SUPPORTING INFORMATION

Halogen bonds direct the solid state architectures of a multivalent iodopropargylcalix[4]arene

Maria Chiara Gullo, Laura Baldini, Alessandro Casnati, Luciano Marchiò*

Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze, 17/a, 43124 Parma, Italy.

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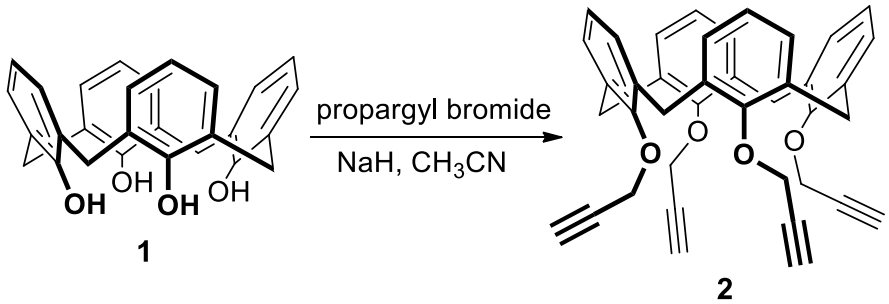
1. Synthesis

General information

The reactions were performed under a nitrogen atmosphere by using oven-dried glassware. Dry solvents were prepared according to standard procedures, distilled before use, and stored over 3 or 4 Å molecular sieves. *N*-iodomorpholine·HI was synthesized according to literature procedures.[1] The remaining reagents and all of the solvents were obtained from commercial sources and were used without further purification. Analytical TLC was performed by using prepared plates of silica gel (Merck 60 F-254 on aluminum) and was visualized with UV light. ^{1}HNMR spectra were recorded with Bruker AV300 and Bruker AV400 spectrometers, (observation of ^{1}H nuclei at 300 and 400 MHz, respectively); ^{13}CNMR spectra were recorded with proton decoupling with a Bruker AV400 spectrometer (observation of ^{13}C nuclei at 100 MHz). All chemical shifts are reported in part per million (ppm) by using the residual peak of the deuterated solvent, the values of which are referred to tetramethylsilane (δ=0 ppm) as internal standard. Mass spectra were recorded in ESI mode with a single quadrupole instrument SQ Detector, Waters. Melting points were determined with an Electrothermal apparatus in closed capillaries.

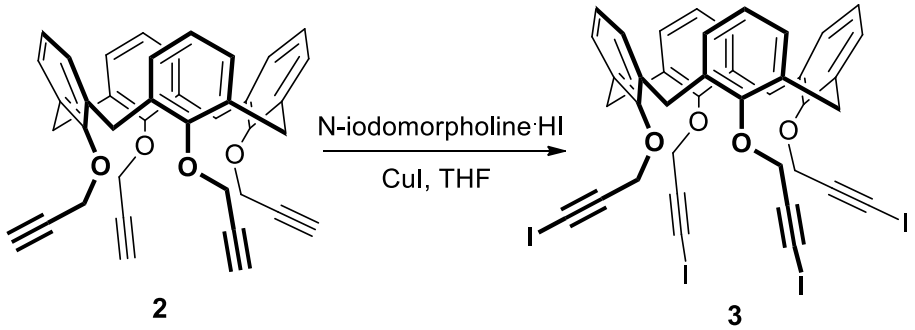
Synthesis of 25,26,27,28-tetrakis(propargyloxy)calix[4]arene 2



NaH (60% in oil, 1.1 g, 28.3 mmol) was added to a stirred solution of 25,26,27,28-tetrahydroxycalix[4]arene **1** (2.0 g, 4.71 mmol) in 100 mL of dry acetonitrile cooled to 0°C with an ice bath. After 2 hours, propargyl bromide (80% in toluene, 2.2 mL, 20.2 mmol) was added and the mixture was stirred overnight at room temperature. After TLC analysis (CH_2Cl_2/hexane 6:4, v/v) had revealed the complete conversion of calixarene **1**, the reaction was quenched with water

