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Azacalixquinarenes: from Canonical to (Poly-)Zwitterionic Macrocycles

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ABSTRACT: Azacalixquinarenes, a new family of macrocycles constituted of diaminobenzoquinone diimine units linked by dinitrobenzene rings are synthesized by selected oxidation of the parent azacalixarenes. Crystallographic analyses of two compounds demonstrated the presence of (uncharged) canonical and zwitterionic quinones within a single structure. The electron-withdrawing nature of the dinitrobenzene moieties can trigger the intramolecular H-transfer that generates zwitterionic-ground state quinones. The nature of the N-substituents and the polarity of the solvent have a crucial impact on the equilibrium between the canonical and zwitterionic forms that present distinct optical and electrochemical properties. Thus, within [4]- and [6]-membered macrocycles, poly-zwitterionic structures can be reached, as demonstrated experimentally and theoretically using first-principle approaches.

INTRODUCTION

Heteroatom-bridged calixarenes are an evolved class of calixarene macrocycles in which the introduction of a bridging heteroatom in lieu of a methylene link provides additional features such as: (i) the tuning of the cavity size and of the conformation (e.g. 1,3-alternate structure); (ii) new redox properties; and (iii) conjugation between the units of the macrocyclic oligomer. Beyond the wide range of heteroatom-containing calixarenes developed during the past decades, azacalixarenes (ACA) demonstrated an undeniable versatility regarding structure-properties shaping. Since seminal works in the late nineties on polyazacalixarenes, this family has been growing to incorporate tricyclic moieties, pyridine units, and covalently-bonded metallic centers conferring unusual reactivity. Noteworthy, ACA macrocycles were valorized for carbon dioxide uptake, fullerene or anions complexation and demonstrated to be relevant as hole- and spin-containing architectures. In 2013, the azacalixphyrin (ACP, Figure 1) was reported as the only known “azacalixarene-like” derivative introducing four oxidized tetraaminobenzene units that promote a stable bis-zwitterionic ground electronic state. Consequently ACP can be viewed as a masked conjugated azacalixquinone. Its aromatic core involving 18 π-electrons confers to the ACP a strong absorption ca. 900 nm that can be tuned by substitution of the peripheral imine functions (Figure 1, R = H, aryl, alkyl).
The zwitterionic form was found to dominate in both solution and solid states. Diimine, can be also stabilized under a zwitterionic ground state if it is functionalized with strongly electron-withdrawing groups.

Figure 1. Previously reported azalixphyrin macrocycle (top) and illustration of the canonical-zwitterionic equilibrium in 2,5-diaminobenzoquinone diimines (bottom).

Chart 1. Scope of the study (only the canonical form is represented).

Interestingly, we recently reported that the constituting unit of ACP, the monocyclic 2,5-diamino benzoquinone diimine, can be also stabilized under a zwitterionic ground state if it is functionalized with strongly electron-withdrawing aromatic substituents (EWG, Figure 1).9 In the case of quinone 1a featuring 5-fluoro-2,4-dinitrophenyl moieties (Chart 1), the zwitterionic form was found to dominate in both solution and solid states.
With the aim to combine several of these systems in a single molecule and study the impact on the canonical/zwitterionic equilibrium, we naturally focused our attention on the elaboration of macrocyclic architectures of types 2 or 3 presenting an alternation of quinones and aromatic rings substituted with EWG. We report herein their synthesis from ACA precursors and demonstrate that these macrocycles (2a-c and 3a), named azacalixquinaranes (ACQ), can be seen as “hemi-azacalixphyrins”, i.e. an intermediary class of ACA-ACP derivatives featuring an alternation of dinitro-substituted aromatic rings and diaminobenzoquinone diimine rings. As for model compounds 1a-d, the quinoidal fragments within ACQs can be either stabilized under canonical (uncharged) or zwitterionic forms depending on given parameters (N-substituents, solvent), allowing to reach unprecedented poly-zwitterionic systems.

RESULTS AND DISCUSSION

Synthesis. The access to the target ACQs 2a-c was envisaged by chemical oxidation of the azacalix[4]arene precursors (Scheme 1). Therefore, the preparation of ACA 7a-c was carried out following a well-established strategy starting from precursors 4a-c, incorporating octylamine or selected aniline moieties, which were reduced under acidic conditions in the presence of Sn(II) salts or Fe powder, then substituted by 1,5-difluoro-2,4-dinitrobenzene (DFDNB) to afford the adducts 6a-c.30–34

Scheme 1. Synthesis of compounds 1a-d, 2a-c and 3a (quinones only represented under their canonical forms).

