† Electronic Supplementary Information

Molecular structure, spectroscopic signatures and reactivity analyses of paracetamol hydrochloride monohydrate salt using density functional theory calculations

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Part I. FIGURES

Powder X-ray Diffraction (PXRD)

PXRD patterns for the samples were collected using an Empyrean X-ray diffractometer (PANalytical, The Netherlands) equipped with a PIXel3D detector and a monochromatic Cu Kα radiation X-Ray tube (1.54056Å). The tube voltage and amperage were set at 45 kV and 40 mA, respectively. Sample was prepared for analysis by pressing a thin layer of the sample onto a metal sample holder. Instrument calibration was performed using a silicon reference standard. Each sample was scanned 2θ range of 5° to 40°, increasing at a step size of 0.02° 2θ. The data were processed using High Score Plus Version 3.0 software (PANalytical, The Netherlands).

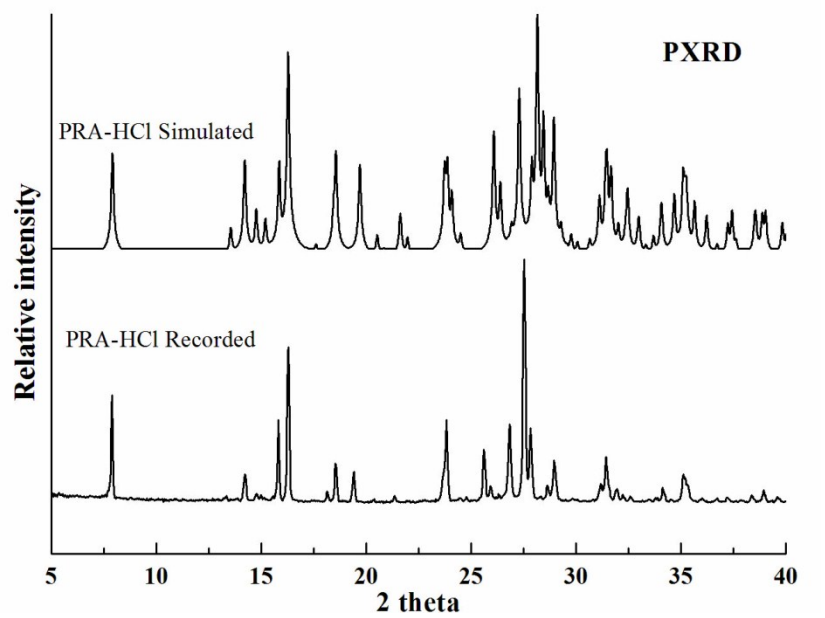

Fig.S1 PXRD overlapped of prepared PRA-HCl with its simulated pattern.

Differential scanning calorimetry (DSC)

The DSC profiles of the solid samples were generated in the range of (30–200 °C) using a TA Q1000 DSC instrument with a refrigerated cooling unit. Temperature calibration was performed using an indium metal standard at the respective heating rate. Samples (1–2 mg) were crimped in non-hermetic aluminum pans and scanned at a heating rate of 10 °C/min under a continuously purged dry nitrogen atmosphere (flow rate 50 mL/min) using a similar empty pan as a reference. The data were collected in triplicate for each sample and analyzed using a TA Instruments Universal Analysis 2000 version 4.5A software.

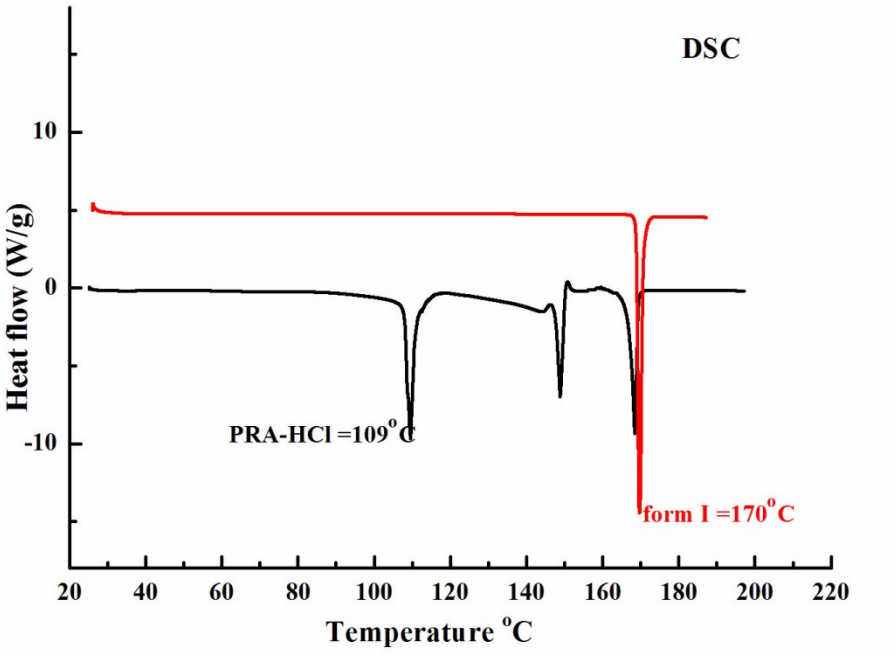

Fig.S2 DSC plot of form I (melting point 170 ^{O}C) and PRA-HCl (melting point 109 ^{O}C)

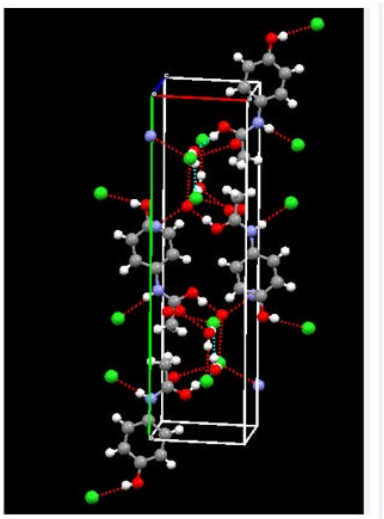

Fig.S3 Interactions between the molecules that are held together through hydrogen bonds in the crystal lattice of Paracetamol hydrochloride monohydrate salt (Cambridge Crystallographic Database (CSD) reference code is LATBUF)

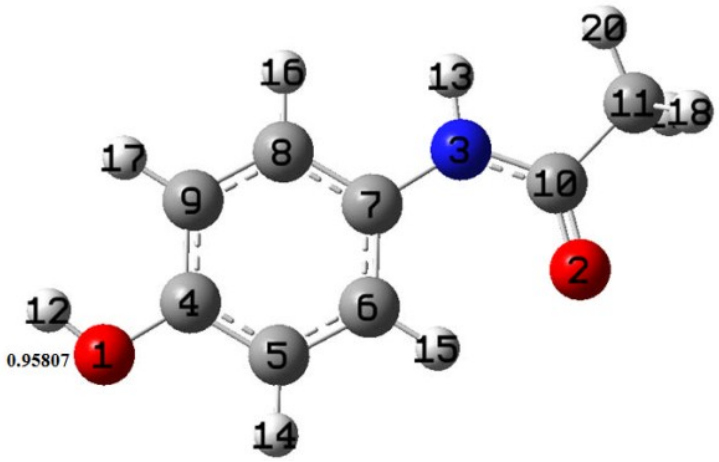

Fig.S4 Optimized geometry of the ground state of the form I using wB97X-D level of theory

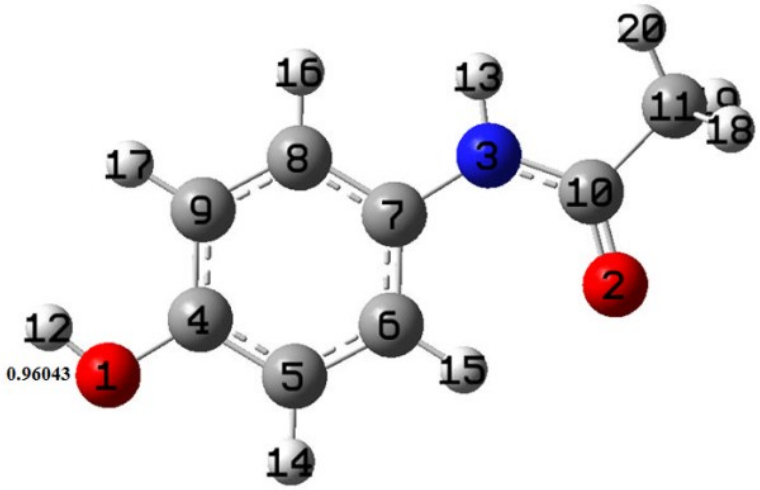

Fig.S5. Optimized geometry of the ground state of the form I using M062X level of theory

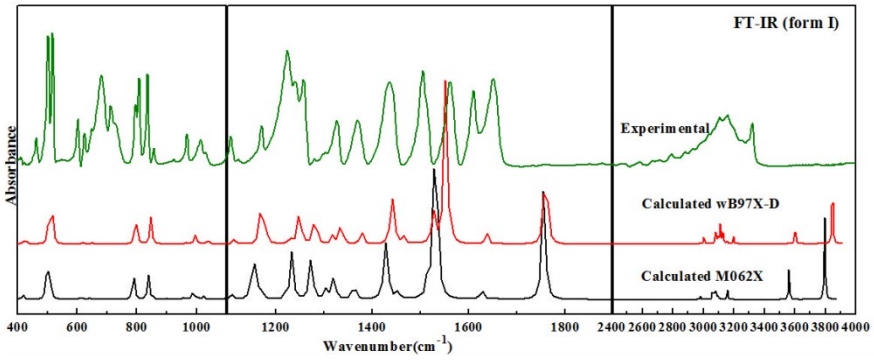

Fig.S6 Experimental and calculated FT-IR absorbance spectra for form I in the region 400-3800 cm^{-1}

