Supporting information

Ion channel-like crystallographic signatures in modified guanine-potassium/sodium interactions

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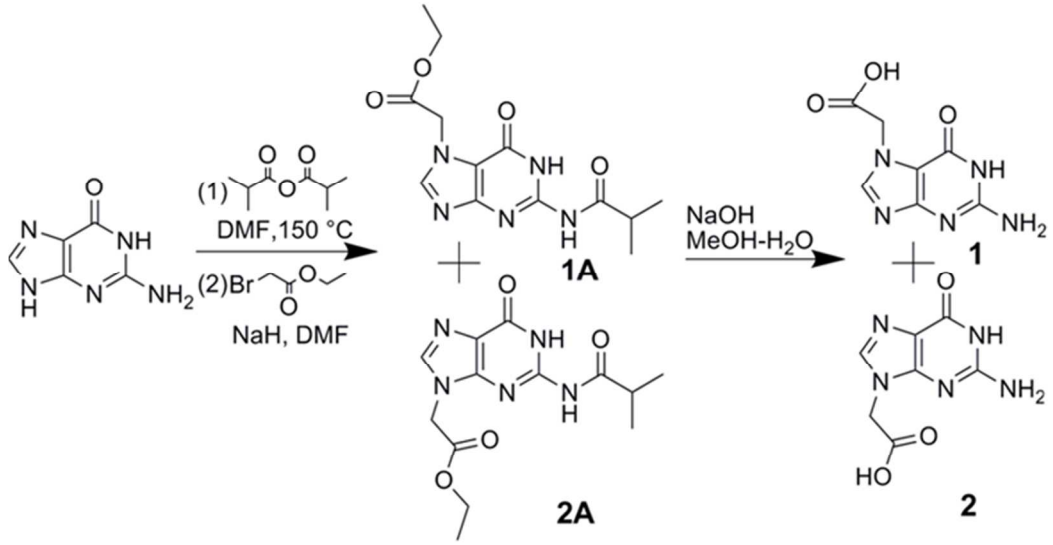
General procedures: ^{1}H and ^{13}C NMR spectra were obtained on a JEOL-DELTA2 500 model spectrometer operating at 500 MHz. The spectra were recorded in DMSO–d_6, D_2O solutions and the chemical shifts were referenced with respect to tetramethylsilane. High resolution (ESI^+ and ESI^- modes) mass spectra were obtained on WATERS HAB 213 machine, Department of Chemistry, IIT Kanpur. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F_{254}) were used, and compounds were visualized with a UV light at 254 nm. Flash chromatographic separations were performed on Merck 230-400 mesh silica gel. All solvents were distilled prior to use by using standard procedures. Solvents were evaporated using rotary evaporator under reduced pressure. The Au(111) surface (No. N9807A-FG) was purchased from Agilent Technologies. All STM images were recorded using Agilent Technologies 5500 instrument (Tip no. N9801A) in constant current mode at 298 K.

SCHEME1: Synthesis of **1** and **2**.



Synthesis of N^2-Isobutyrylguanine: N^2-Isobutyrylguanine was prepared based on literature procedure.[1] Isobutyric anhydride (21.36 g, 135 mmol) was added to a suspension of guanine (7.56 g, 50 mmol) in anhydrous DMF (100 ml). The reaction mixture was heated at 150 °C for 2 hours, cooled to room temperature and evaporated under reduced pressure. Saturated aqueous $NaHCO_3$ solution was added to the obtained crude product until effervescences ceases. Then, the solution was filtered and the residue was washed with water (2×20 ml) and dried under vacuum (8.83 g, 80% Yield). The obtained compound was used in the next step without further purification.

Synthesis of 1A and 2A: The compounds **1A** and **2A** were prepared based on literature procedure.[2] To a suspension of N^2-isobutyrylguanine (6.63 g, 30 mmol) in anhydrous DMF (250 ml), NaH (0.72 g, 30 mmol) was added at 0 °C under N_2 atmosphere. Ethylbromoacetate (3.67 ml, 33 mmol) was added dropwise over a period of 30 minutes *(Caution: Ethybromoacetate causes severe eye irritation)* and reaction was quenched with methanol after 2 hours of stirring. The solvents were evaporated and compounds were isolated by flash column chromatography eluting with methanol/chloroform respectively to afford yellowish-white powders.

