Electronic Supplementary Material for

Fluorescent calix[4]arene chemosensor for acidic and basic amino acids in pure aqueous media

Yao-Wei Xu[a], Li-Lin Tan[a], Jun-Min Liu*[a], Li-Min Xiao[c], Shao-Yong Li[b], Cheng-Yong Su*[a]

[a] MOE Laboratory of Bioinorganic and Synthetic Chemistry/KLGHEI of Environment and Energy Chemistry, State Key Laboratory of Optoelectronic Materials and Technologies, School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China. E-mail: liujunm@mail.sysu.edu.cn, cesscy@mail.sysu.edu.cn

[b] Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics (Theranostics), School of Pharmacy, Basic Medical Research Center, Tianjin Medical University, Tianjin 300070, China.

Table of Contents

1. Apparatus and reagents

All reactions were carried out under anhydrous conditions in dry solvents, using argon or nitrogen and monitored by thin-layer chromatography (TLC) using silica gel plates from Merck (60F254). Fluorescence spectra were recorded on a Shimadzu RF-5301PC spectrometer. UV-Vis spectra were recorded on a Shimadzu UV-2450 spectrometer. MALDI-TOF MS was run on a Bruker Daltonics ultrafleXtreme MALDI-TOF/TOF mass spectrometer. ESI-MS data were obtained using a JEOL The AccuTOF CS JMS-T100CS mass spectrometer. NMR spectra were recorded on a Bruker Ascend 400 MHz or Varian Mercury Plus 300 MHz nuclear magnetic resonance spectroscopy. Chemical shifts of NMR are given in ppm relative to tetramethylsilane. Elemental analyses were carried out with a Vario EL Element Analyzer. A Delta 320 pH-meter [Mettler-Toledo Instruments (Shanghai) Co., China] was used for pH measurements. All of naturally occurring amino acids were of analytical grade and used without further purification.

2. Synthesis of 2 and 3

2.1 Synthesis of 3

4 (200 mg, 0.21 mmol), 5'-formyl-2,2'-bithiophene-5-boronic acid (400 mg, 1.68 mmol), Pd(dppf)Cl_2 (77 mg, 0.11 mmol), K_2CO_3 (580 mg, 4.2 mmol) was added to a flask under nitrogen atmosphere, and then toluene (8 mL) and methanol (8 mL) was added. The reaction mixture was stirred at room temperature for about 15 min and then refluxed at 80 ˚C. After completion of the reaction as monitored by TLC, the mixture was cooled and evaporated to dryness. The residue was dissolved in dichloromethane and the organic content was washed with water and brine. The combined organic extracts were subsequently dried over anhydrous $MgSO_4$, filtered and evaporated to afford a crude product which was further purified by silica-gel column chromatography using petroleum ether and ethyl acetate as the eluant (2:1, v/v) to yield 220 mg yellow solid. Yield: 75%. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 9.75 (s, 4H), 7.51 (d, J = 3.9 Hz, 4H), 7.04 (d, J = 3.8 Hz, 8H), 6.94 (s, 8H), 6.81 (d, J = 3.6 Hz, 4H), 4.50 (d, J = 13.3 Hz, 4H), 3.96 (t, J = 7.3 Hz, 8H), 3.25 (d, J = 13.5 Hz, 4H), 2.01-1.86 (m, 8H), 1.51-1.42 (m, 8H), 1.03 (t, J = 7.3 Hz, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 182.2, 157.1, 147.5, 146.5, 141.1, 137.4, 135.5, 134.0, 127.8, 127.0, 125.9, 123.5, 123.1, 75.4, 32.5, 31.3, 19.6, 14.3; MALDI-TOF: *m/z* 1416.300 ($[M]^+$);1439.292 ($[M+Na]^+$);1455.259 ($[M+K]^+$); Elemental Analysis: Calcd for $C_{80}H_{72}O_8S_8$: C, 67.76; H, 5.12. Found: C, 67.72; H, 5.15.

2.2 Synthesis of 2

A mixture of **3** (142 mg, 0.10 mmol) and cyanoacetic acid (102 mg, 1.2 mmol) was added acetonitrile (60 mL) and toluene (20 mL) under nitrogen atmosphere, and then piperidine (1.9 g, 22.5 mmol) was added. The reaction solution was refluxed at 90 ˚C for 5 h. After cooling to room temperature, the resulting mixture was neutralized to pH 2-3 with 0.5 M aqueous HCl and extracted with dichloromethane. The extract was washed successively with water and brine and dried over anhydrous $MgSO_4$, filtered and evaporated to afford a crude product which was further purified by silica-gel column chromatography using ethyl acetate and acetic acid as the eluant (1:1, v/v) to yield 157 mg yellow solid. Yield: 93%. ^{1}H-NMR (400 MHz, DMF-d_7) δ (ppm): 8.36 (s, 4H), 7.81 (d, J = 4.4 Hz, 4H), 7.36 (d, J = 3.8 Hz, 4H), 7.30 (d, J = 4.0 Hz, 4H), 7.24 (s, 8H), 7.13 (d, J = 3.9 Hz, 4H), 4.56 (d, J = 13.1 Hz, 4H), 4.18-3.96 (m, 8H), 3.52 (d, J = 13.5 Hz, 4H), 2.13-1.89 (m, 8H), 1.70-1.47 (m, 8H), 1.09 (t, J = 7.3 Hz, 12H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ (ppm): 163.3, 156.5, 145.9, 145.8, 140.8, 135.0, 133.2, 132.8, 127.7, 126.7, 125.4, 123.9, 123.5, 116.3, 97.2, 74.5, 31.8, 29.0, 22.1, 18.9, 13.9; MALDI-TOF: *m/z* 1684.310 ($[M]^+$); 1707.302 ($[M+Na]^+$); 1723.270 ($[M+K]^+$); Elemental Analysis: Calcd for $C_{92}H_{76}N_4O_{12}S_8$: C, 65.53; H, 4.54; N, 3.32. Found: C, 65.52; H, 4.51; N, 3.35.

3.

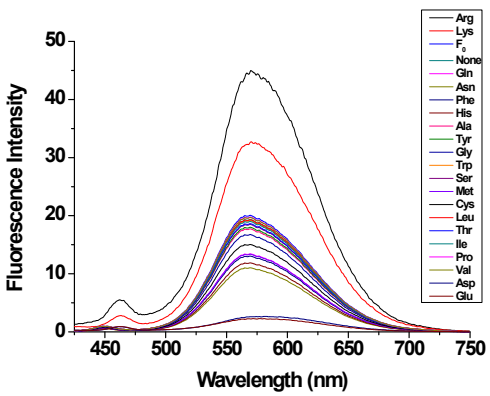

Figure S1. The change of fluorescence intensity of **2** with 10 equiv. of amino acids in sodium phosphate buffer solution (0.1 M, pH 7.8), λ_{ex} = 400 nm, [**2**] = 5.0 × 10^{-6} M, [Glu] = [Asp] = [Val] = [Pro] = [Ile] = [Thr] = [Leu] = [Cys] = [Met] = [Ser] = [Trp] = [Gly] = [Tyr] = [Ala] = [His] = [Phe] = [Asn] = [Gln] = [Lys] = [Arg] = 0.02 M.

4.

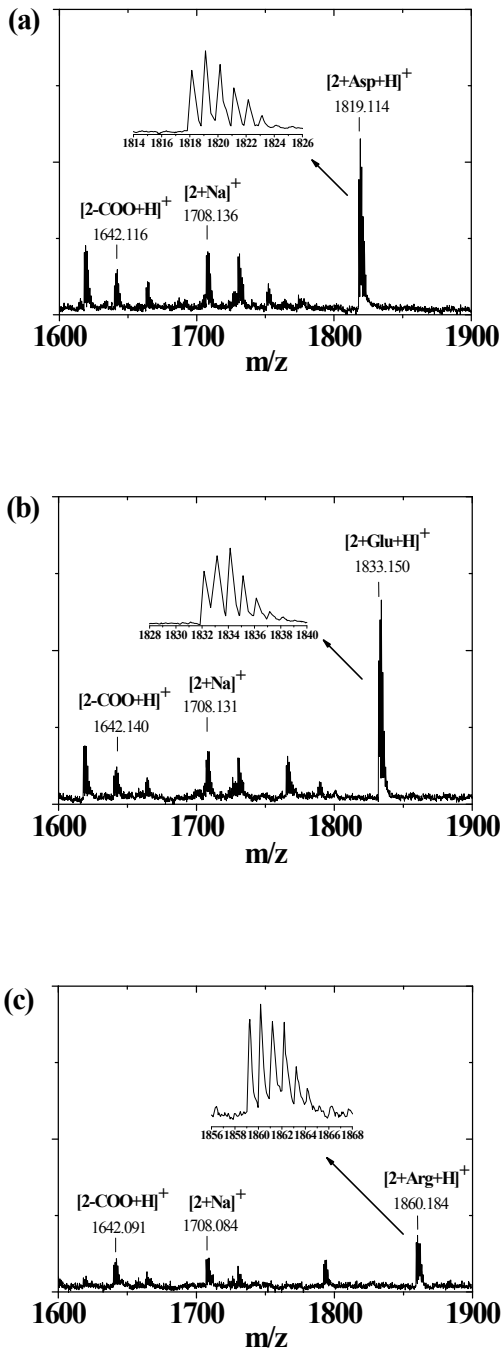

Figure S2. ESI MS spectra of (a) **2** and Asp, (b) **2** and Glu, and (c) **2** and Arg in 1 : 1 molar ratio.