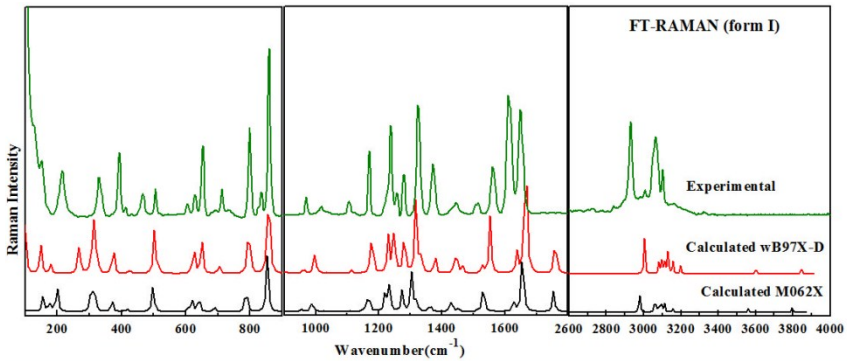

Fig.S7. Experimental and calculated FT-Raman spectra for form I in the region 100-3800 cm^{-1}

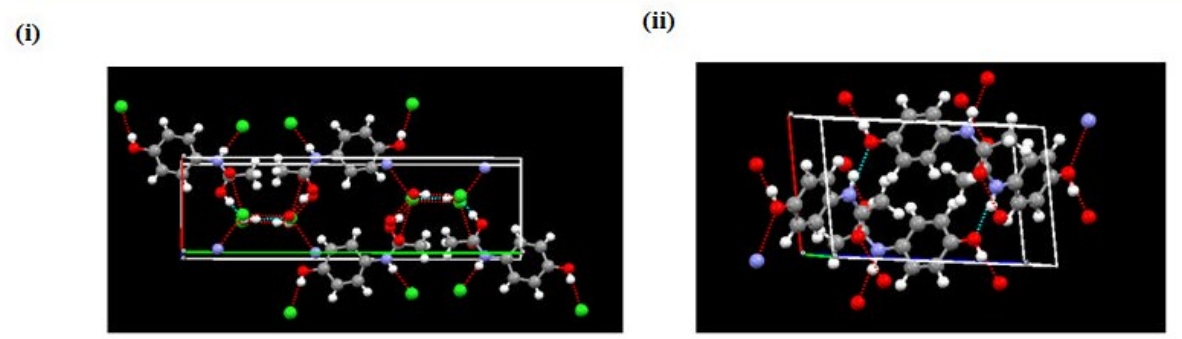

Fig.S8. Hydrogen bonding pattern in PRA-HCl (i) and form I (ii)

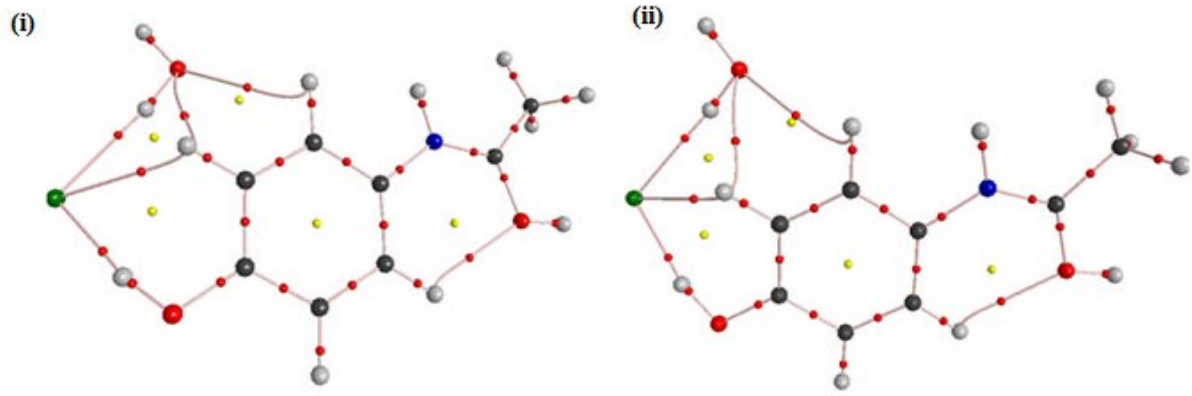

Fig.S9 Molecular graph of PRA-HCl using wB97X-D/6-311++G (d, p) (i) and M062X/6-311++G (d, p) (ii) method: bond critical points (small red spheres), ring critical points (small yellow sphere), bond paths (pink lines).

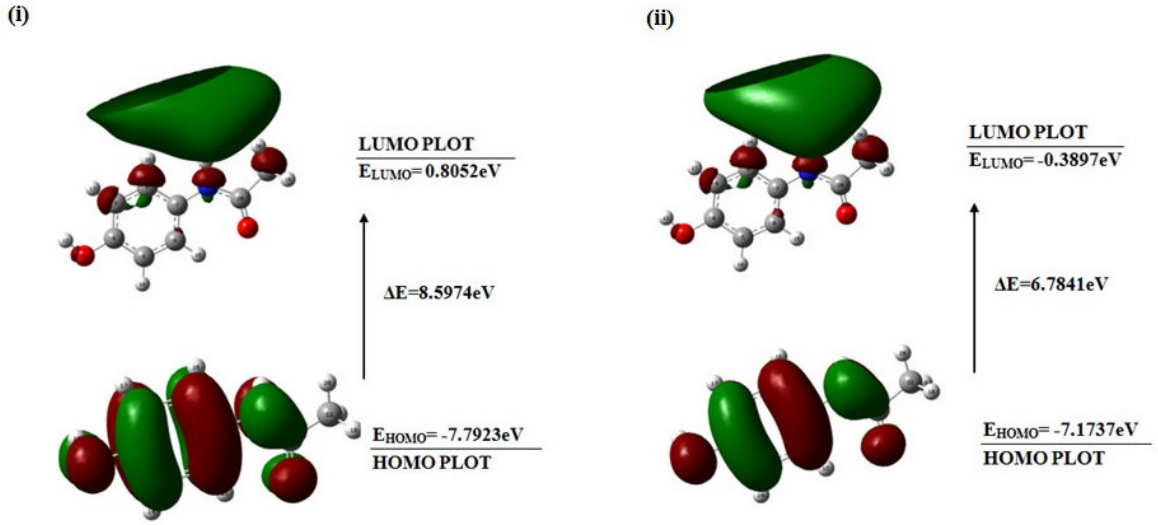

Fig.S10 HOMO-LUMO ~~energy band gap~~ energy gap of form I calculated at wB97X-D (i) and M062X (ii) level of theory.

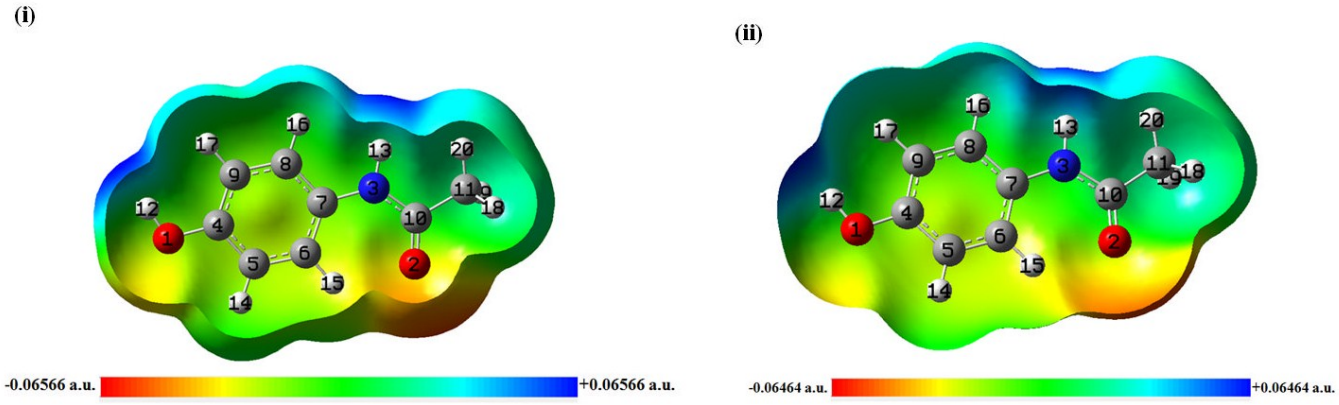

Fig.S11 Molecular electrostatic potential (MEP) formed by mapping of total density over electrostatic potential in the gas phase for the form I using wB97X-D (i) and M062X (ii) level of theory.

