Supplementary Information

The inositol phosphate isomers

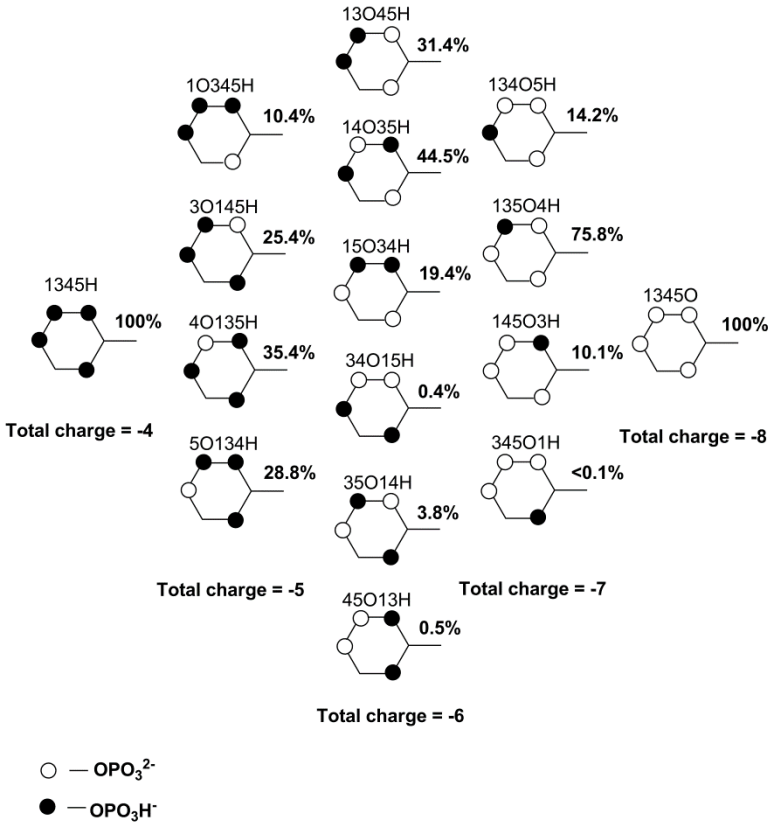


Fig. S1 The sixteen Ins(1,3,4,5)P_4 isomers. Results from Borkovec and Spiess.[1] The horizontal line indicates the axial hydroxyl group 2. Circles represent phosphate groups 1, 3, 4, and 5. Filled in circles represent mono-protonated phosphate groups, and empty circles represent fully deprotonated phosphate groups. The names given to, microstate probability and total charges of, each isomer are indicated.

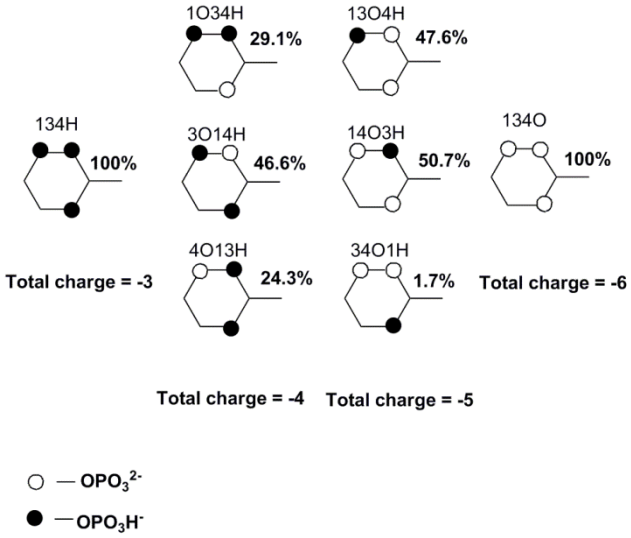


Fig. S2 The eight Ins(1,3,4)P_3 isomers studied in this paper. Diagram format adapted from that of Borkovec and Spiess.[1] The horizontal line indicates the axial hydroxyl group 2. Circles represent phosphate groups 1, 3 and 4. Filled in circles represent mono-protonated phosphate groups, and empty circles represent fully deprotonated phosphate groups. The names given to, microstate probability and total charges of, each isomer are indicated.

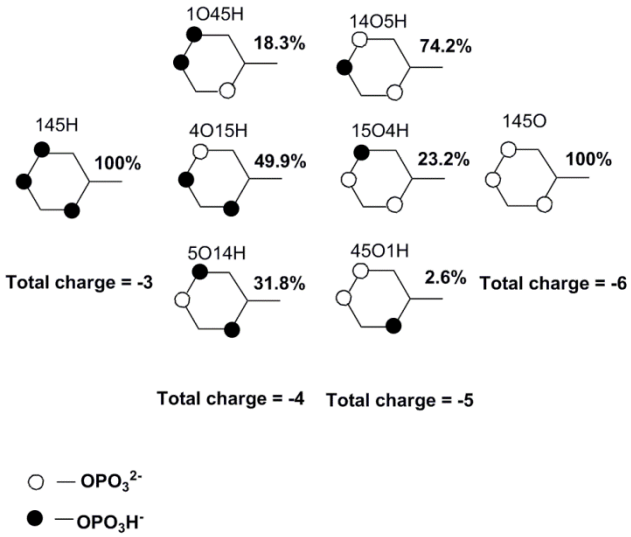


Fig. S3 The eight Ins(1,4,5)P_3 isomers studied in this paper. Diagram format adapted from that of Borkovec and Spiess.[1] The horizontal line indicates the axial hydroxyl group 2. Circles represent phosphate groups 1, 4, and 5. Filled in circles represent mono protonated phosphate groups, and empty circles represent fully deprotonated phosphate groups. The names given to, microstate probability and total charges of, each isomer are indicated.

Macro-state and micro-state probabilities

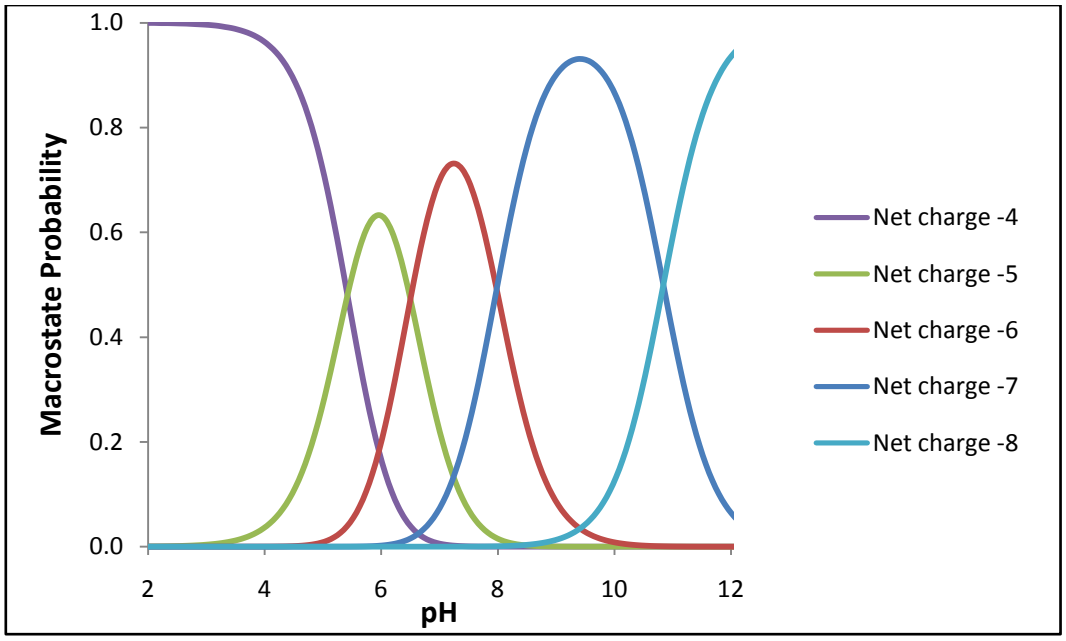
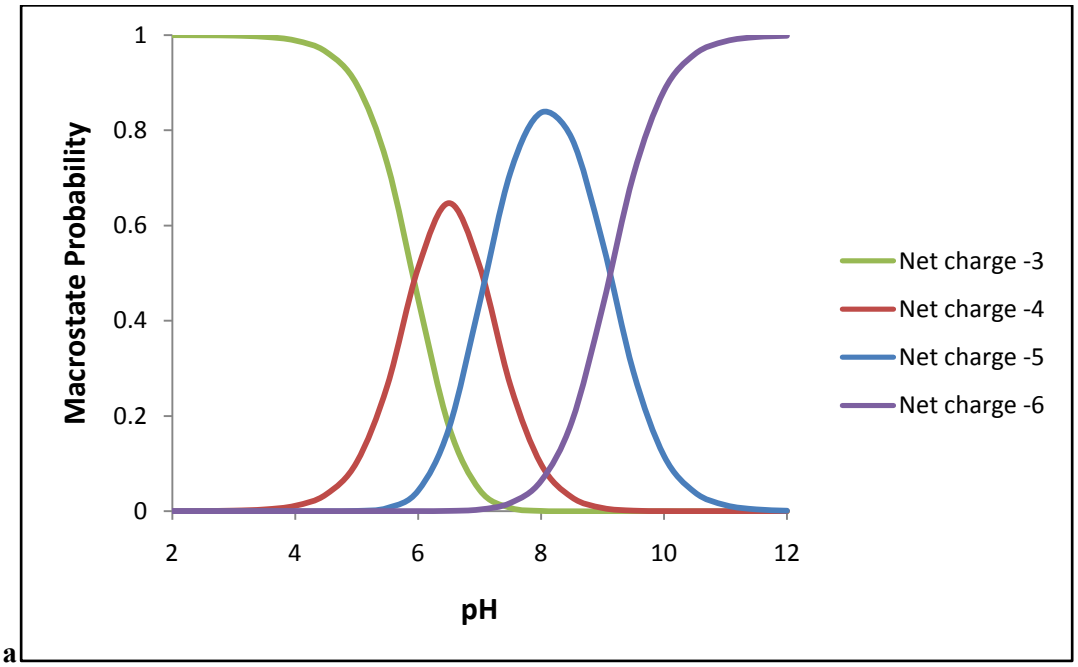
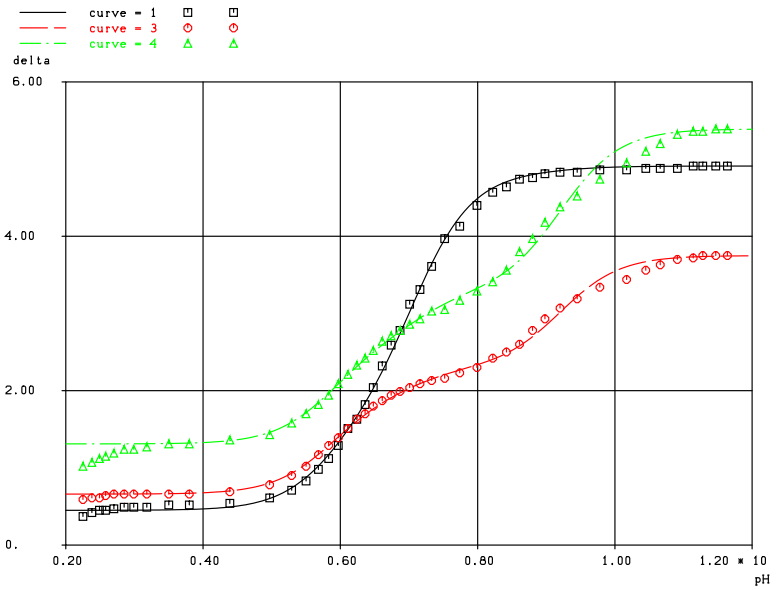