1A: (2.8 g, 50% Yield). HRMS: $(M+H)^+$ calculated: 308.1359, found: 308.1358; ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 1.07(d, 6H, two isobutyl CH_3's), 1.16 (t, 3H, ethyl CH_3), 2.70 (septet, 1H, isobutyl CH), 4.13 (q, 2H, ethyl CH_2), 5.16 (s, 2H, CH_2), 8.10 (s, 1H, C8-H), 11.55 (s, 1H, N1-H), 12.11 (s, 1H, N2-H); ^{13}C NMR (125 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 14.50, 19.39, 35.24, 47.85, 61.87, 112.22, 145.44, 147.77, 153.17, 157.38, 168.38, 180.50.

2A: (2.578 g, 46% Yield). HRMS: $(M+H)^+$ calculated: 308.1359, found: 308.1355; ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 1.06 (d, 6H, two isobutyl CH_3's), 1.17 (t, 3H, ethyl CH_3), 2.72 (septet, 1H, isobutyl CH), 4.13 (q, 2H, ethyl CH_2), 4.97 (s, 2H, CH_2), 7.92 (s, 1H, C8-H); ^{13}C NMR (125 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 14.53, 19.38, 35.21, 44.81, 62.05, 120.21, 140.79, 148.68, 149.52, 155.36, 168.20, 180.75.

Synthesis of N7-(carboxymethyl)guanine (1) and N9-(carboxymethyl)guanine (2): Compound **1A** (**2A**) (50 mg) was dissolved in methanol (4 ml) and aqueous solution of 2N NaOH was added. The solution was stirred for 48 hours at ambient temperature. The product **1**(**2**) was precipitated out on neutralization with aqueous 2N HCl solution and it was collected via filtration and dried under vacuum. **1**: (25 mg, 73% Yield). HRMS: $(M-H)^-$ calculated: 208.0476, found: 208.0473; ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 4.83(s, 2H, CH_2), 6.18 (s, 2H, NH_2), 7.77 (s, 1H, C8-H), 10.89 (s, 1H, N1-H); ^{13}C NMR (125 MHz, DMSO-d_6, 25 °C, TMS): δ (ppm) 47.81, 109.03, 144.28, 153.32, 155.17, 159.96, 170.05; **2**: (23 mg, 67% Yield). HRMS: $(M-H)^-$ calculated: 208.0476, found: 208.0479; ^{1}H NMR (500 MHz, D_2O, 25 °C, TMS): δ (ppm) 4.49 (s, 2H, CH_2), 7.60 (s, 1H, C8-H); ^{13}C NMR (125 MHz, D_2O, 25 °C, TMS): δ (ppm) 46.54, 115.60, 140.56, 151.65, 153.74, 158.94, 174.36.

Synthesis of G7K: Compound **1** (1 eq., 0.01 g), anhydrous K_2CO_3 (4 eq., 0.026 g) were dissolved in methanol/water mixture (1:2, 4 ml). The obtained clear solution was slow evaporated and crystals of **G7K** were isolated after a month and they dried under high vacuum (0.006 g, 42% Yield). HRMS (positive mode): $[L+K]^+$ calculated: 248.0186, found: 248.0190; $[(L–H)+2K]^+$ calculated: 285.9750, found: 285.9747; $[(L–H)+L+2K]^+$ calculated: 495.0299, found: 495.0302; $[2(L–H)+3K]^+$ calculated: 532.9863, found: 532.9858; $[3L+K]^+$ calculated: 666.1284, found: 666.1294; $[3(L–H)+4K]^+$ calculated: 779.9977, found: 779.9961; $[(L–H)+3L+2K]^+$ calculated: 913.1397 found: 913.1411; $[2(L–H)+2L+3K]^+$ calculated: 951.0961, found: 951.0975; HRMS (negative mode): $[2(L–H)+K]^-$ calculated: 455.0589, found: 455.0583; $[2(L–H)+L+K]^-$ calculated: 664.1138, found: 664.1124; $[3(L–H)+2K]^-$ calculated: 702.0703, found: 702.0727; $[3(L–H)+L+2K]^-$ calculated: 911.1251, found: 911.1286 where L= N7-(carboxymethyl)guanine (**1**).

Synthesis of G9K: Compound **2** (1 eq., 0.01 g), anhydrous K_2CO_3 (4 eq., 0.026 g) were dissolved in methanol/water mixture (1:2, 4 ml). The obtained clear solution was slow evaporated and crystals of **G9K** were isolated after a month and they dried under high vacuum (0.005 g, 31% Yield). HRMS (positive mode): $[L+K]^+$ calculated: 248.0186, found: 248.0188; $[2L+K]^+$ calculated: 457.0735, found: 457.0753 where L= N9-(carboxymethyl)guanine (**2**).

