ACADÉMIE DES SCIENCES
INSTITUT DE FRANCE

Comptes Rendus. Chimie
Supplementary material to the article available at:
https://doi.org/10.5802/crchim.290

Structural and in silico studies of 2-pyridyl-decorated 2-amino-1,3,5-triazine with a potency against SARS-CoV-2 proteins

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Supplementary Table S1. Thermodynamic parameters of the isomers of NH_2Py_2T

Thermodynamic parameter	**1w**	**2w**	**3w**	**1g**	**2g**	**3g**
Self-consistent field energy (a.u.)	−830.169	−830.169	−830.169	−830.151	−830.151	−830.147
Total energy (thermal) ($kcal{\cdot}mol^{-1}$)	146.343	146.354	146.329	146.392	146.416	145.767
Electronic energy (thermal) ($kcal{\cdot}mol^{-1}$)	0.000	0.000	0.000	0.000	0.000	0.000
Translational energy (thermal) ($kcal{\cdot}mol^{-1}$)	0.889	0.889	0.889	0.889	0.889	0.889
Rotational energy (thermal) ($kcal{\cdot}mol^{-1}$)	0.889	0.889	0.889	0.889	0.889	0.889
Vibrational energy (thermal) ($kcal{\cdot}mol^{-1}$)	144.565	144.577	144.552	144.615	144.638	143.990
Total heat capacity (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	57.184	57.182	57.199	57.165	57.137	55.099
Electronic heat capacity (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	0.000	0.000	0.000	0.000	0.000	0.000
Translational heat capacity (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	2.981	2.981	2.981	2.981	2.981	2.981
Rotational heat capacity (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	2.981	2.981	2.981	2.981	2.981	2.981
Vibrational heat capacity (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	51.223	51.221	51.238	51.204	51.175	49.137
Total entropy (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	129.924	129.599	128.956	127.972	127.579	120.785
Electronic entropy (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	0.000	0.000	0.000	0.000	0.000	0.000
Translational entropy (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	42.451	42.451	42.451	42.451	42.451	42.451
Rotational entropy (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	33.773	33.771	33.770	33.768	33.763	33.763
Vibrational entropy (thermal) ($cal{\cdot}mol^{-1}{\cdot}K^{-1}$)	53.700	53.377	52.736	51.753	51.366	44.572
Zero-point vibrational energy (thermal) ($kcal{\cdot}mol^{-1}$)	136.966	136.975	136.956	137.011	137.049	137.061
Rotational constants (GHz)						
A	0.69060	0.70101	0.71069	0.69521	0.69922	0.71238
B	0.22388	0.22189	0.21949	0.22306	0.22340	0.22033
C	0.16925	0.16865	0.16838	0.16969	0.16931	0.16853

Supplementary Table S2. Selected bond lengths (Å), bond and dihedral angles (°) in the optimized isomers of NH_2Py_2T

	1w	**2w**	**3w**	**1g**	**2g**	**3g**
Bond length						
N1–C1	1.349	1.347	1.347	1.345	1.344	1.341
C1–N2	1.349	1.349	1.347	1.345	1.343	1.341
N2–C2	1.329	1.329	1.332	1.328	1.329	1.337
C2–N3	1.341	1.343	1.339	1.342	1.342	1.335
N3–C3	1.341	1.337	1.339	1.342	1.333	1.335
C3–N1	1.329	1.33	1.332	1.328	1.336	1.337
N4–C4	1.342	1.342	1.342	1.339	1.339	1.338
C4–C5	1.399	1.399	1.399	1.400	1.400	1.401
C5–C6	1.391	1.391	1.391	1.390	1.390	1.390
C6–C7	1.391	1.391	1.391	1.391	1.391	1.391
C7–C8	1.395	1.395	1.395	1.395	1.395	1.395
C8–N4	1.334	1.334	1.334	1.332	1.332	1.331
N5–C9	1.342	1.342	1.342	1.339	1.339	1.338
C9–C10	1.399	1.399	1.400	1.400	1.401	1.401
C10–C11	1.391	1.391	1.391	1.390	1.390	1.390
C11–C12	1.391	1.391	1.391	1.391	1.391	1.391
C12–C13	1.395	1.395	1.395	1.395	1.396	1.395
C13–N5	1.334	1.334	1.334	1.332	1.332	1.331
C1–N6	1.345	1.345	1.345	1.351	1.353	1.357
C3–C5	1.499	1.499	1.499	1.498	1.498	1.498
C2–C10	1.499	1.499	1.499	1.498	1.497	1.498
Bond angle						
N1–C1–N2	125.01	124.74	124.43	125.59	125.39	125.04
C1–N2–C2	114.84	114.85	115.12	114.53	114.53	114.77
N2–C2–N3	124.88	125.12	125.14	12.02	125.15	125.16
C2–N3–C3	115.56	115.35	115.06	115.30	115.39	115.10
N3–C3–N1	124.88	124.84	125.14	125.02	124.90	125.16
C3–N1–C1	114.84	115.10	115.12	114.53	114.64	114.77
N4–C4–C5	122.42	122.42	122.45	122.63	122.59	122.61
C4–C5–C6	118.89	118.91	118.89	118.75	118.78	118.74
C5–C6–C7	118.82	118.82	118.81	118.80	118.80	118.80
C6–C7–C8	118.20	118.18	118.20	118.15	118.13	118.14
C7–C8–N4	123.56	123.58	123.58	123.67	123.68	123.66
C8–N4–C4	118.11	118.09	118.07	118.00	118.01	118.05
N5–C9–C10	122.42	122.43	122.45	122.63	122.82	122.61
C9–C10–C11	118.89	118.88	118.89	118.75	118.59	118.74
C10–C11–C12	118.82	118.82	118.81	118.80	118.84	118.80

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Supplementary Table S2. (continued)

	1w	2w	3w	1g	2g	3g
Bond length						
C11–C12–C13	118.20	118.20	118.21	118.15	118.21	118.15
C12–C13–N5	123.56	123.57	123.57	123.66	123.64	123.66
C13–N5–C9	118.11	118.09	118.08	118.00	117.90	118.04
N1–C1–N6	117.49	117.70	117.79	117.20	117.57	117.47
N2–C1–N6	117.49	117.56	117.79	117.20	117.03	117.48
N1–C3–C4	118.54	116.74	116.55	118.22	116.78	116.45
N3–C3–C4	116.58	118.42	118.31	116.75	118.31	118.39
C3–C4–N4	117.64	117.58	117.56	117.47	117.44	117.43
C3–C4–C5	119.94	120.01	119.99	119.91	119.97	119.97
N2–C2–C9	118.54	118.42	116.55	118.23	118.62	116.45
N3–C2–C9	116.58	116.46	118.31	116.75	116.23	118.39
C2–C9–N5	117.64	117.67	117.56	117.46	117.72	117.43
C2–C9–C10	119.94	119.90	119.99	119.91	119.46	119.96
Dihedral angle						
N1–C3–C4–N4	5.62	178.78	168.42	−11.98	−178.86	172.80
N3–C3–C4–C5	5.53	178.72	168.00	−11.73	−178.84	172.57
N1–C3–C4–C5	−174.32	−1.25	−11.65	167.86	1.16	−7.22
N3–C3–C4–N4	−174.53	−1.26	−11.93	168.42	1.15	−7.41
N2–C2–C9–N5	5.62	−6.08	−168.44	−11.96	−0.09	−173.12
N3–C2–C9–C10	5.53	−6.02	−168.02	−11.72	−0.06	−172.89
N2–C2–C9–C10	−174.32	173.81	−11.62	167.88	179.88	6.91
N3–C2–C9–N5	−174.53	174.09	11.92	168.44	179.97	7.09
N1–C1–N6–H1	−0.10	0.51	−2.01	0.35	4.60	−9.74
N1–C1–N6–H2	179.91	179.60	178.00	0.36	−4.25	9.73
N2–C1–N6–H2	−0.10	−0.39	2.01	−179.65	176.12	−171.04
N2–C1–N6–H1	179.91	−179.48	178.00	−179.64	−175.77	171.04

