Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

SUPPLEMENTARY INFORMATION FOR:

Cation-π Interactions: Computational Analyses of the Aromatic Box Motif and the Fluorination Strategy for Experimental Evaluation.

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In our studies on the effects of fluorination on cation-π binding, we found several instances of substituent patterns that produced edge-on binding geometries that were competitive with the cation-π interactions. We summarize those results here, while noting that it is quite possible that the M06/6-31G** level of theory that performs well for cation-π interactions is less appropriate for binding interactions of this type. As such, quantitative comparisons should be made with caution.

Tetramethylammonium. Upon monofluorination of benzene, NMe_4^+ ions deviated significantly from the face of the benzene, regardless of whether one, two, or three methyl groups were *en face*. The binding energies were roughly equal to the cation-π interaction with benzene (Figure S1a-c). When more than one fluorine was introduced, NMe_4^+ ions did not exhibit clear local minima in a typical cation-π binding geometry. Rather, the tetramethylammonium cation favored the side of the benzene that was fluorinated. The cation-fluorine binding appeared to be competitive with cation-π binding to the unfluorinated ring (Table S2; Figure S2a-c). As expected, NMe_4^+-fluorine binding scaled with the number of methyl groups facing the fluorine.

Guanidinium. Upon monofluorination of benzene, the stacked guanidinium deviated significantly from the center of the benzene face, favoring the side of the benzene containing a fluorine, although the stacked arrangement was maintained (Figure S1d). However, the guanidinium side-on interaction with the aromatic fluorine is lower in energy than the stacked guanidinium-benzene interaction and competitive with the T-shaped interaction. (Table S2; Figure S2d). Similar results have been seen in the binding of guanidinium to phenol. In the stacked geometry the calculated binding energy to fluorobenzene was 10.1 kcal/mol, more favorable than the stacked interaction with the parent benzene.

The T-shaped guanidinium-aromatic interaction was also probed with fluorination. In fluorobenzene as well as 1,3-difluorobenzene complexes, the position of the guanidinium relative to the center of the aromatic molecule did not change. However, with 1,2,3-trifluorobenzene, the T-shaped guanidinium complex deviated significantly from the unfluorinated complex, with the guanidinium ion favoring the fluorinated side of the benzene. As with stacked interactions, symmetrically-substituted fluorinated benzenes can bind to guanidinium in a T-shaped conformation without significant deviation of the cation from the face of the aromatic molecule.

Indole-Tetramethylammonium: Unlike with studies of NMe_4^+-fluorobenzene, 5-fluoroindole as well as 5,7-difluoroindole and 5,6,7-trifluoroindole bound tetramethylammonium in a cation-π geometry. It was only when a fourth fluorine is added to make 4,5,6,7-tetrafluoroindole that the tetramethylammonium cation deviates from the center of the benzene, and binds in an offset geometry (Figure S3) with an energy of 10.0 kcal/mol, roughly the same as for trifluoroindole. The fluorine-cation binding energy of 5-fluoroindole with tetramethylammonium is 13.8 kcal/mol.

Table S1: *En face* Binding Energies (kcal/mol)[a]

	Benzene	F-Benzene
Sodium	26.8	22.7
Potassium	20.3	17.7
Ammonium	19.5	16.2
Tetramethylammonium (1)	6.5	6.3[b]
Tetramethylammonium (2)	8.7	9.0[b]
Tetramethylammonium (3)	10.8	10.7[b]
Guanidinium (T-Shaped)	14.9	12.3
Guanidinium (Stacked)	8.6	10.1[b]

