Electronic Supplementary Material (ESI) for RSC Advances

From building blocks of proteins to drugs: A quantum chemical study on structure-property relationships of phenylalanine, tyrosine and dopa

Aravindhan Ganesan*‡, Narges Mohammadi and Feng Wang*

eChemistry Laboratory, Department of Chemistry and Biotechnology, School of Science, Faculty of Sciences, Engineering and Technology, Swinburne University of Technology, Hawthorn, Victoria 3122, Australia.

*Corresponding authors

Aravindhan Ganesan: aganesan@daad-alumni.de

Feng Wang: fwang@swin.edu.au

Supplementary Information

‡ Current Address: Research School of Chemistry, Australian National University, Canberra, ACT 0200 Australia.

SI.1: Comparison of the calculated and experimental geometries of L-tyr and L-dopa.

Parameters	L-phe	L-tyr			L-dopa		
	This Work*	This Work*	Exp[1]	|Δ|	This Work*	Exp[2]	|Δ|
$C_{(1)}=O_{(1)}$/Å	1.20	1.20	1.24	0.04	1.20	1.25	0.05
$C_{(1)}$-$O_{(2)}$/Å	1.34	1.34	1.26	0.08	1.34	1.25	0.09
$C_{(1)}$-$C_{(\alpha)}$/Å	1.55	1.55	1.53	0.02	1.55	1.54	0.01
$C_{(\alpha)}$-N/Å	1.47	1.47	1.49	0.02	1.47	1.46	0.01
$C_{(\alpha)}$-$C_{(\beta)}$/Å	1.55	1.55	1.54	0.01	1.55	1.53	0.02
$C_{(\beta)}$-$C_{(\gamma)}$ /Å	1.51	1.51	1.51	0.00	1.51	1.51	0.00
$C_{(4)}$-$O_{(3)}$/Å		1.37	1.37	0.00	1.37	1.37	0.00
$C_{(3)}$-$O_{(4)}$/Å					1.36	1.36	
R_6/Å	8.37	8.38	8.36	0.02	8.38	8.37	-0.01
$O_{(1)}=C_{(1)}$-$O_{(2)}$/^{0}	123.29	123.23	126.40	3.17	123.18	126.10	2.92
$C_{(1)}$-$C_{(\alpha)}$-N/^{0}	109.02	108.96	109.70	0.74	108.87	110.00	1.14
$C_{(1)}$-$C_{(\alpha)}$-$C_{(\beta)}$/^{0}	111.84	111.81	111.10	0.71	111.82	109.80	2.02
N-$C_{(\alpha)}$-$C_{(\beta)}$/^{0}	116.30	116.03	110.80	5.23	115.96	110.60	5.36
$C_{(\alpha)}$-$C_{(\beta)}$-$C_{(\gamma)}$/^{0}	114.01	114.09	114.50	0.41	113.98	114.00	0.02
$C_{(3)}$-$C_{(4)}$-$C_{(5)}$/^{0}	119.57	119.54	120.20	0.66	118.97	120.30	1.33
$O_{(1)}=C_{(1)}$-$O_{(2)}$-H/^{0}	177.81	177.79			177.40		
$O_{(1)}=C_{(1)}$-$C_{(\alpha)}$-N/^{0}	-165.72	-165.75			-165.47		
$O_{(2)}$-$C_{(1)}$-$C_{(\alpha)}$-N/^{0}	16.59	16.40			16.40		
$O_{(1)}=C_{(1)}$-$C_{(\alpha)}$-$C_{(\beta)}$/^{0}	-35.71	-36.19			-36.04		
$O_{(2)}$-$C_{(1)}$-$C_{(\alpha)}$-$C_{(\beta)}$/^{0}	146.60	146.11			145.83		
$C_{(1)}$-$C_{(\alpha)}$-$C_{(\beta)}$-$C_{(\gamma)}$/^{0}	-73.89	-73.36			-72.36		
N-$C_{(\alpha)}$-$C_{(\beta)}$-$C_{(\gamma)}$/^{0}	52.25	52.52			53.25		

*B3LYP/6-311G**

SI.2: Intra-molecular H-bonds of the aromatic molecules (Å) with a cut-off of 2.80 Å.

