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# Deprotonation reactions of the non-rigid bis-(2,5-diamidopyrrole) induced by anions

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## ABSTRACT

The molecular structures of 4-aminomethyl-phenylamino-bis-(3,4-dichloro-5-phenylcarbamoyl-1*H*-pyrrole-2-carboxamide), $\mathbf{L}H_2$, its deprotonated species and fluoride, chloride and hydroxide complexes were obtained by geometry optimizations using the density functional theory (DFT) calculations. Energetics, thermodynamic properties and equilibrium constants of deprotonation processes of the compound in the presence and absence of fluoride, chloride and hydroxide ions were computed at the B3LYP/6-31G(d) level with zero point vibration energy (ZPVE) corrections. In gas phase, the fluoride and hydroxide ions are able to form complexes with the deprotonated species of the compounds and finally the compounds became the free deprotonated form. However, the chloride ions prefer to form the dichloride complexes without the deprotonation processes of the compound. The B3LYP/6-31G(d)-optimized data of $\mathbf{L}^{2-}$ also shows a strong support for its X-ray crystallographic structure.

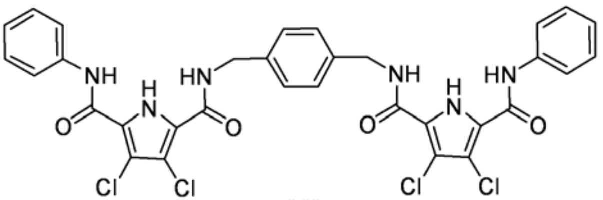
*Keywords:* anion coordination; computational chemistry; 2,5-diamidopyrrole; DFT; deprotonation.

## INTRODUCTION

Pyrrole-containing amide groups which appended to the 2,5-positions of the pyrrole ring have been used as anion receptors (Camiolo *et al.*, 2002). To enhance the anions binding properties of these receptors, the functional groups, quite often are electron withdrawing groups, must be attached into the structure of the compounds. For examples, the nitro group is the one that has been also used as electron withdrawing groups to the amide links. The chlorine moieties were added in 3- and 4-positions of the pyrrole rings increasing the acidity of pyrrole NH groups and therefore allow the receptors to form the stronger hydrogen bonds to the putative anionic guests (Camiolo *et al.*, 2003). Not only the anion binding affinity of these receptors has been improved but also the unusual deprotonation process at the NH-pyrrolic proton was obtained in the presence of fluoride and hydroxide ions (Gale, 2002). However, chloride ion, in this case, prefers to induce the complexation process than acts as the catalyst in the deprotonation reaction (Light *et al.*, 2005;

Light *et al.*, 2005). These processes have been studied using the molecular models calculating with the molecular orbital theory, the density functional theory (DFT) (Navakhun and Ruangpornvisuti, 2006; Navakhun and Ruangpornvisuti, 2007; Navakhun and Ruangpornvisuti, 2008).

In this work, 4-aminomethyl-phenylamino-bis-(3,4-dichloro-5-phenylcarbamoyl-1*H*-pyrrole-2-carboxamide), **L**$H_2$, containing two 3,4-dichloro-2,5-diamido pyrrole subunits and non-rigid linker, 1,4-dimethylphenyl group, has been theoretically investigated using DFT method. The geometrical structures of all species were evaluated in terms of stabilities and thermodynamic properties of all deprotonation reactions with and without anions ($F^-$, $Cl^-$ and $OH^-$) comparing to the X-ray crystallographic data.



$LH_2$

## METHODOLOGY

Geometries of various species of compounds **L**$H_2$**,** its deprotonated species, fluoride, chloride and hydroxide complexes were optimized using density functional theory (DFT) method. DFT calculations have been performed with the Becke's three-parameter exchange functional with the Lee–Yang–Parr correlation functional (B3LYP). All geometry optimizations have been carried out using the MO computations at the B3LYP/6-31G(d) level. All calculations were performed with the GAUSSIAN03 program. The molecular graphics of all related species were generated with the GAUSSVIEW 3.07 program.

The standard enthalpy $\Delta H_{298}$ and Gibbs free energy changes $\Delta G_{298}$ of all deprotonation of **L**$H_2$ systems have been derived from the frequency calculations at the B3LYP/6-31G(d) level of theory. Deprotonation constant, $K$ at 298.15 K and 1 atm for all reactions is evaluated using a thermodynamic equation $\Delta G^O = - RT \ln K$.

