Electronic Supplementary Material (ESI) for Chemical Science

SUPPORTING INFORMATION

Aromatic Reactivity Revealed: Beyond Resonance Theory & Frontier Orbitals

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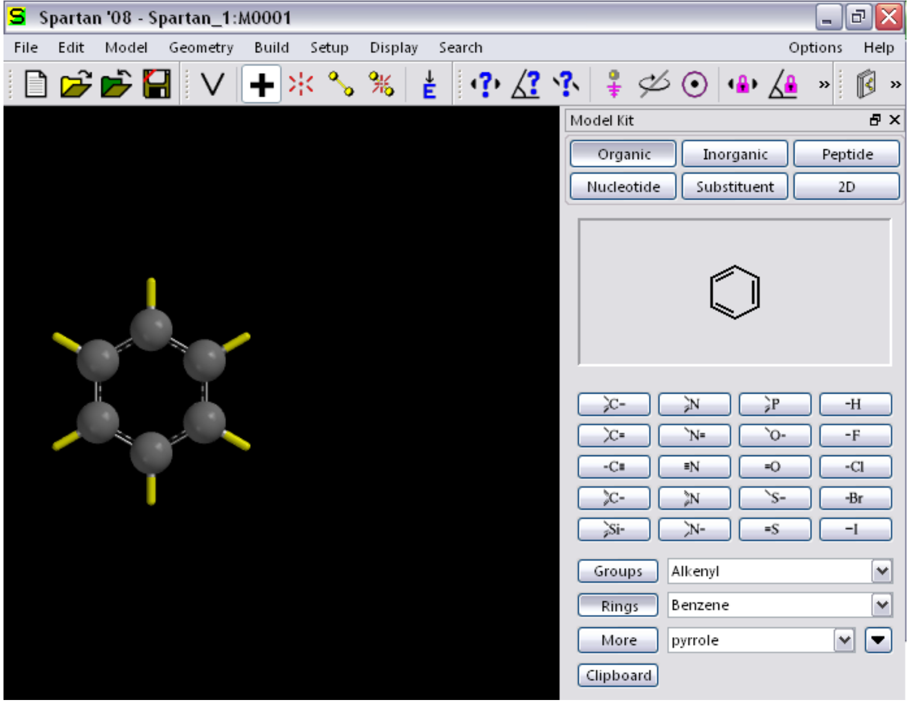
Methods

Minimised geometries and molecular surfaces were calculated using *Spartan '08* with DFT/B3LYP/6-311G*, unless otherwise indicated. ionisation energies and electrostatic potentials are plotted on the 0.002 electrons/bohr^3 density surface. Ionisation energy surfaces emphasising minima are scaled from the average local ionisation energy minimum on the molecular surface, $\bar{I}_{\mathrm{S,min}}$ (red) to $\bar{I}_{\mathrm{S,min}}$ +0.4 eV (blue) of each molecule. A step-by-step guide describing how this was done is provided on the following page. $\bar{I}_{\mathrm{S}\ meta}$ and $\bar{I}_{\mathrm{S}\ para}$ values for the plots in Figures 3 and S17 were taken on the 0.002 electrons/bohr^3 average local ionisation energy surface directly over the centre of the carbon atoms perpendicular to the plane of the aromatic ring as shown in Figure S1.

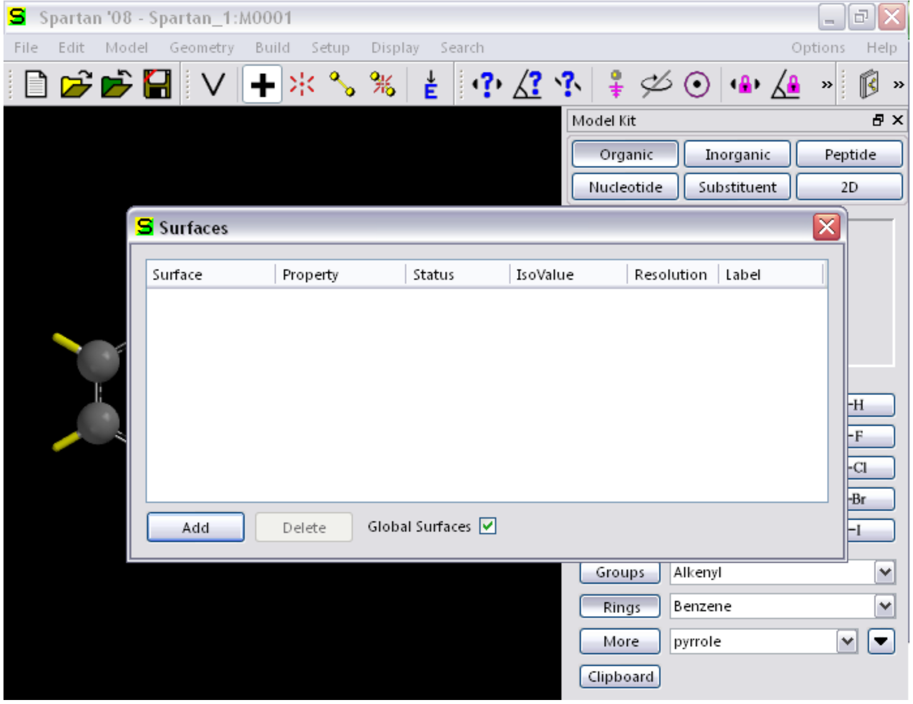
Step-by-step guide for calculating ionisation energy surfaces using Spartan '08:

1) Open the 'Model Kit' structure drawing tool by selecting 'New' from the 'File' menu, and draw a structure of interest. Using benzene as an example, click the "Rings" button and left click in the drawing window.



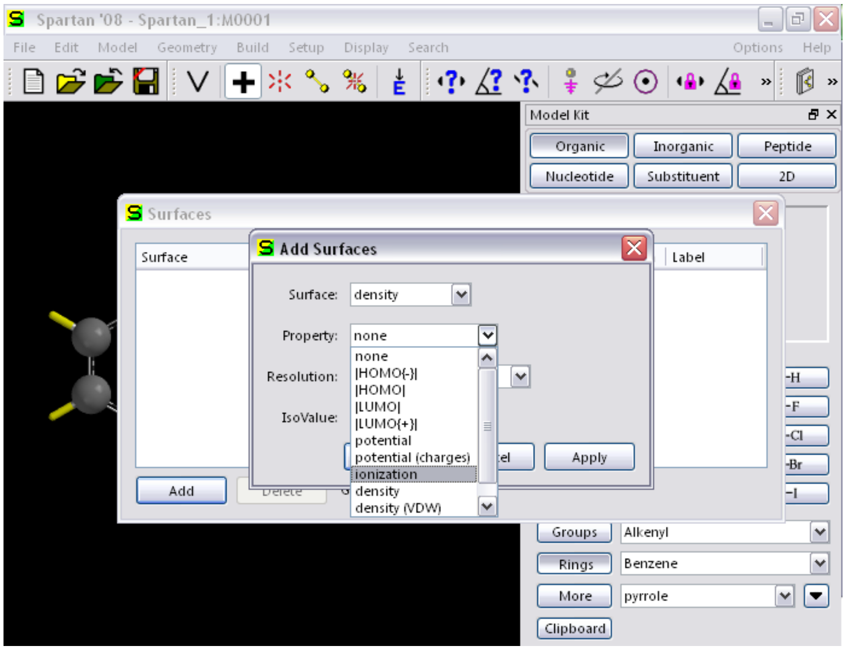
Groups: Alkenyl
Rings: Benzene
More: pyrrole

2) Click the 'Setup' menu and select 'Surfaces' to open the surfaces window.



Global Surfaces ☑

3) Click the ‘Add’ button and select ‘ionization’ from the ‘Property’ drop-down menu. Additionally, electrostatic surfaces can be added by selecting ‘potential’, while the HOMO and LUMO visualisations are available under the ‘Surface’ drop-down menu.



Surface: density

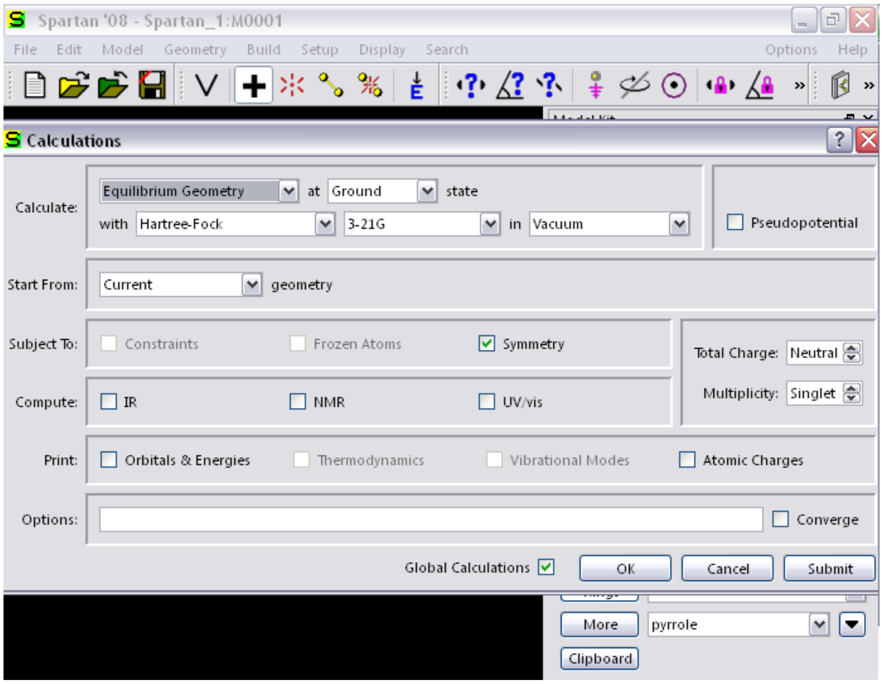
Property: none

Groups: Alkenyl

Rings: Benzene

More: pyrrole

4) Select ‘Calculations’ from the ‘Setup’ menu in the main program window. In the window that opens, select ‘Density Functional’ from the ‘with’ menu, then select the required functional and basis set. In this work, the B3LYP functional was used with the 6-311G* basis set. Click ‘Submit’ to save and start the calculation.



Calculate: Equilibrium Geometry at Ground state
with Hartree-Fock 3-21G in Vacuum
☐ Pseudopotential

Start From: Current geometry

Subject To: ☐ Constraints ☐ Frozen Atoms ☑ Symmetry

Total Charge: Neutral

Multiplicity: Singlet

Compute: ☐ IR ☐ NMR ☐ UV/vis

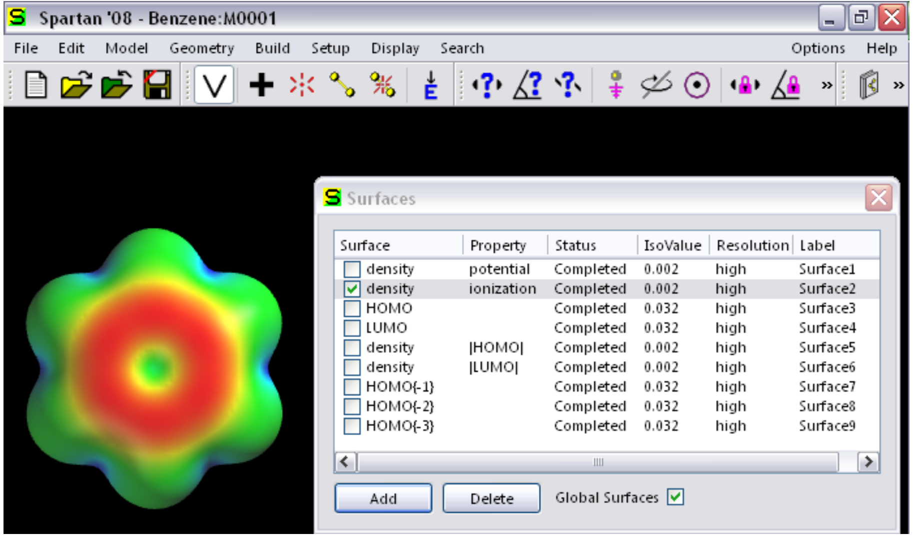
Print: ☐ Orbitals & Energies ☐ Thermodynamics ☐ Vibrational Modes ☐ Atomic Charges

Options: ☐ Converge

Global Calculations ☑

More: pyrrole

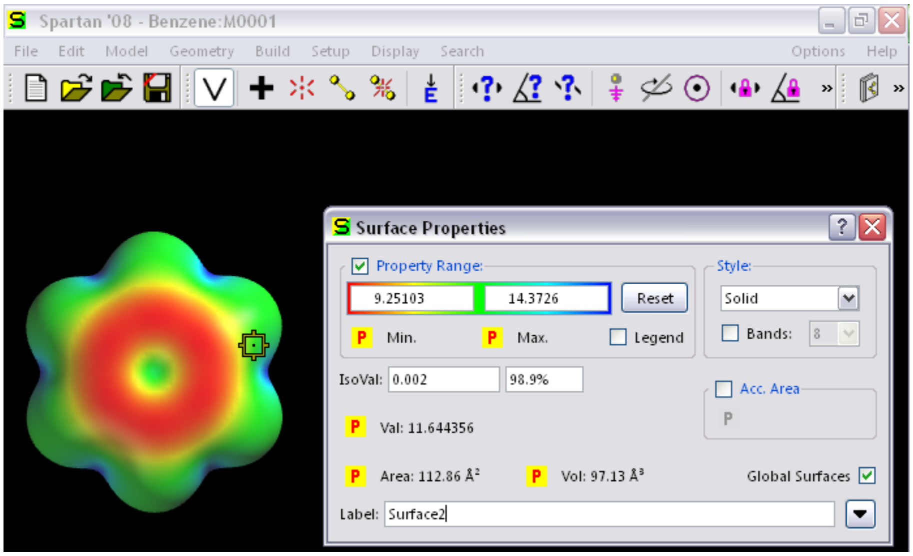
5) After the calculation is complete, open the surfaces window by selecting ‘Surfaces’ from the ‘Setup’ menu, and check the box to the left of the ‘density’ ‘ionization’ entry.



	Surface	Property	Status	IsoValue	Resolution	Label
☐	density	potential	Completed	0.002	high	Surface1
☑	density	ionization	Completed	0.002	high	Surface2
☐	HOMO		Completed	0.032	high	Surface3
☐	LUMO		Completed	0.032	high	Surface4
☐	density	|HOMO|	Completed	0.002	high	Surface5
☐	density	|LUMO|	Completed	0.002	high	Surface6
☐	HOMO{-1}		Completed	0.032	high	Surface7
☐	HOMO{-2}		Completed	0.032	high	Surface8
☐	HOMO{-3}		Completed	0.032	high	Surface9

Global Surfaces ☑

6) To scale the surface appropriately, open the properties window by selecting ‘Properties’ from the Display menu in the main program, and left-click click anywhere on the surface of the molecule.