Parameters	L-phe	L-tyr	L-dopa
$N^{\cdots}H\text{-}O_{(2)}$	1.89	1.88	1.89
$O_{(1)}{}^{\cdots}H\text{-}C_{(\alpha)}$	2.81	2.81	2.81
$O_{(1)}{}^{\cdots}H\text{-}C_{(\beta)}$	2.55	2.55	2.58
$O_{(1)}{}^{\cdots}H\text{-}C_{(2)}$	2.61	2.59	2.54
$O_{(3)}{}^{\cdots}H\text{-}C_{(5)}$		2.57	2.60
$O_{(3)}{}^{\cdots}H\text{-}C_{(3)}$		2.69	
$O_{(4)}{}^{\cdots}H\text{-}O_{(3)}$			2.13
$O_{(4)}{}^{\cdots}H\text{-}C_{(2)}$			2.71

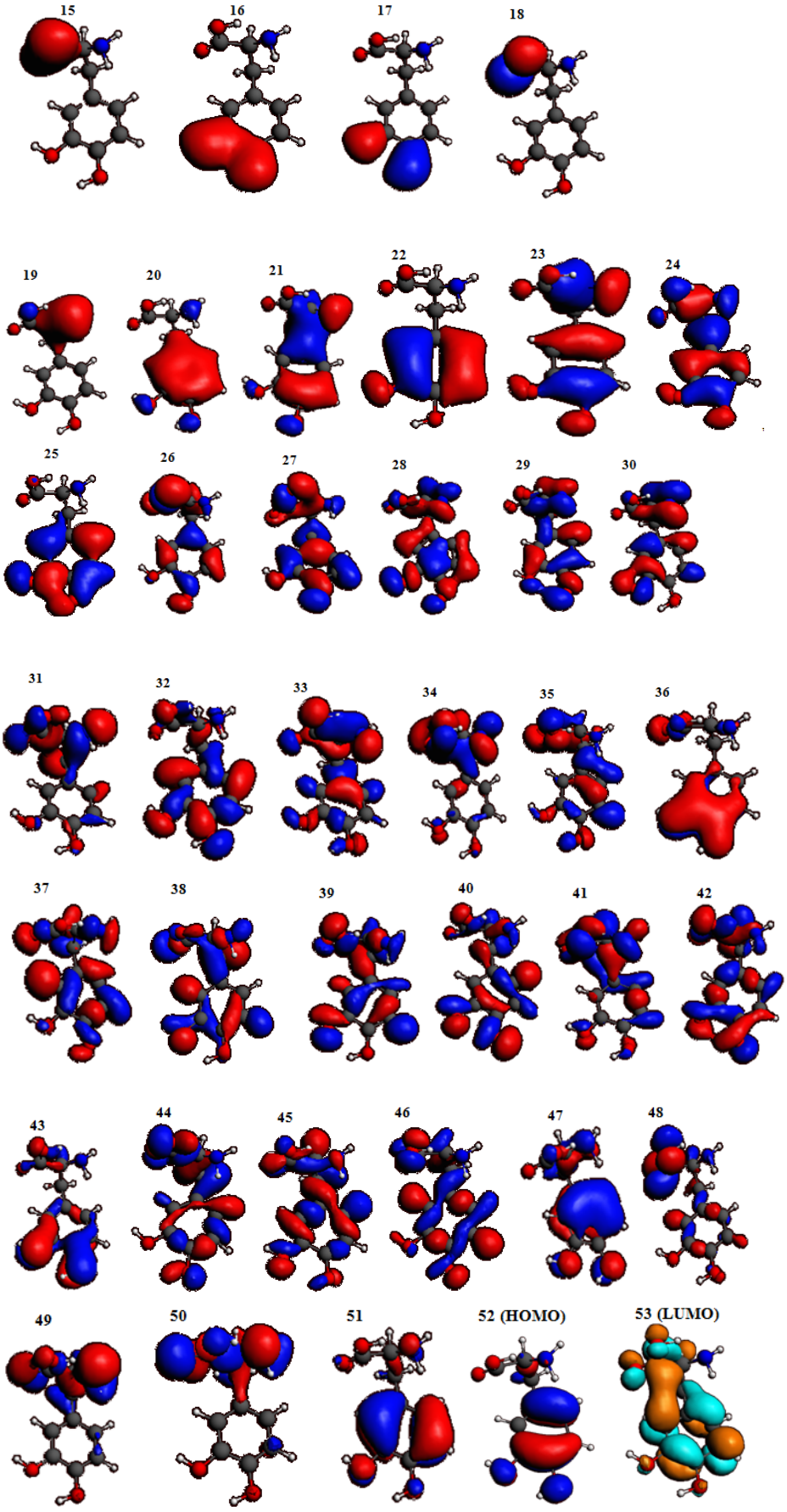
SI.2 discussion:

