	O-H_2N	OH		N1-Nε + N2-Nε + O2-H2N
ER_C6	13.93	9.78	8.82	8.03	OH - NH		C7(O0-N2) + C7(O1-N3)	
ER_T5	14.53	12.09	9.98	8.32			C10(O0-N3)	N2-Nε + O0-H_2N + O1-HO
ER_C7	14.58	12.28	14.36	13.97	OH - NH	N2	C7(O0-N2) + C7(O1-N3)	O0-H_2N

ER_T6	14.77	12.39	12.11	9.49	OH-NH_2	NH_2	C7(O1-N3)	N1-Nε + N2-Nε
ER_C8	15.58	11.61	12.16	11.07			C5(N1-O1) + C5(N2-O2)	N2-O + N3-HNη + O2-HO
ER_T7	16.11	14.08	15.88	14.64		NH_2		N2-Nε + O1-HO
ER_T8	17.32	14.15	14.77	13.23			C7(O1-N3)	N1-H2N + N2-Nε
ER_C9	18.69	14.61	15.69	14.08			C7(O1-N3)	N1-O
ER_T9	19.09	13.10	14.15	11.55		NH_2	C7(O1-N3)	N1-Nε
ER_C10	19.12	12.11	11.78	7.36			C5(N1-O1) + C7(O1-N3)	N2-O
ER_Z16	20.33	18.60	16.20	16.03	A		C7(O0-N2) + C7(O1-N3)	
ER_T10	20.48	17.58	19.92	19.78			C7(O0-N2) + C7(O1-N3)	N1-O + O1-HO
ER_C11	21.04	16.09	16.51	13.81			C7(O0-N2) + C7(O1-N3)	O2-H_2N
ER_C12	25.11	18.57	17.33	13.20			C7(O0-N2) + C7(O1-N3)	

Energies are given in kcal/mol.

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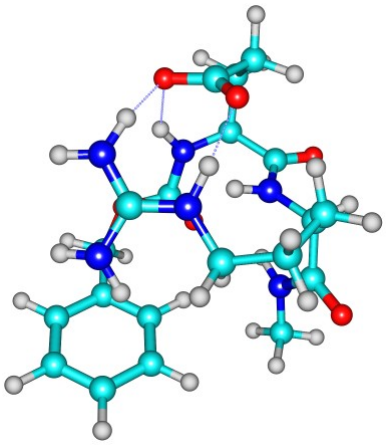

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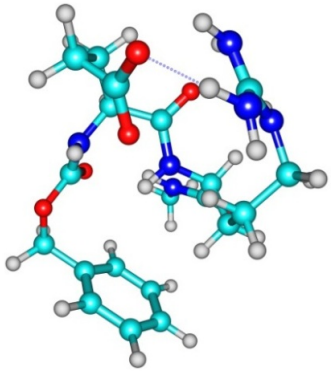

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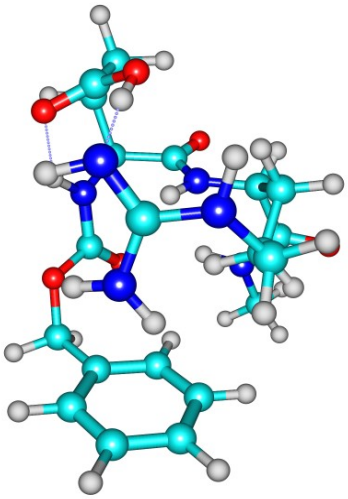

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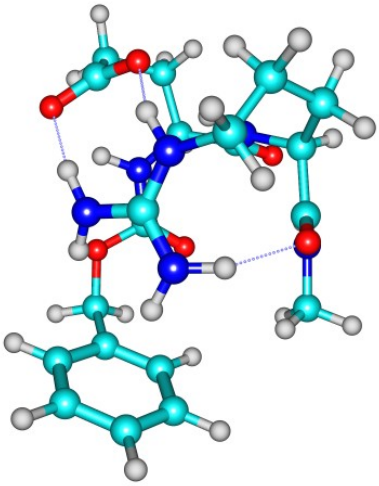

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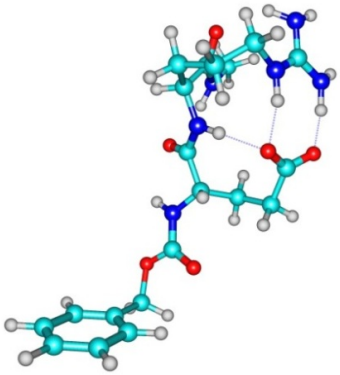

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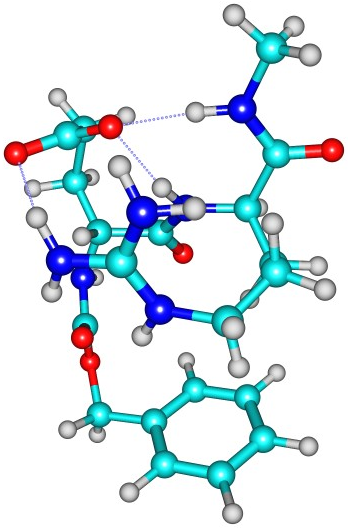

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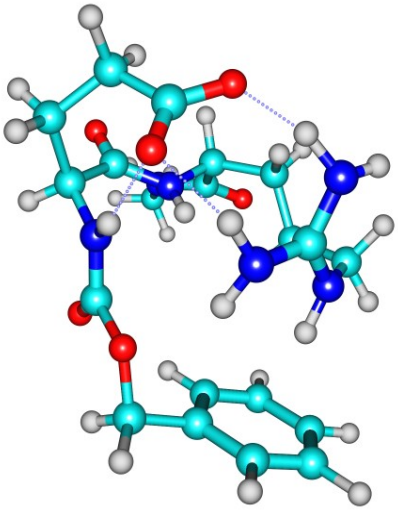

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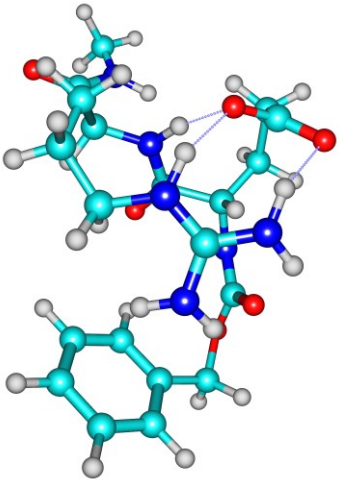

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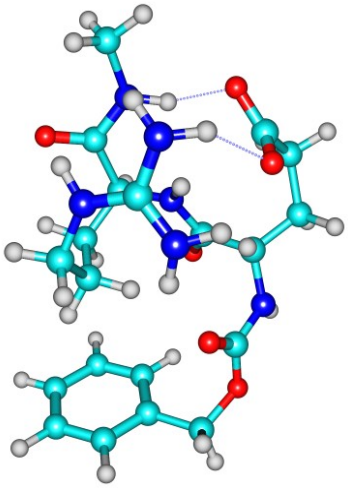

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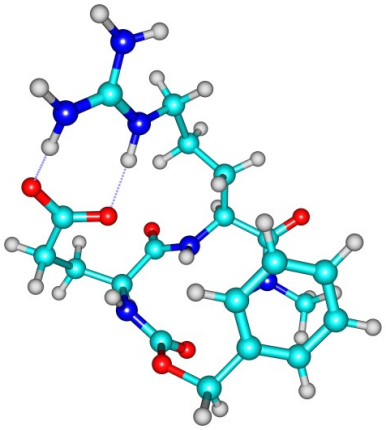
ER_C2

ER_Z10



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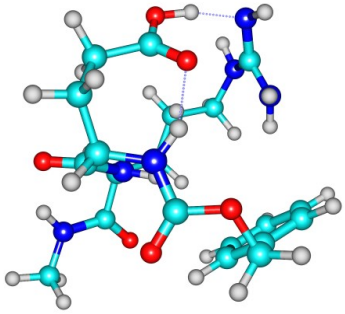

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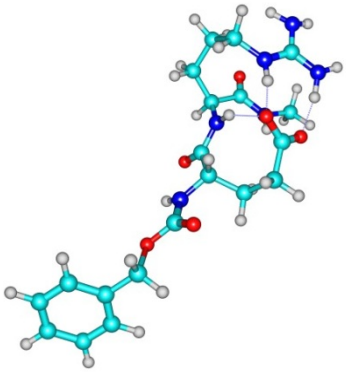

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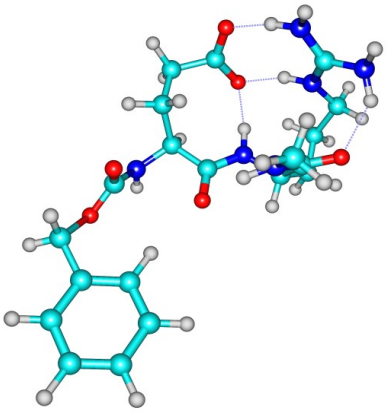

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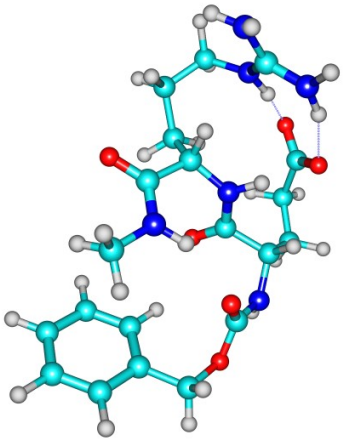

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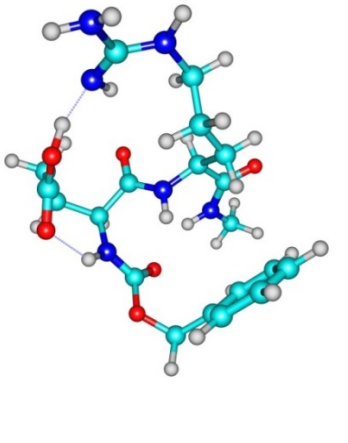

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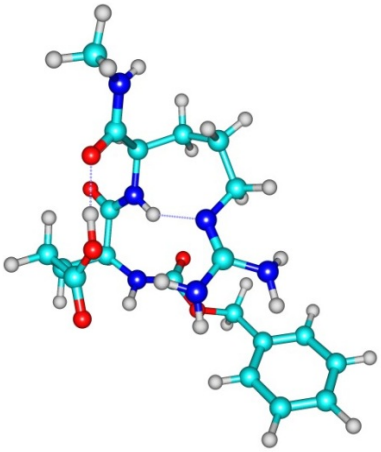

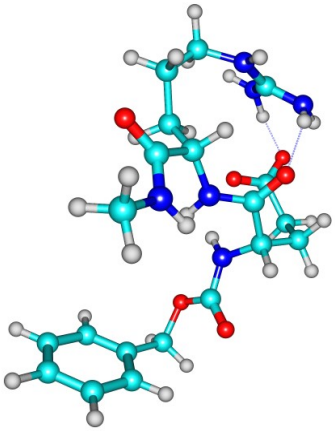

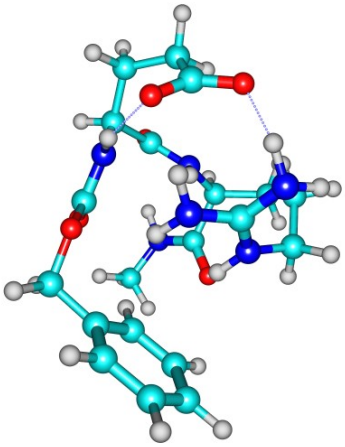

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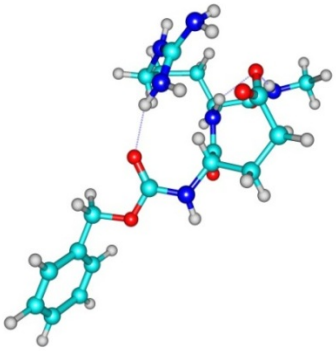

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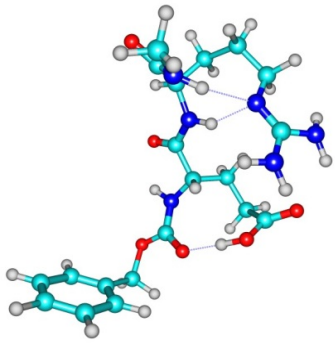

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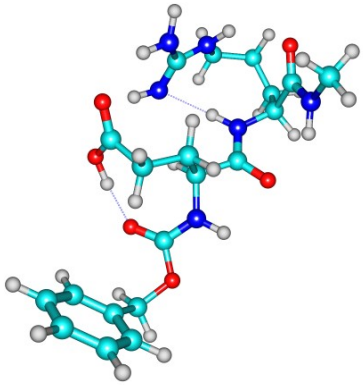

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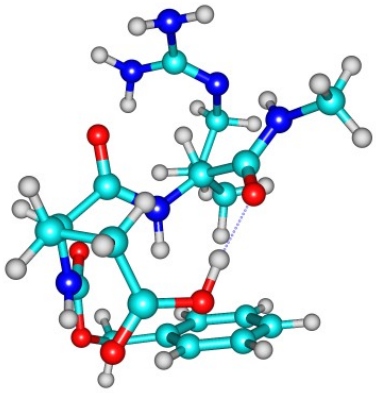

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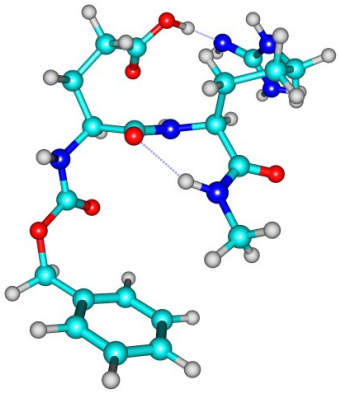

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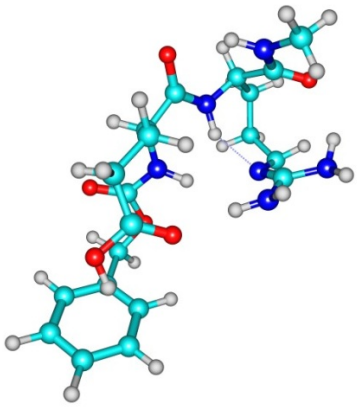

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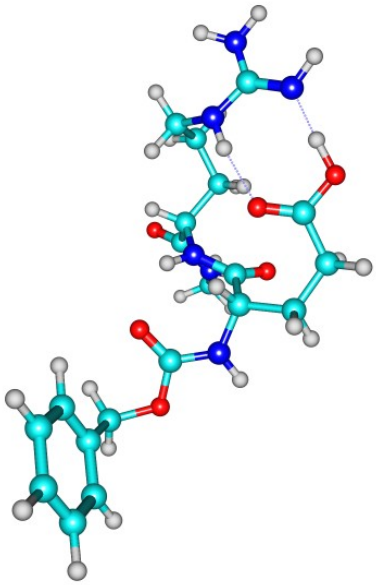

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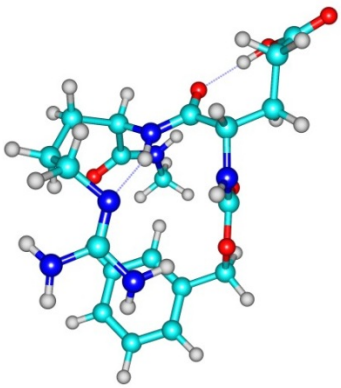

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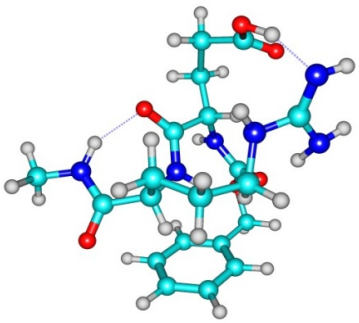

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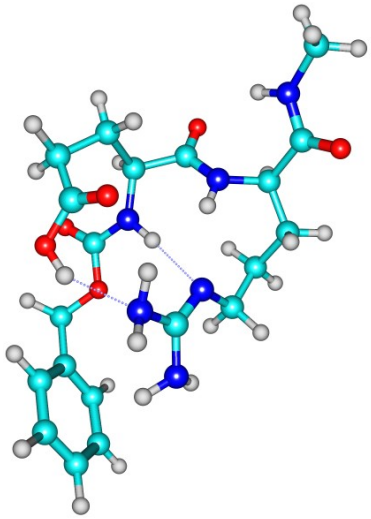

