# ChemComm

## COMMUNICATION

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Cite this: Chem. Commun., 2021, 57, 6983

Received 22nd May 2021, Accepted 17th June 2021

DOI: 10.1039/d1cc02691g

rsc.li/chemcomm

Published on 18 June 2021. Downloaded by University of Cambridge on 9/1/2021 6:20:03 AM.

### Pyrrole-bridged quinones: $\pi$ -electronic systems that modulate electronic structures by tautomerism and deprotonation<sup>†</sup>

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A new series of  $\pi$ -extended quinone derivatives containing a pyrrole bridge exhibited NH/OH-type tautomerization and anion binding along with deprotonation that induced near-infrared absorption and ion-pairing assemblies.

Modulation of the electronic structures of  $\pi$ -electronic systems is essential for the control of properties in dispersed and assembled states.<sup>1</sup> The electronic structures can be controlled by associating specific species (guests) via suitable noncovalent interactions.<sup>2</sup> Further facile modifications can be achieved by changing the location of protons, that is, protonation, deprotonation and intramolecular displacement (tautomerism) (Fig. 1a). Acids and bases, as  $\pi$ -electronic systems, are converted to their charged states by deprotonation and protonation, respectively, and can thus be used as molecular sensors and bio-probes.3 On the other hand, tautomerism is an intramolecular proton transfer that provides isomeric structures with the sites of competitive  $pK_a$  values, inducing different electronic structures and properties.<sup>4</sup> A  $\pi$ -electronic system bearing a mobile proton is pyrrole, which is a five-membered heteroaromatic ring and a building unit of extended  $\pi$ -systems such as porphyrins. Porphyrin has two NH and two N sites inside the macrocycle, thus exhibiting protonation, deprotonation<sup>5</sup> and tautomerism.<sup>6</sup> The modification of pyrrole units in conjunction with proton-accepting and electron-withdrawing  $\pi$ -units, even in acyclic forms, results in  $\pi$ -electronic systems exhibiting intramolecular and intermolecular NH proton migration and corresponding electronic properties. A candidate proton-accepting and electron-withdrawing  $\pi$ -unit attached to pyrrole is *p*-quinone methide.  $\pi$ -Electronic systems substituted with two p-quinone methide moieties on both sides exhibit unique electronic properties, including near-infrared

absorption and diradical properties.<sup>7,8</sup> In this study, pyrrolebridged quinones were synthesized as  $\pi$ -electronic systems that exhibit tautomerism between quinoidal (NH) and phenol (OH) forms and anion-binding and deprotonation behaviours (Fig. 1b). This study will lead to ion-pairing assemblies whose properties are modulated by external conditions.

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The precursors of the target pyrrole-bridged quinones, which included tert-butyl groups for stabilization, were synthesized via multistep reactions. Firstly, 5-(4-acetoxy-3,5-di-tertbutylphenyl)pyrrol-2-yl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane was obtained by the Ir<sup>I</sup>-catalyzed reaction<sup>9</sup> of the corresponding pyrrole and bis(pinacolato)diboron (Fig. 2a). The boronic acid ester was converted to 2,5-bis(4-acetoxy-3,5-di-tert-butylphenyl) pyrrole 1a in 53% yield by Suzuki coupling with 1-acetoxy-4bromo-2,6-di-tert-butylbenzene in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> and  $K_2CO_3$ .<sup>10</sup> The  $\beta$ -positions of **1a** exhibited reactivity, as seen in the bromination using N-bromosuccinimide (NBS) to afford  $\beta$ -brominated **1b** in 79% yield.<sup>11</sup> Furthermore, tetraaryl-substituted 1c was synthesized in 40% yield by Suzuki coupling between 1b and phenylboronic acid. After several trials, pyrrole-based quinoidal derivatives 2a-c were obtained



(e.g., 2-pyridone; left: tautomerism, right: protonation/deprotonation) and (b) tautomerization of quinoidal pyrrole, as a parent structure, which is observed as the quinoidal (NH) and phenol (OH) form (left) and a deprotonated form (right).