The Table SI.2 presents all the possible H-bonds in L-phe, L-tyr and L-dopa that are ≤ 2.80 Å cut-off. In L-phe, there are four major H-bonds, three within the amino acid moiety, such as $O_{(1)}{}^{\cdots}H\text{-}C_{(\alpha)}$, $N^{\cdots}H\text{-}O_{(2)}$ and $O_{(1)}{}^{\cdots}H\text{-}C_{(\beta)}$, and one between the carbonyl and phenyl ring, i.e., $O_{(1)}{}^{\cdots}H\text{-}C_{(2)}$. Nevertheless substitution of an OH group in the para position (of phenyl ring) in L-tyr causes a few additional H-bonds, such as $O_{(3)}{}^{\cdots}H\text{-}C_{(5)}$ and $O_{(3)}{}^{\cdots}H\text{-}C_{(3)}$. On the other hand, L-dopa, when compared to L-phe, has three additional H-bonds including $O_{(3)}{}^{\cdots}H\text{-}C_{(5)}$, $O_{(4)}{}^{\cdots}H\text{-}O_{(3)}$ and $O_{(4)}{}^{\cdots}H\text{-}C_{(2)}$; those are formed due to the OH substituent on its catechol side chain. These additional bonds in L-dopa tend to affect its other H-bonds, especially those arising from the carbonyl group. For instance, the $O_{(1)}{}^{\cdots}H\text{-}C_{(2)}$ bond in L-phe and L-tyr is 2.61 Å, which becomes stronger in L-dopa with a distance of 2.54 Å. This indicates that additional OH groups in the phenyl ring tend to also affect the intra-molecular interactions between the side chains. Indeed strong intra-molecular H-bonds between amino and carboxyl groups in the amino acid moiety on one end and the H-bonds with the catechol OH groups on the other end greatly affects the flexibility in the structure of L-dopa. Lack of flexibility, therefore, may attribute to lesser number of conformers in L-dopa when compared to its amino acid precursors, L-phe and L-tyr.