These intermediates were converted to the corresponding azacalix[4]arene 7a-c using one equivalent of tetraaminobenzenes 4a-c in refluxing acetonitrile. For compound 6d, previously unknown, the reaction was carried out at room temperature and a low concentration of 5d (10⁻³ M) was necessary to reach a moderate yield (43%, Table S1). Such poor efficiency is presumably imputable to a lack of regioselectivity during the nucleophilic aromatic substitution of the electron-rich adduct 5d on DFDNB. Unfortunately, for the same reason, it was impossible to reach the corresponding azacalix[4]arene 6d using classical conditions. The synthesis of azacalix[6]arenes 8a was more straightforward and allowed the isolation of the macrocycle in only one step from octylamine-decorated tetraaminobenzene 5a, with however a poor 5% yield.35 Note that the formation of higher order macrocycles was not observed.
As expected, series of azacalix[4]arenes 7a-c and azacalix[6]arene 8a could be oxidized to the corresponding azacalixquinarenes 2a-c and 3a using 2 and 3 equivalents of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), respectively. The reaction proceeded rapidly, nevertheless purification was more tedious for aryl-substituted quinones 2b-c which revealed a poor solubility in organic solvents. In contrast, macrocycles 2a and 3a, featuring octyl chains, show a surprisingly good solubility in dichloromethane and were obtained in 82% and 90% yields, respectively. Eventually, care was taken to verify that the ACQ 2a could be converted to the corresponding ACP by reducing the nitro functions in presence of Pd/C and excess hydrazine in refluxing tetrahydrofuran for 2 days. Following a classical workup and overnight aerial oxidation, the expected bis-zwitterionic ACP-C8 (Figure 1, ACP with R = C<sub>8</sub>H<sub>17</sub>) was isolated in a 97% yield (see Experimental Section for details).

With the perspective to study them as model compounds, the quinone 1a-d were prepared from the aromatic derivatives 6a-d, following their treatment with a stoichiometric amount of DDQ in degassed chloroform. The compounds were conveniently purified either by precipitation or by flash column chromatography and finally isolated with good yields (67-80%).

**Structural analysis.** X-ray quality crystals could be obtained for quinone 1b by slow evaporation of an acetonitrile solution. All H-atoms were found experimentally for 1b, as well as the H-atoms for the central cycles and amines in 2a and 3a, except the one for amine N6 in 3a (see Figure 4) that was introduced at geometrical position. Unlike the previously reported crystal structure of 1a, featuring a zwitterionic ground state, the molecule 1b presents an alternation of single and double bonds in both subunits of the quinoidal ring (BLA ca. 0.10 Å; Figure 2). Thus, the presence of slightly electron-donating aromatic substituents in 1b promotes an unequivocal canonical ground state. This unexpected result, which helps to rationalize the optical properties of ACQ 2b (see below), is consistent with theoretical predictions and experimental evidences that aryl-substituted ACPs tend to stabilize canonical tautomers due to the extent of delocalization brought by the aryl substituents. 31, 34

![Figure 2](image.png)

*Figure 2.* Single crystal structures of canonical 1b with selected bond lengths (Å). Anisotropic displacement ellipsoids plot at the 50 percent probability level.

Single crystals of 2a were obtained from a dichloromethane-acetonitrile solution and the structure is presented in Figure 3. Considering the striking effect of the environment on the ground state structure of the ACQs (*vide infra*), it is worth to underline that crystals of 2a obtained from acetone or dimethylformamide solutions gave rise to the exact same structure and packing. An unusual solid-state structure is evidenced for this ACQ corresponding to the mixed form 2c-2a (Scheme 2), which presents two aromatic dinitrobenzene moieties binding two oxidized rings, one of them being a zwitterion structure, the other being a canonical structure. The former ring is characterized by two 6π-electrons subunits, one cationic and the other anionic, linked by single bonds (1.50 Å). Within each cyanine systems, the bond length alternation nearly vanishes (BLA ca. 0.01 Å) due to the strong delocalization of the charges along the trimethine motifs. Surprisingly,
for both oxidized rings, the two 6π-electrons subsystems are not belonging to the same plane, with an angle of 6° for the zwitterionic system and 4° for the canonical one. One can notice that the presence of these two quinone rings within ACQ 3a also induces a strong distortion of the 1,3-alternate configuration, compared to parent analogous ACA structures. The only acidic hydrogen atom borne by the macrocyclic core is involved in a 1.98 Å hydrogen bond with one of the peripheral nitro function. The distance between the two oxidized ring centroids is 6.86 Å, this value being close to the one found in unsubstituted ACP (6.65 Å) and standing out from classical 1,3-alternate ACA 7a, which presents a distance of 4.74 Å between the two octyl-substituted aromatic rings. The angle formed between the two planes of the quinone rings is ca. 110°, which is comparable to the data measured for unsubstituted ACP (see Table S3).

![Diagram](image)

**Figure 3.** Single crystal structure of 2a. Selected bond lengths (Å) and the electronic structure of each rings are indicated: zwitterionic (z), canonical (c) and aromatic (Ar). N-octyl chains are omitted for clarity. Anisotropic displacement ellipsoids plot at the 50 percent probability level.

**Scheme 2.** Possible H-transfers and tautomeric structures of series 1a-d, azacalix[4]quinarenes 2a-c and azacalix[6]quinarene 3a. c and z stand for canonical and zwitterionic, respectively. Note that only one structure for compounds containing at least one c unit is shown here but other (generally less stable) tautomers can be drawn, see Schemes S1, S2, and S3 in the ESI.

