Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Carbocation-π Interaction: Evaluation of the Stabilization by Phenylalanine of a Biochemical Carbocation Intermediate

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Computational Details

All Density Functional Theory calculations were performed with the M06/cc-pVTZ method[1,2] using the Gaussian 09, revision A.02 software.[3] The ultrafine grid option was employed together with the weighting scheme of Stratman, Scuseria and Frisch.[4] Vibrational frequency calculations confirmed that π complex **1** is a local minima. Because the structures for complexes **2**, and **3** are not fully optimized, vibrational frequency calculations were not performed on these systems, and thus all reported energies do not include zero-point vibrational corrections. All atomic charges were calculated using the NBO method.[5]

To determine a representative magnitude of the basis set superposition error (BSSE), M06/cc-pVTZ counterpoise calculations[6] were conducted on Model **2** resulting in a correction of 0.0006699 hartrees (0.4 kcal/mol).

CCSD(T)[7] calculations were performed with the cc-pVTZ basis set[2] using the CFOUR v1.0 suite of programs[8].

Table S1. M06/cc-pVTZ optimized geometries (Å) and energies (hartrees) for *t*-butyl cation, ethylbenzene, and π complex **1**.

t-butyl cation coordinates

Atom Label	x	y	z
C	0.00000000	5.00222498	-0.00155786
C	1.26980025	5.03615040	-0.70799768
C	-1.24980025	4.95615040	-0.72799768
C	-0.01000000	4.97318976	1.44620334
H	1.28910285	3.96344028	-1.23451779
H	2.17265419	5.12624454	-0.02261632
H	1.24387881	5.77638156	-1.58902013
H	-1.70910285	3.88344028	-0.43451778
H	-1.99265419	5.68624454	-0.24261632
H	-1.16387881	5.05638156	-1.84902013
H	0.83873571	4.40444242	1.86567696
H	-0.97873571	4.70444242	1.88567696
H	0.21000000	6.04404806	1.72317101

Energy = –157.4696698;

Table S1. (continued)

Ethylbenzene coordinates

Atom Label	x	y	z
C	-1.57640963	0.46403626	-0.42621899
C	-0.19991236	0.37779027	-0.54180676
C	0.61414649	1.44547094	-0.18611248
C	0.01515891	2.60296387	0.29435804
C	-1.36062721	2.69520330	0.41223724
C	-2.16122922	1.62463159	0.05134633
H	-2.19553887	-0.37656367	-0.71297597
H	0.25710221	-0.53178530	-0.91803199
H	0.64142941	3.44346432	0.57567245
H	-1.81033413	3.60717831	0.78403530
H	-3.23758365	1.69564181	0.13926523
C	2.10618866	1.32899455	-0.25798302
H	2.38418471	0.66568178	-1.08154451
H	2.54115957	2.30668632	-0.48285854
C	2.68598662	0.79855780	1.04474159
H	2.27510876	-0.18631800	1.27572690
H	3.77197918	0.71124407	0.99776839
H	2.43368640	1.46039117	1.87570206

Energy = –310.7231012

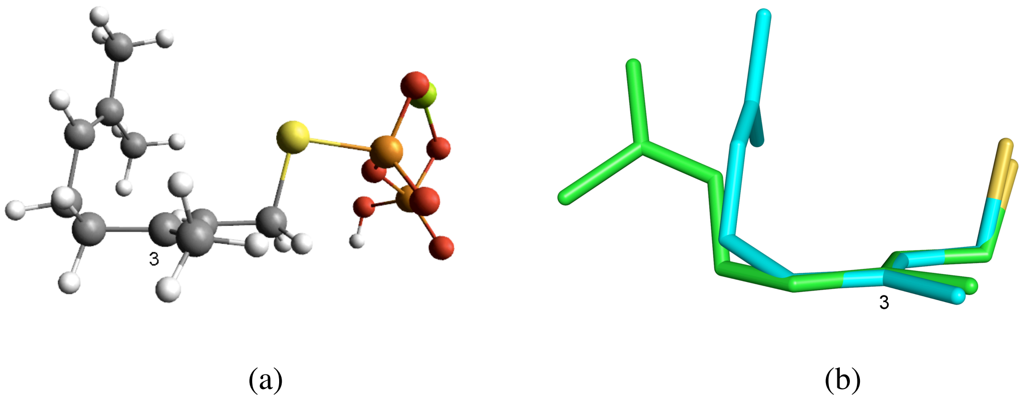
Table S1. (continued)