5.

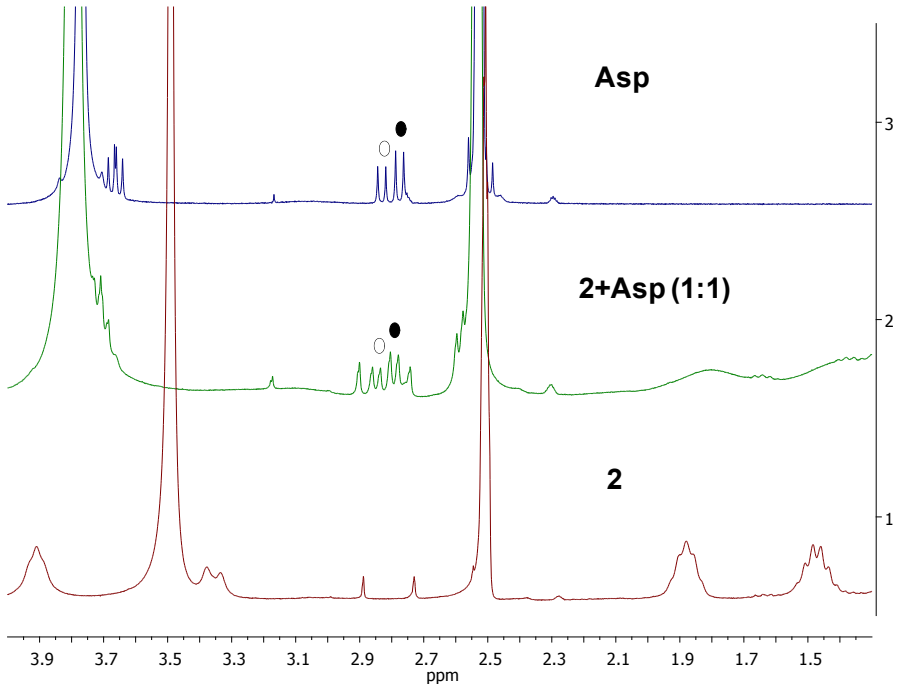

Figure S3. Partial ^{1}H NMR spectra of **2**, Asp, and a 1 : 1 mixture of **2** and Asp in DMSO-d_6/D_2O.

6.

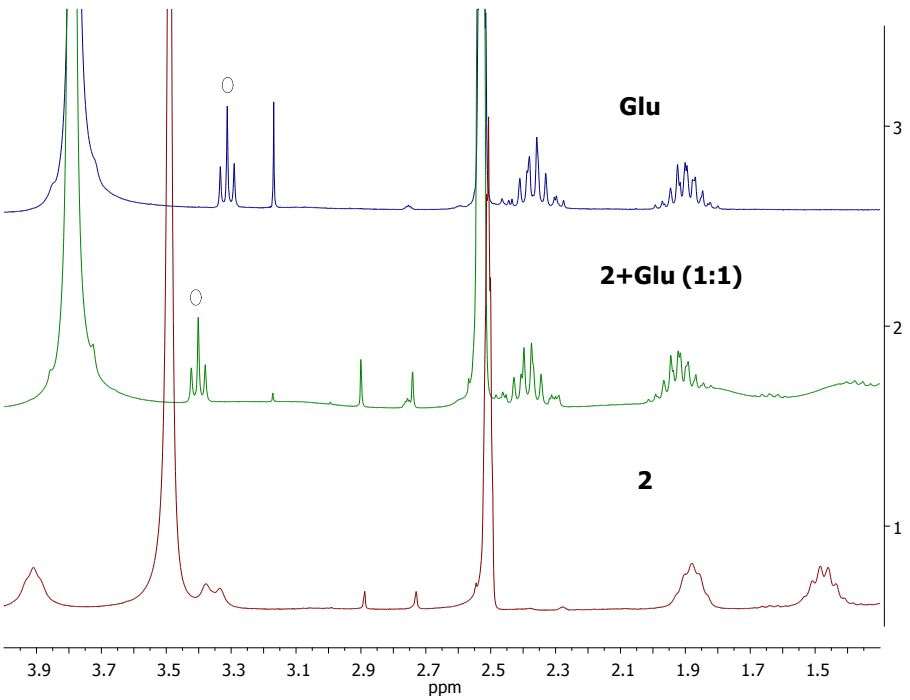

Figure S4. Partial ^{1}H NMR spectra of **2**, Glu, and a 1 : 1 mixture of **2** and Glu in DMSO-d_6/D_2O.

7.

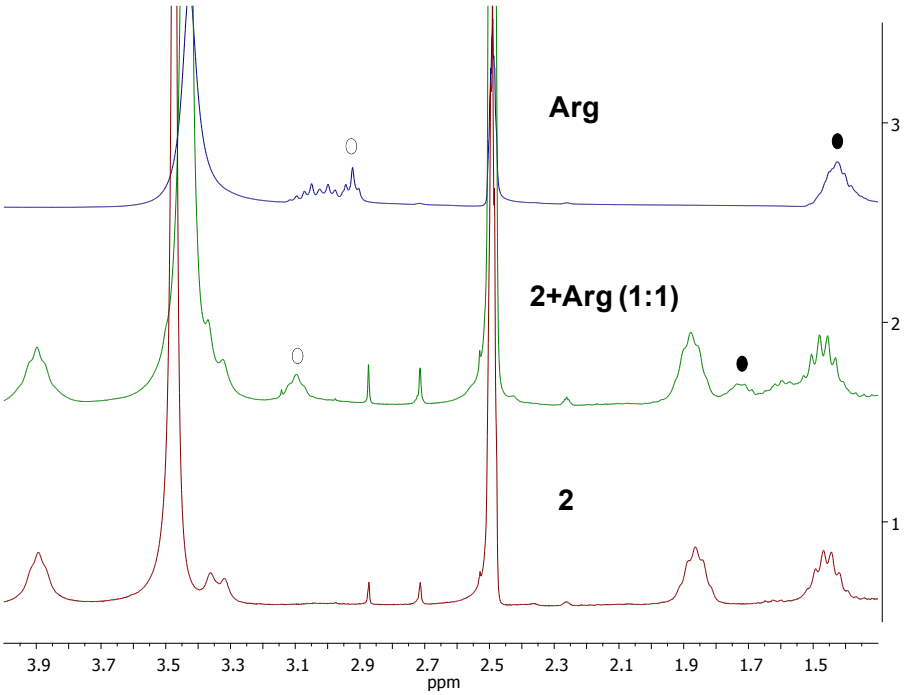

Figure S5. Partial ^{1}H NMR spectra of **2**, Arg, and a 1 : 1 mixture of **2** and Arg in DMSO-d_6/D_2O.

8.

Table S1 Cartesian coordinates of **2** from B3LYP/6-31G optimization.

atom	x	y	z		atom	x	y	z
O(1)	-2.8428	-4.5346	0.4320		C(39)	-3.0404	-7.6164	4.2078
O(2)	0.3271	-6.1338	-0.2754		C(40)	-3.5551	-9.0596	4.3272
C(3)	-0.7459	-4.2471	2.7514		C(41)	0.6710	-7.5739	-0.3644
O(4)	-2.0161	-5.4651	-2.8695		C(42)	-0.5560	-8.3958	-0.0074
C(5)	-6.3856	-0.1532	0.9082		C(43)	-0.2790	-9.9109	-0.0650
C(6)	3.8716	-3.9153	-0.7336		C(44)	-1.5136	-10.7510	0.2987
C(7)	3.3914	-4.2525	0.5476		C(45)	-3.2927	-5.9202	0.1346
C(8)	2.1753	-4.9223	0.7251		C(46)	-4.7312	-6.2298	0.5482
C(9)	0.6092	-3.9900	2.4555		C(47)	-5.0969	-7.6971	0.2453
C(10)	1.0388	-2.6606	2.4027		C(48)	-6.5392	-8.0454	0.6464
C(11)	0.1559	-1.5841	2.6192		C(49)	-2.4585	-5.7747	-4.2505
C(12)	-1.2074	-1.8797	2.8023		C(50)	-2.9088	-7.2276	-4.2978
C(13)	-1.6767	-3.1940	2.8582		C(51)	-1.7759	-8.2460	-4.0814
C(14)	-0.6765	-1.4737	-2.5866		C(52)	-2.2669	-9.7009	-4.1423
C(15)	0.2328	-2.5314	-2.7660		C(53)	1.9476	0.2421	2.7960
C(16)	-0.1806	-3.8667	-2.8043		C(54)	2.0911	1.6543	2.8149
C(17)	0.8630	-4.9866	-2.8782		C(55)	0.9116	2.3583	2.6791
C(18)	0.6544	-0.2123	2.6417		S(56)	-0.4853	1.2003	2.4957
C(19)	5.1662	-3.2691	-0.9244		S(57)	5.9767	-2.3731	0.4385
C(20)	-0.2466	-0.0789	-2.6228		C(58)	7.3842	-1.9713	-0.6515
C(21)	-2.0282	-1.7986	-2.3540		C(59)	7.1692	-2.4978	-1.9091
C(22)	1.4530	-5.3054	-0.4213		C(60)	5.9507	-3.2123	-2.0567
C(23)	-5.1813	-1.8313	-0.5102		S(61)	-6.8356	0.8944	-0.5130
O(24)	-1.1810	-5.5766	2.9353		C(62)	-7.9183	1.8998	0.5586
C(25)	-1.5571	-4.1411	-2.6951		C(63)	-7.8733	1.4202	1.8523
C(26)	-2.4824	-3.1184	-2.3980		C(64)	-7.0328	0.2921	2.0422
C(27)	-3.9388	-3.4277	-2.0489		S(65)	1.5108	0.3644	-2.4545
C(28)	-4.3107	-2.9161	-0.6623		C(66)	1.0958	2.1272	-2.6693
C(29)	1.5851	-5.1238	2.1150		C(67)	-0.2675	2.2736	-2.8282
C(30)	3.0480	-4.1935	-1.8461		C(68)	-1.0036	1.0595	-2.8040
C(31)	1.8318	-4.8697	-1.7073		C(69)	0.6838	3.7689	2.6863
C(32)	-5.4596	-1.2696	0.7526		C(70)	-0.5045	4.4640	2.4982
C(33)	-3.1778	-3.4488	2.9701		C(71)	-0.4022	5.8670	2.5845
C(34)	-3.7312	-3.4735	0.4959		C(72)	0.8770	6.3463	2.8481
C(35)	-4.8006	-1.8078	1.8807		S(73)	2.0418	4.9239	2.9923
C(36)	-3.9385	-2.8998	1.7689		C(74)	1.4531	7.6330	3.0383
C(37)	-0.9730	-6.0933	4.3084		C(75)	0.9544	8.9250	3.0381
C(38)	-1.5148	-7.5140	4.3780		C(76)	-0.4370	9.3163	2.7988

