

Selenium in proteins: Conformational changes induced by Se substitution on methionine, as studied in isolated model peptides by optical spectroscopy and quantum chemistry

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Table S1 : Comparison of the experimental N-H stretch frequencies of the 4 conformers of **Ac-Sem-Phe-NH₂** with relevant theoretical data obtained for the lowest energy conformers of each backbone family (see Figure 2). Also given are, for each conformation: H-bond network and side chain orientations; relative enthalpies (ΔH , 0 K) and Gibbs free energies (ΔG , 300 K), both in kJ/mol. ; theoretical N-H stretch vibrational frequencies (cm^{-1}) and average and maximum deviations ($\langle \delta \rangle$ and δ_{max} resp.) of the theoretical frequencies with respect to experimental frequencies of conformers A-D. These latter criteria can be used to guide the assignment, since typical discrepancy with experimental data is less than 20 cm^{-1} for free NH or NH...OC H-bonds. The best match conformations are indicated here in red in the eight last columns.

Experiment																	
	Conformer		NH stretch frequencies (cm^{-1})														
	A		3354	3381	3434	3520											
	D		3332	3389	3437	3519											
	B		3272	3381	3452	3520											
	C		3329	3422	3440	3539											
Theory			NH stretch frequencies (cm^{-1})														
	ΔH (0 K) kJ/mol	ΔG (300 K) kJ/mol	NH _{Sem}	NH ₂ symm.	NH _{Phe}	NH ₂ antis.	A		D		B		C				
							$\langle \delta \rangle$	δ_{max}	$\langle \delta \rangle$	δ_{max}	$\langle \delta \rangle$	δ_{max}	$\langle \delta \rangle$	δ_{max}	$\langle \delta \rangle$	δ_{max}	
$6_{\text{E}}^{\delta} - \pi_{\text{E}^{+}} - 10$	0.0	0.0	3331	3388	3448	3527	13	23	5	11	19	59	14	34			
$6_{\text{A}}^{\delta} - \pi_{\text{E}^{+}} - 10$	5.3	4.6	3354	3393	3447	3528	8	13	11	22	27	82	18	29			
$5_{\text{E}^{+}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{L}}$	9.4	6.0	3332	3373	3453	3521	12	22	9	16	18	60	21	49			
$5_{\text{E}^{+}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{L}}$	6.7	9.0	3316	3365	3460	3520	20	38	16	24	17	44	27	57			
$5_{\text{E}^{+}} - 7_{\text{A}}^{\delta} - 7_{\text{L}}$	13.3	9.6	3308	3399	3459	3522	23	46	15	24	16	36	20	23			
$5_{\text{E}^{+}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{D}}$	5.8	8.0	3315	3360	3454	3524	21	39	17	29	17	43	26	62			
$5_{\text{A}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{L}}$	8.5	9.0	3277	3378	3462	3528	29	77	25	55	6	10	32	52			
$5_{\text{A}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{L}}$	11.4	10.0	3260	3374	3454	3516	31	94	27	72	6	12	39	69			
$5_{\text{A}} - 7_{\text{A}}^{\delta} - 7_{\text{L}}$	13.7	12.4	3249	3394	3458	3520	36	105	28	83	11	23	36	80			
$5_{\text{A}} - 7_{\text{E}^{+}}^{\delta} - f$	14.3	7.6	3274	3432	3447	3559	46	80	38	58	24	51	23	55			
$5_{\text{A}} - 7_{\text{E}^{+}}^{\delta} - 7_{\text{D}}$	10.9	14.3	3267	3361	3451	3524	32	87	28	65	7	20	37	62			
$5_{\text{E}^{+}} - 7_{\text{E}^{+}}^{\delta}/5_{\text{A}} - \pi$	12.6	7.6	3351	3426	3444	3540	19	45	21	37	38	79	8	22			
$5_{\text{A}} - 7_{\text{E}^{+}}^{\delta}/5_{\text{A}} - \pi$	16.9	11.5	3319	3425	3442	3538	26	44	18	36	30	47	4	10			