π complex **1** coordinates

Atom Label	x	y	z
C	0.08628342	0.01616597	0.07781404
C	-0.14759326	0.06695873	1.49838827
C	1.38592512	-0.41542788	-0.42719546
C	-0.88932963	0.58207361	-0.84598796
C	-1.28211660	-3.07181126	2.23193254
C	-2.42297626	-2.52999686	1.64635480
C	-2.47101167	-2.33165089	0.28002822
C	-1.38602520	-2.66554755	-0.53012141
C	-0.25255685	-3.21487725	0.07107505
C	-0.19924094	-3.42216628	1.43752761
H	0.77092555	0.16115621	2.07739767
H	-0.90952869	0.78749996	1.78975143
H	-0.55399326	-0.93691264	1.76576846
H	1.92158639	-1.05553526	0.27069252
H	1.33888648	-0.84865936	-1.42471596
H	1.97394779	0.51284033	-0.51950977
H	-1.89802883	0.60462509	-0.43826183
H	-0.85842265	0.13287987	-1.83709909
H	-0.57726698	1.63273915	-0.97001216
H	-1.24992712	-3.24078951	3.29998842
H	-3.27640662	-2.27712042	2.26149180
H	-3.36969755	-1.93352384	-0.17969218
H	0.58216408	-3.51347152	-0.55550653
H	0.67938043	-3.86733933	1.88566978
C	-1.48914557	-2.57390607	-2.02034528
H	-2.16949389	-1.76261919	-2.29779631
H	-0.50948212	-2.34049891	-2.45276557
C	-1.99876634	-3.88209940	-2.61271545
H	-2.07954202	-3.81899245	-3.69654244
H	-1.32624407	-4.70527395	-2.36813960
H	-2.98273914	-4.12723809	-2.21105960

Energy = –468.2187521

Comparison of the conformation of the hydrocarbon backbone of isolated GSPPMg^{2+} with that found for GSPPMg^{2+} bound to GPPMT in monomer A of the X-ray structure 3VC1.

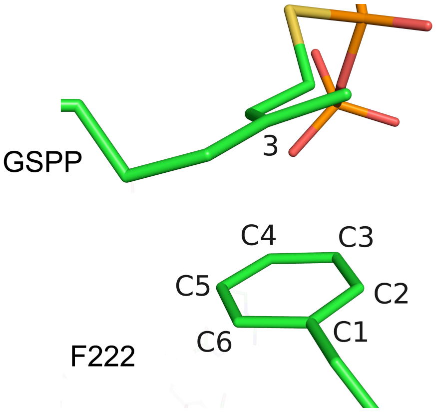


(a) (b)

Figure S1. a) The minimum energy conformation of GSPP complexed to Mg^{2+} (calculated at M06/cc-pVTZ). b) Comparison of the M06/cc-pVTZ optimized conformation (shown in blue) of the –S–C1–C2–C3–C4–C5–C6–C7– backbone with the corresponding backbone conformation (shown in green) for GSPPMg^{2+} bound to GPPMT in monomer A of the X-ray structure.[9,10]

To determine if the hydrocarbon backbone of isolated GSPPMg^{2+} differs from that found for GSPPMg^{2+} when it is bound to GPPMT, we have optimized the geometry of the GSPP–Mg^{2+} complex, and the minimum energy conformation calculated at M06/cc-pVTZ is shown in Figure S1(a). To show the difference between this minimum energy conformation and that found in monomer A of the X-ray structure 3VC1, we have superimposed the two backbones so that the positions of C2, C3 and C4 correspond as closely as possible. As shown in Figure S1(b), although the positions of S and C1 in the two structures are also very similar, those of C6, C7, C8 and C9 are very different. These results show that the C1-C7 backbone of GSPPMg^{2+} bound to GPPMT is much more extended than that calculated for isolated GSPPMg^{2+}.

Table S2. Bond lengths and angles defining the position of C3 of GSPP with respect to the aromatic ring of F222. The correspondences between the atom designations shown in the Figure and those in the X-ray structure[9] are 3 ≡ C3/303 GST; C1 ≡ CG/222 PHE; C2 ≡ CD1/222 PHE; C3 ≡ CE1/222 PHE; C4 ≡ CZ/222 PHE; C5 ≡ CE2/222 PHE; and C6 ≡ CD2/222 PHE.