Stepwise deprotonation reactions (equations (1) and (2)) of the system in the absence and presence of each anion, $X^-$ (fluoride, chloride and hydroxide ions) and complexation reactions (equation (3)) are described by the following equations.

Stepwise deprotonation reactions :

System without $X^-$:

$$LH_2 \rightleftharpoons LH^- + H^+ \rightleftharpoons L^{2-} + 2H^+ \qquad (1)$$

System with $X^-$ :

$$LH_2 + 2X^- \rightleftharpoons [LH_2.X]^- + X^- \rightleftharpoons LH^- + HX + X^-$$
$$\rightleftharpoons [LH.X]^{2-} + HX \rightleftharpoons L^{2-} + 2HX \qquad (2)$$

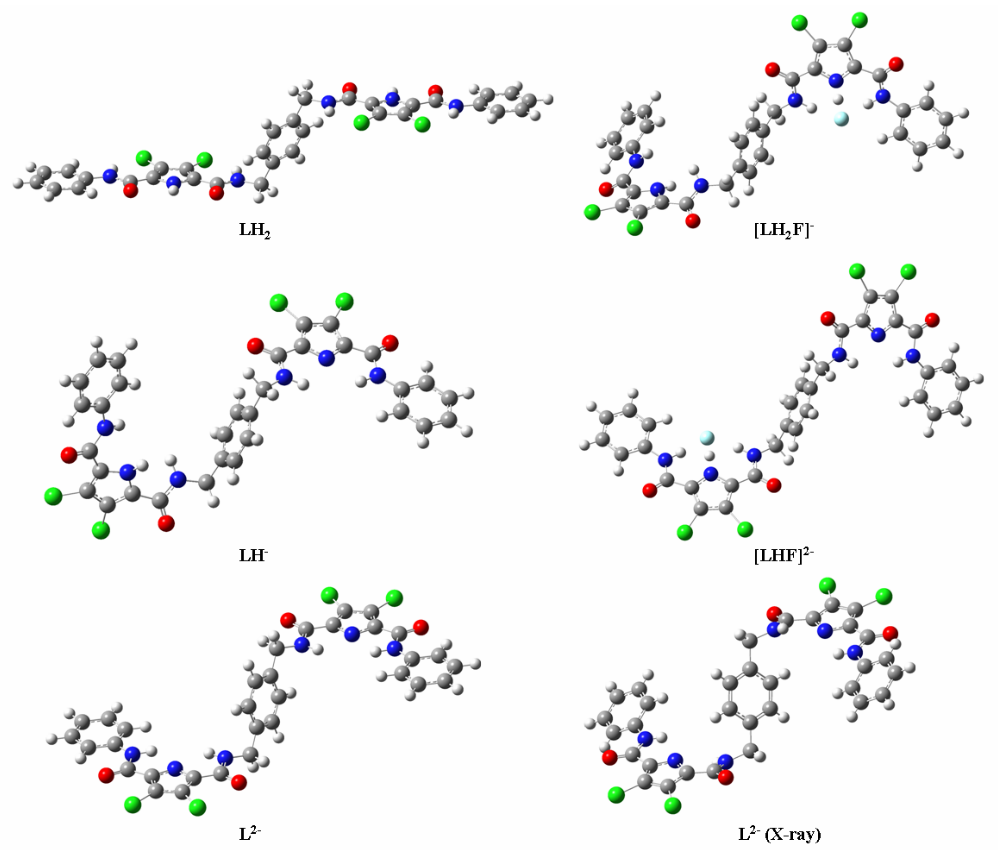
Complexation reactions :

$$LH_2 + 2X^- \rightleftharpoons [LH_2.X]^- + X^- \rightleftharpoons [LH_2.2X]^{2-} \qquad (3)$$

## RESULTS AND DISCUSSION

### 1. Geometrical structure and energetic stability

The B3LYP/6-31G(d)-optimized structures calculated in gas phase of deprotonated species, neutral form and the various fluoride, chloride and hydroxide complexes of the compound are shown in Figure 1 and 2. The B3LYP/6-31G(d)-optimized geometrical data for the deprotonated forms of **L**$^{2-}$ is in good agreement with its corresponding X-ray crystallographic data. The B3LYP/6-31G(d)-optimized energy of the specie **L**$^{2-}$ (E = –3703.02607664 au) are more stable than its corresponding X-ray crystallographic structure (E = –3702.65389093 au) by 233.55 kcal mol$^{-1}$. Both of the B3LYP/6-31G(d)-optimized and X-ray geometries of the species **L**$^{2-}$ are not the planar structures which usually occurs in the rigid structures as the previous results. Two pyrrole rings are in the difference planes linked by dimethyl-phenyl group. However, they are almost parallel and the deprotonated compound is similar Z like structure. The distances between two pyrrole rings are 4.20 and 4.12 Å for the B3LYP/6-31G(d)-optimized and X-ray structures respectively.



