

## Dimerization of aromatic ureido pyrimidinedione derivatives: Observation of an unexpected tautomer in the solid state

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### ELECTRONIC SUPPLEMENTARY INFORMATION

#### 1. SYNTHESIS

**1-(5,5-diallyl-4,6-dioxo-1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl-urea (2).** NaH (80 mg, 2.0 mmol, 60% in mineral oil) was taken in 10 ml dry DMF. To this solution 1.0 equiv. of 5,5-diallyl-2-amino-1H-pyrimidine-4,6-dione (414 mg, 2.0 mmol) was slowly added. The reaction mixture was heated at 70°C for 2 hours to form the sodium salt. A solution of CH<sub>2</sub>Cl<sub>2</sub> containing phenyl isocyanate (0.36 mL, 2.0 mmol) was added drop-wise to the above DMF solution and refluxed at 70°C for 12 hours. The reaction mixture was quenched with acetic acid (0.11 mL, 2.0 mmol), the solvents were removed under vacuum; the residue was dissolved in CHCl<sub>3</sub>, washed with brine solution and water, and the organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to give the crude product, which was further purified by column chromatography (SiO<sub>2</sub>, 9:1 CHCl<sub>3</sub>/Hexane) to give a white solid product Phenyl-DDAA (~80mg, 12%). Upon recrystallization from CHCl<sub>3</sub>, white crystals were obtained (48 mg, 8%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ, ppm. = 12.61 (s, 1H, NH), 11.27 (s, 1H, NH), 10.44 (s, 1H, NH), 7.61-7.59 (d, 2H, CH-benzene), 7.33-7.28 (t, 2H, CH-benzene), 7.19 (s, CHCl<sub>3</sub>), 7.11-7.07 (t, 1H, CH-benzene), 5.66-5.57 (m, 2H, -CH<sub>2</sub>CHCH<sub>2</sub>), 5.56-5.05 (t, 4H, -CH<sub>2</sub>CHCH<sub>2</sub>), 2.73-2.67 (d, 4H, -CH<sub>2</sub>CHCH<sub>2</sub>), \*2.10 (Acetone), \*1.48 (water). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ, ppm. = 180.17, 170.94, 156.21, 155.68, 137.73, 130.74, 129.20, 124.80, 121.19, 120.33, 77.48/77.16/76.84 (CHCl<sub>3</sub>), 58.70, 42.92. MS (FAB): 326 (M+H)<sup>+</sup>.

**1-(5,5-diallyl-4,6-dioxo-1,4,5,6-tetrahydro-pyrimidin-2-yl)-1-naphthyl-urea (3).** Compound **3** was prepared using the same procedure described for compound **2** by reacting 1-naphthyl isocyanate (0.67 mL, 4.0 mmol) with 5,5-diallyl-2-amino-1H-pyrimidine-4,6-dione (828 mg, 4mmol) Na-salt. Yield. 8.3%.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm. = 12.57 (s, 1H, NH), 11.21 (s, 1H, NH), 10.49 (s, 1H, NH), 7.90-7.7.85 (m, 2H, CH-Np), 7.76-7.74 (m, 1H, CH-Np), 7.64-7.62 (m, 1H, CH-Np), 7.49-7.44 (m, 3H, CH-Np), 5.64-5.59 (m, 2H, -CH<sub>2</sub>CHCH<sub>2</sub>), 5.12-5.07 (t, 4H, -CH<sub>2</sub>CHCH<sub>2</sub>), 2.64-2.60 (d, 4H, -CH<sub>2</sub>CHCH<sub>2</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ ppm. = 180.79, 171.35, 157.11, 154.74, 134.69, 132.01, 129.20, 128.91, 127.57, 125.88, 123.59, 121.33, 58.95, 43.11. MS (FAB): 377 (M+H)<sup>+</sup>.