Finally, ACQ 3a was crystallized from evaporation of a solution in acetone and stands as one of the rare example of six-membered azacalix-derivatives (Figure 4). The structure reveals that 3a crystallizes with two independent molecules in the asymmetric unit that stack together through two π-π ring interactions between, on one hand, two of their canonical c cycles and, on the other hand, two of their aromatic cycles. Indeed the distance between the cen-
troids is equal to 4.359(4) Å between the canonical cycles and 4.270(4) Å between the aromatic ones, while the dihedral angles are equal to 7.5(3)° and 1.6(3)° respectively. The slippage between the centroids is equal to 2.443 Å and 2.497 Å for the canonical and the aromatic rings respectively. In both independent molecules the macrocycle presents three aromatic dinitrobenzene moieties, two canonical quinones and one zwitterionic ring, thus corresponding to the structure zcc-3a in Scheme 2. It is worthy to note that both acidic hydrogen atoms (NH) borne by the central core are symmetrically distributed and involved in H-bonds with the closest nitro functions. The 1,2,4,5-alternate structure (u,d,u,d,d) is very similar to the parent 8a, with however a distortion brought by the zwitterionic ring. Note that one dinitro aromatic ring is folded inside the cavity and occupies the available space.

Figure 4. Single crystal structures of 3a. The electronic structure of each rings are indicated: zwitterionic (z), canonical (c) and aromatic (Ar). N-octyl chains are omitted for clarity. Anisotropic displacement ellipsoids plot at the 50 percent probability level.

Photophysical properties. The electronic absorption spectra of the quinones recorded in acetone solution (ca. 2·10⁻⁵ M) are compiled in Figure 5. As a model compound, alkyl-substituted compound 1a exhibits a characteristic broad absorption band centered at ca. 700 nm, which is the fingerprint of the zwitterionic form z-1a. This transition is attributed to an intramolecular charge transfer (ICT) from the anionic trimethine to the cationic one (cyanine-to-cyanine ICT), its intensity depending on the proportion of ground-state zwitterion in solution. This analysis is corroborated by theoretical calculations (see Figure S34 and Table S9 in the ESI). Quinones 1b and 1c, which possess trimethoxyaniline and m-trifluoromethylaniline moieties do not present such transition, which hints at a prominent canonical ground-state for these compounds, the strong UV band and its tail in the visible region being classical features of tetra-substituted diamino benzoquinone diimines. In contrast, the absorption of p-dimethylanilinoaniline-substituted 1d shows a pan-chromatic absorption spanning from 400 to 800 nm. Two main transitions can be identified at 654 and 570 nm, and are counter-intuitively theoretically attributed to the forms c-1d and z-1d, respectively (vide infra). In any case, this result
underlines that, for aniline substituted quinones 1b-d, very electron-rich auxochromes are needed to trigger the proton transfer and subsequently observe the presence of the zwitterion. The solvatochromism of this series has been recorded in different solvents ranging from toluene to DMSO and shows a very low impact on the absorption of canonical compounds 1b-c, while a moderate hyperchromic effect is observed for 1a and 1d in solvent of high polarity due to the generation of the zwitterionic forms (Figure S30).

**Figure 5.** Electronic absorption spectra of the quinones in acetone.

The absorption solvatochromism of the macrocycle 2a is particularly interesting since a strong evolution of the lower energy transition is monitored depending on the solvent (Figure 6). Going from toluene to dichloromethane solution, the molar extinction coefficient increases from ca. 720 to 4200 M⁻¹cm⁻¹. In acetone, a transition centered at 660 nm starts to emerge and ultimately becomes the most intense band in DMSO (ε = 6800 M⁻¹cm⁻¹). With the help of theory (Figure S46 and Table S16 in the ESI), the hyperchromic shift in the less polar solvents compared to 2a-1a is attributed to the stronger absorbance of zc-2a in solution (tripling of the oscillator strength compared to 1a), while the growing blue-shifted transition corresponds to the bis-zwitterionic zzz-2a. In a different way, the ACQ 2b presents characteristic "canonical-type" absorption spectra with negligible differences in the range of solvents screened. In contrast, the macrocycle 2c shows the apparition of a band at 700 nm in the most polar solvents such as DMF and DMSO (ε = 4200 M⁻¹cm⁻¹). Such behavior is tentatively assigned to the formation of mixed species zc-2c following intramolecular proton transfer in the corresponding bis-canonical macrocycle. Finally, the [6]-membered macrocycle 3a exhibits a very similar progression of absorption that of 2a. The broad transition at ca. 650-700 nm observed in toluene and dioxane potentially implies the presence of at least one zwitterionic quinone among the three oxidized rings of 3a (see tautomer zcc-3a in Figure 4 and Scheme 2). The growing transition noticed in DMSO is most probably due to the evolution towards species zzc-3a and/or zzz-3a (see calculations below).

