Supporting Information for

Chiral Helicity Induced by Hydrogen Bonding and Chirality of Podand Histidyl Moieties

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General Comments

All reagents and solvents were purchased from commercial sources and were further purified by the standard methods, if necessary. Melting points were determined on a Yanagimoto Micromelting Point Apparatus and were uncorrected. Infrared spectra were obtained with a Perkin Elmer Model 1605 FT-IR. ^{1}H NMR spectra were recorded on a Varian MERCURY 300 (300 MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra were run on a JEOL JMS-DX303HF mass spectrometer.

Preparation of *N,N'*-bis{(*S*)-(+)-1-methoxycarbonyl-2-(4-imidazoyl)ethyl}-2,6-pyridinedicarboxamide (L-BHisPA) and *N,N'*-bis{(*R*)-(-)-1-methoxycarbonyl-2-(4-imidazoyl)ethyl}-2,6-pyridinedicarboxamide (D-BHisPA).

2,6-Pyridinedicarboxylic acid (418 mg, 2.5 mmol) was treated with thionyl chloride (912 μL, 12.5 mmol) and 1,4-dioxane (5 mL) at 80 ℃ for 24 h. Thionyl chloride and 1,4-dioxane were then removed under reduced pressure to give the acid chloride as a white solid.

To a solution of the corresponding histidyl methyl ester dihydrochloride (1.21 g, 5.0 mmol) and triethylamine (4.2 mL, 30 mmol) in dichloromethane (30 mL) was slowly added a solution of the acid chloride in dichloromethane (30 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h and at room temperature for 12 h. The resulting mixture was diluted with dichloromethane (30 mL), washed with saturated $NaHCO_3$ aqueous solution and brine, and dried over $MgSO_4$. White solid was obtained by evaporation of the dichloromethane solution in vacuo. L-BHisPA and D-BHisPA were isolated in 83% and 79% yields, respectively, by recrystallization from methanol/ether.

L-BHisPA: mp 198-199 °C (uncorrected); IR (KBr): 3394, 3126, 1743, 1666 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 8.23 (d, 2H, J = 7.5 Hz), 8.12 (t, 1H, J = 7.5 Hz), 7.57 (s, 2H), 6.93 (s, 2H), 4.93 (dd, 2H, J = 8.7, 5.1 Hz), 3.76 (s, 6H), 3.36-3.19 (m, 4H); EI-MS *m/z* 469 (M^+); Anal. Calcd for $C_{21}H_{23}N_7O_6 \cdot H_2O$: C, 51.74; H, 5.17; N, 20.11. Found: C, 51.57; H, 5.01; N, 20.16.

D-BHisPA: mp 198-199 °C (uncorrected); IR (KBr): 3394, 3126, 1743, 1666 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 8.23 (d, 2H, J = 7.5 Hz), 8.12 (t, 1H, J = 7.5 Hz), 7.57 (s, 2H), 6.93 (s, 2H), 4.93 (dd, 2H, J = 8.7, 5.1 Hz), 3.76 (s, 6H), 3.36-3.19 (m, 4H); EI-MS *m/z* 469 (M^+); Anal. Calcd for $C_{21}H_{23}N_7O_6 \cdot H_2O$: C, 51.74; H, 5.17; N, 20.11. Found: C, 51.51; H, 4.78; N, 19.83.

Preparation of { (*S*)-(+)-1-methoxycarbonyl-2-(4-imidazoyl)ethyl}-2-pyridinecarboxamide (L-HisPA) and { (*R*)-(-)-1-methoxycarbonyl-2-(4-imidazoyl)ethyl}-2-pyridinecarboxamide (D-HisPA).

Picolinic acid (616 mg, 5.0 mmol) was treated with thionyl chloride (912 µL, 12.5 mmol) and 1,4-dioxane (5 mL) at 80 °C for 24 h. Thionyl chloride and 1,4-dioxane were then removed under reduced pressure to give the the acid chloride as a white solid. To a solution of

the corresponding histidyl methyl ester dihydrochloride (1.21 g, 5.0 mmol) and triethylamine (4.2 mL, 30 mmol) in dichloromethane (30 mL) was slowly added a solution of the acid chloride in dichloromethane (30 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h and at room temperature for 12 h. The resulting mixture was diluted with dichloromethane (30 mL), washed with saturated $NaHCO_3$ aqueous solution and brine, and dried over $MgSO_4$. White solid was obtained by evaporation of the dichloromethane solution in vacuo. L-HisPA and D-HisPA were isolated in 70% and 79% yields, respectively, by recrystallization from methanol/ether.