(50 mL) and extracted with CH_2Cl_2 (2x50 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to dryness under reduced pressure. After recrystallization of the crude mixture from CH_2Cl_2/ethanol, **2** was isolated in 67% yield (1.81 g, 3.16 mmol) as a white solid. M.p. 164-165°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.76 – 6.66 (m, 12H, ArH); 4.80 (d, J=2,4 Hz, 8H, OCH_2); 4.66 (d, J=13.6 Hz, 4H, ArCHAr ax); 3.25 (d, J=13.6 Hz, 4H, ArCHAr eq); 2.49 (t, J=2.4 Hz, 4H, C≡CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 155.0 (Ar); 135.4 (Ar); 128.3 (Ar); 123.3 (Ar); 80.5 (*C*≡CH); 74.7 (C≡*C*H); 61.2 (OCH_2); 31.9 ($ArCH_2Ar$). ESI-MS: m/z calcd for $C_{40}H_{32}O_4$+Na^+: 599.2 $[M+Na]^+$; found: 599.3; m/z calcd for $C_{40}H_{32}O_4$+K^+: 615.2 $[M+K]^+$; found: 615.3.

Synthesis of 25,26,27,28-tetrakis(3-iodopropargyloxy)calix[4]arene 3



CuI (13.5 mg, 0.07 mmol) was added to a stirred solution of calixarene **2** (800 mg, 1.39 mmol) in dry THF (50 mL). After 30 min, *N*-iodomorpholine·HI (3.78 g, 11.1 mmol) was added and the mixture was stirred in the dark for 4 hours. After TLC analysis (hexane/AcOEt 8:2, v/v) had revealed the complete conversion of calixarene **2**, 10 mL of a saturated solution of NH_4Cl were added. The mixture was extracted with Et_2O (3x25 mL) and the combined organic layers were washed with $Na_2S_2O_3$ (sat., 2x20 mL), dried over Na_2SO_4 and evaporated to dryness under reduced pressure affording **3** as a yellow solid in 86% yield (1.29 g, 1.19 mmol). M.p. 185-187°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.76-6.65 (m, 12H, ArH); 4.90 (s, 8H, OCH_2); 4.58 (d, J=13.5 Hz, 4H, ArCHAr ax); 3.23 (d, J=13.5 Hz, 4H, ArCHAr eq). ^{13}C NMR (100 MHz, CDCl3) δ (ppm): 155.0 (Ar); 135.4 (Ar); 128.3 (Ar); 123.3 (Ar); 91.5 (*C*≡CI); 63.0 (OCH_2); 31.8 ($ArCH_2Ar$); 29.7 (C≡*C*I). ESI-MS: m/z calcd for $C_{40}H_{28}I_4O_4$+Na^+: 1102.8 $[M+Na^+]$; found: 1103.5; m/z calcd for $C_{40}H_{28}I_4O_4$+K^+: 1118.8 $[M+K^+]$; found: 1119.4.

2. Crystallization conditions

X-Ray quality crystals of calixarenes **2** and **3** were separately obtained by the slow evaporation (3 days) of a CH_2Cl_2 solution (15 mg in 3 mL).

The co-crystals of **3** and **bipy** were prepared by the slow evaporation (3 days) of a chloroform solution of calixarene **3** with 2 equivalents of **bipy** (30 mg of **3** and 9 mg of **bipy**).

3. X-Ray diffraction

A summary of data collection and structure refinement for **2**, **3**, and **3-bipy** is reported in Table S1. Single crystal data were collected with a *Bruker D8 PhotonII*, Mo Kα: λ = 0.71073 Å. The data collection strategy covered the sphere of reciprocal space.[2] Absorption correction was applied using the program SADABS[3] for **2** and **3-bipy**. Crystals of **3** were non-merohedral twins and the absorption correction was applied with the TWINABS program.[4] The structures were solved with the ShelXT[5] structure solution program using Intrinsic Phasing and refined with the ShelXL[6] refinement package using Least Squares minimisation. Graphical material was prepared with the Mercury 3.9 program.[7]

Table S1. Crystal data and structure refinement for **2**, **3** and the co-crystal **3-bypy**.