**1-(5,5-diallyl-4,6-dioxo-1,4,5,6-tetrahydro-pyrimidin-2-yl)-2-naphthyl-urea (4).** Compound **4** was prepared using the same procedure employed for compound **2** by reacting 2-naphthyl isocyanate (0.67 mL, 4.0 mmol) with 5,5-diallyl-2-amino-1H-pyrimidine-4,6-dione (828mg, 4mmol) Na-salt. Yield 11% (165 mg)

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm. = 12.64 (s, 1H, NH), 11.26 (s, 1H, NH), 10.29 (s, 1H, NH), 8.19 (s, 1H, CH-Np), 7.86-7.79 (m, 2H, CH-Np), 7.84-7.82 (m, 1H, CH-Np), 7.85-7.70 (m, 3H, CH-Np), 7.61-7.59 (t, 1H, CH-Np), 7.46-7.33(m, 2H, CH-Np), 5.66-5.59 (m, 2H,  $-\text{CH}_2\text{CHCH}_2$ ), 5.15-5.07 (t, 4H,  $-\text{CH}_2\text{CHCH}_2$ ), 2.75-2.72(d, 4H,  $-\text{CH}_2\text{CHCH}_2$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  ppm. = 184.00, 170.77, 158.33, 155.36, 133.97, 130.93, 130.72, 130.26, 128.99, 127.95, 127.74, 126.72, 125.38, 121.26, 121.04, 120.04, 117.12 58.68, 42.88ppm. MS (FAB): 377 (M+H) $^+$ .

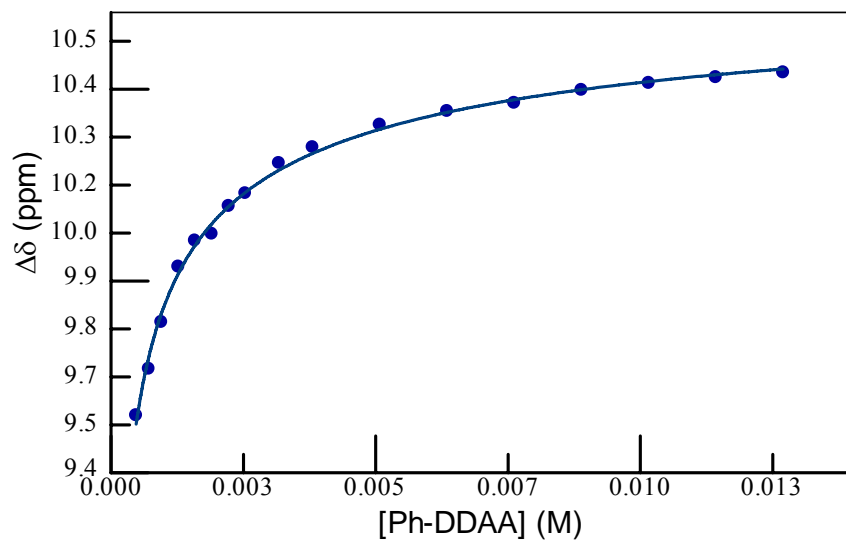
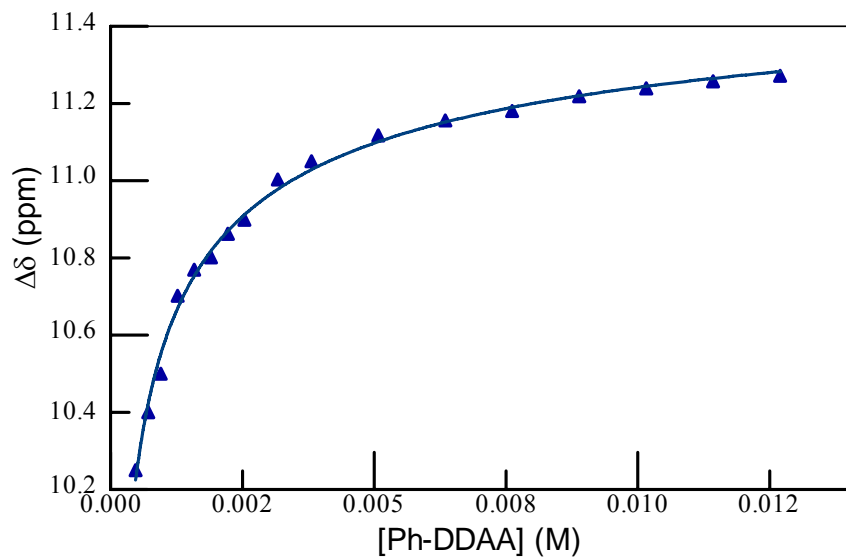
## 2. EXPERIMENTAL DETAILS ON X-RAY WORK