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<sup>†</sup> Electronic supplementary information (ESI) available: Synthetic procedures, analytical data, computational details and cif files for the single-crystal X-ray analysis. CCDC 2076439-2076443. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1cc02691g



Fig. 2 (a) Synthesis of pyrrole-bridged quinones 2a-c and (b) singlecrystal X-ray structures of (i) 2a and (ii) 2c with atom numbering. Atom colour code in (b) and following figures: brown, pink, blue and red refer to carbon, hydrogen, nitrogen and oxygen, respectively.

in 66–74% yields by reactions of **1a–c** with excess anhydrous FeCl<sub>3</sub> for 5 min in CH<sub>2</sub>Cl<sub>2</sub> (Fig. 2a).<sup>12,13</sup> Longer reaction time (>10 min) resulted in lower yields of **2a–c** due to the formation of byproducts. The characterization of the obtained compounds was conducted using <sup>1</sup>H and <sup>13</sup>C NMR and ESI-TOF-MS. It is noteworthy that the <sup>1</sup>H NMR spectra revealed the presence of the quinoidal form **2a–c**<sub>NH</sub> and phenol form **2a–c**<sub>OH</sub>, where the ratios were dependent on the solvent polarity (*vide infra*).

Single-crystal X-ray analysis revealed the exact geometries and packing structures of **2a,c** in the solid state (Fig. 2b and Fig. S16, S17, ESI<sup>†</sup>), exhibiting the quinoidal forms (**2a,c**<sub>NH</sub>). Hydrogen bonding of water molecules with the pyrrole NH and carbonyl unit of the *p*-quinone methide moieties was observed. The bond lengths in the quinone methide moieties ( $C^{2(2')}-C^{3(3')}$ ,  $C^{5(5')}-C^{6(6')}$ ) of **2a,c** were in the range of 1.34–1.36 Å, suggesting double bond characters of quinoidal structures. The dihedral angles between *p*-quinone methide moieties and the core pyrrole unit of **2c** were 10.2° and 14.8°, which were slightly larger than those of **2a** (8.5° and 10.2°), due to steric hindrance by the  $\beta$ -phenyl rings. These values of **2c** were smaller than those of tetraarylpyrroles, such as 2,3,4,5-tetraphenylpyrrole (25.2° and 34.3°),<sup>14</sup> due to the quinoid structure.

The tautomerism of **2a–c** between the quinoidal and phenol forms was examined by UV/vis absorption spectra (Fig. S39–S41, ESI<sup>†</sup>). A blue solution with an absorption maximum ( $\lambda_{max}$ ) at 625 nm was detected for **2a** in CH<sub>2</sub>Cl<sub>2</sub> (Fig. 3a(i)), which was ascribed to the quinoidal form **2a**<sub>NH</sub> (observed in the green region) by electronic transition spectra simulated by time-dependent density functional theory (TD-DFT) (Fig. S32, ESI<sup>†</sup>).<sup>16</sup> No notable differences were observed in the UV/vis absorption spectra in more polar solvents (MeOH and CH<sub>3</sub>CN). In contrast, absorption bands observed at 400–500 nm in *n*-hexane were correlated with the theoretical spectrum of **2a**<sub>OH</sub>. Polar and less polar solvents induced the preferred formation of the quinoidal and phenol forms,



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Fig. 3 (a) UV/vis absorption spectra of (i) **2a** and (ii) **2b** (0.010 mM) in CH<sub>3</sub>CN (dielectric constant<sup>15</sup>  $v_r$ : 35.94; red), MeOH (32.66; orange), acetone (20.56; blue), CH<sub>2</sub>Cl<sub>2</sub> (8.93; green) and *n*-hexane (1.88; light blue) and photographs under visible light and (b) <sup>1</sup>H NMR spectra of (i) **2a** and (ii) **2b** in CD<sub>2</sub>Cl<sub>2</sub> at 20 °C.

respectively. On the other hand, **2b,c** in CH<sub>2</sub>Cl<sub>2</sub> showed brown and green colours, respectively, derived from their phenol forms at  $\lambda_{max}$  of 462 and 467 nm, respectively (Fig. 3a(ii)).<sup>17</sup> In MeOH and CH<sub>3</sub>CN, the absorption of **2b** at ~450 nm (purple region) decreased, while new absorption bands were observed at ~600–850 nm (650 and 830 nm in CH<sub>3</sub>CN). Furthermore, in acetone, **2b** showed a dark green solution with a large and sharp absorption at 830 nm, which was also observed in CH<sub>3</sub>CN. This peak was assigned to the deprotonated species (red region, *vide infra*).<sup>7a</sup> **2a,c** also exhibited small absorptions at ~800 nm in acetone.

