Supplementary Information

for

Self-assembly of 3,5-Bis(ethoxycarbonyl)pyrazolate Anions and Ammonium Cations of β-Phenylethylamine and Homoveratrylamine into Hetero-Double-stranded Helical Structures

by

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1. Experimental Section

The starting materials were purchased from commercial sources and used without further purifications. Pyrazole-3,5-dicarboxylic acid (Aldrich), and sodium hydroxide (Merck). Phenethylamine and homoveratrylamine hydrochlorides were purchased from Sigma-Aldrich.

The solvents were dried using standard techniques. Melting points were determined in a Reichert–Jung hot-stage microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova-300 spectrometer. The chemical shifts are reported in parts per million (ppm) from tetramethylsilane but were measured against the solvent signals. FAB mass spectra were obtained on a VG AutoSpec spectrometer using a *m*-nitrobenzyl alcohol (NBA) matrix. IR spectra were recorded with a Perkin-Elmer 681 S2 spectrometer. Elemental analyses were provided by the *Departamento de Análisis, Centro de Química Orgánica "Manuel Lora Tamayo", CSIC, Madrid, Spain*.

Diethyl* 1*H*-*pyrazole-3,5-dicarboxylate [L]. The titled compound was obtained from pyrazole-3,5-dicarboxylic acid as previously described.[1] Yield 80%. Mp 54-55 ^{o}C (*n*-hexane) (lit.,[1] m.p. 53-54 ^{o}C). Found: C, 50.80; H, 5.51; N, 13.34 %. Calcd for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20 %. ν_{max}(KBr)/cm^{-1} 3260 (NH) and 1730 (CO). δ_H(300 MHz; DMSO-d_6; Me_4Si) 14.62 (1 H, s, NH), 7.18 (1 H, s, 4-H), 4.31 (4H, c, 7-H), 1.31 (6H, t, 8-H). δ_C(75 MHz; DMSO-d_6; Me_4Si) 160.89 (C-6, br s), 158.98 (C-6´, br s), 143.56 (C-3, vbr s), 134.74 (C-5, vbr s), 110.83 (C-4), 60.87 (C-7), 14.10 (C-8). m/z (FAB-MS) 213 (MH^+, 100 %), 425 ($2MH^+$, 19).

Sodium 3,5-bis(ethoxycarbonyl)pyrazolate 1[H$_{-1}$L]Na. To a solution of diethyl 1*H*-pyrazole-3,5-dicarboxylate (50 mg, 0.23 mmol) in anhydrous ethanol (30 mL) vigorously stirred at 25 ^{o}C, sodium hydroxide (9 mg, 0.23 mmol) dissolved in anhydrous ethanol (10 mL) was slowly added. When the addition was complete the reaction was allowed to proceed for 1h, and then the organic solvent was partially evaporated. A solid was formed which, after it was filtered off and dried *in vacuo* gave compound **1** as a crystalline solid

(54 mg, 97%). Mp 213-214 °C (lit.,[2] m.p. 212-214 °C). Found; C, 46.03; H, 4.68; N, 12.10 %. Calcd for $C_9H_{11}N_2O_4Na$: C, 46.15; H, 4.70; N, 11.96 %. ν_{max}(KBr)/cm^{-1} 1670 (CO). δ_H(300 MHz; DMSO-d_6; Me_4Si) 6.69 (1H, s, 4-H), 4.16 (4H, c, 7-H), 1.25 (6H, t, 8-H). δ_C (75 MHz; DMSO-d_6; Me_4Si) 163.64 (C-6,6´), 142.39 (C-3,5), 111.15 (C-4), 58.48 (C-7), 14.45 (C-8). m/z (FAB-MS) 491 [$(2M + Na)^+$, 22 %], 257 [$(M + Na)^+$, 100], 235 (MH^+, 13).

Preparation of Solid Binuclear Ammonium Pyrazolate complexes 2 and 3.

A solution of sodium salt **1** (200 mg, 0.85 mmol) in chloroform (10 mL) was heated at 30 °C until a clear solution was obtained. Then, it was slowly cooled to room temperature and a solution of the corresponding ammonium chloride (0.85 mmol) in chloroform (5 mL) was added dropwise under stirring. The reaction mixture was allowed to proceed for 24 h. The small amount of the resulting insoluble salt was filtered off and the clear solution evaporated *in vacuum* to afford the corresponding ammonium pyrazolate complex as a pure solid in almost quantitative yield.