☑ Property Range: 9.25103 14.3726

☐ Legend

Style: Solid

☐ Bands: 8

IsoVal: 0.002 98.9%

Val: 11.644356

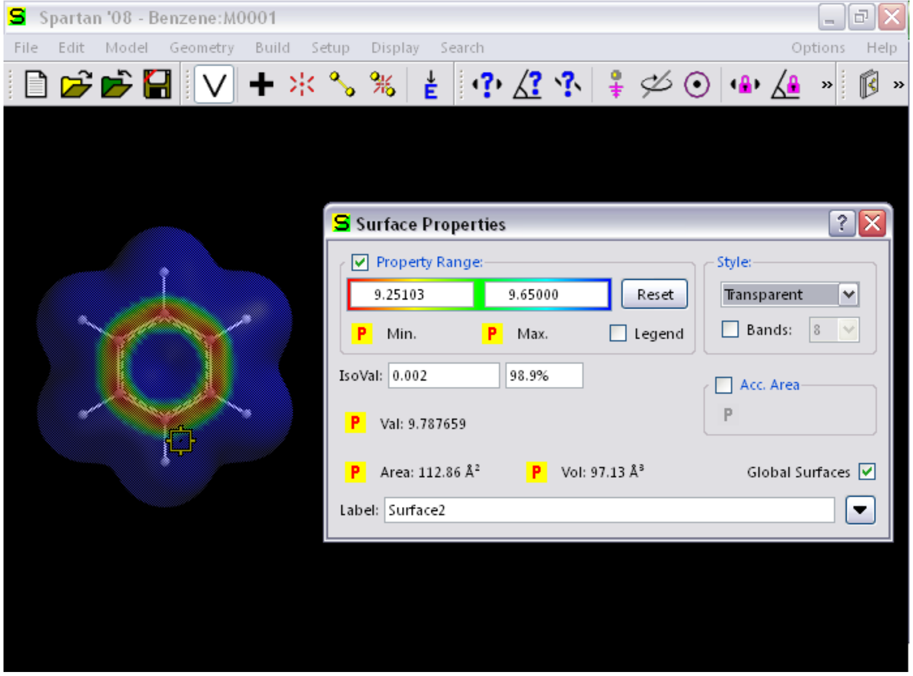
Area: 112.86 Å²

Vol: 97.13 Å³

Global Surfaces ☑

Label: Surface2

7) The surface can be scaled by changing the values in the 'Property Range' boxes. The procedure used in this work leaves the minimum value unchanged and the maximum value is adjusted to the min+0.4 eV. The surface can be made transparent by selecting this option from the 'Style' drop-down menu. Furthermore, the model can be changed to 'Ball and Spoke' via the 'Model' menu in the main program window. To read a value from a specific point on the surface, place the cursor over that point. The value at the cursor point is shown on the left of the properties window as "Val: 9.787659" eV in this example.



☑ Property Range: 9.25103 9.65000
Min. Max. ☐ Legend
Style: Transparent
☐ Bands: 8
IsoVal: 0.002 98.9%
☐ Acc. Area
Val: 9.787659
Area: 112.86 Å² Vol: 97.13 Å³
Global Surfaces ☑
Label: Surface2

Method Selection:

We quickly established that average local ionisation energy calculations performed using Density Functional Theory (DFT) successfully rank the relative nucleophilicities of aromatic carbons and heteroatoms where previously used Hartree-Fock (HF) methods sometimes fail (Figure S2) [25, 61-63]. Indeed, average local ionisation energies calculated using DFT have been shown to be theoretically robust ,[61] and were also employed in the most detailed assessment of local average ionisation energies prior to the present study (21 aromatic molecules)[20].

Correlations of average local ionisation energy minima calculated using DFT and various basis sets against experimental reactivity parameters were also found to be better than corresponding calculations performed using HF (Figures S16-S17).

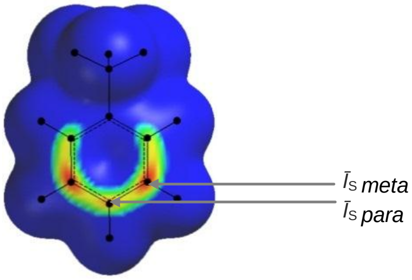


Figure S1. Example showing the positions on the 0.002 electrons/bohr^3 average local ionisation energy surface corresponding to $\bar{I}_{S\ meta}$ and $\bar{I}_{S\ para}$ in the example of trifluoromethyl benzene.

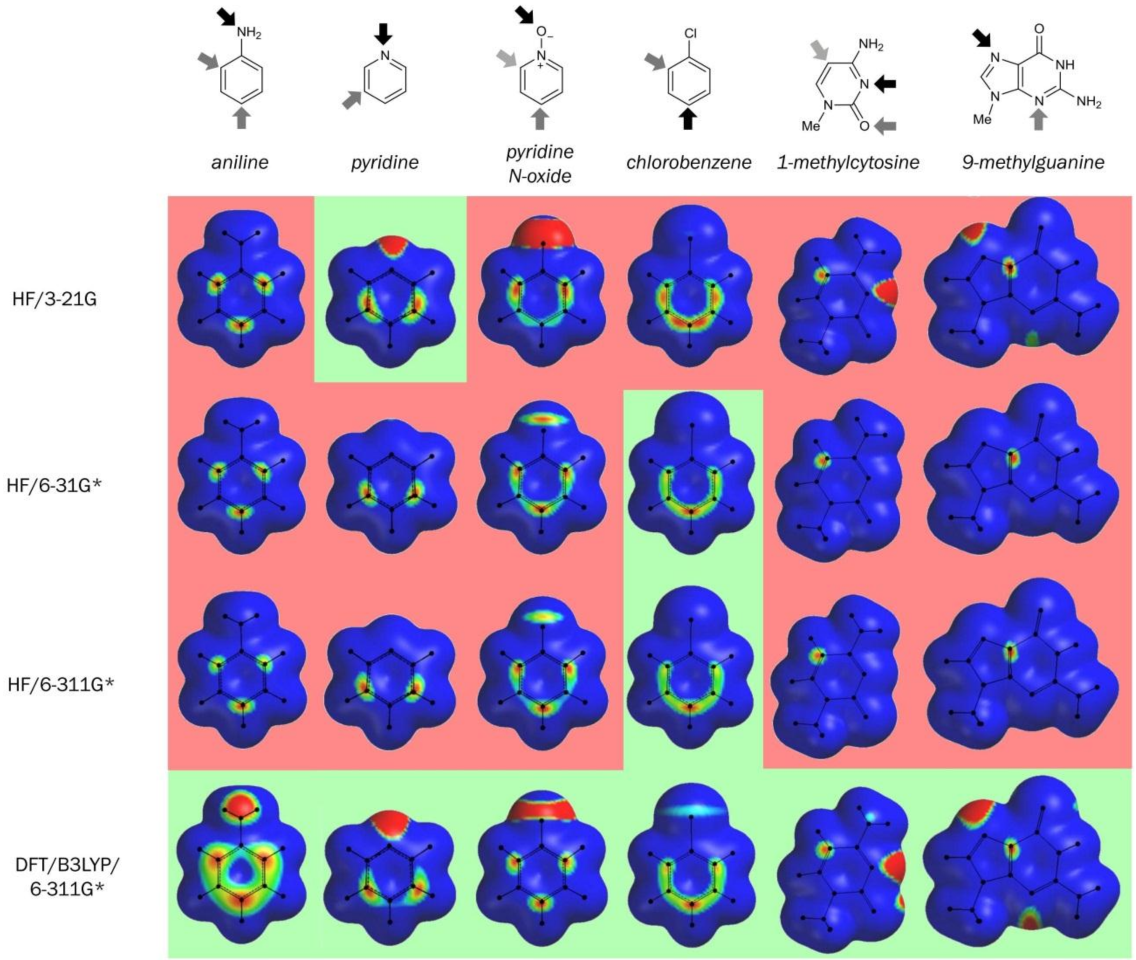


Figure S2. Experimental reactivity patterns for a range of aromatic substrates and corresponding average local ionisation energy surfaces at the 0.002 electrons/bohr^3 surface calculated using the methods shown. Examples where the calculation correctly ranks the relative nucleophilicities of different reactive sites are highlighted with a green background. References for the observed reactivity patterns are given in the captions of other Supporting Figures.

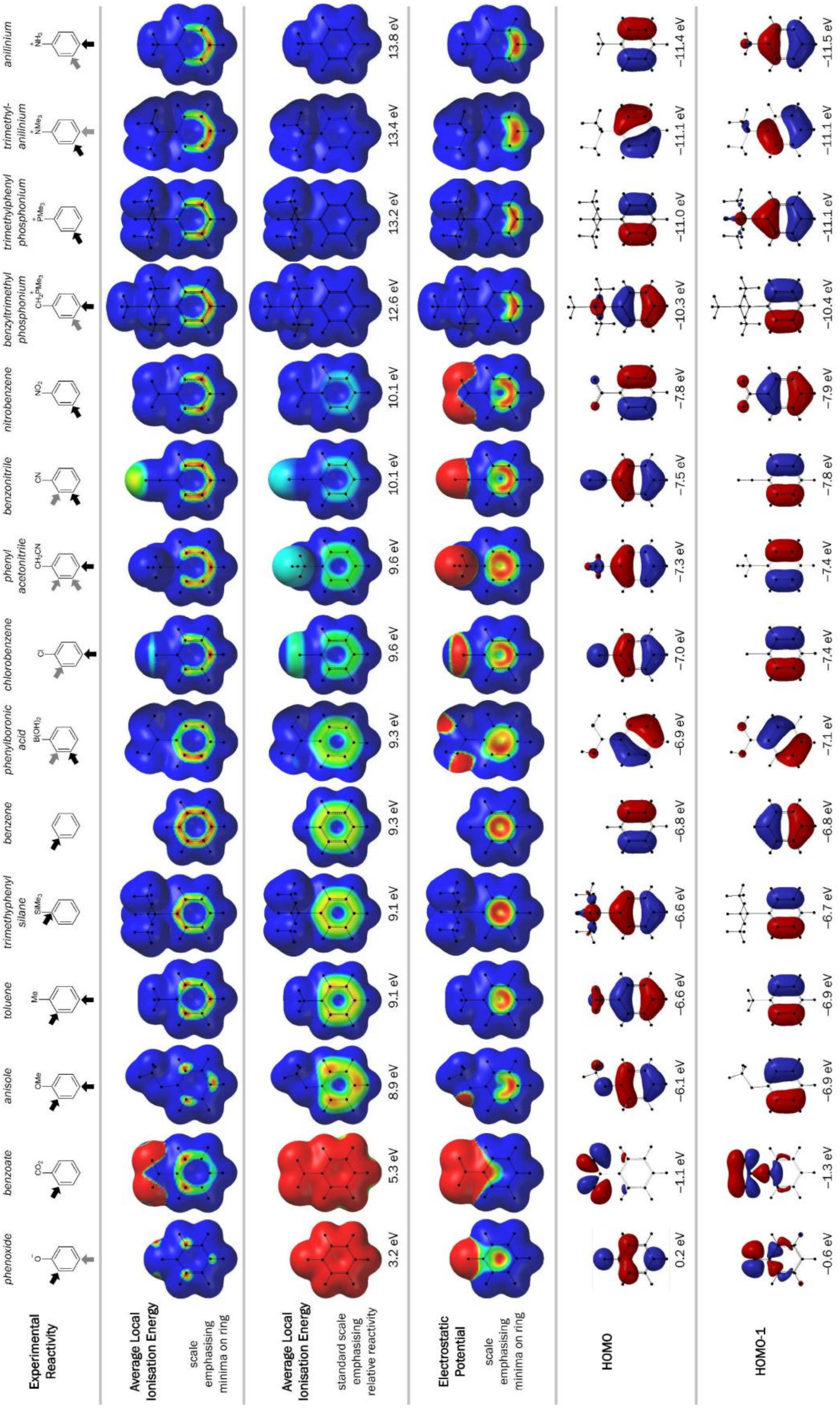

Experimental Reactivity
Average Local Ionisation Energy
scale emphasising minima on ring
Average Local Ionisation Energy
standard scale emphasising relative reactivity
Electrostatic Potential
scale emphasising minima on ring
HOMO
HOMO-1
phenoxide
O⁻
3.2 eV
0.2 eV
−0.6 eV
benzoate
CO₂⁻
5.3 eV
−1.1 eV
−1.3 eV
anisole
OMe
8.9 eV
−6.1 eV
−6.9 eV
toluene
Me
9.1 eV
−6.6 eV
−6.9 eV
trimethylphenyl silane
SiMe₃
9.1 eV
−6.6 eV
−6.7 eV
benzene
9.3 eV
−6.8 eV
−6.8 eV
phenylboronic acid
B(OH)₂
9.3 eV
−6.9 eV
−7.1 eV
chlorobenzene
Cl
9.6 eV
−7.0 eV
−7.4 eV
phenyl acetonitrile
CH₂CN
9.6 eV
−7.3 eV
−7.4 eV
benzonitrile
CN
10.1 eV
−7.5 eV
−7.8 eV
nitrobenzene
NO₂
10.1 eV
−7.8 eV
−7.9 eV
benzyltrimethyl phosphonium
CH₂P⁺Me₃
12.6 eV
−10.3 eV
−10.4 eV
trimethylphenyl phosphonium
P⁺Me₃
13.2 eV
−11.0 eV
−11.1 eV
trimethyl-anilinium
N⁺Me₃
13.4 eV
−11.1 eV
−11.1 eV
anilinium
N⁺H₃
13.8 eV
−11.4 eV
−11.5 eV

Figure S3 (on preceding page). Comparison of surface-encoded ionisation energy surfaces, electrostatic potentials, HOMO and HOMO-1 lobes of monosubstituted benzenes in relation to their experimental reactivity in electrophilic aromatic substitution reactions. Surface-encoded ionisation energies account for the reactivity of monosubstituted benzenes and the magnitude of these minima correspond with the relative nucleophilicities of these molecules. There is no obvious link between purely electrostatic or orbital-based models and the reactive behaviour of this series of molecules. The ionisation energy surfaces emphasising the relative reactivity of different molecules in the second row are plotted on a standardised scale from 8.7 eV (red) to 10.7 eV (blue). Electrostatic potentials are scaled from the lowest potential on each aromatic ring (red) to this value plus 15 kJ mol^{-1} (blue). HOMO and HOMO-1 lobes correspond to 0.032 electrons/bohr^3. References for the observed reactivity patterns are given in the captions of the other Supporting Figures.