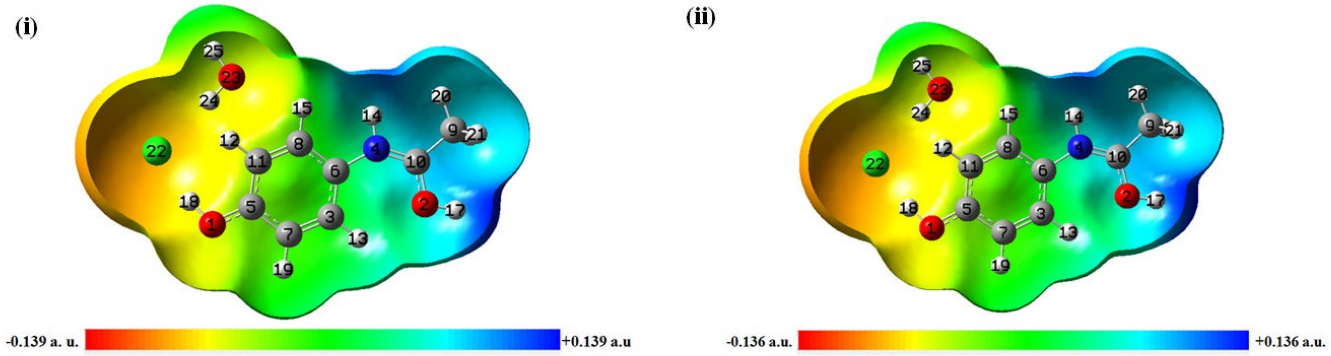

Fig.S12 Molecular electrostatic potential (MEP) formed by mapping of total density over electrostatic potential in the gas phase for the PRA-HCl using wB97X-D (i) and M062X (ii) level of theory

Part II. TABLES

Table S1 The experimental and calculated geometric parameters of PRA-HCl

Geometrical parameter	Experimental	Calculated optimised parameters	
		wB97X-D	M062X
Bond length(Å)			
O1-C5	1.36740	1.31442	1.31380
O1-H18	0.77636	1.01098	1.01817
O2-C10	1.28955	1.31816	1.32057
O2-H17	0.89226	0.96099	0.96366
C3-C6	1.38818	1.40018	1.40135
C3-C7	1.38619	1.38038	1.37991
C3-H13	0.95660	1.07947	1.07886
N4-C6	1.42998	1.41916	1.42111
N4-C10	1.30385	1.29416	1.29377
N4-H14	0.83265	1.01346	1.01531
C5-C7	1.38436	1.40867	1.40953
C5-C11	1.39060	1.40767	1.40890
C6-C8	1.39055	1.39961	1.40022
C7-H19	0.90958	1.08316	1.08250
C8-C11	1.38536	1.37054	1.37171
C8-H15	0.97486	1.08760	1.08736
C9-C10	1.48705	1.49012	1.48967
C9-H16	0.95434	1.09468	1.09352
C9-H20	0.99389	1.09000	1.08823
C9-H21	0.91871	1.09464	1.09328
C11-H12	0.93994	1.07974	1.07991
H18-Cl22	2.33422	1.96687	1.92975
Cl22-H24	2.27748	2.24899	2.25254
O23-H24	0.82440	0.97795	0.97770
O23-H25)	0.85312	0.95758	0.95919
Bond angle(º)			
C5-O1-H18	105.78625	109.68667	109.74251
C10-O2-H17	113.70125	111.36218	111.49552
C6-C3-C7	119.41436	118.94966	118.80901
C6-C3-H13	121.34886	121.50750	121.65067
C7-C3-H13	119.23305	119.52428	119.52585
C6-N4-C10	130.59158	133.61881	133.28968
C6-N4-H14	114.16720	112.14254	112.09688
C10-N4-H14	115.20180	114.23347	114.59325
O1-C5-C7	117.64867	118.99409	118.95926
O1-C5-C11	122.87441	122.15502	122.24087
C7-C5-C11	119.47296	118.84913	118.79947
C3-C6-N4	124.22122	124.81757	124.90367
C3-C6-C8	119.76704	120.43975	120.45720
N4-C6-C8	116.01036	114.71245	114.62059
C3-C7-C5	121.03545	121.05053	121.24008
C3-C7-H19	122.35471	120.49870	120.53479
C5-C7-H19	116.60932	118.40427	118.18232
C6-C8-C11	120.52404	120.36251	120.45697
C6-C8-H15	118.91791	121.53027	121.39273
C11-C8-H15	120.53576	118.06654	118.11568
C10-C9-H16	109.91647	109.68405	109.65323
C10-C9-H20	111.08790	111.48434	111.61460
C10-C9-H21	109.54061	109.66549	109.72449
H16-C9-H20	110.29352	108.59035	108.58094
H16-C9-H21	105.55530	108.55847	108.52880
H20-C9-H21	110.30069	108.79958	108.67492
O2-C10-N4	119.85843	118.41701	117.97896
O2-C10-C9	120.73835	119.82313	119.79369
N4-C10-C9	119.40288	121.75983	122.22728
C5-C11-C8	119.75611	120.08501	119.97290
C5-C11-H12	121.42798	119.31827	119.56579
C8-C11-H12	118.81511	120.48828	120.38187
O1-H18-Cl22	171.02612	166.46103	166.49120
H18-Cl22-H24	110.43713	103.13822	104.04524
H24-O23-H25	102.65058	103.08172	103.31641
Cl22-H24-O23	169.64754	168.00703	166.89119

Dihedral angle (º)			
H18-O1-C5-C7	-167.16164	-159.66488	-159.25626
H18-O1-C5-C11	13.56781	19.84723	20.50982
C5-O1-H18-Cl22	173.73147	35.08597	33.60096
H17-O2-C10-N4	-174.52358	179.28710	178.90036
H17-O2-C10-C9	5.26614	-0.77328	-1.00441
C7-C3-C6-N4	-178.47683	-175.60152	-175.82629
C7-C3-C6-C8	1.07802	2.28999	2.52072
H13-C3-C6-N4	0.81518	2.82355	2.78324
H13-C3-C6-C8	-179.62996	-179.28494	-178.86975
C6-C3-C7-C5	0.45197	0.25213	0.22749
C6-C3-C7-H19	-179.27768	177.73232	177.80415
H13-C3-C7-C5	-178.85515	-178.20476	-178.41220
H13-C3-C7-H19	1.41520	-0.72457	-0.83555
C10-N4-C6-C3	-12.70767	-4.82733	0.10860
C10-N4-C6-C8	167.72229	177.17375	-178.32403
H14-N4-C6-C3	164.86354	174.27433	178.34212
H14-N4-C6-C8	-14.70651	-3.72458	-0.09052
C6-N4-C10-O2	2.62953	-1.02327	-1.44290
C6-N4-C10-C9	-177.16300	179.03834	178.45941
H14-N4-C10-O2	-174.92142	179.88922	-179.64286
H14-N4-C10-C9	5.28605	-0.04917	0.25945
O1-C5-C7-C3	179.02459	175.10263	175.29551
O1-C5-C7-H19	-1.23085	-2.42908	-2.33651
C11-C5-C7-C3	-1.67911	-4.42579	-4.47871
C11-C5-C7-H19	178.06546	178.04250	177.88926
O1-C5-C11-C8	-179.37516	-173.36717	-173.70839
O1-C5-C11-H12	0.95427	2.86581	3.06341
C7-C5-C11-C8	1.36704	6.14562	6.05805
C7-C5-C11-H12	-178.30353	-177.62140	-177.17015
C3-C6-C8-C11	-1.38191	-0.55938	-0.92233
C3-C6-C8-H15	-179.67399	-178.19431	-178.74189
N4-C6-C8-C11	178.20853	177.53517	177.58649
N4-C6-C8-H15	-0.08355	-0.09976	-0.23307
C6-C8-C11-C5	0.15071	-3.71081	-3.42621
C6-C8-C11-H12	179.82989	-179.89922	179.82864
H15-C8-C11-C5	178.41503	174.00467	174.46354
H15-C8-C11-H12	-1.90580	-2.18374	-2.28161
H16-C9-C10-O2	48.42166	59.53182	60.76146
H16-C9-C10-N4	-131.78767	-120.53063	-119.13913
H20-C9-C10-O2	170.77175	179.84136	-178.87731
H20-C9-C10-N4	-9.43758	-0.22110	1.22210
H21-C9-C10-O2	-67.12544	-59.59914	-58.35033
H21-C9-C10-N4	112.66523	120.33840	121.74907
O1-H18-Cl22-H24	1.71564	-30.69836	-29.80798
H18-Cl22-H24-O23	-119.70919	-87.40457	-79.35208
H25-O23-H24-Cl22	8.54346	-75.25507	-84.57859

Table S2 Experimental and theoretical vibrational wavenumbers (cm^{-1}) of form I with potential energy distribution (PED)

Unscaled	**Scaled wB97X-D**	**Scaled M062X**	**FT-IR**	**FT-Raman**	**Assignment(%PED)**
3924	3846	3796	3321	-	[ν(O1H12)](100)
3676	3603	3562	3255	-	[ν(N3H13)](100)
3264	3199	3157	3159	-	R[ν(CH)](97)
3222	3157	3111			R[ν(CH)](97)
3194	3130	3093	3107	3102	R[ν(CH)](99)
3176	3113	3078			R[ν(CH)](99)
3162	3098	3065		3066	$\nu_a(C11H_3)$](100)
3145	3082	3059	3036		$\nu_a(C11H_3)$](99)
3066	3004	2978	2993	2981	$\nu_s(C11H_3)$](99)
1796	1760	1755	1651	1648	[ν(C10=O2)](77)+[ν(C10=N3)](5)
1700	1666	1656			R[ν(CC)(60) + δ_a(11)+δ_{in}(CH)(10)]
1671	1638	1627	1610	1611	R[ν(CC)(62)+δ_a'(7)] +[ρ(N3H13)](6)
			1562	1561	[ρ(N3H13)](37)+[ν(C10=N3)](17)+R[ν(N3C7)(12)+ν(CC)(7)+δ_{in}(CH)(6)]
1584	1553	1532			
1559	1527	1516	1504	1515	R[δ_{in}(CH)(42)+ν(CC)(29)+ν(O1C4)(9)]+[ρ(N3H13)](8)
1496	1466	1453		1477	$\delta_a(C11H_3)$(75)+ρ'$(C11H_3)$(6)+$\delta_{sym}(C11H_3)$(5)
1479	1449	1433	1435	1446	δ_a'$(C11H_3)$(84)+ρ$(C11H_3)$(7)
1470	1441	1427			R[ν(CC)(30)+δ_{in}(CH)(19)+(C4H12O1)(6)]+[ρ(N3H13)](6)+δ_a(C11H_3) (6)+[ν(C10=N3)](5)