atom	x	y	z		atom	x	y	z
O(77)	-1.3970	8.5653	2.5493		H(118)	2.0734	-2.4549	2.1531
O(78)	-0.6102	10.6802	2.8768		H(119)	-1.9224	-1.0701	2.9099
C(79)	1.8883	9.9760	3.3032		H(120)	1.2890	-2.3109	-2.8760
N(80)	2.6835	10.8105	3.5311		H(121)	0.3443	-5.9454	-2.8624
C(81)	-8.6561	2.9960	0.0158		H(122)	1.4242	-4.9198	-3.8186
S(82)	-9.7102	4.0161	1.0744		H(123)	-2.7314	-1.0128	-2.0998
C(83)	-10.1861	5.0482	-0.3781		H(124)	-5.6618	-1.4220	-1.3942
C(84)	-9.5392	4.5693	-1.5129		H(125)	-4.0958	-4.5062	-2.1210
C(85)	-8.7073	3.4528	-1.2956		H(126)	-4.6064	-2.9574	-2.7819
C(86)	-11.0932	6.1094	-0.1056		H(127)	1.0444	-6.0691	2.1674
C(87)	-11.6932	7.0907	-0.8771		H(128)	2.3983	-5.1542	2.8512
C(88)	-11.5143	7.2900	-2.3174		H(129)	3.3518	-3.8562	-2.8319
O(89)	-12.2491	8.3564	-2.7863		H(130)	-3.3417	-4.5248	3.0575
O(90)	-10.8032	6.6189	-3.0865		H(131)	-3.5697	-2.9762	3.8794
C(91)	-12.5722	7.9943	-0.2004		H(132)	-4.9537	-1.3568	2.8559
N(92)	-13.2875	8.7157	0.3901		H(133)	0.1001	-6.0656	4.5373
C(93)	2.1285	3.1152	-2.6715		H(134)	-1.4925	-5.4328	5.0161
S(94)	1.7480	4.8531	-2.9970		H(135)	-1.0128	-8.1217	3.6126
C(95)	3.5332	5.2843	-2.8312		H(136)	-1.2260	-7.9344	5.3528
C(96)	4.2594	4.1323	-2.5481		H(137)	-3.3178	-7.2001	3.2320
C(97)	3.4924	2.9529	-2.4626		H(138)	-3.5297	-6.9883	4.9672
C(98)	3.8548	6.6565	-3.0269		H(139)	-3.3112	-9.4876	5.3077
C(99)	5.0328	7.3843	-3.0133		H(140)	-3.1042	-9.7051	3.5624
C(100)	6.3744	6.8571	-2.7492		H(141)	-4.6429	-9.1066	4.2037
O(101)	6.6816	5.6801	-2.4880		H(142)	1.5002	-7.7802	0.3261
O(102)	7.3368	7.8392	-2.8173		H(143)	1.0167	-7.7918	-1.3844
C(103)	4.9279	8.7844	-3.2891		H(144)	-0.8870	-8.1105	0.9991
N(104)	4.8016	9.9282	-3.5261		H(145)	-1.3684	-8.1378	-0.6970
C(105)	8.4908	-1.2152	-0.1545		H(146)	0.5467	-10.1600	0.6175
S(106)	9.8714	-0.7775	-1.2376		H(147)	0.0632	-10.1831	-1.0743
C(107)	10.7023	0.0935	0.1590		H(148)	-2.3448	-10.5473	-0.3876
C(108)	9.9095	-0.0031	1.2976		H(149)	-1.8577	-10.5248	1.3159
C(109)	8.7058	-0.7160	1.1237		H(150)	-1.2942	-11.8234	0.2507
C(110)	11.9566	0.6908	-0.1500		H(151)	-2.5824	-6.5192	0.7027
C(111)	12.8847	1.4183	0.5750		H(152)	-3.1308	-6.0992	-0.9310
C(112)	14.0539	1.8518	-0.1267		H(153)	-4.8613	-6.0347	1.6214
N(113)	15.0001	2.1888	-0.7365		H(154)	-5.4326	-5.5686	0.0216
C(114)	12.7838	1.7862	1.9903		H(155)	-4.3984	-8.3637	0.7713
O(115)	13.8707	2.5190	2.4110		H(156)	-4.9580	-7.8912	-0.8288
O(116)	11.8607	1.5057	2.7752		H(157)	-7.2602	-7.4136	0.1131
H(117)	3.9870	-4.0101	1.4228		H(158)	-6.6962	-7.8945	1.7215

atom	x	y	z
H(159)	-6.7748	-9.0907	0.4169
H(160)	-3.2775	-5.0945	-4.5175
H(161)	-1.6207	-5.5912	-4.9364
H(162)	-3.6947	-7.3786	-3.5447
H(163)	-3.3765	-7.4014	-5.2783
H(164)	-1.3049	-8.0511	-3.1103
H(165)	-0.9995	-8.0875	-4.8447
H(166)	-2.7216	-9.9261	-5.1152
H(167)	-3.0219	-9.8957	-3.3701
H(168)	-1.4423	-10.4062	-3.9889
H(169)	2.7880	-0.4286	2.9214
H(170)	3.0483	2.1472	2.9376
H(171)	7.8853	-2.3833	-2.7144
H(172)	5.6707	-3.7026	-2.9805
H(173)	-8.4477	1.8673	2.6551
H(174)	-6.9281	-0.1999	3.0009
H(175)	-0.7332	3.2415	-2.9714
H(176)	-2.0763	1.0269	-2.9465
H(177)	-1.4403	3.9563	2.2990
H(178)	-1.2324	6.5468	2.4618
H(179)	2.5226	7.5991	3.2364
H(180)	-1.5490	10.9080	2.7070
H(181)	-9.6863	5.0406	-2.4735
H(182)	-8.1459	2.9778	-2.0907
H(183)	-11.3839	6.1667	0.9415
H(184)	-12.1051	8.4624	-3.7507
H(185)	5.3299	4.1738	-2.4112
H(186)	3.9288	1.9851	-2.2481
H(187)	2.9854	7.2744	-3.2428
H(188)	8.2203	7.4558	-2.6311
H(189)	10.2224	0.4451	2.2290
H(190)	7.9958	-0.8695	1.9271
H(191)	12.2567	0.5465	-1.1861
H(192)	13.7714	2.7506	3.3590

9.

Table S2 Cartesian coordinates of the **2**–Asp complex from B3LYP/6-31G optimization.