Monomer	R(3–C1) Å	R(3–C2) Å	R(3–C6) Å	∠3–C1–C4°	∠3–C2–C5°	∠3–C6–C3°	∠C2–3–C1°	∠C6–3–C1°
A	3.85	3.98	3.95	80.2	74.3	75.9	20.2	20.6
B	3.84	3.96	3.97	81.7	75.9	76.4	20.5	20.4
C	3.85	3.97	4.00	79.9	75.7	74.5	20.3	20.3
D	3.96	4.13	4.06	80.9	75.0	77.2	19.4	20.0
E	3.76	3.77	4.08	80.9	81.0	68.9	21.4	20.2
F	3.91	3.99	4.09	80.5	77.7	73.8	20.2	19.7
G	3.95	4.11	4.13	83.4	77.7	77.5	19.9	19.6
H	3.95	4.11	4.07	81.1	75.8	77.0	19.6	19.9
I	3.94	3.86	4.16	76.4	79.9	67.3	20.4	19.4
J	3.89	4.06	4.03	82.1	74.8	77.3	20.1	20.3
K	3.90	4.11	3.98	81.0	73.1	78.1	20.0	20.1
L	3.84	3.92	3.96	78.5	75.4	73.6	20.4	20.7
Mean	3.89 ± 0.04	4.00 ± 0.07	4.04 ± 0.05	80.5 ± 1.1	76.4 ± 1.4	74.8 ± 2.2	20.2 ± 0.3	20.1 ± 0.2

Table S3. Cartesian coordinates (Å) and M06/cc-pVTZ energies (hartrees) for model complex **2**, the F222 mimic, and its binding partner (Figure 6).

Model **2** coordinates

Atom Label	x	y	z
C	64.666000	28.864000	65.258000
C	66.084000	29.378000	65.561000
O	67.037000	28.579000	65.775000
N	66.229000	30.696000	65.531000
C	67.534000	31.332000	65.764000
C	67.712000	31.945000	67.158000
O	68.759000	32.548000	67.449000
C	67.799000	32.408000	64.706000
C	67.907999	31.860999	63.314001
C	68.949999	31.026993	62.976006
C	66.978999	32.214000	62.329001
C	69.067001	30.513003	61.662999
C	67.101998	31.728999	61.016000
C	68.119999	30.854002	60.687001
N	66.714000	31.817000	68.010000
C	66.775000	32.444000	69.333000
C	71.185006	35.440003	52.958004
C	69.694005	35.422003	53.272004
C	69.428005	34.524003	54.506004
C	69.818002	33.184002	54.493003
C	68.830007	35.036003	55.666005
C	69.566998	32.337990	55.604006
C	68.587996	34.230993	56.764006
C	68.973022	32.877024	56.727997
O	68.723968	32.038975	57.801065
Mg	73.950006	30.743002	55.822004
P	71.628005	29.412002	57.748005
P	73.155009	31.640004	58.749006
C	71.145445	32.800158	60.305567
O	72.279005	28.246002	58.438005
O	71.898006	30.672002	58.648003

S	72.070990	33.385989	58.811015
C	69.971223	33.698033	60.651933
O	72.221005	29.703002	56.407004
O	73.992007	31.764003	57.511005
C	70.040029	34.639041	61.715934
O	70.122984	29.350991	57.713006
O	73.821004	31.426002	60.043005
C	68.946995	35.579976	62.188034
C	67.741009	35.722009	61.238001
C	68.045005	36.500003	59.957005
C	67.136005	37.341003	59.422004
C	67.359005	38.095003	58.152004
C	65.837005	37.521003	60.133005
C	71.287997	34.475998	62.534016
H	64.600442	27.854286	65.605964
H	68.715903	32.903395	64.948431
H	66.994954	33.113535	64.731096
H	69.678998	30.764798	63.714046
H	66.164593	32.861488	62.578801
H	69.879683	29.862867	61.414457
H	66.403733	32.038772	60.266758
H	68.184477	30.442640	59.701340
H	68.245498	30.536041	65.692445
H	65.660491	31.021382	66.286595
H	65.833713	32.257372	69.806337
H	66.677234	30.836379	68.202434
H	66.930179	33.498524	69.239203
H	67.535706	32.020079	69.954705
H	64.479092	28.919931	64.205937
H	63.932853	29.470058	65.747989
H	69.362721	36.418031	53.479556
H	69.158351	35.036184	52.429912
H	68.555559	36.069565	55.702459
H	70.314179	32.788401	53.631488
H	68.112173	34.633621	57.633704
H	69.832931	31.302083	55.571513
H	69.157398	31.194926	57.655041