1406	1378	1362	1369	1372	$\delta_{sym}(C11H_3)(81)+[\nu(C10C11)](8)+\delta_a(C11H_3)(7)$
1363	1335	1321	1327	1324	$R[\nu(CC)(60)+\delta_{in}(CH)](19)+\delta(C4H12O1)(14)]$
			1302		$R[\delta_{in}(CH)(42)+\nu(CC)(12)+\nu(N3C7)(10)+\nu(O1C4)(6)$
1345	1318	1305			$]+[\nu(C10=N3)](8)$
1307	1281	1274	1280	1280	$R[\nu(O1C4)](35)+R[\nu(CC)](32)+R[\delta_{in}(CH)](14)$
			1257	1257	$[\rho(N3H13)](17)+R[\delta_{in}(CH)](18)+\nu(N3C7)(9)$
1274	1249	1234			$+\nu(O1C4)(8)+\nu(CC)(13)+\delta tri(8)]+[\nu(C10=N3)](10)$
			1224	1238	$R[\nu(N3C7)(21)+\delta tri(9)]+[\nu(C10=N3)](14)+[\nu(C10C11)](11)+[\delta$
1255	1230	1221			$_{sci}(C10C11)](5)+[\rho(C10C11)](5)$
1203	1179	1168	1170	1170	$R[\delta_{in}(CH)(65)+\delta(C4H12O1)(12)]+R[\nu(CC)](9)$
1194	1170	1154			$R[\delta(C4H12O1)(42)+\delta_{in}(CH)(15)+\nu(CC)(22)]$
1137	1114	1108	1107	1106	$R[\delta_{in}(CH)(63)+\nu(CC)(24)]$
			1031	1035	$\rho(C11H_3)(41)+\rho'(C11H_3)(32)+\delta_a'(C11H_3)(9)+$
1060	1038	1026			$[\omega(C10C11)](17)$
1035	1014	1004	1014	1017	$R[\delta_{tri}(39)+\nu(CC)(39)+\delta_{in}(CH)(10)]$
				994	$\rho'(C11H_3)(35)+\rho(C11H_3)(26)+[\nu(C10C11)](8)+R[\delta_{tri}](6)+[\nu(C1$
1018	997	988			$0=N3)](5)$
1002	982	965	968	969	$R[\delta_{out}(CH)(86)+puck(5)+\tau_a'(5)]$
				950	$[\nu(C10C11)](30)+[\delta_{sci}(C10C11)](17)+[\nu(C10=N3)](15)+[\delta_{sci}(N$
981	961	955			$3H13)]\ 15)+R[\nu(CC)](5)$
927	909	899	923	915	$R[\delta_{out}(CH)](77)+\ R[puck](14)$
			856	860	$R[\nu(CC)(46)+\delta_a(14)+\nu(N3C7)(10)+\nu(O1C4)(8)]+[\delta_{sci}(N3H13)]($
876	858	853			$6)$
864	846	838	835	836	$R[\delta_{out}(CH)(71)+\delta_{out}(C4O1)(9)+\tau_a(8)]$
814	798	790	806	798	$R[\delta_{out}(CH)\ (80)+\delta_{out}(C7N3)(5)+\tau_a\ (5)]$
			796		$R[\delta_{tri}(27)+\nu(O1C4)(16)+\nu(CC)(6)+\nu(N3C7)(5)]+[\delta_{sci}(N3H13)]($
812	796	788			$12)+[\nu(C10C11)](8)+[\delta_{sci}(C10C11)](6)$
717	703	688	711	711	$R[puck(65+\delta_{out}(C4O1)(15)+\delta_{out}(C7N3)(14)]$
663	650	641	650	653	$R[\delta_a'(55)+\delta_{in}(C4O1)(6)+\delta_{in}(C7N3)(5)]+[\nu(C10C11)](6)$
			624	628	$R[\delta_a'(19)+\delta_a(9)]+[\omega(C10C11)](15)+[\delta_{sci}(C10C11)](13)+[\nu(C10$
639	627	620			$C11)](11)+[\delta_{sci}(N3H13)](6)+\rho(C11H_3)(5)$
630	617	609	603	605	$[\omega(C10C11)](49)+[\tau(C10=N3)](9)+\rho'(C11H_3)(8)+\ \rho(C11H_3)(6)$
528	517	509	516	514	$R[\delta_{out}(C4O1)](31)+R[\tau_a](30)+R[\delta_{out}(C7N3)](27)$
524	513	502			$[\omega(N3H13)](46)+[\tau(C10=N3)](24)+[\omega(C10C11)](15)$
513	502	497	501	505	$[\rho(C10C11)](38)+R[\delta_a](34)+[\delta_{sci}(C10C11)](7)+\rho'(C11H_3)(6)$
436	427	418	422	431	$R[\delta_{in}(C4O1)(52)+\delta a'(18)+\delta_{in}(C7N3)(14)]+[\delta_{sci}(C10C11)](7)$
422	414	407	412	414	$R[\tau_a'(81)+\delta_{out}(CH)(11)]$
			-	393	$R[puck(35)+\delta_{out}(C4O1)(19)+\delta_{out}(C7N3)(18)+\delta_{out}(C9H17)(6)]+$
382	374	370			$[\tau(C10=N3)](6)$
			-	329	$[\rho(C10C11)](28)+R[\delta_{in}(C7N3)(15)+\delta_a(12)+\delta_{in}(C4O1)(9)+\nu(N3$
329	323	320			$C7)(6)]+[\delta_{sci}(C10C11)](14)+[\delta_{sci}(N3H13)](5)$
			-		$R[\delta_{in}(C7N3)](23)+\delta_a(10)+\delta_{in}(C4O1)(9)+\nu(N3C7)(5)+\nu(CC)(5)]$
					$+[\delta_{sci}(N3H13)](18)+[\delta_{sci}(C10C11)](9)+[\nu(C10=N3)](9)+[\rho(C10$
318	311	307			$C11)](5)$
274	269	200	-	286	$R[\tau(C4O1)(90)+\tau_a'(5)+\delta_{out}(C4O1)(3)]$
183	179	176	-	171	$R[\tau_a(57)+\delta_{out}(CH)(9)]+[\tau(C10=N3)](13)+[\omega(N3H13)](10)$
			-	152	$[\delta_{sci}(N3H13)](46)+R[\delta_{in}(C7N3)(33)+\delta_{in}(C4O1)(3)]+$
152	149	156			$[\rho(C10C11)](9)$
99.4	97.4	76.7	-		$[\tau(C10C11)](77)+[\omega(C10C11)](7)+R[\tau_a]\ (6)$
			-	-	$[\tau(C10=N3)](32)+[\omega(N3H13)](23)+R[\tau_a(15)+\delta out(C7N3)(6)]+$
63.7	62.5	56			$[\tau(C10C11)]12)+[\omega(C10C11)](4)$
			-	-	$R[\tau(C7N3)(62)+\delta_{out}(C7N3)(8)+\delta_{out}(CH)(3)]+$
					$[\tau(C10C11)](13)+[\tau(C10=N3)](5)+[\omega(C10C11)](4)+[\omega(N3H13)$
34.5	33.8	33.1			$](3)$

Table S3 Experimental and theoretical vibrational wavenumbers (cm^{-1}) of PRA-HCl and their assignments using wB97X-D/ 6-311++G (d, p) level of theory

Unscaled	Scaled	FT-IR	FT-Raman	PED
3954	3875			$[\nu(O23H25)](56)+[\delta(H25O23Cl22)](44)$
3889	3811			$[\nu(O2H17)](100)$
3599	3527	3323		$[\nu(N4H14)](99)$
3570	3498	3248		$[\nu(O23H24)](67)+[\nu(H24Cl22)](28)$
3251	3186	3176	3175	$R[\nu(CH)](94)$
3250	3185			$R[\nu(CH)](93)$
3221	3157	3163	3149	$R[\nu(CH)](99)$
3174	3110	3109	3102	$R[\nu(CH)](97)$
3162	3098			$[\nu_a(C9H_3)](100)$
3115	3053	3065,	3071	$[\nu_a(C9H_3)](99)$