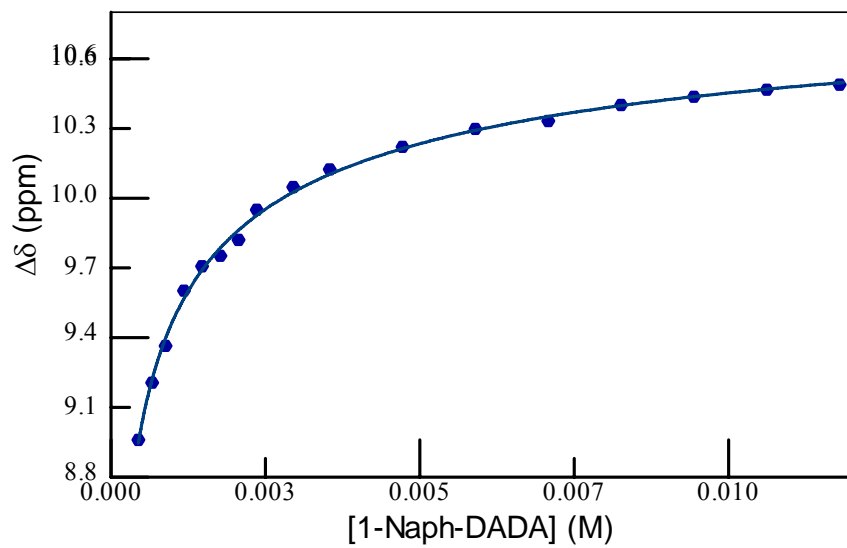
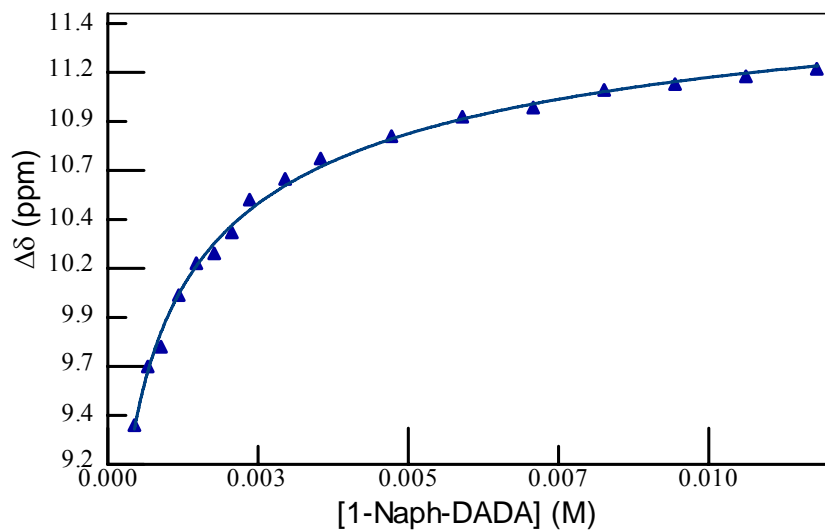
Crystals of **2** - **4** were mounted in a Cryoloop<sup>TM</sup> with a drop of Paratone oil and placed in the cold nitrogen stream of the Kryoflex<sup>TM</sup> attachment of the Bruker APEX CCD diffractometer. A full sphere of data was collected using either a combination of three sets of 400 scans in  $\omega$  ( $0.5^\circ$  per scan) at  $\varphi = 0, 90$  and  $180^\circ$  plus two sets of 800 scans in  $\varphi$  ( $0.45^\circ$  per scan) at  $\omega = -30$  and  $210^\circ$  (for **2** and **3**) using the SMART software package<sup>1</sup> or 606 scans in  $\omega$  ( $0.3^\circ$  per scan) at  $\varphi = 0, 120$  and  $240^\circ$  (for **4**) using the APEX2 software suite.<sup>2</sup> The raw data were reduced to  $F^2$  values using the SAINT+ software<sup>3</sup> and a global refinements of unit cell parameters employing 7690 - 9940 reflections chosen from the full data sets were performed. Multiple measurements of equivalent reflections provided the basis for empirical absorption corrections as well as a correction for any crystal deterioration during the data collection (SADABS<sup>4</sup>). The structures were solved by direct methods and refined by full-matrix least-squares procedures using either the SHELXTL (for **2** and **3**)<sup>5</sup> or APEX2 (for **4**)<sup>1</sup> program packages. Hydrogen atoms attached to carbon were placed in calculated positions and included as riding contributions with isotropic displacement parameters tied to those of the attached non-hydrogen atoms while those attached to nitrogen were refined with isotropic displacement parameters.