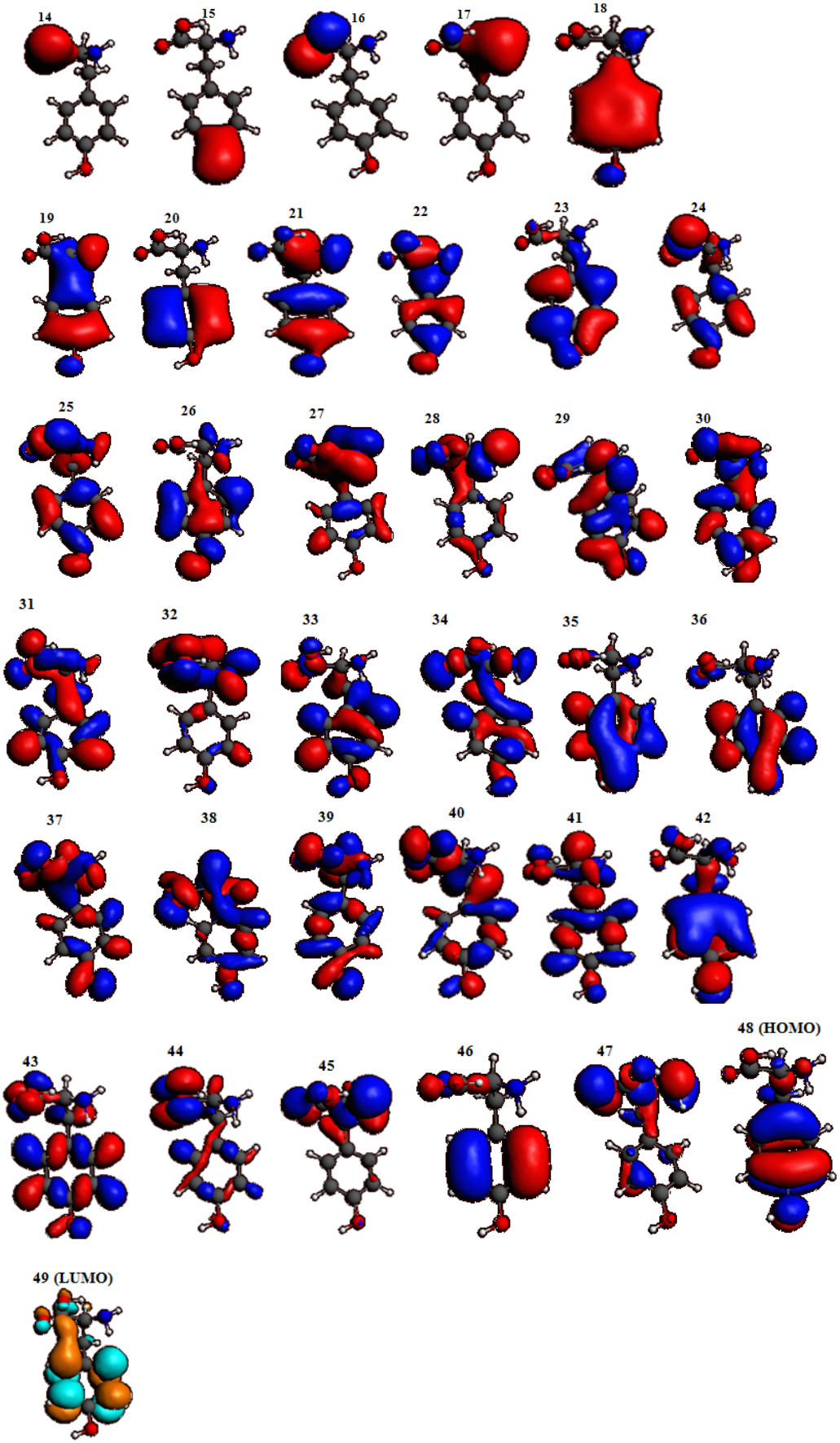
SI.3: Valence vertical IPs of L-phe, L-tyr and L-dopa calculated using the SAOP/et-pVQZ and OVGF/6-311G** models (eV). OVGF polestrengths are given in parantheses.