3037	2976	2972	2987	[ν_s($C9H_3$)](100)
2930	2871	2887	2876	[ν(O1H18)](92)+[ν(H18Cl22)](7)
1782	1747	-	1685	[ν(C10=N4)](60)+[ρ(N4H14)](9)+[ν(C10O2)](5)
1683	1649	1653	1623	[δ(H25O23Cl22)](51)+[τ(C8O23)](32)+[δ(H24O23H25)](14)
				R[ν(CC)(33)+ν(C5O1)(11)+δ_a'(7)]+[δ(C11C8O23)](10)+[τ(C8O23)](9)+[δ(H25O23Cl22)](8)
1664	1631			
		1610	1604	R[ν(CC)(37)+δ_a'(9)+δ_{in}(C5O1)(7)+δ(C5H18O1)(6)]+[δ(C5O1Cl22)](10)+[τ(C8O23)](6)+[ρ(N4H14)](5)
1646	1613			
		1564	1577	[ρ(N4H14)](39)+[ν(C10O2)](13)+[δ(C5O1Cl22)](6)+R[δ(C5H18O1)(5)+ν(C5C11)(5)]
1585	1553			
1562	1531	1508	1509	R[ν(C5O1)(43)+δ_{in}(CH)(10)+ν(C6C8)(5)]+[δ(C5O1Cl22)](23)
		1473		R[ν(CC)](27)+δ(C5H18O1)(14)+δ_{in}(CH)(12)+δ_{in}(C5O1)(5)+[δ(C11C8O23)] 10)+[δ(C5O1Cl22)](7)
1521	1491			
1477	1447	1435	1455	δ_a'($C9H_3$)(50)+δ_a($C9H_3$)(18)+δ_{sym}($C9H_3$)(8)
1461	1432		1420	δ_a($C9H_3$)(65)+δ_a'($C9H_3$)(25)+ρ($C9H_3$)(7)
1457	1428	1410		R[ν(CC)(44)+δ(C5H18O1)(19)+δ_{in}(C3H13)(7)]+[δ(C11C8O23)](12)
1437	1409			δ_{sym}($C9H_3$)(54)+[ν(C9C10)](13)+δ_a'($C9H_3$)(5)
		1362	1375	δ_{sym}($C9H_3$)(17)+[ν(C10O2)](12)+R[ν(C5O1)(6)+δ_{in}(CH)(11)+ν(CC)(5)]+[δ(C10H17O2)](5)+[δ_{sci}(C9C10)](5)
1391	1363			
1382	1355	1344	1344	R[ν(C5O1)](54)+[δ(C5O1Cl22)](32)
		1284	1284	[δ(C10H17O2)](17)+R[δ_{in}(C3H13)](10)+ν(CC)](15)+ν(N4C6)](7)]+[ν(C10O2)](7)+[ρ(N4H14)](6)+[τ(C8O23)](5)
1321	1295			
		1259	1274	R[δ_{in}(CH)(28)+δ_{in}(C5O1)(14)+ν(CC)(26)+δ(C5H18O1)(8)]+[δ(C5O1Cl22)](6)
1291	1266			
		1244	1228	[δ(C10H17O2)](18)+R[ν(N4C6)(15)+ν(CC)(10)+δ_{in}(CH)(9)]+[ν(C10O2)](8)+[ρ(N4H14)](8)+[ν(C10=N4)](5)
1263	1237			
		1173	1181	[δ(C10H17O2)](18)+R[δ_{in}(CH)(25)+ν(N4C6)(11)+ν(CC)(11)+δ_{tri}(6)]+[ν(H12Cl22)](7)
1210	1186			
				R[δ_{in}(CH)](42)+ν(C5O1)(7)+ν(N4C6)(7)+ν(CC)(11)]+[ν(H12Cl22)](8)
1193	1169			
1141	1118	1109	1121	R[δ_{in}(CH)(47)+ν(CC)(15)]+[ν(H12Cl22)](7)+[δ(C11C8O23)] (6)
1059	1038	1041	1041	ρ($C9H_3$)(59)+ρ'($C9H_3$)(19)+[ω(C9C10)](9)+δ_a($C9H_3$)(7)
1048	1027	1016	1015	ρ'($C9H_3$)(55)+ρ($C9H_3$)(16)+δ_a'($C9H_3$)(6)
1026	1005		993	R[δ_{out}(CH)(42)+δ_{tri}(15)]+[ν(H12Cl22)](9)+[δ(H25O23Cl22)](8)
1018	998	970	983	R[δ_{out}(CH)](42)+δ_{tri}(11)]+[ν(H12Cl22)](19)+[τ(C8O23)](5)
961	941	947	950	R[δ_{out}(CH)(74) +puck(11)]
		935		[ν(C9C10)](34)+[ν(C10O2)](21)+[δ_{sci}(C9C10)](8)+[δ_{sci}(N4H14)](7)+[δ(C10H17O2)](6)
950	931			
901	883			R[τ(C5O1)(79)+δ_{out}(C8H15)(6)]
		856	861	[δ(C5O1Cl22)](17)+[τ(C8O23)](14)+R[δ_{out}(C8H15)(11)+ν(C5O1)(10)+δ_a'(7)]
878	861			
868	851			R[δ_{out}(CH)(29)+δ_{out}(C5O1)(8)+τ_a'(8)+ν(C5O1)(6)+δ_a'(5)]
		822	800	R[δ_{out}(CH)(22)+[τ(C8O23)](15)+ν(C5O1)(10)+δ_{out}(C5O1)(9)+δ_{tri}(8)]+[δ(C5O1Cl22)](5)+[δ_{sci}(N4H14)](5)
829	812			
		808		R[δ_{out}(CH)(27)+δ_{out}(C5O1)(7)+δ_{tri}(6)+ν(C5O1)(11)]
822	806			+[δ(C5O1Cl22)](16)+[δ_{sci}(N4H14)](5)
		796		[ω(N4H14)](50)+[τ(C10=N4)](21)+R[δ_{out}(C8H15)](8)+[τ(C8O23)](7)
791	775			
		712	707	[τ(C8O23)](32)+R[puck(19)+δ_{out}(C5O1)(12)+δ_{out}(CH)(5)]+
728	714			[δ(H25O23Cl22)](17)+[ν(H24Cl22)](6)
		687	684	R[puck(29)+δ_{out}(C5O1)(12)]+[τ(C8O23)](18)+[δ(H25O23Cl22)](16)+ν(H24Cl22)](10)
692	678			
659	646	646	647	R[δ_a(23)+δ_{in}(C5O1)(12)+δ_a'(7)]+[τ(C8O23)](21)+[ν(H12Cl22)](7)
		623	622	R[δ_a'](48)+[δ(C5O1Cl22)](13)+[τ(C8O23)](10)+[δ_{sci}(C9C10)](5)+[δ_{sci}(N4H14)](5)
622	609			
		602	599	[ω(C9C10)](51)+[ω(N4H14)](13)+R[δ_{out}(N4C6)](6)+[τ(C10=N4)](5)+ρ($C9H_3$)(5)
594	582			
		519	510	R[δ_{out}(C5O1)(23)+τ_a'(20)+δ_{out}(N4C6)(10)+puck(8)+τ_a(6)]+[δ(C5O1Cl22)](8)+[δ(H25O23Cl22)](6)
519	508			
		503	479	[ρ(C9C10)](19)+R[δ_a'(17)+δ_a(10)+δ_{in}(C5O1)(6)]+[τ(C8O23)](15)+[δ(H25O23Cl22)](8)
491	481			
472	463	443	445	R[δ_{in}(C5O1)(37)+δ_a'(8)]+ [δ(C5O1Cl22)](37)
427	419		414	[δ(H25O23Cl22)](34)+[τ(C8O23)](30)+R[τ_a(14) +τ_a'(9)]
386	378	-	389	[δ(H25O23Cl22)](58)+[τ(C8O23)](37)+[δ(H25O23C8)](5)
375	368	-	370	[δ(H25O23Cl22)](53)+[τ(C8O23)](35)+[δ(H25O23C8)](5)
353	346	-	339	[δ(H25O23Cl22)](41)+[τ(C8O23)](34)+[τ(C10O2)](7)
		-		R[δ_{in}(N4C6)(20)+δ_a'(16)+δ_{in}(C5O1)(6)]+[δ_{sci}(C9C10)](16)+[δ(C11C8O23)](8)+[ρ(C9C10)](8)+[δ_{sci}(N4H14)](5)+[ν(H18Cl22)](5)
339	332			
		-		[δ(C5O1Cl22)](34)+[δ(H25O23Cl22)](18)+R[δ_a'](8)+[ρ(C9C10)](6)+[δ(C11C8O23)](5)
327	320			
219	214	-	213	[δ(C5O1Cl22)](54)+[ν(H18Cl22)](13)+[ν(H24Cl22)](12)+[δ(C11C8

				O23)](5)
208	204	-		[τ(C8O23)](59)+[ν(H24Cl22)](9)+[δ(C5O1Cl22)](7)+ R[τ_a'](6)
176	172	-	185	[τ(C8O23)](52)+[δ(H25O23Cl22)](28)+[δ(H25O23C8)](16)
169	166	-	156	[τ(C8O23)](73)+[δ(H25O23C8)](16)+[δ(H25O23Cl22)](6)
152	149	-		[ν(H24Cl22)](53)+[τ(C8O23)](19)+[δ(H25O23Cl22)](19)
139	137	-		[τ(C8O23)](41)+[δ(H25O23Cl22)](26)+[δ(C11C8O23)](14)+[ν(H24 Cl22)](9)+[τ(C9C10)] (5)
135	132	-	-	[τ(C8O23)](65)+[δ(H25O23Cl22)](14)+[δ(C11C8O23)](11)+[δ(C5 O1Cl22)](6)
93.4	91.5	-	-	[ν(H12Cl22)](30)+[ν(H24Cl22)](21)+[δ(H25O23C8)](17)+[τ(C8O2 3)](10)+[δ(H25O23Cl22)](7)
76.4	74.8	-	-	[δ(C5O1Cl22)](45)+[δ(H25O23C8)](14)+R[τ(C5O1)](8)+[ν(H12Cl2 2)](8)+[δ(C11C8O23)](7)
37	36.2	-	-	[τ(C8O23)](65)+[δ(H25O23C8)](16)+[δ(C6C8O23)] (9)+[δ(C11C8O23)](7)
31.3	30.6	-	-	[δ(C5O1Cl22)](42)+[δ(C11C8O23)](22)+[δ(H25O23Cl22)](10)+[δ(H25O23C8)](6)+R[τ(C5O1)](5)+[δ(C6C8O23)](5)
22.9	22.4	-	-	[δ(H25O23C8)](24)+[δ(C5O1Cl22)](15)+[τ(N4C6)](15)+[τ(C8O23)](11)+[δ(C6C8O23)](8)+[δ(C11C8O23)](7)

Table S4 Experimental and theoretical vibrational wavenumbers (cm^{-1}) of PRA-HCl and their assignments using M062X/ 6-311++G (d, p) level of theory