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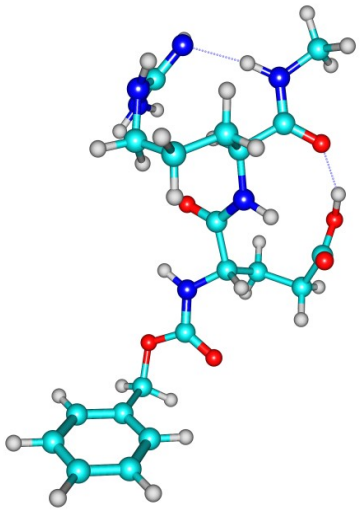

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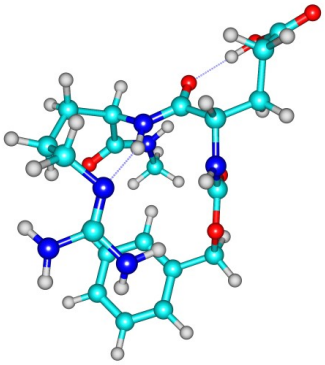

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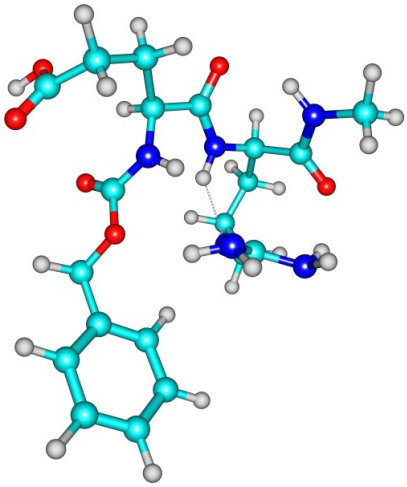

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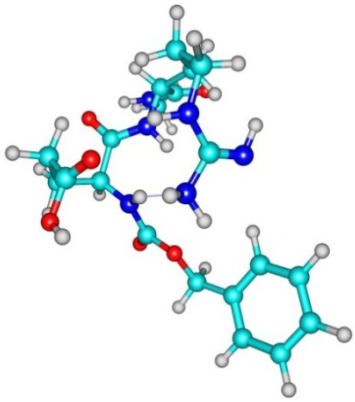

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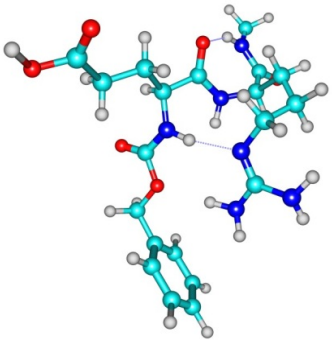

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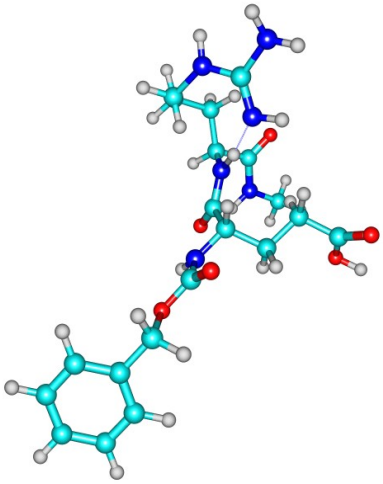

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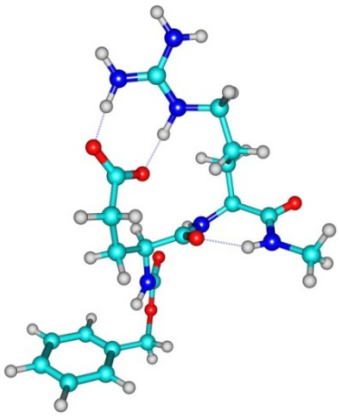

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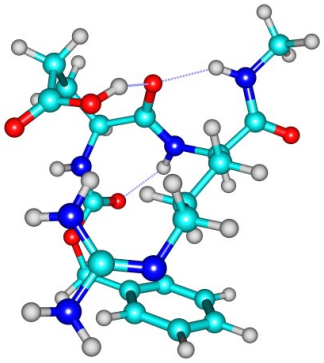

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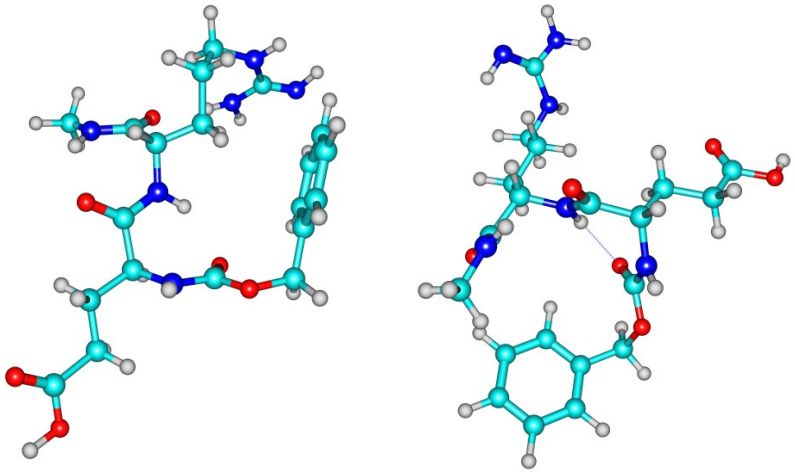
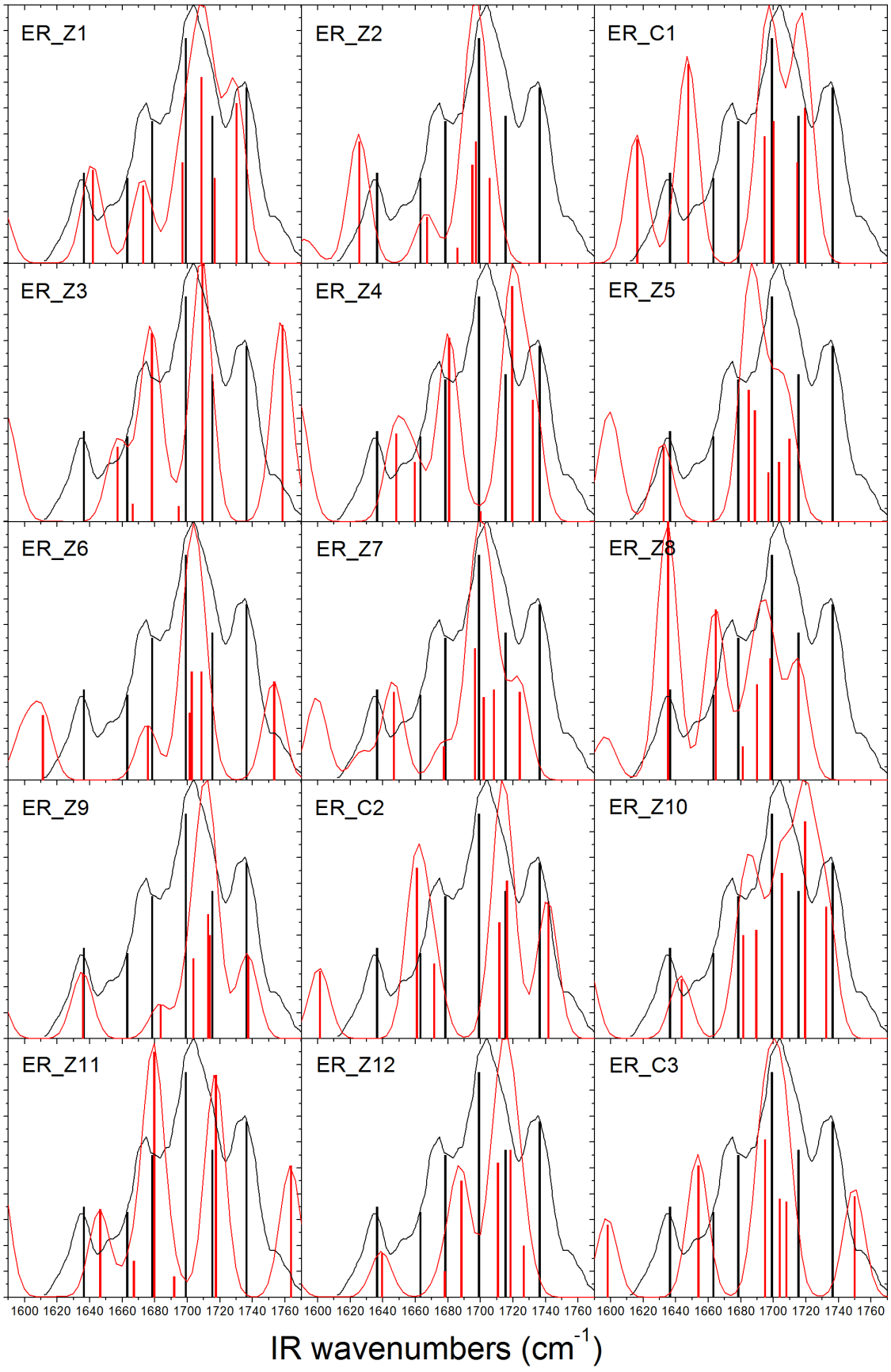


Figure SI-2. Conformations of Z-Glu-Arg-NHMe, optimized with the M05-2x functional employed with the 6-311+G(d,p) basisset.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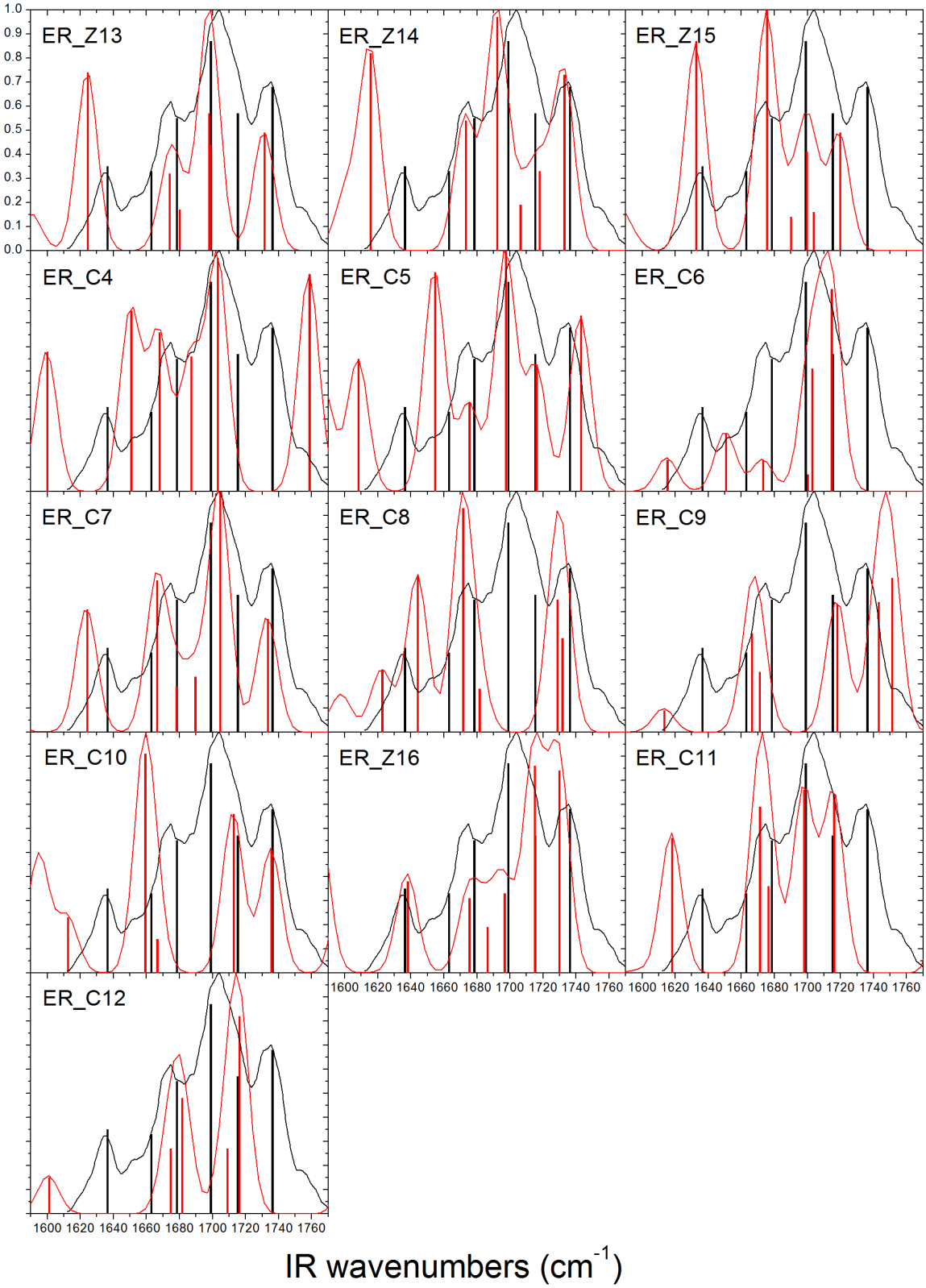
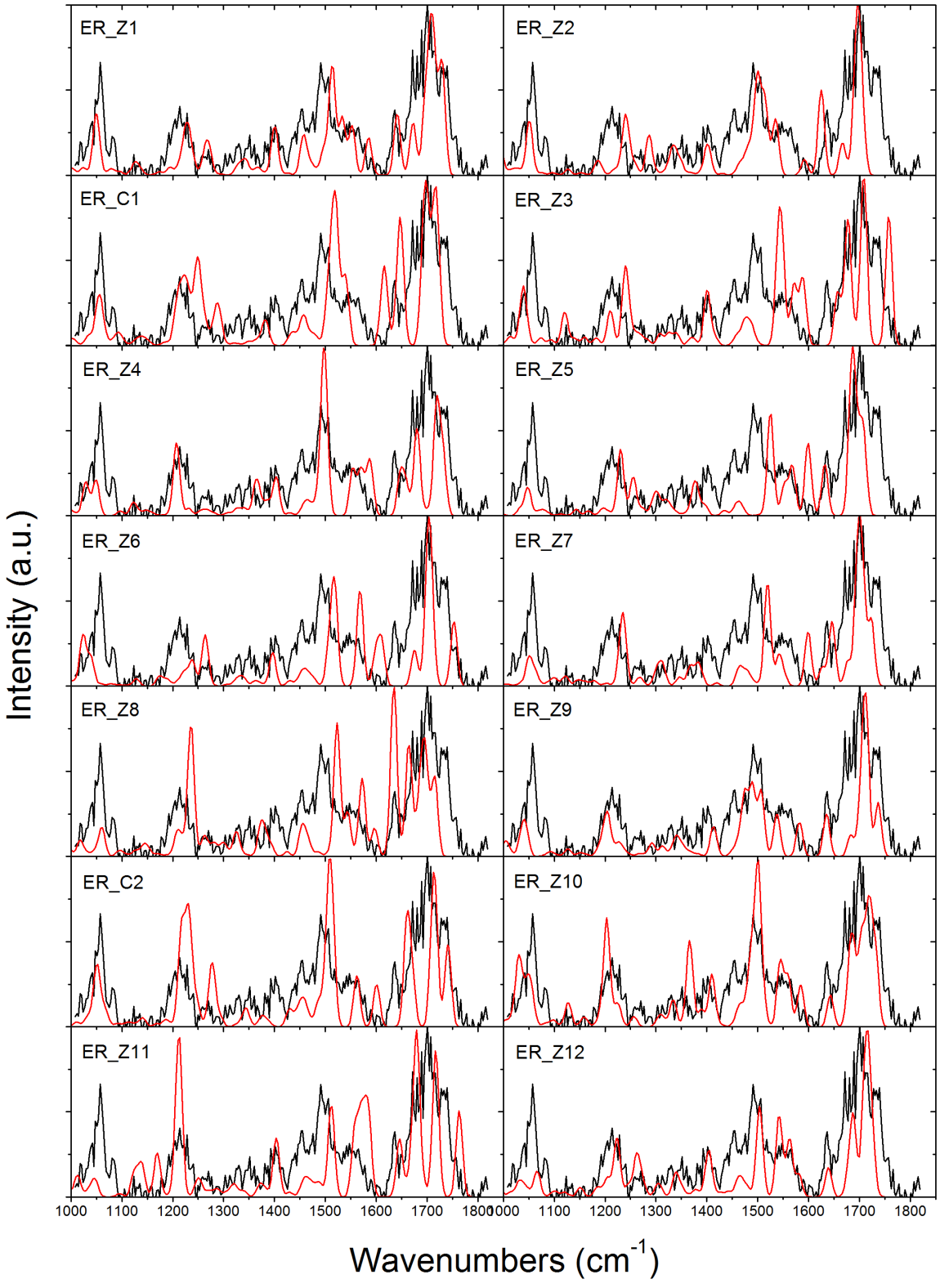