L-phe			L-tyr				L-dopa		
MOs	**SAOP**	**OVGF**	**MOs**	**SAOP**	**OVGF**	**EXP[3]**	**MOs**	**SAOP**	**OVGF**
44a	-10.49	-8.96(0.90)	48a	-9.88	-8.14(0.90)	8.47	52a	-9.60	-7.85(0.90)
43a	-10.70	-9.18(0.90)	47a	-10.61	-9.26(0.89)	9.40	51a	-10.27	-8.71(0.90)
42a	-10.78	-9.75(0.90)	46a	-10.69	-9.71(0.90)	9.60	50a	-10.64	-9.76(0.90)
41a	-11.66	-10.91(0.90)	45a	-11.55	-10.86(0.90)	10.80	49a	-11.55	-10.88(0.90)
40a	-12.17	-11.12(0.90)	44a	-12.09	-11.13(0.90)		48a	-12.12	-11.22(0.90)
39a	-12.46	-11.79(0.90)	43a	-12.40	-11.60(0.85)	11.30	47a	-12.33	-11.34(0.85)
38a	-12.50	-11.92(0.90)	42a	-12.56	-11.88(0.90)		46a	-12.52	-11.91(0.90)
37a	-13.13	-12.19(0.83)	41a	-12.72	-12.02(0.90)		45a	-12.75	-12.21(0.90)
36a	-13.31	-12.81(0.90)	40a	-13.05	-12.70(0.90)		44a	-13.06	-12.73(0.90)
35a	-13.80	-13.36(0.90)	39a	-13.65	-13.38(0.90)		43a	-13.57	-13.34(0.90)
34a	-14.10	-13.74(0.89)	38a	-14.08	-13.68(0.90)		42a	-13.62	-13.33(0.89)
33a	-14.50	-14.17(0.89)	37a	-14.39	-14.23(0.90)		41a	-14.06	-13.70(0.89)
32a	-14.54	-14.37(0.88)	36a	-14.52	-14.24(0.87)		40a	-14.21	-14.18(0.90)
31a	-14.91	-14.74(0.89)	35a	-14.57	-14.39(0.88)		39a	-14.58	-14.47(0.89)
30a	-15.40	-15.24(0.89)	34a	-14.80	-14.67(0.89)		38a	-14.74	-14.72(0.89)
29a	-15.49	-15.42(0.88)	33a	-14.98	-15.04(0.89)		37a	-14.82	-14.79(0.89)
28a	-15.69	-15.58(0.88)	32a	-15.38	-15.22(0.89)		36a	-15.04	-14.84(0.85)
27a	-16.03	-15.95(0.89)	31a	-15.57	-15.67(0.88)		35a	-15.23	-15.14(0.89)
26a	-16.81	-16.87(0.89)	30a	-16.02	-16.02(0.88)		34a	-15.43	-15.41(0.89)
25a	-16.94	-17.03(0.86)	29a	-16.34	-16.29(0.88)		33a	-16.03	-16.04(0.89)
24a	-17.88	-18.08(0.89)	28a	-16.73	-16.88(0.89)		32a	-16.18	-16.28(0.88)
23a	-18.75		27a	-17.78	-18.07(0.89)		31a	-16.68	-16.89(0.89)
22a	-19.19		26a	-17.83	-18.13(0.86)		30a	-17.46	-17.82(0.88)
21a	-19.34		25a	-18.80		18.65	29a	-17.84	-18.19(0.87)
20a	-20.75		24a	-19.14			28a	-17.99	-18.29(0.88)
19a	-22.51		23a	-19.76		19.40	27a	-18.78	
18a	-22.88		22a	-20.67			26a	-19.14	
17a	-23.90		21a	-22.38		21.15	25a	-20.16	
16a	-25.77		20a	-22.94		22.75	24a	-20.70	
15a	-27.38		19a	-23.75		24.30	23a	-22.37	
14a	-30.05		18a	-25.68		25.90	22a	-22.78	
13a	-32.11		17a	-27.26		28.00	21a	-23.73	
			16a	-29.94			20a	-25.61	
			15a	**-31.26**		32.40	19a	-27.25	
			14a	-32.00		34.00	18a	-29.97	
							17a	**-30.86**	
							16a	**-31.58**	
							15a	-32.03	