Fig. S4 Variation of the macrostate probabilities as a function of pH, for *myo*-inositol 1,3,4,5-tetrakisphosphate in 0.2 M KCl. . Results from Borkovec and Spiess.[1]



a



b

Fig. S5. a Variation of the macrostate probabilities as a function of pH, for *myo*-inositol 1,3,4-trisphosphate in Et_4NClO_4 10% D_2O. **b** The site-specific titration curve for Ins(1,3,4)P_3 obtained from the chemical shifts of ^{31}P-NMR resonances compared with model calculations. The black, red and green lines represent phosphate groups 1, 3 and 4 respectively. [Titration curves for Ins(1,3,4,5)P_4 and Ins(1,4,5)P_3 have previously been published.] [1, 2]

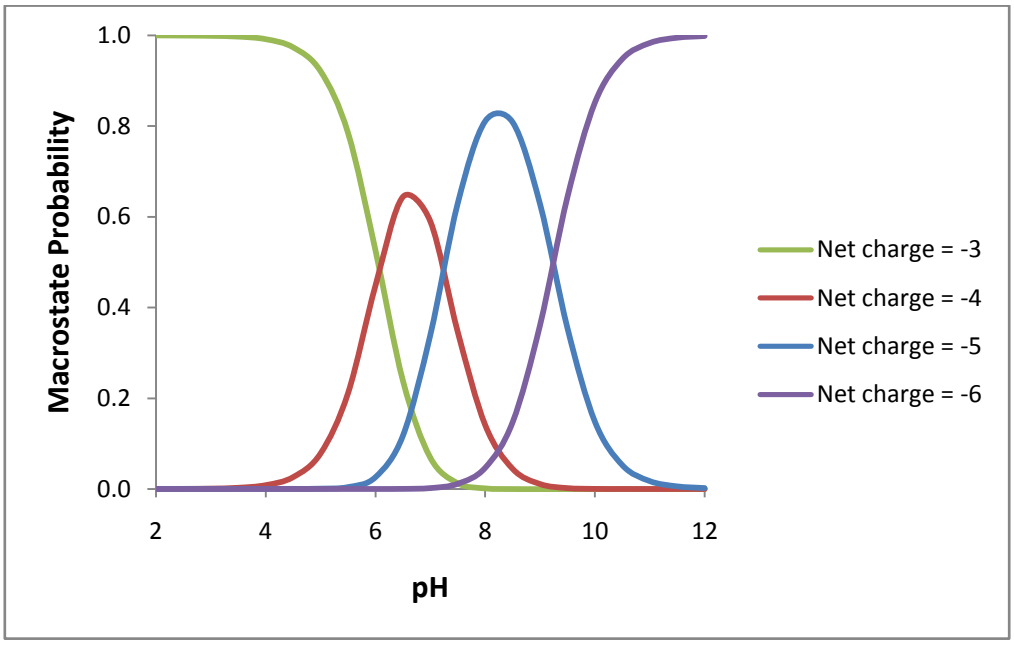


Fig. S6 Variation of the macrostate probabilities as a function of pH, for *myo*-inositol 1,4,5-trisphosphate in Et_4NClO_4 10% D_2O.

Parameters for -7 subset of Ins(1,3,4,5)P_4

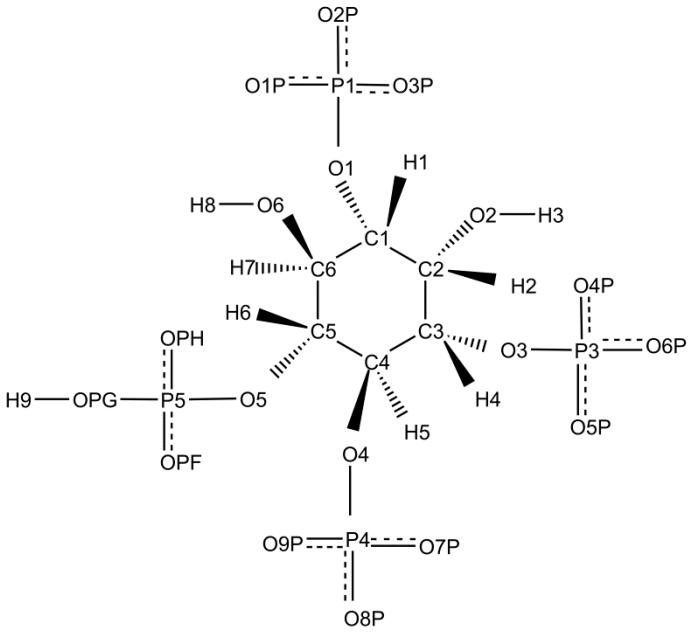


Fig. S7 The atomic labelling scheme for the -7 isomer, 134O5H, of Ins(1,3,4,5)P_4.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.117757	P4	P	1.317919
O1	OS	-0.448797	O7P	O2	-0.978916
C2	CT	-0.068199	O8P	O2	-0.984588
O2	OH	-0.747007	O9P	O2	-0.946876
C3	CT	0.434004	P5	P	1.237755
O3	OS	-0.605511	OPF	O2	-0.903200
C4	CT	-0.099412	OPG	OH	-0.777543
O4	OS	-0.569890	OPH	O2	-0.876920
C5	CT	0.339144	H1	HC	0.063415
O5	OS	-0.575180	H2	HC	0.063970
C6	CT	0.081703	H3	HO	0.525382
O6	OH	-0.802417	H4	HC	0.028067
P1	P	1.235244	H5	HC	0.190370
O1P	O2	-0.962850	H6	HC	0.125465
O2P	O2	-0.934394	H7	HC	0.133349
O3P	O2	-0.972889	H8	HO	0.561546
P3	P	1.265233	H9	HY	0.407729
O4P	O2	-0.937750			
O5P	O2	-0.969482			
O6P	O2	-0.966231			

Table S1 Atom names, atom-types and charge parameters for the -7 134O5H isomer of Ins(1,3,4,5)P_4.

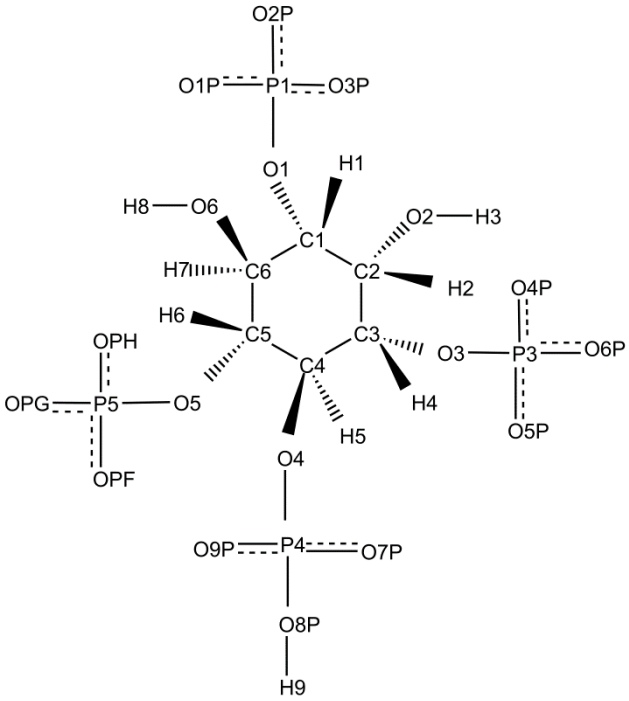


Fig. S8 The atomic labelling scheme for the -7 isomer, 135O4H, of Ins(1,3,4,5)P_4.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.047183	P4	P	1.192988
O1	OS	-0.434424	O7P	O2	-0.924064
C2	CT	-0.032919	O8P	OH	-0.817703
O2	OH	-0.703820	O9P	O2	-0.886364
C3	CT	0.195195	P5	P	1.207011
O3	OS	-0.475412	OPF	O2	-0.956737
C4	CT	0.102599	OPG	O2	-0.929827
O4	OS	-0.501788	OPH	O2	-0.915979
C5	CT	0.071796	H1	HC	0.085212
O5	OS	-0.493347	H2	HC	0.108458
C6	CT	0.156312	H3	HO	0.478342
O6	OH	-0.707886	H4	HC	0.037208
P1	P	1.189999	H5	HC	0.127693
O1P	O2	-0.929198	H6	HC	0.154855
O2P	O2	-0.932105	H7	HC	0.095770
O3P	O2	-0.971362	H8	HO	0.432421
P3	P	1.180819	H9	HY	0.560674
O4P	O2	-0.922530			
O5P	O2	-0.935212			
O6P	O2	-0.953857			

Table S2 Atom names, atom-types and charge parameters for the -7 135O4H isomer of Ins(1,3,4,5)P_4.