Supplementary Table S3. Values of the selected vibrations in the IR and Raman spectra (Figure 3) of the isomers of NH_2Py_2T

Molecular vibration (PED, %)[a]	Frequency (cm^{-1})	IR intensity	Raman intensity
1w			
ν_{as}(N6–H1 + N6–H2) (100)	3733	115.6	105.4
ν_{s}(N6–H1 + N6–H2) (100)	3604	209.8	429.1
βH1–N6–H2 (66); νC1–N6 (19)	1628	517.4	164.2
ν(C5–C6 + C7–C8 + C12–C13 + C3–N1) (42); β(H7–C10–C11 + H9–C12–C13) (10)	1620	41.3	1085.5
ν(C5–C6 + C7–C8 + C10–C11 + C12–C13) (56)	1619	15.2	490.7
ν_{s}(C2–N2 + C3–N1) (67)	1568	1364.9	382.6
ν_{as}(C1–N1 + C3–N3) (39); β(C6–C7–C8 + C11–C12–C13 + C2–C9–N5 + C3–C4–N4 + C4–C3–N1 + C7–C8–N4 + C9–C2–N2 + C12–C13–N5 + C4–N4–C8 + N1–C1–N6 + N2–C2–N3) (13)	1546	1174.5	469.8
β(H6–C8–N4 + H10–C13–N5) (21); ν(C2–C9 + C2–N3 + C3–N3) (14); ν(C2–N3 + C3–N3 + C4–N4 + C8–N4 + C9–N5) (10)	1506	0.0	779.6
ν(C1–N6) (25); β(H1–N6–H2) (16); β(C5–C6–C7 + C10–C11–C12 + C1–N1–C3 + C2–N3–C3 + C4–N4–C8 + C9–N5–C13) (15); β(H6–C8–N4 + H10–C13–N5) (12);	1487	256.4	1.7
β(H4–C6–C7 + H5–C7–C8 + H8–C11–C12 + H9–C12–C13) (47); ν(C2–C9 + C3–C4 + C2–N2 + C3–N1) (11)	1464	21.0	343.0
ν(C2–C9 + C3–C4 + C2–N2 + C3–N1) (52); β(H4–C6–C7 + H5–C7–C8 + H8–C11–C12 + H9–C12–C13) (17)	1415	334.7	277.5
ν(C2–C9 + C2–N3 + C3–N3) (40); β(H6–C8–N4 + H10–C13–N5) (16)	1385	306.6	1266.2
β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5) (43); β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5) (39); ν(C5–C6 + C6–C7 + C7–C8 + C10–C11 + C11–C12 + C12–C13) (28); ν(C6–C7 + C7–C8 + C11–C12 + C12–C13) (23); ν(C4–N4 + C8–N4 + C9–N5 + C13–N5) (12)	1011	10.9	436.9
2w			
ν_{as}(N6–H1 + N6–H2) (100)	3733	116.1	104.4
ν_{s}(N6–H1 + N6–H2) (100)	3604	209.4	422.1
β(H1–N6–H2 + C1–N1–C3 + C2–N3–C3 + N1–C3–N3) (54); νC1–N6 (30)	1628	622.7	75.7

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Supplementary Table S3. (continued)

Molecular vibration (PED, %)[a]	Frequency (cm^{-1})	IR intensity	Raman intensity
ν_{as}(C5–C6 + C7–C8) (26); ν_{as}(C10–C11 + C12–C13) (12)	1621	19.9	445.3
ν_{as}(C10–C11 + C12–C13) (34); ν_{as}(C5–C6 + C7–C8) (12)	1619	1.7	1074.2
ν(C2–N2 + C3–N1 + C3–N3) (47)	1566	1327.4	374.7
ν(C1–N1 + C2–N2 + C3–N1) (40); ν(C2–N2 + C3–N1 + C3–N3) (11)	1549	1223.2	461.9
β(H1–N6–H2 + C1–N1–C3 + C2–N3–C3 + N1–C3–N3) (17); β(H6–C8–N4 + H10–C13–N5) (16); ν_s(C2–C9 + C3–C4) (11); ν(C5–C6 + C10–C11 + C4–N4 + C9–N5) (10)	1506	58.6	653.0
β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4) (34); ν_s(C4–N4 + C8–N4) (15)	1498	72.0	223.4
β(H4–C6–C7 + H5–C7–C8) (45)	1461	38.4	318.9
ν(C2–C9 + C3–C4 + C2–N2 + C3–N1) (49); β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4) (10)	1411	347.9	357.9
ν_s(C2–C9 + C3–C4) (20)	1389	306.0	1207.5
β(C5–C6–C7 + C6–C7–C8 + C7–C8–N4) (42)	1010	22.2	383.3
3w			
ν_{as}(N6–H1 + N6–H2) (100)	3733	116.6	103.4
ν_s(N6–H1 + N6–H2) (100)	3604	209.0	415.5
βH1–N6–H2 (69); νC1–N6 (18)	1629	667.2	63.0
ν(C5–C6 + C6–C7 + C7–C8 + C10–C11 + C11–C12 + C12–C13 + C4–N4 + 8C–N4 + C9–N5 + C13–N5) (42); β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4 + H10–C13–N5) (11); β(C7–C8–N4 + C12–C13–N5 + C4–N4–C8 + C9–N5–C13) (11)	1622	4.7	614.6
ν_{as}(C10–C11 + C12–C13) (59); βC4–N4–C8 (10)	1619	4.7	706.7
ν(C5–C6 + C6–C7 + C10–C11 + C11–C12 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (58); β(H4–C6–C7 + H9–C12–C13) (12)	1613	4.3	442.0
ν_s(C2–N2 + C3–N1) (59)	1563	1295.8	341.8
ν_{as}(C1–N2 + C2–N3) (52)	1553	1248.1	423.0
β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4) (22); ν(C2–N3 + C3–N1 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (11); ν(C5–C6 + C6–C7 + C7–C8 + C10–C11 + C11–C12 + C12–C13 + C3–N4 + C9–N5) (10); ν_s(C2–C9 + C3–C4) (10)	1507	141.7	521.2

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Supplementary Table S3. (continued)