Table S2 : Comparison of the experimental N-H stretch frequencies of the 4 conformers of **Ac-Met-Phe-NH₂** with relevant theoretical data obtained for the lowest energy conformers of each backbone family (see Figure 2). Also given are, for each conformation: H-bond network and side chain orientations; relative enthalpies (ΔH , 0 K) and Gibbs free energies (ΔG , 300 K), both in kJ/mol. ; theoretical N-H stretch vibrational frequencies (cm^{-1}) and average and maximum deviations ($\langle \delta \rangle$ and δ_{max} resp.) of the theoretical frequencies with respect to experimental frequencies of conformers A-D. These latter criteria can be used to guide the assignment, since typical discrepancy with experimental data is less than 20 cm^{-1} for free NH or $\text{NH} \cdots \text{OC}$ H-bonds. The best match conformations are indicated here in red in the four last columns.

Experiment											
	Conformer		NH stretch frequencies (cm^{-1})								
	A		3359	3385	3436	3518					
	B		3340	3359	3449	3518					
Theory											
			NH stretch frequencies (cm^{-1})								
	ΔH (0 K) kJ/mol	ΔG (300 K) kJ/mol	NH _{sem}	NH ₂ symm.	NH _{phe}	NH ₂ antis.	A		B		
							$\langle \delta \rangle$	δ_{max}	$\langle \delta \rangle$	δ_{max}	
$6^{\delta}_{\text{a}} - \pi_{\text{g}^{+}} - 10$	4.3	2.3	3360	3391	3445	3527	6	9	16	32	
$6^{\delta}_{\text{g}^{-}} - \pi_{\text{g}^{+}} - 10$	0.0	0.0	3341	3389	3444	3527	10	18	12	30	
$5_{\text{g}^{+}} - 7^{\delta}_{\text{g}^{-}} - 7_{\text{L}}$	10.0	6.0	3332	3375	3454	3522	15	27	8	16	
$5_{\text{g}^{+}} - 7^{\delta}_{\text{g}^{+}} - 7_{\text{L}}$	7.6	6.7	3314	3369	3459	3521	22	45	12	26	
$5_{\text{g}^{+}} - 7^{\delta}_{\text{a}} - 7_{\text{L}}$	13.9	9.0	3321	3398	3457	3522	19	38	17	39	
$5_{\text{g}^{+}} - 7^{\delta}_{\text{g}^{-}} - 7_{\text{D}}$	6.6	7.6	3322	3361	3451	3525	21	37	7	18	
$5_{\text{a}} - 7^{\delta}_{\text{g}^{+}} - 7_{\text{L}}$	9.7	8.7	3291	3376	3460	3527	28	68	22	49	
$5_{\text{a}} - 7^{\delta}_{\text{g}^{-}} - 7_{\text{L}}$	12.1	9.8	3274	3379	3454	3517	28	85	23	66	
$5_{\text{a}} - 7^{\delta}_{\text{a}} - 7_{\text{L}}$	13.2	10.1	3248	3397	3456	3522	37	111	35	92	
$5_{\text{a}} - 7^{\delta}_{\text{g}^{+}} - \text{f}$	16.4	10.7	3330	3431	3435	3546	46	80	31	72	
$5_{\text{a}} - 7^{\delta}_{\text{g}^{-}} - 7_{\text{D}}$	11.7	6.4	3271	3361	3450	3524	33	88	19	69	
$5_{\text{g}^{+}} - 7\delta/5_{\text{a}} - \pi$	11.7	6.4	3351	3426	3444	3540	19	45	27	66	
$5_{\text{a}} - 7\delta/5_{\text{a}} - \pi$	14.3	9.6	3319	3425	3442	3538	26	44	27	66	