**Figure 6.** UV-Vis-NIR absorption solvatochromism of 2c, 2a and 3a in toluene (---), 1,4-dioxane (---), ethyl acetate (---), dichloromethane (---), acetone (---), N,N-dimethylformamide (---) and dimethylsulfoxide (---).

**Cyclic voltammetry.** The redox properties of compounds 1a-d, 2a-c and 3a were analyzed by recording their cyclic voltammograms (CV) in DCM and in DMF solutions (containing 0.1 M of [([Bu4N]+PF6]-) and using ferrocene as an internal standard (Figures S28 and S29). The corresponding oxidation and reduction half-wave potential E1/2 values are given versus the oxidation potential of ferrocene and are listed in Table S4. In DCM, each CV features up to three irreversible reduction waves and up to two oxidation ones. In DMF, no oxidation potential values of compounds 1c and 2c are reported since these processes are occurring out of the solvent electro-chemical window.
For the 1a-d series, the first reduction processes centered on the most electron-accepting di-nitro-fluorobenzene moieties have $E_{1/2}$ values that are not strongly affected by the nature of the N-ssubstituents nor by the solvent polarity. For example, in both solvents, the replacement of the electron-withdrawing $\textit{m}$-trifluoromethylphenyl groups of 1c by electron-donating $\textit{p}$-dimethylaminophenyl ones in 1d induces a cathodic shift of the first reduction wave by less than 50 mV. In contrast, in the four membered macrocycle 2a-c series, where the fluorine atoms have been replaced by tetraaminobenzoquinone moieties, such variation of the $N$-substitution has a noticeable effect on the first reduction $E_{1/2}$ values. For example, the first reduction waves located at $–1.06 \text{ V (DCM)}$ and $–1.00 \text{ V (DMF)}$ for 2a (Figure 7) are found at $–0.78 \text{ V (DCM)}$ and at $–0.84 \text{ V (DMF)}$ when studying 2c. The first oxidation potential values are significantly affected by the nature of the $N$-substituents and/or by the solvent polarity. For example, in DCM, when going from 1b and 2b to 1c and 2c, the increasing electron-accepting strength of the $N$-substituents produces an anodic shift of the first oxidation wave by more than 250 mV. The variation of the first oxidation $E_{1/2}$ value with the solvent polarity can also be used as an additional proof of the occurrence of a canonical/zwitterionic balance. Indeed, if the solvent polarity has a limited impact on the location of the oxidation of the canonical 1b and 2b compounds, it induces, for the oxidation $E_{1/2}$ values of compounds 1a, 2a and 3a, a significant variation of more than 150 mV. This canonical/zwitterionic equilibrium is probably responsible for the decrease of the electrochemical gaps ($\geq 200 \text{ mV}$) of 1a, 2a and 3a when changing DCM by DMF (Figure 7), while those of 1b and 2b are only slightly affected ($\leq 50 \text{ mV}$).

**Figure 7.** Cyclic voltammograms of compound 2a in DCM (black) and DMF (red) solutions.

**Theoretical calculations.** In order to obtain further insights into the underlying electronic structures and evaluate the relative stabilities of the various tautomers, DFT and TD-DFT calculations have been performed on all the systems studied herein. Let us first compare the crystallographic structures with the one modelled in gas phase for 1b, 2a, and 3a. For the two former compounds, we have performed a full tautomeric search, i.e., modelling not only structures presenting rings of $z$ and/or $c$ forms (displayed in Scheme 2), but also accounting for other possible types of rings (see Schemes S1 and S2 in the ESI). For 1b, among the four tautomers considered, theory predicts that the canonical $c$ form is the most stable by more than 2 kcal.mol$^{-1}$ compared to the other forms, which is in perfect agreement with the X-ray structure. One notices that the $a$ and $x$ tautomers (see the ESI for representation) are much less stable ($\geq 10 \text{ kcal.mol}^{-1}$, Table S5) than the $z$ and $c$ structures, which is also consistent with our previous work on a similar compound.\(^9\) The BLA determined for 1b is ca. 0.07 Å, only slightly smaller than in the XRD (vide supra). For 2a, among the thirteen different tautomers considered, it turns out that the macrocycles presenting a least one ring of type $a$ or $x$ are very unlikely with relative free energies exceeding 15 kcal.mol$^{-1}$ (Table S6) which is perfectly consistent with the results obtained for 1b. While only the $zc$-2a structure has been evidenced experimentally, theory predicts that the $cc$ structure is slightly more stable than $zc$. However, the computed difference (1 kcal.mol$^{-1}$) is within DFT error bar and could be overcome by crystal packing effects, not accounted for in the calculations. In $zc$-2a, the DFT determined CC bond lengths in the zwitterionic cycle are 1.386 and 1.389 Å (external side), and 1.388 and 1.405 Å (internal side), in very good match with the experimental values (Figure 3). For 3a, according to the previous observations, only the possible tautomers that combine $z$ and/or $c$ type of rings have been taken into account (Scheme S3 and Table S7). Due to its strongly distorted structure, for a given tautomer, several non-equivalent conformers can be drawn and a full conformational search has therefore been performed. It turns out that, in gas phase, only the $zc$ form in the exact same conformation as the crystallographic structure was found to be stable, the other structures being less stable by at least 3 kcal.mol$^{-1}$.