atom	x	y	z		atom	x	y	z
O(1)	-5.3662	-2.7201	0.8102		C(39)	-6.7468	-4.9141	4.9738
O(2)	-3.4330	-5.8037	0.3885		C(40)	-7.8289	-5.9636	5.2722
C(3)	-3.2606	-3.1663	3.0542		C(41)	-3.8103	-7.2321	0.4999
O(4)	-5.4064	-4.3634	-2.3402		C(42)	-5.2626	-7.3180	0.9393
C(5)	-6.3888	2.8407	0.6093		C(43)	-5.7497	-8.7747	1.0635
C(6)	0.6679	-5.4659	-0.5000		C(44)	-7.2191	-8.8723	1.5034
C(7)	0.2083	-5.3510	0.8260		C(45)	-6.4240	-3.7604	0.6953
C(8)	-1.1584	-5.4112	1.1364		C(46)	-7.8081	-3.3093	1.1585
C(9)	-1.9744	-3.6294	2.7096		C(47)	-8.8382	-4.4525	1.0531
C(10)	-0.9741	-2.6836	2.4659		C(48)	-10.2445	-4.0274	1.5044
C(11)	-1.2276	-1.3015	2.5275		C(49)	-6.0200	-4.6033	-3.6680
C(12)	-2.5434	-0.8756	2.7808		C(50)	-7.1423	-5.6181	-3.5008
C(13)	-3.5711	-1.7896	3.0261		C(51)	-6.6628	-7.0214	-3.0902
C(14)	-2.2146	-1.6090	-2.5549		C(52)	-7.8189	-8.0205	-2.9280
C(15)	-1.9858	-2.9942	-2.6129		C(53)	0.9878	-0.5106	1.5198
C(16)	-3.0166	-3.9282	-2.4870		C(54)	1.9096	0.5649	1.5870
C(17)	-2.6772	-5.4217	-2.3806		C(55)	1.5436	1.5910	2.4366
C(18)	-0.1307	-0.3641	2.3117		S(56)	-0.0700	1.2200	3.2046
C(19)	2.0902	-5.4099	-0.8429		S(57)	3.2127	-4.2351	-0.0110
C(20)	-1.1070	-0.6659	-2.6856		C(58)	4.5852	-4.7705	-1.0941
C(21)	-3.5288	-1.1670	-2.3068		C(59)	4.1442	-5.7543	-1.9544
C(22)	-2.0717	-5.6208	0.0860		C(60)	2.7712	-6.1016	-1.8165
C(23)	-6.2174	0.6184	-0.5336		S(61)	-7.1136	3.6299	-0.8660
O(24)	-4.2545	-4.0925	3.4331		C(62)	-7.0871	5.2496	-0.0267
C(25)	-4.3320	-3.4466	-2.3530		C(63)	-6.5687	5.1098	1.2452
C(26)	-4.5923	-2.0686	-2.1965		C(64)	-6.1857	3.7885	1.5922
C(27)	-5.9836	-1.5572	-1.8213		S(65)	0.5976	-1.2346	-2.3835
C(28)	-5.9741	-0.7592	-0.5224		C(66)	1.2313	0.4359	-2.7433
C(29)	-1.6610	-5.1213	2.5459		C(67)	0.1850	1.2794	-3.0503
C(30)	-0.2869	-5.5749	-1.5325		C(68)	-1.1030	0.6701	-3.0168
C(31)	-1.6588	-5.6167	-1.2619		C(69)	2.2752	2.7604	2.7992
C(32)	-6.1170	1.4079	0.6305		C(70)	1.8839	3.8505	3.5728
C(33)	-5.0057	-1.2839	3.1597		C(71)	2.8905	4.8024	3.8193
C(34)	-5.6474	-1.3682	0.7071		C(72)	4.1289	4.5036	3.2522
C(35)	-5.7261	0.7707	1.8301		S(73)	4.0041	2.9268	2.3072
C(36)	-5.4814	-0.6019	1.8817		C(74)	5.4265	5.0656	3.3065
C(37)	-4.2199	-4.4535	4.8698		C(75)	5.9961	6.1400	3.9771
C(38)	-5.3213	-5.4680	5.1410		C(76)	5.2965	7.1127	4.8107

atom	x	y	z		atom	x	y	z
O(77)	4.0741	7.1652	5.0332		H(118)	0.0295	-3.0224	2.2365
O(78)	6.1617	8.0335	5.3636		H(119)	-2.7780	0.1839	2.7433
C(79)	7.4144	6.2539	3.8549		H(120)	-0.9723	-3.3548	-2.7404
N(80)	8.5825	6.2221	3.7175		H(121)	-3.5960	-5.9737	-2.1839
C(81)	-7.5632	6.4172	-0.6965		H(122)	-2.2556	-5.7869	-3.3255
S(82)	-7.5706	8.0245	0.1349		H(123)	-3.7171	-0.1102	-2.1489
C(83)	-8.2846	8.8113	-1.3733		H(124)	-6.4722	1.0891	-1.4786
C(84)	-8.4597	7.8427	-2.3567		H(125)	-6.6614	-2.4110	-1.7469
C(85)	-8.0668	6.5416	-1.9859		H(126)	-6.3728	-0.9117	-2.6190
C(86)	-8.5257	10.2097	-1.2814		H(127)	-2.5691	-5.6895	2.7489
C(87)	-9.0359	11.1618	-2.1488		H(128)	-0.8965	-5.4244	3.2724
C(88)	-9.4970	10.9267	-3.5191		H(129)	0.0517	-5.5718	-2.5640
O(89)	-9.9474	12.0826	-4.1177		H(130)	-5.6534	-2.1306	3.3968
O(90)	-9.5102	9.8448	-4.1332		H(131)	-5.0755	-0.5665	3.9868
C(91)	-9.1194	12.5024	-1.6564		H(132)	-5.6293	1.3510	2.7418
N(92)	-9.1728	13.5905	-1.2158		H(133)	-3.2316	-4.8696	5.1046
C(93)	2.6425	0.6729	-2.6869		H(134)	-4.3595	-3.5414	5.4662
S(94)	3.3662	2.2261	-3.2826		H(135)	-5.1763	-6.3308	4.4763
C(95)	5.0456	1.6121	-2.8755		H(136)	-5.1897	-5.8374	6.1690
C(96)	4.9567	0.3401	-2.3374		H(137)	-6.8637	-4.5371	3.9506
C(97)	3.6421	-0.1737	-2.2353		H(138)	-6.8780	-4.0509	5.6432
C(98)	6.1578	2.4352	-3.2641		H(139)	-7.7469	-6.3373	6.3006
C(99)	7.5024	2.2612	-3.0606		H(140)	-7.7396	-6.8254	4.5982
C(100)	8.1217	1.1545	-2.2606		H(141)	-8.8345	-5.5461	5.1480
O(101)	8.9963	0.4096	-2.7049		H(142)	-3.1449	-7.7166	1.2278
O(102)	7.6416	0.9614	-0.9887		H(143)	-3.6574	-7.7166	-0.4743
C(103)	8.4134	3.1147	-3.7496		H(144)	-5.3696	-6.8005	1.9012
N(104)	9.1482	3.8173	-4.3386		H(145)	-5.8826	-6.7767	0.2145
C(105)	5.8784	-4.1567	-1.0097		H(146)	-5.1158	-9.3147	1.7820
S(106)	7.2710	-4.8476	-1.9351		H(147)	-5.6243	-9.2856	0.0976
C(107)	8.3595	-3.4875	-1.3364		H(148)	-7.8790	-8.3677	0.7868
C(108)	7.6341	-2.6499	-0.5008		H(149)	-7.3702	-8.4030	2.4838
C(109)	6.2801	-3.0204	-0.3215		H(150)	-7.5433	-9.9162	1.5796
C(110)	9.6950	-3.5188	-1.8378		H(151)	-6.0301	-4.5529	1.3302
C(111)	10.8056	-2.7113	-1.7001		H(152)	-6.4370	-4.1107	-0.3395
C(112)	11.9700	-3.0993	-2.4389		H(153)	-7.7581	-2.9577	2.1981
N(113)	12.9045	-3.4665	-3.0485		H(154)	-8.1539	-2.4584	0.5559
C(114)	10.9329	-1.4915	-0.8924		H(155)	-8.5005	-5.3059	1.6586
O(115)	12.0562	-0.8116	-1.1435		H(156)	-8.8790	-4.8096	0.0133
O(116)	10.0934	-1.1314	-0.0177		H(157)	-10.6199	-3.1963	0.8947
H(117)	0.9302	-5.2327	1.6288		H(158)	-10.2392	-3.6963	2.5503

atom	x	y	z		atom	x	y	z
H(159)	-10.9575	-4.8552	1.4187		C(196)	11.0433	3.3738	1.2590
H(160)	-6.3974	-3.6490	-4.0571		C(197)	11.1357	1.9420	0.7823
H(161)	-5.2438	-4.9724	-4.3518		O(198)	10.0820	1.1785	1.1288
H(162)	-7.8564	-5.2362	-2.7582		O(199)	8.9767	3.8881	-0.7726
H(163)	-7.6849	-5.6792	-4.4557		O(200)	7.4804	3.0695	0.7475
H(164)	-6.1027	-6.9427	-2.1505		O(201)	12.1111	1.5145	0.1308
H(165)	-5.9567	-7.3952	-3.8467		H(202)	9.3205	2.2611	2.9491
H(166)	-8.3817	-8.1325	-3.8633		H(203)	8.9710	3.7985	3.5937
H(167)	-8.5233	-7.6873	-2.1552		H(204)	9.6478	4.9200	1.8002
H(168)	-7.4511	-9.0119	-2.6399		H(205)	11.4593	4.0002	0.4652
H(169)	1.1294	-1.3669	0.8732		H(206)	11.6893	3.4979	2.1379
H(170)	2.8241	0.5916	1.0058		H(207)	10.0700	0.2391	0.6975
H(171)	4.7954	-6.2121	-2.6894		H(208)	7.5944	2.9002	1.7525
H(172)	2.2928	-6.8625	-2.4211					
H(173)	-6.4585	5.9500	1.9207					
H(174)	-5.7523	3.5483	2.5544					
H(175)	0.3359	2.3234	-3.2988					
H(176)	-2.0102	1.2111	-3.2569					
H(177)	0.8771	3.9455	3.9604					
H(178)	2.7529	5.6985	4.4072					
H(179)	6.1564	4.5043	2.7278					
H(180)	5.6616	8.6796	5.9061					
H(181)	-8.8687	8.1030	-3.3217					
H(182)	-8.1477	5.6932	-2.6544					
H(183)	-8.2500	10.6303	-0.3162					
H(184)	-10.2464	11.8898	-5.0318					
H(185)	5.8235	-0.2267	-2.0279					
H(186)	3.4304	-1.1647	-1.8511					
H(187)	5.8949	3.2946	-3.8763					
H(188)	7.2713	1.7624	-0.5309					
H(189)	8.0884	-1.7774	-0.0558					
H(190)	5.5969	-2.4530	0.2992					
H(191)	9.8766	-4.3611	-2.5027					
H(192)	12.1399	0.0657	-0.6433					
C(193)	8.6891	3.6274	0.3924					
N(194)	8.9783	3.2017	2.7723					
C(195)	9.6135	3.8427	1.6003					

10.