Figure SI-3. Comparison of the experimental IR-UV ion dip spectrum of Z-Glu-Arg-NHMe (black trace) with spectra calculated for various isomers. The black sticks represent the deconvoluted experimental spectrum. The red traces are the theoretical spectra of the optimized structures of Z-Glu-Arg-NHMe, where the red sticks represent the individual computed frequencies and intensities.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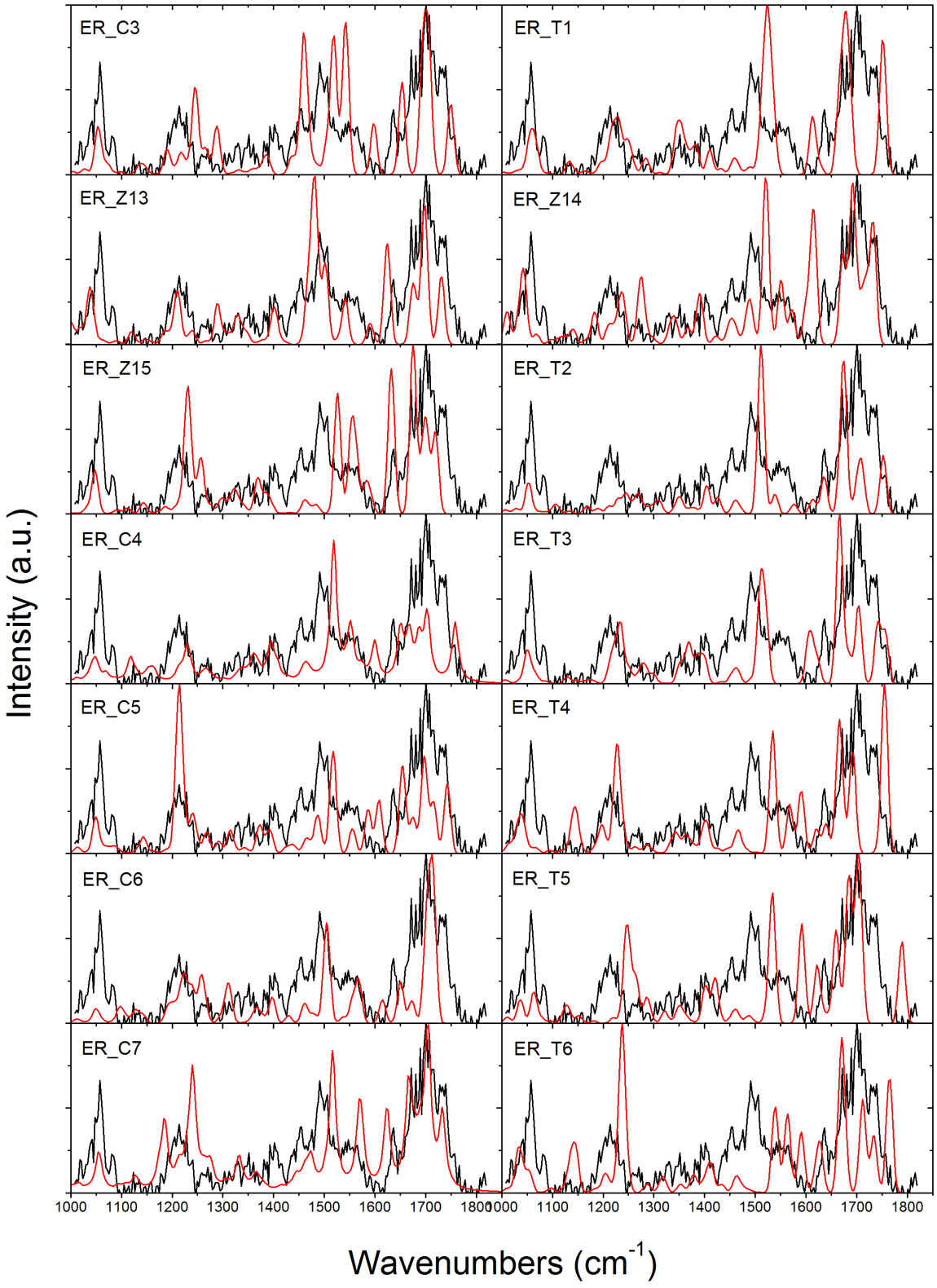
ER_Z11
ER_Z12
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)


ER_C3
ER_T1
ER_Z13
ER_Z14
ER_Z15
ER_T2
ER_C4
ER_T3
ER_C5
ER_T4
ER_C6
ER_T5
ER_C7
ER_T6
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)

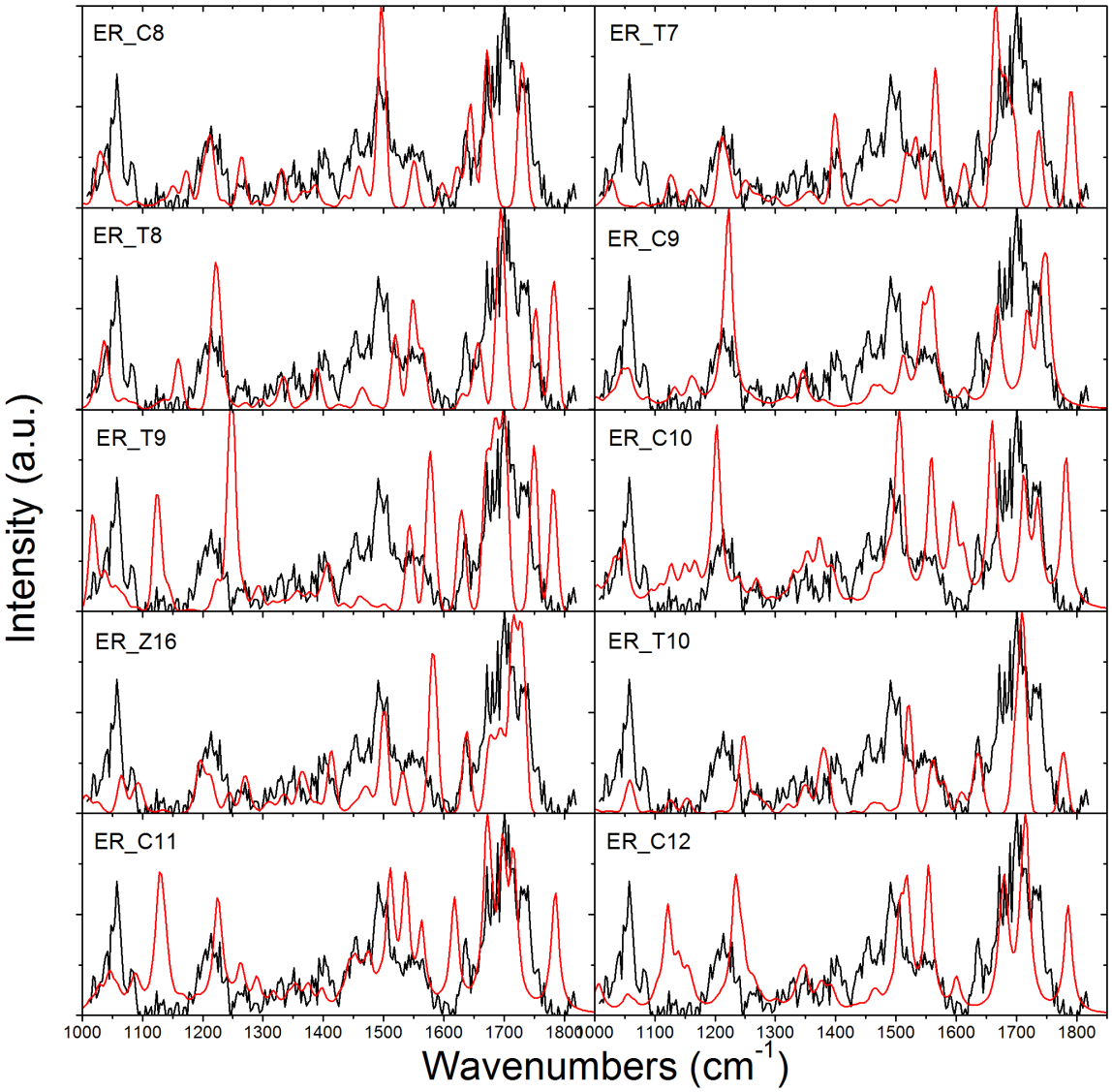


Figure SI-4. Experimental IR-UV ion-dip spectrum of Z-Glu-Arg-NHMe (black trace) and the theoretical spectra of the optimized structures (red trace).

Table SI-2. Frequencies and intensities of the six deconvoluted Gaussians in the Amide I region in the experimental spectrum of Z-Glu-Arg-NHMe compared to the computed bands for the optimized structures, which are listed in order of increasing relative energy.

Exp	ν_1	I_1	ν_2	I_2	ν_3	I_3	ν_4	I_4	ν_5	I_5	ν_6	I_6		
	1634.4	0.29	1657.3	0.18	1675.4	0.58	1698.7	0.78	1713.5	0.6	1736.0	0.68		
Calculations	$\Delta\nu_1$	ΔI_1	$\Delta\nu_2$	ΔI_2	$\Delta\nu_3$	ΔI_3	$\Delta\nu_4$	ΔI_4	$\Delta\nu_5$	ΔI_5	$\Delta\nu_6$	ΔI_6	$\sum(\lvert\Delta\nu\rvert)$	$\sum(\lvert\Delta I\rvert)$
ER_Z1	7.0	0.07	15.1	0.12	21.2	-0.19	9.4	-0.06	2.8	-0.27	-6.4	-0.06	61.7	0.77
ER_Z2	-9.4	0.18	9.3	0.00	9.9	-0.52	-4.2	-0.40	-16.8	-0.13	-30.9	-0.35	80.5	1.59
ER_C1	-18.6	0.19	-10.2	0.59	18.5	-0.09	0.8	-0.23	0.5	-0.21	-17.0	-0.08	65.7	1.39
ER_Z3	22.1	0.00	8.7	-0.11	2.3	0.15	-4.5	-0.72	-4.9	0.40	21.9	0.08	64.3	1.47
ER_Z4	13.2	0.05	1.7	0.05	4.8	0.13	0.8	-0.74	5.4	0.31	-4.4	-0.21	30.3	1.48
ER_Z5	-2.5	0.00	26.9	0.33	12.6	-0.15	-2.3	-0.59	-10.6	-0.37	-26.7	-0.36	81.6	1.80
ER_Z6	-23.7	-0.04	17.9	0.03	25.4	-0.32	3.5	-0.36	-5.3	-0.18	16.9	-0.30	92.7	1.23
ER_Z7	11.9	0.05	19.6	-0.05	20.7	-0.07	2.7	-0.46	-5.9	-0.25	-12.4	-0.34	73.1	1.22
ER_Z8	0.3	0.71	6.8	0.48	5.2	-0.45	-9.4	-0.41	-16.0	-0.13	-21.1	-0.22	58.7	2.39
ER_Z9	0.9	-0.04	25.7	-0.05	27.7	-0.27	13.5	-0.30	-0.3	-0.20	0.8	-0.36	68.9	1.21
ER_C2	-33.6	-0.03	3.0	0.48	-4.4	-0.29	12.3	-0.33	2.2	0.01	5.1	-0.15	60.7	1.29
ER_Z10	8.5	-0.06	23.6	0.22	13.4	-0.16	5.9	-0.14	5.4	0.24	-4.1	-0.17	61.0	0.98
ER_Z11	11.6	0.05	9.3	-0.04	3.8	0.37	-7.3	-0.70	3.5	0.26	27.2	-0.17	62.6	1.60
ER_Z12	4.6	-0.12	20.2	-0.08	12.4	-0.13	11.5	-0.26	4.3	-0.03	-9.9	-0.48	62.9	1.10
ER_C3	-36.8	-0.01	-3.9	0.33	18.8	0.03	4.7	-0.40	-6.1	-0.23	13.4	-0.29	83.6	1.29
ER_Z13	-10.4	0.45	16.3	0.14	4.2	-0.41	-1.3	-0.21	-15.2	-0.16	-5.1	-0.19	52.4	1.55
ER_Z14	-19.4	0.53	15.4	0.36	16.4	0.39	7.2	-0.59	3.9	-0.27	-3.7	0.05	66.0	2.19
ER_Z15	-2.3	0.58	17.6	0.82	14.2	-0.44	0.5	-0.37	-10.3	-0.44	-16.7	-0.19	61.6	2.84
ER_C4	-34.9	0.29	-6.9	0.57	-8.0	0.08	-12.0	-0.22	-10.8	0.37	22.2	0.22	94.8	1.75
ER_C5	-26.5	0.26	-3.2	0.73	-0.4	-0.21	-1.6	0.22	2.0	-0.08	6.5	0.05	40.3	1.55
ER_C6	-19.7	-0.16	-7.1	0.06	-2.8	-0.45	1.0	-0.71	-11.2	-0.09	-21.9	0.16	63.5	1.63
ER_C7	-10.8	0.22	8.7	0.45	2.1	-0.39	-9.6	-0.55	-9.4	0.40	-3.1	-0.21	43.7	2.21
ER_C8	-12.2	-0.03	-13.6	0.47	-4.2	0.35	-17.5	-0.60	14.8	-0.05	-4.7	-0.29	67.1	1.79
ER_C9	-21.6	-0.20	8.6	0.23	-4.9	-0.33	18.9	-0.25	29.1	-0.06	14.8	-0.04	97.8	1.11
ER_C10	-22.3	-0.06	1.5	0.73	-9.3	-0.44	13.5	-0.12	21.7	-0.09	46.0	0.14	114.3	1.58
ER_Z16	3.2	0.09	17.7	0.13	10.5	-0.39	-2.4	-0.45	0.9	0.26	-6.6	0.16	41.4	1.48
ER_C11	-16.9	0.27	13.5	0.51	0.4	-0.22	-1.1	-0.02	2.1	0.14	48.6	-0.05	82.6	1.21
ER_C12	-33.8	-0.14	16.7	0.09	5.7	-0.10	9.8	-0.51	2.2	0.22	49.4	-0.15	117.7	1.22

Deconvolution and assignment of the Z-Glu-Arg-NHMe spectrum in the Amide I region

The Amide I region of the experimental spectrum of Z-Glu-Arg-NHMe is deconvoluted into 6 Gaussian functions, each Gaussian representing a vibrational mode of Z-Glu-Arg-NHMe. The obtained frequencies and relative intensities are compared with the theoretically obtained frequencies and relative intensities of the DFT calculations. The sum of the deviations in frequencies and relative intensities with respect to the computed ones are given in the last two columns of Table SI-2.

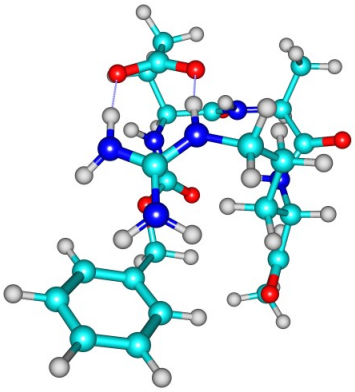
The closest agreement between experimental and calculated frequencies is found for structure ER_Z4, with the sum of the absolute frequency deviations between theory and experiment being 30 cm^{-1}. However, there is a large mismatch between the relative intensities, resulting in a completely different shape of the overall feature (see Supporting Information: Fig SI-3).