Synthesis of G7Na: Similar to **G7K** procedure except using Na_2CO_3 instead of K_2CO_3. (0.003 g, 27% Yield). HRMS (positive mode): $[L+Na]^+$ calculated: 232.0447, found: 232.0446; $[(L–H)+2Na]^+$ calculated: 254.0272, found: 254.0271; $[2L+Na]^+$ calculated: 441.0995, found: 441.0974; $[(L–H)+L+2Na]^+$ calculated: 463.0820, found: 463.0802; $[2(L–H)+3Na]^+$ calculated: 485.0645, found: 485.0667; $[2(L–H)+4Na–H]^+$ calculated: 507.0465, found: 507.0497; [(L–

H)+2L+2Na]$^+$ calculated: 672.1369, found: 672.1373; [(L–H)+3L+2Na]$^+$ calculated: 881.1918, found: 881.1983; HRMS (negative mode): [2(L–H)+Na]$^-$ calculated: 439.0850, found: 439.0829; [2(L–H)+2Na–H]$^-$ calculated: 461.0670, found: 461.0649; [2(L–H)+L+Na]$^-$ calculated: 648.1399, found: 648.1375; [3(L–H)+2Na]$^-$ calculated: 670.1224, found: 670.1172; [3(L–H)+3Na–H]$^-$ calculated: 692.1043, found: 692.0975; [4(L–H)+3Na]$^-$ calculated: 901.1598, found: 901.1489 where L= N7-(carboxymethyl)guanine (**1**).

STM sample preparation: Dried crystals of **G7K** and **G9K** were dissolved in H_2O. 10^{-9} M concentrated **G7K** and **G9K** samples were deposited on Au(111) surface respectively and dried using high vacuum. Then the surfaces were imaged with STM at 298 K.

Crystal structure refinement details for G7K, G9K and **G7Na:** Single Crystals of **G7K**, **G9K** and **G7Na** were coated with light hydrocarbon oil and mounted in the 100 K dinitrogen stream of a Bruker SMART APEX CCD diffractometer equipped with CRYO Industries low-temperature apparatus and intensity data were collected using graphite-monochromated Mo Kα radiation. The data integration and reduction were processed with the SAINT software.[3] An absorption correction was applied.[4] Structures were solved by the direct method using SHELXS-97 and refined on *F*2 by a full-matrix least-squares technique using the SHELXL-97 program package.[5] Non-hydrogen atoms were refined anisotropically. In the refinement, hydrogens were treated as riding atoms using the SHELXL default parameters. Crystal structure refinement parameters are given in Table S1 whereas H-bonding parameters are provided in Table S2. CCDC contains the supplementary crystallographic data for this paper with deposition numbers of CCDC 862440, 862441, 907744 for **G7K, G9K** and **G7Na** respectively. Copies of this information can be

obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK. [Fax: +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk]. In **G9K** [$K(C_7H_6N_5O_3)_2.H^+.9H_2O$], the proton in the formula was added to balance the overall charge of complex, although it cannot be determined in structural refinement. It may come from protonated solvent molecules or from proton attached to oxygen or nitrogen atoms in ligand.[6]

Table S1: Crystallographic data for **G7K**, **G9K** and **G7Na**.

Identification code	**G7K**	**G9K**	**G7Na**
Empirical formula	$C_7H_{12}K_1N_5O_6$	$C_{14}H_{30}K_1N_{10}O_{15}$	$C_7H_{12}Na_1N_5O_7$
*M*r	301.32	617.58	301.21
crystal system	Monoclinic	Monoclinic	Monoclinic
space group	$P2_1/c$	C2/c	$P2_1/c$
a/Å	16.239(5)	17.936(7)	17.566(5)
b/Å	9.884(4)	9.590(3)	9.743(3)
c/Å	7.574(3)	14.730(5)	7.361(2)
α/°	90	90	90
β/°	100.516(5)	104.700(11)	96.875(5)
γ/°	90	90	90
Volume/ Å^3	1195.3(8)	2450.8(15)	1250.7(6)
Z	4	4	4
Dx /Mg m^{-3}	1.674	1.674	1.600
F(000)	624	1292	624
μ/ mm^{-1}	0.479	0.312	0.169
θ range for data collection/ °	2.42 to 28.4	2.35 to 26.00	2.39 to 28.38
Limiting indices	-21<=h<=21, -13<=k<=10, -8<=l<=10	-20<=h<=22, -11<=k<=8, -16<=l<=18	-23<=h<=17, -12<=k<=13, -9<=l<=9
Reflections collected	7615	6766	7906
unique reflections	2936	2407	3074
R(int)	0.0381	0.0497	0.0432
Completeness to *θ*	97.8	99.9	98.2
T_{max} / T_{min}	0.9360/0.9103	0.9576/0.9402	0.9669/0.9621
Data / restraints / parameters	2936/9/196	2407/13/218	3074/19/205
Goodness-of-fit on F^2	1.208	1.070	1.083
*R*1 and *R*2 [$I>2\sigma(I)$]	0.0539, 0.1347	0.0476, 0.1155	0.0553, 0.1355
*R*1 and *R*2 (all data)	0.0796, 0.2098	0.0646, 0.1306	0.0890, 0.1747
Largest diff. peak and hole/e.A^{-3}	0.660 and -0.798	0.780 and -0.386	0.668 and -0.446
CCDC No.	**862440**	**862441**	**907744**