Molecular vibration (PED, %)[a]	Frequency (cm^{-1})	IR intensity	Raman intensity
β(H3–C5–C6 + H5–C7–C8 + H7–C10–C11 + H8–C11–C12 + H6–C8–N4 + H10–C13–N5) (45); ν_s(C9–N5 + C13–N5) (23)	1500	9.1	227.2
β(H4–C6–C7 + H5–C7–C8 + H8–C11–C12 + H9–C12–C13) (48); β(C7–C8–N4 + C12–C13–N5 + C4–N4–C8 + C9–N5–C13) (14)	1462	35.4	649.9
ν(C2–N2 + C3–N1 + C3–N3) (47)	1408	348.9	371.0
ν_s(C2–C9 + C3–C4) (26); β(H4–C6–C7 + H5–C7–C8 + H8–C11–C12 + H9–C12–C13) (11)	1394	294.2	1070.7
ν(C5–C6 + C6–C7 + C10–C11 + C11–C12 + C4–N5 + C8–N4 + C9–N5 + C13–N5) (72)	1290	40.3	313.5
β(C5–C6–C7 + C10–C11–C12 + C7–C8–N4 + C12–C13–N5 + C1–N2–C2 + C2–N3–C3 + C4–N4–C8 + C9–N5–C13 + N1–C3–N3) (42); ν(C2–N3 + C3–N1 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (20); β(C5–C6–C7 + C10–C11–C12 + C7–C8–N4 + C12–C13–N5 + C2–N3–C3 + C4–N4–C8 + C9–N5–C13 + N1–C3–N3 + N2–C2–N3) (13)	1009	25.6	508.8
1g			
ν_{as}(N6–H1 + N6–H2) (100)	3751	67.0	55.0
ν_s(N6–H1 + N6–H2) (100)	3614	122.9	210.9
βH1–N6–H2 (61); νC1–N6 (26)	1639	695.3	2.2
ν(C7–C8 + C10–C11 + C2–N2) (55); β(H7–C10–C11 + H9–C12–C13 + H6–C8–N4) (13)	1624	0.3	508.1
ν(C6–C7 + C7–C8 + C2–N2 + C3–N1) (53)	1585	456.2	98.9
ν_{as}(C1–N1 + C3–N3) (57); β(C2–C9–N5 + C3–C4–N4 + C4–C3–N1 + C9–C2–N2 + N2–C2–N3) (14)	1561	642.8	92.4
β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4 + H10–C13–N5) (32); ν(C3–C4 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (24)	1506	0.0	239.0
β(H4–C6–C7 + H5–C7–C8 + H8–C11–C20 + H9–C12–C13) (44); ν(C2–C9 + C3–C4 + C2–N2 + C3–N1) (11)	1466	11.9	103.0
ν(C2–C9 + C3–C4 + C2–N2 + C3–N1) (44); β(H4–C6–C7 + H5–C7–C8 + H8–C11–C20 + H9–C12–C13) (15)	1423	222.8	70.6

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Supplementary Table S3. (continued)

Molecular vibration (PED, %)[a]	Frequency (cm^{-1})	IR intensity	Raman intensity
ν(C3–C4 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (21); β(H3–C5–C6 + H7–C10–C11 + H6–C8–N4 + H10–C13–N5) (17); ν_{as}(C1–N1 + C2–N3) (16)	1391	123.6	418.3
β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5) (43); β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5) (34); ν(C5–C6 + C6–C7 + C7–C8 + C10–C11 + C11–C12 + C12–C13) (28); ν(C5–C6 + C6–C7 + C7–C8) (20); ν_{s}(C4–N4 + C8–N4) (11); ν(C3–C4 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (10)	1011	3.1	140.2
2g			
ν_{as}(N6–H1 + N6–H2) (100)	3751	61.7	55.9
ν_{s}(N6–H1 + N6–H2) (100)	3615	111.5	206.6
βH1–N1–H2 (61); νC1–N6 (22)	1639	652.7	5.5
ν_{as}(C5–C6 + C7–C8) (43); β(C7–C8–N4 + C4–N4–C8) (12)	1623	7.3	263.0
ν_{as}(C10–C11 + C12–C13) (48); β(C2–C9–N5 + C3–C4–N4 + C4–C3–N1 + C9–C2–N2 + C9–N5–C13) (10)	1622	8.8	404.8
ν(C2–N2 + C3–N1 + C3–N3) (56)	1581	526.7	104.8
ν(C1–N2 + C2–N2 + C2–N3 + C3–N1) (51); β(C2–N3–C3 + N1–C3–N3) (12)	1570	649.4	110.4
β(H6–C8–N4 + H10–C13–N5) (14); β(H3–C5–C6 + H6–C8–N14) (12); ν_{s}(C2–C9 + C3–C4) (12); ν_{s}(C11–C12 + C12–C13 + C9–N5) (11)	1506	6.9	246.8
ν(C3–C4 + C1–N2 + C2–N2 + C3–N1 + C3–N3) (53)	1416	234.7	116.9
ν_{s}(C2–C9 + C3–C4) (22); ν(C2–N2 + C2–N3 + C3–N1 + C3–N3) (16)	1398	147.1	410.7
β(C10–C11–C12 + C11–C12–C13 + C12–C13–N5) (42); β(C5–C6–C7 + C4–N4–C8) (39); ν_{s}(C9–N5 + C13–N5) (31); ν(C5–C6 + C6–C7 + C7–C8 + C11–C12 + C12–C13) (19)	1011	0.9	134.0
3g			
ν_{as}(N6–H1 + N6–H2) (100)	3744	54.1	56.0
ν_{s}(N6–H1 + N6–H2) (100)	3612	93.4	203.6

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Supplementary Table S3. (continued)

Molecular vibration (PED, %)[a]	Frequency (cm^{-1})	IR intensity	Raman intensity
βH1–N6–H2 (65); ν(C1–N6 + C2–N2 + C3–N1 + C9–N5 + C13–N5) (11); ν_s(C2–N2 + C3–N1) (10)	1640	572.1	8.8
ν(C5–C6 + C7–C8 + C10–C11 + C12–C13 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (61); β(H7–C10–C11 + H6–C8–N4 + H10–C13–N5) (11)	1622	0.1	454.1
ν(C5–C6 + C10–C11 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (62)	1621	37.1	238.2
ν_s(C1–N2 + C2–N3) (47)	1581	716.4	109.2
ν_s(C2–N2 + C3–N1) (52); ν(C1–N6 + C2–N2 + C3–N1 + C9–N5 + C13–N5) (12)	1570	507.7	81.0
β(H7–C10–C11 + H10–C13–N5) (29); ν(C2–N3 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (17); ν(C5–C6 + C6–C7 + C7–C8 + C11–C12 + C12–C13 + C4–N4) (13); ν_s(C2–C9 + C3–C4) (11)	1506	19.4	225.1
β(H4–C6–C7 + H5–C7–C8 + H8–C11–C12 + H9–C12–C13) (32); β(C10–C11–C12 + C7–C8–N4 + C1–N2–C2 + C2–N3–C3 + C4–N4–C8 + C9–N5–C13) (11)	1461	3.3	311.4
ν(C3–C4 + C2–N2 + C3–N1 + C3–N3) (48)	1409	257.7	125.8
β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5 + C1–N2–C2 + N1–C3–N3) (15); ν_s(C2–C9 + C3–C4) (14)	1403	148.5	374.0
β(C5–C6–C7 + C6–C7–C8 + C10–C11–C12 + C11–C12–C13 + C7–C8–N4 + C12–C13–N5 + C1–N2–C2 + N1–C3–N3) (32); ν(C2–N3 + C4–N4 + C8–N4 + C9–N5 + C13–N5) (20)	1009	9.4	193.7

[a]ν—stretching, ν_s—symmetric stretching, ν_{as}—antisymmetric stretching, β—bending.