For a general review of nitration by electrophilic aromatic substitution[64]

Phenoxide anion:
Reimer-Tiemann reaction[32, 65]
Allylation[66]
Kolbe-Schmitt reaction[31]
Chlorination[29]

Benzoate anion
Chlorination[38]
Bromination[39]

Anisole
Bromination[30,35]
Chlorination[29, 30, 67]
Iodination[30, 68, 69]
Nitration[70]
Formylation[71]

Toluene
Chlorination[30, 67, 72-74]
Bromination[75,30, 35, 74, 76]
Iodination[30, 36]
Nitration[70, 77, 78]

Trimethylphenyl silane
In Pd-catalysed cross coupling reactions[79]
Review[80]
Desilylation (reaction with H$^+$)[81]
Bromination[82]
Chlorination[83]
Iodination[84, 85]
Nitration[85]
Fluorination[86]

Phenylboronic acid
Nitration[87]

Chlorobenzene and other halobenzenes
Nitration[28, 70, 78]
Chlorination[29, 30, 67]
Bromination [30,35]
Iodination[36]

Phenylacetonitrile
Nitration[42, 88]

Benzonitrile
Nitration[34, 37, 78]
Bromination[75,35]
Chlorination[34]
Iodination[36]

Nitrobenzene
Nitration[34, 78]
Iodination[89, 90 91]
Bromination[30, 75,35]
Chlorination[30, 34]

Benzyltrimethyl phosphonium cation
Nitration[92]

Trimethylphenyl phosphonium cation
Nitration[41, 92]

Trimethyl anilinium cation
Nitration[41, 93]

Anilinium cation
Nitration[93, 94]

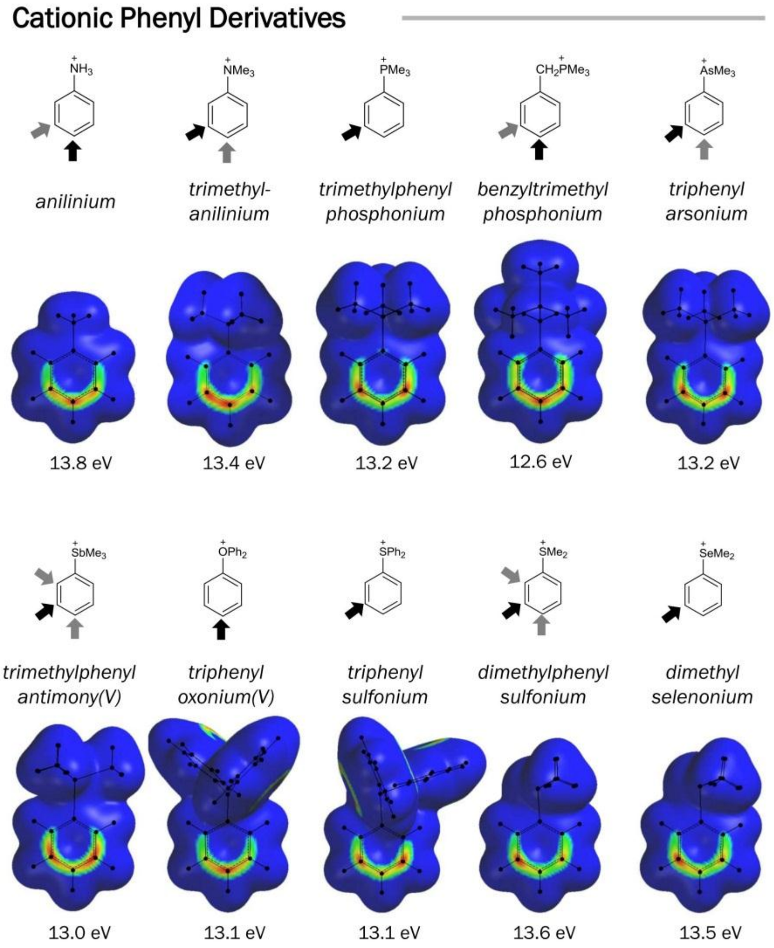


Figure S4. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\ min}$) at the 0.002 electrons/bohr^3 surface for cationic monosubstituted benzenes. Calculations were performed using the LACVP combination of basis sets where DFT/B3LYP/6-311G* was not supported. References for the observed reactivity patterns are given below.

Anilinium cation
Nitration[93, 94]

Trimethyl anilinium cation
Nitration[41, 93]

Trimethylphenyl phosphonium cation
Nitration[41, 92]

Benzyltrimethyl phosphonium cation
Nitration[92]

Trimethylphenyl arsonium cation
Nitration[41, 92]

Trimethylphenyl antimony(V) cation
Nitration[92]

Triphenyl oxonium cation
Nitration[41, 95]

Triphenyl sulfonium cation
Nitration[96]

Dimethylphenyl sulfonium cation
Nitration[41]

Dimethyl selenonium cation
Nitration[41]

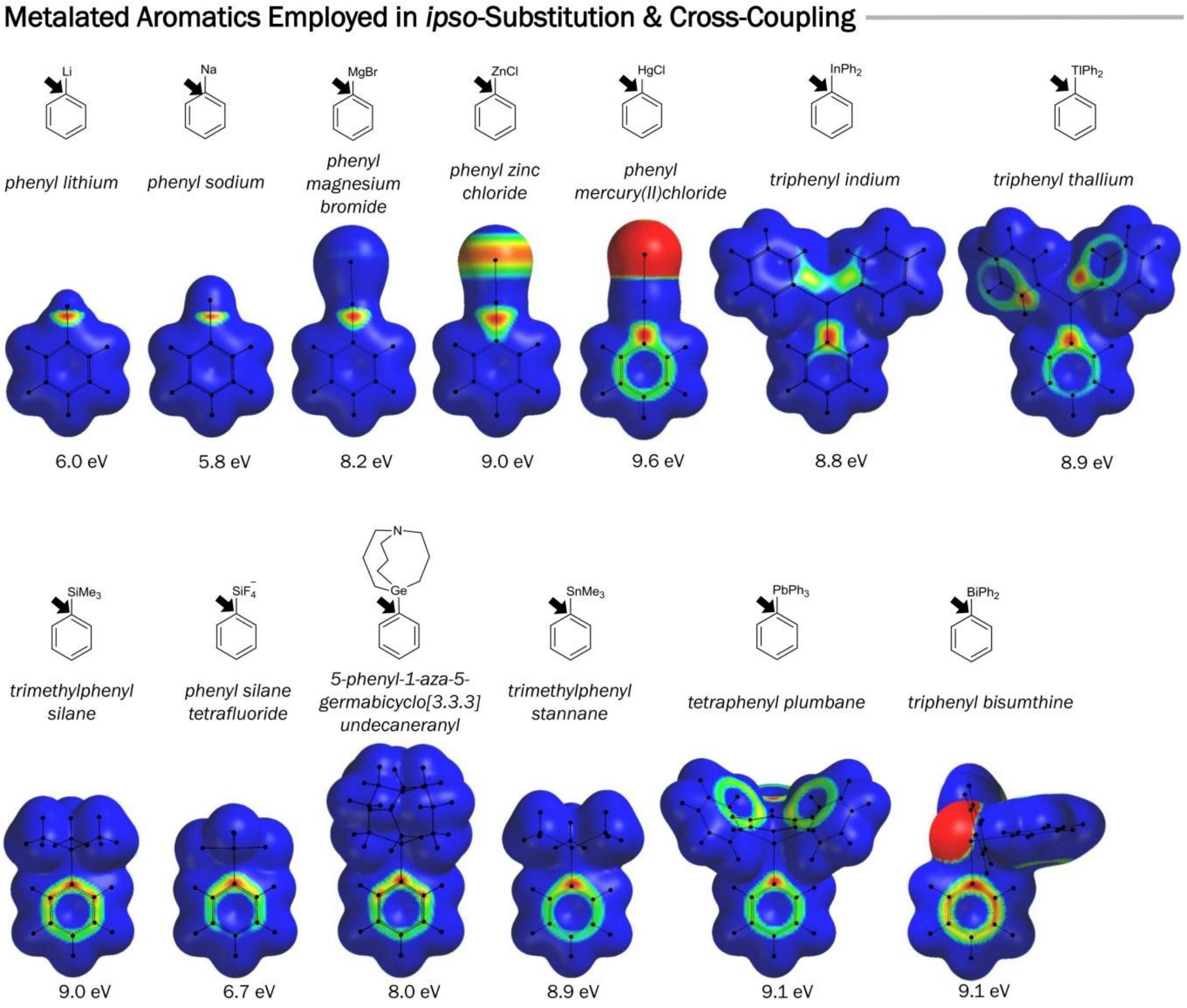


Figure S5. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\,\min}$) at the 0.002 electrons/bohr^3 surface for phenyl derivatives used in metal-catalysed cross-coupling reactions and *ipso*-substitution reactions. Calculations were performed using the LACVP combination of basis sets where DFT/B3LYP/6-311G* was not supported. References for the observed reactivity patterns are given below.

General:
For excellent general overview of metal-catalysed cross coupling reactions[14, 79]

For other more specific literature*:*

Phenyl lithium
General[9]
ipso-Fluorination[97]

Phenyl sodium
General[98]

Phenyl zinc chloride
ipso-Bromination[99]

Phenyl mercury(II)chloride
In Pd-catalysed cross coupling reactions[100]
ipso-nitration and nitrosation[101]

Triphenyl indium
In metal-catalysed cross-coupling reactions[102]

Trimethylphenyl silane
Review[80]

Desilylation (reaction with H^+)[81]
ipso-Bromination[82]
ipso-Chlorination[83]
ipso-Iodination[84, 85]
ipso-Nitration[85]
ipso-Fluorination[86]

5-Phenyl-1-aza-5-germabicyclo[3.3.3]undecane
In metal-catalysed cross-coupling reactions[79]

Trimethylphenyl stannane
ipso-Fluorination[86]
ipso-Nitration, Nitrosation[101]
In Pd-catalysed cross coupling reactions[100]

Tetraphenyl plumbane
ipso-Nitration, Nitrosation[101]

Triphenyl bismuthine
ipso-Nitrosation[101]

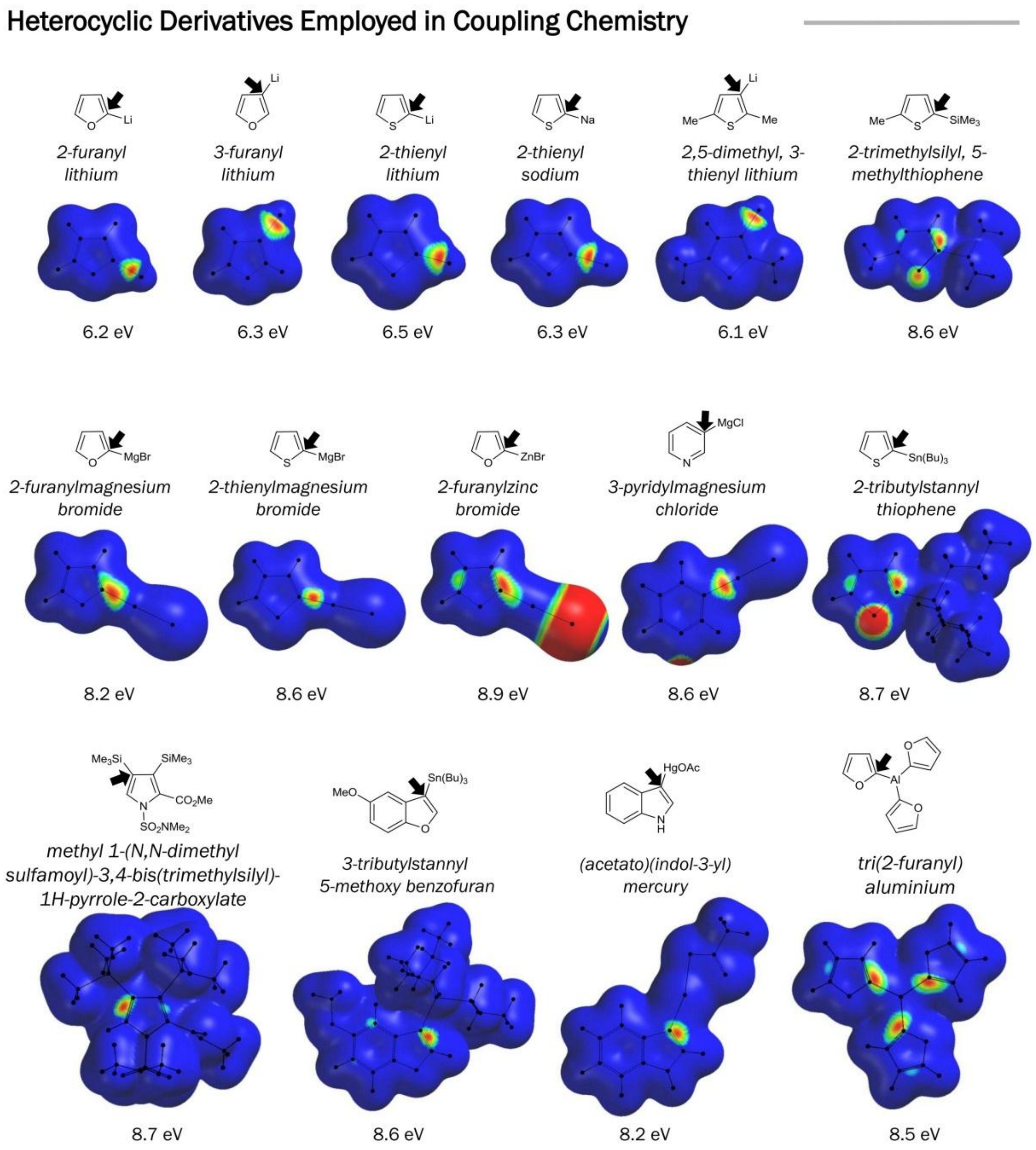


Figure S6. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{\mathrm{S,\,min}}$) at the 0.002 electrons/bohr^3 surface for heterocycles used in metal-catalysed cross-coupling reactions. Calculations were performed using the LACVP combination of basis sets where DFT/B3LYP/6-311G* was not supported. References for the observed reactivity patterns are given below.