L-HisPA: mp 174-175 °C (uncorrected); IR (KBr): 3348, 3116, 1728, 1658 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 8.62 (ddd, 1H, J = 5.4, 1.8, 0.9 Hz), 8.05 (ddd, 1H, J = 7.5, 1.5, 0.9 Hz), 7.94 (td, 1H, J = 7.5, 1.8 Hz), 7.63 (s, 1H), 7.54 (ddd, 1H, J = 7.5, 5.4, 1.5 Hz), 6.89 (s, 1H), 4.91 (dd, 1H, J = 7.2, 5.4 Hz), 3.74 (s, 3H), 3.25-3.21 (m, 2H); EI-MS *m/z* 274 (M^+); Anal. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.14; N, 20.43. Found: C, 56.56; H, 5.21; N, 20.26.

D-HisPA: mp 174-175 °C (uncorrected); IR (KBr): 3348, 3116, 1728, 1658 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 8.62 (ddd, 1H, J = 5.4, 1.8, 0.9 Hz), 8.05 (ddd, 1H, J = 7.5, 1.5, 0.9 Hz), 7.94 (td, 1H, J = 7.5, 1.8 Hz), 7.63 (s, 1H), 7.54 (ddd, 1H, J = 7.5, 5.4, 1.5 Hz), 6.89 (s, 1H), 4.91 (dd, 1H, J = 7.2, 5.4 Hz), 3.74 (s, 3H), 3.25-3.21 (m, 2H); EI-MS *m/z* 274 (M^+); Anal. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.14; N, 20.43. Found: C, 56.89; H, 5.06; N, 20.38.

X-ray Structure Analysis.

All measurements for L-BhisPA, D-BhisPA, and D-HisPA were made on a Rigaku RAXIS-RAPID Imaging Plate diffractometer with graphite monochromated Mo Kα radiation. All measurements for L-HisPA were made on a Rigaku AFC5R diffractometer with graphite

monochromated Mo Kα radiation and a rotating anode generator. The structures of L-BHisPA, D-BHisPA, L-HisPA, and D-HisPA were solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The H atoms involved in hydrogen bonding were located in electron density maps. The remainder of the H atoms were placed in idealized positions and allowed to ride with the C atoms to which each was bonded. Crystallographic details are given in Table S1.

Table S1. Crystallographic Data for L-BHisPA, D-BHisPA, L-HisPA, and D-HisPA

	L-BHisPA	D-BHisPA	L-HisPA	D-HisPA
formula	$C_{21}H_{23}N_7O_6 \cdot H_2O$	$C_{21}H_{23}N_7O_6 \cdot H_2O$	$C_{13}H_{14}N_4O_3$	$C_{13}H_{14}N_4O_3$
fw	487.47	487.47	274.28	274.28
cryst syst	orthorhombic	orthorhombic	orthorhombic	orthorhombic
space group	$C222_1$ (No. 20)	$C222_1$ (No. 20)	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)
a, Å	12.317(1)	9.105(1)	9.650(2)	9.6490(6)
b, Å	9.1373(9)	12.297(1)	16.262(2)	16.3212(9)
c, Å	22.507(2)	22.403(3)	8.872(2)	8.8998(6)
V, Å^3	2533.1(4)	2508.4(5)	1392.2(3)	1401.6(1)
Z	4	4	4	4
D_{calcd}, g cm^{-3}	1.278	1.291	1.308	1.300
μ(Mo Kα), cm^{-1}	0.98	0.99	0.90	0.95
T, °C	23	23	23	23
λ(Mo Kα), Å	0.71069	0.71069	0.71069	0.71069
R^a	0.089	0.074	0.091	0.038
$R_w{}^b$	0.211	0.183	0.136	0.128

$^a R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. $^b R_w = [\Sigma w(F_o{}^2 - F_c{}^2)^2/\Sigma w(F_o{}^2)^2]^{1/2}$.