Table S3 Cartesian coordinates of the **2**–Glu complex from B3LYP/6-31G optimization.

atom	x	y	z		atom	x	y	z
O(1)	-5.3488	-2.9968	0.9585		C(39)	-6.3400	-5.3729	5.0191
O(2)	-3.3663	-5.8824	0.0563		C(40)	-7.3806	-6.4618	5.3243
C(3)	-3.0320	-3.4512	2.9317		C(41)	-3.7122	-7.3244	0.0949
O(4)	-5.4939	-4.5491	-2.3091		C(42)	-5.1088	-7.4810	0.6723
C(5)	-6.5574	2.5259	0.9756		C(43)	-5.5489	-8.9564	0.7401
C(6)	0.7012	-5.5675	-0.9542		C(44)	-6.9531	-9.1273	1.3411
C(7)	0.2899	-5.5438	0.3927		C(45)	-6.3837	-4.0598	0.8879
C(8)	-1.0637	-5.5681	0.7480		C(46)	-7.7501	-3.6538	1.4385
C(9)	-1.7724	-3.8958	2.4812		C(47)	-8.7536	-4.8234	1.3755
C(10)	-0.7750	-2.9434	2.2514		C(48)	-10.1433	-4.4438	1.9108
C(11)	-1.0095	-1.5651	2.4167		C(49)	-6.2928	-4.7077	-3.5486
C(12)	-2.3147	-1.1533	2.7483		C(50)	-7.2811	-5.8469	-3.3441
C(13)	-3.3352	-2.0753	2.9984		C(51)	-6.6285	-7.2343	-3.2139
C(14)	-2.6462	-1.4677	-2.7489		C(52)	-7.6607	-8.3580	-3.0306
C(15)	-2.2701	-2.8177	-2.8680		C(53)	1.2817	-0.7594	1.5800
C(16)	-3.1876	-3.8575	-2.6728		C(54)	2.1732	0.3415	1.6921
C(17)	-2.7142	-5.3140	-2.7071		C(55)	1.7050	1.3919	2.4554
C(18)	0.0881	-0.6142	2.2554		S(56)	0.0377	1.0022	3.0899
C(19)	2.1153	-5.6170	-1.3155		S(57)	3.3761	-4.9009	-0.2151
C(20)	-1.7262	-0.3643	-3.0090		C(58)	4.6893	-5.4170	-1.3723
C(21)	-3.9603	-1.1816	-2.3304		C(59)	4.1332	-6.0574	-2.4601
C(22)	-2.0189	-5.6658	-0.2815		C(60)	2.7147	-6.1646	-2.4280
C(23)	-6.4474	0.3297	-0.2252		S(61)	-6.8166	3.4759	-0.5577
O(24)	-3.9996	-4.3979	3.3311		C(62)	-7.1566	4.9794	0.4196
C(25)	-4.5243	-3.5247	-2.3766		C(63)	-7.0513	4.6964	1.7667
C(26)	-4.9043	-2.1890	-2.1295		C(64)	-6.7241	3.3490	2.0703
C(27)	-6.2791	-1.8196	-1.5698		S(65)	0.0783	-0.5725	-2.8988
C(28)	-6.1572	-1.0384	-0.2661		C(66)	0.3117	1.1911	-3.3101
C(29)	-1.4975	-5.3773	2.1956		C(67)	-0.9138	1.7968	-3.4985
C(30)	-0.2906	-5.5202	-1.9568		C(68)	-2.0324	0.9396	-3.3359
C(31)	-1.6528	-5.5505	-1.6384		C(69)	2.3295	2.6319	2.7973
C(32)	-6.2274	1.1058	0.9311		C(70)	1.7626	3.7504	3.3964
C(33)	-4.7529	-1.5804	3.2736		C(71)	2.6467	4.8204	3.6310
C(34)	-5.6690	-1.6512	0.9067		C(72)	3.9621	4.5956	3.2335
C(35)	-5.6627	0.4713	2.0604		S(73)	4.0940	2.9060	2.5027
C(36)	-5.3820	-0.8959	2.0649		C(74)	5.1651	5.3516	3.2919
C(37)	-3.8374	-4.8604	4.7302		C(75)	5.4689	6.6237	3.7558
C(38)	-4.8990	-5.9119	5.0192		C(76)	4.5399	7.5984	4.3318

atom	x	y	z		atom	x	y	z
O(77)	3.3172	7.4644	4.5167		H(118)	0.2110	-3.2795	1.9519
O(78)	5.1787	8.7698	4.6801		H(119)	-2.5456	-0.0931	2.7921
C(79)	6.8374	7.0277	3.6621		H(120)	-1.2438	-3.0651	-3.1201
N(80)	7.9755	7.3050	3.5668		H(121)	-3.5775	-5.9612	-2.5495
C(81)	-7.4792	6.2084	-0.2329		H(122)	-2.2900	-5.5488	-3.6910
S(82)	-7.8162	7.7043	0.7268		H(123)	-4.2375	-0.1561	-2.1136
C(83)	-8.1046	8.6496	-0.8304		H(124)	-6.8635	0.7991	-1.1121
C(84)	-7.9305	7.8025	-1.9203		H(125)	-6.8629	-2.7316	-1.4293
C(85)	-7.5903	6.4750	-1.5923		H(126)	-6.8238	-1.2011	-2.2945
C(86)	-8.4425	10.0208	-0.6623		H(127)	-2.4090	-5.9402	2.3975
C(87)	-8.7348	11.0583	-1.5322		H(128)	-0.7091	-5.7500	2.8616
C(88)	-8.7660	10.9796	-2.9947		H(129)	0.0092	-5.4376	-2.9970
O(89)	-9.0900	12.1885	-3.5698		H(130)	-5.3646	-2.4351	3.5714
O(90)	-8.5393	9.9795	-3.6990		H(131)	-4.7412	-0.8698	4.1091
C(91)	-9.0356	12.3270	-0.9433		H(132)	-5.4340	1.0563	2.9452
N(92)	-9.2785	13.3520	-0.4225		H(133)	-2.8279	-5.2734	4.8506
C(93)	1.6190	1.7662	-3.3601		H(134)	-3.9370	-3.9957	5.4006
S(94)	1.8224	3.5520	-3.5673		H(135)	-4.8029	-6.7207	4.2816
C(95)	3.6515	3.3679	-3.4377		H(136)	-4.6735	-6.3537	6.0013
C(96)	3.9678	2.0228	-3.2785		H(137)	-6.5496	-4.9194	4.0430
C(97)	2.8584	1.1527	-3.2359		H(138)	-6.4225	-4.5668	5.7633
C(98)	4.3926	4.5825	-3.4901		H(139)	-7.2047	-6.9149	6.3080
C(99)	5.7185	4.9067	-3.2634		H(140)	-7.3417	-7.2654	4.5775
C(100)	6.7841	3.9660	-2.8960		H(141)	-8.3975	-6.0534	5.3222
O(101)	6.7217	2.7267	-2.9390		H(142)	-2.9684	-7.8471	0.7117
O(102)	7.9239	4.6049	-2.4624		H(143)	-3.6523	-7.7294	-0.9246
C(103)	6.0757	6.2888	-3.3470		H(144)	-5.1245	-7.0374	1.6760
N(104)	6.3468	7.4301	-3.4209		H(145)	-5.8120	-6.9077	0.0571
C(105)	6.0567	-5.1191	-1.0752		H(146)	-4.8240	-9.5297	1.3364
S(106)	7.4054	-5.8363	-2.0444		H(147)	-5.5294	-9.3917	-0.2698
C(107)	8.6351	-4.8874	-1.0488		H(148)	-7.7032	-8.5871	0.7501
C(108)	7.9671	-4.1511	-0.0788		H(149)	-6.9932	-8.7383	2.3665
C(109)	6.5637	-4.2838	-0.0902		H(150)	-7.2472	-10.1823	1.3724
C(110)	10.0030	-5.0808	-1.4005		H(151)	-5.9358	-4.8509	1.4870
C(111)	11.1817	-4.4318	-1.0777		H(152)	-6.4479	-4.3981	-0.1492
C(112)	12.3846	-4.9529	-1.6524		H(153)	-7.6467	-3.3167	2.4791
N(113)	13.3493	-5.4195	-2.1338		H(154)	-8.1542	-2.8037	0.8725
C(114)	11.3161	-3.2091	-0.2773		H(155)	-8.3596	-5.6745	1.9494
O(115)	12.5277	-2.6471	-0.3418		H(156)	-8.8436	-5.1689	0.3347
O(116)	10.3702	-2.7085	0.3976		H(157)	-10.5768	-3.6179	1.3335
H(117)	1.0393	-5.5408	1.1786		H(158)	-10.0876	-4.1236	2.9586