H	71.474812	34.426186	52.776105
H	71.872719	32.597819	61.084847
H	70.714544	31.846627	60.004256
H	69.203168	33.033017	61.154932
H	68.585613	35.220710	63.128858
H	69.380027	36.549656	62.319022
H	67.019078	36.306396	61.769235
H	67.498676	34.728081	60.924481
H	68.993451	36.375351	59.477616
H	66.497967	38.692370	57.935981
H	68.214817	38.728315	58.258784
H	67.523975	37.404445	57.351496
H	65.826381	36.915580	61.015189
H	65.718529	38.549162	60.404579
H	65.034361	37.227377	59.489229
H	71.219017	35.080472	63.414208
H	71.399257	33.449349	62.814193
H	72.135351	34.781993	61.956705
C	71.938397	36.021493	54.168735
H	71.437483	36.902981	54.510738
H	71.962250	35.296812	54.955608
H	72.938916	36.268710	53.881083
C	71.564512	36.184848	51.664644
H	72.614485	36.079650	51.487470
H	71.020642	35.770348	50.841665
H	71.322094	37.222069	51.766165
C	69.345527	34.113627	59.370615
H	68.286782	34.294265	59.414982
H	69.884638	34.949082	58.940183
H	69.494685	33.267247	58.746335

Energy (complex 2) = –3354.4890721; Energy (F222 mimic) = –726.5906212

Energy (binding partner) = –2627. 8751000

Table S4. Calculated NBO[5] charges on the tertiary carbon atom

Molecule	*t*-butyl cation	π complex **1**	structure **2** (C3)
NBO charge	0.613	0.583	0.590

Estimate of the carbocation-π binding contribution to the stabilization energy of complex 2

In addition to a contribution from carbocation-π binding, the total stabilization energy calculated for complex **2** may contain components from other attractive interactions, such as that between the F222 mimic and the (–diphosphate–Mg^{2+}–) moiety. To estimate the contribution that carbocation-π binding *alone* makes to the stabilization energy of complex **2**, calculations were performed on complex **3**, shown in Figure S2, in which the (–diphosphate–Mg^{2+}–) fragment has been replaced by a methyl group. The calculated binding energy for this complex is –13.6 kcal/mol.

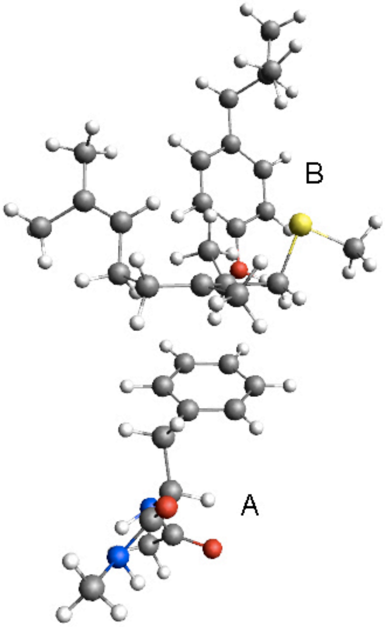


Figure S2. Complex **3** constructed from model structure **2** by replacing the (–diphosphate–Mg^{2+}–) fragment with a methyl group. The fragment labeled A is the F222 mimic, that labeled B is a model of the carbocation species, and the separation of these two binding partners is identical to that in model structure **2**.

Because the NBO[5] charge (0.651) on C3 in complex **3** is larger than the value of 0.590 calculated for model structure **2**, we have rescaled the binding energy for complex **3** by the ratio of these charges, producing an estimate of –12.3 kcal/mol for the carbocation-π binding contribution to the stabilization energy for complex **3**. Although approximate, this analysis suggests that the contribution from the attractive interaction between the (–diphosphate–Mg^{2+}–) fragment and F222 is approximately 2 kcal/mol.

Table S5. Cartesian coordinates (Å) and M06/cc-pvtz energies (hartrees) for complex **3** and binding partners A and B