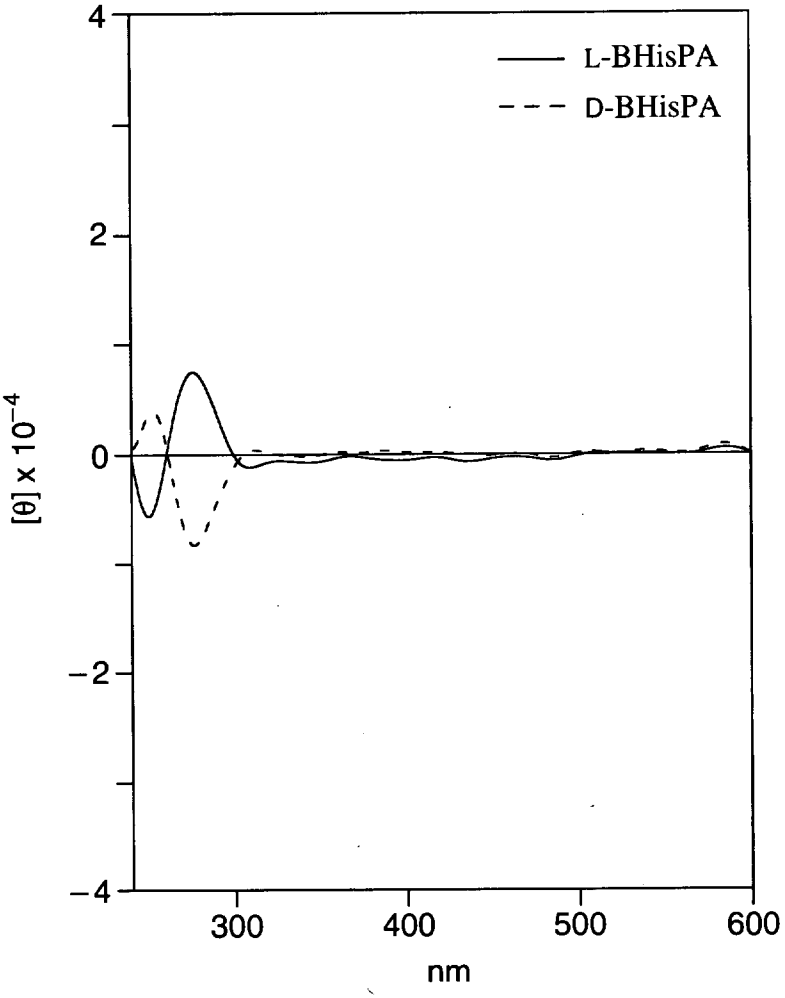

Figure S1. CD spectra of L-BHisPA and D-BHisPA in CH_2Cl_2 (5.0×10^{-5} M).

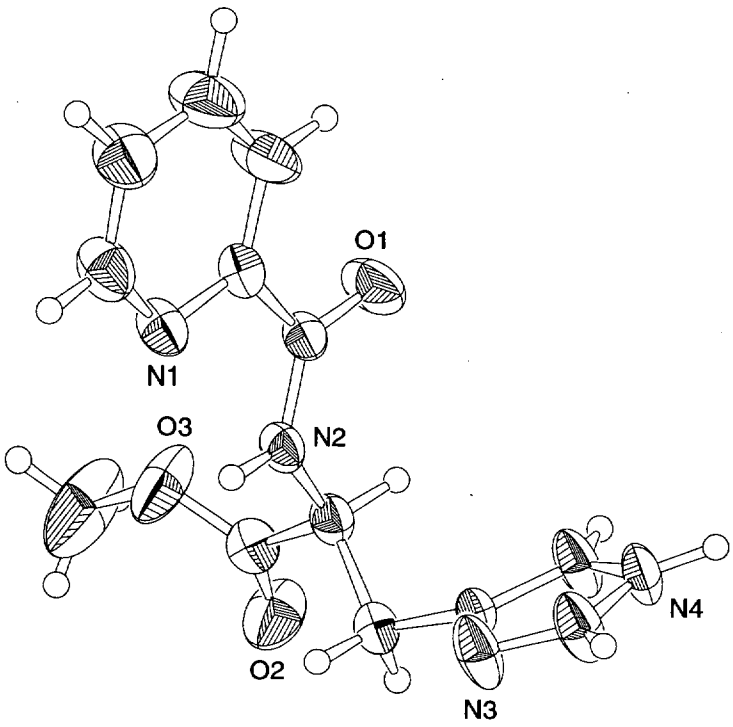

Figure S2. Molecular structure of L-HisPA.