Let us now turn towards an analysis of the results obtained in solution. We have chosen DMSO as reference solvent except when noted. For 1a, only the $z$ form, presenting a band at 602 nm according to TD-DFT (Table S9), is likely to exist in DMSO, the $c$ tautomer being 5 kcal.mol$^{-1}$ less stable. As stated above, this 602 nm transition involves a significant CT between the two cyanine subunits (Figure S55), consistent with our previous work.\(^9\) In contrast, for 1b and 1c, theory finds that the canonical form is preferred by at least 4 kcal.mol$^{-1}$ (Tables S10 and S12). The $c$-1b and $c$-1c compounds pre-
sent their lowest absorption at 527 and 495 nm, respectively (Figures S36 and S39). There is therefore a clear agreement with the experimental spectra observed for these three species: only the c structures are present and their spectra are blueshifted compared to z-1a. Eventually for 1d, DFT returns almost isoenergetic z and c tautomers, which are therefore likely to coexist in solution (Table S4). This can explain the broad long-wavelength band obtained in the experimental spectra. Unexpectedly, the absorption band at the longest wavelength is attributed to the c-1d (651 nm, f=0.49) whereas the first significant absorption of z-1d appears at 540 nm, f=0.85, see Table S15 and Figure S43). This is because the Si state of z-1d, computed at 667 nm is totally dark. As can be seen in Figures S41 and S42, all the lowest dipole-allowed transitions present a significant CT character, the p-amino-phenyl moieties acting as donor groups and the central core acting as acceptor.

For 2a, the free energies and UV-Vis spectra have been calculated in both DCM and DMSO. The results are displayed in the ESI. The computed free energies indicate that the cc forms are not likely to be present in solution (> 5 kcal.mol\(^{-1}\)), whereas the difference between the zc and zz forms increases when going from DCM to DMSO hinting that the ratio of the latter increases with solvent polarity as expected (Table S16). For both zc and zz, the absorption spectra computed in the two solvents are extremely similar (see Figure S51), with the first dipole-allowed absorption of zz appearing at smaller wavelength than the one of zc (565 and 621 nm, respectively, see Table S17), for the same reason as in 1d (i.e., the first transition in zz is forbidden). Therefore, the experimentally observed solvatochromism, that is, the increase of the intensity of the blueshifted zwitterionic band when going from DCM to DMSO (see Figure 8), is due to the changes in the relative population of the tautomers rather than a direct solvent effect on their individual spectra. In the zc-2a structure, the band at 621 nm is clearly centered on the z cycle (Figure S48). For 2b, theory predicts that the cc tautomer is the most stable and that the zz structure is unlikely (relative free energy of 3.8 kcal.mol\(^{-1}\), Table S19) whereas the zc tautomer is only 1.1 kcal.mol\(^{-1}\) above cc. Given the computed spectra (Figure S52), one can therefore probably attribute the small extension of the foot of the band toward the red in 2b to the formation of a small amount of zc. For 2c, theory predicts that only the cc exists in solution, the free energies of the other zc and zz forms being relatively high, e.g., 3.8 kcal.mol\(^{-1}\) for zc (Table S21). This is the only theoretical result not consistent with experiment that returns the presence of zwitterionic forms in the most polar solvents (vide infra).

Figure 8. Theoretical absorption spectra of different tautomeric forms of azacalixquinarenes 2a and 3a computed in DMSO. The theoretical spectra are obtained using a broadening Gaussian with a FWHM of 2500 cm\(^{-1}\) to convolute the stick spectrum.

As previously shown and consistently with the experiments, theory predicts that the most stable form of 3a in gas phase corresponds to the zcc tautomer. Interestingly, going to DCM and DMSO leads to markedly different results (Table S22). Indeed, unsurprisingly, the more polar is the solvent, the more the “z-heavy” structures are stabilized. Indeed, in DCM (DMSO), theory predicts that the zcc (zzz) form is the most stable one. The theoretical spectra of these three species are given in Figures 8 and S50 and one notices that the long-wavelength absorption band presents a nearly equal position in zcc, zcc and zzz, whereas its intensity is roughly proportional to the ratio of zwitterionic rings. The lowest electronic transitions for these three species have been characterized (Figure 9). The long-wavelength bright states (> 550 nm) are localized on the zwitterionic part(s) for the three tautomers of 3a, whereas the canonical moieties are related to absorption at higher energies (ca. 470 nm).
EXPERIMENTAL SECTION & THEORETICAL DETAILS

Reagents. All reagents were purchased from Alfa-Aesar or Sigma-Aldrich and used as received. When heating was required, oil bathes were used. Column chromatography were performed using Silica 60M (0.04-0.063 mm) purchased from Macherey-Nagel. Compounds 1a,\textsuperscript{35} 6a and 7a,\textsuperscript{36} 6b-c and 7b-c,\textsuperscript{36} 8a\textsuperscript{34} were prepared following previously reported protocols.