Supplementary Table S4. Selected values for the calculated absorption spectra (Figure 5) of the isomers of NH_2Py_2T

λ_{max} (nm)	Osc. strength	Transition	λ_{max} (nm)	Osc. strength	Transition
		1w			**1g**
307.39	0.1859	HOMO → LUMO (95.5%)	301.50	0.0781	HOMO−1 → LUMO (90.0%)
273.99	0.2852	HOMO−4 → LUMO (96.2%)	298.22	0.0480	HOMO−4 → LUMO (53.0%)
272.29	0.1690	HOMO−3 → LUMO (89.1%)			HOMO−2 → LUMO (13.7%)
248.63	0.2338	HOMO−3 → LUMO+1 (91.4%)			HOMO−1 → LUMO+1 (8.8%)
239.90	0.0904	HOMO−8 → LUMO (68.5%)			HOMO → LUMO (21.3%)
		HOMO−3 → LUMO+2 (13.0%)	265.59	0.2232	HOMO−5 → LUMO (94.9%)
236.89	0.1782	HOMO−4 → LUMO+1 (89.2%)	264.65	0.1133	HOMO−3 → LUMO (82.3%)
217.11	0.1319	HOMO−8 → LUMO+1 (32.5%)	247.50	0.1439	HOMO−6 → LUMO+1 (17.2%)
		HOMO−7 → LUMO (10.9%)			HOMO−3 → LUMO+1 (66.9%)
		HOMO−4 → LUMO+2 (25.5%)	242.72	0.0855	HOMO−6 → LUMO+1 (60.5%)
		HOMO−3 → LUMO+3 (15.6%)			HOMO−3 → LUMO+1 (23.0%)
208.96	0.1056	HOMO−7 → LUMO+1 (19.3%)	236.34	0.1109	HOMO−6 → LUMO (51.7%)
		HOMO−4 → LUMO+3 (35.2%)			HOMO−3 → LUMO+2 (18.5%)
		HOMO−3 → LUMO+2 (36.1%)	233.62	0.0857	HOMO−5 → LUMO+1 (72.0%)
199.15	0.0954	HOMO−7 → LUMO+1 (8.9%)			HOMO → LUMO+2 (14.6%)
		HOMO−4 → LUMO+3 (13.0%)	228.36	0.0564	HOMO−7 → LUMO (18.9%)
		HOMO → LUMO+4 (57.6%)			HOMO−5 → LUMO+1 (8.1%)
		HOMO → LUMO+7 (10.1%)			HOMO−1 → LUMO+3 (8.8%)
199.07	0.2619	HOMO−7 → LUMO+1 (24.5%)			HOMO → LUMO+2 (53.5%)
		HOMO−4 → LUMO+3 (34.8%)	215.31	0.0954	HOMO−8 → LUMO+1 (31.7%)
		HOMO → LUMO+4 (20.6%)			HOMO−7 → LUMO (18.0%)
187.57	0.1605	HOMO−7 → LUMO+2 (60.9%)			HOMO−5 → LUMO+2 (19.2%)
		HOMO−4 → LUMO+5 (26.2%)			HOMO−3 → LUMO+3 (17.1%)
186.85	0.3787	HOMO−9 → LUMO (37.4%)	209.66	0.0695	HOMO−7 → LUMO+1 (18.8%)
		HOMO−7 → LUMO+3 (10.2%)			HOMO−5 → LUMO+3 (38.9%)
		HOMO → LUMO+5 (30.0%)			HOMO−3 → LUMO+2 (29.2%)
184.92	0.2990	HOMO−8 → LUMO+2 (57.9%)	196.82	0.2328	HOMO−7 → LUMO+1 (27.7%)
		HOMO−4 → LUMO+5 (19.7%)			HOMO−5 → LUMO+3 (29.5%)
184.00	0.1206	HOMO−8 → LUMO+3 (64.7%)			HOMO−2 → LUMO+6 (14.6%)
		HOMO−7 → LUMO+2 (15.0%)	195.64	0.1146	HOMO−7 → LUMO+1 (9.1%)
		HOMO−3 → LUMO+5 (10.4%)			HOMO−5 → LUMO+3 (8.4%)
181.42	0.1070	HOMO−6 → LUMO+4 (8.9%)			HOMO−4 → LUMO+4 (8.6%)
		HOMO−2 → LUMO+6 (46.4%)			HOMO−2 → LUMO+6 (37.1%)
		HOMO−1 → LUMO+7 (19.6%)			HOMO−1 → LUMO+5 (15.2%)

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Supplementary Table S4. (continued)

λ_{max} (nm)	Osc. strength	Transition	λ_{max} (nm)	Osc. strength	Transition
180.31	0.1037	HOMO−10 → LUMO (21.6%)	184.28	0.1299	HOMO−8 → LUMO+3 (41.4%)
		HOMO−9 → LUMO+1 (16.3%)			HOMO−7 → LUMO+2 (9.7%)
		HOMO−8 → LUMO+2 (9.4%)			HOMO−3 → LUMO+7 (9.5%)
		HOMO−3 → LUMO+5 (27.1%)	183.18	0.2194	HOMO−8 → LUMO+2 (23.1%)
		HOMO → LUMO+8 (12.3%)			HOMO−6 → LUMO+4 (9.3%)
					HOMO−1 → LUMO+8 (14.2%)
					HOMO−1 → LUMO+9 (10.8%)
			181.87	0.1795	HOMO−8 → LUMO+2 (13.8%)
					HOMO−6 → LUMO+4 (27.2%)
					HOMO−4 → LUMO+5 (9.3%)
					HOMO−1 → LUMO+8 (20.6%)
		2w			**2g**
304.76	0.1491	HOMO−1 → LUMO (9.4%)	299.33	0.1163	HOMO−5 → LUMO (12.7%)
		HOMO− → LUMO+ (86.2%)			HOMO−1 → LUMO (77.8%)
275.95	0.2462	HOMO−4 → LUMO (40.4%)	271.37	0.1329	HOMO−4 → LUMO (25.0%)
		HOMO−2 → LUMO (51.0%)			HOMO−3 → LUMO (66.2%)
273.29	0.2206	HOMO−4 → LUMO (53.7%)	267.45	0.2059	HOMO−4 → LUMO (69.8%)
		HOMO−2 → LUMO (34.5%)			HOMO−3 → LUMO (25.0%)
254.73	0.2062	HOMO−2 → LUMO+1 (54.0%)	251.94	0.1610	HOMO−3 → LUMO+1 (36.2%)
		HOMO → LUMO+1 (25.4%)			HOMO−1 → LUMO+1 (45.6%)
243.57	0.0813	HOMO−8 → LUMO (10.5%)	239.32	0.1667	HOMO−8 → LUMO (12.9%)
		HOMO−7 → LUMO (13.7%)			HOMO−7 → LUMO (35.3%)
		HOMO−4 → LUMO+1 (47.7%)			HOMO−4 → LUMO+1 (19.8%)
		HOMO−2 → LUMO+1 (8.1%)			HOMO−3 → LUMO+1 (14.6%)
240.63	0.1185	HOMO−8 → LUMO (17.6%)	229.72	0.2010	HOMO−8 → LUMO (37.1%)
		HOMO−7 → LUMO (46.2%)			HOMO−4 → LUMO+1 (37.0%)
234.48	0.2122	HOMO−8 → LUMO (38.3%)	217.85	0.0623	HOMO−7 → LUMO+1 (21.3%)
		HOMO−4 → LUMO+1 (36.1%)			HOMO−3 → LUMO+2 (8.7%)
218.63	0.0740	HOMO−7 → LUMO (8.2%)			HOMO−3 → LUMO+3 (35.9%)
		HOMO−7 → LUMO+1 (30.2%)			HOMO−1 → LUMO+3 (12.9%)
		HOMO−4 → LUMO+2 (13.8%)	214.69	0.0409	HOMO−8 → LUMO (19.8%)
		HOMO−3 → LUMO+2 (9.5%)			HOMO−8 → LUMO+1 (27.9%)
		HOMO−2 → LUMO+2 (16.9%)			HOMO−3 → LUMO+ 2(43.1%)
200.72	0.0884	HOMO−7 → LUMO+1 (25.1%)	199.62	0.1127	HOMO−7 → LUMO+1 (24.8%)
		HOMO−6 → LUMO+2 (29.0%)			HOMO−4 → LUMO+3 (28.2%)
		HOMO−4 → LUMO+2 (20.3%)			HOMO → LUMO+6 (19.1%)
199.09	0.1185	HOMO−8 → LUMO+1 (31.4%)	195.55	0.0952	HOMO−8 → LUMO+1 (35.5%)
		HOMO−4 → LUMO+3 (21.8%)			HOMO−4 → LUMO+2 (22.6%)