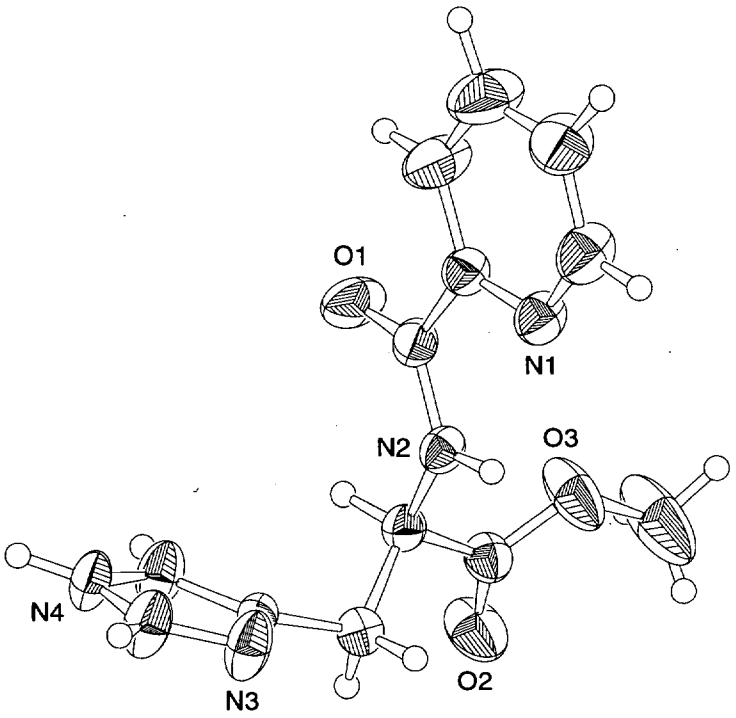

Figure S3. Molecular structure of D-HisPA.

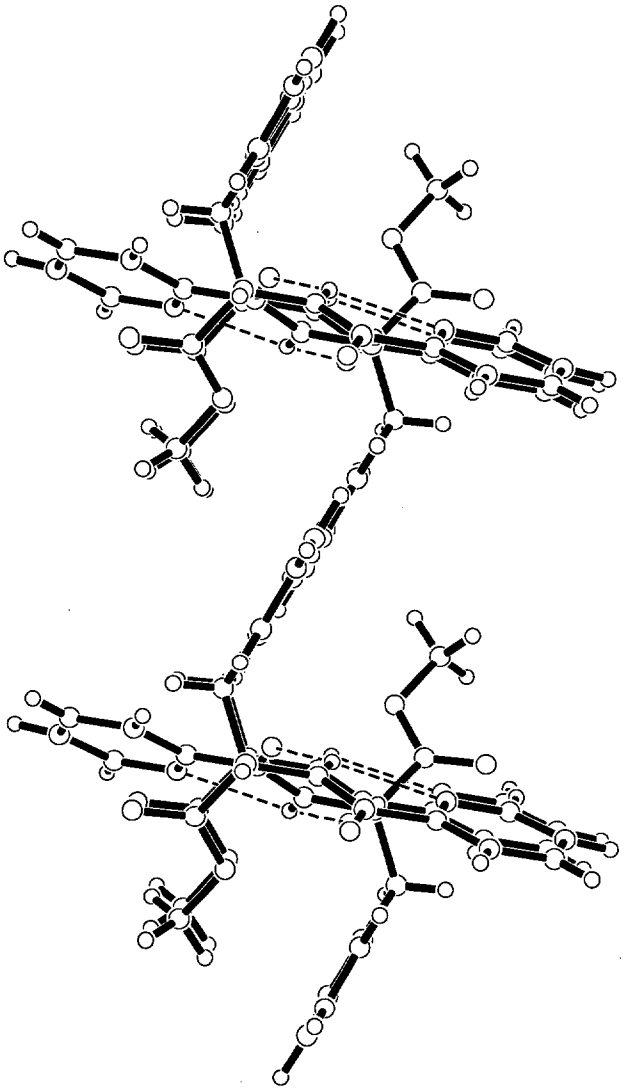

Figure S4. A hydrogen-bonded network in the crystal packing of L-HisPA. Projection down the *a* axis. Each molecule is connected to four neighboring molecules by intermolecular hydrogen bonds.