The next closest match between computed and experimental frequencies is found for ER_Z16 with a summed absolute deviation of 41.4 cm^{-1}. However, the energy of this structure is calculated to be 20.3 kcal/mol higher than the lowest energy structure. Moreover, this structure also shows a large mismatch in relative intensities. The calculated spectrum of ER_Z16 is shown together with the experimental spectrum in the bottom panel of Figure 7, showing a strong absorption at 1585 cm^{-1} which is not observed in the experimental spectrum.

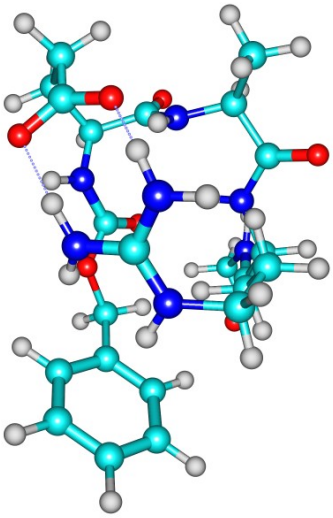
The experimental spectrum of ER_C7 in the Amide I region is shown in Figure SI-3. At first glance, there is a fairly good agreement between theory and experiment and only the lowest frequency vibration is shifted to the red by 11 cm^{-1}. However, upon comparing the individual vibrations (Table SI-2), one observes a large mismatch in relative intensities. In addition, the experimental spectrum shows a moderately strong band at 1713 cm^{-1}, which shifts to 1689 cm^{-1}. In the calculated spectrum of ER_C7 leading to the conclusion that this structure is unlikely to be responsible for the observed spectrum.

The relative intensities are thus important for assigning the experimental spectrum to one of the theoretical structures. The structure with the lowest deviation in relative intensity is ER_Z1. In addition, the deviation in frequency is also fairly low. The experimental spectrum together with computed spectrum of ER_Z1 is shown in the top trace of Figure 7 in the 1000 – 1850 cm^{-1} range. Besides the good match in the Amide I region, the remainder of the spectrum is also in good agreement with the experimental spectrum. To conclude, the experimental spectrum of Z-Glu-Arg-NHMe is assigned to ER_Z1.

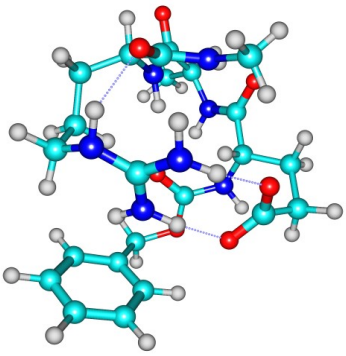
EAR_Z1



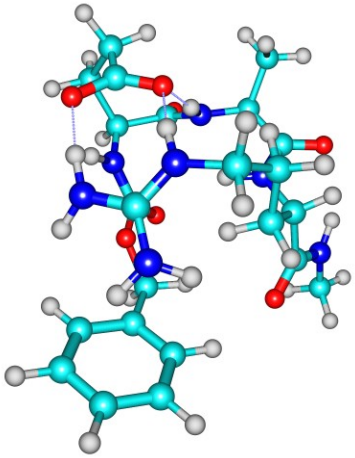
EAR_Z2



EAR_Z3



EAR_Z4



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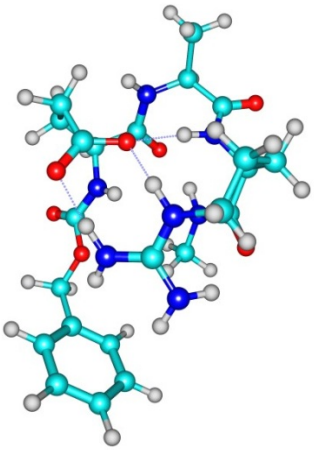

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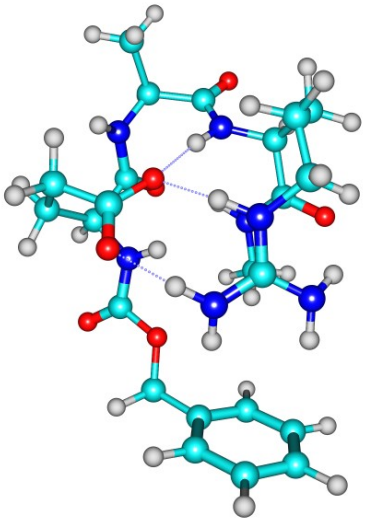
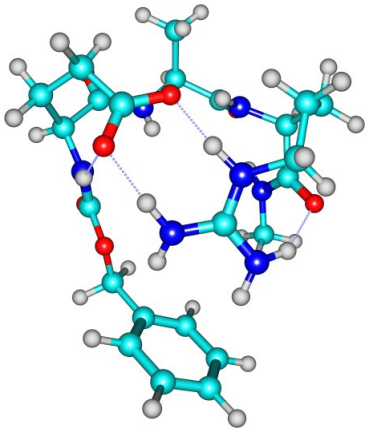


EAR_Z7



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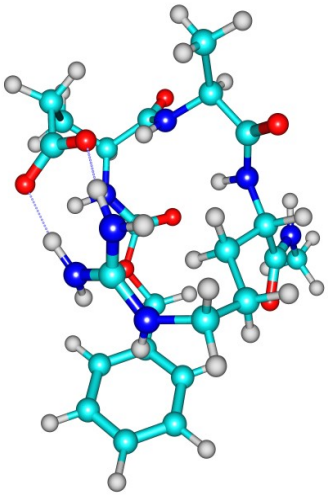

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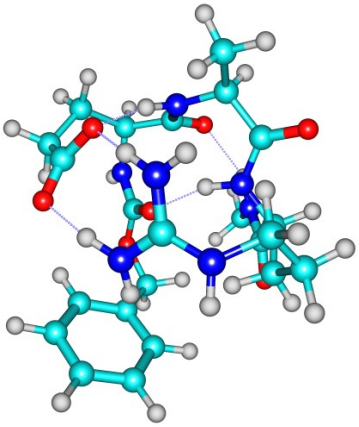

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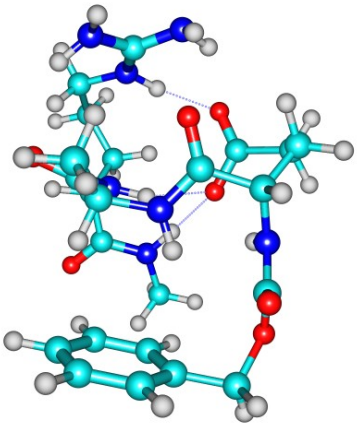

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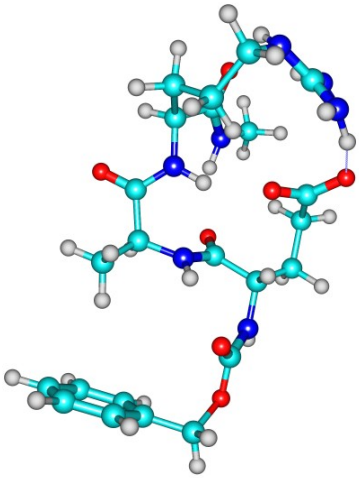

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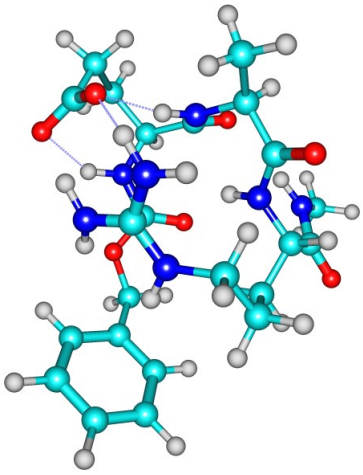

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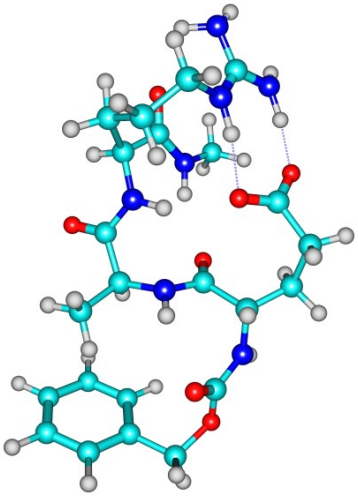

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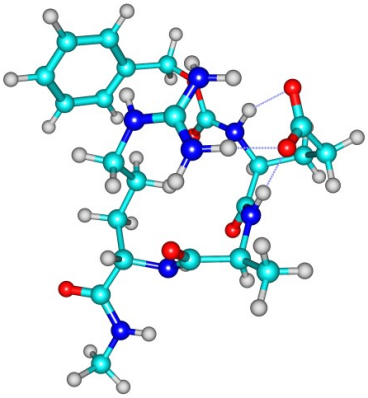

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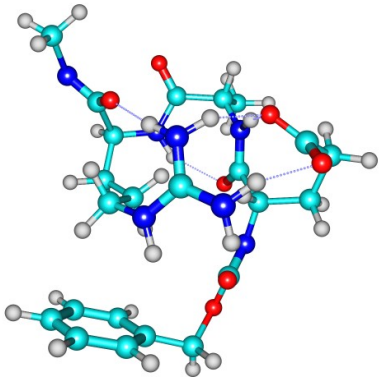

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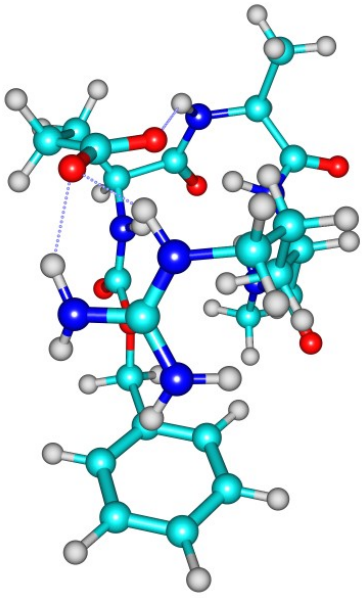

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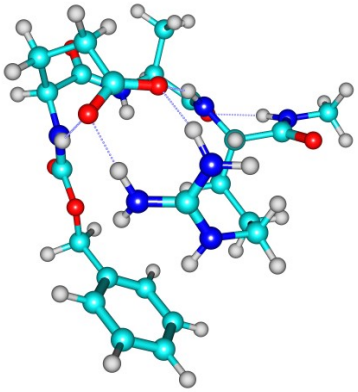

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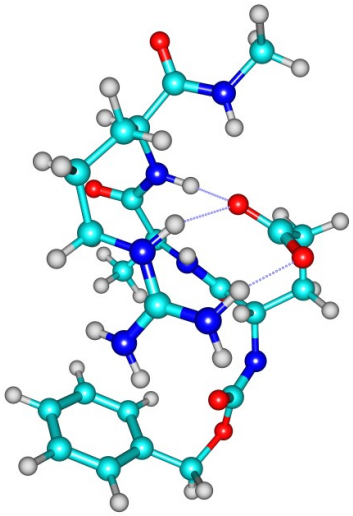

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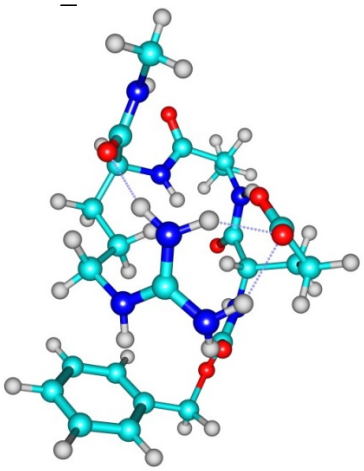

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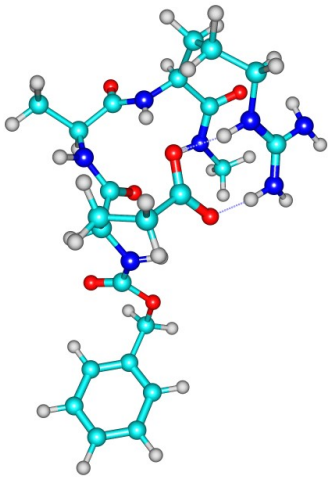

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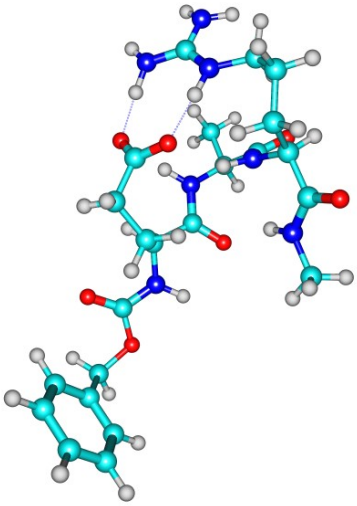

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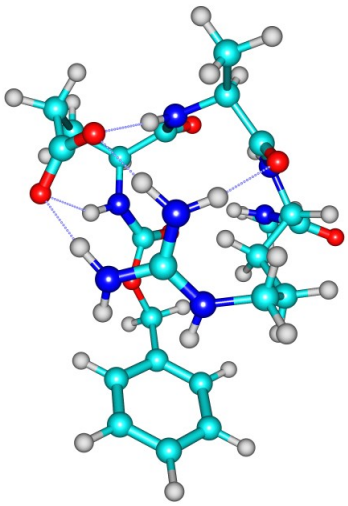

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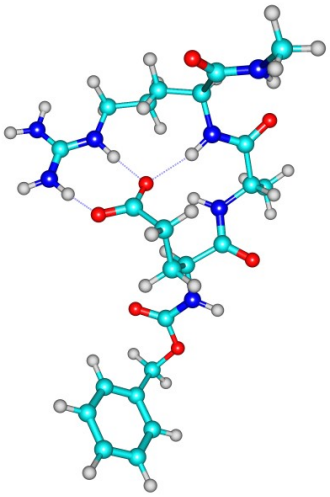

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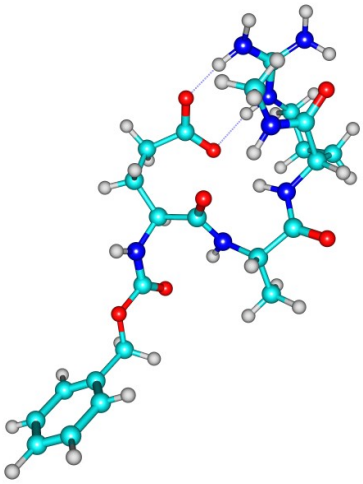

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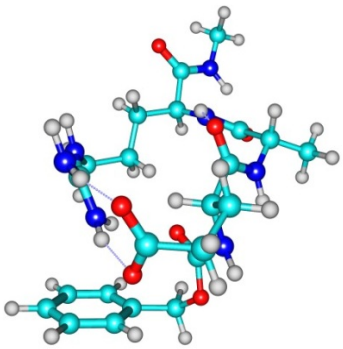

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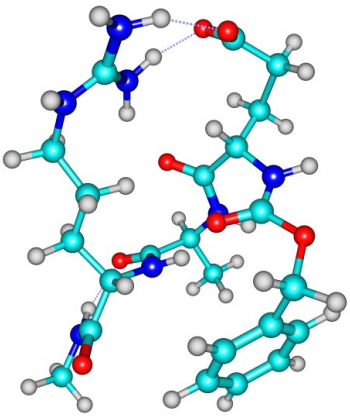

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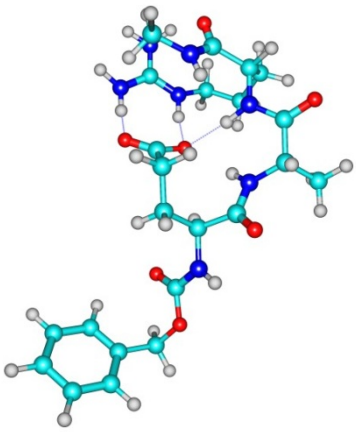