Phenethylamine complex 2 $[H_{-1}L]_2(R^1\text{-}NH_3)_2$. Reaction of sodium salt **1** (200 mg, 0.85 mmol) with phenethylamine hydrochloride (0.85 mmol) gave **2** (95%). Mp 108-110 °C (EtOH) as a white solid. Found: C, 61.12; H, 6.88; N, 12.45 %. Calcd for $C_{34}H_{46}N_6O_8$: C, 61.25; H, 6.95; N, 12.60 %. ν_{max}(KBr)/cm^{-1} 2758, 2656, 2555, 2489, 2131 (NH_3^+) and 1720 (CO), 1704 (CO). δ_H(300 MHz; DMSO-d_6; Me_4Si) 7.30-7.15 (10H, m, H_{Arom}), 7.12 (2H, s, 4-H), 4.25 (8H, c, *J* 6.7, 7-H), 2.83 (4H, t, *J* 6.6, α-H), 2.70 (4H, t, *J* 6.6, β-H), 1.27 (12H, t, *J* 6.7, 8-H). δ_C(75 MHz; DMSO-d_6; Me_4Si) 161.13 (C-6,6´), 140.40 (C-3,5), 139.25 (C-1´), 128.66 (C-3´), 128.39 (C-2´), 126.17 (C-4´), 110.92 (C-4), 60.10 (C-7), 42.15 (C-α), 37.01 (C-β), 14.23 (C-8). m/z (FAB-MS) 546 [$(M+1)^+$ - $C_8H_{11}N$, 2 %], 425 [$(2L+1)^+$, 22], 334 [$(M/2 +1)^+$, 13], 289 [$(M/2)^+ - 2C_2H_5)^+$, 6], 275 [$(M/2)^+ - 2C_2H_6O)^+$, 4], 213 [$(L+1)^+$, 100], 122 [$(C_8H_{11}N)^+$, 40].

After this compound was redissolved in ethanol and the solution slowly allowed evaporating we obtained crystals valid for X-ray diffraction.

Homoveratrylamine complex 3 $[H_{-1}L]_2(R^2\text{-}NH_3)_2$. Reaction of sodium salt **1** (200 mg, 0.85 mmol) with homoveratrylamine hydrochloride (0.85 mmol) gave **3** (95%). Mp 115-117 °C (EtOH) as a white solid. Found: C, 57.74; H, 6.76; N, 10.46 %. Calc. for $C_{38}H_{54}N_6O_{12}$: C, 58.00; H, 6.92; N, 10.68 %. ν_{max}(KBr)/cm^{-1} 2835, 2758, 2674, 2591, 2495, 2149 (NH_3^+) and

1719, 1705 (CO). δ_H(300 MHz; DMSO-d_6; Me_4Si) 7.11 (2H, s, 4-H), 6.90-6.60 (6H, m, H_{Arom}), 4.25 (8H, c, *J* 7.1, 7-H), 4.12 (6H, brs, NH_3^+), 3.71 (6H, s, MeO), 3.69 (6H, s, MeO), 2.79 (4H, t, *J* 7.0, α-H), 2.60 (4H, t, *J* 7.0, β-H), 1.27 (12H, t, *J* 7.0, 8-H) ppm. δ_C(75 MHz; DMSO-d_6; Me_4Si) 160.77 (C-6,6´), 148.62 (C-3´), 147.14 (C-4´), 140.07 (C-3,5), 132.12 (C-1´), 120.43 (C-6´), 112.51 (C-5´), 111.86 (C-2´), 110.95 (C-4), 60.27 (C-7), 55.50 (MeO), 55.36 (MeO), 42.94 (C-α), 37.80 (C-β), 14.21 (C-8). m/z (FAB-MS) 606 [$(M+1)^+$ - $C_{10}H_{15}NO_2$, 1.5 %], 425 [$(2L+1)^+$, 21], 394 [$(M/2 + 1)^+$, 6], 366 [$(M/2)^+ – C_2H_5)^+$, 1], 335 [$(M/2)^+ – 2C_2H_5)^+$, 1], 213 [$(L+1)^+$, 79], 182 [$(C_{10}H_{15}NO_2)^+$, 100].

After this compound was re-dissolved in ethanol and the solution slowly allowed evaporating we obtained crystals valid for X-ray diffraction.