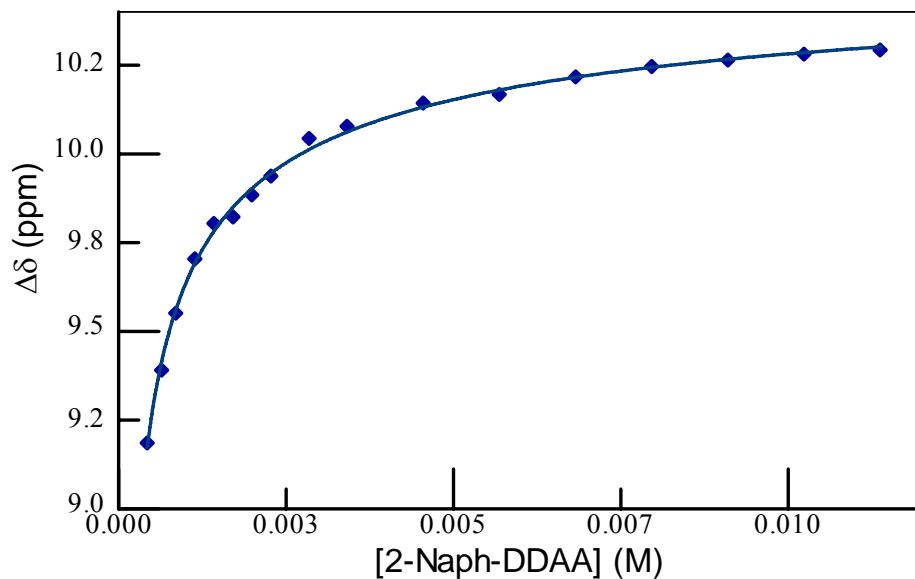
### References:

1. Bruker-AXS, SMART, Version 5.625, Madison, WI (2000).
2. Bruker-AXS, APEX2, Version 2.1-0, Madison, WI (2006).
3. Bruker-AXS, SAINT+, Version 6.35A (for **2** and **3**), Madison, WI (2002) or Version 7.34A (for **4**), Madison, WI (2006).
4. Sheldrick, G. M., SADABS, Version 2.05 (for **2** and **3**). University of Göttingen, Germany (2002) or Version 2007/2 (for **4**) University of Göttingen, Germany (2007).
5. a. Bruker-AXS, SHELXTL, Version 6.10, Madison, WI (2000). b. Sheldrick, G.M., SHELXS97 and SHELXL97. University of Göttingen, Germany (1997).