General
For an excellent overviews of metal-catalysed cross coupling reactions[79, 103]
2-Furanyl lithium
Reaction with carbonyls[104]

3-Furanyl lithium
Reaction with aldehydes[105 106-109]
Reaction with ketones[110]
2-Thienyl lithium
Reaction with esters[111, 112]
Reaction with amides[113, 114]
Reaction with Weinreb amides[115]
Reaction with carbonyl[116]
Reaction with Vilsmeier reagent[117-119]
Reaction with carbon dioxide[120]

Reaction with carbonates[121]

2-Thienyl sodium
General[98]
2,5-Dimethyl, 3-thienyl lithium
With alkenes[122]

2-Trimethylsilyl, 5-methylthiophene:
ipso-substitution[123-126]

2-Furanylmagnesium bromide
Reaction oxycarbenium ions [127]

2-Thienylmagnesium bromide
Reaction with carbonyls[128 129, 130]
Reaction with esters[131]
Reaction with Weinreb amides[132]
Reaction with alkenes [133, 134]

2-Furanyl zinc bromide
Negishi coupling[135, 136]

2-Pyridylmagnesium chloride
Kumada coupling[137]

2-Tributylstannyl thiophene:
Stille coupling[138, 139]

Methyl 1-(N,N-dimethylsulfamoyl)-3,4-bis(trimethylsilyl)-1H-pyrrole-2-carboxylate
ipso-substitution[140]
ipso-Iodination during formal total synthesis of lukianol A[141]

3-Tributylstannyl 5-methoxybenzofuran
Stille coupling[138]

(Acetato)(indol-3-yl) mercury
Pd-catalysed cross-coupling[142]

Tri(2-furanyl) aluminium
Reaction with an epoxide[143]

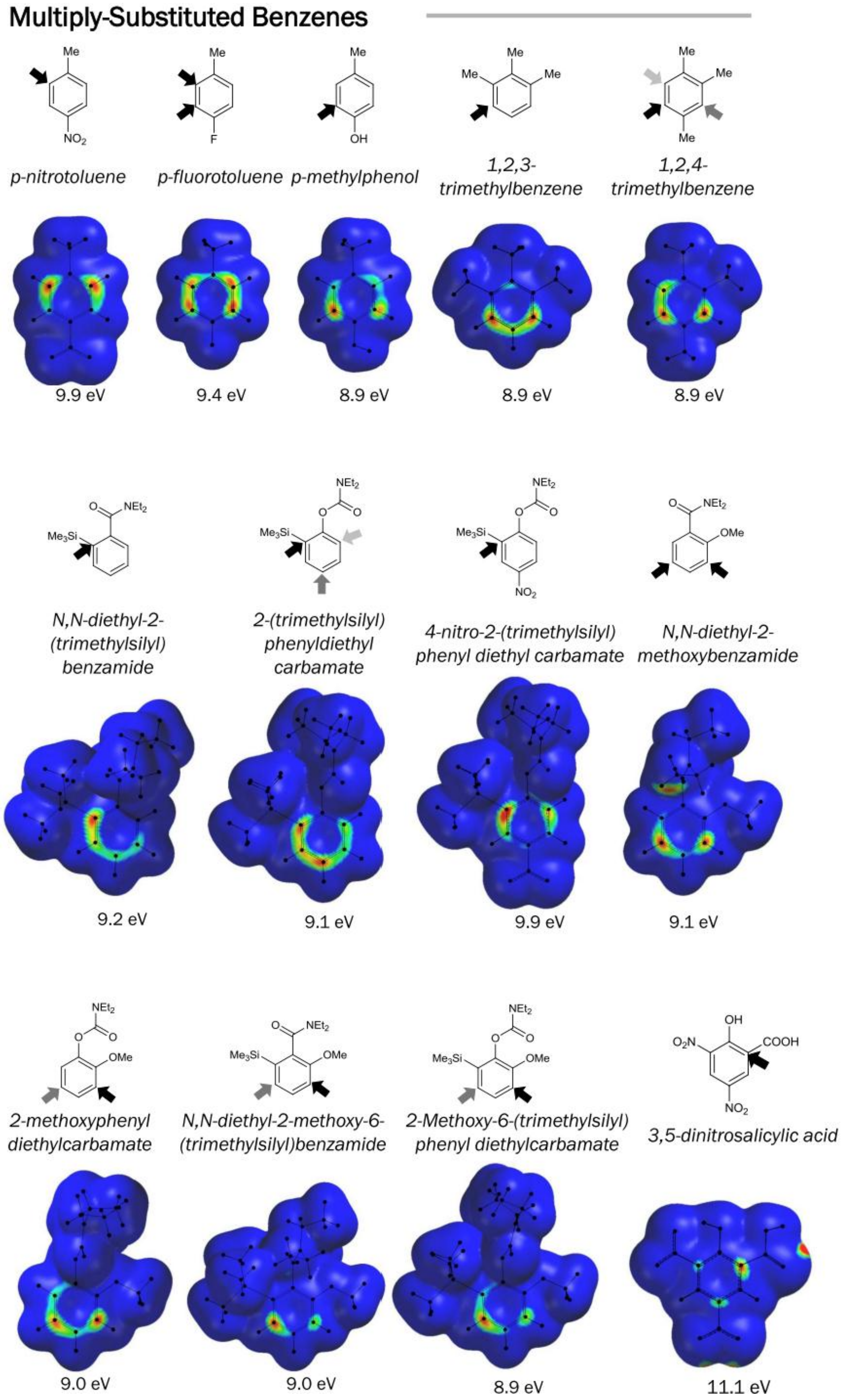


Figure S7. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\,\mathrm{min}}$) at the 0.002 electrons/bohr^3 surface for multiply-substituted benzenes. References for the observed reactivity patterns are given below.

***p*-Nitrotoluene**
Bromination[144,35]

***p*-Fluorotoluene**
Nitration[145]

***p*-Methylphenol**
Bromination[146]

1,2,3-Trimethylbenzene
Nitration[43]

1,2,4-Trimethylbenzene
Nitration[43]

N,N-diethyl-2-(trimethylsilyl)benzamide
Iodination, bromination, chlorination, *ipso*-borodesilylation[83]

2-(trimethylsilyl)phenyl diethylcarbamate
Iodination, bromination, chlorination, nitrosation, *ipso*-borodesilylation[83]

4-nitro-2-(trimethylsilyl)phenyl diethylcarbamate
Bromination[83]

N,N-diethyl-2-methoxybenzamide
Nitration[83]

2-Methoxyphenyl diethylcarbamate
Nitration[83]

N,N-diethyl-2-methoxy-6-(trimethylsilyl)benzamide
Nitration[83]

2-Methoxy-6-(trimethylsilyl)phenyl diethylcarbamate
Nitration[83]

3,5-dinitrosalicylic acid
Nitration[147]

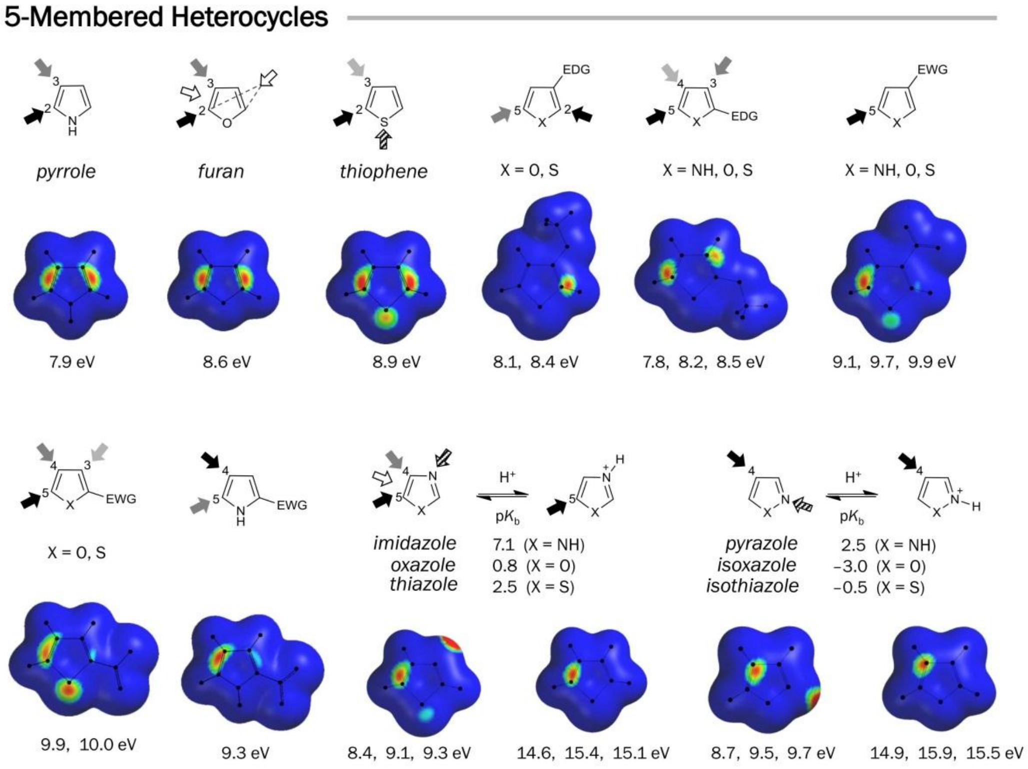


Figure S8. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{\mathrm{S,\,min}}$) at the 0.002 electrons/bohr^3 surface for 5-membered heterocyclic rings. References for the observed reactivity patterns are given below.

For a general review of the substitution of 5-membered rings[148]

Pyrroles
Nitration[77, 149, 150]
Nitration: reversal of 2– vs. 3–substitution ratio upon *N*–substitution of pyrroles[151]
Halogenation[152, 153]
Acetylation: mostly in the 2–position, 3–position minor product[154]
Formylation in 2–position[71]

2- and 3-EDG pyrroles
Note that electron–rich pyrroles tend to be highly reactive and unstable.
Formylation (EDG = 2–Me)[155]

2-EWG-pyrroles
Bromination (EWG = NO_2)[49, 50]
Nitration, halogenation and acetylation (EWG = $COCCl_3$)[48]
Nitration (EWG = $COCH_3$)[51]

3-EWG-pyrroles
Alkylation, halogenation (EWG = COPh)[156]
Acylation (EWG = COPh–*p*–OMe)[157]
Formylation (EWG = COOEt)[158]

Thiophenes
Nitration[77, 159, 160]
Bromination, chlorination[30, 67, 161]
Acylation[162]
Formylation[71, 163]
Addition at sulfur (hashed arrow)[164]

2-EDG thiophenes
Bromination, Chlorination (EDG = OMe)5–position most reactive [165-167] 3– and 5–positions[139, 168]
Iodination (EDG = Me, OMe, OC=OMe)[69, 169]
Nitration (EDG = Me)[160]
Formylation (EDG = OMe) 5–position most reactive[71]

2-EWG thiophene

(EWG = NO_2, CN and CHO) 5–position most reactive, 4–position 2nd most reactive, 3–position 3rd most reactive[159]
Chlorination (EWG = Cl, Br)[67]
Nitration (EWG = Cl)[160]
Iodination (EWG = Cl, Br, I, CN, NO_2, CHO, $COCH_3$, CO_2CH_3)[69, 169]

3-EDG thiophenes

Bromination (EDG = alkyl, OMe)[170,167, 171]
Iodination (EDG = alkyl)[172]

3-EWG thiophenes

(EWG = NO_2, CN and CHO) 5–position most reactive, 2–position 2nd most reactive, 4–position 3rd most reactive[159]
Hydroxyalkylation (EWG = Cl)[173]

Furans

Note that some of the substitution reactions of furans may not–proceed through a typical electrophilic aromatic substitution reaction mechanism, but through an addition–elimination mechanism, although the position of the initial attack of the incoming electrophile determines the regiochemistry of the final product as in a typical EAS reaction mechanism.
Nitration[77, 174]
Formylation[71]
Bromination[175]
Acetylation[176]
Oxidation with osmium tetroxide (unfilled arrow)[177]

2–EDG furans

Formylation (EDG = alkyl)[178]
Michael addition (EDG = OMe)[179 180]
Acylation (EDG = alkyl)[181]
Chlorination (EDG = *t*–Bu)[152]

2–EWG furans

Nitration (EWG = NO_2)[182, 183]

3–EDG furans

Formylation, acylation (EWG = OMe, alkyl)[184 185]

3–EWG furans

Formylation (EWG = COOMe)[186]

Oxazole

pK_a of conjugate acid = 0.8[187]
Oxazoles tend to undergo addition rather than substitution (unfilled arrow)[188]

Imidazole and cation

pK_a of conjugate acid = 7.1[189]
Nitration[190]
Bromination[191]
Oxidation with osmium tetroxide (unfilled arrow)[192]

Thiazole

pK_a of conjugate acid = 2.5[187]
Nitration[193]

Pyrazole and cation

pK_a of conjugate acid = 2.5[194]
Iodination[195, 196]
Bromination and Chlorination[197]
Nitration[190, 198]

Isothiazole

pK_a of conjugate acid = –0.5[187]
Halogenation[199, 200]
Nitration[200]

Isoxazole

pK_a of conjugate acid = –3.0[187]
Nitration[201-203]
Bromination[204, 205]

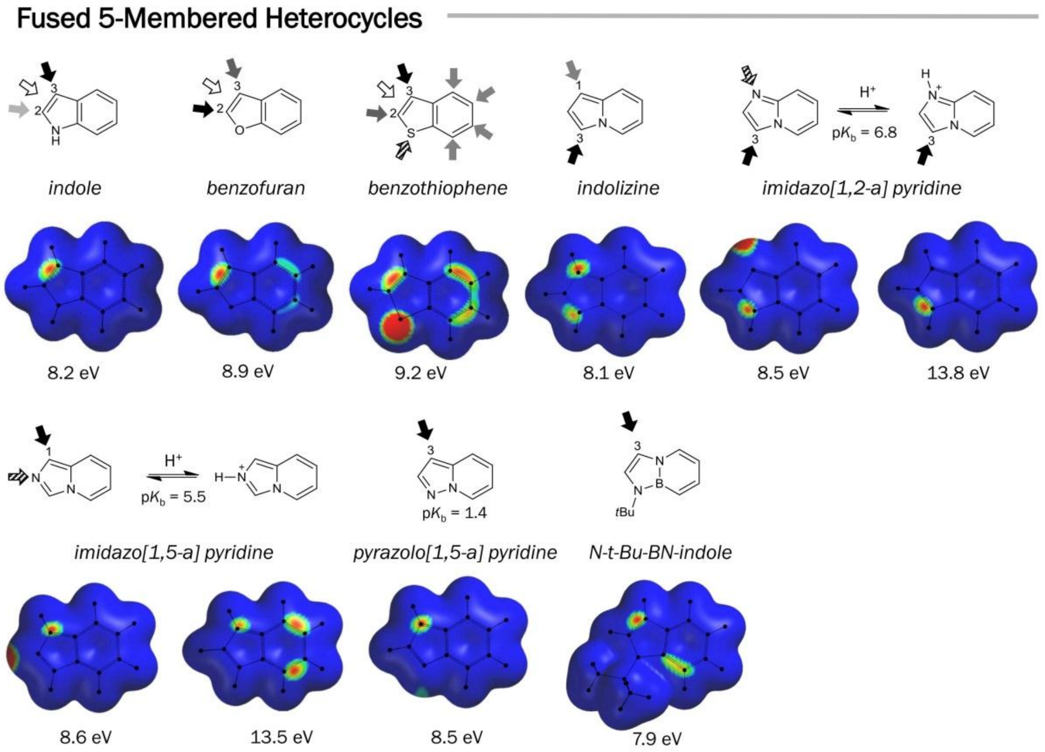


Figure S9. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\,\min}$) at the 0.002 electrons/bohr^3 surface for fused 5-membered heterocycles. References for the observed reactivity patterns are given below.