Unscaled	Scaled	FT-IR	FT-Raman	PED
3957	3838			[ν(O23H25)](57)+[δ(H25O23Cl22)](42)
3879	3763			[ν(O2H17)](100)
3598	3490	3248		[ν(O23H24)](70)+[ν(H24Cl22)](24)
3567	3460	3323		[ν(N4H14)](99)
3277	3179	3176	3175	R[ν(CH)](98)
3261	3163	3163	3149	R[ν(CH)](94)
3207	3111	3109	3102	R[ν(CH)](98)
3172	3078	3065	3071	[$\nu_a(C9H_3)$](100)
3164	3069			R[ν(CH)](98)
3123	3029			[$\nu_a(C9H_3)$](99)
3055	2964	2972	2987	[$\nu_s(C9H_3)$](100)
2787	2704	2887	2876	[ν(O1H18)](93)+[ν(H18Cl22)](6)
1783	1730	-	1685	[ν(C10=N4)](61)+[ρ(N4H14)](7)+[ν(C10O2)](5)
1672	1622	1653	1623	[δ(H25O23Cl22)](19)+R[ν(CC)(25)+ν(C5O1)(8)+δ_a'(6)]+[δ(C11C8O23)](7)+[τ(C8O23)](6)+[δ(H24O23H25)](6)
1663	1613			[δ(H25O23Cl22)](49)+[τ(C8O23)](27)+[δ(H24O23H25)](16)
1644	1595	1610	1604	R[ν(C3C6)(44)+δ_a'(8)+δ_{in}(C5O1)(6)+δ(C5H18O1)(5)]+[δ(C5O1Cl22)](7)+[τ(C8 O23)](6)
1565	1518	1508	1509	R[ν(C5O1)(39)+ν(CC)(5)+δ_{in}(CH)](10)]+[δ(C5O1Cl22)](17)
1560	1514	1564	1577	[ρ(N4H14)](24)+R[ν(C5O1)(15)+ν(C5C11)(6)]+[δ(C5O1Cl22)](15)+[ν(C10O2)](11)
1522	1477	1473		R[ν(CC)(38)+δ_{in}(CH)(7)+δ(C5H18O1)(6)]+[δ(C11C8O23)] 12)
1483	1439	1435	1455	δ_a'($C9H_3$)(59)+δ_{sym}($C9H_3$)(10)+δ_a($C9H_3$)(10)+[ν(C10O2)](5)
1475	1431		1420	$\delta_a(C9H_3)$(76)+ δ_a'($C9H_3$)(14)+ρ($C9H_3$)(6)
1446	1403	1410		R[ν(CC)(41)+R[δ(C5H18O1)(25)+δ_{in}(CH)(5)]+[δ(C11C8O23)](6)+[δ(C5O1Cl22)](5)
1432	1390	1362	1375	$\delta_{sym}(C9H_3)$(56)+[ν(C9C10)](11)+δ_a'($C9H_3$)(9)+[ρ(N4H14)](6)
1389	1348			R[ν(C5O1)](43)+δ_{in}(CH)(5)]+[δ(C5O1Cl22)](26)+δ_{sym}($C9H_3$)(5)
1383	1342	1344	1344	R[ν(C5O1)(41)+δ_{in}(CH)(11)]+[δ(C5O1Cl22)](20)
1321	1281	1284	1284	[δ(C10H17O2)](20)+R[δ_{in}(CH)(11)+ν(CC)(10)+ν(N4C6)(9)]+[ρ(N4H14)](8)+[ν(C10O2)](7)
1282	1243	1259	1274	R[δ_{in}(CH)(23)+δ(C5H18O1)(14)+ν(C5C11(27)+δ_{in}(C5O1)(12)]+[δ(C5O1Cl22)](6)
1254	1216	1244	1228	[δ(C10H17O2)](18)+R[ν(N4C6)(14)+ν(CC)(9)+δ_{in}(CH)(9)]+[ρ(N4H14)](11)+[ν(C10O2)](8)+[ν(C10=N4)](5)
1212	1176	1173	1181	[δ(C10H17O2)](19)+R[δ_{in}(CH)(28)+ν(N4C6)(10)+δ_{tri}(6)+ν(CC)(10)]+[ν(H12Cl2 2)](6)
1190	1154			R[δ_{in}(CH)(38)+ν(N4C6)(10)+ν(CC)(7)+ν(C5O1)(7)]+[δ(C10H17O2)](5)+[ν(H12Cl22)](5)
1153	1119	1109	1121	R[δ_{in}(CH)(49)+ν(CC)(19)]+[ν(H12Cl22)](7)+δ(C11C8O23)(5)
1057	1025	1041	1041	ρ($C9H_3$)(49)+ρ'($C9H_3$)(28)+[ω(C9C10)](9)+δ_a($C9H_3$)(8)
1043	1012	1016	1015	ρ'($C9H_3$)(45)+ρ($C9H_3$)(26)+δ_a'($C9H_3$)(6)
1019	988		993	R[δ_{tri}(43)+ν(CC)(32)+δ_{in}(CH)(5)]
1008	978	970	983	R[δ_{out}(CH)](66) +[ν(H12Cl22)](16)
966	938	947	950	R[δ_{out}(CH)(78)+puck(11)]
955	927	935		[ν(C9C10)](35)+[ν(C10O2)](24)+[δ_{sci}(N4H14)](8)+[δ_{sci}(C9C10)](8)

				+[δ(C10H17O2)](5)+[ν(C10=N4)](5)
885	859	856	861	R[τ(C5O1)(18)+ν(C5O1)(13)+ν(CC)(23)+δ_a'(9)]+[δ(C5O1Cl22)](12)
876	850			R[δ_{out}(CH)(22)+τ(C5O1)(21)+δ_{out}(C5O1)(8)+ν(C5O1)(5)+τ_a'(5)]+[δ(C5O1Cl22)](10)+[τ(C8O23)](6)
859	833	822	800	R[δ_{out}(CH)(43)+τ(C5O1)](14)+δ_{out}(C5O1)(13)+τ_a'(9)]
829	804	808		R[δ_{out}(CH)(49)+δ_{out}(C5O1)(7)+δ_{tri}(5)]+[τ(C8O23)](9)
820	795			[δ(C5O1Cl22)](15)+ν(C5O1)(14)+δ_{tri}(12)+τ(C5O1)(5)+δ_{out}(CH)(5)]+[δ_{sci}(N4H14)](9)+[δ_{sci}(C9C10)](5)
789	766	796		[ω(N4H14)](47)+[τ(C10=N4)](21)+R[δ_{out}(CH)](13)
707	686	687	684	R[puck(39)+δ_{out}(C5O1)(21)]+[τ(C8O23)](14)+[δ(H25O23Cl22)](5)
673	653	712	707	[τ(C8O23)](28)+[ν(H24Cl22)](19)+[δ(H25O23Cl22)](18)+R[puck] (12)
653	633	646	647	[τ(C8O23)](30)+R[δ_a(16)+δ_{in}(C5O1)(8)]+[ν(H24Cl22)](9)+[δ(H25O23Cl22)](5)+[ν(H12Cl22)](5)
619	601	623	622	R[δ_a'](46)+[δ(C5O1Cl22)](11)+[τ(C8O23)](9)+[δ_{sci}(C9C10)](7)+[δ_{sci}(N4H14)](6)
594	576	602	599	[ω(C9C10)](50)+[ω(N4H14)](13)+R[δ_{out}(N4C6)](7)+[τ(C10=N4)](5)+ρ($C9H_3$)(5)
515	500	519	510	R[δ_{out}(C5O1)(21)+τ_a'(19)+δ_{out}(N4C6)(11)+puck(10)+τ_a(7)]+[δ(H25O23Cl22)](8)+[δ(C5O1Cl22)](6)
486	471	503	479	[ρ(C9C10)](21)+R[δ_a'(20)+δ_a(9)]+[τ(C8O23)](12)+[δ(H25O23Cl22)](8)+[δ(C5O1Cl22)](5)+[δ_{sci}(C9C10)](5)
465	452	443	445	R[δ_{in}(C5O1)(39)+δ_a'(6)]+δ(C5O1Cl22)](32)
424	411		414	[δ(H25O23Cl22)](40)+[τ(C8O23)](25)+R[τ_a(13)+τ_a'(8)]+[δ(H25O23C8)](5)
397	385	-	389	[δ(H25O23Cl22)](63)+[τ(C8O23)](24)+[δ(H25O23C8)](13)
379	367	-	370	[δ(H25O23Cl22)](30)+[τ(C10O2)](25)+[τ(C8O23)](10)+[ω(C9C10)](9)+[δ(H25O23C8)](8)
359	349	-	339	[δ(H25O23Cl22)](33)+[τ(C8O23)](14)+[τ(C10O2)](12)+[δ(H25O23C8)](9)+R[δ_{out}(N4C6)](8)+[τ(C10=N4)](5)
331	321	-		R[δ_a'(19)+δ_{in}(N4C6)(15)]+[ρ(C9C10)](14)+[δ_{sci}(C9C10)](12)+[δ(H25O23C8)](6)+[ν(H18Cl22)](5)
322	312	-		[δ(C5O1Cl22)](35)+R[δ_{in}(N4C6)](12)+[δ(C11C8O23)](7)+[δ_{sci}(N4H14)](7)+[δ_{sci}(C9C10)](6)
274	266	-		[τ(C8O23)](67)+[δ(H25O23Cl22)](21)+[δ(H25O23C8)](12)
216	209	-	213	[δ(C5O1Cl22)](48)+[ν(H18Cl22)](16)+[ν(H24Cl22)](14)
211	204	-	185	[τ(C8O23)](32)+[δ(C5O1Cl22)](15)+R[τ_a'](12)+[ν(H24Cl22)](8)+[ν(H12Cl22)](6)
179	174	-		[ν(H24Cl22)](52)+[δ(H25O23Cl22)](33)+[τ(C8O23)](6)
167	162	-		[δ(H25O23Cl22)](47)+[ν(H24Cl22)](41)+[τ(C9C10)](5)
152	148	-	156	[ν(H24Cl22)](44)+[δ(H25O23Cl22)](34)+[δ(C5O1Cl22)](11)
128	125	-	-	[τ(C8O23)](62)+[δ(C11C8O23)](19)+[δ(H25O23Cl22)](11)+[δ(C5O1Cl22)](7)
95.2	92.3	-	-	[ν(H12Cl22)](34)+[δ(H25O23Cl22)](26)+[τ(C8O23)](11)+[ν(H24Cl22)](10)+[δ(C5O1Cl22)](5)
78.5	76.1	-	-	[δ(C5O1Cl22)](44)+R[τ(C5O1)(9)+τ_a'(5)]+[δ(C11C8O23)](8)+[τ(C8O23)](5)+[δ(H25O23Cl22)](5)
44.9	43.5	-	-	[δ(H25O23Cl22)](28)+[δ(C6C8O23)](26)+[δ(C11C8O23)](13)+[τ(C8O23)](12)+[δ(C5O1Cl22)](10)
35.8	34.7	-	-	[δ(C5O1Cl22)](25)+[τ(N4C6)](19)+[δ(C11C8O23)](13)+[δ(H25O23C8)](11)+[τ(C8O23)](10)+[τ(C9C10)](5)+R[δ_{out}(N4C6)](3)
22.8	22.1	-	-	[δ(C5O1Cl22)](40)+[δ(C11C8O23)](19)+[δ(H25O23C8)](12)+R[τ(C5O1)](6)+[ν(H24Cl22)](6)+[δ(H25O23Cl22)](5)