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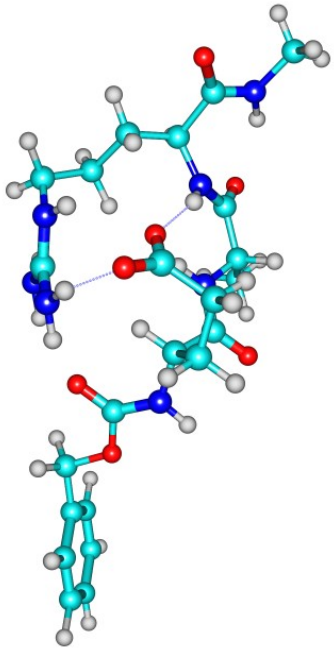

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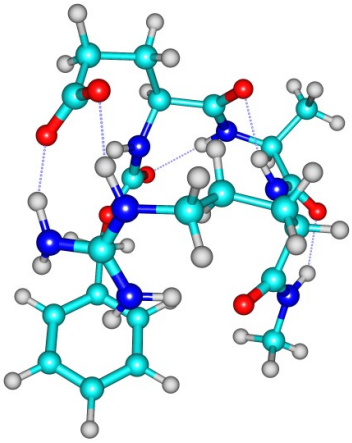

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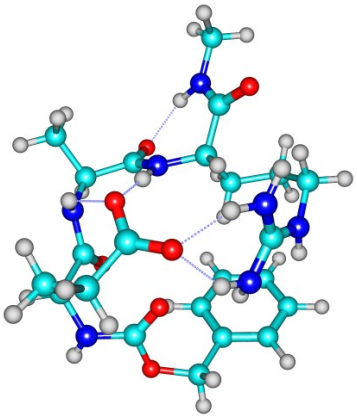

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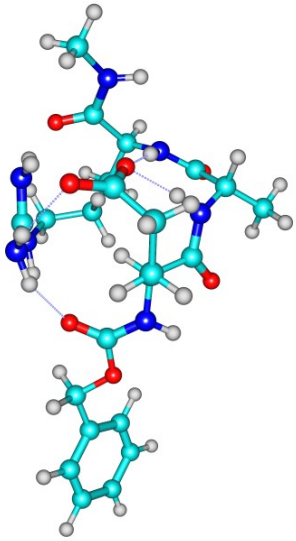

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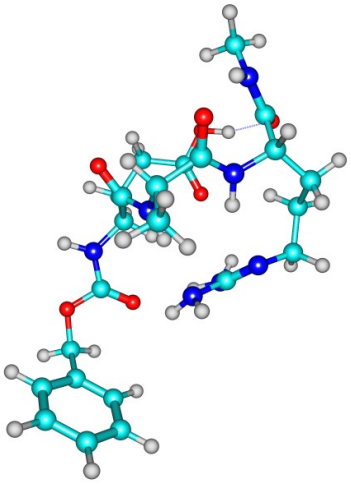
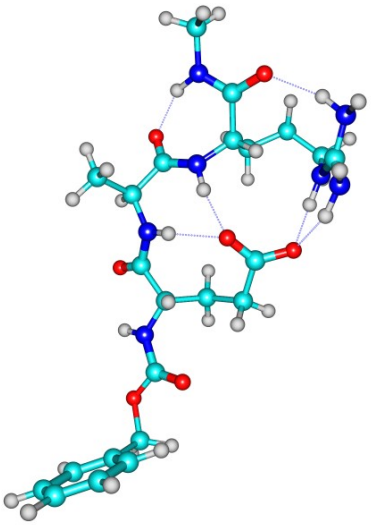


EAR_Z32



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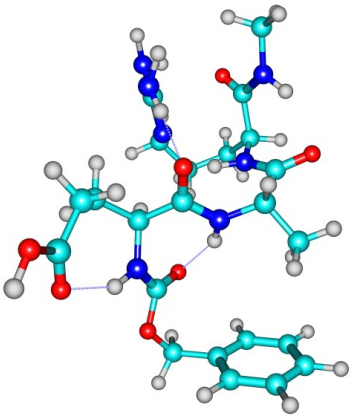

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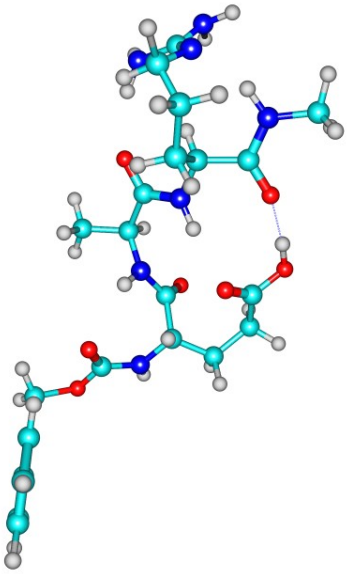
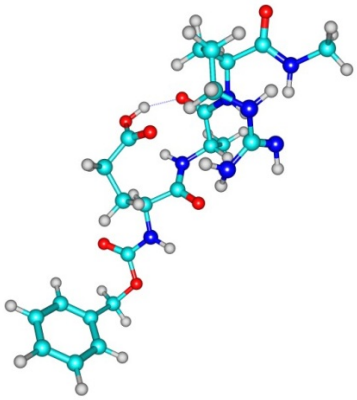


EAR_C1



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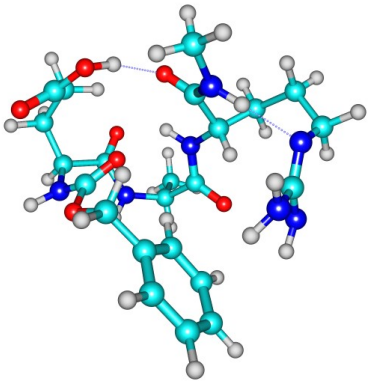

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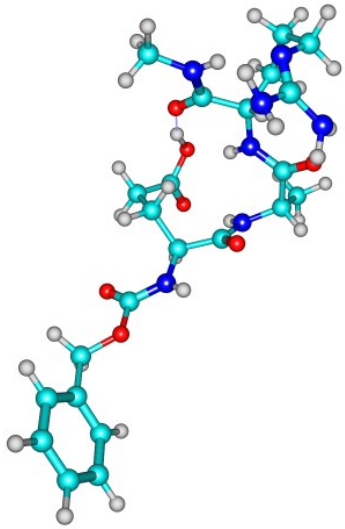

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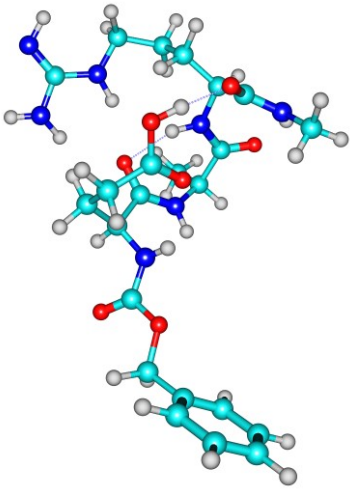
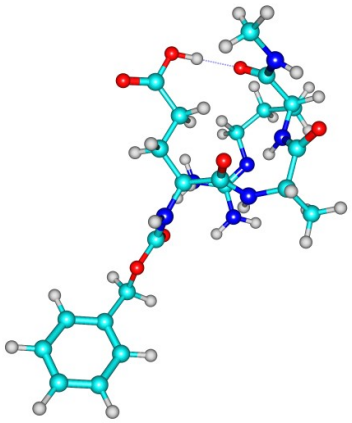


EAR_T6



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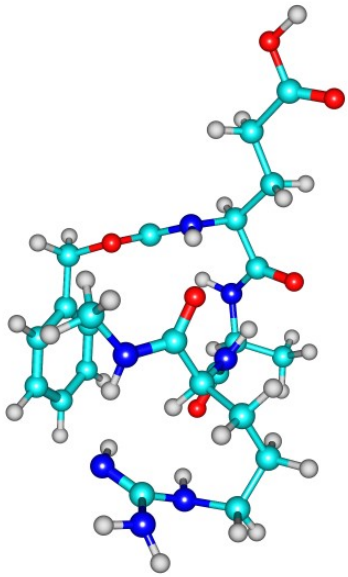

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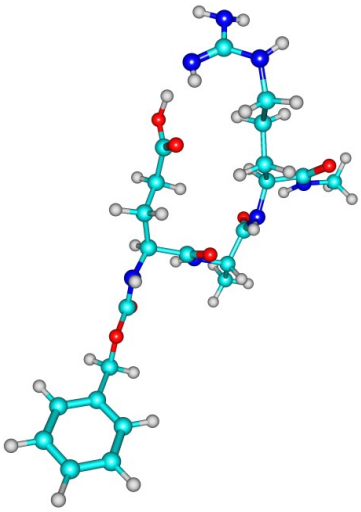

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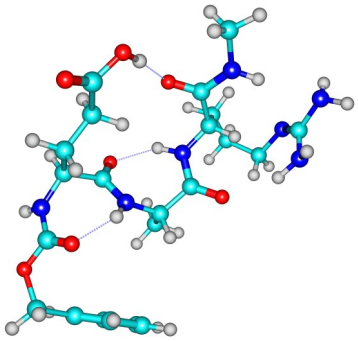
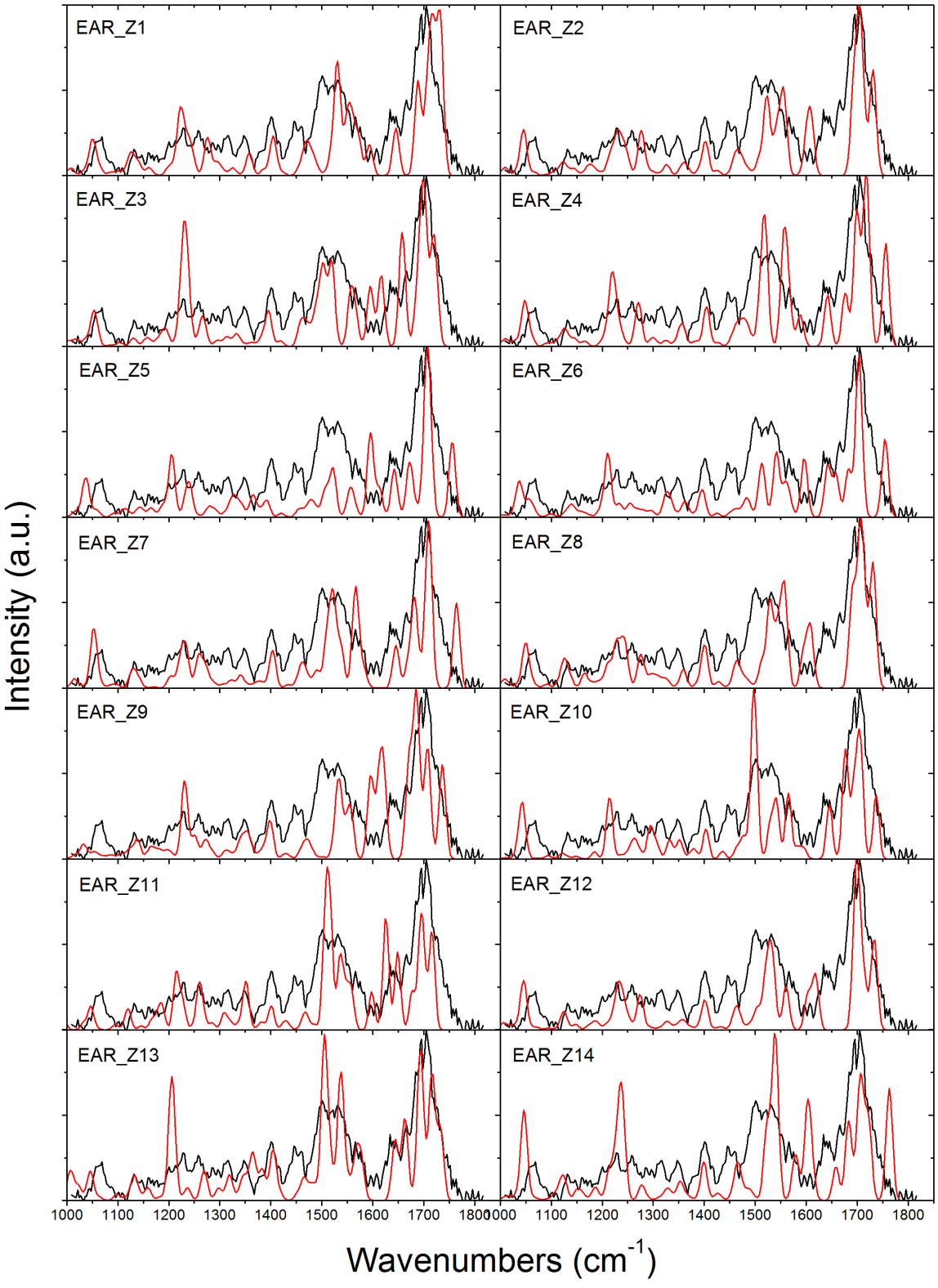
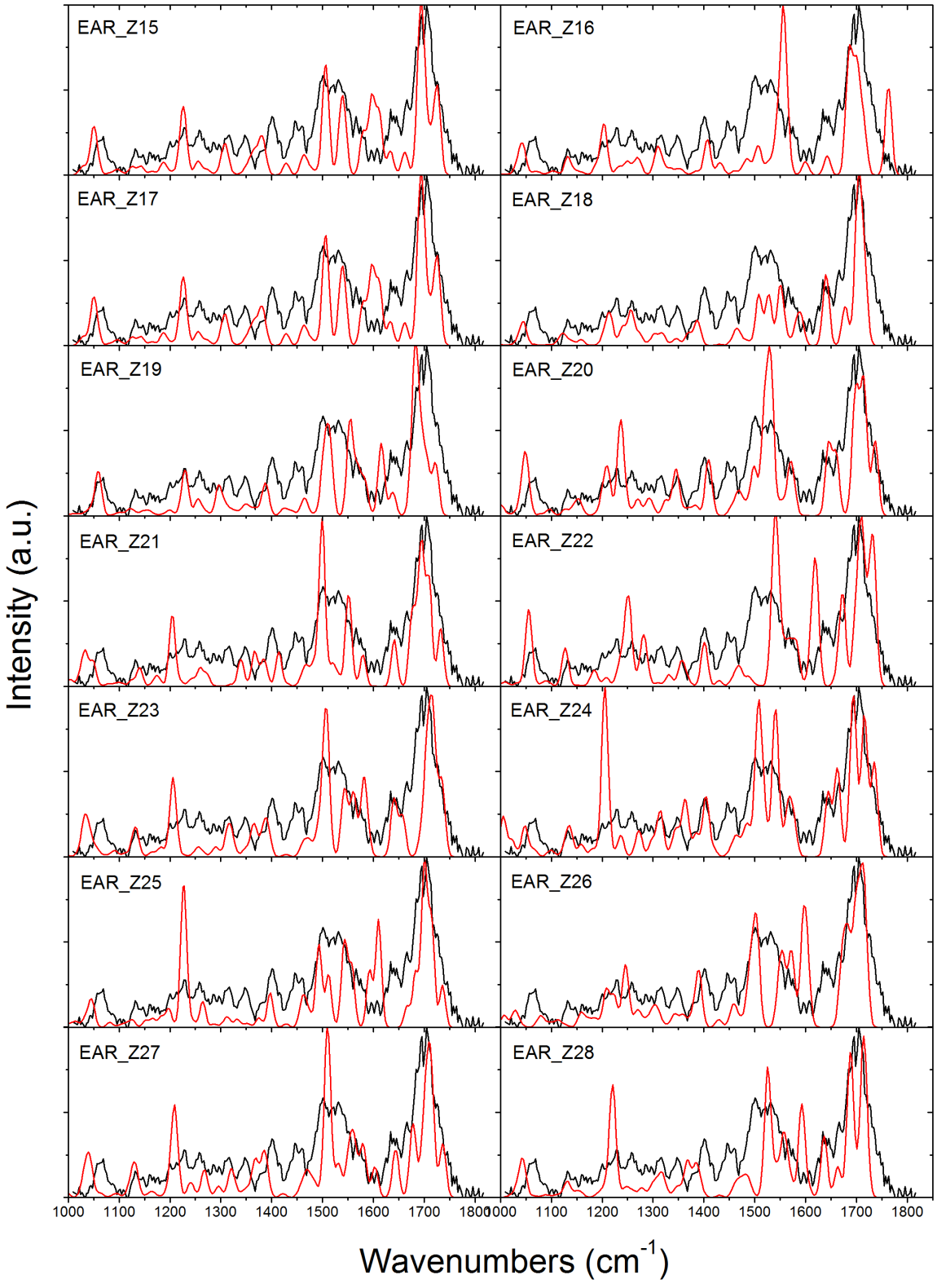
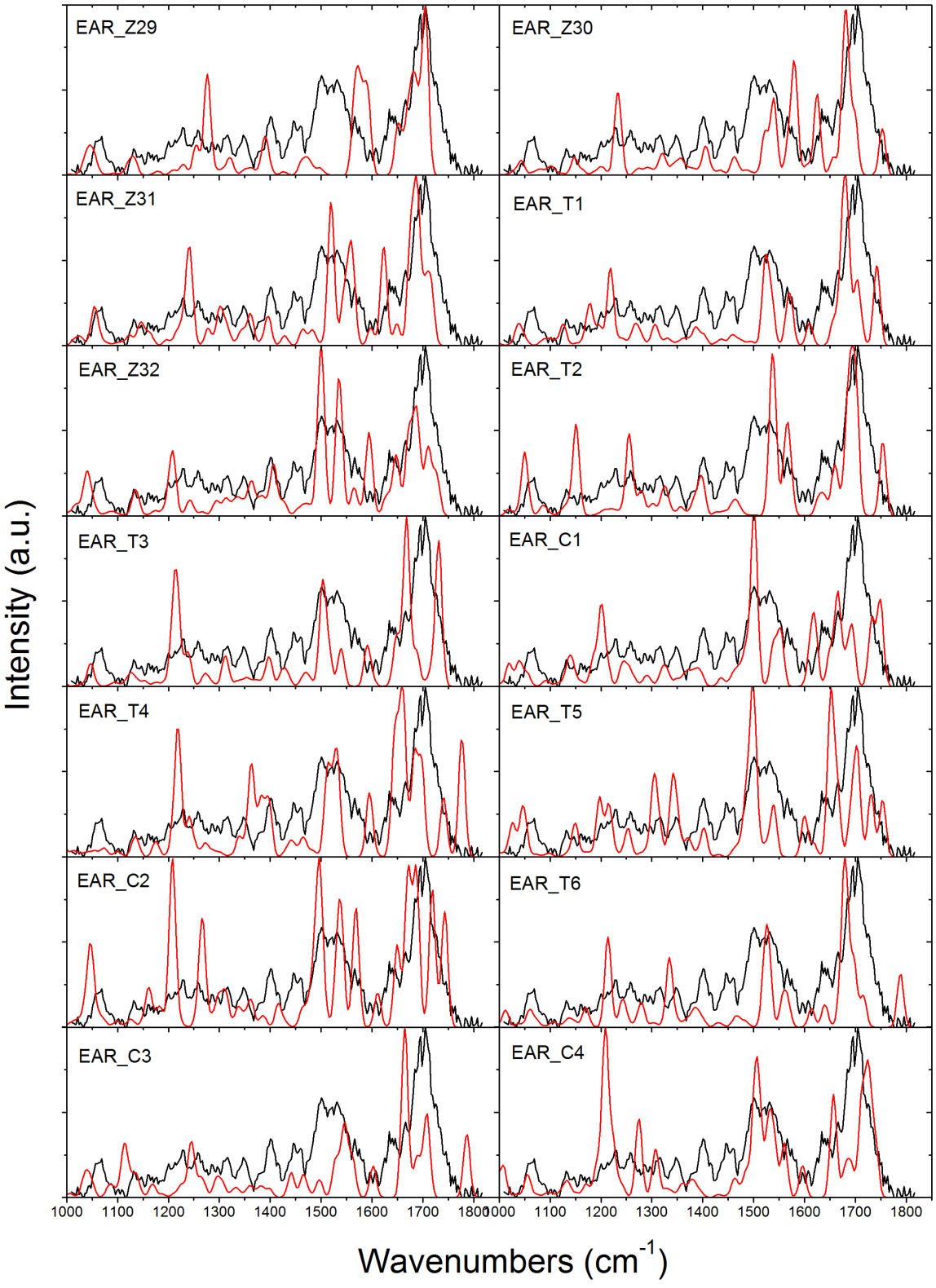