	2	**3**	**3-bipy**
Empirical formula	$C_{40}H_{32}O_4$	$C_{40}H_{28}I_4O_4$	$C_{71}H_{53}Cl_3I_4N_6O_4$
Formula weight	576.65	1080.22	1668.14
Temperature/K	100	190	150
Crystal system	orthorhombic	monoclinic	triclinic
Space group	Pbca	$P2_1/c$	P-1
a/Å	16.0724(8)	17.7984(8)	11.6837(9)
b/Å	15.3888(7)	18.2952(8)	15.192(1)
c/Å	24.395(1)	11.6487(5)	18.959(1)
α/°	90	90	86.236(2)
β/°	90	101.041(2)	78.894(2)
γ/°	90	90	83.118(2)
Volume/$Å^3$	6033.6(5)	3722.9(3)	3275.2(4)
Z	8	4	2
ρ_{calc}g/cm^3	1.270	1.927	1.691
μ/mm^{-1} (Mo Kα)	0.081	3.387	2.079
F(000)	2432	2048	1632
Crystal size/mm^3	0.24 × 0.24 × 0.18	0.27 × 0.21 × 0.17	0.19 × 0.17 × 0.11
2θ range (°)	5.552 to 52.064	5.026 to 50.054	5.048 to 51.512
Reflections collected	87688	6533	39892
N_{Indep} (R_{int})	5936 (0.0579)	6533 (0.0432)	12433 (0.0764)
Data/restraints/parameters	5936/0/397	6533/28/469	12433/0/793
Goodness-of-fit on F^2	1.039	1.086	1.025
R_1 [I>=2σ (I)]	0.0404	0.0870	0.0539
wR_2 [I>=2σ (I)]	0.1068	0.1617	0.1200
$\Delta\rho_{min/max}$ (e $Å^{-3}$)	0.34/-0.30	3.41/-3.26	1.55/-1.37

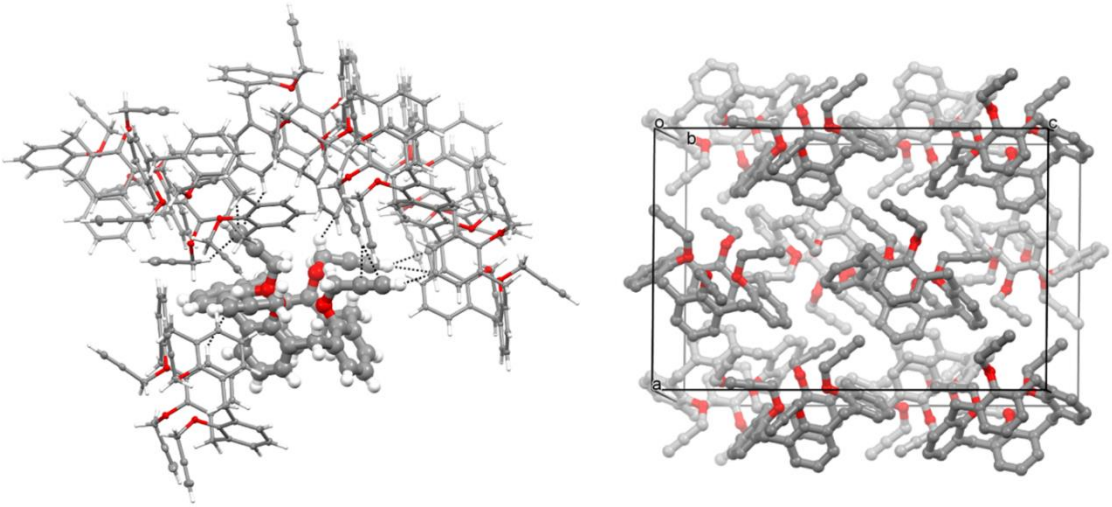


Figure S1. Left, portion of the crystal packing of **2** with short contacts depicted as dashed bonds. Right, crystal packing as viewed along the *b* crystallographic axis.