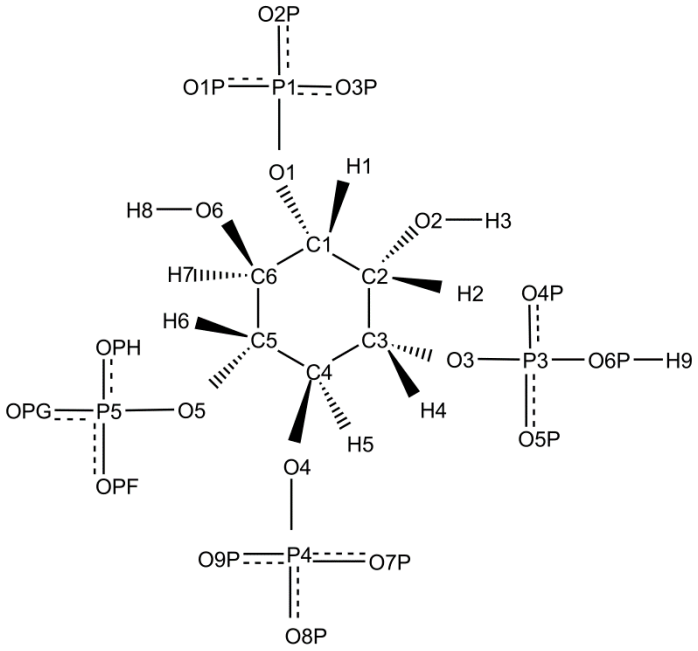


Fig. S9 The atomic labelling scheme for the -7 isomer, 145O3H, of Ins(1,3,4,5)P_4.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.006741	P4	P	1.189919
O1	OS	-0.503965	O7P	O2	-0.913490
C2	CT	0.033204	O8P	O2	-0.866078
O2	OH	-0.642457	O9P	O2	-0.815196
C3	CT	0.003195	P5	P	1.211726
O3	OS	-0.452007	OPF	O2	-0.963710
C4	CT	0.059906	OPG	O2	-0.945254
O4	OS	-0.460097	OPH	O2	-0.929396
C5	CT	0.091729	H1	HC	0.126984
O5	OS	-0.440696	H2	HC	0.159233
C6	CT	0.176233	H3	HO	0.356530
O6	OH	-0.816590	H4	HC	0.106468
P1	P	1.228585	H5	HC	0.132802
O1P	O2	-0.942964	H6	HC	0.153732
O2P	O2	-0.948476	H7	HC	0.118083
O3P	O2	-0.968999	H8	HO	0.506506
P3	P	1.301262	H9	HY	0.545725
O4P	O2	-0.958930			
O5P	O2	-0.981268			
O6P	OH	-0.958989			

Table S3 Atom names, atom-types and charge parameters for the -7 145O3H isomer of Ins(1,3,4,5)P_4.

Parameters for Ins(1,3,4)P_3

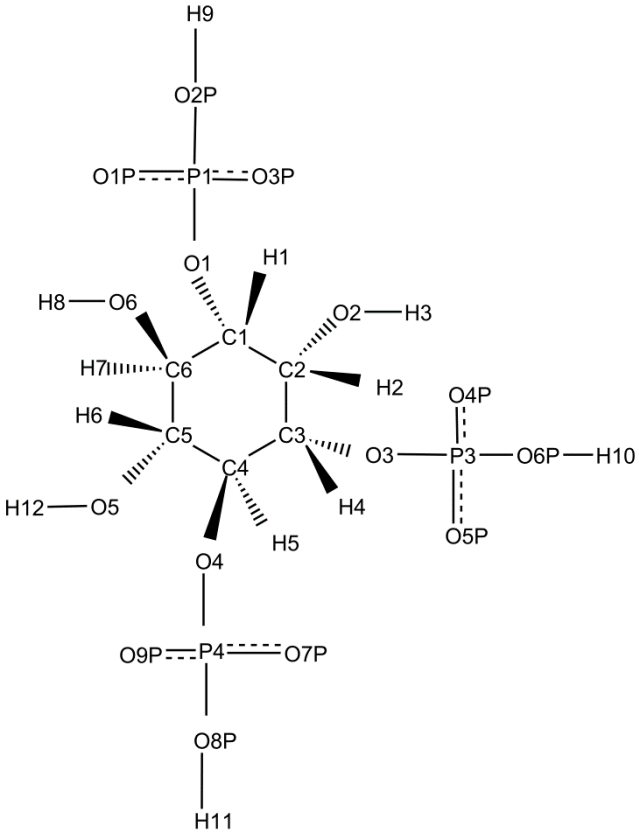


Fig. S10 The atomic labelling scheme for the -3 isomer, 134H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.026167	P4	P	1.166716
O1	OS	-0.489475	O7P	O2	-0.764846
C2	CT	0.016310	O8P	OH	-0.706027
O2	OH	-0.572080	O9P	O2	-0.788397
C3	CT	0.033117	H1	HC	0.115401
O3	OS	-0.415327	H2	HC	0.147393
C4	CT	0.015759	H3	HO	0.389555
O4	OS	-0.421136	H4	HC	0.122738
C5	CT	0.084103	H5	HC	0.158137
O5	OH	-0.576136	H6	HC	0.101065
C6	CT	0.094965	H7	HC	0.112812
O6	OH	-0.688429	H8	HO	0.434482
P1	P	1.279995	H9	HY	0.390760
O1P	O2	-0.817592	H10	HY	0.399866
O2P	OH	-0.710467	H11	HY	0.374215
O3P	O2	-0.826135	H12	HO	0.404141
P3	P	1.194680			
O4P	O2	-0.801728			
O5P	O2	-0.806739			
O6P	OH	-0.677859			

Table S4 Atom names, atom-types and charge parameters for the -3 134H isomer of Ins(1,3,4)P_3.

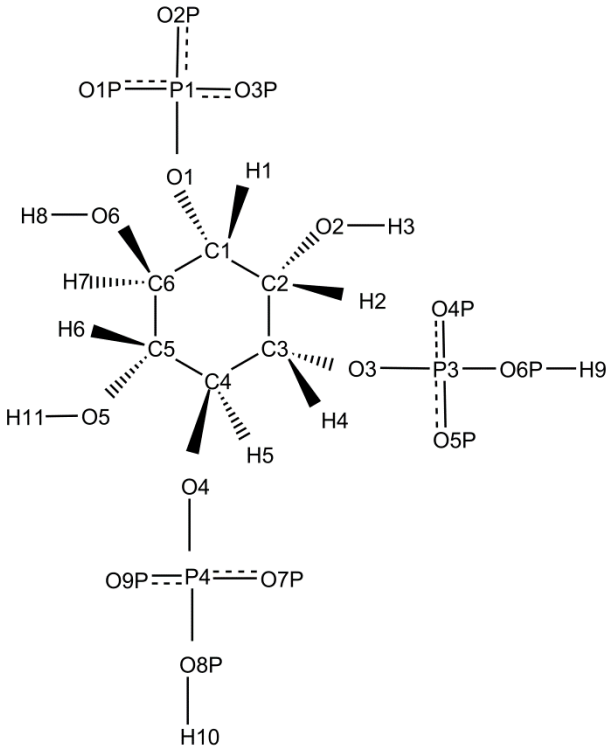


Fig. S11 The atomic labelling scheme for the -4 isomer, 1O34H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.013873	P4	P	1.213326
O1	OS	-0.481823	O7P	O2	-0.821135
C2	CT	0.005823	O8P	OH	-0.738796
O2	OH	-0.655457	O9P	O2	-0.770203
C3	CT	0.056183	H1	HC	0.134167
O3	OS	-0.396201	H2	HC	0.152707
C4	CT	0.023906	H3	HO	0.408877
O4	OS	-0.403256	H4	HC	0.102235
C5	CT	0.017627	H5	HC	0.175038
O5	OH	-0.645426	H6	HC	0.081161
C6	CT	0.146188	H7	HC	0.087772
O6	OH	-0.590467	H8	HO	0.344114
P1	P	1.239783	H9	HY	0.396609
O1P	O2	-0.893159	H10	HY	0.392188
O2P	O2	-0.914398	H11	HO	0.412141
O3P	O2	-0.914600			
P3	P	1.164657			
O4P	O2	-0.819055			
O5P	O2	-0.821157			
O6P	OH	-0.703241			

Table S5 Atom names, atom-types and charge parameters for the -4 1O34H isomer of Ins(1,3,4)P_3.

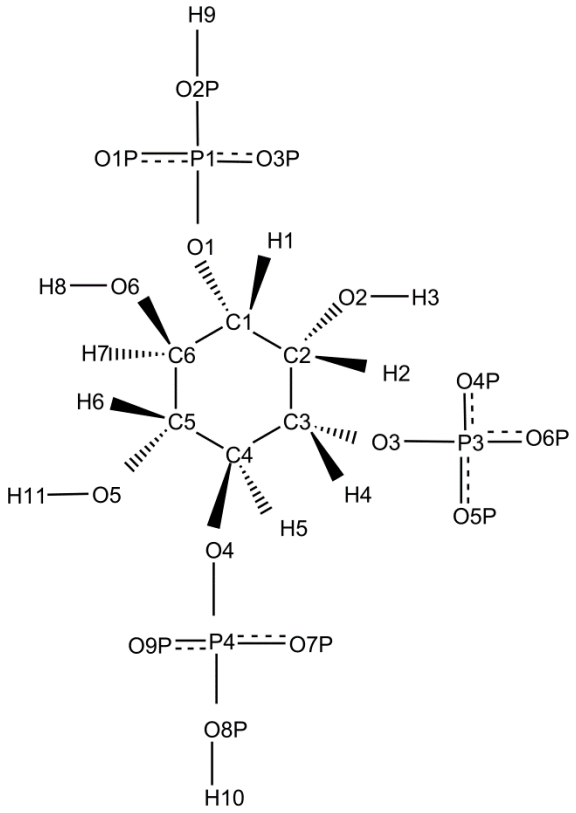


Fig. S12 The atomic labelling scheme for the -4 isomer, 3O14H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.072263	P4	P	1.255551
O1	OS	-0.461066	O7P	O2	-0.836377
C2	CT	-0.014129	O8P	OH	-0.770734
O2	OH	-0.668403	O9P	O2	-0.782726
C3	CT	0.105859	H1	HC	0.090043
O3	OS	-0.453311	H2	HC	0.122794
C4	CT	0.069741	H3	HO	0.467576
O4	OS	-0.457824	H4	HC	0.055265
C5	CT	0.061335	H5	HC	0.139178
O5	OH	-0.688663	H6	HC	0.059415
C6	CT	0.161356	H7	HC	0.117431
O6	OH	-0.656745	H8	HO	0.373293
P1	P	1.277991	H9	HY	0.419020
O1P	O2	-0.846400	H10	HY	0.391397
O2P	OH	-0.731569	H11	HO	0.440484
O3P	O2	-0.878450			
P3	P	1.198443			
O4P	O2	-0.868236			
O5P	O2	-0.871682			
O6P	O2	-0.892117			

Table S6 Atom names, atom-types and charge parameters for the -4 3O14H isomer of Ins(1,3,4)P_3.