Table S3 : Detailed parameters of the NBO(i)→NBO(j) interactions at play in the 7^δ and 6^δ NH···Se H-bonds in several conformers of interest of the Ac-Sem-Phe-NH₂ capped dipeptide together with the NH···Se H-bond of the intermolecular *trans*-N-methylacetamide···SeMe₂ complex. Interaction energies E(2) are given in kcal/mol ; NBO occupancy is close to 2 for the donor NBOs considered. Depending on the conformation considered, several donor NBOs to the σ* NBO of the H-bonded NH have been found : namely the two Se lone pairs NBOs (lp_{Se}(1) and lp_{Se}(2)), a π orbital of a C-C bond of the ring (π_{CC Phe}) as well as the two lone pairs NBOs (lp_{OPhe}(1) and lp_{OPhe}(2)) of the neighbouring carbonyl O atom of the Phe residue in extended conformations

Se-compounds											
	Side chain	NH···Se distance (pm)	E(2) NBO stabilization energies (kcal/mol) for interaction from a donor NBO to the acceptor σ* _{NH} NBO								
Ac-Sem-Phe-NH₂			donors								
conformation			lp _{Se} (1)	lp _{Se} (2)	π _{CC Phe}	lp _{OPhe} (1)	lp _{OPhe} (2)	ΣE _{HB}	ΣE _{NH}	σ* _{NH} population (e)	Calc'd frequency
5_a - 7^δ_{g+} - 7_L	ag+a	249.5	0.83	12.39				13.22	13.22	0.0684	3274
5_a - 7^δ_{g-} - 7_L	ag+a	259.2	0.83	9.28	1.27			10.11	11.38	0.0631	3291
5_{g+} - 7^δ/5_a - π	ag+a	271.4	0.26	4.72		0.19	0.59	4.98	5.17	0.0497	3325
6^δ_a - π_{g+} - 10	g+g-a	250.7	1.38	7.47				8.85	8.85	0.053	3360
5_{g+} - 7^δ_{g-} - 7_L	ag+g+	262.6	0.96	6.3				7.26	7.26	0.0558	3332
5_{g+} - 7^δ_{g+} - 7_L	ag+g+	267.9	1.02	5.5	1.37			6.52	7.89	0.0583	3314
5_{g+} - 7^δ/5_a - π	ag+g+	276.1	0.56	2.66		0.29	0.98	3.22	4.49	0.0464	3357
6^δ_{g-} - π_{g+} - 10	g+g-g-	248.5	1.14	10.29				11.43	11.43	0.0567	3341
t-MMA···SeMe₂											
6^δ_a - π_{g+} - 10		261.4	0.43	7.24				7.67	7.67	0.0515	3355

Table S4 : Detailed parameters of the NBO(i)→NBO(j) interactions at play in the 7^δ and 6^δ NH···Se H-bonds in several conformers of interest of the Ac-Met-Phe-NH₂ capped dipeptide together with the NH···Se H-bond of the intermolecular *trans*-N-methylacetamide···SMe₂ complex. Interaction energies E(2) are given in kcal/mol ; NBO occupancy is close to 2 for the donor NBOs considered. Depending on the conformation considered, several donor NBOs to the σ* NBO of the H-bonded NH have been found : namely the two S lone pairs NBOs (lp_S(1) and lp_S(2)), a π orbital of a C-C bond of the ring (π_{CC Phe}) as well as the two lone pairs NBOs (lp_{OPhe}(1) and lp_{OPhe}(2)) of the neighbouring carbonyl O atom of the Phe residue in extended conformations