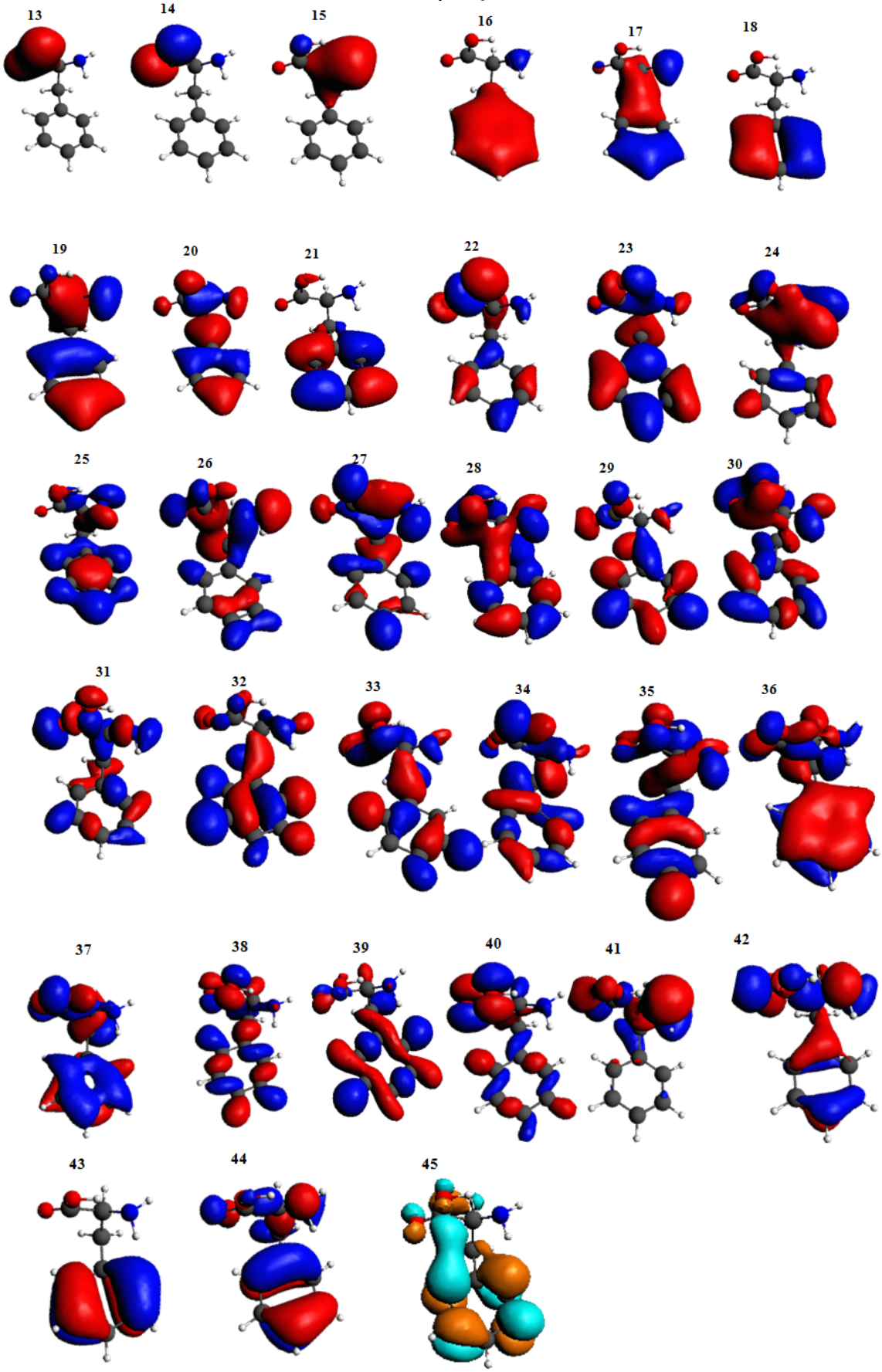
SI.4: Valence MOs of L-DOPA from SAOP/et-pVQZ calculations



SI.5: Valence MOs of L-tyr from SAOP/et-pVQZ calculations



SI.6: Valence MOs of L-Phe from SAOP/et-pVQZ calculations



References (Supplementary information):

1. M. N. Frey, T. F. Koetzle, M. S. Lehmann and W. C. Hamilton, *J. Chem. Phys.*, 1973, 58, 2547-2556.
2. A. Mostad, T. Ottersen and C. Romming, *Acta Chem. Scand.*, 1970, 24, 1864-1865.
3. O. Plekan, V. Feyer, R. Richter, M. Coreno and K. C. Prince, *Mol. Phys.*, 2008, 106, 1143-1153.