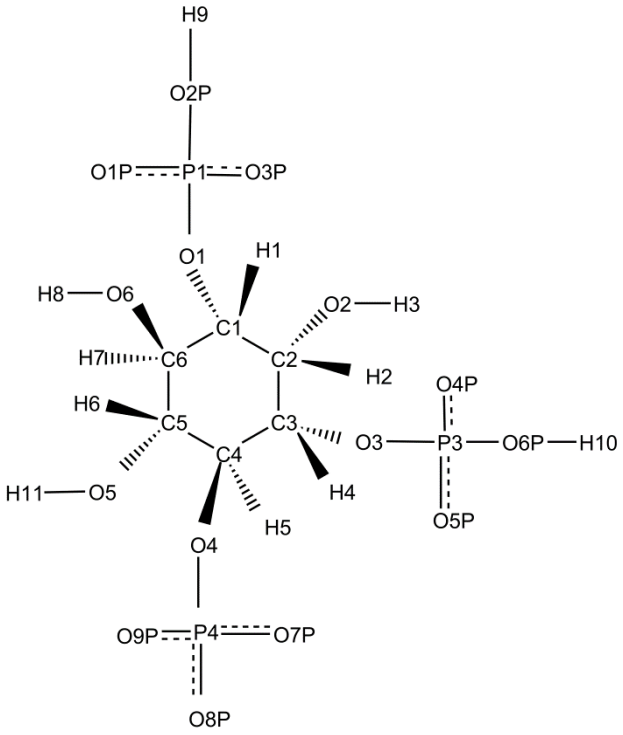


Fig. S13 The atomic labelling scheme for the -4 isomer, 4O13H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.089514	P4	P	1.263174
O1	OS	-0.477931	O7P	O2	-0.866728
C2	CT	0.052506	O8P	O2	-0.864020
O2	OH	-0.692575	O9P	O2	-0.778957
C3	CT	0.012065	H1	HC	0.043870
O3	OS	-0.498877	H2	HC	0.079555
C4	CT	0.059773	H3	HO	0.493696
O4	OS	-0.470764	H4	HC	0.060752
C5	CT	0.115809	H5	HC	0.139882
O5	OH	-0.694383	H6	HC	0.039880
C6	CT	0.304750	H7	HC	0.068769
O6	OH	-0.716496	H8	HO	0.399989
P1	P	1.228516	H9	HY	0.399106
O1P	O2	-0.791703	H10	HY	0.505024
O2P	OH	-0.733626	H11	HO	0.445125
O3P	O2	-0.837263			
P3	P	1.268020			
O4P	O2	-0.904410			
O5P	O2	-0.884146			
O6P	OH	-0.857895			

Table S7 Atom names, atom-types and charge parameters for the -4 4O13H isomer of Ins(1,3,4)P_3.

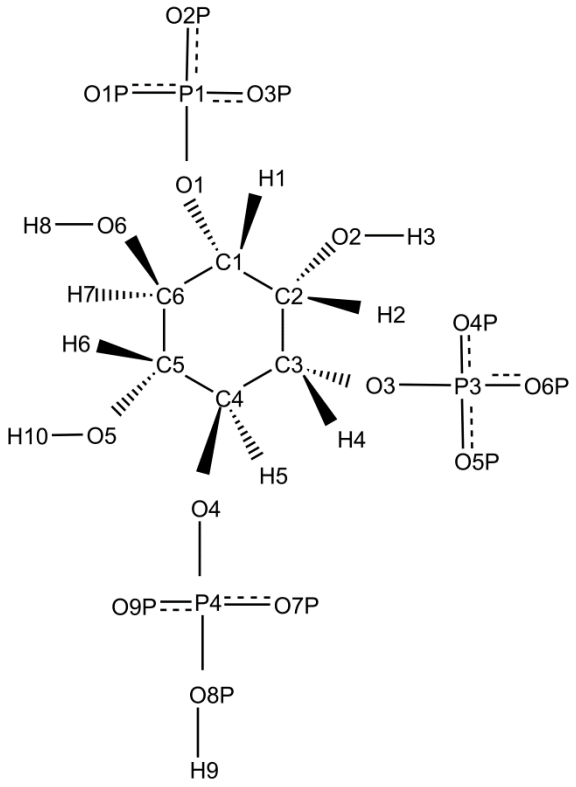


Fig. S14 The atomic labelling scheme for the -5 isomer, 13O4H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	-0.003102	P4	P	1.208483
O1	OS	-0.534171	O7P	O2	-0.846325
C2	CT	0.149444	O8P	OH	-0.778596
O2	OH	-0.703444	O9P	O2	-0.846236
C3	CT	0.062347	H1	HC	0.069463
O3	OS	-0.430819	H2	HC	0.128716
C4	CT	0.067332	H3	HO	0.444990
O4	OS	-0.418057	H4	HC	0.062523
C5	CT	0.045715	H5	HC	0.154233
O5	OH	-0.605886	H6	HC	0.087999
C6	CT	0.143878	H7	HC	0.099654
O6	OH	-0.745361	H8	HO	0.476636
P1	P	1.279962	H9	HY	0.392864
O1P	O2	-0.925510	H10	HO	0.367580
O2P	O2	-0.895923			
O3P	O2	-0.926509			
P3	P	1.184179			
O4P	O2	-0.914494			
O5P	O2	-0.920363			
O6P	O2	-0.931200			

Table S8 Atom names, atom-types and charge parameters for the -5 13O4H isomer of Ins(1,3,4)P_3.

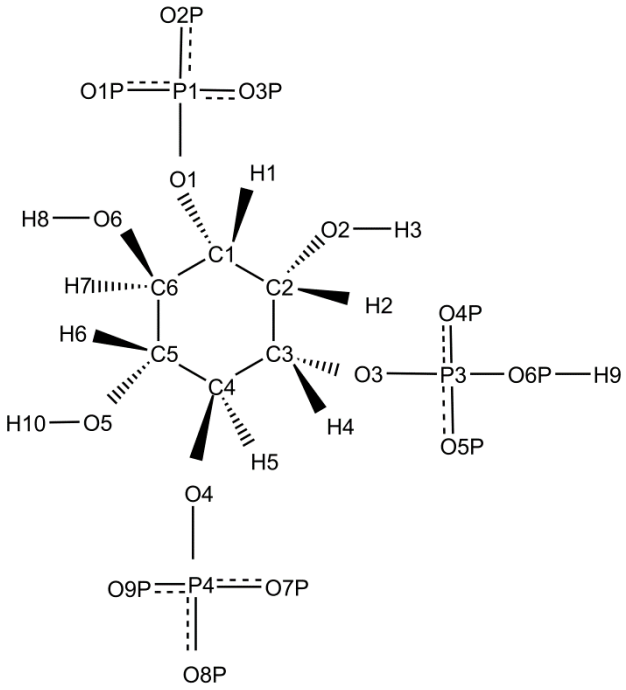


Fig. S15 The atomic labelling scheme for the -5 isomer, 14O3H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.070152	P4	P	1.219236
O1	OS	-0.442699	O7P	O2	-0.930081
C2	CT	-0.018542	O8P	O2	-0.932143
O2	OH	-0.618062	O9P	O2	-0.908273
C3	CT	0.024692	H1	HC	0.086566
O3	OS	-0.413644	H2	HC	0.136713
C4	CT	0.053059	H3	HO	0.367943
O4	OS	-0.475342	H4	HC	0.106689
C5	CT	0.129298	H5	HC	0.141007
O5	OH	-0.578109	H6	HC	0.040145
C6	CT	0.140422	H7	HC	0.050217
O6	OH	-0.730523	H8	HO	0.470253
P1	P	1.211355	H9	HY	0.419862
O1P	O2	-0.911127	H10	HO	0.339030
O2P	O2	-0.902376			
O3P	O2	-0.923113			
P3	P	1.261596			
O4P	O2	-0.849748			
O5P	O2	-0.843178			
O6P	OH	-0.791275			

Table S9 Atom names, atom-types and charge parameters for the -5 14O3H isomer of Ins(1,3,4)P_3.

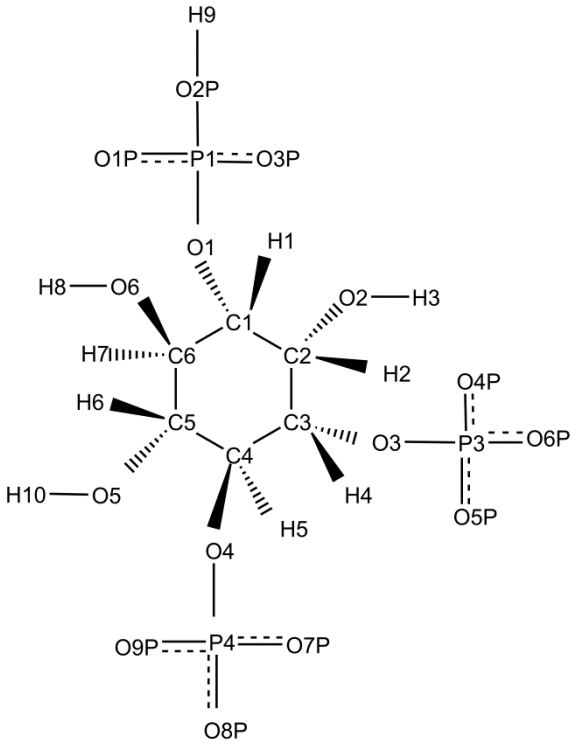


Fig. S16 The atomic labelling scheme for the -5 isomer, 34O1H, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.037401	P4	P	1.201063
O1	OS	-0.467116	O7P	O2	-0.917930
C2	CT	0.025270	O8P	O2	-0.923224
O2	OH	-0.693213	O9P	O2	-0.892820
C3	CT	0.205926	H1	HC	0.066587
O3	OS	-0.456932	H2	HC	0.102833
C4	CT	0.011744	H3	HO	0.467797
O4	OS	-0.474859	H4	HC	0.017168
C5	CT	0.178663	H5	HC	0.100665
O5	OH	-0.723483	H6	HC	0.028056
C6	CT	0.197837	H7	HC	0.073528
O6	OH	-0.704797	H8	HO	0.380850
P1	P	1.239234	H9	HY	0.415835
O1P	O2	-0.851133	H10	HO	0.462981
O2P	OH	-0.724754			
O3P	O2	-0.897006			
P3	P	1.191210			
O4P	O2	-0.883131			
O5P	O2	-0.889307			
O6P	O2	-0.906946			

Table S10 Atom names, atom-types and charge parameters for the -5 34O1H isomer of Ins(1,3,4)P_3.