**LH$_2$**

**[LH$_2$F]$^-$**

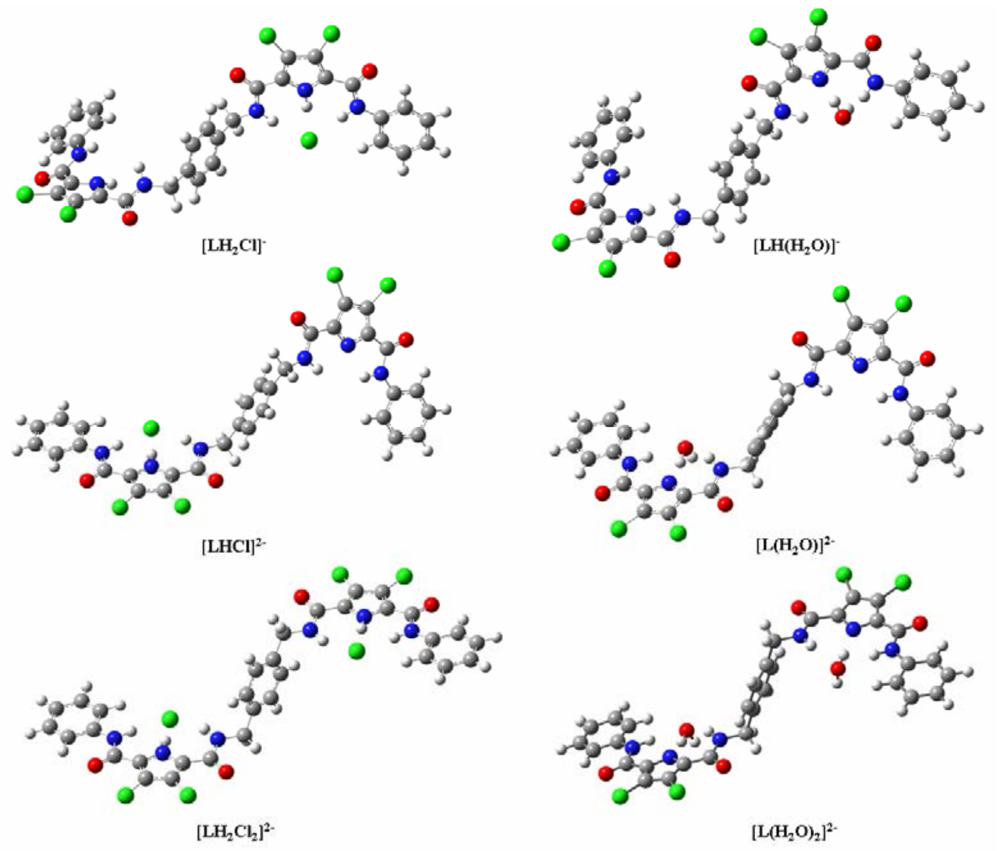
**LH$^-$**

**[LHF]$^{2-}$**

**L$^{2-}$**

**L$^{2-}$ (X-ray)**

**Figure 1** The B3LYP/6-31G(d)-optimized structures of the various species of **L**H$_2$ and their fluoride complexes



$[LH_2Cl]^-$ $[LH(H_2O)]^-$

$[LHCl]^{2-}$ $[L(H_2O)]^{2-}$

$[LH_2Cl_2]^{2-}$ $[L(H_2O)_2]^{2-}$

**Figure 2** The B3LYP/6-31G(d)-optimized structures of the chloride and hydroxide complexes of $\mathbf{L}H_2$

## 2. Reaction energies and thermodynamic quantities

The overall deprotonation processes via complexation pathway of the fluoride, chloride and hydroxide complexes (equations (2) and (3)) of the compound are more preferable than the system of the absence of an anion (equation (1)). Relative energies of all related species based on mass balance of $\mathbf{L}H_2$+2$X^-$ ($X^-$ = $F^-$, $Cl^-$ and $OH^-$) computed at the B3LYP/6-31G(d) with ZPVE correction levels are listed in Table 1.