Complex **3** coordinates

Atom Label	x	y	z
C	64.666000	28.864000	65.258000
C	66.084000	29.378000	65.561000
O	67.037000	28.579000	65.775000
N	66.229000	30.696000	65.531000
C	67.534000	31.332000	65.764000
C	67.712000	31.945000	67.158000
O	68.759000	32.548000	67.449000
C	67.799000	32.408000	64.706000
C	67.908000	31.861000	63.314000
C	68.950000	31.027000	62.976000
C	66.979000	32.214000	62.329000
C	69.067000	30.513000	61.663000
C	67.102000	31.729000	61.016000
C	68.120000	30.854000	60.687000
N	66.714000	31.817000	68.010000
C	66.775000	32.444000	69.333000
C	71.185006	35.440003	52.958004
C	69.694005	35.422003	53.272004
C	69.428005	34.524003	54.506004
C	69.818005	33.184003	54.493004
C	68.830005	35.036003	55.666004
C	69.567004	32.338002	55.604004
C	68.588006	34.231003	56.764005
C	68.973009	32.877001	56.728004
O	68.723982	32.038982	57.801052
C	71.133953	32.775026	60.307091
S	72.070991	33.385989	58.811014
C	69.943527	33.655561	60.667000
C	70.040022	34.639041	61.715952
C	68.946996	35.579980	62.188030
C	67.741008	35.722008	61.238001
C	68.045005	36.500003	59.957005
C	67.136005	37.341003	59.422004

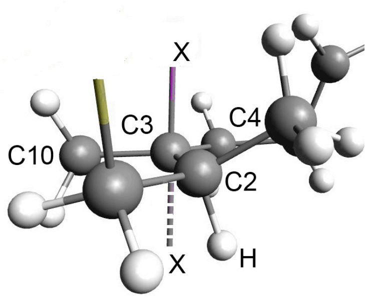
C	67.359005	38.095003	58.152004
C	65.837005	37.521003	60.133005
C	71.288000	34.475999	62.534012
H	64.600442	27.854286	65.605964
H	68.715903	32.903395	64.948431
H	66.994954	33.113535	64.731096
H	69.678998	30.764798	63.714046
H	66.164593	32.861488	62.578801
H	69.879683	29.862867	61.414457
H	66.403733	32.038772	60.266758
H	68.184477	30.442640	59.701340
H	68.245498	30.536041	65.692445
H	65.660491	31.021382	66.286595
H	65.833713	32.257372	69.806337
H	66.677234	30.836379	68.202434
H	66.930179	33.498524	69.239203
H	67.535706	32.020079	69.954705
H	64.479092	28.919931	64.205937
H	63.932853	29.470058	65.747989
H	69.362721	36.418031	53.479556
H	69.158351	35.036184	52.429912
H	68.555559	36.069565	55.702459
H	70.314179	32.788401	53.631488
H	68.112172	34.633614	57.633710
H	69.832926	31.302082	55.571511
H	69.157379	31.194915	57.655046
H	71.474812	34.426186	52.776105
H	71.865974	32.579562	61.083531
H	70.720270	31.816093	59.997448
H	69.171721	32.983861	61.118095
H	68.585613	35.220711	63.128858
H	69.380027	36.549656	62.319021
H	67.019078	36.306396	61.769235
H	67.498676	34.728081	60.924481
H	68.993451	36.375351	59.477616
H	66.497967	38.692370	57.935981
H	68.214817	38.728315	58.258784

H	67.523975	37.404445	57.351496
H	65.826381	36.915580	61.015189
H	65.718529	38.549162	60.404579
H	65.034361	37.227377	59.489229
H	71.219017	35.080473	63.414208
H	71.399256	33.449349	62.814194
H	72.135351	34.781993	61.956705
C	71.938397	36.021493	54.168735
H	71.437483	36.902981	54.510738
H	71.962250	35.296812	54.955608
H	72.938916	36.268710	53.881083
C	71.564512	36.184848	51.664644
H	72.614485	36.079650	51.487470
H	71.020642	35.770348	50.841665
H	71.322094	37.222069	51.766165
C	69.363374	34.123180	59.374683
H	68.307213	34.318993	59.401773
H	69.924164	34.964668	58.985323
H	69.518049	33.294701	58.726952
C	73.009460	31.874436	58.757331
H	73.679078	31.899795	57.923144
H	73.570856	31.770837	59.662318
H	72.342580	31.044045	58.654261

Energy (fragment A) = –726.5906212; Energy (fragment B) = –1333.2338595;

Energy (complex **3**) = –2059.8462203.

Figure S3. Bond angles in the C2 – C3 – C4 fragment of model structure **2** (X – C3 – X is the pyramidal axis – it is equivalent to the three-fold axis if C3 were trigonal planar)



∢ X – C3 – C10 = 94.1° ∢ X – C3 – C4 = 91.5° ∢ X – C3 – C2 = 92.7°

∢ H – C2 – C3 = 95.7° ∢ H – C2 – C3 – X = –160.4°

Notes and References

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