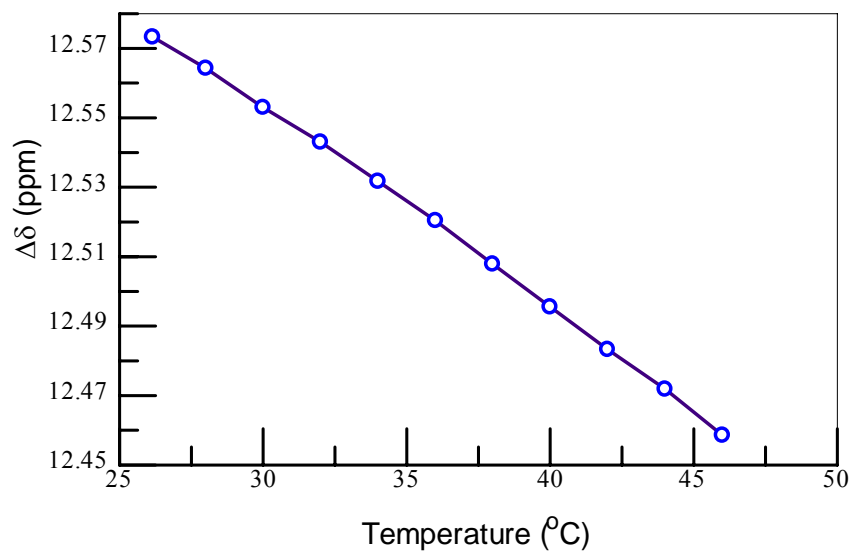
### 3. PLOTS OF NH PROTON CHEMICAL SHIFTS AS A FUNCTION OF CONCENTRATION

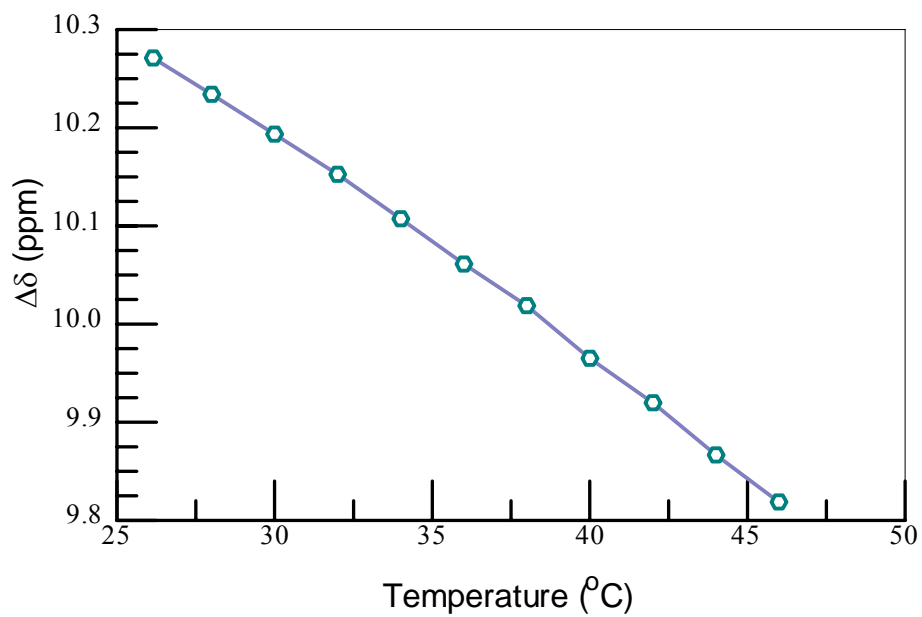
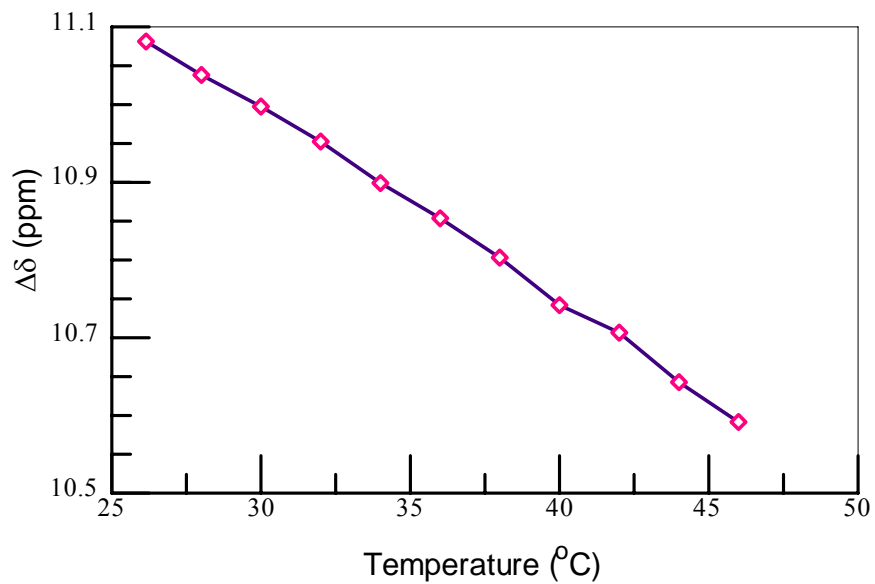