Relative energy profiles of the compound computed at the B3LYP/6-31G(d) with ZPVE correction for deprotonation processes without an anion and in the presence of the fluoride ion are shown in Figure 3. Figure 4 shows other relative energy profiles with the chloride and hydroxide ions. Reaction energies and thermodynamic quantities of the deprotonated species of the compounds $\mathbf{L}H_2$ computed at the B3LYP/6-31G(d) level are shown in Table 1. The relative stabilities of all the species of the compound are in decreasing order: $\mathbf{L}H_2 > \mathbf{L}H^- > \mathbf{L}^{2-}$. In the absence of an anion, the relative energies of the mono and deprotonated species are 335.52 and 672.77 kcal mol$^{-1}$, respectively. The result suggests that the deprotonated species do not exist in the system without an anion.

**Table 1** Reaction energies and thermodynamic quantities of deprotonated species of **L**$H_2$ and its equilibrium constants, computed at the B3LYP/6-31G(d) level of theory

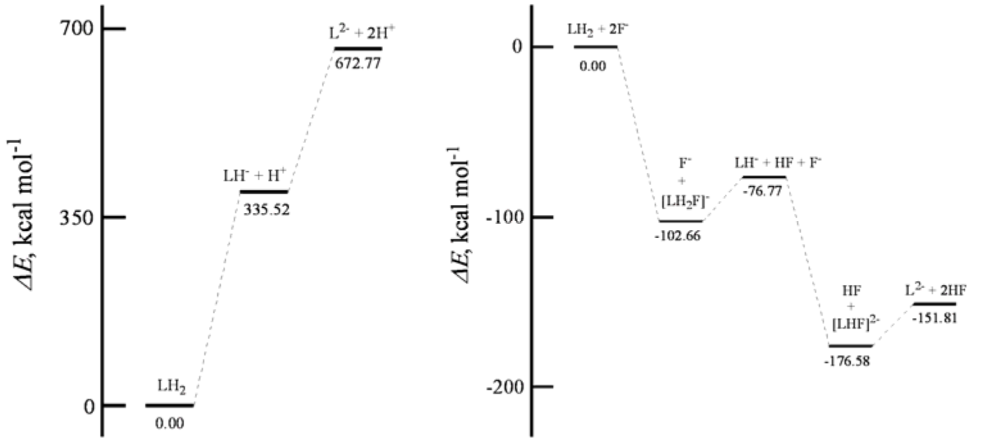
| System/reaction | $\Delta E_0$ [a] | $\Delta H_{298}$ [a] | $\Delta G_{298}$ [a] | $K_{298}$ |
|---|---|---|---|---|
| $LH_2 \rightarrow LH^- + H^+$ | 335.52 | 335.68 | 334.14 | [b] |
| $LH^- \rightarrow L^{2-} + H^+$ | 337.25 | 337.02 | 337.95 | [b] |
| $LH_2 + F^- \rightarrow [LH_2.F]^-$ | -102.66 | -103.20 | -95.42 | $1.57 \times 10^{70}$ |
| $[LH_2.F]^- \rightarrow LH^- + HF$ | 25.89 | 27.19 | 15.84 | $2.22 \times 10^{-12}$ |
| $LH^- + F^- \rightarrow [LH.F]^{2-}$ | -99.81 | -100.69 | -90.89 | $7.38 \times 10^{66}$ |
| $[LH.F]^{2-} \rightarrow L^{2-} + HF$ | 24.77 | 26.02 | 15.12 | $7.51 \times 10^{-12}$ |
| $LH_2 + Cl^- \rightarrow [LH_2.Cl]^-$ | -32.65 | -32.10 | -26.06 | $1.50 \times 10^{19}$ |
| $[LH_2.Cl]^- \rightarrow LH^- + HCl$ | 31.33 | 31.53 | 21.57 | $1.37 \times 10^{-16}$ |
| $LH^- + Cl^- \rightarrow [LH.Cl]^{2-}$ | -29.66 | -29.51 | -21.39 | $5.42 \times 10^{15}$ |
| $[LH.Cl]^{2-} \rightarrow L^{2-} + HCl$ | 30.07 | 30.29 | 20.69 | $5.98 \times 10^{-16}$ |
| $[LH_2.Cl]^- + Cl^- \rightarrow [LH_2.Cl_2]^-$ | -22.32 | -23.94 | -9.18 | $5.69 \times 10^{6}$ |
| $LH_2 + OH^- \rightarrow [LH(H_2O)]^-$ | -99.96 | -99.71 | -92.14 | $6.05 \times 10^{67}$ |
| $[LH(H_2O)]^- \rightarrow LH^- + H_2O$ | 12.04 | 11.25 | 1.97 | $3.53 \times 10^{-2}$ |
| $LH^- + OH^- \rightarrow [L(H_2O)]^{2-}$ | -97.33 | -97.41 | -88.06 | $6.06 \times 10^{64}$ |
| $[L(H_2O)]^{2-} \rightarrow L^{2-} + H_2O$ | 11.15 | 11.29 | 1.70 | $5.59 \times 10^{-2}$ |
| $[LH(H_2O)]^- + OH^- \rightarrow [L(H_2O)_2]^{2-}$ | -96.90 | -96.97 | -88.05 | $5.94 \times 10^{64}$ |
| *Overall reactions:* | | | | |
| $LH_2 \rightarrow L^{2-} + 2H^+$ | 672.77 | 672.71 | 672.08 | [b] |
| $LH_2 + 2F^- \rightarrow L^{2-} + 2HF$ | -151.81 | -150.69 | -155.35 | [c] |
| $LH_2 + 2Cl^- \rightarrow L^{2-} + 2HCl$ | -0.90 | 0.22 | -5.19 | $6.62 \times 10^{3}$ |
| $LH_2 + 2Cl^- \rightarrow [LH_2.Cl_2]^-$ | -54.98 | -56.03 | -35.25 | $8.52 \times 10^{25}$ |
| $LH_2 + 2OH^- \rightarrow L^{2-} + 2H_2O$ | -174.11 | -173.58 | -176.52 | [c] |
| $LH_2 + 2OH^- \rightarrow [L(H_2O)_2]^{2-}$ | -196.86 | -196.69 | -180.18 | [c] |