Analytical methods and apparatus. NMR spectra were recorded on a JEOL ECS400 NMR spectrometer at room temperature, otherwise noted. NMR chemical shifts are given in ppm (δ) relative to Me$_4$Si with solvent resonances used as internal standards (CDCl$_3$; 7.26 ppm for 'H and 77.2 for $^{13}$C[‘H]; Acetone-\textit{d}$_6$: 2.05 ppm for 'H and 29.8 for $^{13}$C[‘H]; DMSO-\textit{d}$_6$: 2.50 ppm for 'H and 39.5 for $^{13}$C[‘H]). UV-Vis-NIR absorption spectra were recorded on a VARIAN CARY 50 SCAN spectrophotometer at room temperature. NMR peak assignments were confirmed using a DEPT-135 method. Optical properties were recorded in spectrophotoochemical grade solvents. HRMS (ESI) and MS (ESI) analyses were performed on a QStar Elite (Applied Biosystems SCIEX) or a SYNAPT G2 HDMS (Waters) spectrometers by the “Spectropole” of the Aix-

CONCLUSION

A new class of macrocycle, the azacalixquinarene family has been synthesized by partial oxidation of azacalixarenes. Single crystal structures highlighted that the cavity volume in four-membered macrocycles was higher than in the parent ACA due to the distortion brought by the imine functions. Importantly, [4]- and [6]-membered ACQs 2a and 3a presented one of their quinone cycle under zwitterionic electronic structure at the solid state. The nature of the $N$-substituents influences the ground state of the quinone units, alkyl chains and strong electron-donating aryl moieties allowed to promote a zwitterionic character. The evolution of the absorption profiles observed in solution was rationalized by TD-DFT, highlighting the preponderance of zwitterionic units in polar environment. This fine, easily tunable balance between the presence of canonical and zwitterionic moieties within a same macrocyclic architecture paves the way to several sensing applications.

Figure 9. Representation of the TD-DFT electron density difference for the three lowest excited-states of 3a in three of its tautomeric forms. The blue and red regions respectively indicate decrease and increase of density upon photon absorption (contour threshold: 0.0008 au).
Marseille University. These two instruments were equipped with an ESI or MALDI source spectrometer, and a TOF mass analyzer.

**Single Crystal X-ray Diffraction.** Suitable crystals for compounds 1b, 2a and 3a were obtained from slow evaporation from acetonitrile, dichloromethane/acetonitrile and acetone respectively. They were mounted on a Rigaku Oxford Diffraction SuperNova diffractometer and measured at 203 K, 250 K and 150 K respectively, at the Cu radiation (\(\lambda=1.54184\) Å). Data collection, reduction and multiscan ABSPACK correction were performed with CrysalisPro (Rigaku Oxford Diffraction). Using Olex2\textsuperscript{a} the structures were solved with the ShelXT\textsuperscript{a} structure solution program using Intrinsic Phasing and refined with ShelXL\textsuperscript{a} using least-square minimization. Crystals of 1b were found to be twins and all H-atoms were determined experimentally. Structures of 2a and 3a revealed severe disorder for the octylamine moieties and hard constraints were applied during the refinement process. For both compounds the H-atoms for the central cycles and the amines were found experimentally except for atom N6 in 3a. The remaining H-atoms were introduced at geometrical positions and all H-atoms were refined with riding coordinates to their parent atoms and with their Uiso parameters constraint to 1.2Ueq(parent atoms) for the CH, CH\textsubscript{2} and NH and 1.5Ueq(parent atoms) for the CH\textsubscript{3}. Compound 3a crystallized with 2 independent molecules in the asymmetric unit.

**Electrochemistry.** Cyclic voltammetry (CV) data were recorded using a BAS 100 (Bioanalytical Systems) potentiostat and the BASsooW software (v.2.3). All the experiments were conducted under an argon atmosphere in a standard one-compartment using a three electrodes setup: a Pt working electrode (Ø = 1.6 mm), a Pt counter electrode and an Ag/AgCl reference electrode (filled with a 3 M NaCl solution). Tetra-n-butylammonium hexafluorophosphate ([TBA][PF\textsubscript{6}]) was used as supporting electrolyte (10 M). The solvent effects were modeled through the well-known Polarizable Continuum Model (PCM). All calculations have been made with Gaussian-16\textsuperscript{a}, replacing the alkyl chains C\textsubscript{6}H\textsubscript{13} by methyl groups in all the calculations for the sake of computational time. We have used the PBE0\textsuperscript{a} global hybrid functional for all our calculations. For compounds 1a-d and 2a, we have optimized the ground-state geometry with the 6-31++G(d,p) basis set, whereas larger compounds 2b-c and 3a have been optimized using the more compact 6-31G(d) atomic basis set. We verified the absence of imaginary frequencies by computing analytically the Hessian at the same level of theory. The excited-state calculations were performed with TD-DFT determined with the CAM-B3LYP\textsuperscript{b} exchange-correlation functional in combination with the 6-31++G(d,p) atomic basis set. This functional has been preferred to PBE0 as several charge transfer states are considered in this study. The solvent effects were modeled through the well-known Polarizable Continuum Model (PCM). Extra computational details are available in Section VII of the SI.