Figure SI-5. Conformations of Z-Glu-Ala-Arg-NHMe, optimized with the M05-2x functional employed with the 6-311+G(d,p) basis set.


EAR_Z1
EAR_Z2
EAR_Z3
EAR_Z4
EAR_Z5
EAR_Z6
EAR_Z7
EAR_Z8
EAR_Z9
EAR_Z10
EAR_Z11
EAR_Z12
EAR_Z13
EAR_Z14
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)


EAR_Z15
EAR_Z16
EAR_Z17
EAR_Z18
EAR_Z19
EAR_Z20
EAR_Z21
EAR_Z22
EAR_Z23
EAR_Z24
EAR_Z25
EAR_Z26
EAR_Z27
EAR_Z28
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)


EAR_Z29
EAR_Z30
EAR_Z31
EAR_T1
EAR_Z32
EAR_T2
EAR_T3
EAR_C1
EAR_T4
EAR_T5
EAR_C2
EAR_T6
EAR_C3
EAR_C4
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)

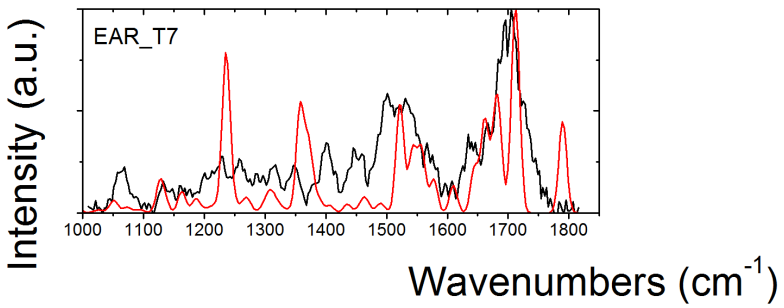


Figure SI-6. Experimental IR-UV ion-dip spectrum of Z-Glu-Ala-Arg-NHMe (black trace) and the theoretical spectra of the optimized structures for Z-Glu-Ala-Arg-NHMe (red trace).

Table SI-3. ZPE-corrected energies (ZPE), Gibbs free energies at 300 K (ΔG) and intramolecular interactions for the optimized structures of Z-Glu-Ala-Arg-NHMe. The employed basis set for the M05-2X and B3LYP functionals is 6-311+G(d,p).

	M05-2X		B3LYP		Interactions			
	ZPE	Gibbs	ZPE	Gibbs	SC - SC	Disp. Int.	BB - BB	BB - SC
EAR_Z1	0.00	0.00	2.56	5.86	A	2 x NH_2	C10(O0-N3)	N1-O^1 + N2-O^2
EAR_Z2	0.73	0.47	3.47	6.28	B	NH_2 + Nε	C10(O0-N3)	N1-O^1 + N2-O^2
EAR_Z3	1.11	2.54	4.07	7.73	B	NH_2	C10(O0-N3) + C10(O1-N4)	O3-(H_2N + Hε)
EAR_Z4	1.85	1.31	2.67	5.61	A	2 x NH_2	C7(O2-N4)	N1-O^1 + N2-O^2
EAR_Z5	1.90	2.09	5.16	8.20	A	2 x NH_2	C10(O1-N4)	N1-O^1 + N2-O^1 + N3-O^1 + O4-H_2N
EAR_Z6	2.13	1.96	4.65	7.88	A	2 x NH_2	C10(O1-N4)	N3-O + O3-H_2N
EAR_Z7	2.85	2.82	3.46	7.12	A	2 x NH_2	C7(O2-N4)	N1-O^1 + N3-O^2 + O3-H_2N
EAR_Z8	3.03	3.42	5.67	8.88	B	NH_2 + Nε	C10(O0-N3)	N1-O^1 + N2-O^2
EAR_Z9	3.91	5.82	5.93	8.89	B	NH_2	C10(O0-N3) + C10(O1-N4)	N2-O
EAR_Z10	4.40	5.12	6.33	8.62	C*	N2		N1-O^1 + N3-O^1 + N4-O^1 + O1-(H_2N)^1 + O2-(H_2N)^2
EAR_Z11	4.82	4.67	5.61	7.42	C		C7(O0-N2) + C10(O1-N4)	N3-O + O3-H_2N
EAR_Z12	5.16	5.08	7.41	8.72	B	NH_2 + Nε	C10(O0-N3) + C10(O1-N4)	N1-O^1 + N2-O^2
EAR_Z13	5.52	4.30	4.25	5.01	A		C7(O0-N2) + C10(O1-N4)	N3-O + O3-H_2N
EAR_Z14	5.52	5.73	6.67	9.20	B	HE	C7(O1-N3)	N1-O^1 + N2-O^2 + O2-H_2N
EAR_Z15	6.07	5.97	7.52	11.60	B		C5(N1-O1) + C7(O1-N3)	N2-O + O0-(H_2N)^1+ O3-(H_2N)^2
EAR_Z16	6.10	7.21	9.13	11.29	C*	2 x NH_2	C10(O1-N4)	N1-O^1 + N2-O^1 + N3-O^1
EAR_Z17	6.74	6.85	7.40	10.39	B	NH_2 + Nε	C7(O2-N4)	N1-O^1 + N3-O^2
EAR_Z18	6.79	5.86	7.45	8.46	A	NH_2	C5(N1-O1)	N2-O^1 + N3-O^1 + N4-O^1 + O0-H_2N
EAR_Z19	6.87	6.45	7.24	10.47	C	HE	C5(N1-O1) + C7(O2-N4)	N2-O + O0-(H_2N)^1 + O3-(H_2N)^2
EAR_Z20	7.17	6.87	4.34	6.29	A		C10(O1-N4)	N1-O^1 + N3-O^2 + O3-NH2
EAR_Z21	7.17	4.26	3.58	3.95	A		C5(N1-O1) + C10(O1-N4)	N2-O^1 + N3-O^2
EAR_Z22	7.43	8.35	9.09	12.12	B	NH_2 + Nε	C13(O0-N4) + C7(O1-N3)	N1-O^1 + N2-O^2 + O2-H_2N
EAR_Z23	7.46	3.02	0.00	0.00	A		C5(N1-O1) + C7(O2-N4)	N2-O^1 + N3-O^1
EAR_Z24	7.74	6.30	4.28	4.71	A		C7(O0-N2) + C10(O1-N4)	N3-O + O3- H_2N
EAR_Z25	8.01	7.10	4.50	6.40	B	NH_2	C7(O1-N3) + C7(O2-N4)	O0- H_2N
EAR_Z26	9.07	8.11	8.17	10.40	B		C10(O0-N3) + C7(N2-O4)	O1- H_2N
EAR_Z27	9.49	7.20	4.96	6.16	A		C5(N1-O1)	N2-O^1 + N3-O^1 + O3-H_2N

EAR_Z28	9.56	7.33	4.07	5.81	O-H_2N		C5(N1-O1) + C7(O2-N4)	O0- H_2N + N2-O^1 + N3-O^1
EAR_Z29	9.88	9.65	8.06	10.93	A	2 x NH_2	C7(O0-N2) + C7(O1-N3) + C7(O2-N4)	N1-O + O3-H_2N
EAR_Z30	10.03	10.34	11.36	14.50	C	NH_2 + Nε	C7(O2-N4)	N2-O^1 +N3-O^1 + O0-H_2N
EAR_Z31	10.11	10.07	8.33	10.31	C		C5(N1-O1)	N2-O^1 +N3-O^1 + O0-$(H_2N)^1$ + O3-$(H_2N)^2$
EAR_T1	11.96	11.01	12.17	14.04	O-H_2N		C7(O2-N4)	O0-$(NH_2)_2$ + N2-H_2N + N3-Nε + O3-HO
EAR_Z32	15.02	11.53	7.85	8.36	C*		C5(N1-O1) + C7(O2-N4)	N2-O^1 +N3-O^1 + O3-H_2N
EAR_T2	18.03	15.54	14.53	14.59			C7(O0-N2) + C7(O2-N4)	N1-O+ O1-$(H_2N)^1$ + O3-$(H_2N)^2$ + N3-Nε
EAR_T3	18.04	15.21	12.26	12.74			C7(O0-N2) + C5(N3-O3)	N3-O + O3-HO + N4-Nε + O2-H_2N
EAR_C1	18.30	17.31	15.73	17.00			C5(N1-O1)	N3-NηH + N4-NηH + O1-H_2N + O2-HO
EAR_T4	18.52	17.87	21.37	23.85		NH_2	C7(O1-N3) + C5(N3-O3)	O3-HO + N4-Nε
EAR_T5	20.00	15.59	15.61	15.59			C5(N1-O1) + C5(N3-O3)	N2-O + N3-OH + N4-Nε + O2-H_2N + O3-HO
EAR_C2	19.72	16.17	14.36	13.66			C7(O1-N3) + C7(O2-N4)	N1-O + O1-Hε + O3-HO
EAR_T6	20.38	18.42	16.66	17.97			C7(O2-N4)	O0-(H_2N + H_2N) + N2-NH_2 + N3-Nε + O4-HO
EAR_C3	21.54	18.44	19.60	19.95		NH	C11(N1-O3) + C7(O0-N2) + C7(O1-N3)	O2-Hε
EAR_C4	21.56	18.02	13.17	12.02	OH - NH		C7(O0-N2) + C7(O1-N3) + C7(O2-N4)	
EAR_T7	24.06	21.24	19.33	19.18			C7(O0-N2) + C7(O1-N3) + C5(N3-O3)	O3-HO + N4-$(NH_2)^1$ + O2-$(H_2N)^2$

Energies are given in kcal/mol.

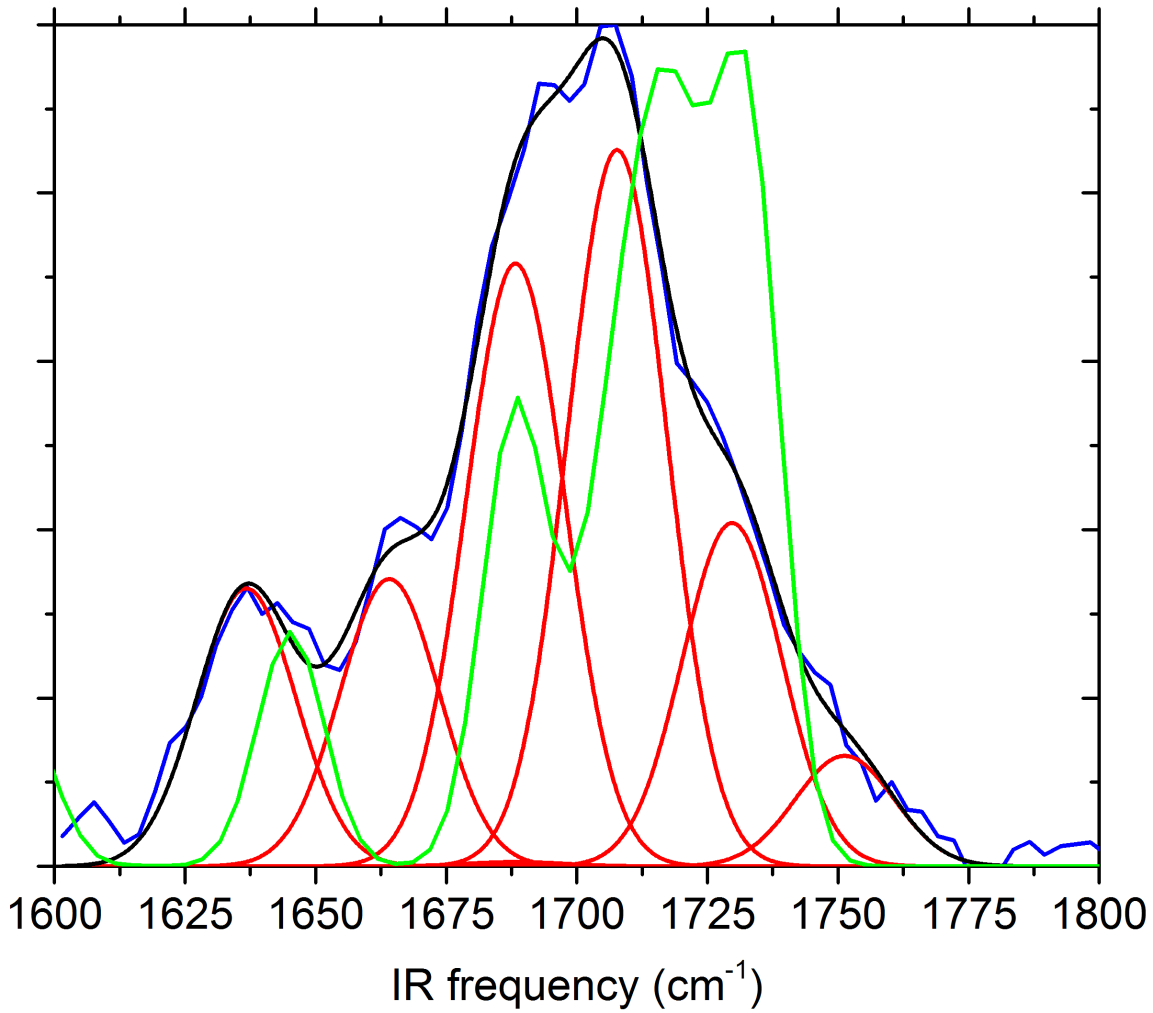


Figure SI- 7. Seven Gaussian functions, each representing a vibrational mode in the Amide I region of Z-Glu-Arg-NHMe (red), the sum of the six Gaussian functions (black), the experimental IR-UV spectrum (blue) and the computed spectrum of the proposed structure (EAR_Z1) of Z-Glu-Arg-NHMe (green).