Table S5 Geometrical parameters for intra and inter molecular hydrogen bonds in PRA-HCl: bond length (Å), bond angle (◦) and sum of van der Waal radii of interacting atoms (r_H + r_A) in Å.

Interactions(D-H…A)	**d_{D-H}(Å)**	**d_{H-A}(Å)**	**d_{D-A}(Å)**	**D-H…A(°)**	**(r_H+r_A)(Å)**
		wB97X-D			
O1-H18···Cl22	1.01098	1.96687	2.95924	166.46103	2.95
C11-H12···Cl22	1.07974	2.56882	3.28557	123.11189	2.95
O23-H24···Cl22	0.97795	2.24899	3.21203	168.00703	2.95
H25-O23···H15	0.95758	2.70488	3.48258	138.75454	2.72
H17-O2···H13	0.96099	2.27846	3.09155	141.82953	2.72
		M062X			
O1-H18···Cl22	1.01817	1.92975	2.92942	166.49120	2.95
C11-H12···Cl22	1.07991	2.56809	3.26961	121.87602	2.95
O23-H24···Cl22	0.97770	2.25254	3.21243	166.89119	2.95
H25-O23···H15	0.95919	2.70684	3.48759	138.95430	2.72
H17-O2···H13	0.96366	2.25863	3.06888	141.10424	2.72

Table S6 Second order perturbation theory analysis of Fock matrix in NBO Basis for PRA-HCl using wB97X-D level of theory

Donor NBO (i)	ED(i)/e	Acceptor NBO (j)	ED(j)/e	E(2)[a](Kcal mol^{-1})	E(j)-E(i)[b]	F(i,j)[c]
Unit 1						
σ O1-H18	1.97801	σ*C5-C7	0.02823	5.85	1.42	0.081
σ O2-H17	1.98445	σ*N4-C10	0.03030	5.76	1.51	0.084
σ C3-C6	1.97247	σ*C6-C8	0.02194	6.08	1.45	0.084
σ C3-C7	1.97402	σ*N4-C6	0.03595	6.37	1.24	0.079
σ N4-H14	1.97631	σ*O2-C10	0.02684	7.99	1.22	0.088
σ C6-C8	1.97099	σ* C3-C6	0.02407	5.91	1.44	0.082
σ C9-C10	1.98511	σ*N4-C6	0.03595	5.44	1.29	0.075
σ C9-H16	1.97297	π*N4-C10	0.35983	6.63	0.63	0.063
σ C9-H20	1.98351	σ*O2-C10	0.02684	7.03	1.08	0.078
σ C9-H21	1.97306	π*N4-C10	0.35983	6.50	0.63	0.063
LP(1) O1	1.97050	σ*C5-C11	0.03142	8.98	1.26	0.095
LP(1) O2	1.97172	σ*C9-C10	0.01868	7.33	1.18	0.083
LP(2) O2	1.81405	π*N4-C10	0.35983	67.00	0.45	0.161
LP(1) C6	1.16360	π*C3-C7	0.30791	79.08	0.25	0.146
LP(1) C6	1.16360	π*N4-C10	0.35983	102.83	0.11	0.107
LP(1) C6	1.16360	π*C8-C11	0.27464	69.76	0.27	0.143
Unit 1 to unit 3						
π C8-C11	1.70963	σ*O23-H24	0.03307	0.05	0.89	0.006
π C8-C11	1.70963	σ*O23-H25	0.00058	0.11	0.91	0.010
σ C11-H12	1.97498	σ*O23-H24	0.03307	0.05	1.16	0.007
σ C11-H12	1.97498	σ*O23-H25	0.00058	0.08	1.18	0.009
Unit 2 to unit 1						
LP(1) Cl22	1.99898	σ*O1-H18	0.11330	2.15	1.18	0.046
LP(2) Cl22	1.99522	σ*C11-H12	0.01950	0.81	0.84	0.023
LP(3) Cl22	1.95618	σ*O1-H18	0.11330	0.44	0.79	0.017
LP(3) Cl22	1.95618	σ*C8-C11	0.01394	0.16	1.02	0.012
LP(3) Cl22	1.95618	π* C8-C11	0.27464	0.45	0.41	0.013
LP(3) Cl22	1.95618	σ*C11-H12	0.01950	1.50	0.89	0.033
LP(4) Cl22	1.88114	σ*O1-C5	0.01886	0.06	0.86	0.006
LP(4) Cl22	1.88114	σ*O1-H18	0.11330	45.80	0.80	0.171
LP(4) Cl22	1.88114	σ*C8-C11	0.01394	0.15	1.02	0.011
LP(4) Cl22	1.88114	π* C8-C11	0.27464	0.24	0.42	0.009
LP(4) Cl22	1.88114	σ*C11-H12	0.01950	0.48	0.89	0.019
Unit 2 to unit 3						
LP(1) Cl22	1.99898	σ*O23-H24	0.03307	0.39	1.28	0.020
LP(2) Cl22	1.99522	σ*O23-H24	0.03307	0.08	0.84	0.007
LP(3) Cl22	1.95618	σ*O23-H24	0.03307	12.61	0.89	0.095
LP(4) Cl22	1.88114	σ*O23- H24	0.03307	0.15	0.90	0.011
Unit 3 to unit 1						
σ O23-H24	1.99816	π*C8-C11	0.27464	0.08	0.89	0.008
σ O23-H24	1.99816	σ*C11-H12	0.01950	0.18	1.37	0.014
LP(1) O23	1.99646	σ*C8-H15	0.01421	0.07	1.12	0.008
LP(2) O23	1.99364	σ*C5-C11	0.03142	0.16	1.07	0.012
LP(2) O23	1.99364	σ*C6-C8	0.02194	0.12	1.06	0.010
LP (2) O23	1.99364	σ*C8-H15	0.01421	0.21	0.94	0.012
LP (2) O23	1.99364	σ*C11-H12	0.01950	0.47	1.00	0.019

[a]E(2) means energy of hyper conjugative interaction (stabilization energy),
[b]Energy difference between donor (i) and acceptor (j) NBO orbitals,
[c]F(i,j) is the Fock matrix element between i and j NBO orbitals.

Table S7 Second order perturbation theory analysis of Fock matrix in NBO Basis for PRA-HCl using M062X level of theory

Donor NBO (i)	ED(i)/e	Acceptor NBO (j)	ED(j)/e	E(2)[a](Kcal mol^{-1})	E(j)-E(i)[b]	F(i,j)[c]
Unit 1						
σ O1-H18	1.97595	σ*C5-C 7	0.02862	5.79	1.38	0.080
σ O2-H17	1.98449	σ*N4-C10	0.03031	5.58	1.48	0.081