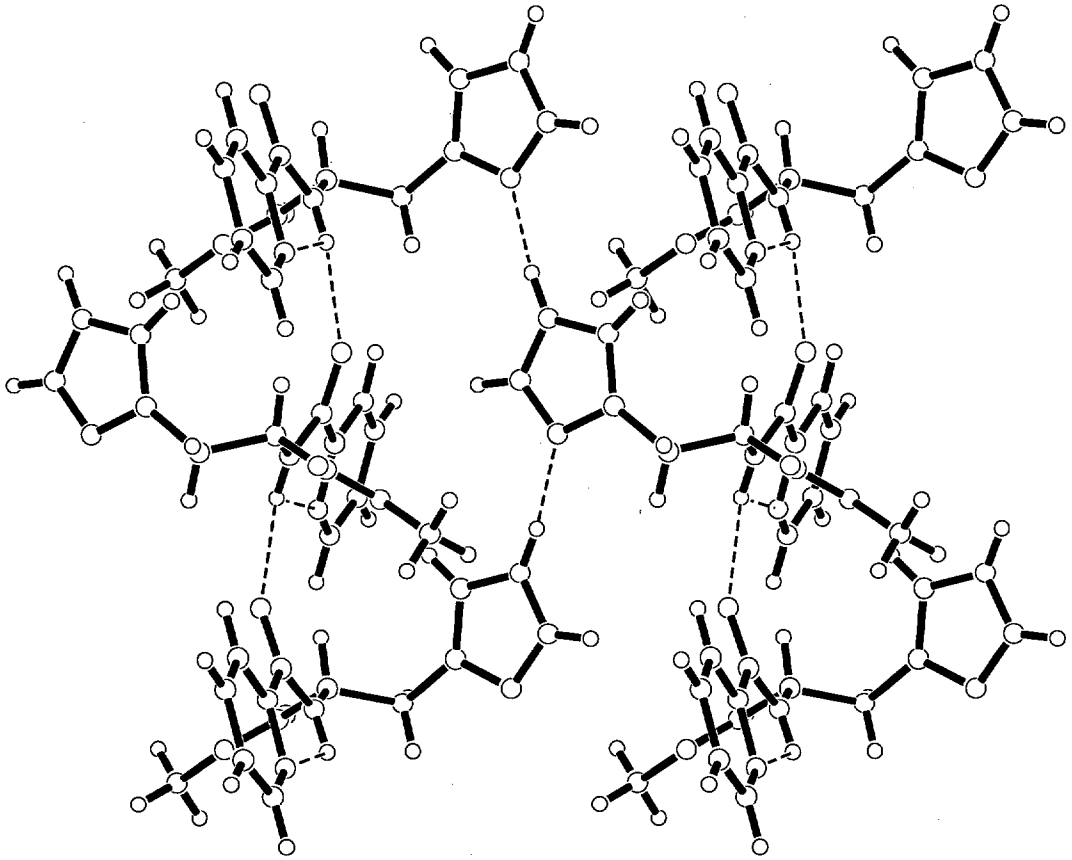

Figure S5. A hydrogen-bonded network in the crystal packing of L-HisPA. Projection down the *b* axis. Each molecule is connected to four neighboring molecules by intermolecular hydrogen bonds.