Indole
Formylation[71, 206]
Mannich reaction[207]
Halogenation[208]
Nitration[77]
Oxidation with osmium tetroxide (unfilled arrow)[209]

Benzofuran
Nitration[77, 210, 211]
Formylation[212]
Hydroxyalkylation[173]
Addition at carbon (unfilled arrow)[213]

Benzothiophene
Halogenation[214-217]
Nitration[77, 215, 218]
Acetylation[219]
Hydroxyalkylation[173]
Addition at carbon (unfilled arrow)[213]
Addition at sulfur (hashed arrow)[164]
Indolisine
Nitrosylation, formylation[220]
Acylation[221]
Nitration[222]

Imidazo[1,2-a]pyridine and cation
pK_a of conjugate acid = 8.3[223]
Bromination[224]
Chlorination[224]
Acylation[225]
Nitration[224]

Imidazo[1,5-a]pyridine and cation
pK_a of conjugate acid = 5.5[223]
Acylation[226]
Nitration[227]

Pyrazolo[1,5-a]pyridine
pK_a of conjugate acid = 1.4[223]
Formylation, acylation[228]

N-tert-Bu-BN-Indole
Bromination, Mannich Reaction, Michael Addition, Deuteriation, Acylation[56]

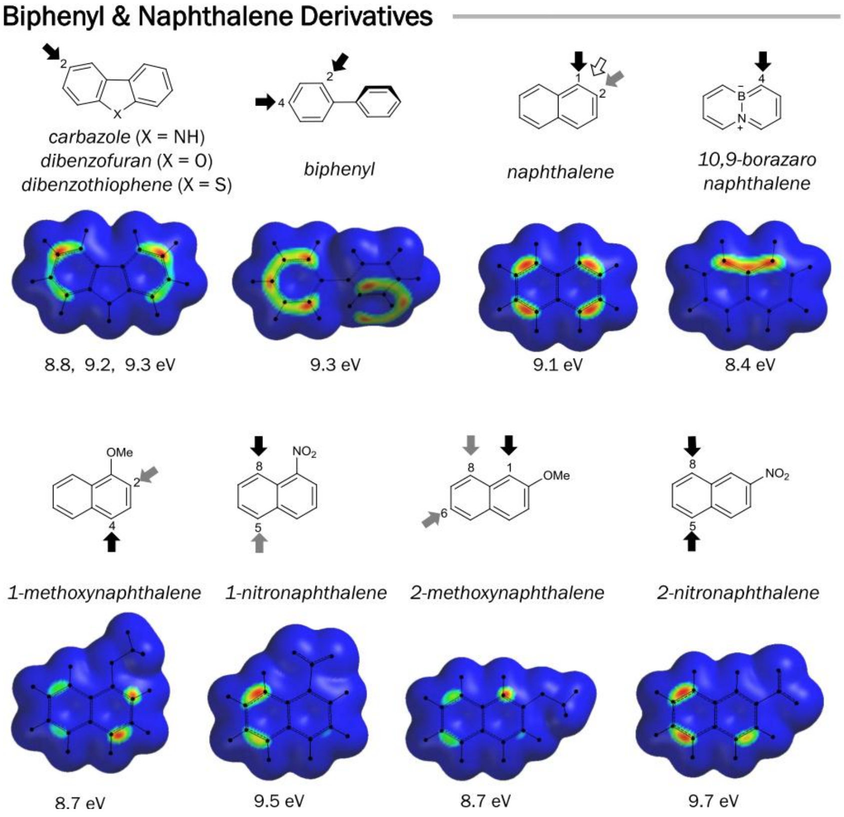


Figure S10. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\ min}$) at the 0.002 electrons/bohr^3 surface for biphenyl and naphthalene derivatives. References for the observed reactivity patterns are given below.

Carbazole
Bromination[229, 230]
Alkylation[231]

Dibenzofuran
Halogenations, Friedel-Crafts and protodetritiation reactions (note that some nitration reactions follow a charge-transfer mechanism to gives the 3-product rather than the 2-product) [52]
Iodination[232, 233]
Alkylation, acylation[234]

Dibenzothiophene
Halogenation[214]

Biphenyl
Nitration[70, 235-237]
Chlorination[67]

Naphthalene
Nitration[70, 235]
Halogenation[67, 214]
Acylation[238]
Addition & oxidation reactions[239]
Reaction with ethyl diazoacetate (unfilled arrow)[240]
Oxidation with osmium tetroxide (unfilled arrow)[241]

10,9–Borazaronaphthalene
Bromination and deuteration[242]

1–Methoxynaphthalene
Nitration[243]
Iodination[69]

1–Nitronaphthalene
Nitration[46, 244, 245]

2–Methoxynaphthalene
Nitration[243]
Bromination[246]
Iodination[68, 69, 247]

2–Nitronaphthalene
Nitration[248]

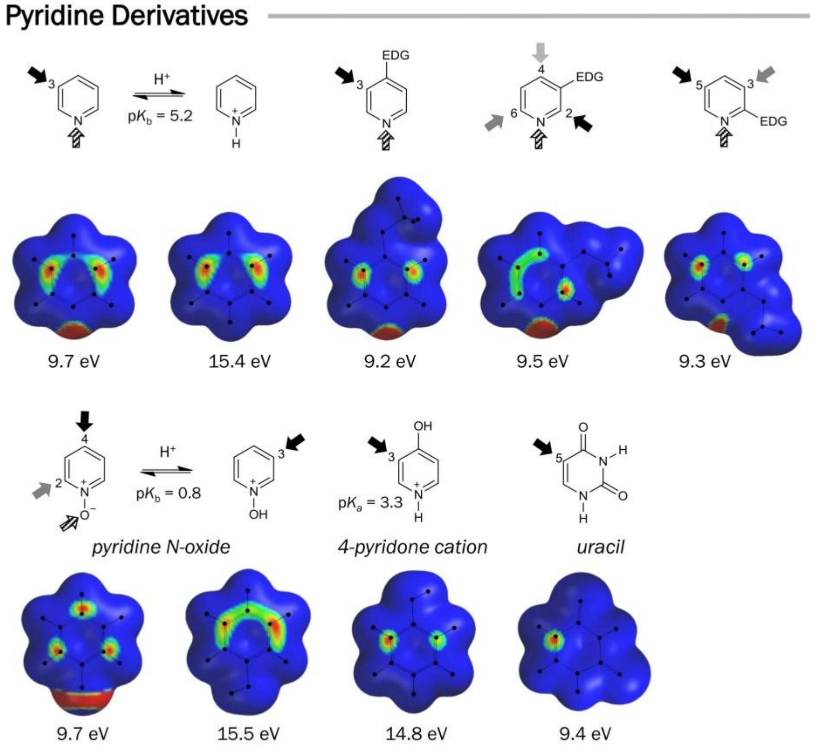


Figure S11. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\,min}$) at the 0.002 electrons/bohr^3 surface for pyridine derivatives. References for the observed reactivity patterns are given below.

Pyridine and cation
pK_a of conjugate acid = 5.2[249]
Halogenation[250]
Nitration[251 252]

4–EDG pyridines
Bromination (EDG = OMe, OH, NH_2)[253]
Nitration (EDG = OMe)[254]

3–EDG pyridines
Bromination (EDG = OMe, OH, NH_2)[253]

2–EDG pyridines
Bromination (EDG = OMe, OH, NH_2)[253, 255]
Chlorination (EDG = NH_2)[256]

Pyridine N–Oxide
pK_a of conjugate acid = 0.8[257]
Bromination[252, 258]

Pyridinium N–Oxide cation
Nitration[252]
Chlorination[259]

4–Pyridone cation
pK_a = 3.3[249]
Nitration[255, 260, 261]

Uracil
Phenylsulfenylation[262]
Bromination[263]
Iodination[264, 265]{#338, 266, 267]
Nitration[160]

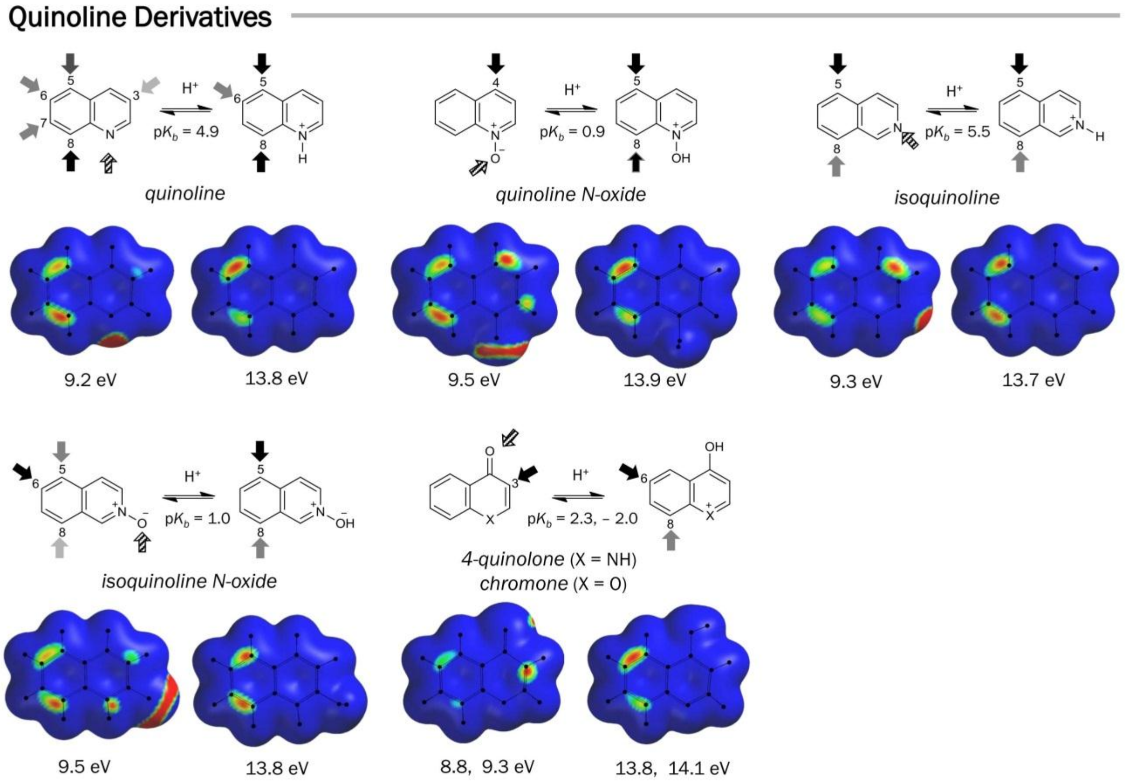


Figure S12. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{\mathrm{S,\,min}}$) at the 0.002 electrons/bohr^3 surface for quinoline derivatives. References for the observed reactivity patterns are given below.

Quinoline and cation
pK_a of conjugate acid = 4.9[249]
Bromination[268-271]
Chlorination[272]
Iodination[273]
Nitration[190, 252, 274-276]
Fluorination[277]

Quinoline N–Oxide and cation
pK_a of conjugate acid = 0.9[278]
Nitration[252, 279, 280]
Nitration with N_2O_5[281]

Isoquinoline and cation
pK_a of conjugate acid = 5.5[249]
Nitration[276, 282, 283]
Bromination[270, 284, 285] in 5 and 8–positions in strong acid [271]

Isoquinoline N–Oxide
pK_a of conjugate acid = 1.0[286]
Nitration[287]

Isoquinolinium N–oxide cation
Nitration[280, 288]

4–Quinolone (X = NH)
pK_a of conjugate acid = 2.3[249]
Nitration[289]

Chromone (X = O)
pK_a of conjugate acid = –2.0[290]
Bromination[291]
Mannich reaction[292]

4–Hydroxyquinolin–1–ium cation (X = NH)
Nitration[293-295]

4–Hydroxychromenylium cation (X =O)
Nitration[296, 297]

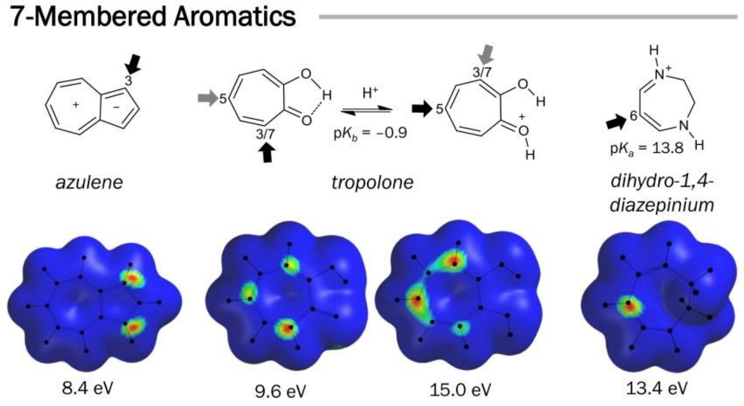


Figure S13. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\ min}$) at the 0.002 electrons/bohr^3 surface for 7-membered aromatics. References for the observed reactivity patterns are given below.