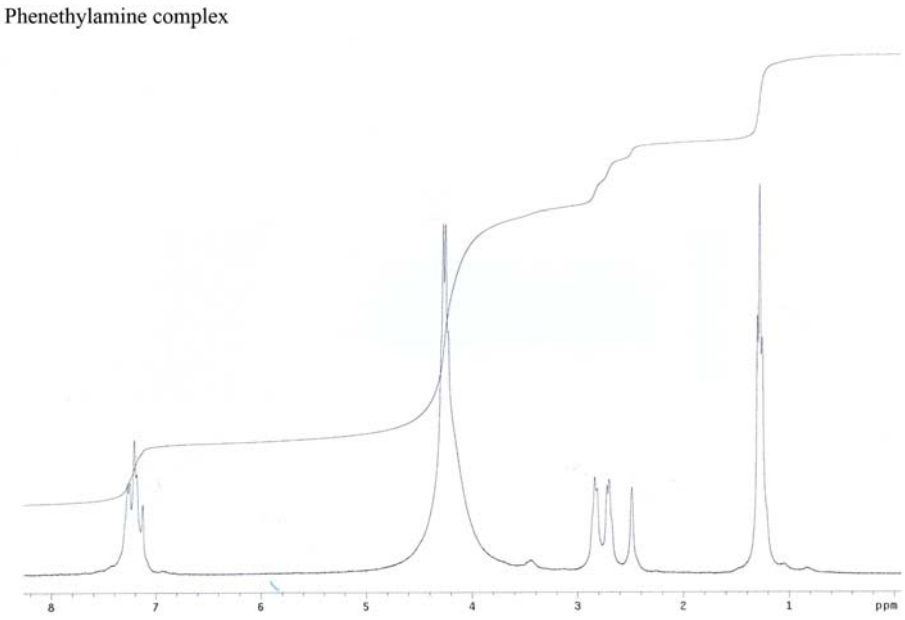
References

1. L. Iturrino, P. Navarro, M. I. Rodríguez-Franco, M. Contreras, J. A. Escario, A. Martínez and M. R. Pardo, *Eur. J. Med. Chem*. 1987, **22**, 445-451.

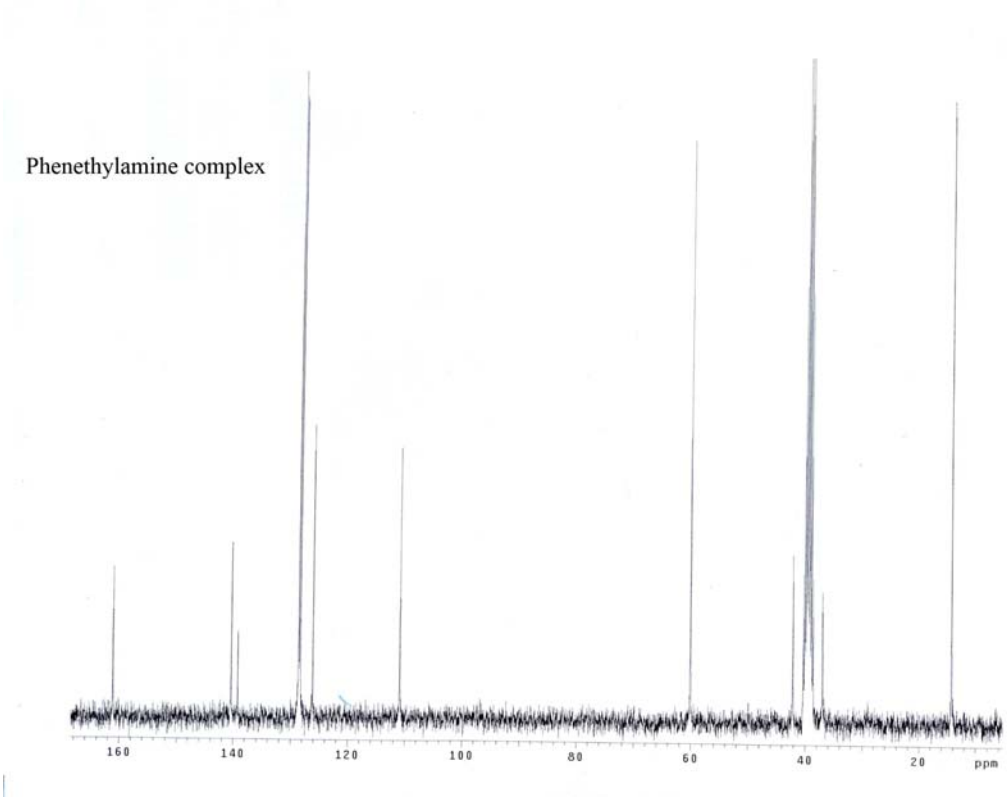
2. F. Reviriego, M. I. Rodríguez-Franco, P. Navarro, E. García-España, M. Liu-González, B. Verdejo and A. Domènech, *J. Am. Chem. Soc.* 2006, **128**, 16458.