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Supplementary Table S4. (continued)

λ_{max} (nm)	Osc. strength	Transition	λ_{max} (nm)	Osc. strength	Transition
		HOMO−2 → LUMO+3 (9.2%)			HOMO−0 → LUMO+5 (9.6%)
		HOMO → LUMO+4 (18.8%)	186.59	0.1007	HOMO−8 → LUMO+2 (8.0%)
188.28	0.2512	HOMO−8 → LUMO+3 (26.3%)			HOMO−7 → LUMO+2 (20.0%)
		HOMO−2 → LUMO+5 (34.7%)			HOMO−3 → LUMO+7 (30.3%)
187.17	0.3226	HOMO−9 → LUMO (32.8%)			HOMO−1 → LUMO+7 (8.1%)
		HOMO−2 → LUMO+5 (9.2%)	185.56	0.0731	HOMO−7 → LUMO+2 (22.1%)
		HOMO → LUMO+5 (28.0%)			HOMO−8 → LUMO+4 (40.7%)
185.10	0.2359	HOMO−7 → LUMO+2 (41.9%)	184.44	0.1970	HOMO−7 → LUMO+3 (25.1%)
		HOMO−4 → LUMO+5 (19.7%)			HOMO−1 → LUMO+10 (37.4%)
		HOMO → LUMO+8 (10.5%)			HOMO−0 → LUMO+9 (12.2%)
184.09	0.1056	HOMO−8 → LUMO+2 (8.3%)	183.89	0.0781	HOMO−7 → LUMO+2 (13.4%)
		HOMO → LUMO+6 (12.8%)			HOMO−6 → LUMO+4 (20.3%)
		HOMO → LUMO+8 (17.1%)			HOMO−3 → LUMO+10 (8.0%)
182.29	0.1346	HOMO−7 → LUMO+3 (34.3%)			HOMO−1 → LUMO+7 (12.3%)
		HOMO−1 → LUMO+7 (25.1%)	182.61	0.3277	HOMO−8 → LUMO+2 (26.2%)
180.64	0.1912	HOMO−10 → LUMO (11.9%)			HOMO−4 → LUMO+7 (11.5%)
		HOMO−9 → LUMO+1 (16.0%)			HOMO−3 → LUMO+7 (11.9%)
		HOMO−8 → LUMO+3 (8.3%)	180.27	0.1398	HOMO−9 → LUMO+1 (19.3%)
		HOMO−7 → LUMO+2 (8.8%)			HOMO−8 → LUMO+3 (11.7%)
		HOMO−2 → LUMO+5 (17.0%)			HOMO → LUMO+9 (8.4%)
		HOMO → LUMO+8 (13.9%)			
		3w			**3g**
300.63	0.1085	HOMO−1 → LUMO (64.4%)	294.00	0.1313	HOMO−2 → LUMO (92.8%)
		HOMO → LUMO (32.3%)	273.57	0.0633	HOMO−3 → LUMO (92.7%)
273.45	0.4037	HOMO−4 → LUMO (93.6%)	270.22	0.2637	HOMO−4 → LUMO (86.6%)
255.89	0.2071	HOMO−3 → LUMO+1 (25.1%)	253.35	0.1765	HOMO−8 → LUMO (12.4%)
		HOMO−2 → LUMO+1 (55.5%)			HOMO−3 → LUMO+1 (72.9%)
250.86	0.0676	HOMO−1 → LUMO+1 (55.3%)	236.66	0.3247	HOMO−8 → LUMO (64.1%)
		HOMO → LUMO+1 (32.2%)			HOMO−3 → LUMO+1 (18.8%)
237.72	0.2455	HOMO−8 → LUMO (70.3%)	230.15	0.1514	HOMO−7 → LUMO (32.7%)
		HOMO−2 → LUMO+1 (9.5%)			HOMO−4 → LUMO+1 (46.7%)
232.68	0.1609	HOMO−7 → LUMO (41.7%)	215.24	0.0223	HOMO−3 → LUMO+2 (8.8%)
		HOMO−4 → LUMO+1 (40.5%)			HOMO−2 → LUMO+3 (71.4%)
		HOMO−2 → LUMO+2 (8.4%)			HOMO → LUMO+4 (10.6%)
198.14	0.0803	HOMO−8 → LUMO+1 (13.0%)	207.08	0.0314	HOMO−8 → LUMO+1 (27.9%)
		HOMO−6 → LUMO+3 (13.3%)			HOMO−4 → LUMO+3 (40.7%)

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Supplementary Table S4. (continued)

λ_{max} (nm)	Osc. strength	Transition	λ_{max} (nm)	Osc. strength	Transition
		HOMO−4 → LUMO+3 (21.3%)			HOMO−3 → LUMO+2 (26.3%)
		HOMO−1 → LUMO+4 (14.4%)	195.68	0.1326	HOMO−8 → LUMO+1 (27.2%)
		HOMO−1 → LUMO+5 (8.1%)			HOMO−4 → LUMO+3 (38.2%)
		HOMO → LUMO+5 (12.6%)	186.42	0.0775	HOMO−9 → LUMO (8.2%)
197.53	0.1016	HOMO−8 → LUMO+1 (14.8%)			HOMO−2 → LUMO+7 (14.7%)
		HOMO−6 → LUMO+3 (27.0%)			HOMO−1 → LUMO+8 (14.8%)
		HOMO−4 → LUMO+3 (26.8%)			HOMO → LUMO+9 (43.7%)
		HOMO → LUMO+5 (12.6%)	184.17	0.2828	HOMO−7 → LUMO+2 (44.8%)
190.76	0.0817	HOMO−9 → LUMO (27.7%)			HOMO−4 → LUMO+7 (13.6%)
		HOMO−1 → LUMO+5 (38.2%)			HOMO−2 → LUMO+7 (12.2%)
		HOMO → LUMO+5 (21.4%)			HOMO → LUMO+11 (10.3%)
190.26	0.1027	HOMO−8 → LUMO+2 (10.2%)	182.90	0.2314	HOMO−8 → LUMO+2 (45.3%)
		HOMO−3 → LUMO+4 (28.9%)			HOMO−2 → LUMO+10 (18.9%)
		HOMO−2 → LUMO+5 (28.5%)	182.74	0.1012	HOMO−1 → LUMO+8 (14.2%)
187.43	0.3340	HOMO−9 → LUMO (49.5%)			HOMO → LUMO+11 (47.5%)
		HOMO−1 → LUMO+5 (16.1%)	181.85	0.1773	HOMO−8 → LUMO+3 (37.7%)
186.24	0.1356	HOMO−8 → LUMO+3 (11.9%)			HOMO−7 → LUMO+2 (14.1%)
		HOMO−7 → LUMO+2 (29.4%)			HOMO−4 → LUMO+6 (12.2%)
		HOMO−4 → LUMO+5 (36.3%)			HOMO−3 → LUMO+8 (9.0%)
		HOMO−2 → LUMO+8 (10.1%)	181.69	0.1152	HOMO−9 → LUMO+1 (11.9%)
184.11	0.1286	HOMO−5 → LUMO+4 (11.1%)			HOMO−8 → LUMO+2 (10.3%)
		HOMO−3 → LUMO+4 (9.6%)			HOMO−7 → LUMO+3 (56.3%)
		HOMO−1 → LUMO+8 (11.5%)	180.46	0.1271	HOMO−9 → LUMO+1 (28.0%)
		HOMO → LUMO+6 (41.3%)			HOMO−8 → LUMO+2 (11.1%)
183.83	0.2332	HOMO−8 → LUMO+2 (32.4%)			HOMO−2 → LUMO+8 (14.7%)
		HOMO−1 → LUMO+8 (18.7%)			HOMO−2 → LUMO+10 (14.1%)
		HOMO → LUMO+6 (12.9%)			
		HOMO → LUMO+8 (8.9%)			
182.11	0.1027	HOMO−8 → LUMO+3 (28.4%)			
		HOMO−7 → LUMO+2 (15.2%)			
		HOMO−1 → LUMO+7 (33.8%)			
181.72	0.2447	HOMO−9 → LUMO+1 (30.3%)			
		HOMO−2 → LUMO+5 (16.0%)			
		HOMO−1 → LUMO+8 (18.4%)			
		HOMO → LUMO+8 (8.6%)			