Azulene
Iodination[68]

Tropolone and cation
pK_a of conjugate acid of tropolone = –0.9[298]
Azo–coupling, nitrosation, nitration, sulfonation, halogenation, hydroxylation, hydroxymethylation, Reimer–Tiemann reaction[299, 300]

Dihydro–1,4–diazepinium cation
pK_a = 13.4 (5,7–dimethyl derivative)[301]
Bromination[302-304]
Nitration[47, 305]

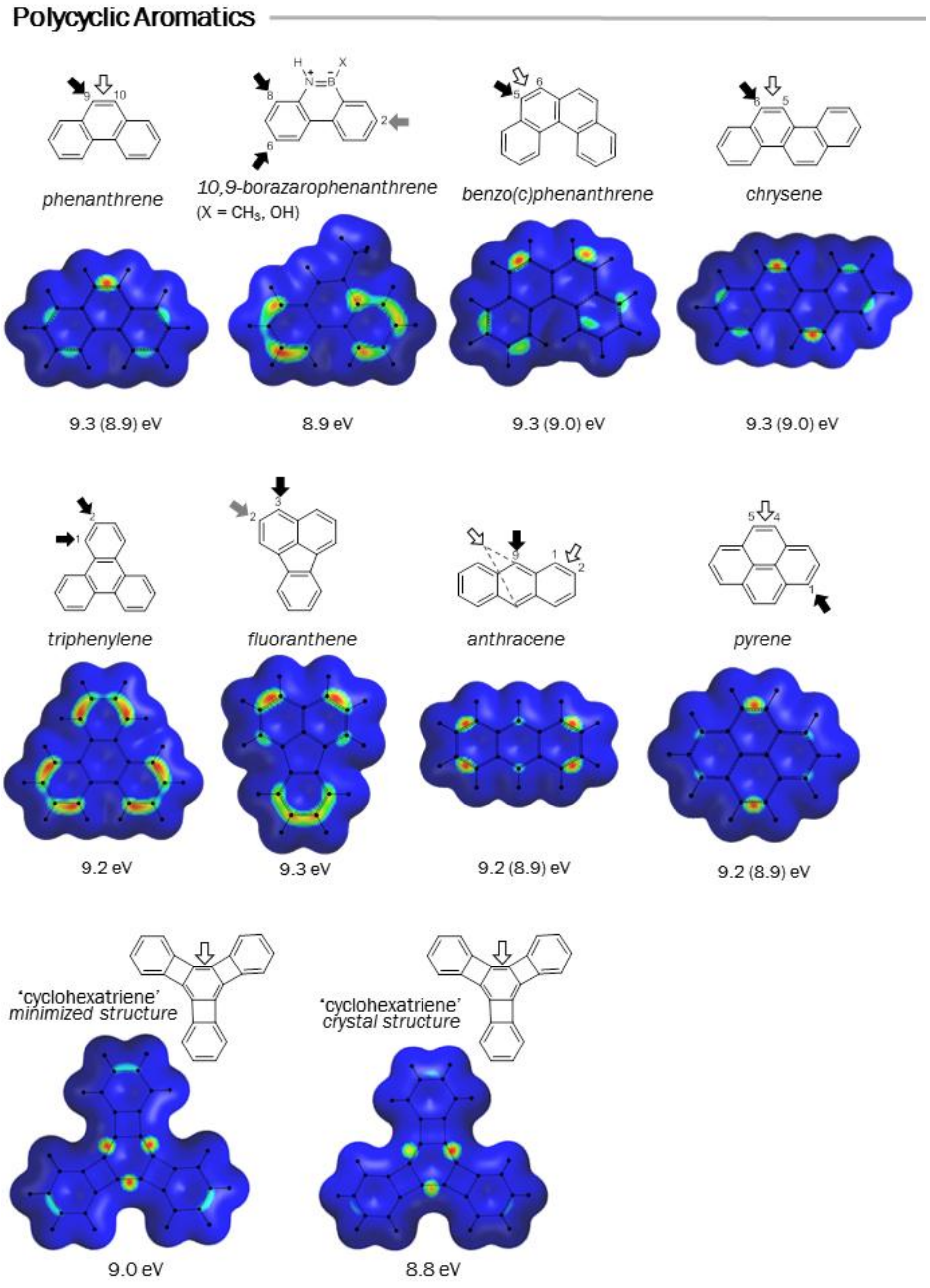


Figure S14. Experimental reactivity patterns and corresponding calculated average local ionisation energy surfaces and minimum values ($\bar{I}_{S,\,min}$) at the 0.002 electrons/bohr^3 surface for polycyclic aromatics. Values in parentheses refer to the values taken over regions with double-bond character as discussed in the main text. References for the observed reactivity patterns are given below.

Phenanthrene
Nitration[235]
Halogenation[67, 214]
Bromination[306]
Addition & oxidation reactions (unfilled arrow)[240, 241, 307, 308]

10–Methyl–10,9–Borazarophenanthrene
Bromination and chlorination[55]

Nitration and chlorination[54]
Acetylation[53]
Steric congestion inhibits reaction at carbon 4[53]

10–Hydroxy–10,9–Borazarophenanthrene

Bromination and chlorination[55]
Nitration and chlorination[54]
Acetylation[53]

Benzo(c)phenanthrene

Acylation[238]
Bromination, nitration, acetylation[309]
Oxidation with osmium tetroxide (unfilled arrow)[310]

Chrysene

Nitration[235, 311]
Halogenation[214]
Acetylation[312]
Acylation[238, 313]
Oxidation with osmium tetroxide (unfilled arrow)[310, 314]

Triphenylene

Small electrophiles react preferentially in the most reactive 1–position, while larger electrophile react in the 2–position due to the steric hindrance in the 1–position.

1–chlorination and 1–deuteriation[315]
mostly 1–nitration, some 2–nitration[316 311]
mostly 2–nitration, some 1–nitration[235, 311]
2–halogenation[214]
2-acylation[238]

Fluoranthene

mostly 3–nitration, some 8–nitration [311]

Anthracene

Acylation[238]
Halogenation[67, 214, 306]
Nitration[317]
Addition & Oxidation reactions (unfilled arrow)[307, 308, 318, 319]
[241 240, 320]

Pyrene

Acylation[238]
Nitration[235, 311]
Halogenation[67, 214]
Oxidation with osmium tetroxide (unfilled arrow)[321]
Reaction with ethyl diazoacetate (unfilled arrow)[240]

‘Cyclohexatrine’

Epoxidation and hydrogenation {#1240}[57, 59]

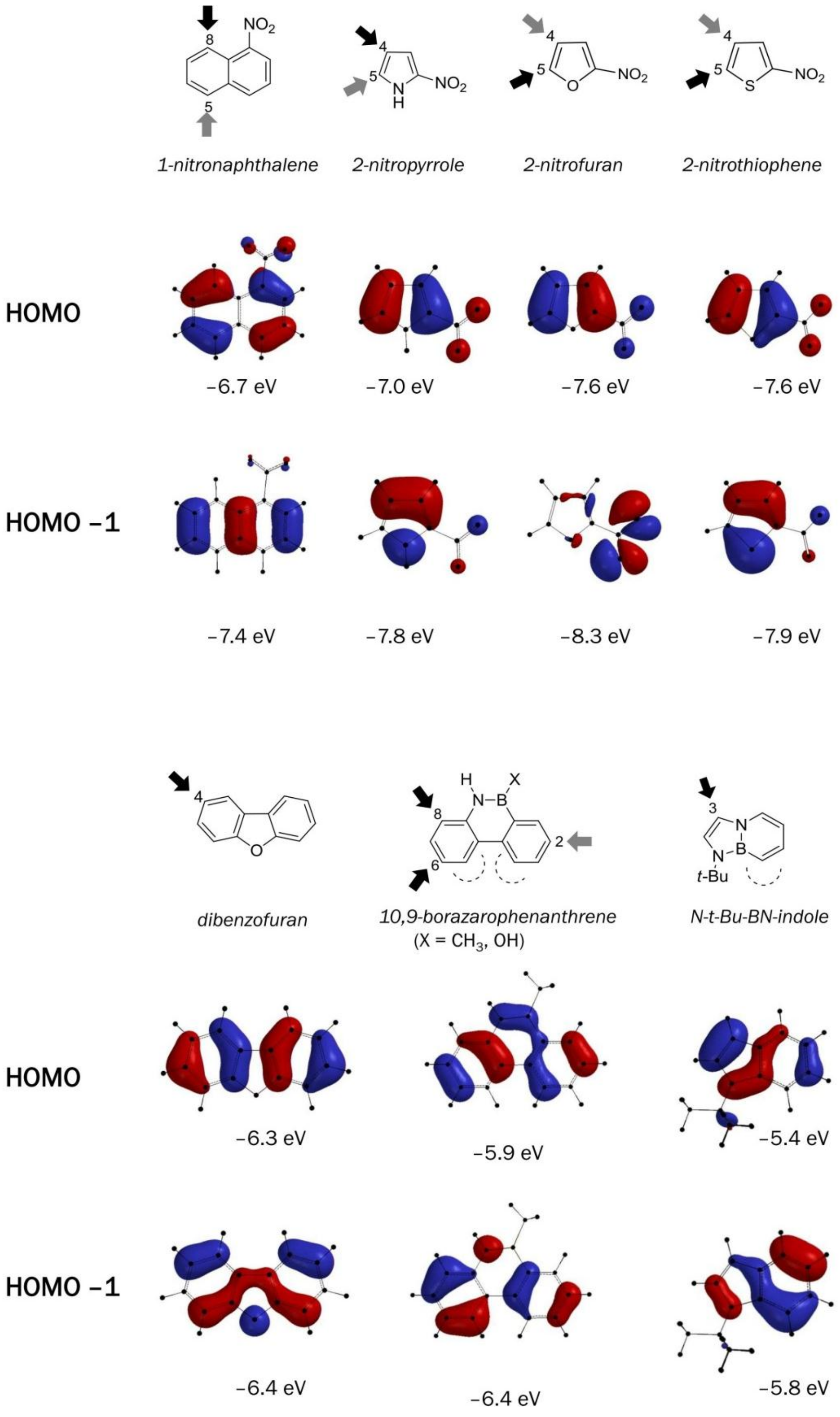


Figure S15. HOMOs and HOMO–1 orbitals and energies for theoretically challenging aromatic molecules calculated using DFT/B3LYP/6-311G*. The locations of the largest HOMO lobes indicate that the Frontier Molecular Orbital approximation for predicting nucleophilicity fails in many situations.

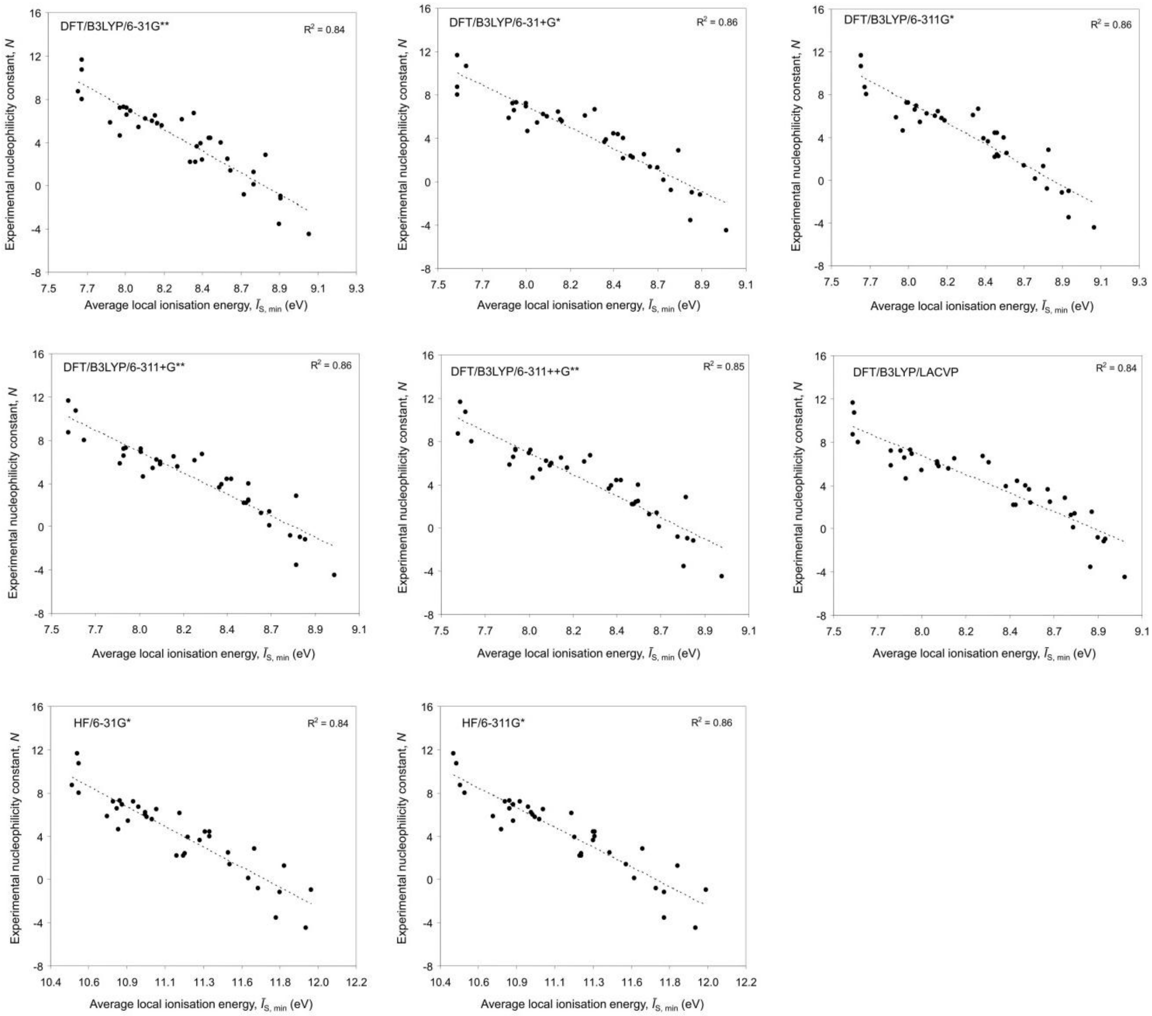


Figure S16. Correlations of experimental nucleophilicity parameters, N with average local ionisation energy minima $\bar{I}_{S,\min}$ calculated using the methods indicated at the 0.002 electrons/bohr^3 surface (Table S3).

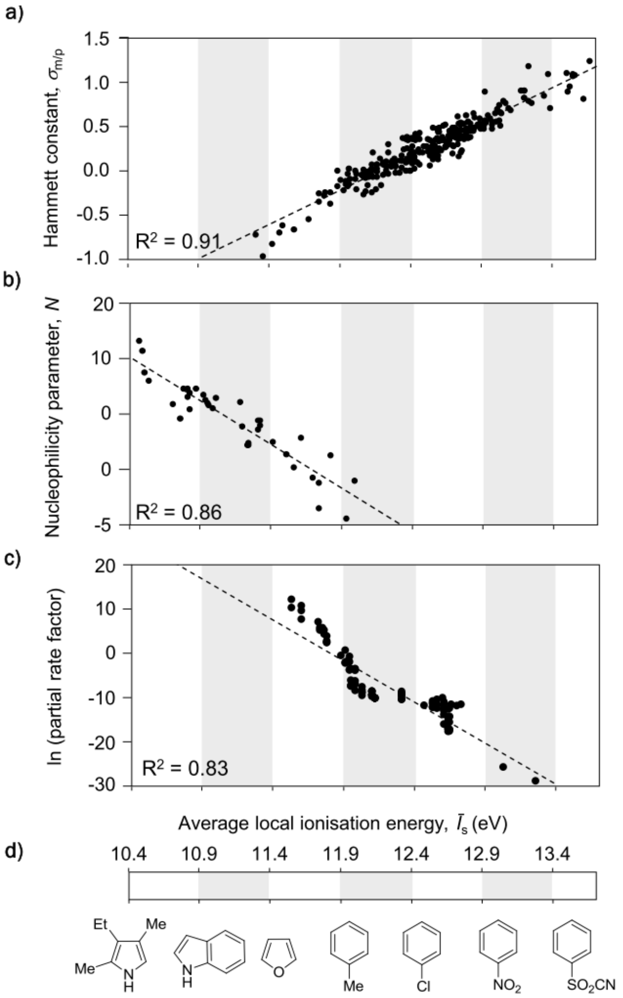


Figure S17. Correlations of experimental reactivity parameters with average local ionisation energies calculated using HF/6-311G* at the 0.002 electrons/bohr^3 surface: (**a**), Average local ionisation energies taken over the *meta* and *para* positions vs. the corresponding Hammett substituent constants. (**b**), Nucleophilicity parameters determined by Mayr and co-workers. (**c**), Experimental partial rate factors for a range of electrophilic substitution reactions at different carbon positions in substituted benzenes. (**d**), A scale of average local ionisation energies including representative examples. Tables S1-S3 contain the associated data and references. The main text contains a version of this figure plotted using DFT/B3LYP/6-311G* values.