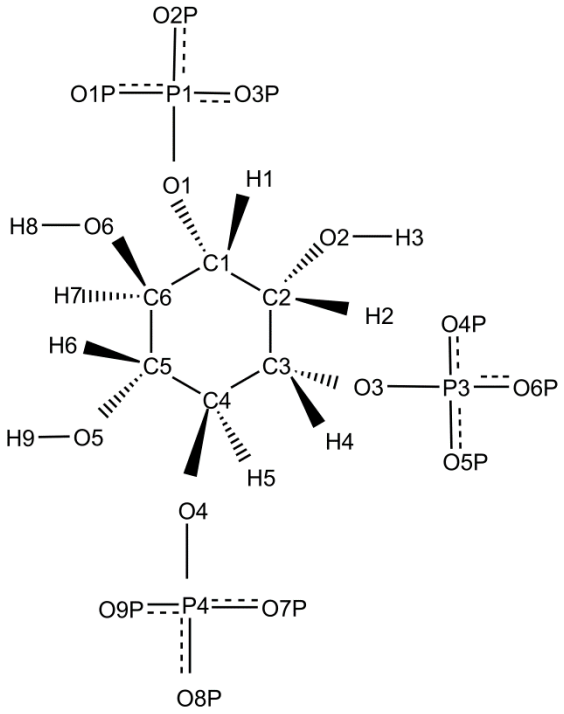


Fig. S17 The atomic labelling scheme for the -6 isomer, 134O, of Ins(1,3,4)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.099410	P4	P	1.178651
O1	OS	-0.460188	O7P	O2	-0.953596
C2	CT	-0.001150	O8P	O2	-0.940626
O2	OH	-0.700301	O9P	O2	-0.910834
C3	CT	0.076315	H1	HC	0.062498
O3	OS	-0.418785	H2	HC	0.116046
C4	CT	0.045328	H3	HO	0.452761
O4	OS	-0.475477	H4	HC	0.039055
C5	CT	0.189355	H5	HC	0.120064
O5	OH	-0.645536	H6	HC	0.062599
C6	CT	0.141750	H7	HC	0.067401
O6	OH	-0.795789	H8	HO	0.495746
P1	P	1.214789	H9	HO	0.358485
O1P	O2	-0.940650			
O2P	O2	-0.921997			
O3P	O2	-0.951626			
P3	P	1.175458			
O4P	O2	-0.910339			
O5P	O2	-0.924442			
O6P	O2	-0.944377			

Table S11 Atom names, atom-types and charge parameters for the -6 134O isomer of Ins(1,3,4)P_3.

Parameters for Ins(1,4,5)P_3

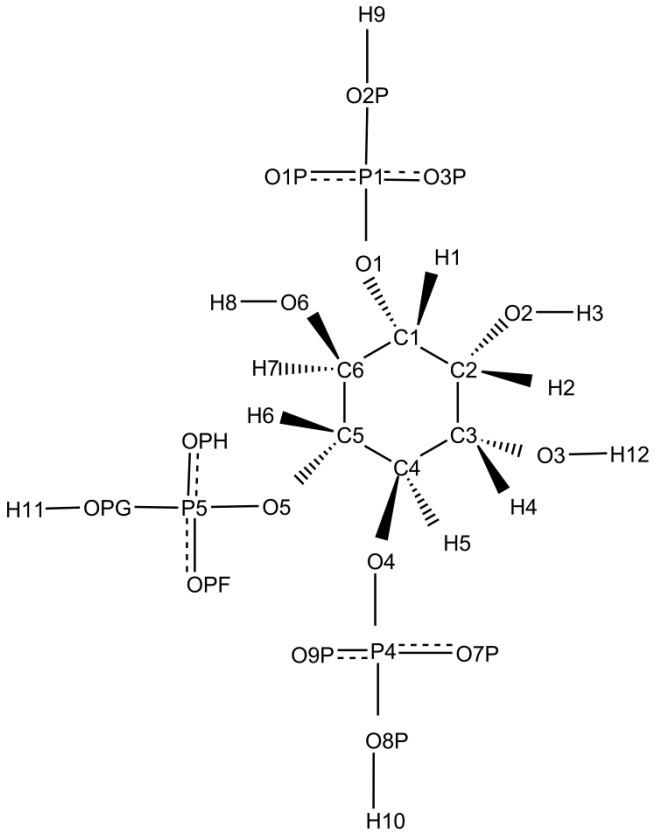


Fig. S18 The atomic labelling scheme for the -3 isomer, 145H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	-0.003428	P5	P	1.226935
O1	OS	-0.375440	OPF	O2	-0.817259
C2	CT	0.056775	OPG	OH	-0.706381
O2	OH	-0.637025	OPH	O2	-0.759779
C3	CT	0.200366	H1	HC	0.081431
O3	OH	-0.717646	H2	HC	0.094212
C4	CT	0.143371	H3	HO	0.414492
O4	OS	-0.526876	H4	HC	0.030619
C5	CT	0.094299	H5	HC	0.104241
O5	OS	-0.493987	H6	HC	0.105801
C6	CT	0.094423	H7	HC	0.126715
O6	OH	-0.638022	H8	HO	0.440763
P1	P	1.184252	H9	HY	0.410595
O1P	O2	-0.814009	H10	HY	0.423189
O2P	OH	-0.718754	H11	HY	0.395164
O3P	O2	-0.775982	H12	HO	0.450229
P4	P	1.265521			
O7P	O2	-0.822373			
O8P	OH	-0.703148			
O9P	O2	-0.833284			

Table S12 Atom names, atom-types and charge parameters for the -3 145H isomer of Ins(1,4,5)P_3.

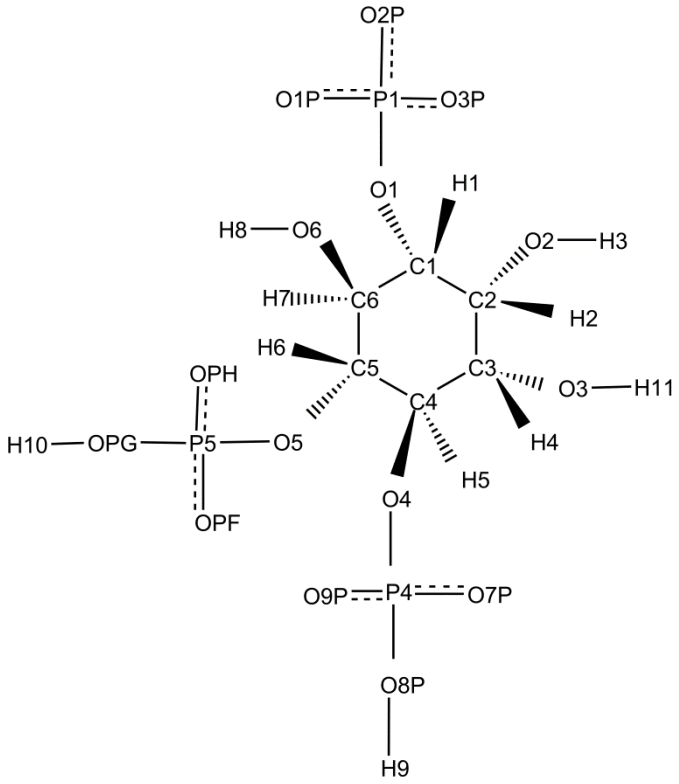


Fig. S19 The atomic labelling scheme for the -4 isomer, 1O45H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	-0.039018	P5	P	1.252494
O1	OS	-0.461582	OPF	O2	-0.836610
C2	CT	0.161807	OPG	OH	-0.755304
O2	OH	-0.608807	OPH	O2	-0.832421
C3	CT	0.004464	H1	HC	0.096019
O3	OH	-0.678101	H2	HC	0.070252
C4	CT	-0.002448	H3	HO	0.355665
O4	OS	-0.469206	H4	HC	0.109754
C5	CT	0.006673	H5	HC	0.166066
O5	OS	-0.475620	H6	HC	0.157070
C6	CT	0.120731	H7	HC	0.087597
O6	OH	-0.608184	H8	HO	0.444720
P1	P	1.223028	H9	HY	0.431623
O1P	O2	-0.875360	H10	HY	0.411765
O2P	O2	-0.888313	H11	HO	0.467021
O3P	O2	-0.899907			
P4	P	1.277407			
O7P	O2	-0.842191			
O8P	OH	-0.725433			
O9P	O2	-0.845654			

Table S13 Atom names, atom-types and charge parameters for the -4 1O45H isomer of Ins(1,4,5)P_3.

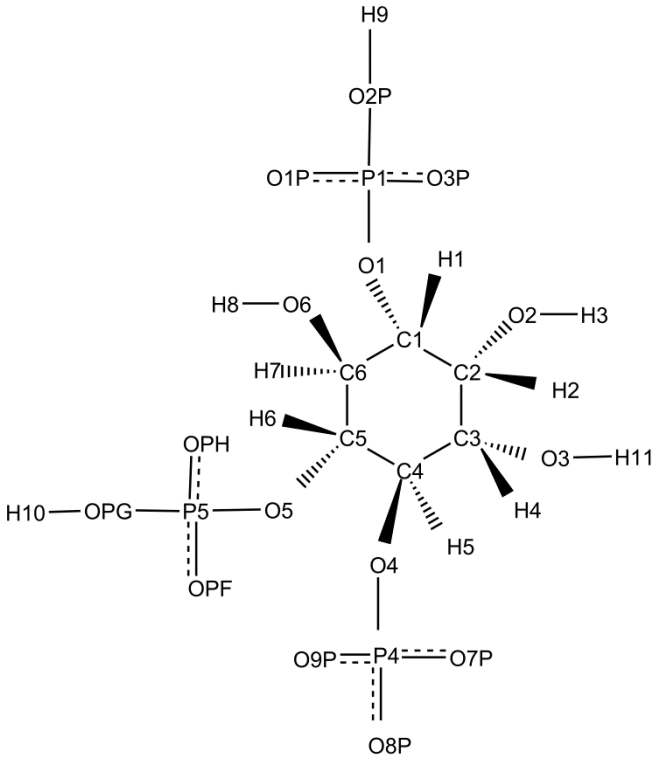


Fig. S20 The atomic labelling scheme for the -4 isomer, 4O15H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.111359	P5	P	1.213028
O1	OS	-0.445064	OPF	O2	-0.830230
C2	CT	-0.031348	OPG	OH	-0.689157
O2	OH	-0.594418	OPH	O2	-0.842498
C3	CT	0.112454	H1	HC	0.101737
O3	OH	-0.773570	H2	HC	0.099001
C4	CT	0.051656	H3	HO	0.381256
O4	OS	-0.415319	H4	HC	0.016769
C5	CT	0.041130	H5	HC	0.135732
O5	OS	-0.485044	H6	HC	0.115100
C6	CT	0.090340	H7	HC	0.085285
O6	OH	-0.649986	H8	HO	0.412040
P1	P	1.266738	H9	HY	0.389808
O1P	O2	-0.850465	H10	HY	0.395041
O2P	OH	-0.743070	H11	HO	0.449366
O3P	O2	-0.861430			
P4	P	1.228040			
O7P	O2	-0.791778			
O8P	O2	-0.848067			
O9P	O2	-0.844437			

Table S14 Atom names, atom-types and charge parameters for the -4 4O15H isomer of Ins(1,4,5)P_3.