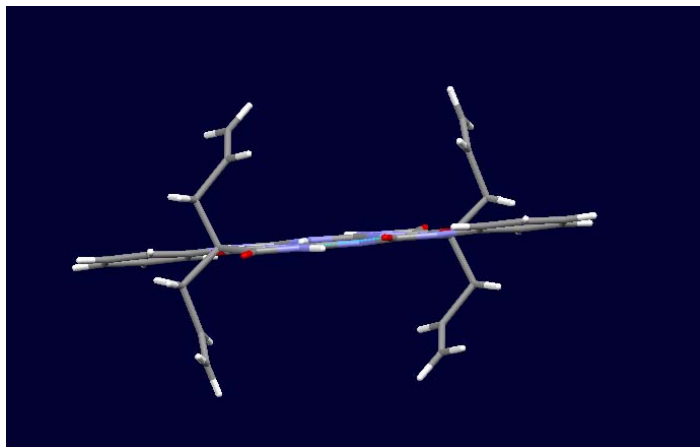


4. PLOTS OF NH PROTON CHEMICAL SHIFTS AS A FUNCTION OF TEMPERATURE FOR COMPOUND **2**.

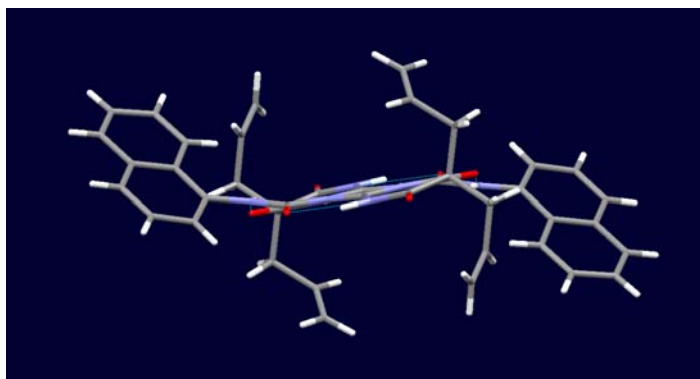




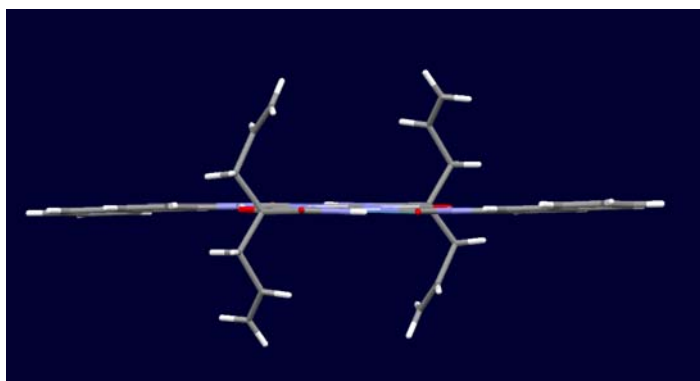
## 5. SIDE VIEWS OF THE DIMERS ( $2_2$ - $4_2$ ) IN THE SOLID STATE



DDAA  $2_2$  dimer.



DADA  $3_2$  dimer



DDAA  $4_2$  dimer.