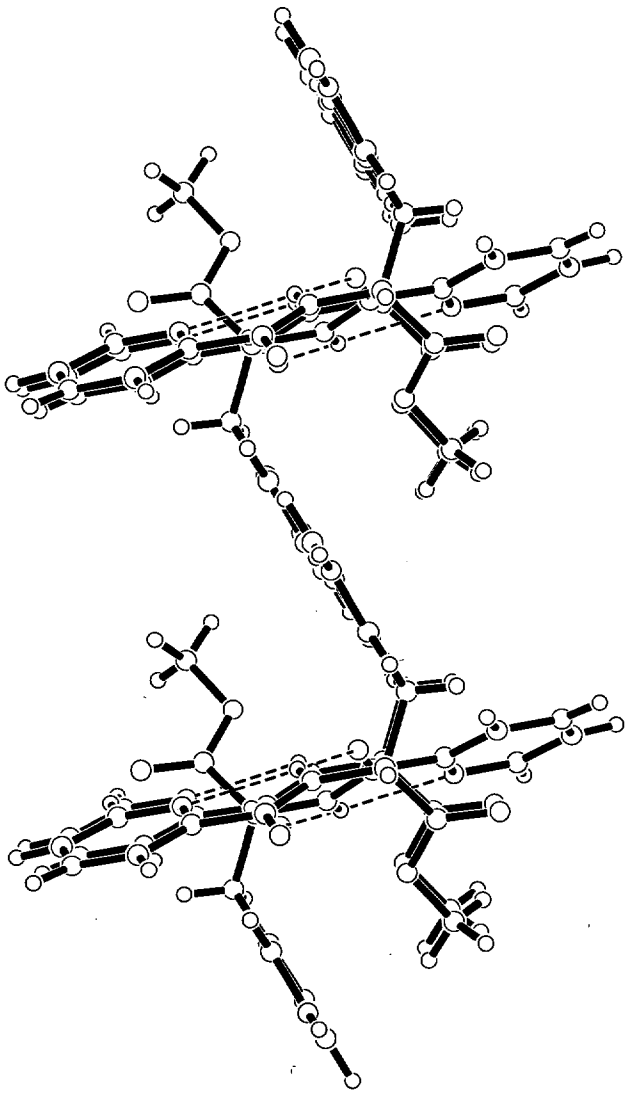

Figure S6. A hydrogen-bonded network in the crystal packing of D-HisPA. Projection down the *a* axis. Each molecule is connected to four neighboring molecules by intermolecular hydrogen bonds.

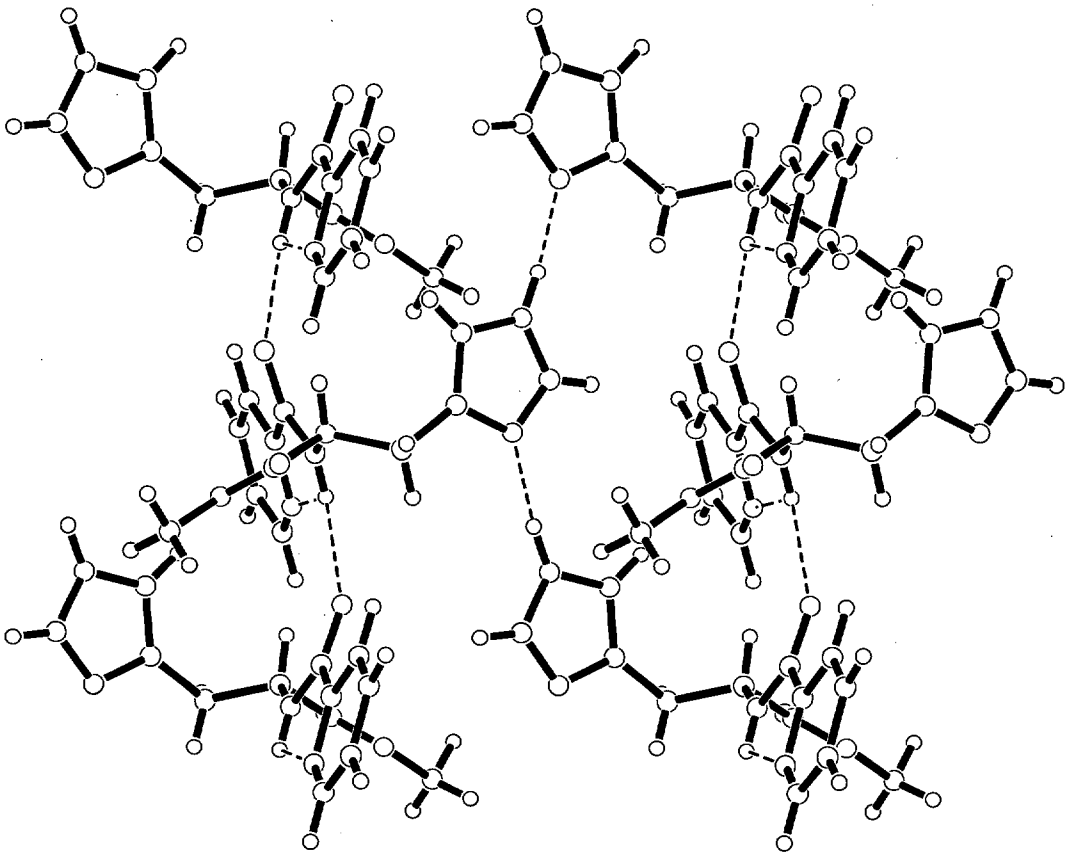

Figure S7. A hydrogen-bonded network in the crystal packing of D-HisPA. Projection down the *b* axis. Each molecule is connected to four neighboring molecules by intermolecular hydrogen bonds.