2. NMR Spectra

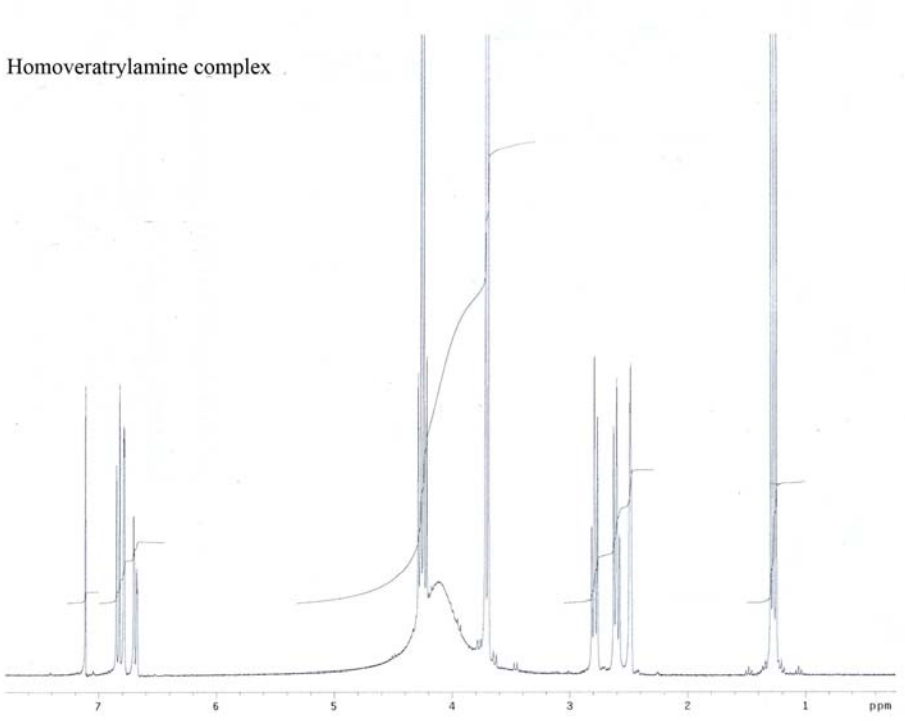
a) ^{1}H NMR [300 MHz, DMSO-d_6] of **2**



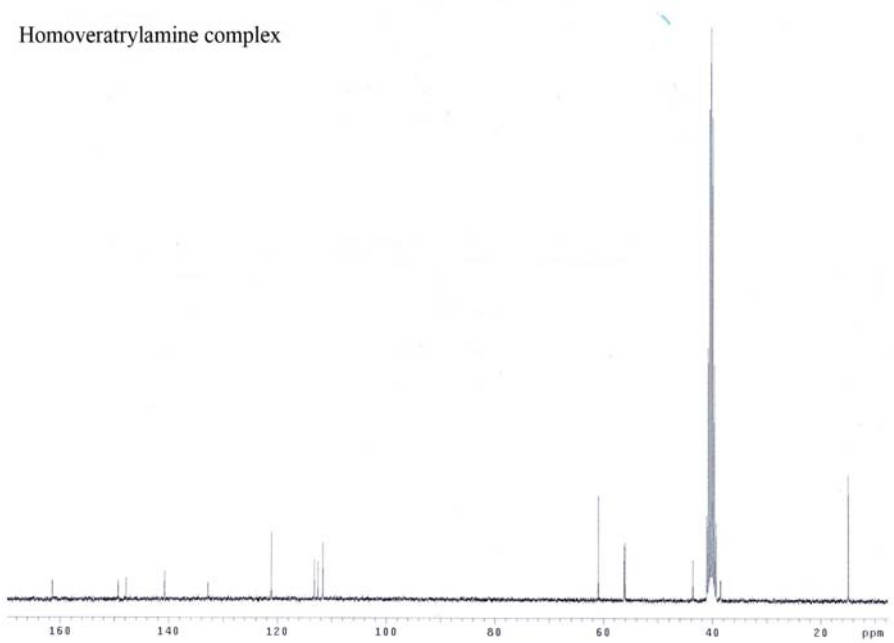
b) ^{13}C NMR (75 MHz, DMSO-d_6) of **2**