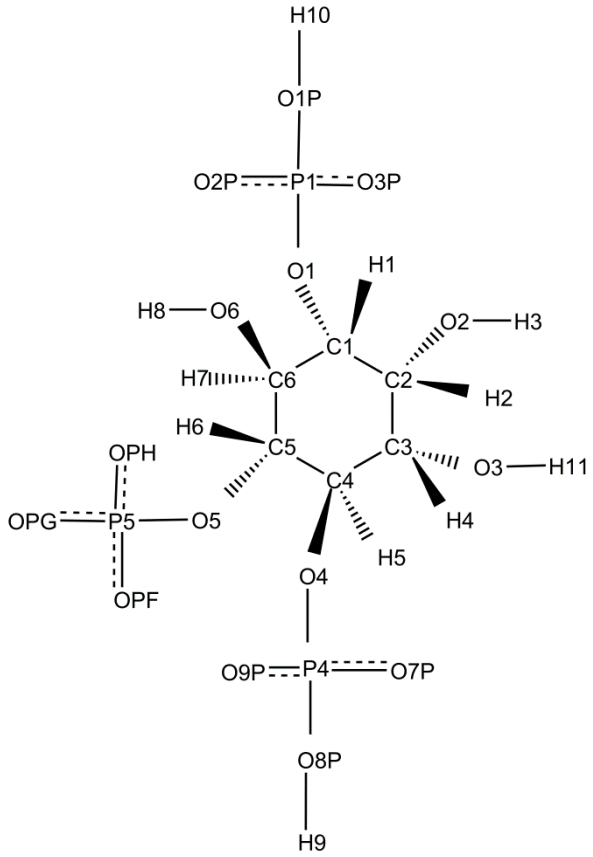


Fig. S21 The atomic labelling scheme for the -4 isomer, 5O14H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	-0.037659	P5	P	1.244112
O1	OS	-0.448720	OPF	O2	-0.857172
C2	CT	0.159940	OPG	O2	-0.767015
O2	OH	-0.600046	OPH	O2	-0.845105
C3	CT	0.001685	H1	HC	0.098839
O3	OH	-0.675061	H2	HC	0.061157
C4	CT	0.010303	H3	HO	0.356062
O4	OS	-0.480484	H4	HC	0.108611
C5	CT	0.034527	H5	HC	0.151342
O5	OS	-0.465733	H6	HC	0.136592
C6	CT	0.117153	H7	HC	0.057280
O6	OH	-0.690010	H8	HO	0.405840
P1	P	1.207573	H9	HY	0.427543
O1P	OH	-0.756050	H10	HY	0.434525
O2P	O2	-0.850812	H11	HO	0.463072
O3P	O2	-0.863802			
P4	P	1.288862			
O7P	O2	-0.850101			
O8P	OH	-0.723337			
O9P	O2	-0.853911			

Table S15 Atom names, atom-types and charge parameters for the -4 5O14H isomer of Ins(1,4,5)P_3.

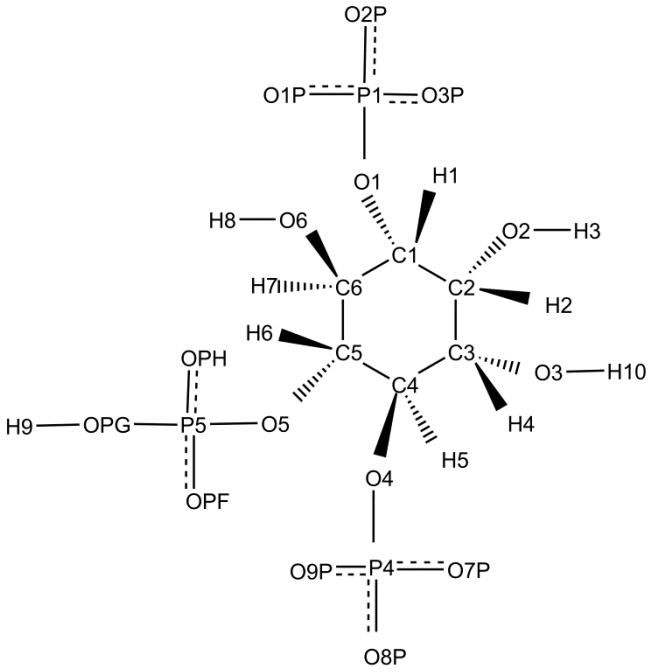


Fig. S22 The atomic labelling scheme for the -5 isomer, 14O5H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.054765	P5	P	1.236822
O1	OS	-0.440888	OPF	O2	-0.867150
C2	CT	0.024615	OPG	OH	-0.772361
O2	OH	-0.662364	OPH	O2	-0.846114
C3	CT	0.134880	H1	HC	0.099288
O3	OH	-0.780696	H2	HC	0.086050
C4	CT	0.091978	H3	HO	0.399519
O4	OS	-0.455165	H4	HC	0.043416
C5	CT	-0.002006	H5	HC	0.115366
O5	OS	-0.440875	H6	HC	0.128156
C6	CT	0.009215	H7	HC	0.124742
O6	OH	-0.576623	H8	HO	0.425521
P1	P	1.219324	H9	HY	0.399494
O1P	O2	-0.899464	H10	HO	0.509231
O2P	O2	-0.917181			
O3P	O2	-0.933231			
P4	P	1.238708			
O7P	O2	-0.930884			
O8P	O2	-0.895867			
O9P	O2	-0.920221			

Table S16 Atom names, atom-types and charge parameters for the -5 14O5H isomer of Ins(1,4,5)P_3.

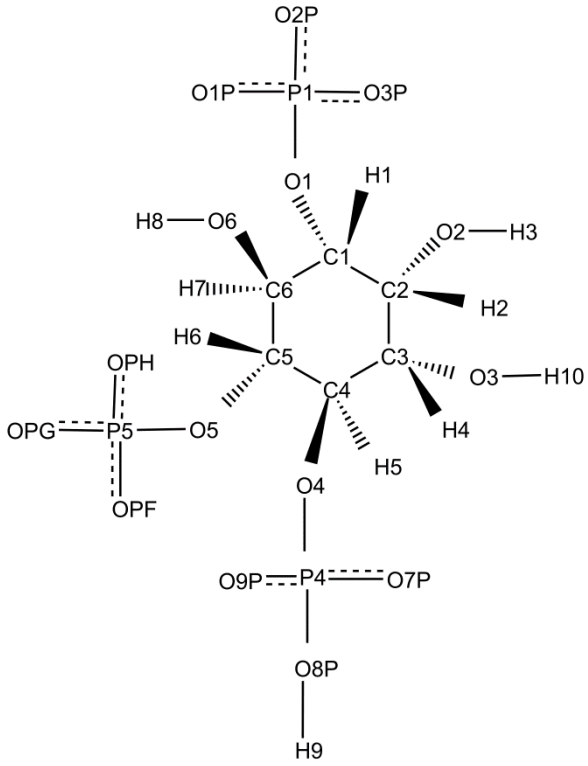


Fig. S23 The atomic labelling scheme for the -5 isomer, 15O4H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.093358	P5	P	1.251949
O1	OS	-0.457615	OPF	O2	-0.886672
C2	CT	0.058093	OPG	O2	-0.850299
O2	OH	-0.660481	OPH	O2	-0.794703
C3	CT	0.010834	H1	HC	0.063921
O3	OH	-0.735515	H2	HC	0.082650
C4	CT	-0.041722	H3	HO	0.401282
O4	OS	-0.468270	H4	HC	0.106106
C5	CT	0.015168	H5	HC	0.172481
O5	OS	-0.465439	H6	HC	0.151560
C6	CT	0.167962	H7	HC	0.063872
O6	OH	-0.656771	H8	HO	0.419118
P1	P	1.209228	H9	HY	0.498680
O1P	O2	-0.903891	H10	HO	0.494850
O2P	O2	-0.921357			
O3P	O2	-0.940705			
P4	P	1.285844			
O7P	O2	-0.927680			
O8P	OH	-0.904959			
O9P	O2	-0.930875			

Table S17 Atom names, atom-types and charge parameters for the -5 15O4H isomer of Ins(1,4,5)P_3.

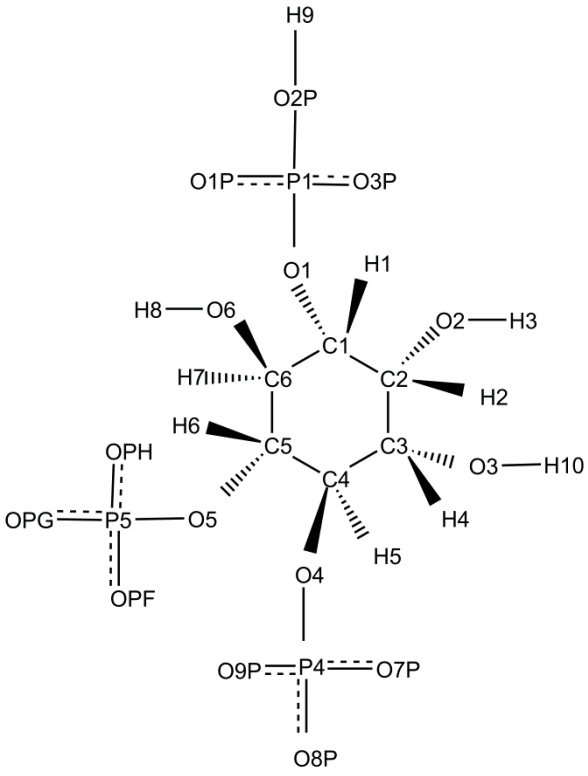


Fig. S24: The atomic labelling scheme for the -5 isomer, 45O1H, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.087423	P5	P	1.242584
O1	OS	-0.448677	OPF	O2	-0.924361
C2	CT	0.004243	OPG	O2	-0.939798
O2	OH	-0.613024	OPH	O2	-0.906461
C3	CT	0.125078	H1	HC	0.092954
O3	OH	-0.806299	H2	HC	0.072999
C4	CT	0.020970	H3	HO	0.382530
O4	OS	-0.409337	H4	HC	0.010699
C5	CT	0.012637	H5	HC	0.133287
O5	OS	-0.464182	H6	HC	0.108357
C6	CT	0.155764	H7	HC	0.051842
O6	OH	-0.718157	H8	HO	0.476855
P1	P	1.269872	H9	HY	0.403111
O1P	O2	-0.868173	H10	HO	0.454019
O2P	OH	-0.774796			
O3P	O2	-0.887605			
P4	P	1.239405			
O7P	O2	-0.887221			
O8P	O2	-0.869846			
O9P	O2	-0.826693			

Table S18 Atom names, atom-types and charge parameters for the -5 45O1H isomer of Ins(1,4,5)P_3.