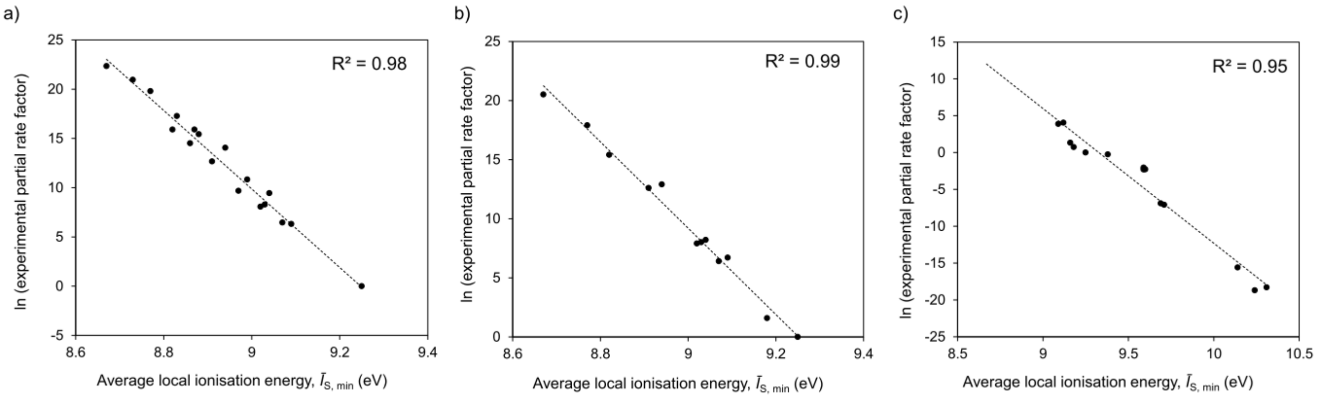
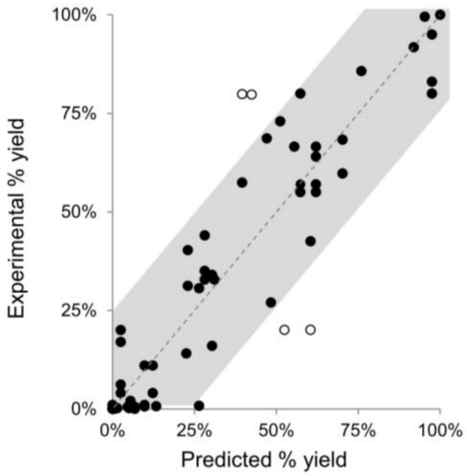


Figure S18. Correlation of experimental partial rate factors for (**a**) bromination, (**b**) chlorination, and (**c**) nitration taken from individual experimental studies vs. average local ionisation minima taken over each reactive position calculated using DFT/B3LYP/6-311G* at the 0.002 electrons/bohr^3 surface. Table S2 contains the associated data and references.



$$experimental\ \%\ \text{yield at position}\ j = \frac{n_j f_j}{\sum_j n_j f_j} \times 100\%$$

$$predicted\ \%\ \text{yield at position}\ j = \frac{n_j \exp(m\, \bar{I}_{S,j})}{\sum_j n_j \exp(m\, \bar{I}_{S,j})} \times 100\%$$

Figure S19. Correlation of experimental percentage yields (from Figure 4) and those derived from partial rate factors for a range of electrophilic aromatic substitution reactions (y-axis) vs. those predicted using the equation given above (x-axis). n_j is the number of equivalent aromatic positions j that are available for substitution, f_j is the experimental partial rate factor at each position j (Table S2), m is the gradient of the graph determined in Figure 3c (m = –21.194), and $\bar{I}_{S,j}$ is the average local ionisation energy taken over each position j (calculated using B3LYP/6-311G* at the 0.002 electrons/bohr^3 surface). Figure 4 in the main text and Table S2 contain the associated data and references. In general, yields can be predicted with ±25% accuracy. The outliers marked with hollow circles correspond to examples where steric effects have an important influence on the observed product ratios (iodobenzene and some polymethylbenzenes), which are not taken into account in the ionisation energy model.

Table S1. Hammett σ_m and σ_p substituent constants and corresponding calculated average local ionisation energy values $\bar{I}_{S\,meta}$ and $\bar{I}_{S\,para}$ taken directly over the centre of the carbons in the *meta* and *para* positions when viewed perpendicular to the plane of the ring (as shown in Figure S1). [a] Entry numbers refer to Table I of reference [26].

				DFT/B3LYP/6-311G*		HF/B3LYP/6-311G*	
Entry[a]	**Substituent**	σ_m	σ_p	$\bar{I}_S$ ***meta* /eV**	$\bar{I}_S$ ***para* /eV**	$\bar{I}_S$ ***meta* /eV**	$\bar{I}_S$ ***para* /eV**
2	Br	0.39	0.23	9.69	9.61	12.63	12.56
5	Cl	0.37	0.23	9.71	9.60	12.64	12.53
7	SO_2Cl	1.20	1.11	10.42	10.54	13.24	13.51
15	F	0.34	0.06	9.62	9.41	12.61	12.30
18	SO_2F	0.80	0.91	10.38	10.50	13.24	13.52
28	I	0.35	0.18	9.71	9.66	12.62	12.60
31	NO	0.62	0.91	9.98	10.14	12.74	12.93
32	NO_2	0.71	0.78	10.13	10.24	13.02	13.26
37	N_3	0.37	0.08	9.42	9.41	12.53	12.13
43	H	0.00	0.00	9.25	9.25	12.13	12.13
45	OH	0.12	–0.37	9.32	8.96	12.39	11.84
49	SH	0.25	0.15	9.49	9.27	12.46	12.19
50	$B(OH)_2$	–0.01	0.12	9.31	9.43	12.17	12.34
51	NH_2	–0.16	–0.66	9.09	8.62	12.20	11.58
52	NHOH	–0.04	–0.34	9.18	8.87	12.21	11.76
53	SO_2NH_2	0.53	0.60	9.88	9.96	12.76	12.97
59	$NHNH_2$	–0.02	–0.55	9.21	8.76	12.33	11.68
60	SiH_3	0.05	0.10	9.43	9.48	12.27	12.37
61	CBr_3	0.28	0.29	9.79	9.83	12.65	12.71
62	$CClF_2$	0.42	0.46	9.87	9.91	12.72	12.82
66	CCl_3	0.40	0.46	9.86	9.92	12.69	12.79
70	CF_3	0.43	0.54	9.83	9.90	12.70	12.83
75	OCF_3	0.38	0.35	9.81	9.74	12.73	12.64
76	$SOCF_3$	0.63	0.69	9.99	10.08	12.95	13.11
78	SO_2CF_3	0.83	0.96	10.33	10.45	13.21	13.53
80	OSO_2CF_3	0.56	0.53	9.96	9.91	13.01	12.98
81	SCF_3	0.40	0.50	9.83	9.94	12.67	12.86
84	CN	0.56	0.66	10.06	10.10	12.94	13.05
85	NC	0.48	0.49	9.98	9.90	12.83	12.72
89	N=C=O	0.27	0.19	9.69	9.50	12.65	12.40
90	OCN	0.67	0.54	10.05	9.87	13.04	12.78
91	SO_2CN	1.10	1.26	10.51	10.64	13.38	13.67
92	N=C=S	0.48	0.38	9.87	9.71	12.98	12.81
93	SCN	0.51	0.52	10.04	10.09	12.89	13.04
94	SeCN	0.61	0.66	10.00	10.08	12.86	13.00
97	$C(NO_2)_3$	0.72	0.82	10.44	10.52	13.39	13.63
102	$OCHCl_2$	0.38	0.26	9.89	9.79	12.75	12.61

103	CHF_2	0.29	0.32	9.61	9.64	12.52	12.56
104	$OCHF_2$	0.31	0.18	9.72	9.51	12.67	12.54
105	$SOCHF_2$	0.54	0.58	9.95	9.99	12.89	13.03
106	SO_2CHF_2	0.75	0.86	10.16	10.31	13.03	13.35
107	$SCHF_2$	0.33	0.37	9.78	9.82	12.66	12.78
109	$NHSO_2CF_3$	0.44	0.39	9.82	9.69	12.80	12.83
111	NHCN	0.21	0.06	9.72	9.40	12.76	12.28
117	CHO	0.35	0.42	9.78	9.89	12.58	12.75
118	COOH	0.37	0.45	9.63	9.78	12.47	12.71
119	CH_2Br	0.12	0.14	9.57	9.56	12.43	12.41
120	CH_2Cl	0.11	0.12	9.58	9.58	12.44	12.43
121	OCH_2Cl	0.25	0.08	9.56	9.28	12.61	12.17
122	CH_2F	0.12	0.11	9.37	9.32	12.34	12.23
123	OCH_2F	0.20	0.02	9.52	9.21	12.56	12.12
124	SCH_2F	0.23	0.20	9.73	9.78	12.59	12.70
125	CH_2I	0.10	0.11	9.59	9.58	12.45	12.40
126	NHCHO	0.19	0.00	9.41	9.21	12.40	12.01
127	$CONH_2$	0.28	0.36	9.58	9.65	12.42	12.60
133	Me	–0.07	–0.17	9.19	9.11	12.09	11.96
139	$NHCONH_2$	–0.03	–0.24	9.25	8.98	12.25	11.84
142	OMe	0.12	–0.27	9.24	8.91	12.28	11.79
143	CH_2OH	0.00	0.00	9.52	9.52	12.40	12.40
144	SOMe	0.52	0.49	9.72	9.73	12.64	12.70
147	S(O)OMe	0.50	0.54	9.70	9.76	12.56	12.75
148	SO_2Me	0.60	0.72	10.01	10.10	12.89	13.10
150	OSO_2Me	0.39	0.36	9.57	9.37	12.69	12.39
151	SMe	0.15	0.00	9.49	9.51	12.29	12.37
152	SSMe	0.22	0.13	9.61	9.62	12.49	12.56
154	NHMe	–0.21	–0.70	9.04	8.57	12.16	11.48
155	CH_2NH_2	–0.03	–0.11	9.10	9.08	12.02	11.95
158	$N(COF)_2$	0.58	0.57	10.00	10.05	12.93	12.98
160	$COCF_3$	0.63	0.80	10.00	10.17	12.80	13.06
161	$SCOCF_3$	0.48	0.46	9.87	9.95	12.72	12.85
162	$OCOCF_3$	0.56	0.46	9.89	9.81	12.81	12.68
165	CF_2CF_3	0.47	0.52	9.86	9.94	12.74	12.90
166	OCF_2CF_3	0.48	0.28	9.78	9.61	12.80	12.50
167	$SO_2CF_2CF_3$	0.92	1.08	10.33	10.49	13.21	13.55
169	$N(CF_3)_2$	0.40	0.53	9.91	9.95	12.77	12.89
175	$C\equiv CH$	0.21	0.23	9.56	9.50	12.43	12.41
176	OCF_2CHFCl	0.35	0.28	9.77	9.69	12.68	12.58
177	$NHCOCF_3$	0.30	0.12	9.69	9.52	12.70	12.33
179	OCF_2CHF_2	0.34	0.25	9.66	9.48	12.66	12.36
180	SCF_2CHF_2	0.38	0.47	9.74	9.82	12.59	12.76
185	CH_2CF_3	0.12	0.09	9.51	9.50	12.41	12.42

186	CH_2SOCF_3	0.25	0.24	9.65	9.66	12.56	12.59
187	$CH_2SO_2CF_3$	0.29	0.31	9.77	9.80	12.66	12.74
188	CH_2SCF_3	0.12	0.15	9.45	9.50	12.41	12.38
189	CH_2CN	0.16	0.18	9.67	9.65	12.58	12.55
193	$CH{=}CH_2$	0.06	–0.04	9.34	9.26	12.23	12.11
198	oxiranyl	0.05	0.03	9.36	9.30	12.23	12.17
199	$OCH{=}CH_2$	0.21	–0.09	9.46	9.14	12.47	12.01
200	COMe	0.38	0.50	9.61	9.74	12.46	12.61
201	SCOMe	0.39	0.44	9.50	9.51	12.38	12.47
202	OCOMe	0.39	0.31	9.50	9.39	12.43	12.25
203	COOMe	0.37	0.45	9.55	9.66	12.37	12.61
205	$SCH{=}CH_2$	0.26	0.20	9.53	9.39	12.38	12.41
210	NHCOOMe	–0.02	–0.17	9.32	9.03	12.30	11.89
211	NHCOMe	0.21	0.00	9.30	9.09	12.25	11.89
212	CONHMe	0.35	0.36	9.50	9.57	12.44	12.54
214	CH_2CONH_2	0.06	0.07	9.59	9.54	12.54	12.47
219	Et	–0.07	–0.15	9.20	9.12	12.11	11.97
221	OCH_2CH_3	0.10	–0.24	9.21	8.88	12.27	11.80
222	CH(OH)Me	0.08	–0.07	9.34	9.29	12.21	12.14
223	CH_2OMe	0.08	0.01	9.30	9.25	12.17	12.13
224	SO_2Et	0.66	0.77	9.98	10.08	12.85	13.08
225	SEt	0.18	0.03	9.48	9.50	12.34	12.43
230	NHEt	–0.24	–0.61	9.03	8.55	12.13	11.50
231	$N(Me)_2$	–0.16	–0.83	8.99	8.54	12.10	11.43
236	N=NNMe2	–0.05	–0.03	9.13	8.96	12.13	11.96
239	$PO(OMe)_2$	0.42	0.53	9.60	9.73	12.44	12.65
250	$C{\equiv}CF_3$	0.41	0.51	9.94	9.95	12.80	12.83
251	$CF{=}CFCF_3$–*t*	0.39	0.46	9.88	9.89	12.73	12.84
253	$CF_2CF_2CF_3$	0.44	0.48	9.88	9.97	12.75	12.92
254	$CF(CF_3)_2$	0.37	0.53	9.85	9.91	12.75	12.88
255	$SO_2CF_2CF_3$	0.92	1.09	10.33	10.48	13.21	13.57
256	$SO_2CF(CF_3)_2$	0.92	1.10	10.33	10.48	13.19	13.55
257	$SCF_2CF_2CF_3$	0.45	0.48	9.87	9.94	12.72	12.90
258	$SCF(CF_3)_2$	0.48	0.51	9.88	9.95	12.70	12.89
262	$CH(CN)_2$	0.53	0.52	9.99	9.99	12.91	12.92
263	$CHC{=}HCF_3$–*c*	0.16	0.17	9.61	9.63	12.43	12.43
264	$CH{=}HCF_3$–*t*	0.24	0.27	9.74	9.71	12.59	12.55
266	CH=HCN–*t*	0.24	0.17	9.91	9.90	12.77	12.75
267	C=CMe	0.21	0.03	9.25	9.13	12.14	11.97
268	$N(Me)COCF_3$	0.41	0.39	9.81	9.82	12.68	12.72
269	CH=CHCHO	0.24	0.13	9.80	9.80	12.62	12.60
270	cyclopropyl	–0.07	–0.21	9.20	9.16	12.07	12.02
272	$CH{=}CHCH_3$	0.02	–0.09	9.26	9.14	12.14	11.98
276	COEt	0.38	0.48	9.53	9.65	12.35	12.59