c) ^{1}H NMR [300 MHz, DMSO-d_6] of **3**



d) ^{13}C NMR (75 MHz, DMSO-d_6) of **3**



*3.- **Crystallographic Data***

. Data collection of compounds **2** and **3** was performed at 293 K on a Nonius Kappa-CCD single crystal diffractometer, using Mo K_α radiation (λ=0.7173 Å). Data collection strategy was calculated with the program Collect.[1] Data reduction and cell refinement were performed with the programs HKL Denzo and Scalepack .[2]

The crystal structure was solved by direct methods, using the program SIR-97.[3]Anisotropic least-squares refinement was carried out with SHELXL-97.[4] All non hydrogen atoms were anisotropically refined except C8 and C9. These atoms and their respective hydrogens were refined as a two half-occupancy systems due to the occurrence of disorder in this part of the chain. The hydrogen atoms were located in calculated positions using HFIX cards.

Geometrical calculations were made with PARST.[5] The crystallographic plots were made with ORTEP.[6]

1. **COLLECT,** Nonius BV, 1997-2000
2. **DENZO-SCALEPACK** Otwinowski, Z. & Minor, W., **"Processing of X-ray Diffraction Data Collected in Oscillation Mode ",** *Methods in Enzymology, **Volume 276:** Macromolecular Crystallography, **part A,*** p.307-326, 1997**,** Carter,C. W. Jr. & Sweet, R. M., Eds., Academic Press.
3. **SIR97 -** Altomare A., Burla M.C., Camalli M., Cascarano G.L., Giacovazzo C. , Guagliardi A., Moliterni A.G.G., Polidori G.,Spagna R. (1999) J. Appl. Cryst. **32,** 115-119.
4. **SHELX97 -** Sheldrick, G. M. (1997). SHELX97. Programs for Crystal Structure Analysis (Release 97-2). University of Göttingen, Germany.
5. **PARST -** (a) Nardelli, M. Comput. Chem. 1983, **7**, 95-97. (b) Nardelli, M. J**.** *Appl. Crystallogr.* 1995, **28,** 659
6. **ORTEP3** for Windows - Farrugia, L. J. (1997) J. Appl. Cryst. **30**, 565.

4.-Table of Selected Hydrogen bonds for compounds 2 and 3.

Compound (2)

Donor-H	Donor...Acceptor	H...Acceptor	Donor-H.....Acceptor
N3 -H3A	N3 ...N1 (1)	H3A ...N1 (1)	N3 -H3A ...N1 (1)
0.89	2.867(.005)	1.99	169
1.03	1.85	167 (**)	

N3	-H3B	N3	...N2'	(2)	H3B	...N2'	(2)	
0.89		2.839(.005)			1.964			167
1.03			1.82			166	(**)	

N3	-H3C	N3	...N2	(3)	H3C	...N2	(3)	
0.89		3.093(.005)			2.20			175
1.03			2.06			175	(**)	

(**) Values normalized following G.A.Jeffrey & L.Lewis, Carbohydr.Res. (1978).60,179; R.Taylor, O.Kennard, Acta Cryst.(1983).B39,133.

Equivalent positions:

(0) x,y,z

(1) x-1/2,-y+1/2,+z-1/2

(2) -x,-y,-z

(3) x-1/2,-y-1/2,+z-1/2

(4) -x+1,-y+1,-z

(5) -x,-y-1,-z

Compound (3)

Donor-H	Donor...Acceptor	H...Acceptor	Donor-H.....Acceptor
N3 -H3A	N3 ...N2' (1)	H3A ...N2' (1)	N3 -H3A ...N2' (1)
0.89	2.865 (.003)	1.98	171
1.03	1.84	171	(**)
N3 -H3B	N3 ...N2 (2)	H3B ...N2 (2)	N3 -H3B ...N2 (2)
0.89	2.965(.003)	2.11	160
1.03	1.98	158	(**)
N3 -H3C	N3 ...N1 (3)	H3C ...N1 (3)	N3 -H3C ...N1 (3)
0.89	2.873(.003)	2.03	158
1.03	1.90	156	(**)

(**) Values normalized following G.A.Jeffrey & L.Lewis, Carbohydr.Res. (1978).60,179; R.Taylor, O.Kennard, Acta Cryst.(1983).B39,133.