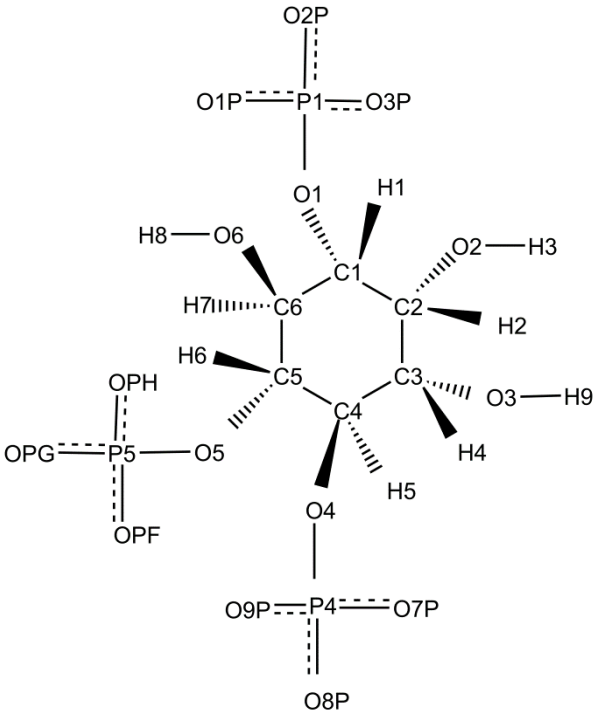


Fig. S25 The atomic labelling scheme for the -6 isomer, 145O, of Ins(1,4,5)P_3.

Atom	ff99SB atom-type	Charge	Atom	ff99SB atom-type	Charge
C1	CT	0.016906	P5	P	1.203981
O1	OS	-0.527083	OPF	O2	-0.952231
C2	CT	0.177777	OPG	O2	-0.932364
O2	OH	-0.706669	OPH	O2	-0.914822
C3	CT	0.033974	H1	HC	0.076586
O3	OS	-0.779108	H2	HC	0.074195
C4	CT	0.237039	H3	HO	0.400246
O4	OS	-0.582251	H4	HC	0.052579
C5	CT	0.184988	H5	HC	0.074156
O5	OS	-0.531031	H6	HC	0.081296
C6	CT	0.328378	H7	HC	0.051773
O6	OH	-0.843179	H8	HO	0.483837
P1	P	1.229021	H9	HO	0.478490
O1P	O2	-0.928954			
O2P	O2	-0.948844			
O3P	O2	-0.958965			
P4	P	1.225175			
O7P	O2	-0.943621			
O8P	O2	-0.933546			
O9P	O2	-0.927729			

Table S19 Atom names, atom-types and charge parameters for the -6 145O isomer of Ins(1,4,5)P_3.

Parameters for PtdIns(4,5)P_2

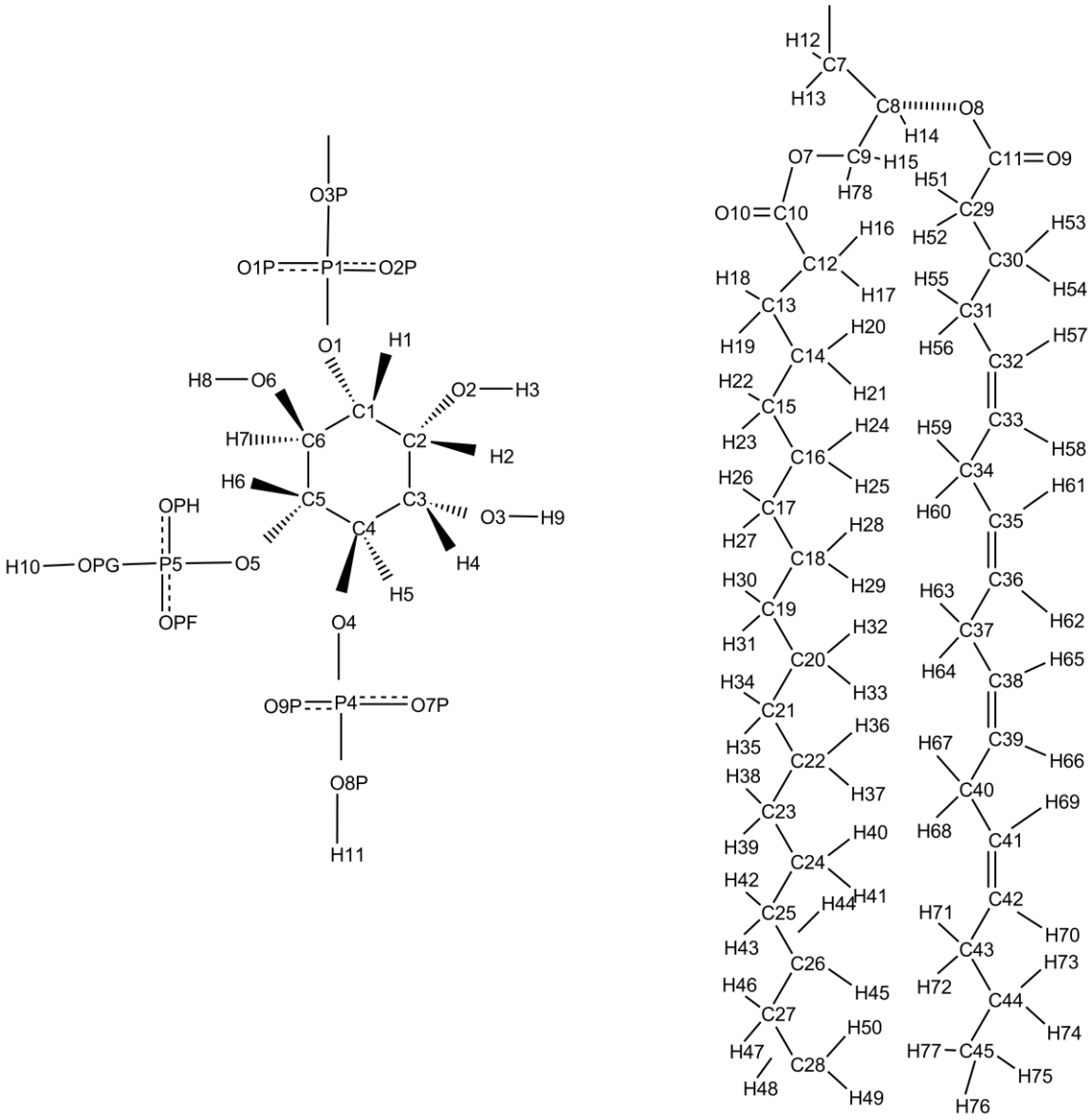


Fig. S26 The atomic labelling scheme for PtdIns(4,5)P_2. The fatty acid chains in this study are stearic acid at the 1-position and 5,8,11,14-octadecatetranoic acid at the 2-position. For ease of visualization the inositol phosphate head-group and phosphatidate tail are drawn separately. These are bonded via atoms O3P and C7.

Table S20 Atom names, atom-types and charge parameters for PtdIns(4,5)P_2. The charge parameters were generated using the same method as for the inositol phosphates. Atom-types for the inositol phosphate head-groups were taken from the ff99SB force field, whilst atom-types for the phosphatidate tail were applied from the GAFF force field and assigned by analogy to DOPC and DMPC.[3, 4] Table is shown on following page.

Atom	ff99SB atom-type	Charge
C1	CT	-0.007892
O1	OS	-0.329293
C2	CT	0.010483
O2	OH	-0.626480
C3	CT	0.201160
O3	OS	-0.711258
C4	CT	0.093514
O4	OS	-0.511775
C5	CT	0.072878
O5	OS	-0.475200
C6	CT	0.060429
O6	OH	-0.583651
P1	P	1.103976
O1P	O2	-0.759492
O2P	O2	-0.763350
O3P	O2	-0.436470
P4	P	1.271394
O7P	O2	-0.823214
O8P	O2	-0.708211
O9P	O2	-0.830577
P5	P	1.215553
OPF	O2	-0.813687
OPG	O2	-0.702181
OPH	O2	-0.753531
H1	HC	0.118738
H2	HC	0.092943
H3	HO	0.422891
H4	HC	0.046657
H5	HC	0.125644
H6	HC	0.135720
H7	HC	0.108962
H8	HO	0.409780
H9	HO	0.453225
H10	HY	0.385921
H11	HY	0.430612

Atom	GAFF atom-type	Charge
C7	c3	0.006650
H12	hc	0.076003
H13	hc	0.083821
C8	c3	0.018888
H14	hc	0.136849
C9	c3	0.019275
H15	hc	0.158297
O7	os	-0.523019
08	os	-0.356749
C10	c	0.824405
C11	c	0.686414
O9	o	-0.578146
O10	o	-0.650149
C12	c3	-0.096916
H16	hc	0.067229
H17	hc	0.025102
C13	c3	-0.341768
H18	hc	0.170640
H19	hc	0.188647
C14	c3	-0.236287
H20	hc	0.139592
H21	hc	0.116649
C15	c3	-0.421411
H22	hc	0.145919
H23	hc	0.183324
C16	c3	-0.224487
H24	hc	0.146202
H25	hc	0.140452
C17	c3	-0.391526
H26	hc	0.135910
H27	hc	0.193092
C18	c3	-0.315155
H28	hc	0.143265
H29	hc	0.166881
C19	c3	-0.224105
H30	hc	0.140014