Quantitative analyses of the tautomers  $2\mathbf{a}_{\rm NH}$  and  $2\mathbf{a}_{\rm OH}$  were conducted using <sup>1</sup>H NMR. In CD<sub>2</sub>Cl<sub>2</sub>, pyrrole NH, quinone methide CH, and pyrrole CH signals of  $2\mathbf{a}_{\rm NH}$  were observed at 8.25, 7.39/7.28 and 7.44 ppm, respectively, whereas quinone methide CH, phenol CH, pyrrole CH and OH signals of  $2\mathbf{a}_{\rm OH}$  appeared at 8.43/7.54, 8.05, 7.68/7.44 and 5.79 ppm, respectively.  $2\mathbf{a}_{\rm NH}$  was a major tautomer with an integration ratio of 89 : 11 (Fig. 3b(i)), providing an equilibrium constant of 0.12 for NH/OH tautomerization ( $K_{\rm T} = [2\mathbf{a}_{\rm OH}]/$ [ $2\mathbf{a}_{\rm NH}$ ]) and the Gibbs energy ( $\Delta G$ ) of 1.23 kcal mol<sup>-1</sup> at 20 °C (Table 1). The observation was consistent with the theoretically estimated stability of 1.38 kcal mol<sup>-1</sup> for  $2\mathbf{a}_{\rm NH}$  compared to  $2\mathbf{a}_{\rm OH}$ at the PCM-B3LYP/6-31+G(d,p)[CH<sub>2</sub>Cl<sub>2</sub>]//B3LYP/6-31+G(d,p) level

**Table 1**  $K_T (K_T = [\mathbf{2}_{OH}]/[\mathbf{2}_{NH}])$  and  $\Delta G$  (kcal mol<sup>-1</sup>) values of  $\mathbf{2a-c}$  in several solvents at 20 °C

	2a	2 <b>b</b>	2 <b>c</b>
$CD_2Cl_2$	$K_{\rm T}: 0.12,$	Only $2\mathbf{b}_{\mathrm{OH}}$	$K_{\rm T}: 1.24,$ $\Lambda G: -0.13$
$CDCl_3$	$K_{\rm T}$ : 0.26, $\Lambda C$ : 0.78	Only $2b_{OH}$	$K_{\rm T}$ : 2.19,
CD <sub>3</sub> CN	Only $2a_{\rm NH}$	a	Only $2c_{\rm NH}$

 $^a$  A mixture of  $\mathbf{2b}_{\mathrm{NH}},\,\mathbf{2b}_{\mathrm{OH}}$  and  $\mathbf{2b}^-$ .

(Fig. S20, ESI<sup>†</sup>).<sup>16,18</sup> However, **2b** existed only as **2b**<sub>OH</sub> (Fig. 3b(ii)), whereas **2c** showed the tautomers with a  $K_{\rm T}$  value of 1.24 and  $\Delta G$  of -0.13 kcal mol<sup>-1</sup> at 20 °C in CD<sub>2</sub>Cl<sub>2</sub> (Table 1 and Fig. S47, ESI<sup>†</sup>). The preferred tautomers were controlled by pyrrole  $\beta$ -substituents and resulting pyrrole NH acidities, based on the rather competitive p $K_{\rm a}$  values of pyrrole and phenol (23.0 and 18.0, respectively, in DMSO).<sup>19</sup>