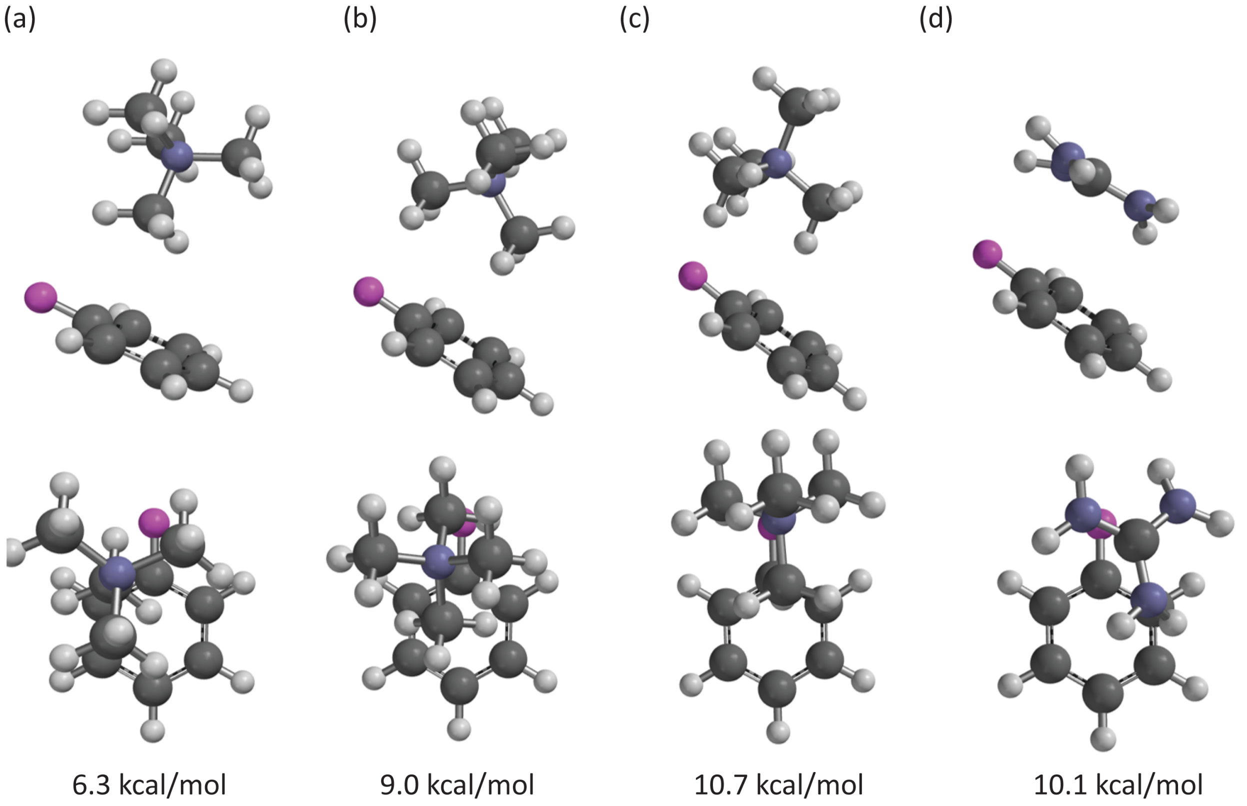
[a] M06/6-31G** calculations; full geometry optimization. [b] Structure is substantially offset from the center of the ring. See Figure S1.

Table S2: *En side* Binding Energies (kcal/mol)[a]

	F-Benzene	1,3-F_2-Benzene	1,2,3-F_3-Benzene
Sodium	22.1	19.7	27.5
Potassium	17.1	14.9	21.6
Ammonium	15.9	13.3	18.5
Tetramethylammonium (1)	5.9	4.8	-
Tetramethylammonium (2)	7.9	6.5	8.4
Tetramethylammonium (3)	10.6	9.0	-
Guanidinium	14.2	12.3	14.8

[a] M06/6-31G** calculations; full geometry optimization in all cases.

Figure S1: Geometry-minimized structures of tetramethylammonium binding to fluorobenzene with (a) one, (b) two, and (c) three methyl groups down as well as (d) guanidinium binding in a stacked fashion; alternate views of all structures below. Binding energies computed at M06/6-31G** and all structures are geometry minimized.



6.3 kcal/mol 9.0 kcal/mol 10.7 kcal/mol 10.1 kcal/mol

Figure S2: Binding of various ions to the side of a fluorobenzene molecule. Binding energies computed at M06/6-31G** and are all geometry minimized structures. NMe_4^+ ions were computed with (a) one, (b) two and (c) three methyl groups facing the fluorine. (d) Guanidinium binding to the side of fluorobenzene.

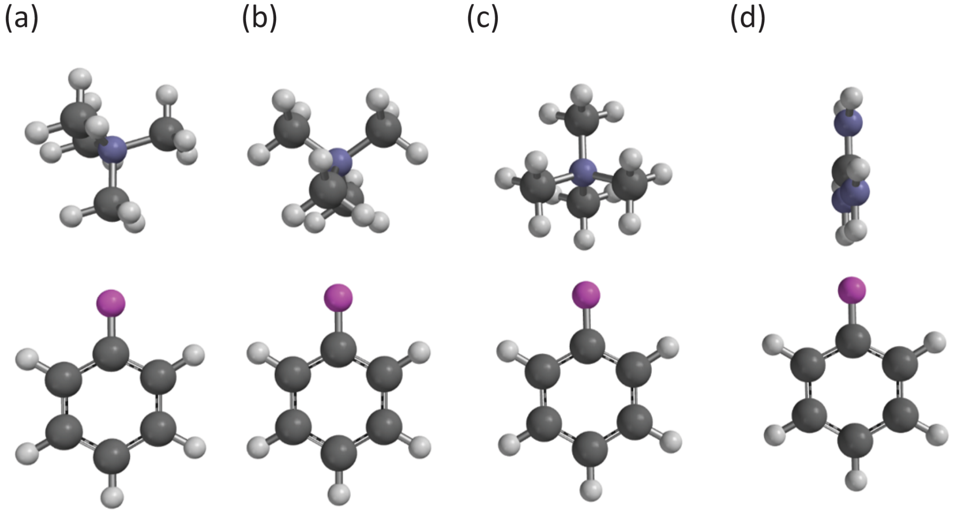


Figure S3: Geometry-minimized structures of tetramethylammonium binding with (a) indole, (b) 5,6,7-trifluoroindole, and (c) 4,5,6,7-tetrafluoroindole with alternate views of all complexes below. Binding energies computed at M06/6-31G** and all structures are geometry minimized.