Equivalent positions:

(0) x,y,z

(1) x+1,+y,+z

(2) -x+1/2,+y-1/2,-z+1/2

(3) -x+1/2,+y+1/2,-z+1/2

(4) -x,-y+1,-z

(5) x+1,+y-1,+z

(6) x,+y-1,+z

(7) x,+y+1,+z

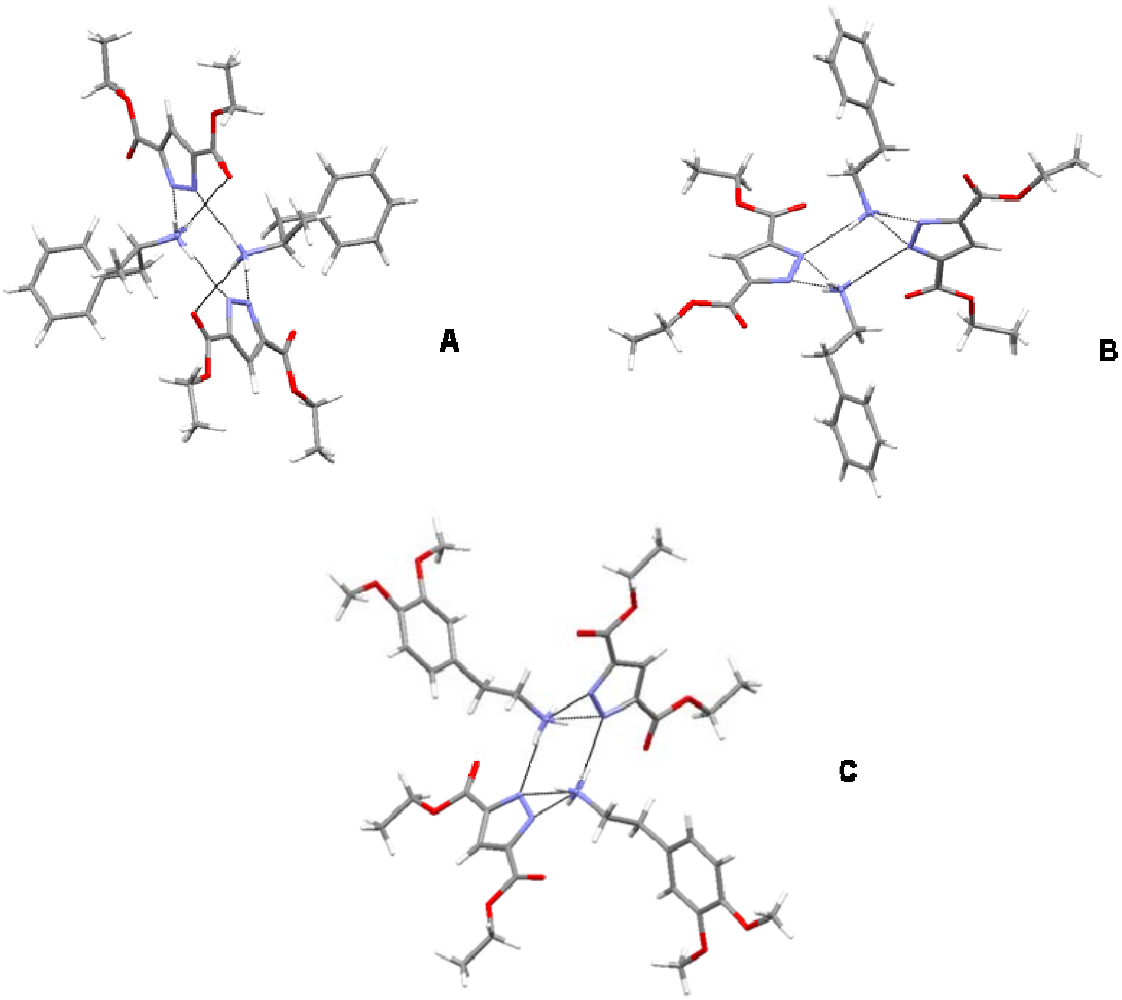


Figure S1. View along the b-axes showing the hydrogen bond pattern (dotted lines) of crystal structures **1 (A),** (ref. 11) **2 (B)** and **3(C)**.