atom	x	y	z		atom	x	y	z
H(159)	-10.8362	-5.2911	1.8560		C(196)	10.2287	2.5006	1.7957
H(160)	-6.8116	-3.7632	-3.7560		C(197)	11.4166	1.9037	1.0242
H(161)	-5.6082	-4.9154	-4.3818		C(198)	11.4451	0.4030	0.9474
H(162)	-7.8866	-5.6339	-2.4522		O(199)	10.2656	-0.2033	1.1490
H(163)	-7.9724	-5.8469	-4.1999		H(200)	10.2904	-1.2000	0.9500
H(164)	-5.9342	-7.2224	-2.3649		O(201)	9.6764	3.5549	-0.8190
H(165)	-6.0243	-7.4325	-4.1117		O(202)	8.7083	5.4049	0.0986
H(166)	-8.3544	-8.4008	-3.8796		H(203)	8.9154	5.5509	2.4580
H(167)	-8.2566	-8.2027	-2.1223		H(204)	9.4415	4.3667	3.5214
H(168)	-7.1745	-9.3367	-2.9479		H(205)	11.0339	4.4999	1.5461
H(169)	1.5114	-1.6376	0.9896		H(206)	9.3082	1.9772	1.5285
H(170)	3.1404	0.3687	1.2039		H(207)	10.3761	2.3490	2.8727
H(171)	4.7355	-6.4438	-3.2738		H(208)	12.3802	2.2353	1.4264
H(172)	2.1467	-6.6664	-3.2017		H(209)	11.3729	2.2475	-0.0182
H(173)	-7.2189	5.4470	2.5301		O(210)	12.4910	-0.2297	0.6513
H(174)	-6.6389	2.9872	3.0870		H(211)	8.3236	5.5401	-0.8078
H(175)	-1.0076	2.8449	-3.7570					
H(176)	-3.0513	1.2765	-3.4779					
H(177)	0.7107	3.7926	3.6508					
H(178)	2.3588	5.7590	4.0809					
H(179)	6.0379	4.8272	2.9015					
H(180)	4.5304	9.4038	5.0539					
H(181)	-8.0551	8.1676	-2.9290					
H(182)	-7.4269	5.7105	-2.3419					
H(183)	-8.4827	10.3279	0.3810					
H(184)	-9.0995	12.1011	-4.5468					
H(185)	4.9955	1.7018	-3.1969					
H(186)	2.9590	0.0808	-3.1165					
H(187)	3.7787	5.4521	-3.7167					
H(188)	8.6401	3.9666	-2.1605					
H(189)	8.5093	-3.5268	0.6131					
H(190)	5.9206	-3.7563	0.6035					
H(191)	10.1551	-5.9042	-2.0961					
H(192)	12.5837	-1.7351	0.1190					
C(193)	9.4567	4.2804	0.1777					
N(194)	9.1392	4.5676	2.5744					
C(195)	10.0321	4.0161	1.5585					

11.

Table S4 Cartesian coordinates of the **2**–Lys complex from B3LYP/6-31G optimization.

atom	x	y	z		atom	x	y	z
O(1)	-4.8452	-3.4960	0.9741		C(39)	-5.4222	-5.9088	5.1104
O(2)	-2.5368	-6.1217	0.0440		C(40)	-6.3376	-7.0860	5.4821
C(3)	-2.4314	-3.6589	2.8952		C(41)	-2.6817	-7.5962	0.1103
O(4)	-4.9103	-5.0669	-2.2647		C(42)	-4.0295	-7.9302	0.7273
C(5)	-6.7178	1.8377	1.0402		C(43)	-4.2605	-9.4499	0.8361
C(6)	1.4091	-5.2290	-1.1088		C(44)	-5.6144	-9.7982	1.4746
C(7)	1.0482	-5.2804	0.2520		C(45)	-5.7307	-4.6875	0.9433
C(8)	-0.2741	-5.4993	0.6556		C(46)	-7.1180	-4.4655	1.5453
C(9)	-1.1344	-3.9410	2.4211		C(47)	-7.9566	-5.7597	1.5184
C(10)	-0.2710	-2.8705	2.1720		C(48)	-9.3574	-5.5728	2.1224
C(11)	-0.6757	-1.5316	2.3324		C(49)	-5.7136	-5.3446	-3.4797
C(12)	-2.0172	-1.2890	2.6847		C(50)	-6.5321	-6.6049	-3.2390
C(13)	-2.9056	-2.3324	2.9630		C(51)	-5.6930	-7.8890	-3.1184
C(14)	-2.4919	-1.6549	-2.8176		C(52)	-6.5538	-9.1400	-2.8833
C(15)	-1.9527	-2.9476	-2.9388		C(53)	1.5191	-0.4795	1.5177
C(16)	-2.7233	-4.0926	-2.7058		C(54)	2.2584	0.7317	1.5888
C(17)	-2.0670	-5.4760	-2.7396		C(55)	1.6311	1.7548	2.2690
C(18)	0.2917	-0.4527	2.1457		S(56)	0.0040	1.1912	2.8753
C(19)	2.7977	-5.0653	-1.5274		S(57)	4.0370	-4.3433	-0.4041
C(20)	-1.7161	-0.4520	-3.1030		C(58)	5.3288	-4.5648	-1.6741
C(21)	-3.8192	-1.5313	-2.3629		C(59)	4.7797	-5.1262	-2.8092
C(22)	-1.2443	-5.7249	-0.3397		C(60)	3.3885	-5.4008	-2.7269
C(23)	-6.3919	-0.3355	-0.1625		S(61)	-7.1033	2.7532	-0.4873
O(24)	-3.2631	-4.7184	3.3190		C(62)	-7.5898	4.2109	0.4975
C(25)	-4.0815	-3.9282	-2.3707		C(63)	-7.4340	3.9410	1.8424
C(26)	-4.6207	-2.6483	-2.1235		C(64)	-6.9571	2.6373	2.1388
C(27)	-6.0106	-2.4516	-1.5153		S(65)	0.1014	-0.4535	-3.0223
C(28)	-5.9398	-1.6586	-0.2148		C(66)	0.1259	1.3229	-3.4394
C(29)	-0.6777	-5.3737	2.1195		C(67)	-1.1629	1.7853	-3.6104
C(30)	0.3821	-5.3217	-2.0731		C(68)	-2.1746	0.8066	-3.4280
C(31)	-0.9475	-5.5546	-1.7074		C(69)	2.0869	3.0821	2.5492
C(32)	-6.2278	0.4649	0.9864		C(70)	1.3551	4.1832	2.9735
C(33)	-4.3665	-2.0185	3.2767		C(71)	2.1046	5.3592	3.1795
C(34)	-5.3396	-2.2039	0.9391		C(72)	3.4694	5.2374	2.9374
C(35)	-5.5565	-0.0946	2.0968		S(73)	3.8384	3.5096	2.4035
C(36)	-5.1111	-1.4173	2.0895		C(74)	4.5922	6.1047	3.0438
C(37)	-2.9943	-5.1645	4.7066		C(75)	4.7329	7.4355	3.4074
C(38)	-3.9386	-6.3101	5.0414		C(76)	3.6669	8.3715	3.7656

atom	x	y	z
O(77)	2.4448	8.1447	3.8201
O(78)	4.1618	9.6254	4.0606
C(79)	6.0709	7.9420	3.4438
N(80)	7.1968	8.2797	3.4723
C(81)	-8.0513	5.3982	-0.1486
S(82)	-8.5163	6.8560	0.8162
C(83)	-8.9313	7.7623	-0.7357
C(84)	-8.6968	6.9329	-1.8280
C(85)	-8.2181	5.6475	-1.5056
C(86)	-9.4004	9.0936	-0.5621
C(87)	-9.8106	10.0949	-1.4268
C(88)	-9.8626	10.0096	-2.8882
O(89)	-10.3119	11.1803	-3.4581
O(90)	-9.5551	9.0338	-3.5960
C(91)	-10.2232	11.3295	-0.8330
N(92)	-10.5557	12.3269	-0.3084
C(93)	1.3617	2.0385	-3.4982
S(94)	1.3710	3.8362	-3.7035
C(95)	3.2073	3.8508	-3.5542
C(96)	3.6679	2.5481	-3.4015
C(97)	2.6593	1.5622	-3.3710
C(98)	3.8138	5.1393	-3.5813
C(99)	5.0787	5.6030	-3.2695
C(100)	6.2062	4.7791	-2.8127
O(101)	6.3102	3.5466	-2.9181
O(102)	7.1861	5.5291	-2.2013
C(103)	5.2925	7.0151	-3.3402
N(104)	5.4410	8.1788	-3.4128
C(105)	6.6823	-4.1920	-1.4047
S(106)	7.9926	-4.5730	-2.5914
C(107)	9.2444	-3.8143	-1.4652
C(108)	8.6052	-3.3414	-0.3229
C(109)	7.2116	-3.5483	-0.2935
C(110)	10.5816	-3.8436	-1.9454
C(111)	11.8112	-3.4620	-1.4310
C(112)	12.9523	-3.6730	-2.2682
N(113)	13.8647	-3.8634	-2.9836
C(114)	12.0559	-2.8812	-0.1131
O(115)	13.3907	-2.6299	0.1058
O(116)	11.2065	-2.6221	0.7613
H(117)	1.8165	-5.1748	1.0122
H(118)	0.7434	-3.0820	1.8549
H(119)	-2.3831	-0.2675	2.7284
H(120)	-0.9115	-3.0651	-3.2210
H(121)	-2.8329	-6.2267	-2.5431
H(122)	-1.6498	-5.6704	-3.7354
H(123)	-4.2165	-0.5463	-2.1444
H(124)	-6.8908	0.0779	-1.0343
H(125)	-6.4710	-3.4289	-1.3565
H(126)	-6.6533	-1.9066	-2.2183
H(127)	-1.4983	-6.0537	2.3486
H(128)	0.1765	-5.6400	2.7548
H(129)	0.6235	-5.1915	-3.1233
H(130)	-4.8591	-2.9424	3.5880
H(131)	-4.4203	-1.3124	4.1144
H(132)	-5.3721	0.5166	2.9743
H(133)	-1.9464	-5.4823	4.7790
H(134)	-3.1419	-4.3129	5.3849
H(135)	-3.8024	-7.1083	4.2986
H(136)	-3.6270	-6.7266	6.0110
H(137)	-5.7237	-5.4925	4.1419
H(138)	-5.5424	-5.1024	5.8492
H(139)	-6.0714	-7.5013	6.4622
H(140)	-6.2582	-7.8964	4.7459
H(141)	-7.3880	-6.7763	5.5249
H(142)	-1.8585	-8.0032	0.7132
H(143)	-2.5929	-8.0061	-0.9054
H(144)	-4.0822	-7.4700	1.7222
H(145)	-4.8193	-7.4719	0.1203
H(146)	-3.4509	-9.9032	1.4268
H(147)	-4.2024	-9.9031	-0.1644
H(148)	-6.4447	-9.3852	0.8884
H(149)	-5.6880	-9.3897	2.4906
H(150)	-5.7570	-10.8826	1.5395
H(151)	-5.1600	-5.4090	1.5257
H(152)	-5.7875	-5.0368	-0.0906
H(153)	-7.0215	-4.1142	2.5818
H(154)	-7.6546	-3.6793	0.9971
H(155)	-7.4238	-6.5516	2.0643
H(156)	-8.0493	-6.1106	0.4797
H(157)	-9.9232	-4.8076	1.5768
H(158)	-9.2948	-5.2554	3.1706