Supplementary Table S5. Signals for the calculated ^{1}H NMR spectra of the isomers of NH_2Py_2T, and signals for experimental ^{1}H NMR spectrum of NH_2Py_2T in DMSO-d_6 (see Figure 2 for atoms labelling)

Calculated						Experimental [1]	
Isomer	δ (ppm)	Hydrogen	Isomer	δ (ppm)	Hydrogen	δ (ppm)	Hydrogen
1w	5.43	H1 + H2	**1g**	5.01	H1 + H2	7.56–7.61	H5 + H9
	7.72	H5 + H9		7.35	H5 + H9	7.94	H1 + H2
	8.17	H4 + H8		7.84	H4 + H8	7.98–8.03	H4 + H8
	9.03	H6 + H10		9.01	H6 + H10	8.45–8.48	H3 + H7
	9.33	H3 + H7		9.14	H3 + H7	8.75–8.78	H6 + H10
2w	5.41	H1	**2g**	4.77	H1		
	5.43	H2		4.99	H2		
	7.71	H9		7.32	H9		
	7.74	H5		7.37	H5		
	8.10	H4		7.76	H4		
	8.15	H8		7.84	H8		
	9.01	H10		8.94	H10		
	9.10	H6		9.05	H3		
	9.16	H3		9.06	H6		
	9.37	H7		9.55	H7		
3w	5.36	H1 + H2	**3g**	4.66	H1 + H2		
	7.68	H5 + H9		7.29	H5 + H9		
	8.15	H4 + H8		7.76	H4 + H8		
	9.01	H3 + H7		8.99	H3 + H7		
	9.07	H6 + H10		9.10	H6 + H10		

Supplementary Table S6. Nonlinear optical parameters of the isomers of NH_2Py_2T and urea[a]

Parameter	**1w**	**2w**	**3w**	**1g**	**2g**	**3g**	Urea [2]
μ_x (Debye)	0.0000	−2.7445	0.0001	0.0000	−1.8876	0.0011	
μ_y (Debye)	4.0224	0.5983	5.2761	2.2519	0.4381	3.2899	
μ_z (Debye)	0.0004	0.3775	0.7940	0.0003	0.1509	−0.0354	
μ_D (Debye)	4.0224	2.8342	5.3355	2.2519	1.9436	3.2901	
α_{xx} (a.u.)	370.725	370.596	368.067	285.987	288.475	290.308	
α_{yy} (a.u.)	329.687	329.410	326.946	227.686	229.412	227.793	
α_{zz} (a.u.)	134.661	134.274	137.084	99.944	97.148	98.254	
α_{xy} (a.u.)	0.000	−0.515	0.000	−0.001	−1.324	0.006	
α_{xz} (a.u.)	−3.719	−2.384	−0.004	4.797	0.217	−0.062	
α_{yz} (a.u.)	0.003	−1.622	8.348	0.003	−0.269	3.169	
α (a.u.)	278.358	248.093	277.366	204.539	205.012	205.452	
α (esu)	41.2526×10^{-24}	36.7674×10^{-24}	41.1056×10^{-24}	30.3127×10^{-24}	30.3827×10^{-24}	30.4479×10^{-24}	3.8312×10^{-24}
$\alpha_{isomer}/\alpha_{urea}$	10.8	9.6	10.7	7.9	7.9	7.9	
$\Delta\alpha$ (a.u.)	218.550	205.138	213.904	165.026	169.705	169.755	
$\Delta\alpha$ (esu)	32.3892×10^{-24}	30.4014×10^{-24}	31.7006×10^{-24}	24.4568×10^{-24}	25.150×10^{-24}	25.158×10^{-24}	
β_{xxx} (a.u.)	−0.0004	−47.4516	0.0039	0.0018	−31.0624	0.0332	
β_{yyy} (a.u.)	−63.7707	78.0288	93.2319	−64.9847	65.0538	65.4705	
β_{zzz} (a.u.)	0.0002	−0.0420	−1.3537	0.0002	0.1960	−1.4980	
β_{xyy} (a.u.)	−0.0002	−6.8848	0.0016	0.0006	−6.2167	0.0202	
β_{xxy} (a.u.)	102.9768	−74.1479	−45.9753	68.4641	−50.6366	−33.5237	
β_{xxz} (a.u.)	−0.0023	−0.0187	19.0587	−0.0081	−0.4942	8.4203	
β_{xzz} (a.u.)	0.0003	0.6595	−0.0023	−0.0014	1.1885	−0.0273	
β_{yzz} (a.u.)	−6.6711	5.8180	5.6594	−6.7243	5.9737	4.1979	
β_{yyz} (a.u.)	0.0063	3.6671	−7.0150	0.0047	4.1599	−11.3031	
β_{xyz} (a.u.)	2.4506	−1.8509	−0.0045	−4.3521	0.2714	−0.1038	
β (a.u.)	32.5350	54.6652	53.9850	3.2449	41.6321	36.409	
β (esu)	0.2811×10^{-30}	0.4723×10^{-30}	0.4664×10^{-30}	0.0280×10^{-30}	0.3597×10^{-30}	0.3146×10^{-30}	0.1947×10^{-30}
$\beta_{isomer}/\beta_{urea}$	1.4	2.4	2.4	0.1	1.8	1.6	