In CDCl<sub>3</sub> ( $\varepsilon_r$ (CHCl<sub>3</sub>): 4.81), which is less polar than CD<sub>2</sub>Cl<sub>2</sub>, the *K*<sub>T</sub> values of **2a,c** increased (Table 1 and Fig. S43, S48, ESI<sup>†</sup>). In more polar solvents, such as CD<sub>3</sub>CN, only quinoidal forms  $(2a, c_{NH})$  were observed. On the other hand, 2b existed only as 2b<sub>OH</sub> in CDCl<sub>3</sub> and provided complicated <sup>1</sup>H NMR signals in  $CD_3CN$  and acetone- $d_6$  (Fig. S8 and S46, ESI<sup>†</sup>), suggesting partial deprotonation in polar solvents, which was in agreement with the UV/vis absorption spectra. The control of tautomerism by solvent polarity can be explained by the effective interactions between the pyrrole NH unit and the solvent molecules in the quinoidal forms. The OH site in the phenol forms is less suitable for interactions due to bulky tert-butyl groups. Furthermore, variable-temperature (VT) <sup>1</sup>H NMR in  $CD_2Cl_2$  (1 mM) for 2a revealed decreased  $K_T$  values at lower temperatures, as seen in 0.02 at -40 °C. The temperaturedependent  $K_{\rm T}$  values provided an enthalpy  $\Delta H$  of 4.3 kcal mol<sup>-1</sup> and entropy  $\Delta S$  of 10.5 cal K<sup>-1</sup> mol<sup>-1</sup> via the van't Hoff plots, indicating that  $2a_{\rm NH}$  was more enthalpically stable than  $2a_{\rm OH}$ (Fig. S50, ESI<sup>†</sup>). A similar tendency was observed for 2c, providing smaller  $\Delta H$  and  $\Delta S$  values of 1.8 kcal mol<sup>-1</sup> and 6.3 cal  $K^{-1}$  mol<sup>-1</sup>, respectively, whereas 2b exhibited only  $2b_{OH}$ even at  $-50 \degree C$  (Fig. S51 and S52, ESI<sup>†</sup>). The smaller  $\Delta H$  value in 2c is ascribed to the more distorted geometry of  $2c_{NH}$ , which is seen in the X-ray and optimized structures.

Using pyrrole NH as a hydrogen-bonding donor,<sup>20</sup> quinoidal pyrrole derivatives displayed anion binding *via* the supporting interactions of quinone methide CH sites. In CH<sub>2</sub>Cl<sub>2</sub>, the UV/vis absorption of **2a**, existing mainly as **2a**<sub>NH</sub>, at 625 nm decreased upon the addition of Cl<sup>-</sup> as a tetrabutylammonium (TBA) salt, with the appearance of a new red-shifted absorption at 644 nm ascribed to the Cl<sup>-</sup> complex **2a**<sub>NH</sub>·Cl<sup>-</sup> (Fig. S53, ESI†). UV/vis absorption spectral changes of **2a** in CH<sub>2</sub>Cl<sub>2</sub> revealed a binding constant ( $K_a$ ) of 300 M<sup>-1</sup>, which was larger than that of pyrrole (10 M<sup>-1</sup>),<sup>21</sup> suggesting the electron-withdrawing effect of the *p*-quinone methide units and hydrogen bonding by the quinone methide CH units. On the other hand, **2b,c**, existing mainly in the phenol form in CH<sub>2</sub>Cl<sub>2</sub>, exhibited anion-binding abilities with  $K_a$  values of <1 and 2 M<sup>-1</sup>, respectively,



Fig. 4 (a) UV/vis absorption spectra of  $2a^-$  (solid line), prepared from 2a (broken line) upon the addition of TBAOH, and photographs under visible light in CH<sub>2</sub>Cl<sub>2</sub> (0.010 mM) at 20 °C and (b) <sup>1</sup>H NMR spectrum of  $2a^-$ , prepared from 2a (overlayed in grey) upon the addition of TBAOH (1.5 equiv.) in CD<sub>2</sub>Cl<sub>2</sub> at 20 °C.

for Cl<sup>-</sup>. In the <sup>1</sup>H NMR spectral changes upon the addition of TBACl in CD<sub>2</sub>Cl<sub>2</sub>, the signals of **2a** corresponding to pyrrole NH and quinone methide CH shifted downfield due to hydrogenbonding formation (Fig. S54, ESI†). The signals of **2c**, as a mixture of tautomers, corresponding to pyrrole NH and quinone methide CH in **2c**<sub>NH</sub> shifted downfield, while the signals of **2c**<sub>OH</sub> showed no shifts upon the addition of Cl<sup>-</sup> because of the negligible interaction with Cl<sup>-</sup>. The signals of **2c**<sub>OH</sub> interacted with Cl<sup>-</sup>, suggesting that the tautomeric equilibrium shifted toward the quinoidal form by anion binding (Fig. S56, ESI†). Furthermore, **2b**, which existed as **2b**<sub>OH</sub> in CD<sub>2</sub>Cl<sub>2</sub>, changed to **2b**<sub>NH</sub> by Cl<sup>-</sup> binding in CD<sub>2</sub>Cl<sub>2</sub>. The signals of **2b**<sub>NH</sub> corresponding to pyrrole NH and quinone methide CH at -50 °C gradually emerged upon the addition of Cl<sup>-</sup> (Fig. S55, ESI†).