[a] In kcal $mol^{-1}$.

[b] Very small values.

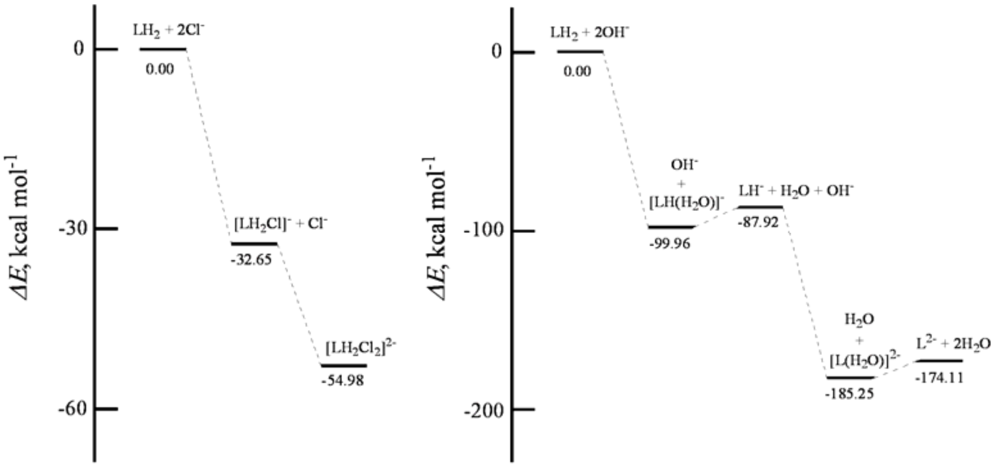
[c] Very large values.

All complexation reactions of the fluoride complexes with the compound **L**$H_2$ are the spontaneous process and the overall reactions energy in the fluoride system is lower than initial of the reaction by 151.81 kcal $mol^{-1}$. In the presence chloride ions, $[LH_2.Cl]^-$ and $[LH_2.Cl_2]^-$ complexes are the dominant species comparing with the deprotonation process. The $[LH_2.Cl_2]^-$ complex is more stable than the $[LH_2.Cl]^-$ complex by 22.33 kcal $mol^{-1}$. However, the deprotonation process in the chloride system is less preferable process than the complexation process with overall reactions energies by -0.90 and -54.98 kcal $mol^{-1}$, respectively. On the other hand, with hydroxide ions, the compound forms the aqua-complexes as $[LH(H_2O)]^-$ and $[L(H_2O)_2]^{2-}$ complexes. The results show the deprotonated protons form the regular water molecules with hydroxide ions and these water molecules have had the hydrogen bonding interactions via $N^{-}_{pyrrole} \cdots H_{water}$ to stabilize these aqua-complexes. The aqua-complexes formation process is more preferable than the normal deprotonation process by 22.75 kcal mol$^{-1}$.