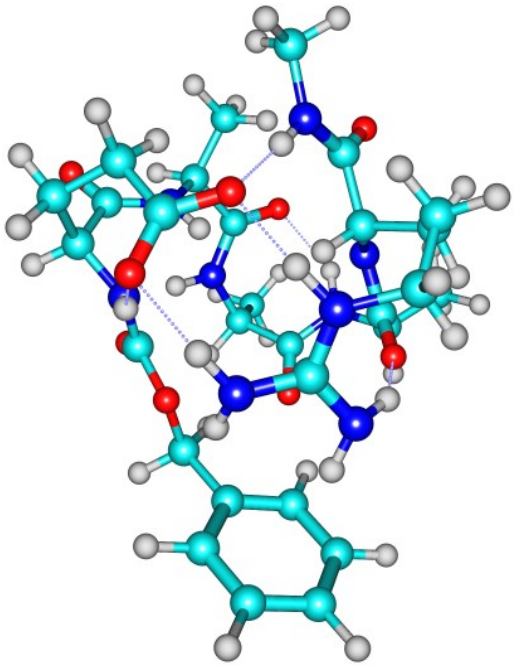
Table SI-4. ZPE-corrected energies (ZPE), Gibbs free energies at 300 K (ΔG) and intramolecular interactions for the optimized structures of Z-Glu-Ala-Ala-Ala-Arg-NHMe. The employed basis set for the M05-2X and B3LYP functionals is 6-311G(d,p).

	M05-2X		B3LYP		Interactions			
	ZPE	Gibbs	ZPE	Gibbs	SC - SC	Disp. Int.	BB - BB	BB - SC
EA3R_Z1	0.00	0.00	0.00	0.00	A	2 x NH_2	C10(O0-N3) + C7(O2-N4) + C5(N5-O5)	O4-H_2N + N1-O^1 + N6-O^2
EA3R_Z2	0.07	0.89	3.71	2.32	B	NH_2 + Nε	C7(O1-N3) + C10(O2-N5) + C10(O3-N6)	N1-O^1 + N4-O^2 + O4- H_2N
EA3R_Z3	0.36	0.49	3.93	1.15	A	NH_2	C5(N1-O1) + C7(O1-N3) + C10(O1-N4) + C10(O2-N5) + C10(O3-N6)	N2-O + O0-(H_2N)^1 + O4-(H_2N)^2
EA3R_Z4	3.18	2.03	3.69	-0.75	A		C5(N1-O1) + C7(O1-N3) + C10(O2-N5) + C10(O3-N6)	N2-O + O0-(H_2N)^1 + O4-(H_2N)^2
EA3R_Z5	3.35	3.52	5.89	3.93	B	NH_2 + Nε	C7(O1-N3) + C10(O2-N5) + C13(O2-N6)	N1-O^1 + N4-O^2 + O4- H_2N
EA3R_Z6	3.81	3.64	6.44	4.92	A		C10(O0-N3) + C7(O2-N4) + C7(O4-N6) + C11(N2-O4)	N1-O
EA3R_Z7	4.86	3.37	7.42	5.26	B		C5(N1-O1) + C11(N2-O4) + C7(O2-N4) + C7(O4-N6)	N3-O + O0-(H_2N)^1 + O3-(H_2N)^2
EA3R_Z8	8.64	5.41	8.61	4.97	C		C7(O0-N2) + C10(O2-N5)	N3-O + O1-(H_2N)^1 + O3-(H_2N)^2
EA3R_Z9	9.07	6.04	7.15	3.23	B		C10(O0-N3) + C13(O1-N5) + C7(O4-N6)	O5-(Nε+H_2N)
EA3R_Z10	9.27	6.27	4.39	-0.34	C		C7(O0-N2) + C7(O3-N5)	N3-O^1 + N4-O^1 + O1-(H_2N)^1 + O4-(H_2N)^2
EA3R_Z11	11.05	7.70	6.17	1.35	O-NH2		C5(N1-O1) + C7(O4-N6)	N2-O^1 + N4-O^1 + N5-O^1 + O5-N + O0 – (H_2N + H_2N)
EA3R_T1	14.84	13.95	18.09	15.00			C10(O0-N3) + C11(N2-O4) + C7(O2-N4)	N5-Nε + N6-Nε + N1-O + O5-HO
EA3R_C1	16.69	15.59	16.41	11.82			C7(O0-N2) + C10(O1-N4)	N3-O + N6-NηH + O4-(Hε + H_2N) + O5-OH
EA3R_T2	17.73	14.62	18.28	13.54			C10(O0-N3) + C14(N2-O5) + C7(O2-N4) + C5(N5-O5)	N1-O + N6-Nε
EA3R_T3	17.95	15.98	17.58	13.35			C5(N1-O1) + C7(O1-N3) + C7(O2-N4)	O0-H_2N + N2-Nε + O3-HO + N5-O

EA3R_T4	21.31	17.84	22.20	15.98		NH_2	C10(O0-N3) + C10(O1-N4) + C10(O2-N5)	N1-Nε
EA3R_C2	33.79	28.46	24.48	16.24			C7(O0-N2) + C7(N3-O5) + C7(N4-O6)	O1- H_2N + N3- NηH
EA3R_C3	40.35	30.33	28.03	18.42			C7(O0-N2) + C7(O1-N3) + C7(O2-N4) + C7(O3-N5) + C7(O4-N6)	O5-Hε

Energies are given in kcal/mol.

EA3R_Z1



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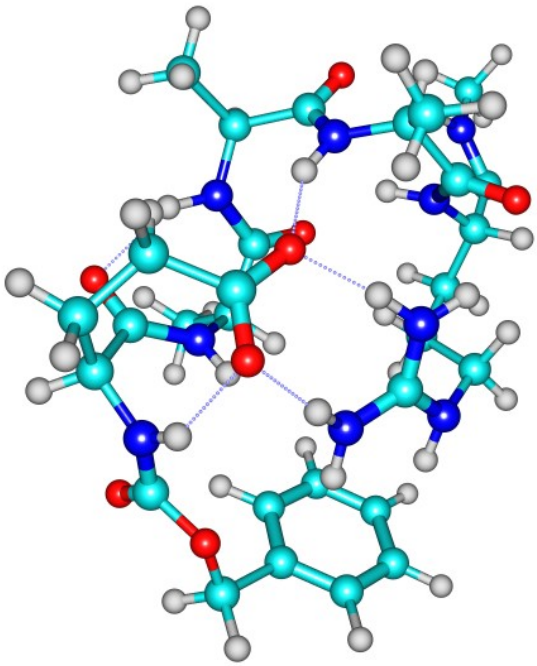

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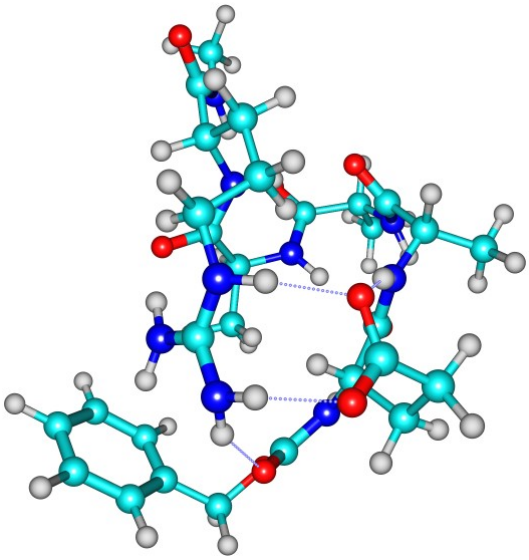

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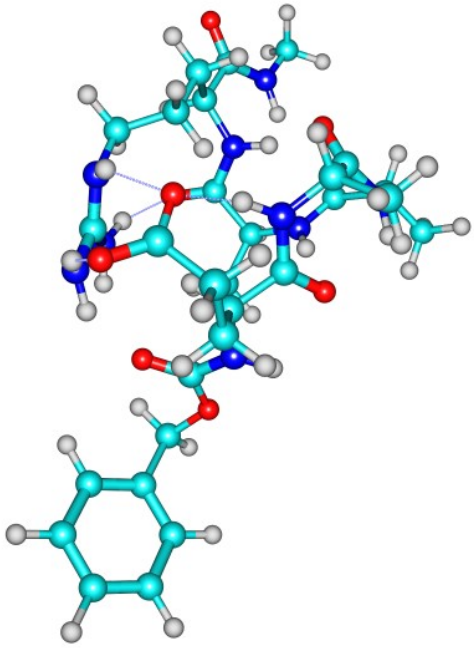

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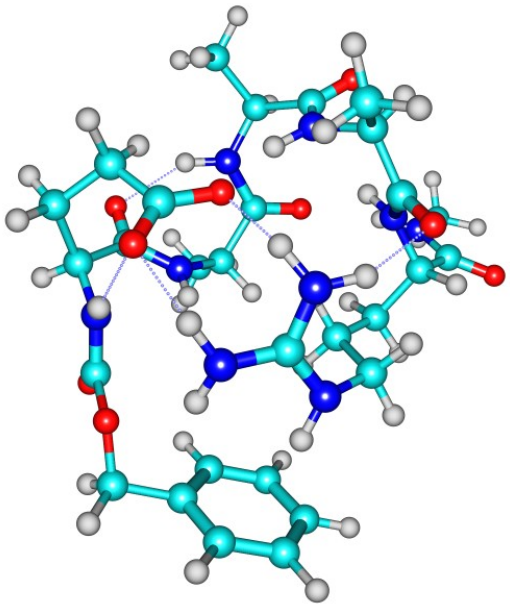

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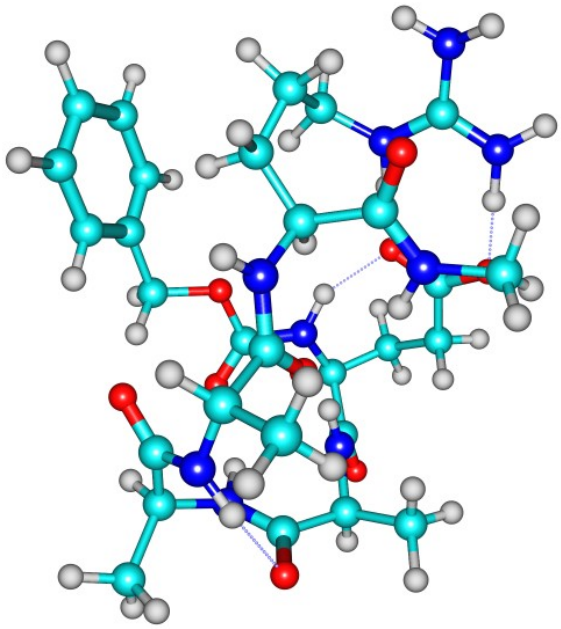

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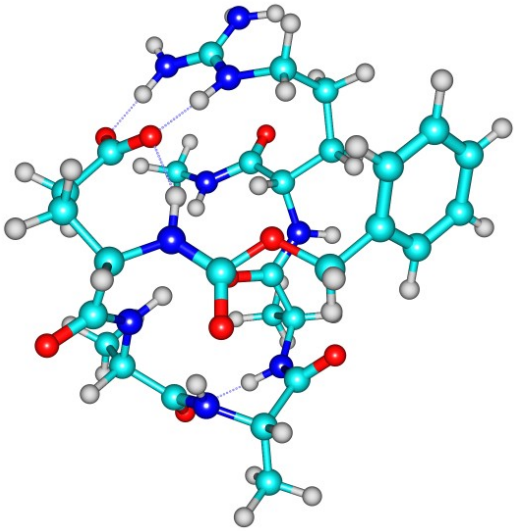

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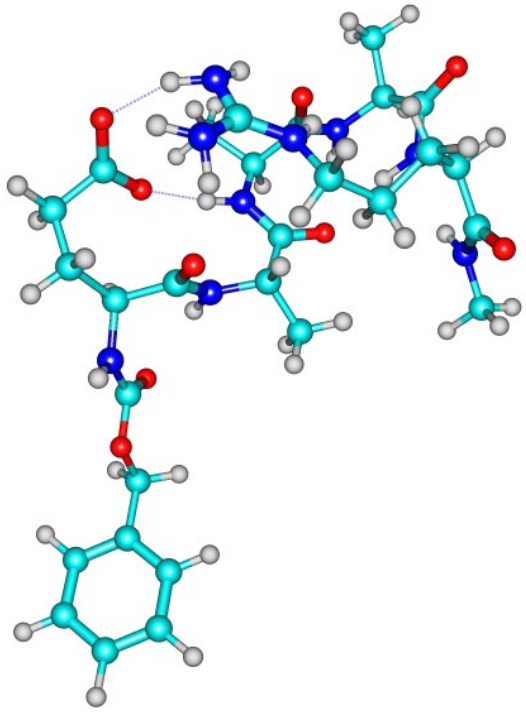
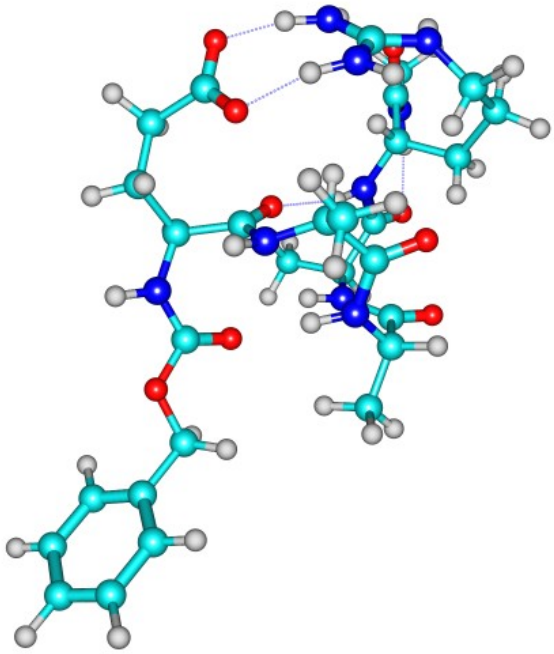
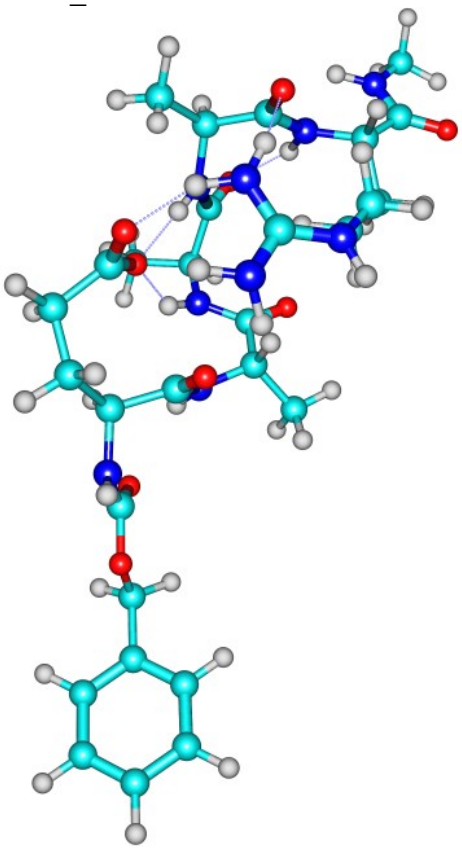