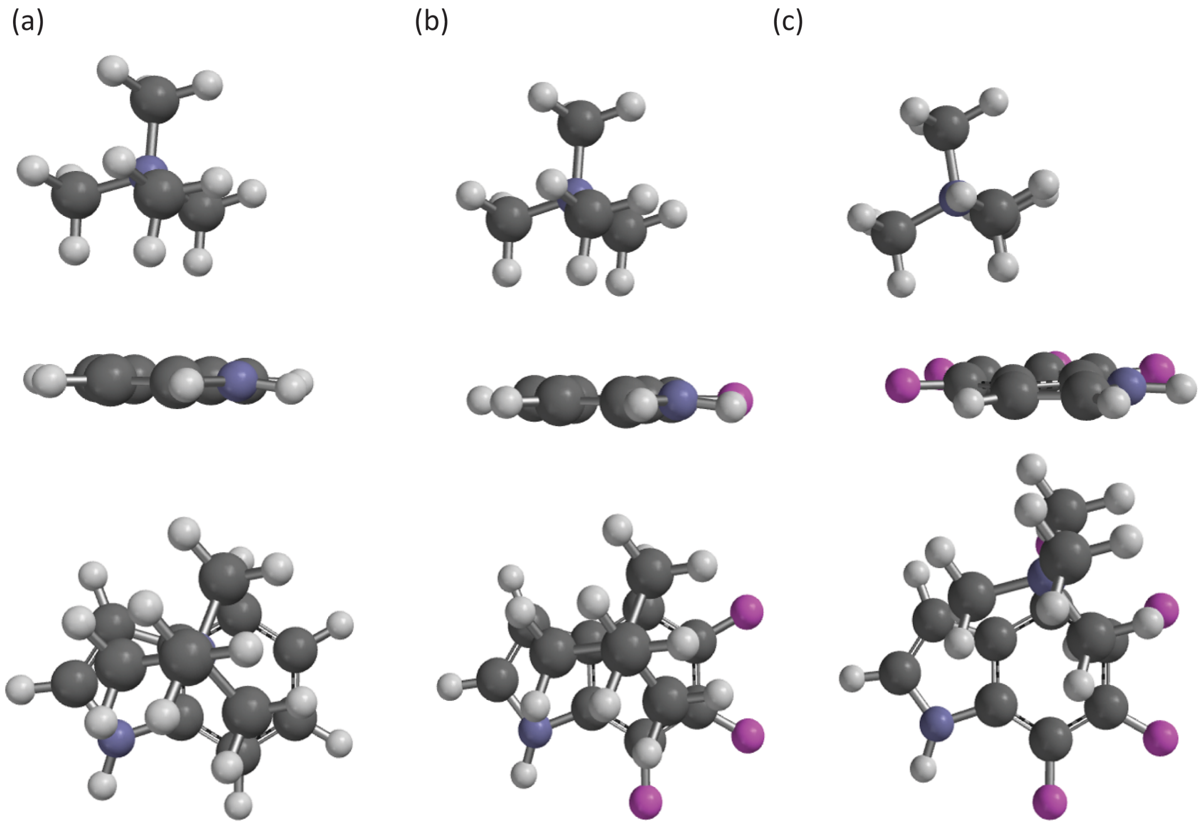


Table S3. Binding energies (kcal/mol) to *ab initio* generated aromatic boxes

	Benzene Rings	Binding Energy	Theoretical[a]	Sum[b]	Discrepancy[c]
Ammonium	3	48.7	58.5	53.4	9.8
	4	59.6	78.0	71.1	18.4
	5	62.3	97.5	-	35.2
TMA	3	30.6	32.4	31.7	1.8
	4	39.2	43.2	42.3	4.0
	5	44.0	54.0	-	10.0

[a] Four times the binding energy for a single ion-benzene complex. [b] Four times the binding energy of a single cation-box aromatic calculated. [c] The difference between the theoretical binding energy and the calculated binding energy.

Figure S4: Geometry-optimized complexes of three benzenes to (a) one ammonium and (b) one tetramethylammonium ion, and complexes of five benzenes to (c) one ammonium and (d) one tetramethylammonium ion.