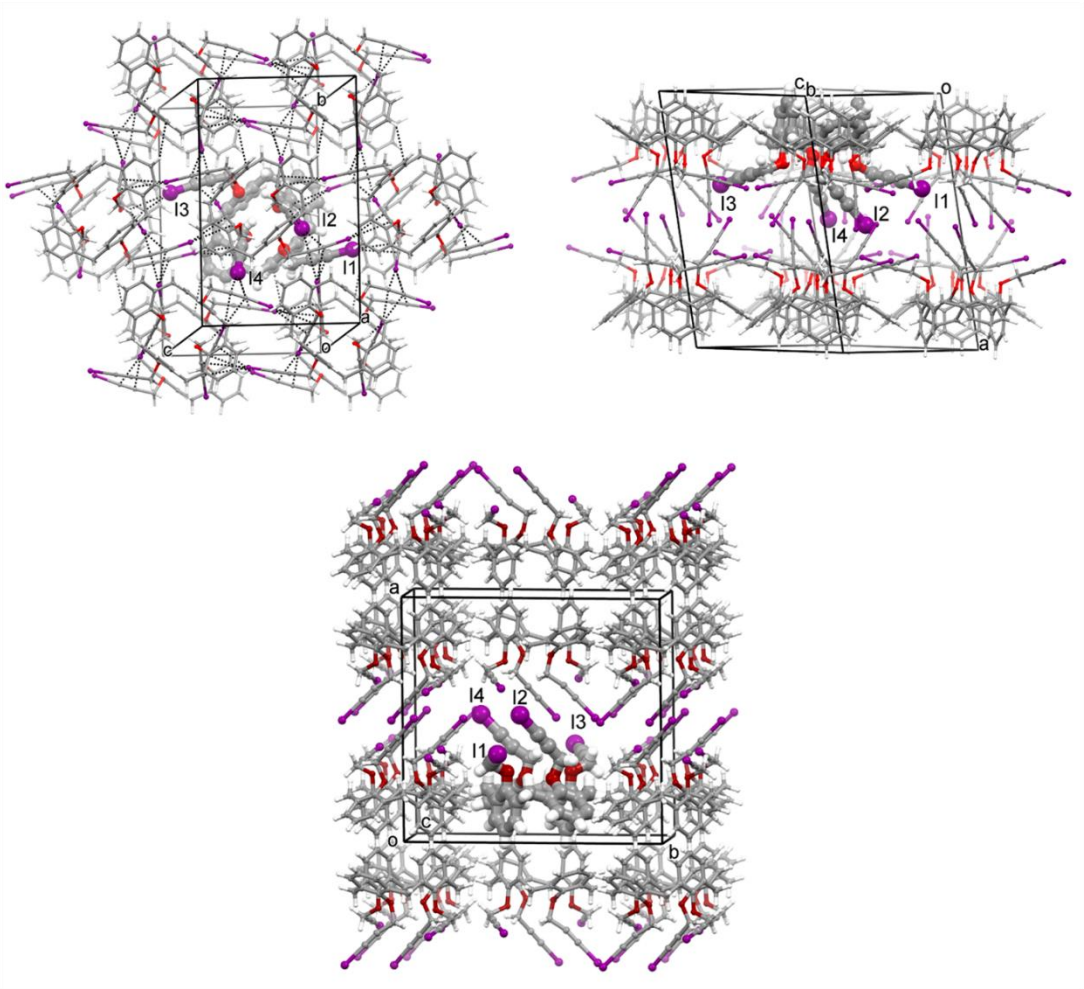


Figure S2. Different projections of the crystal packing of **3**.