**Synthesis of \(N,N'-\text{bis}(4,6\text{-dinitro-1,3-phenylene})\text{bis}(N,N'\text{-dimethylbenzene-1,4-diamine})\) (4d).** In a pressure bomb, compound 4d (1 g, 2.39 mmol, 1 equiv.) and SnCl\textsubscript{2}•2H\textsubscript{2}O (4.136 g, 18.33 mmol, 8 equiv.) were dissolved in 10 mL of concentrated HCl (12 M) and 10 mL of chloroform. The bomb was closed with a Teflon seal and the mixture was stirred at 60 °C for 15 h. The resulting precipitate was filtered, washed several times with concentrated HCl (3 x 20 mL), DCM, Et\textsubscript{2}O and finally dried under vacuum to afford the product as a white powder (739 mg, 72%). The compound was stored at -4 °C to prevent its oxidation to the corresponding quinone. \(1^H\) NMR (DMSO-d\textsubscript{4}, 400 MHz): \(\delta=8.65\) (br s, 2H, NH), 7.66 (d, \(J=9.0\) Hz, 4H, CH), 7.41 (s, 1H, CH), 7.09 (s, 1H, CH), 7.06 (d, \(J=9.0\) Hz, 4H, CH), 3.08 (s, 12H, N(CH\textsubscript{3})\textsubscript{2}). No \(13^C\) NMR spectrum could be recorded owing to the poor stability in solution. HRMS (MALDI) calculated for [M+H]\textsuperscript{+}: 376.2370 (C\textsubscript{22}H\textsubscript{14}N\textsubscript{6}O\textsubscript{4}\textsuperscript{+}), found: 376.2360.

**Synthesis of \(N,N'\text{-bis}(4\text{-dimethylamino})\text{phenyl})\text{benzene-1,2,4,5-tetraamine tetrahydrochloride}\) (5d).** In a pressure bomb, 5d (500 mg, 1.11 mmol, 1 equiv.) and 1,5-difluoro-2,4-dinitrobenzene (227 g, 1.11 mmol, 1 equiv.) were dissolved in 110 mL of acetonitrile. The solution was cooled to 0 °C and degassed under Argon bubbling for
Synthesis of (3E,6E)-N'-((5-fluoro-2,4-dinitrophenyl)imino)-N-((3,4,5-trimethoxyphenyl)-6-((3,4,5-trimethoxyphenyl)imino)cyclohexa-1,4-diene-1,4-diamine (1b). To a solution of compound 6b (100 mg, 0.119 mmol, 1 equiv.) in 3 mL of degassed chloroform was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (22 mg, 0.110 mmol, 1 equiv.) and the mixture was stirred at 25 °C for 30 minutes. After concentration under reduced pressure, the crude residue was washed with ethanol, diethyl ether and pentane to afford the product as a green solid (76 mg, 76%).


Synthesis of (3E,6E)-N'-((5-fluoro-2,4-dinitrophenyl)imino)-N-((3-trifluoromethylphenyl)-6-((3-trifluoromethylphenyl)imino)cyclohexa-1,4-diene-1,4-diamine (1c). To a solution of compound 10c (100 mg, 0.126 mmol, 1 equiv.) in 2 mL of degassed tetrahydrofuran was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (28.7 mg, 0.126 mmol, 1 equiv.) in 2 mL of degassed tetrahydrofuran and the mixture was stirred at room temperature for 4 h. After concentration under reduced pressure, the crude residue was washed with ethanol and diethyl ether to afford the product as a brown solid (80 mg, 80%)


Synthesis of (E)-N'-((E)-5-((4-(dimethylamino)phenyl)amino)-2-((5-fluoro-2,4-dinitrophenyl)imino)cyclohexa-1,2,5-dien-1-ylidene)-N-((5-fluoro-2,4-dinitrophenyl)imino)cyclohexa-1,4-diene-1,4-diamine (1d). To a solution of compound 6d (100 mg, 0.134 mmol, 1 equiv.) in 2 mL of degassed tetrahydrofuran was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (31 mg, 0.134 mmol, 1 equiv.) in 2 mL of degassed tetrahydrofuran and the mixture was stirred at 25 °C for 1 h. After concentration under reduced pressure, the crude residue was washed with ethanol, diethyl ether and pentane to afford the product as a green solid (76 mg, 76%).