**(a)** **(b)**

**Figure 3** Relative energy profiles for deprotonation processes of (a) the absence of anion and (b) the presence of fluoride ion for $LH_2$ computed at the B3LYP/6-31G(d) with ZPVE correction levels.



**(a)** **(b)**

**Figure 4** Relative energy profiles for deprotonation processes of the presence of (a) chloride ion and (b) hydroxride ion for **L**$H_2$ computed at the B3LYP/6-31G(d) with ZPVE corrections

## CONCLUSION

The geometry optimization of the 4-aminomethyl-phenylamino-bis-(3,4-dichloro-5-phenylcarbamoyl-1*H*-pyrrole-2-carboxamide), $\mathbf{L}H_2$, its deprotonated species and fluoride, chloride and hydroxide complexes were carried out at the B3LYP/6-31G(d) level of theory. The B3LYP/6-31G(d)-optimized geometries of deprotonated species of the compound ($\mathbf{L}^{2-}$) show good agreement with the X-ray crystallographic structures. Based on the B3LYP/6-31G(d)-optimized energy with ZPVE correction, $\mathbf{L}^{2-}$ is more stable than the corresponding X-ray crystallographic structures and the deprotonated compound is similar Z like structure. In the absence of an anion, the relative stabilities of all the species of the compound are in decreasing order: $\mathbf{L}H_2 > \mathbf{L}H^- > \mathbf{L}^{2-}$. The deprotonation process occurs in the presence of the fluoride ions, but the complexation reactions prefer in the system with chloride ions. The hydroxide ions can form the aqua-complexes with the compound and stabilize the complexes with $N^-_{pyrrole}\cdots H_{water}$ hydrogen bonds.

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## REFERENCES

Camiolo, S., Gale, P. A., Hursthouse, M. B., Light, M. E. and Shi, A. J. (2002). Solution and solid-state studies of 3,4-dichloro-2,5-diamidopyrroles: formation of an unusual anionic narcissistic dimer. *Chem. Commun.*, 758-759.

Camiolo, S., Gale, P. A., Hursthouse, M. B. and Light, M. E. (2003). Nitrophenyl derivatives of pyrrole 2,5-diamides: structural behaviour, anion binding and colour change signalled deprotonation. *Org. Biomol. Chem. 1*, 741-744.

Gale, P. A., Navakhun, K., Camiolo, S., Light, M. E. and Hursthouse, M. B. (2002). Anion-anion assembly: a new class of anionic supramolecular polymer containing 3,4-dichloro-2,5-diamido-substituted pyrrole anion dimers. *J. Am. Chem. Soc.*, *124*, 11228-11229.

Light, M. E., Gale, P. A., and Navakhun, K. (2005). 1,4-Phenylene-bis-(3,4-dichloro-5-phenylcarbamoyl-1*H*-pyrrole-2-carboxamide) bis(tetrabutylammonium chloride) acetonitrile disolvate. *Acta Cryst.*, *E61*, o1300-o1301.

Light, M. E., Gale, P. A., Navakhun, K. and Maynard-Smith, M. (2005). 4-Aminomethyl-phenylamino-bis-(3,4-dichloro-5-phenylcarbamoyl-1*H*-pyrrole-2-carboxamide) tetrabutylammonium salt. *Acta Cryst.*, *E61*, o1302-o1303.

Navakhun, K. and Ruangpornvisuti, V. (2006). Molecular structures of 3,4-dichloro-2,5-diamido-substituted pyrrole anion dimers, their deprotonation reactions in systems with and without fluoride ion. *J. Mol. Struct.(Theochem)*, *772,* 23-30.

Navakhun, K. and Ruangpornvisuti, V. (2007). A DFT study of chloride and hydroxide anions effects on deprotonations of 3,4-dichloro-2,5-diamido-substituted pyrrole derivatives. *J. Mol. Struct.(Theochem)*, *806,* 145-153.

Navakhun, K. and Ruangpornvisuti, V. (2008). Anion binding of 3,4-dichloro-2,5-diamidopyrrole and anionic self-assembly dimerization of its deprotonated species. *J. Mol. Struct.(Theochem)*, *864*, 26-30.