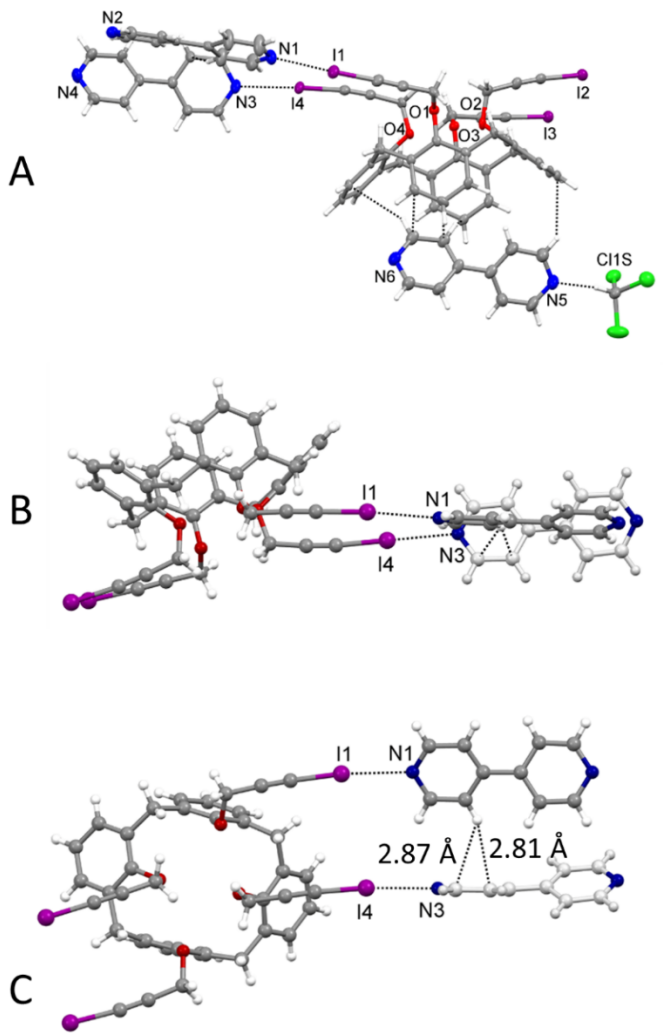


Figure S3. A, asymmetric unit of the co-crystal **3-bypy**. Thermal ellipsoids are depicted at the 30% probability level. B and C, different views of the **bipy** supramolecular dimer. Short contacts are depicted as dashed bonds.

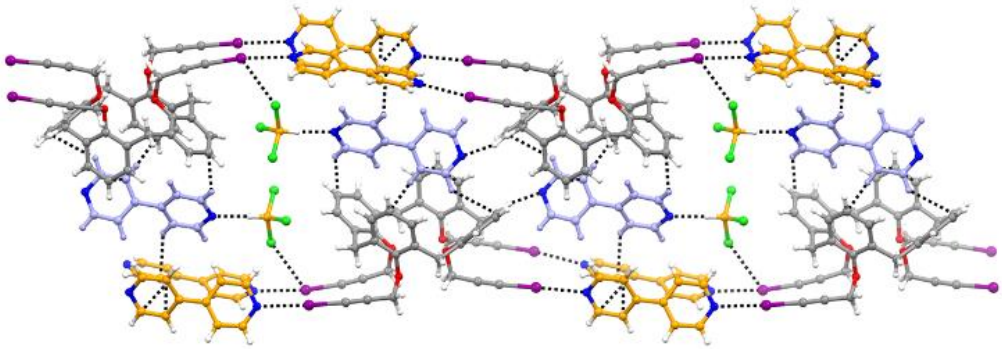


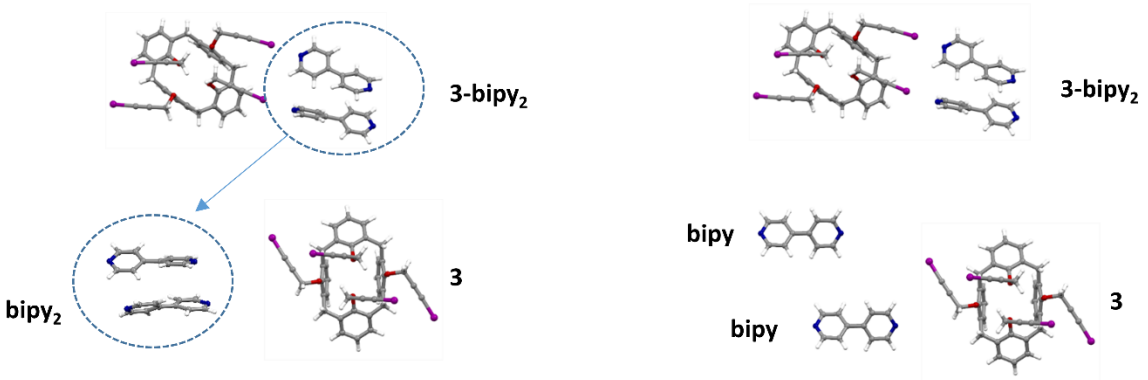
Figure S4. Portion of the crystal packing of the co-crystal **3-bipy**. Short contacts are depicted as dashed bonds. **Bipy** molecules acting as XB acceptor with **3** are depicted in yellow.