atom	x	y	z		atom	x	y	z
H(159)	-9.9334	-6.5045	2.0881		C(196)	8.3976	2.8723	2.1159
H(160)	-6.3612	-4.4812	-3.6781		C(197)	9.4463	2.0078	1.3936
H(161)	-5.0302	-5.4652	-4.3310		C(198)	9.1500	0.4967	1.4276
H(162)	-7.1344	-6.4658	-2.3306		C(199)	9.1091	-0.1183	2.8366
H(163)	-7.2417	-6.7078	-4.0734		N(200)	9.0771	-1.5848	2.7560
H(164)	-4.9768	-7.7692	-2.2963		O(201)	8.8248	4.4887	-0.4203
H(165)	-5.0997	-8.0181	-4.0358		O(202)	7.2594	5.8110	0.5855
H(166)	-7.2634	-9.2943	-3.7059		H(203)	7.9604	6.1235	3.0060
H(167)	-7.1346	-9.0515	-1.9564		H(204)	8.0833	4.7509	3.9721
H(168)	-5.9345	-10.0408	-2.8046		H(205)	9.7412	4.5643	2.0582
H(169)	1.8864	-1.3526	0.9932		H(206)	7.3868	2.6484	1.7501
H(170)	3.2316	0.8562	1.1286		H(207)	8.3972	2.6381	3.1893
H(171)	5.3721	-5.3476	-3.6891		H(208)	10.4320	2.1943	1.8486
H(172)	2.8379	-5.8697	-3.5327		H(209)	9.5213	2.3332	0.3509
H(173)	-7.6708	4.6689	2.6095		H(210)	8.1986	0.2828	0.9220
H(174)	-6.8168	2.2865	3.1533		H(211)	9.9278	-0.0229	0.8508
H(175)	-1.3791	2.8158	-3.8662		H(212)	8.2058	0.2111	3.3649
H(176)	-3.2277	1.0247	-3.5517		H(213)	9.9706	0.2692	3.4178
H(177)	0.2823	4.1382	3.1157		H(214)	9.9176	-1.9869	2.3507
H(178)	1.6820	6.3014	3.4964		H(215)	8.8104	-2.0481	3.6179
H(179)	5.5475	5.6257	2.8137		H(216)	7.0491	6.0878	-0.3456
H(180)	3.4224	10.2292	4.2854					
H(181)	-8.8792	7.2797	-2.8344					
H(182)	-7.9951	4.9005	-2.2575					
H(183)	-9.4501	9.3981	0.4815					
H(184)	-10.3322	11.0893	-4.4345					
H(185)	4.7239	2.3398	-3.3142					
H(186)	2.8742	0.5072	-3.2527					
H(187)	3.1242	5.9369	-3.8509					
H(188)	7.9512	4.9726	-1.8564					
H(189)	9.1308	-2.8443	0.4771					
H(190)	6.6016	-3.2190	0.5385					
H(191)	10.6671	-4.2689	-2.9436					
H(192)	13.5196	-2.2388	0.9959					
C(193)	8.2609	4.8972	0.6204					
N(194)	7.9035	5.1097	3.0408					
C(195)	8.6466	4.4067	2.0012					

12.

Table S5 Cartesian coordinates of the **2**–Arg complex from B3LYP/6-31G optimization.

atom	x	y	z		atom	x	y	z
O(1)	-5.7350	-2.8064	1.0097		C(39)	-6.6273	-5.0852	5.1887
O(2)	-3.8358	-5.7939	0.1699		C(40)	-7.6664	-6.1420	5.5947
C(3)	-3.3693	-3.2684	2.9426		C(41)	-4.1889	-7.2304	0.2655
O(4)	-6.0620	-4.4036	-2.2055		C(42)	-5.5653	-7.3568	0.8976
C(5)	-6.8679	2.7335	1.0038		C(43)	-6.0118	-8.8259	1.0295
C(6)	0.1817	-5.4607	-1.0383		C(44)	-7.3982	-8.9672	1.6779
C(7)	-0.1678	-5.4176	0.3255		C(45)	-6.7879	-3.8552	0.9983
C(8)	-1.5036	-5.4580	0.7440		C(46)	-8.1094	-3.4310	1.6372
C(9)	-2.1313	-3.7381	2.4599		C(47)	-9.1315	-4.5860	1.6396
C(10)	-1.1361	-2.8012	2.1673		C(48)	-10.4737	-4.1912	2.2756
C(11)	-1.3522	-1.4174	2.3044		C(49)	-6.8632	-4.5868	-3.4394
C(12)	-2.6373	-0.9815	2.6784		C(50)	-7.9080	-5.6628	-3.1819
C(13)	-3.6564	-1.8876	2.9873		C(51)	-7.3245	-7.0679	-2.9513
C(14)	-3.0899	-1.4548	-2.7229		C(52)	-8.4121	-8.1293	-2.7230
C(15)	-2.7800	-2.8208	-2.8424		C(53)	0.8633	-0.6564	1.2646
C(16)	-3.7365	-3.8180	-2.6246		C(54)	1.8033	0.4062	1.3198
C(17)	-3.3146	-5.2917	-2.6316		C(55)	1.4572	1.4445	2.1614
C(18)	-0.2492	-0.4907	2.0619		S(56)	-0.1553	1.0985	2.9451
C(19)	1.5774	-5.4536	-1.4719		S(57)	2.8594	-4.6343	-0.4678
C(20)	-2.0950	-0.4141	-2.9618		C(58)	4.1278	-5.0916	-1.6996
C(21)	-4.3861	-1.1036	-2.2999		C(59)	3.5449	-5.7932	-2.7337
C(22)	-2.5045	-5.5919	-0.2364		C(60)	2.1407	-5.9898	-2.6073
C(23)	-6.8190	0.5243	-0.1767		S(61)	-7.1528	3.6715	-0.5322
O(24)	-4.3320	-4.1942	3.3995		C(62)	-7.4457	5.1897	0.4374
C(25)	-5.0520	-3.4229	-2.3131		C(63)	-7.3099	4.9190	1.7843
C(26)	-5.3708	-2.0685	-2.0798		C(64)	-6.9945	3.5702	2.0937
C(27)	-6.7209	-1.6397	-1.5031		S(65)	-0.3196	-0.7705	-2.7974
C(28)	-6.5503	-0.8484	-0.2109		C(66)	0.0714	0.9681	-3.1845
C(29)	-1.8751	-5.2284	2.2039		C(67)	-1.0925	1.6756	-3.4072
C(30)	-0.8575	-5.4681	-1.9933		C(68)	-2.2844	0.9121	-3.2856
C(31)	-2.2029	-5.5121	-1.6113		C(69)	2.1875	2.6290	2.4878
C(32)	-6.5596	1.3084	0.9659		C(70)	1.7720	3.7561	3.1874
C(33)	-5.0599	-1.3731	3.2969		C(71)	2.7583	4.7447	3.3763
C(34)	-6.0406	-1.4570	0.9553		C(72)	4.0059	4.4389	2.8389
C(35)	-5.9761	0.6768	2.0871		S(73)	3.9287	2.7861	2.0257
C(36)	-5.7135	-0.6940	2.0981		C(74)	5.2756	5.0767	2.8091
C(37)	-4.1295	-4.6122	4.8073		C(75)	5.7685	6.2747	3.3026
C(38)	-5.1922	-5.6394	5.1696		C(76)	5.0076	7.2950	4.0249