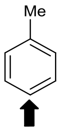
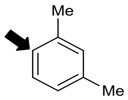
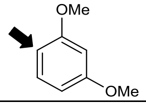
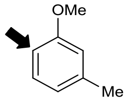
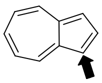
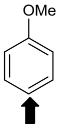
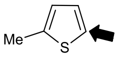
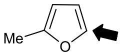
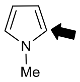
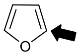
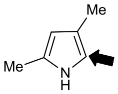
277	COOEt	0.37	0.45	9.60	9.71	12.42	12.60
278	CH_2OCOMe	0.04	0.05	9.46	9.47	12.34	12.30
288	isopropyl	–0.04	–0.15	9.18	9.12	12.06	11.95
294	$OCH_2CH_2CH_3$	0.10	–0.25	9.20	8.87	12.29	11.76
307	$SiMe_3$	–0.04	–0.07	9.24	9.28	12.10	12.17
317	$C(CF_3)_3$	0.55	0.55	9.85	9.94	12.76	12.94
346	$COCHMe_2$	0.38	0.47	9.61	9.72	12.41	12.60
348	$NHCOCH(Me)_2$	0.11	–0.10	9.35	9.09	12.30	11.91
352	$(CH_2)_3CH_3$	–0.08	–0.16	9.18	9.11	12.09	11.96
360	$N(Et)_2$	–0.23	–0.72	8.96	8.44	12.09	11.31
434	$N(C_3H_7)_2$	–0.26	–0.93	8.97	8.47	12.07	11.36
504	$N(C_6H_5)_2$	0.00	–0.22	9.31	9.10	12.23	11.93
527	$Si(C_6H_5)_3$	–0.03	0.10	9.25	9.33	12.08	12.21
529	$C(C_6H_5)_3$	–0.01	0.02	9.20	9.18	12.10	12.07

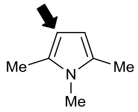
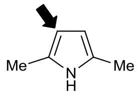
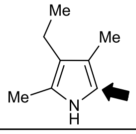
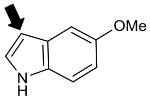
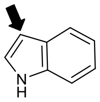
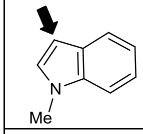
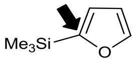
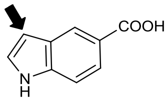
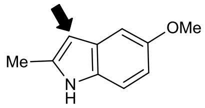
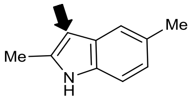
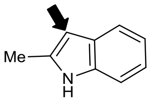
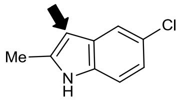
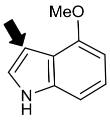
Table S2. Experimental partial rate factors for electrophilic substitution in different positions of aromatic substrates and their corresponding average local ionisation energies, $\bar{I}_{S,\ j}$. Average local ionisation energies were calculated using the methods indicated at the 0.002 electrons/bohr^3 surface (as shown in Figure S1). % yields were calculated from DFT ionisation energies using the equations given in Figure S19. Predicted % yields are and are associated with an error of up to ±25% (Figure S19). Experimental partial rate factors are taken from references[21,44, 74, 322, 323.]

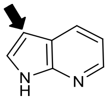
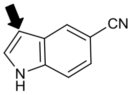
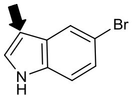
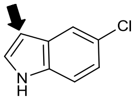
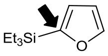
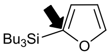
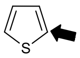
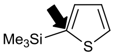
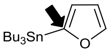
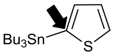
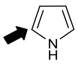
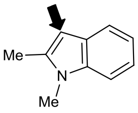
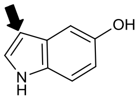
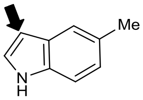
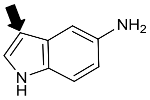
		Ave. Local Ionisation Energy, $\bar{I}_{S,j}$ /eV (predicted % yields)		**In (experimental partial rate factor), ln(f_j) (corresponding % yields where all partial rates known)**							
Compound	**Position, *j***	DFT/B3LYP 6-311G*	HF/ 6-311G*	Bromination	Chlorination	Nitration	Benzylation	Solvolysis	Ethylation	Mercuration	Acetylation
Benzene	1	9.25 (100%)	12.12	0.0 (100%)	0.0 (100%)	0.0 (100%)	0.0 (100%)	0.0	0.0	0.0	0.0
Toluene	2	9.07 (70%)	11.94	6.40 (68%)	6.40 (60%)	-	-	-	-	-	-
	3	9.18 (7%)	12.10	1.70 (1%)	1.59 (0%)	0.74	-	0.67	0.39	0.81	1.57
	4	9.09 (23%)	11.98	7.78 (31%)	6.70 (40%)	3.89	-	3.21	1.75	3.15	6.61
1,2-dimethylbenzene	3	9.02 (60%)	11.91	8.06 (20%)	7.9 (43%)	-	-	-	-	-	-
	4	9.04 (40%)	11.94	9.44 (80%)	8.2 (57%)	-	-	-	-	-	-
1,3-dimethylbenzene	2	8.91 (48%)	11.78	12.66	12.6	-	-	-	-	-	-
	4	8.94 (51%)	11.78	14.05	12.9	-	-	-	-	-	-
	5	9.13 (0%)	12.07	-	-	-	-	-	-	-	-
1,4-dimethylbenzene	2	9.03 (100%)	11.92	8.29 (100%)	8.0 (100%)	-	-	-	-	-	-
1,2,3-trimethylbenzene	4	8.88 (95%)	11.76	15.43 (100%)	-	-	-	-	-	-	-
	5	8.99 (5%)	11.91	10.82 (0%)	-	-	-	-	-	-	-
1,2,4-trimethylbenzene	3	8.86 (52%)	11.76	14.51 (20%)	-	-	-	-	-	-	-
	5	8.87 (42%)	11.75	15.89 (80%)	-	-	-	-	-	-	-
	6	8.97 (5%)	11.88	9.67 (0%)	-	-	-	-	-	-	-
1,3,5-trimethylbenezene	2	8.77 (100%)	11.60	19.8 (100%)	17.9 (100%)	-	-	-	-	-	-
1,2,3,4-tetramethylbenzene	5	8.83 (100%)	11.72	17.27(100%)	-	-	-	-	-	-	-
1,2,3,5-tetramethylbenzene	4	8.73 (100%)	11.60	20.95 (100%)	-	-	-	-	-	-	-
1,2,4,5-tetramethylbenzene	3	8.82 (100%)	11.73	15.89 (100%)	15.4 (100%)	-	-	-	-	-	-
Pentamethylbenzene	6	8.67 (100%)	11.53	22.34 (100%)	20.5 (100%)	-	-	-	-	-	-
Nitrobenzene	2	10.31 (3%)	13.41	-	-	-18.3 (6%)	-	-	-	-	-
	3	10.14 (92%)	13.03	-	-	–15.6 (92%)	-	-	-	-	-
	4	10.24 (6%)	13.26	-	-	–18.7 (2%)	-	-	-	-	-
t-Butylbenzene	2	9.08 (66%)	11.91	-	-	-	-	-	-	-	-
	3	9.16 (17%)	12.03	1.80	1.68	1.34	-	0.62	-	1.22	2.56
	4	9.12 (17%)	11.95	6.70	5.99	4.05	-	2.67	-	2.86	6.49
Chlorobenzene	2	9.66 (28%)	12.66	-	-	-	–1.4 (33%)	-	-	-	-
	3	9.71 (10%)	12.65	–7.09	–8.11	–7.09	–5.4 (1%)	–4.17	–4.17	–2.28	–7.48
	4	9.59 (62%)	12.53	–1.93	–0.97	–2.05	0.0 (67%)	–1.20	–0.62	–1.01	–2.07
Bromobenzene	2	9.65 (31%)	12.70	-	-	-	–1.7 (33%)	-	-	-	-
	3	9.69 (13%)	12.64	–6.93	–1.24	–6.90	–5.6 (1%)	–4.17	-4.24	–2.44	–7.55

	4	9.59 (56%)	12.56	-	1.47	–2.30	–0.3 (67%)	–1.57	–1.57	-	-
Fluorobenzene	2	9.47 (23%)	12.47	–2.79	-	-	–1.6 (14%)	-	-	-	-
	3	9.60 (1%)	12.61	1.52	-	–2.28	–5.9 (0%)	–3.68	–0.83	–1.31	–2.49
	4	9.38 (76%)	12.31	-	-	–0.25	0.9 (86%)	0.76	–0.30	1.08	0.41
Iodobenzene	2	9.71 (26%)	12.73	-	-	-	–1.4 (31%)	-	-	-	-
	3	9.71 (26%)	12.64	-	-	-	–5.1 (1%)	-	-	-	-
	4	9.65 (47%)	12.60	-	-	-	0.1 (69%)	-	-	-	-

Table S3.Experimental nucleophilicity parameters, *N* and corresponding average local ionisation energy minima $\bar{I}_{S,\mathrm{min}}$ taken nearest to the carbons marked with arrows. Average local ionisation energies were calculated with the methods indicated and taken at the 0.002 electrons/bohr^3 surface. This data is plotted graphically in Figures 3, S16 and S17. [a] n.s. denotes entries with atoms not supported by a particular basis set.

Structure	**Nucleophilicity parameter, *N***	**Solvent**	**DFT/B3LYP/ 6-31G***	**DFT/B3LYP/ 6-31G****	**DFT/B3LYP/ 6-31+G***	**DFT/B3LYP/ 6-311G***	**DFT/B3LYP/ 6-311+G****	**DFT/B3LYP/ 6-311++G****	**DFT/B3LYP/ LACVP**	**HF/6-31G***	**HF/6-311G***	**Reference**
	–4.47	DCM	9.02	9.06	9.01	9.07	8.98	8.97	9.02	11.94	11.94	324
	–3.54	DCM	8.86	8.88	8.82	8.92	8.78	8.77	8.84	11.76	11.75	324
	2.48	DCM	8.55	8.57	8.58	8.55	8.53	8.53	8.63	11.47	11.42	324
	0.13	DCM	8.71	8.73	8.68	8.72	8.64	8.64	8.75	11.59	11.57	324
	6.66	ACN	8.34	8.37	8.32	8.38	8.29	8.28	8.28	10.93	10.93	325
	–1.18	DCM	8.86	8.89	8.87	8.88	8.83	8.82	8.91	11.78	11.75	326
	1.26	DCM	8.71	8.73	8.65	8.77	8.60	8.59	8.74	11.81	11.83	324
	3.61	DCM	8.36	8.39	8.37	8.44	8.38	8.38	8.52	11.30	11.32	324
	5.85	DCM	7.83	7.87	7.87	7.89	7.86	7.86	7.80	10.74	10.72	324
	1.36	DCM	8.55	8.59	8.61	8.65	8.64	8.63	8.76	11.48	11.52	324
	10.67	ACN	7.68	7.70	7.65	7.68	7.63	7.63	7.61	10.57	10.50	325

	8.69	ACN	7.66	7.68	7.60	7.70	7.59	7.59	7.60	10.53	10.52	325
	8.01	ACN	7.67	7.70	7.60	7.71	7.67	7.66	7.63	10.57	10.55	325
	11.63	ACN	7.68	7.70	7.60	7.68	7.59	7.60	7.60	10.56	10.48	325
	6.22	DCM	8.05	8.08	8.05	8.07	8.05	8.05	8.04	10.97	10.95	327
	5.55	DCM	8.14	8.18	8.15	8.18	8.16	8.16	8.10	11.01	11.00	327
	5.75	DCM	8.12	8.15	8.14	8.16	8.07	8.07	8.05	10.98	10.97	327
	2.16	DCM	8.33	8.35	8.47	8.48	8.51	8.50	8.44	11.16	11.24	326
	3.97	ACN	8.50	8.53	8.47	8.53	8.53	8.53	8.50	11.36	11.33	327
	7.26	ACN	7.93	7.95	7.91	7.96	7.89	7.89	7.90	10.82	10.82	327
	7.22	ACN	7.91	7.93	7.89	7.95	7.88	7.89	7.85	10.78	10.79	327
	6.91	ACN	7.97	7.99	7.96	8.01	7.97	7.96	7.91	10.83	10.84	327
	6.08	ACN	8.30	8.30	8.27	8.35	8.25	8.25	8.31	11.18	11.19	327
	5.41	ACN	8.00	8.04	8.02	8.03	8.03	8.02	7.96	10.87	10.84	327

	3.87	ACN	8.37	8.41	8.38	8.41	8.39	8.39	8.40	11.23	11.21	[327]
	2.83	ACN	8.76	8.80	8.76	8.80	8.78	8.78	8.71	11.63	11.62	[327]
	4.38	ACN	8.44	8.46	8.44	8.49	8.44	8.44	8.46	11.36	11.33	[327]
	4.42	ACN	8.44	8.47	8.42	8.48	8.42	8.42	8.46	11.33	11.32	[327]
	2.20	DCM	8.36	8.38	8.52	8.50	8.52	8.51	8.45	11.20	11.25	[326]
	2.37	DCM	8.40	8.42	8.51	8.49	8.53	8.52	8.53	11.21	11.25	[326]
	–1.01	DCM	8.86	8.89	8.83	8.92	8.80	8.79	8.92	11.97	12.00	[326]
	–0.80	DCM	8.65	8.67	8.72	8.79	8.75	8.74	8.88	11.65	11.70	[326]
	3.63	DCM	[a]n.s.	n.s.	n.s.	n.s.	n.s.	8.62	n.s.	n.s.	n.s.	[326]
	1.53	DCM	n.s.	n.s.	n.s.	n.s.	n.s.	8.85	n.s.	n.s.	n.s.	[326]
	4.63	DCM	7.88	7.93	7.97	7.93	7.98	7.98	7.88	10.81	10.77	[328]
	6.54	DCM	7.95	7.97	7.90	8.00	7.88	7.88	7.87	10.80	10.82	[327]
	6.44	ACN	8.10	8.14	8.13	8.14	8.14	8.13	8.13	11.04	11.02	[327]
	6.00	ACN	8.08	8.12	8.07	8.12	8.07	8.08	8.04	10.97	10.96	[327]
	7.22	ACN	7.95	7.97	7.96	7.96	7.97	7.97	7.80	10.90	10.88	[327]

Supporting References

1. to 60. are given in the main text.

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