4. Molecular modelling

Computational details

Density functional theory calculations[8] were performed with the Gaussian 16 program suite.[9] The geometries of **2**, **3**, **bipy**, and the adduct **3-bipy$_2$** were optimized starting from the X-ray molecular geometries by using the long-range corrected hybrid density functional with dispersion corrections wB97XD[10,11] with the SDD basis set[12,13] and the MWB46 quasi-relativistic core potential for iodine atoms.[14] Single point calculations were performed with the wB97XD functional using the def2TZVP[15] and the MWB46 core potential for iodine. The molecular electrostatic potential (MEP) was analysed with the MultiWFN program.[16] The energy of the non-covalent interactions between **3** and **bipy**, was estimated by taking into account the energies of the following systems: **3**, **bipy**, **bipy$_2$** dimer, and the adduct **3-bipy$_2$**. In particular, the ΔE value calculated by using the singly optimized bipyridine, hence not involved into any π···π or CH···π interaction, should provide information on all of the weak interactions involving both the calixarene moiety and the two bipyridines bound to it: ΔE2 = E(**3-bipy$_2$**) - [E(**3**) + 2E(**bipy**)].[17] On the other hand, when using the **bipy$_2$** dimer, a more direct estimation of the energy of the XB can be obtained: ΔE1 = E(**3-bipy$_2$**) - [E(**3**) + E(**bipy$_2$**)]. The value of ΔE1 can be associated to the interaction energy of two XB between **3** and the **bipy$_2$** dimer. Moreover, the difference ΔE2-ΔE1, provides information on the interaction energy involving the two **bipy** units in the **3-bipy$_2$**, mainly deriving from π···π or CH···π interactions.

Optimized geometries: wB97XD/SDD with pseudopotential for Iodine
Single point calculations: wB97XD/def2tzvp with pseudopotential for Iodine



$\Delta E_1 = E_{3\text{-bipy2}}-(E_3+E_{bipy2}) = -35.44$ kJ/mol

two XB,
conformational change
(between the isolated molecules
and the molecules in the adduct)

$\Delta E_2 = E_{3\text{-bipy2}}-(E_3+2E_{bipy}) = -45.05$ kJ/mol

two XB, CH-π, π-π,
conformational change

$\Delta E_2 - \Delta E_1 = -9.61$ kJ/mol
(takes into account the CH-π,
between the two bypy)

$\Delta E_1/2 \sim -17$ kJ/mol
(corresponds to the energy of one XB)

Figure S5. Computational scheme used to estimate the energy of the weak interactions.

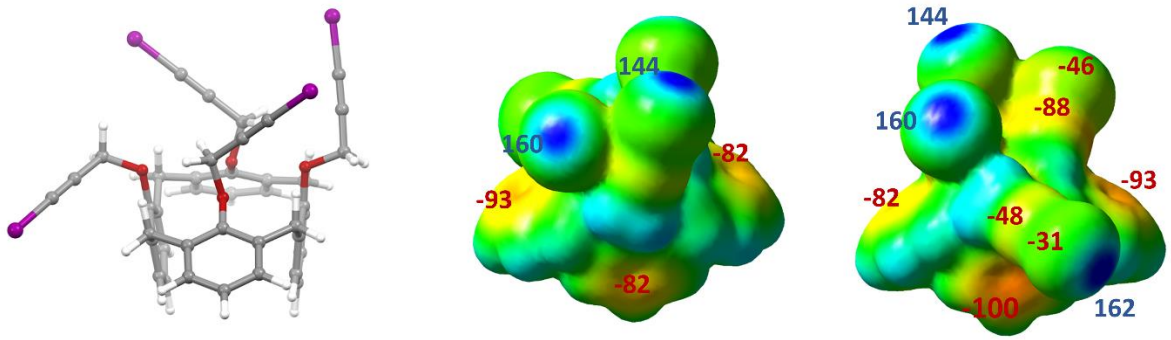


Figure S6. Two views of the DFT optimized geometry of **3**, ωB97XD/SDD. ESP mapped on the 0.001 isodensity surface. Red -0.05; Blue 0.05. The values of the ESP maxima and minima are reported in kJ/mol.

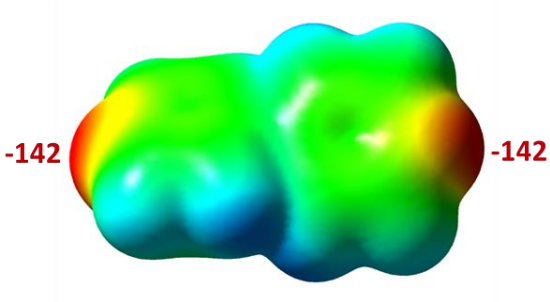


Figure S7. DFT optimized geometry of **bipy**, ωB97XD/SDD. ESP mapped on the 0.001 isodensity surface. Red -0.05; Blue 0.05. The values of the ESP maxima and minima are reported in kJ/mol.

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