The deprotonation of 2a, providing the anionic species 2a<sup>-</sup> upon the addition of tetrabutylammonium hydroxide (TBAOH), was confirmed by the UV/vis absorption spectral changes with the support of theoretical studies (Fig. 4a and Fig. S20, S23, S27, S33, S57, ESI<sup>†</sup>). In CH<sub>2</sub>Cl<sub>2</sub>, the absorption maximum of 2a at 625 nm disappeared, with the appearance of a sharp absorption band of 2a<sup>-</sup> at 773 nm upon the addition of TBAOH. The nearinfrared band was derived from the delocalization of the negative charge and the resulting extended  $\pi$ -electronic state, as seen in cyanine derivatives.<sup>22</sup> No pyrrole NH signal was observed in the <sup>1</sup>H NMR of  $2a^{-}$  in  $CD_2Cl_2$ , while the quinone methide CH signal at the pyrrole N side showed a downfield shift from 7.28 to 8.28 ppm due to hydrogen bonding with the deprotonated N site (Fig. 4b). The signals of the pyrrole CH and neighbouring quinone methide CH exhibited downfield shifts from 7.44 to 7.54 ppm and from 7.39 to 7.51 ppm, respectively (Fig. S58, ESI<sup>+</sup>). Similar deprotonation behaviours of 2b, c were observed in the UV/vis absorption and <sup>1</sup>H NMR spectra (Fig. S57, S59, S60, ESI<sup>†</sup>).



Fig. 5 Single-crystal X-ray structures of (a)  $2b^-$ -TPA<sup>+</sup> and (b)  $2c^-$ -TPA<sup>+</sup> as packing structures (magenta: anions, cyan: TPA<sup>+</sup>) with top views of anions.

The ion-pairing formation of  $2b^-$ , $c^-$  with tetrapropylammonium (TPA) and the corresponding assembled structures were elucidated by single-crystal X-ray analyses (Fig. 5 and Fig. S18, S19, ESI†). Single crystals of the ion pairs  $2b^-$ , $c^-$ -TPA<sup>+</sup> were obtained by the vapour diffusion of *n*-hexane into acetone solutions of the 1:1 mixtures of **2b**,**c** and TPAOH. Alternately stacked anions and TPA<sup>+</sup> provided ion-pairing packing structures, in which TPA<sup>+</sup> was located around the anions with  $O \cdots (H_-)C$  distances of 3.34–3.94 Å between the *p*-quinone methide carbonyl units and TPA<sup>+</sup> methylene groups, suggesting the negative charge localized at the quinone moieties. The C–N bond lengths, for example, of  $2c^-$  (1.36(4) and 1.35(4) Å), were shorter than those of 2c (1.38(2) and 1.38(3) Å), indicating delocalized negative charge to quinone moieties.

In summary, pyrrole-based  $\pi$ -extended quinoidal derivatives, whose electronic states can be controlled by proton migration, such as tautomerism and deprotonation, were synthesized. The quinoidal forms, whose preferences were modulated by pyrrole  $\beta$ -substituents, were stabilized by hydrogen bonding with polar solvents and anions *via* the pyrrole NH. Deprotonated species, exhibiting near-infrared absorption, would be included in diverse fascinating ion-pairing assemblies in combination with  $\pi$ -electronic countercations. Further modification and design of quinone  $\pi$ -electronic molecules exhibiting novel stimuliresponsive electronic properties based on potential open-shell structures are currently under investigation.

This work was supported by JSPS KAKENHI Grant Numbers JP18H01968 for Scientific Research (B) and JP20H05863 for Transformative Research Areas (A) "Condensed Conjugation" and Ritsumeikan Global Innovation Research Organization (R-GIRO) project (2017–2022). Theoretical calculations were partially performed using the Research Center for Computational Science, Okazaki, Japan. We thank Dr Yohei Haketa and Prof. Osamu Tsutsumi, Ritsumeikan University, and Dr Nobuhiro Yasuda, JASRI/SPring-8, for single-crystal X-ray analysis, Prof. Ryo Kitahara and Dr Soichiro Kitazawa, Ritsumeikan University, for <sup>13</sup>C NMR measurements and Prof. Hitoshi Tamiaki, Ritsumeikan University, for various measurements.

#### Conflicts of interest

There are no conflicts to declare.

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