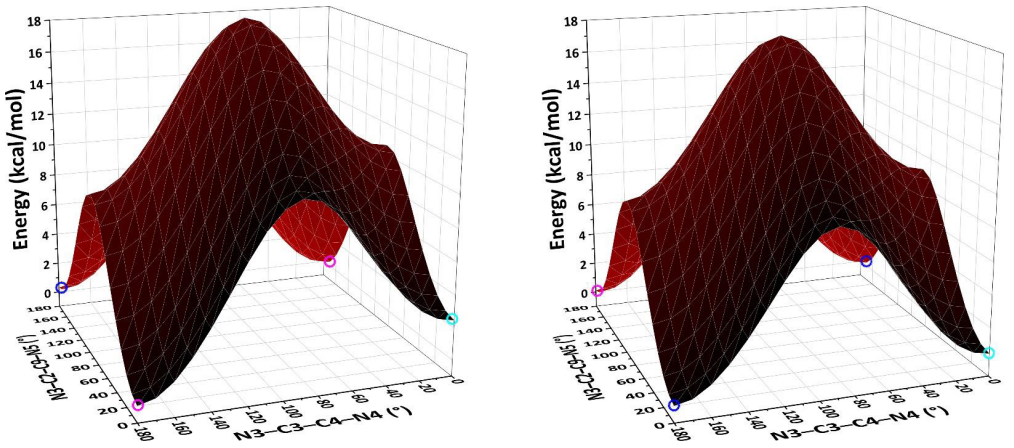
[a]For α 1 a.u. = 0.1482×10^{-24} esu, for β 1 a.u. = 8.6393×10^{-33} esu.

Supplementary Table S7. Best types of interactions and distances of NH_2Py_2T with Mpro, PLpro, Nsp3-AMP and Nsp3-MES

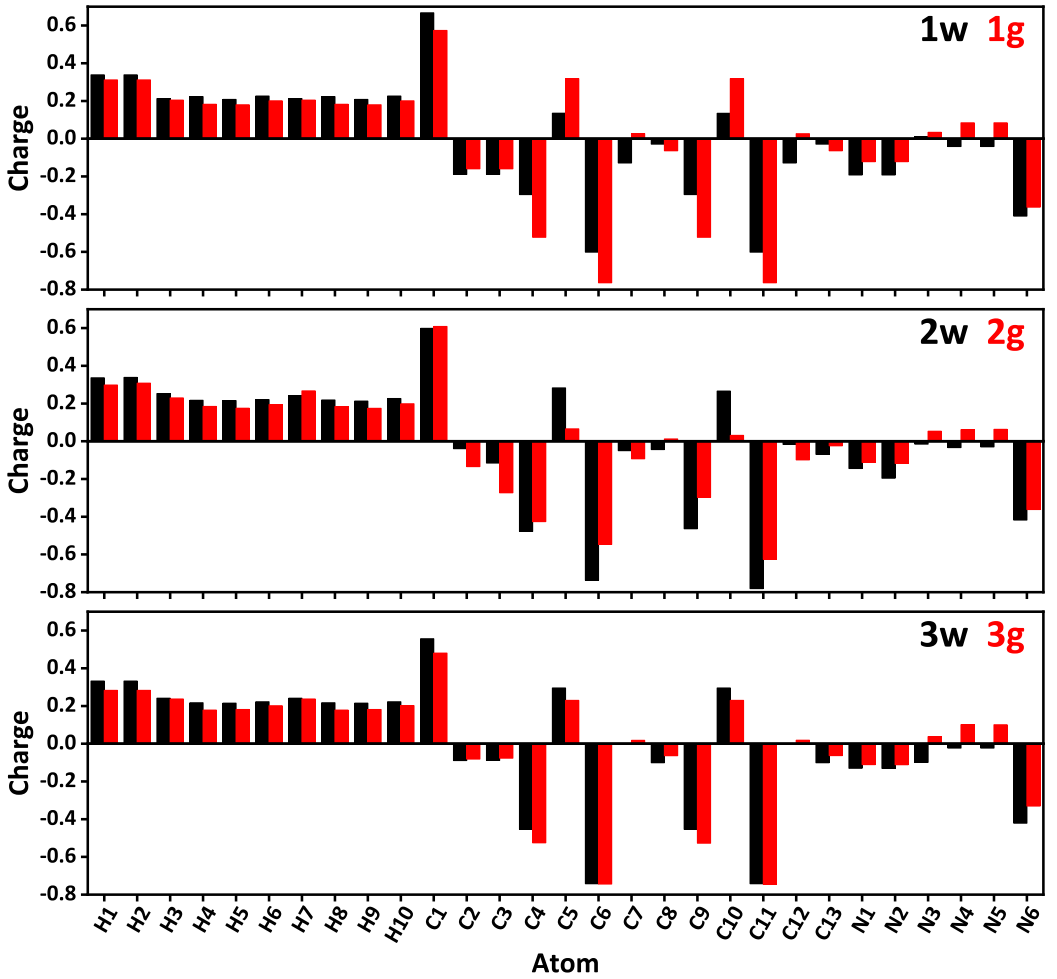
Interaction	Distance (Å)	Bonding	Bonding type
	Mpro–NH_2Py_2T		
:NH_2Py_2T:H - A:LEU141:O	2.00417	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:H - A:HIS163:NE2	2.27944	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:C - A:GLU166:O	3.68890	Hydrogen Bond	Carbon Hydrogen Bond
A:GLU166:HN - :NH_2Py_2T	3.14518	Hydrogen Bond	π···Donor Hydrogen Bond
A:CYS145:SG - :NH_2Py_2T	3.68801	Other	π···Sulfur
A:CYS145:SG - :NH_2Py_2T	5.11777	Other	π···Sulfur
:NH_2Py_2T - A:MET165	5.14145	Hydrophobic	π···Alkyl
	PLpro–NH_2Py_2T		
C:LYS157:HZ2 - :NH_2Py_2T:N	2.08513	Hydrogen Bond	Conventional Hydrogen Bond
C:ASP164:HN - :NH_2Py_2T:N	2.20309	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:C - C:ASP164:O	3.59065	Hydrogen Bond	Carbon Hydrogen Bond
C:GLU167:OE2 - :NH_2Py_2T	3.21013	Electrostatic	π···Anion
C:LYS157:CD - :NH_2Py_2T	3.34765	Hydrophobic	π···Sigma
C:GLY163:C,O - :NH_2Py_2T	3.76158	Hydrophobic	Amide···π Stacked
:NH_2Py_2T - C:CYS155	5.16693	Hydrophobic	π···Alkyl
	Nsp3-AMP–NH_2Py_2T		
A:PHE156:HN - :NH_2Py_2T:N	2.46109	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:H - A:ALA21:O	2.10985	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:H - A:ALA154:O	2.71772	Hydrogen Bond	Conventional Hydrogen Bond
A:VAL155:CA - :NH_2Py_2T:N	3.65923	Hydrogen Bond	Carbon Hydrogen Bond
A:PHE156 - :NH_2Py_2T	5.66828	Hydrophobic	π···π Stacked
:NH_2Py_2T - A:VAL49	4.98464	Hydrophobic	π···Alkyl
:NH_2Py_2T - A:ALA52	4.43473	Hydrophobic	π···Alkyl
:NH_2Py_2T - A:ALA129	4.63418	Hydrophobic	π···Alkyl
:NH_2Py_2T - A:VAL155	4.93637	Hydrophobic	π···Alkyl
	Nsp3-MES–NH_2Py_2T		
B:VAL49:HN - :NH_2Py_2T:N	2.51171	Hydrogen Bond	Conventional Hydrogen Bond
B:GLY130:HN - :NH_2Py_2T:N	2.31750	Hydrogen Bond	Conventional Hydrogen Bond
:NH_2Py_2T:C - B:ALA154:O	3.33627	Hydrogen Bond	Carbon Hydrogen Bond
B:VAL49:HN - :NH_2Py_2T	3.27215	Hydrogen Bond	π···Donor Hydrogen Bond
B:ALA38:CB - :NH_2Py_2T	3.70495	Hydrophobic	π···Sigma
B:PHE132 - :NH_2Py_2T	5.17216	Hydrophobic	π···π T-shaped
:NH_2Py_2T - B:LEU126	4.83753	Hydrophobic	π···Alkyl
:NH_2Py_2T - B:ALA129	4.48782	Hydrophobic	π···Alkyl
:NH_2Py_2T - B:VAL155	5.10269	Hydrophobic	π···Alkyl