atom	x	y	z		atom	x	y	z
O(77)	3.7988	7.2653	4.3164		H(118)	-0.1639	-3.1518	1.8413
O(78)	5.7948	8.3689	4.3804		H(119)	-2.8544	0.0822	2.7037
C(79)	7.1601	6.5257	3.0889		H(120)	-1.7683	-3.1145	-3.1007
N(80)	8.3098	6.6649	2.8946		H(121)	-4.1874	-5.9028	-2.4001
C(81)	-7.7670	6.4165	-0.2197		H(122)	-2.9536	-5.5778	-3.6272
S(82)	-8.0550	7.9277	0.7319		H(123)	-4.6136	-0.0646	-2.0880
C(83)	-8.3708	8.8606	-0.8276		H(124)	-7.2493	0.9911	-1.0581
C(84)	-8.2394	7.9990	-1.9122		H(125)	-7.3357	-2.5280	-1.3432
C(85)	-7.9108	6.6701	-1.5786		H(126)	-7.2541	-1.0096	-2.2265
C(86)	-8.6829	10.2387	-0.6660		H(127)	-2.7788	-5.7820	2.4588
C(87)	-8.9826	11.2711	-1.5395		H(128)	-1.0602	-5.5859	2.8460
C(88)	-9.0549	11.1769	-2.9995		H(129)	-0.6081	-5.4048	-3.0481
O(89)	-9.3765	12.3842	-3.5795		H(130)	-5.6724	-2.2175	3.6210
O(90)	-8.8623	10.1658	-3.6984		H(131)	-5.0174	-0.6538	4.1240
C(91)	-9.2475	12.5508	-0.9571		H(132)	-5.7169	1.2671	2.9600
N(92)	-9.4600	13.5851	-0.4415		H(133)	-3.1212	-5.0334	4.9083
C(93)	1.4289	1.4130	-3.1788		H(134)	-4.1967	-3.7242	5.4508
S(94)	1.8377	3.1586	-3.4165		H(135)	-5.1262	-6.4803	4.4654
C(95)	3.6260	2.7810	-3.1717		H(136)	-4.9417	-6.0411	6.1629
C(96)	3.7825	1.4155	-2.9589		H(137)	-6.8676	-4.6873	4.1957
C(97)	2.5847	0.6729	-2.9653		H(138)	-6.6754	-4.2359	5.8866
C(98)	4.5057	3.8990	-3.2221		H(139)	-7.4616	-6.5352	6.5985
C(99)	5.8493	4.0726	-2.9404		H(140)	-7.6600	-6.9909	4.8987
C(100)	6.7777	3.0347	-2.4697		H(141)	-8.6792	-5.7235	5.6005
O(101)	6.5484	1.8154	-2.4037		H(142)	-3.4271	-7.7402	0.8710
O(102)	7.9857	3.5488	-2.0744		H(143)	-4.1696	-7.6675	-0.7423
C(103)	6.3774	5.3949	-3.0707		H(144)	-5.5428	-6.8798	1.8857
N(104)	6.7977	6.4873	-3.1809		H(145)	-6.2871	-6.7991	0.2890
C(105)	5.4952	-4.7127	-1.5025		H(146)	-5.2723	-9.3829	1.6234
S(106)	6.8039	-5.3920	-2.5522		H(147)	-6.0244	-9.2955	0.0350
C(107)	8.0624	-4.4002	-1.6406		H(148)	-8.1632	-8.4448	1.0903
C(108)	7.4340	-3.6620	-0.6483		H(149)	-7.4055	-8.5412	2.6892
C(109)	6.0342	-3.8377	-0.5719		H(150)	-7.6958	-10.0188	1.7564
C(110)	9.4117	-4.5650	-2.0794		H(151)	-6.3134	-4.6560	1.5632
C(111)	10.6261	-4.0358	-1.6905		H(152)	-6.9244	-4.1869	-0.0339
C(112)	11.7801	-4.4973	-2.4029		H(153)	-7.9324	-3.0967	2.6686
N(113)	12.7002	-4.9013	-3.0121		H(154)	-8.5378	-2.5747	1.0989
C(114)	10.8777	-3.0348	-0.6321		H(155)	-8.7095	-5.4463	2.1789
O(115)	12.1689	-2.7366	-0.4808		H(156)	-9.3002	-4.9232	0.6060
O(116)	9.9663	-2.5029	0.0605		H(157)	-10.9338	-3.3524	1.7389
H(117)	0.6174	-5.3766	1.0745		H(158)	-10.3391	-3.8838	3.3200

atom	x	y	z		atom	x	y	z
H(159)	-11.1821	-5.0273	2.2613		C(196)	11.7063	2.4088	1.5809
H(160)	-7.3328	-3.6293	-3.6985		C(197)	12.6135	1.8205	0.4679
H(161)	-6.1870	-4.8714	-4.2568		C(198)	12.2563	0.3848	0.0482
H(162)	-8.5170	-5.3658	-2.3168		N(199)	12.7235	-0.6906	0.9957
H(163)	-8.5847	-5.6849	-4.0490		C(200)	12.1748	-0.7158	2.3344
H(164)	-6.6480	-7.0342	-2.0888		O(201)	9.8590	2.6266	-0.5370
H(165)	-6.7118	-7.3499	-3.8206		O(202)	9.6103	4.8825	-0.2633
H(166)	-9.0875	-8.1964	-3.5852		N(203)	10.8381	-1.0098	2.3641
H(167)	-9.0209	-7.8879	-1.8425		N(204)	13.0035	-0.4826	3.2989
H(168)	-7.9741	-9.1213	-2.5646		H(205)	9.8929	5.1987	2.2511
H(169)	0.9944	-1.5218	0.6271		H(206)	10.7828	4.1817	3.2674
H(170)	2.7156	0.4169	0.7349		H(207)	11.9253	4.4638	0.9178
H(171)	4.1178	-6.1617	-3.5763		H(208)	10.8711	1.7337	1.7901
H(172)	1.5590	-6.5434	-3.3342		H(209)	12.2745	2.5075	2.5133
H(173)	-7.4471	5.6797	2.5438		H(210)	13.6678	1.8577	0.7737
H(174)	-6.8886	3.2173	3.1116		H(211)	12.5367	2.4381	-0.4361
H(175)	-1.0908	2.7300	-3.6568		H(212)	11.1754	0.2874	-0.0764
H(176)	-3.2681	1.3329	-3.4512		H(213)	12.7237	0.1432	-0.9125
H(177)	0.7574	3.8625	3.5512		H(214)	13.7378	-0.6481	1.1096
H(178)	2.5925	5.6785	3.8933		H(215)	8.9353	4.8222	-0.9893
H(179)	6.0388	4.4917	2.2991		H(216)	10.3461	-0.9913	3.2421
H(180)	5.2545	9.0369	4.8535		H(217)	10.3829	-1.4415	1.5578
H(181)	-8.3857	8.3552	-2.9213		H(218)	12.6060	-0.6054	4.2362
H(182)	-7.7796	5.8950	-2.3237					
H(183)	-8.6899	10.5577	0.3744					
H(184)	-9.4141	12.2860	-4.5547					
H(185)	4.7618	0.9894	-2.7999					
H(186)	2.5602	-0.3995	-2.8149					
H(187)	4.0120	4.8239	-3.5144					
H(188)	8.6183	2.8677	-1.6815					
H(189)	8.0058	-3.0045	-0.0109					
H(190)	5.4179	-3.3152	0.1496					
H(191)	9.5067	-5.2723	-2.9012					
H(192)	12.3928	-1.9422	0.2163					
C(193)	10.1485	3.6846	0.0671					
N(194)	10.3282	4.2888	2.3691					
C(195)	11.1098	3.7843	1.2394					

13.

Table 6 Hydrogen bonds in **2**–Asp complex, **2**–Glu complex, **2**–Lys complex and **2**–Arg complex based on computational study (B3LYP/6-31G).

System	H-bond interaction D–H···A	Distance (Å) D·····A	Distance (Å) H···A	H-bond angle (º) ∠ D–H···A
2–Asp complex	O198–H207···O116	2.579	1.546	176.7
	O115–H1927···O201	2.653	1.643	174.0
	O102–H188···O200	2.736	1.840	148.2
	N194–H202···O198	2.831	2.251	114.7
	N194–H203···N80	3.189	2.458	128.4
2–Glu complex	O199–H200···O116	2.618	1.608	171.1
	O115–H192···O210	2.614	1.599	170.2
	O102–H188···O201	2.622	1.744	143.5
	O202–H211···O102	2.795	1.942	142.3
	N194–H203···N80	3.136	2.278	141.4
2–Lys complex	N200–H214···O116	3.097	2.143	155.6
	O102–H188···O201	2.634	1.749	144.4
	O202–H216···O102	2.802	1.943	143.1
	N194–H203···N80	3.276	2.334	153.7
2–Arg complex	N203–H217···O116	2.880	1.882	164.8
	O102–H188···O201	2.593	1.705	144.4
	O202–H215···O102	2.775	1.924	142.0
	O115–H192···N199	2.583	1.511	170.8
	N194–H205···N80	3.162	2.252	148.4

14.

Table S7 Energies of **2**, Asp, Glu, Lys, Arg and their complexes obtained from computational study (B3LYP/6-31G).

System	E (**2**) (au)	E (amino acid) (au)	E (complex) (au)	$E_s^{\#}$ (kcal/mol)
2–Asp complex	-7857.13125582	-512.132161309	-8369.30584118	-26.6
2–Glu complex		-551.435909807	-8408.62055166	-33.5
2-Lys complex		-496.863285489	-8354.02716767	-20.5
2-Arg complex		-606.329549087	-8463.51109907	-31.6

$^{\#}E_s$ denotes the complex stabilization energy. E_s = E (complex) – [E (**2**) + E (amino acid)].