σ C3-C6	1.97196	σ*C6- C8	0.02224	6.05	1.40	0.082
σ C3-C7	1.97386	σ*N4-C6	0.03670	6.33	1.20	0.078
σ N4-H14	1.97629	σ*O2-C10	0.02676	7.63	1.19	0.085
σ C6-C8	1.97075	σ* C3-C6	0.02443	5.91	1.39	0.081
σ C9-C10	1.98501	σ*N4-C6	0.03670	5.36	1.25	0.073
σ C9-H16	1.97269	π*N4-C10	0.35499	6.09	0.60	0.059
σ C9-H20	1.98366	σ* O2-C10	0.02676	6.71	1.05	0.075
σ C9-H21	1.97362	π*N4-C10	0.35499	5.78	0.60	0.057
LP(1) O1	1.97027	σ*C5-C11	0.03175	8.85	1.23	0.093
LP(1) O2	1.97230	σ* C9-C10	0.01874	7.06	1.16	0.081
LP(2) O2	1.82308	π* N4-C10	0.35499	59.22	0.42	0.148
LP(1) C6	1.16004	π* C3- C7	0.30503	71.41	0.22	0.132
LP(1) C6	1.16004	π*N4- C10	0.35499	102.02	0.09	0.098
LP(1) C6	1.16004	π*C8- C11	0.27586	64.18	0.24	0.131
Unit 1 to unit 3						
πC8-C11	1.71242	σ*O23-H25	0.00065	0.12	0.88	0.010
σC11-H12	1.97492	σ*O23-H25	0.00065	0.08	1.14	0.009
Unit 2 to unit 1						
LP(1) Cl22	1.99878	σ*O1-H18	0.12363	2.77	1.15	0.052
LP(2) Cl22	1.99504	σ* C11-H12	0.01849	0.71	0.80	0.021
LP(3) Cl22	1.96028	σ*O1-H18	0.12363	0.57	0.74	0.019
LP(3) Cl22	1.96028	σ* C8-C11	0.01394	0.17	0.97	0.011
LP(3) Cl22	1.96028	π*C8-C11	0.27586	0.42	0.37	0.012
LP(3) Cl22	1.96028	σ*C11-H12	0.01849	1.18	0.86	0.029
LP(4) Cl22	1.87077	σ*O1-H18	0.12363	47.80	0.75	0.170
LP(4) Cl22	1.87077	σ* C5-C7	0.02862	0.05	0.92	0.006
LP(4) Cl22	1.87077	σ* C8-C11	0.01394	0.14	0.98	0.011
LP(4) Cl22	1.87077	π*C8-C11	0.27586	0.22	0.38	0.008
LP(4) Cl22	1.87077	σ*C11-H12	0.01849	0.37	0.87	0.017
Unit 2 to unit 3						
LP(1) Cl22	1.99878	σ*O23-H24	0.02925	0.39	1.26	0.020
LP(3) Cl22	1.96028	σ*O23-H24	0.02925	10.34	0.86	0.084
LP(4) Cl22	1.87077	σ*O23-H24	0.02925	0.12	0.87	0.009
Unit 3 to unit 1						
σO23-H24	1.99822	π*C8-C11	0.27586	0.08	0.87	0.008
σO23-H24	1.99822	σ* C11-H12	0.01849	0.17	1.35	0.014
LP(1) O23	1.99641	σ*C8-H15	0.01432	0.06	1.10	0.007
LP(2) O23	1.99400	σ* C5-C11	0.03175	0.16	1.04	0.012
LP(2) O23	1.99400	σ*C6-C8	0.02224	0.11	1.03	0.010
LP(2) O23	1.99400	σ*C8-H15	0.01432	0.16	0.92	0.011
LP(2) O23	1.99400	σ* C11-H12	0.01849	0.43	0.99	0.018

[a]E(2) means energy of hyper conjugative interaction (stabilization energy),

[b]Energy difference between donor (i) and acceptor (j) NBO orbitals,

[c]F(i,j) is the Fock matrix element between i and j NBO orbitals.

Table S8 Selected reactivity descriptors as Fukui functions (f_k^+, f_k^-), local softnesses (s_k^+, s_k^-), local electrophilicity indices (ω_k^+, ω_k^-) for PRA-HCl using wB97X-D/6-311++G(d, p)

Atom no.	f_k^+	s_k^+	ω_k^+	Atom no.	f_k^-	s_k^-	ω_k^-	f_k^+/f_k^-	f_k^-/f_k^+
From Hirshfeld atomic charges									
1 O	0.07	0.0114	0.2098	1 O	0.0498	0.0081	0.1491	1.4068	0.7108
2 O	0.0211	0.0034	0.0633	2 O	0.0831	0.0136	0.2489	0.2545	3.9294
3 C	0.0282	0.0046	0.0845	3 C	0.0366	0.006	0.1097	0.7707	1.2975
4 N	0.0015	0.0002	0.0045	4 N	0.1018	0.0166	0.305	0.0148	67.612
5 C	0.0178	0.0029	0.0534	5 C	0.0553	0.009	0.1655	0.3229	3.097
6 C	0.0484	0.0079	0.145	6 C	-0.0055	-0.0009	-0.017	-8.747	-0.114
7 C	0.0414	0.0067	0.1239	7 C	0.0323	0.0053	0.0968	1.281	0.7807
8 C	0.0177	0.0029	0.0531	8 C	0.0352	0.0057	0.1055	0.5035	1.9861
9 C	0.0124	0.002	0.0372	9 C	0.0477	0.0078	0.143	0.2602	3.8436
10 C	0.0400	0.0065	0.1198	10 C	0.1667	0.0272	0.4994	0.2399	4.1681
11 C	0.0296	0.0048	0.0886	11 C	0.0273	0.0045	0.0818	1.0823	0.9239
12 H	0.0076	0.0012	0.0228	12 H	0.0177	0.0029	0.053	0.4294	2.3289
13 H	0.0197	0.0032	0.059	13 H	0.0158	0.0026	0.0472	1.2488	0.8008
14 H	0.0085	0.0014	0.0254	14 H	0.0431	0.0070	0.1292	0.1966	5.087
15 H	0.0167	0.0027	0.0501	15 H	0.0185	0.0030	0.0555	0.9027	1.1078
16 H	0.0158	0.0026	0.0475	16 H	0.0587	0.0096	0.1757	0.2701	3.7024
17 H	0.0165	0.0027	0.0494	17 H	0.0451	0.0074	0.1352	0.3653	2.7376
18 H	0.0217	0.0035	0.0649	18 H	0.0123	0.0020	0.037	1.7538	0.5702
19 H	0.0236	0.0038	0.0705	19 H	0.0256	0.0042	0.0766	0.921	1.0858
20 H	0.0086	0.0014	0.0259	20 H	0.0318	0.0052	0.0952	0.272	3.677

21 H	0.0166	0.0027	0.0498	21 H	0.0598	0.0098	0.1792	0.2777	3.6015
22 Cl	0.4624	0.0754	1.3852	22 Cl	0.0326	0.0053	0.0975	14.202	0.0704
23 O	0.0253	0.0041	0.0759	23 O	-0.0047	-0.0008	-0.014	-5.437	-0.184
24 H	0.0072	0.0012	0.0216	24 H	0.0005	9E-05	0.0016	13.422	0.0745
25 H	0.0215	0.0035	0.0645	25 H	0.0126	0.0021	0.0377	1.7089	0.5852

Table S9 Selected reactivity descriptors as Fukui functions (f_k^+, f_k^-), local softnesses (s_k^+, s_k^-), local electrophilicity indices (ω_k^+, ω_k^-) for PRA-HCl using M062X/6-311++G(d, p)

Atom no.	f_k^+	s_k^+	ω_k^+	Atom no.	f_k^-	s_k^-	ω_k^-	f_k^+/f_k^-	f_k^-/f_k^+
From Hirshfeld atomic charges									
1 O	0.0651	0.0136	0.2677	1 O	0.0242	0.0051	0.0996	2.6888	0.3719
2 O	0.0207	0.0043	0.0852	2 O	0.0423	0.0089	0.174	0.4897	2.0421
3 C	0.0283	0.0059	0.1165	3 C	0.0061	0.0013	0.025	4.6624	0.2145
4 N	0.0025	0.0005	0.0101	4 N	0.0218	0.0046	0.0898	0.1122	8.9102
5 C	0.0179	0.0037	0.0735	5 C	0.0211	0.0044	0.0867	0.8475	1.1799
6 C	0.0472	0.0099	0.194	6 C	0.0003	6E-05	0.0011	170.83	0.0059
7 C	0.0396	0.0083	0.163	7 C	0.015	0.0032	0.0618	2.6353	0.3795
8 C	0.0184	0.0039	0.0755	8 C	0.0101	0.0021	0.0415	1.8222	0.5488
9 C	0.0129	0.0027	0.0529	9 C	0.1126	0.0236	0.463	0.1143	8.7496
10 C	0.0394	0.0083	0.1621	10 C	0.0425	0.0089	0.1746	0.9283	1.0772
11 C	0.0268	0.0056	0.1102	11 C	0.0144	0.003	0.0591	1.8657	0.536
12 H	0.0065	0.0014	0.0266	12 H	0.0091	0.0019	0.0376	0.7092	1.41
13 H	0.0195	0.0041	0.0802	13 H	0.0065	0.0014	0.0268	2.9928	0.3341
14 H	0.0088	0.0018	0.0361	14 H	0.0544	0.0114	0.2236	0.1616	6.1889
15 H	0.0165	0.0035	0.0678	15 H	0.0106	0.0022	0.0435	1.5612	0.6405
16 H	0.0157	0.0033	0.0646	16 H	0.1137	0.0238	0.4675	0.1381	7.239
17 H	0.0166	0.0035	0.0682	17 H	0.239	0.0501	0.9832	0.0694	14.41
18 H	0.0211	0.0044	0.087	18 H	0.0059	0.0012	0.0244	3.5594	0.2809
19 H	0.0228	0.0048	0.094	19 H	0.0119	0.0025	0.0488	1.9243	0.5197
20 H	0.0088	0.0018	0.0361	20 H	0.0849	0.0178	0.3493	0.1034	9.6738
21 H	0.0166	0.0035	0.0682	21 H	0.1257	0.0263	0.5169	0.132	7.5776
22 Cl	0.4754	0.0997	1.9556	22 Cl	0.0196	0.0041	0.0807	24.228	0.0413
23 O	0.0251	0.0053	0.1031	23 O	-0.0044	-9E-04	-0.018	-5.708	-0.1752
24 H	0.0063	0.0013	0.0261	24 H	0.0009	0.0002	0.0036	7.1989	0.1389
25 H	0.0218	0.0046	0.0895	25 H	0.0073	0.0015	0.0301	2.975	0.3361