Supplementary Table S8. Amino acid residues with the strongest fluctuations in complexes of NH_2Py_2T with the applied SARS-CoV-2 proteins, obtained using molecular dynamics

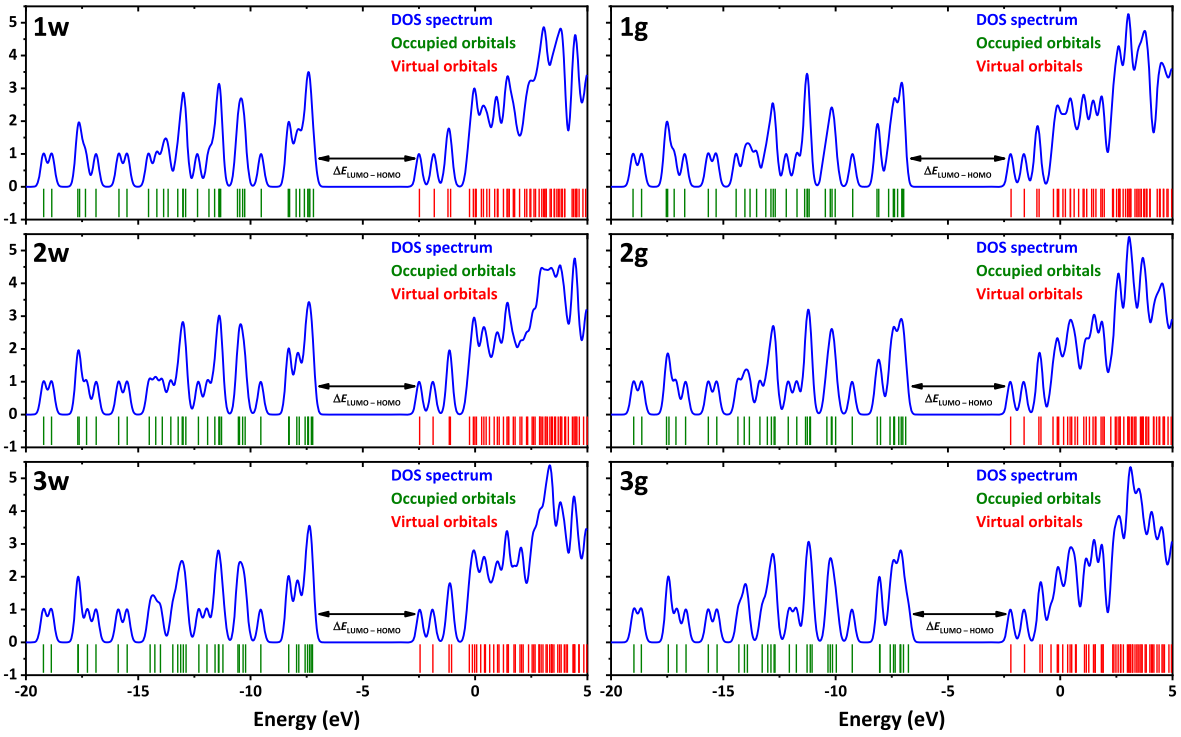
Mpro–NH_2Py_2T	Nsp3-AMP–NH_2Py_2T	Nsp3-MES–NH_2Py_2T
SER1	VAL3	VAL3
ARG4	ASN4	ASN4
LYS5	TYR42	TYR42
GLU47	ASN101	THR71
TYR154	LYS102	ASN72
ALA191	GLN118	LYS76
ALA193	HIS119	LYS102
ALA194	GLU120	GLN118
ARG222	ILE131	HIS119
PHE223	ARG148	GLU120
ASN277	PHE156	ILE131
THR304	GLU170	PHE132
		ARG141
		ARG148
		LEU169



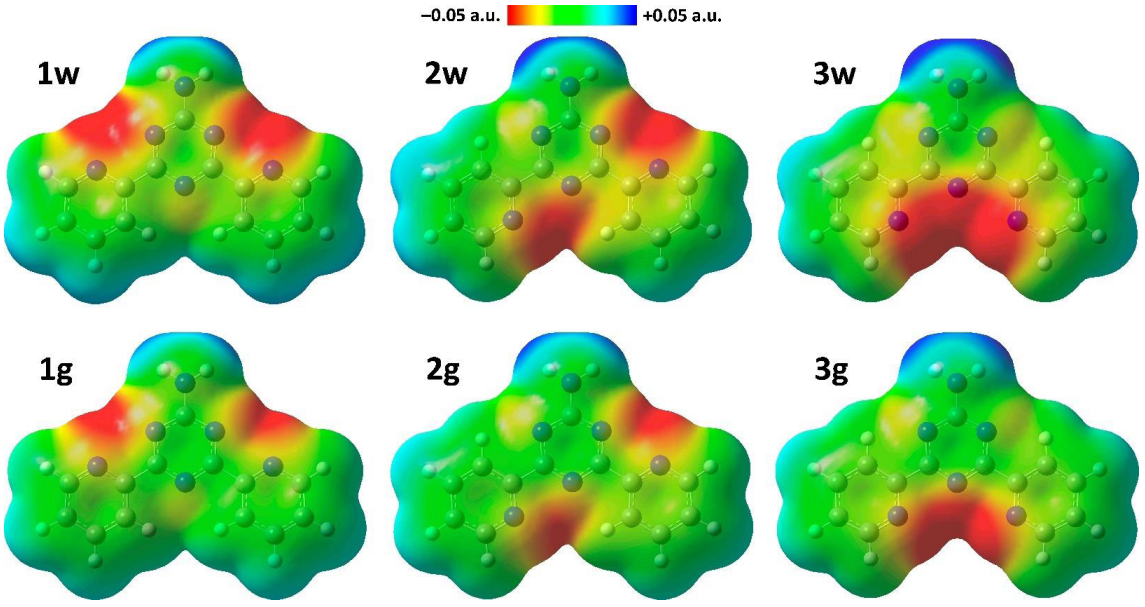
Supplementary Figure S1. Potential energy surface of the optimized structure of NH_2Py_2T in gas phase (left) and in water (right) depending on the N3–C3–C4–N4 and N3–C2–C9–N5 dihedral angles (see Figure 2 for atoms labelling). Circles highlight the isomer 1 (blue), isomer 2 (magenta) and isomer 3 (cyan).



Supplementary Figure S2. Mulliken atomic charges in the isomers of NH_2Py_2T (see Figure 2 for atoms labelling).



Supplementary Figure S3. The density-of-states (DOS) plots of the isomers of NH_2Py_2T.



Supplementary Figure S4. MEP surfaces of the isomers of NH_2Py_2T. Results under 0.02 a.u. isovalue.

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[2] A. Eme, S. M. Sağdınç, *J. Mol. Struct.*, 2017, **1147**, 322-334.