Atom	GAFF atom-type	Charge
H31	hc	0.127449
C20	c3	-0.317377
H32	hc	0.145037
H33	hc	0.156847
C21	c3	-0.313223
H34	hc	0.143451
H35	hc	0.152481
C22	c3	-0.289072
H36	hc	0.146392
H37	hc	0.154311
C23	c3	-0.281396
H38	hc	0.145484
H39	hc	0.151802
C24	c3	-0.326471
H40	hc	0.147397
H41	hc	0.152962
C25	c3	-0.314010
H42	hc	0.146688
H43	hc	0.151281
C26	c3	-0.242019
H44	hc	0.147305
H45	hc	0.151378
C27	c3	-0.385589
H46	hc	0.148809
H47	hc	0.152328
C28	c3	-0.024803
H48	hc	0.017039
H49	hc	0.023122
H50	hc	0.025196
C29	c3	-0.201885
H51	hc	0.067182
H52	hc	0.023592
C30	c3	0.085756
H53	hc	0.82607
H54	hc	0.068043
C31	c3	-0.420171
H55	hc	0.161456
H56	hc	0.145907
C32	c2	-0.111977
H57	hc	0.133058
C33	c2	-0.173807
H58	hc	0.139805
C34	c3	-0.366602
H59	hc	0.177039
H60	hc	0.157694
C35	c2	-0.064823
H61	hc	0.089994
C36	c2	-0.074487
H62	hc	0.092892
C37	c3	-0.326674
H63	hc	0.166166
H64	hc	0.195626
C38	c2	-0.182059
H65	hc	0.110292
C39	c2	-0.079491
H66	hc	0.108238
C40	c3	-0.336421
H67	hc	0.103550
H68	hc	0.207144
C41	c2	-0.070816
H69	hc	0.127505
C42	c2	-0.227918
H70	hc	0.098200
C43	c3	-0.231989
H71	hc	0.168862
H72	hc	0.167289
C44	c3	-0.010990
H73	hc	0.045032
H74	hc	0.070065
C45	c3	-0.306709
H75	hc	0.075239
H76	hc	0.072774
H77	hc	0.066776
H78	hc	0.208214

Calculated binding free energies for individual simulations

Ligand	Charge	Isomer	ΔG in kcal/mol
Ins(1,3,4,5)P_4	-4	1345H	-71.86 ±4.16
	-5	1O345H	-79.43 ±3.06
		3O145H	-60.33 ±16.13†
		4O135H	-86.40 ±5.40
		5O134H	-69.46 ±1.39
	-6	13O45H	-71.90 ±9.09
		14O35H	-65.58 ±6.05
		15O34H	-81.85 ±5.48
		34O15H	-60.81 ±10.64†
		35O14H	-76.50 ±6.99
		45O13H	-96.31 ±5.92
	-7	134O5H	-64.66 ±15.77†
		135O4H	-64.64 ±9.46
		145O3H	-79.41 ±2.49
Ins(1,3,4)P_3	-3	134H	-70.17 ±8.55
	-4	1O34H	-57.97 ±7.53
		3O14H	-72.65 ±9.63
		4O13H	-62.66 ±9.93
	-5	13O4H	-65.22 ±9.55
		14O3H	-63.67 ±11.64†
		34O1H	-53.48 ±4.58
	-6	134O	-61.46 ±9.50
Ins(1,4,5)P_3	-3	145H	-30.01 ±5.09
	-4	1O45H	-32.56 ±11.82†
		4O15H	-42.79 ±3.58
		5O14H	-41.74 ±5.68
	-5	14O5H	-47.08 ±7.09
		15O4H	-27.33 ±8.17
		45O1H	-42.52 ±10.28†
	-6	145O	-32.83 ±12.4†

Table S21 Computationally determined binding free energies (denoted ΔG) for the individual inositol phosphate isomer-PKB PH domain simulations. The free energies of binding were calculated using the MM-PBSA method. The statistical error was estimated from the deviation between block averages. † Larger statistical errors due to multiple possible conformations of binding.

Ligand	Charge	Isomer	ΔG in kcal/mol
Ins(1,3,4,5)P_4 flip	-4	1345H	-41.76 ±6.04
	-5	1O345H	-40.11 ±8.88
		3O145H	-48.99 ±6.94
		4O135H	-78.82 ±6.53
		5O134H	-65.38 ±6.88
	-6	13O45H	-86.08 ±3.99
		14O35H	-55.65 ±3.99
		15O34H	-42.56 ±10.54†
		34O15H	-60.44 ±9.80
		35O14H	-30.32 ±10.53
		45O13H	-62.88 ±8.00
	-7	134O5H	-53.47 ±8.14
		135O4H	-31.02 ±7.09
		145O3H	-50.02 ±12.83†
Ins(1,3,4)P_3 flip	-3	134H	-33.21 ±1.74
	-4	1O34H	-40.69 ±12.6†
		3O14H	-38.35 ±5.38
		4O13H	-52.34 ±5.80
	-5	13O4H	-36.49 ±5.85
		14O3H	-47.87 ±15.50†
		34O1H	-43.65 ±3.67
	-6	134O	-30.15 ±8.01
Ins(1,4,5)P_3 flip	-3	145H	-48.84 ±3.22
	-4	1O45H	-45.90 ±14.79 †
		4O15H	-77.72 ±5.12
		5O14H	-60.81 ±4.14
	-5	14O5H	-59.74 ±9.59
		15O4H	-32.31 ±9.04
		45O1H	-65.51 ±5.26
	-6	145O	-58.36 ±3.47

Table S22 Computationally determined binding free energies (denoted ΔG) for the individual flipped inositol phosphate isomer-PKB PH domain simulations. The free energies of binding were calculated using the MM-PBSA method. The statistical error was estimated from the deviation between block averages. † Larger statistical errors due to multiple possible conformations of binding.

Weighting of inositol phosphate isomers

(a)

Ligand	Charge	Isomer	ΔG (kcalmol^{-1})	Microstate weighted	Macrostate weighted
Ins(1,3,4,5)P_4	-4	1345H	-71.86	-71.86	
				-71.86	-0.42
	-5	1O345H	-79.43	-8.26	
		3O145H	-60.33	-15.32	
		4O135H	-86.40	-30.59	
		5O134H	-69.46	-20.00	
				-74.17	-16.28
	-6	13O45H	-71.90	-22.58	
		14O35H	-65.58	-29.18	
		15O34H	-81.85	-15.88	
		34O15H	-60.81	-0.24	
		35O14H	-76.50	-2.91	
		45O13H	-96.31	-0.48	
				-71.27	-49.85
	-7‡	134O5H	-64.66	-9.18	
		135O4H	-64.64	-49.00	
		145O3H	-79.41	-8.02	
				-66.20	-4.96
					-71.51

‡The -7 345O1H isomer and -8 1345O isomer were not considered in this study, as their *in vitro* probabilities at physiological pH are insignificant.[27]

(b)

Ligand	Charge	Isomer	ΔG (kcalmol^{-1})	Microstate weighted	Macrostate weighted
Ins(1,3,4)P_3	-3	134H	-70.17	-70.17	
				-70.17	-3.37
	-4	1O34H	-57.97	-16.87	
		3O14H	-72.65	-33.85	
		4O13H	-62.66	-15.23	
				-65.95	-33.90
	-5	13O4H	-65.22	-31.04	
		14O3H	-63.67	-32.28	
		34O1H	-53.48	-0.91	
				-64.23	-28.13
	-6	134O	-61.46	-61.46	
				-61.46	-0.02
					-65.61

(c)

Ligand	Charge	Isomer	ΔG ($kcalmol^{-1}$)	Microstate weighted	Macrostate weighted
$Ins(1,4,5)P_3$	-3	145H	-30.01	-30.01	
				-30.01	-2.08
	-4	1O45H	-32.56	-5.96	
		4O15H	-42.79	-21.35	
		5O14H	-41.74	-13.27	
				-40.58	-23.94
	-5	14O5H	-47.08	-34.93	
		15O4H	-27.33	-6.34	
		45O1H	-42.52	-1.11	
				-42.38	-14.37
	-6	145O	-32.83	-32.83	
				-32.83	-0.06
					-40.45

(d)

Ligand	Charge	Isomer	ΔG ($kcalmol^{-1}$)	Microstate weighted	Macrostate weighted
$Ins(1,3,4,5)P_4$ flip	-4	1345H	-41.76	-41.76	
				-41.76	-0.24
	-5	1O345H	-40.11	-4.17	
		3O145H	-48.99	-12.44	
		4O135H	-78.82	-27.90	
		5O134H	-65.38	-18.83	
				-63.35	-13.90
	-6	13O45H	-86.08	-27.03	
		14O35H	-55.65	-24.76	
		15O34H	-42.56	-8.26	
		34O15H	-60.44	-0.24	
		35O14H	-30.32	-1.15	
		45O13H	-62.88	-0.31	
				-61.76	-43.20
	-7‡	134O5H	-53.47	-7.59	
		135O4H	-31.02	-23.51	
		145O3H	-50.02	-5.05	
				-36.16	-2.71
					-60.06

‡The -7 345O1H isomer and -8 1345O isomer were not considered in this study, as their *in vitro* probabilities at physiological pH are insignificant.[27]

(e)

Ligand	Charge	Isomer	ΔG (kcalmol^{-1})	Microstate weighted	Macrostate weighted
Ins(1,3,4)P_3 flip	-3	134H	-33.21	-33.21	
				-33.21	-1.59
	-4	1O34H	-40.69	-11.84	
		3O14H	-38.35	-17.87	
		4O13H	-52.34	-12.72	
				-42.43	-21.81
	-5	13O4H	-36.49	-17.37	
		14O3H	-47.87	-24.27	
		34O1H	-43.65	-0.74	
				-42.38	-18.56
	-6	134O	-30.15	-30.15	
				-30.15	-0.10
					-42.07

(f)

Ligand	Charge	Isomer	ΔG (kcalmol^{-1})	Microstate weighted	Macrostate weighted
Ins(1,4,5)P_3 flip	-3.	145H	-48.84	-48.84	
				-48.84	-3.38
	-4	1O45H	-45.90	-8.40	
		4O15H	-77.72	-38.78	
		5O14H	-60.81	-19.34	
				-66.52	-39.25
	-5	14O5H	-59.74	-44.33	
		15O4H	-32.31	-7.50	
		45O1H	-65.51	-1.70	
				-53.53	-18.15
	-6	145O	-58.36	-58.36	
				-58.36	-0.11
					-60.89

Table S23 Weighting of the binding free energies (denoted ΔG) of the individual inositol phosphate-PKB PH domain simulations for Ins(1,3,4,5)P_4 **(a)**, Ins(1,3,4)P_3 **(b)**, Ins(1,4,5)P_3 **(c)**, flipped Ins(1,3,4,5)P_4 **(d)**, flipped Ins(1,3,4)P_3 **(e)** and flipped Ins(1,4,5)P_3 **(f)** isomers. For each inositol phosphate the isomers are weighted first according to their *in vitro* microstate probability (the probability of a particular arrangement of protonation within a given charge state). The microstate-weighted free energies were then totalled for each charge subset (shown in yellow). These energies were subsequently weighted by their *in vitro* macrostate probability (the probability of a given charge state) at pH7, shown in cyan. These were then totalled to give the overall weighted free energy of binding for each inositol phosphate (shown in red).

Supplementary References

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