S-compounds											
	Side chain	NH···S distance (pm)	E(2) NBO stabilization energies (kcal/mol) for interaction from a donor NBO to the acceptor σ* _{NH} NBO								
Ac-Met-Phe-NH₂			donors								
conformation			lp _{Se} (1)	lp _{Se} (2)	π _{CC Phe}	lp _{OPhe} (1)	lp _{OPhe} (2)	ΣE _{NH}	ΣE _{HB}	σ* _{NH} population	Calc'd frequency
5_a - 7^δ_{g+} - 7_L	ag+a	238.4	1.08	11.21				12.29	12.29	0.0684	3274
5_a - 7^δ_{g-} - 7_L	ag+a	248.9	0.98	7.82	1.26			8.8	10.06	0.0631	3291
5_{g+} - 7^δ_{g+}/5_a - π	ag+a	261.1	0.36	4.07		0.23	0.74	4.43	5.4	0.0497	3325
6^δ_a - π_{g+} - 10	g+g-a	238.8	1.98	6.42				8.4	8.4	0.053	3360
5_{g+} - 7^δ_{g-} - 7_L	ag+g+	248.9	1.46	5.86				7.32	7.32	0.0558	3332
5_{g+} - 7^δ_{g+} - 7_L	ag+g+	253.7	1.53	5.4	1.49			6.93	8.42	0.0583	3314
5_{g+} - 7^δ_{g+}/5_a - π	ag+g+	262.8	0.78	2.44		0.22	0.77	3.22	4.21	0.0464	3357
6^δ_{g-} - π_{g+} - 10	g+g-g-	239.5	1.31	8.68				9.99	9.99	0.0567	3341
t-MMA···SMe₂											
6^δ_a - π_{g+} - 10		246.8	0.71	7.55				8.26	8.26	0.0519	3345