Synthesis of ACQ 2a. To a solution of ACA 7a (50 mg, 0.047 mmol, 1 equiv.) in 2 mL of degassed chloroform was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (22 mg, 0.095 mmol, 2 equiv.) and the mixture was stirred at 25 °C for 4 h. After concentration under reduced pressure, the crude residue was purified by column chromatography over silica gel using dichloromethane as eluent for the product as a brown-green solid (41 mg, 82%).

mg, 52%). R c 0.40 (SiO2, dichloromethane/acetone, 9:1). 1H NMR (DMSO-d6, 400 MHz): δ = 9.54 (br s, 4H, NH), 8.95 (br s, 2H, CH), 7.55 (br s, 2H, CH), 7.11 (br s, 2H, CH), 6.40 (br s, 8H, CH), 6.34 (br s, 2H, CH), 3.67 (br s, 24H, OCH3), 3.67 (br s, 12H, OCH3). Compound was too insoluble to record a 13C{1H} NMR spectrum. HRMS (ESI+) calculated for [M+2H]2+: 927.7 (C69H46N6O10O2), found: 927.8.

**Synthesis of ACQ 2c.** To a solution of compound 7c (80 mg, 0.068 mmol, 1 equiv.) in 2.5 mL of degassed tetrahydrofuran was added dropwise 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (30.72 mg, 0.136 mmol, 2 equiv.) in 2.5 mL of degassed tetrahydrofuran and the mixture was stirred at 25 °C for 19 h. After concentration under reduced pressure, the crude residue was washed with ethanol and was purified by flash column chromatography over neutral aluminium oxide using dichloromethane/acetone (95:5) as eluent to afford the product as a brown solid (30 mg, 90%). R c 0.48 (SiO2, dichloromethane/petroleum ether, 7:3). 1H NMR (DMSO-d6, 400 MHz): δ = 9.80 (br s, 4H, NH), 8.97 (s, 2H, CH), 7.62 – 7.38 (m, 18H, CH), 7.20 (s, 2H, CH), 6.12 (s, 2H, CH). Compound was too insoluble to record a 13C{1H} NMR spectrum. HRMS (ESI+) calculated for [M+2H]2+: 787.4739 (C67H44F3N2O8), found: 787.4737.

**Synthesis of ACQ 3a.** To a solution of ACQ 2a (10 mg, 0.006 mmol, 1 equiv.) in 2 mL of degassed chloroform was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (4.3 mg, 0.018 mmol, 3 equiv.) and the mixture was stirred at 25 °C for 30 minutes. After concentration under reduced pressure, the crude residue was purified by flash column chromatography over silica gel using dichloromethane as eluent to afford the product as a green solid (9 mg, 52%). R c 0.40 (SiO2, dichloromethane/acetone, 9:1). 1H NMR (DMSO-d6, 400 MHz): δ = 8.69 (br s, 2H), 6.67 (br s, 2H), 5.78 (br s, 2H), 3.56 (m, 12H, NCH3), 1.81 (m, 12H, CH), 1.29 (m, 48H, CH). HRMS (ESI+) calculated for [M+2H]2+: 1177.2046 (C82H54F6N2O14), found: 1177.2034 (C82H54F6N2O14), found: 1177.2046.

**Synthesis of ACP-C8 (R=C6H4) from ACQ 2a.** In a Schlenk tube, a solution of compound 2a (35 mg, 0.033 mmol, 1 equiv.) in tetrahydrofuran (15 mL) was added by 5 wt.% Pd/C (21 mg, 0.010 mmol, 30 mol.%), and hydrazine monohydrate (203 µL, 4.169 mmol, 125 equiv.) and the mixture was stirred at 25 °C for 30 minutes. After concentration under reduced pressure, the crude residue was dissolved in 3 mL of methanol (solution instantly turned green, revealing the oxidation of azacalixarene to azacalixphyrin). The solution was bubbled with air for 16 h at 25 °C, then filtered on a Celite (AW) pad which was rinsed with MeOH. The filtrate was evaporated and the solid was taken up in a mixture of dichloromethane and acetone, sonicated for few minutes, filtered and the solid was finally washed with acetonitrile, dichloromethane, diethyl ether and pentane to afford the product as a green powder (9 mg, 52%). R c 0.40 (SiO2, dichloromethane/acetone, 9:1). 1H NMR (acetone-d6, 400 MHz): δ = 8.69 (br s, 2H), 6.67 (br s, 2H), 5.78 (br s, 2H), 3.56 (m, 12H, NCH3), 1.81 (m, 12H, CH), 1.50 (m, 12H, CH), 1.29 (m, 48H, CH), 0.89 (t, J = 6.9 Hz, 18H, CH3). Quinoid units meet relaxation issues that yield uncomplete or unresolved NMR signals. 1H NMR spectrum recorded in DMSO-d6 at 353 K reveals the missing signals (see ESI) No 13C{1H} NMR spectrum could be recorded due to poorly resolved signals and poor solubility. HRMS (ESI+) calculated for [M+2H]2+: 787.4739 (C67H44F3N2O8), found: 787.4737.

**ASSOCIATED CONTENT**

Additional synthetic details, 1H and 13C{1H} NMR spectra, HRMS spectra, crystal data and structures refinements for compounds 2a, 2b and 3a, additional absorption spectra, cyclic voltammograms, theoretical calculations. The Supporting Information is available free of charge on the ACS Publications website at DOI: XXX.

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