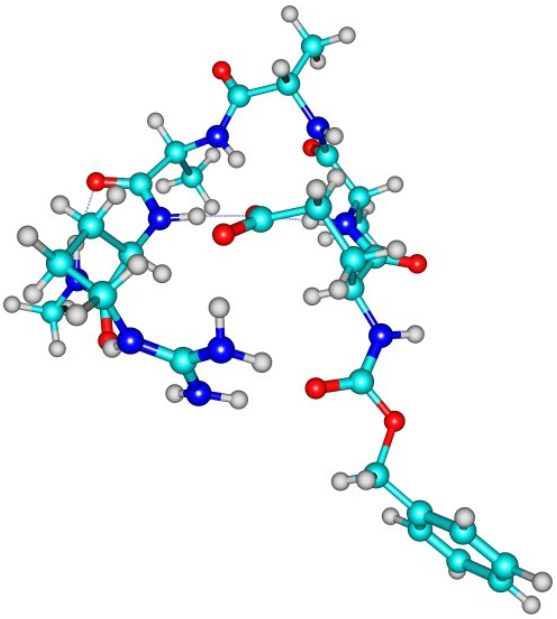
EA3R_Z9



EA3R_10



EA3R_Z11



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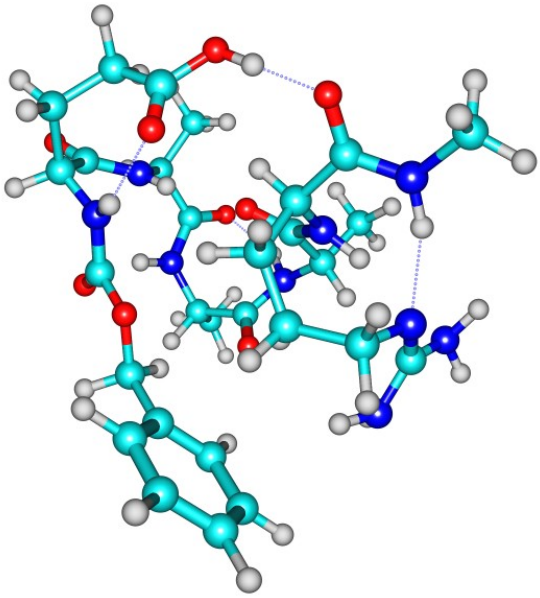

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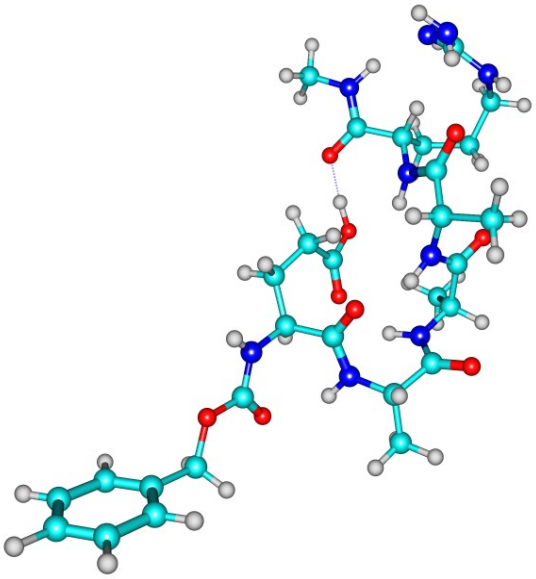

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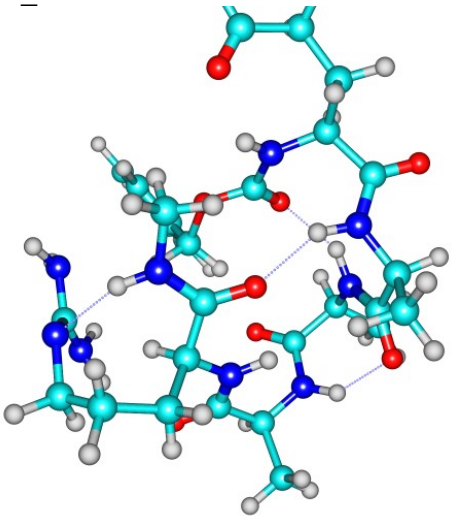

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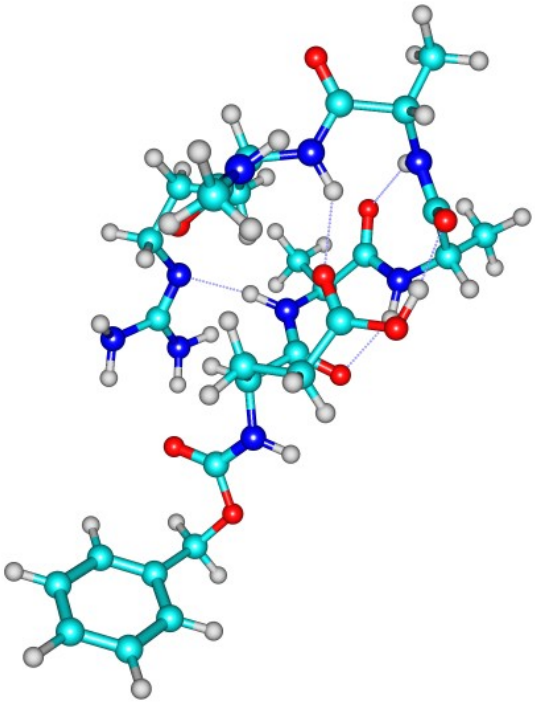

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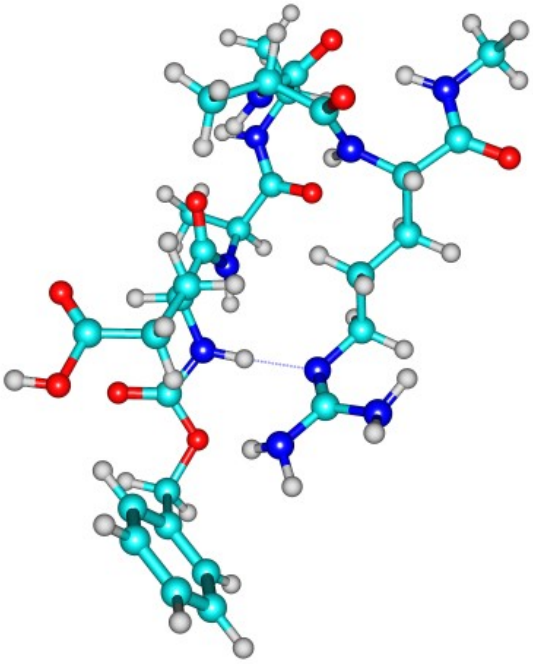

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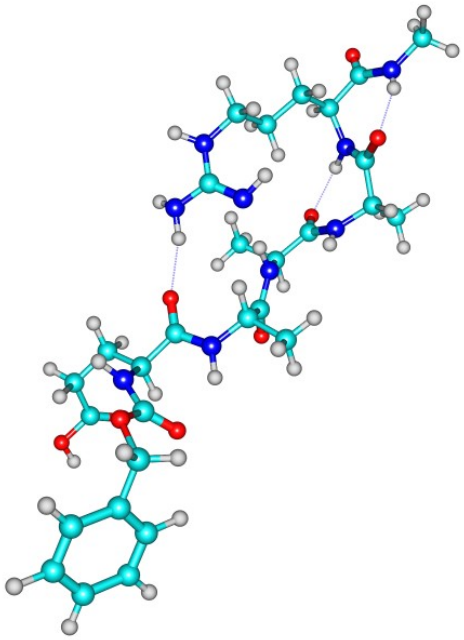

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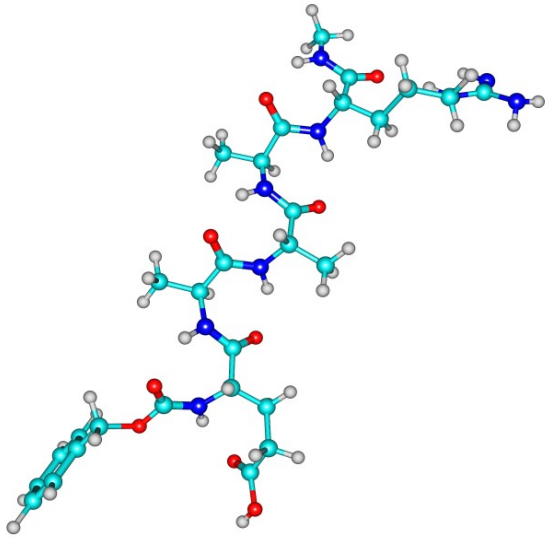
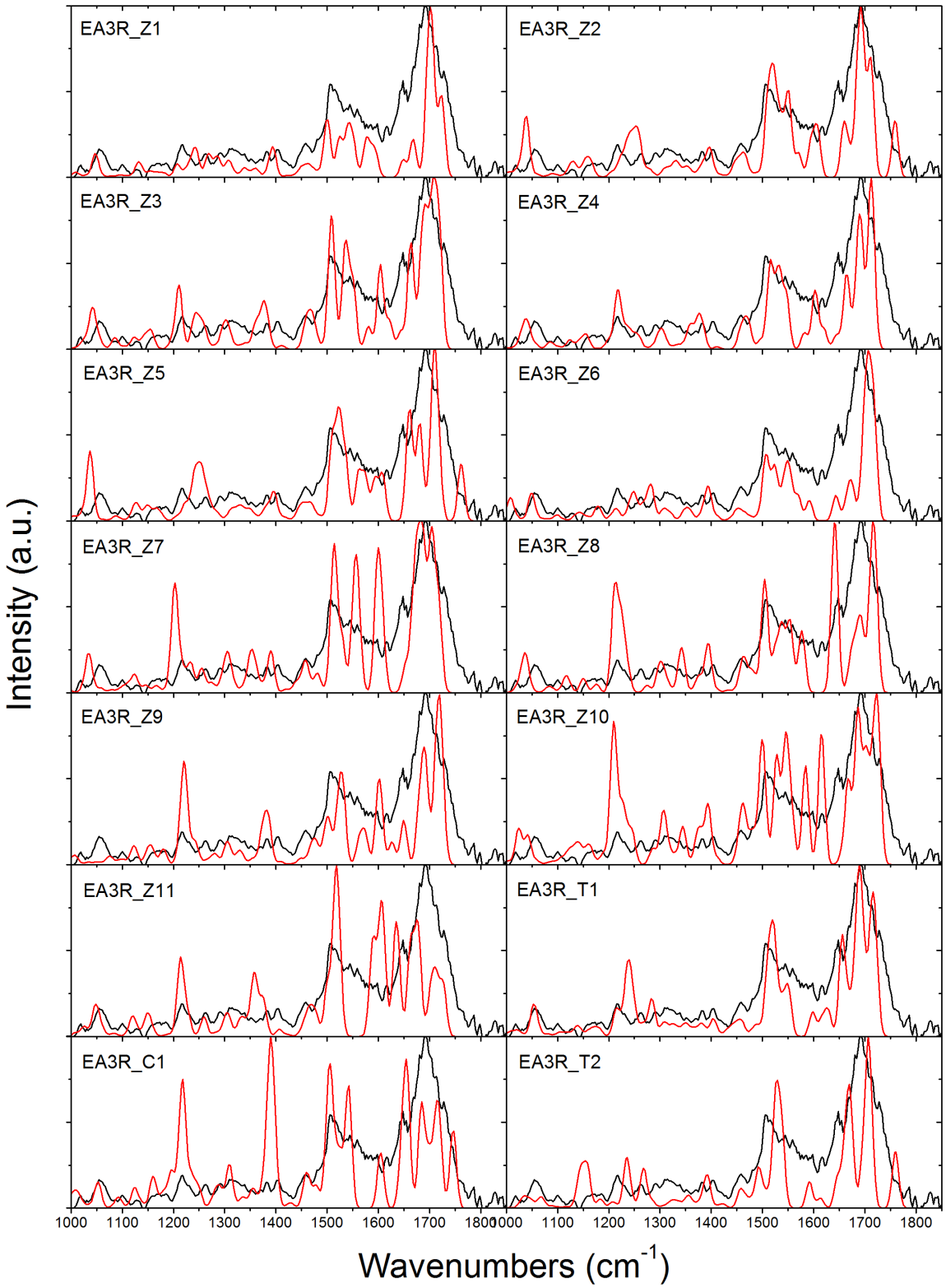


Figure SI-8. Conformations of Z-Glu-Ala-Ala-Ala-Arg-NHMe, optimized with the M05-2x functional employed with the 6-311G(d,p) basis set.


EA3R_Z1
EA3R_Z2
EA3R_Z3
EA3R_Z4
EA3R_Z5
EA3R_Z6
EA3R_Z7
EA3R_Z8
EA3R_Z9
EA3R_Z10
EA3R_Z11
EA3R_T1
EA3R_C1
EA3R_T2
Intensity (a.u.)
1000 1100 1200 1300 1400 1500 1600 1700 1800
Wavenumbers (cm-1)

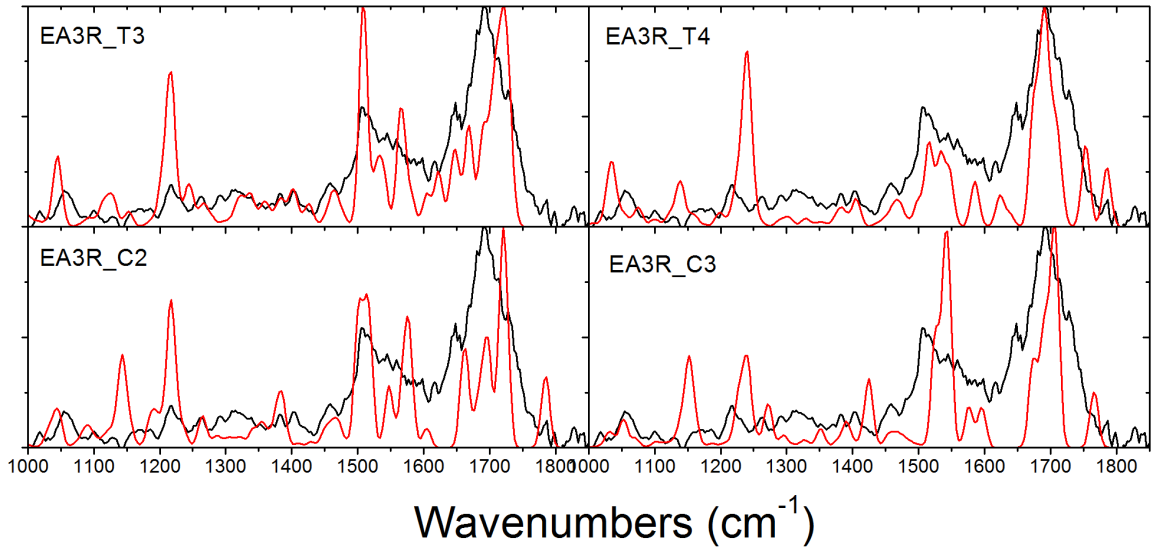


Figure SI-9. Experimental IR-UV ion-dip spectrum of Z-Glu-Ala-Ala-Ala-Arg-NHMe (black trace) and the theoretical spectra of the optimized structures for Z-Glu-Ala-Ala-Ala-Arg-NHMe (red trace).