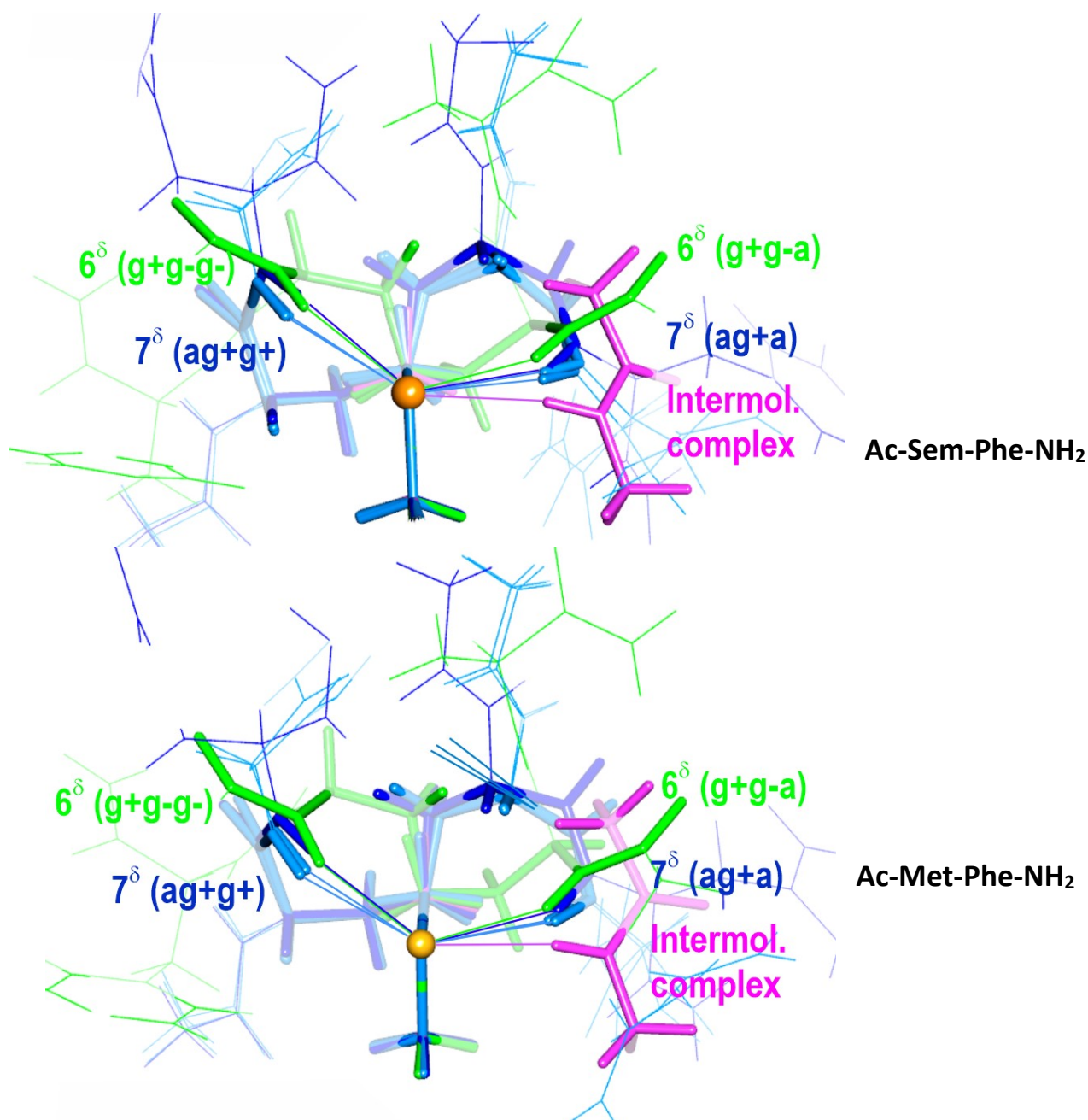


Figure S1 : Comparison of the NH \cdots S/Se approaches of the relevant conformations (5-7 $^{\delta}_{g+/g-}$ -7L light blue, 5-7 $^{\delta}_{5a-\pi}$ dark blue and 6 $^{\delta}$ - π_{g+} -10 green) of the Ac-Sem-Phe-NH₂ (*top panel*) and Ac-Met-Phe-NH₂ (*bottom panel*) compounds, as found at the DFT-D level of theory. The terminal part of all the Sem/Met side chains have been overlaid (Se/S atom in yellow), allowing to distinguish the effect of the χ_3 dihedral orientation (side chain dihedrals between parentheses). For the sake of clarity, front atoms have been omitted and background atoms shaded. For reference, the structure of the intermolecular complex has also been added.

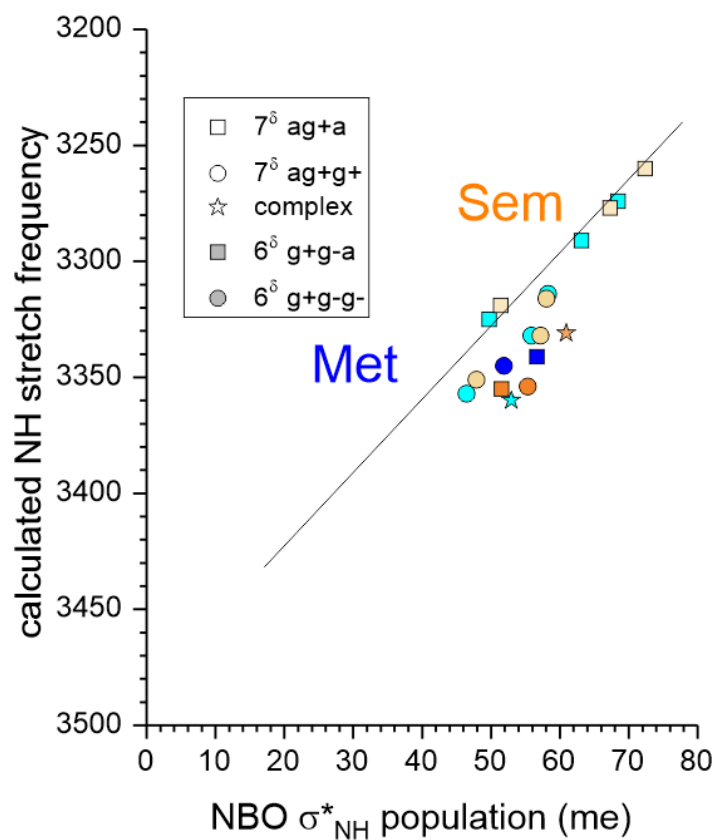


Figure S2 : Calculated NH stretch frequency (scaled harmonic frequencies) vs. the total stabilization energy (noted ΣE_{NH}), taking into account all the interactions that contribute to the electron delocalization towards the σ^*_{NH} interaction, for NH groups involved in a $\text{NH}\cdots\text{S}$ interaction, for all the conformations considered in the present analysis.