Table S2: Selected hydrogen bond distances (Å) and bond angles (°) in **G7K**, **G9K** and **G7Na**.

D—H…A[#]	D…A	H…A	D—H…A
G7K			
N(1)—H(1)…N(3)^{i}	2.887(4)	2.03	174
O3W—H1W3…O(6)^{ii}	2.891(4)	2.10(5)	171(5)
N(2)—H(2A)…N(9)^{i}	2.951(4)	2.09	176
N(2) —H(2B)...O(6)^{iii}	3.007(4)	2.16	169
O1W—H1W1...O(2)^{iv}	2.819(4)	2.02(6)	169(7)
O1W—H2W1...O2W^{v}	2.895(5)	2.10(6)	168(7)
O2W—H1W2...O(2)^{ii}	2.739(4)	1.93(5)	173(6)
O2W—H2W2...O(1)^{vi}	2.891(4)	2.11(3)	163(4)
G9K			
N(1)—H(1)…O(2)^{vii}	2.774(3)	1.95	160
O1W—H1W1...N(7)	2.766(3)	1.83(4)	178(6)
O1W—H2W1...O5W^{viii}	2.733(3)	1.90(4)	179(5)
N(2)—H(2A)…O1W^{ix}	3.043(3)	2.25	153
N(2)—H(2B)…O(1)^{vii}	2.943(3)	2.11	164
O2W—H1W2...O5W^{x}	2.836(3)	2.01(4)	155(4)
O3W—H2W3...N(3)	2.927(3)	2.01(4)	176(3)
O3W—H1W3...O1W^{ix}	2.783(3)	1.85(4)	172(3)
O4W—H2W4...O(6)^{xi}	2.900(3)	1.98(4)	172(3)
O4W—H1W4...O1W^{xii}	2.983(3)	2.16(4)	166(4)
O5W—H1W5...O(6)^{xiii}	2.803(3)	1.95(4)	163(4)
O5W—H1W5...O(2)	2.735(3)	1.84(4)	162(4)
G7Na			
N(1)—H(1)…N(3)^{xiv}	2.876(3)	2.02	177
N(2) —H(2A)...O(6)^{xv}	2.978(3)	2.12	172
N(2)—H(2B)…N(9)^{xiv}	2.906(3)	2.05	174
O2W—H1W2...O(2)^{xvi}	2.837(3)	2.04(3)	164(4)
O3W—H1W3...O(1)^{xvii}	2.784(3)	1.98(3)	170(3)
O3W—H2W3…O4W^{xvii}	2.815(3)	1.99(3)	174(3)
O1W—H2W1...O(2)^{xviii}	2.847(3)	2.04(4)	168(3)
O1W—H1W1...O3W ^{xvi}	2.786(3)	2.05(3)	156(4)

[#]Symmetry of A: (*i*) –x,1/2+y,1/2-z (*ii*) x,3/2-y,1/2+z (*iii*) –x,-1/2+y,1/2-z (*iv*) 1-x,1-y,1-z (*v*) 1-x,2-y,1-z (*vi*) 1-x,1/2+y3/2-z (*vii*) x,1-y,1/2+z (*viii*) –x,y,1/2-z (*ix*) 1/2+x,1/2+y,z (*x*)1/2-x,-1/2+y,1/2-z (*xi*) 1/2+x,-1/2+y,z (*xii*) 1/2-x,1/2-y,1-z (*xiii*) x,1-y,-1/2+z (*xiv*) –x,-1/2+y,3/2-z (*xv*) –x,1/2+y,3/2-z (*xvi*) 1-x,1-y,2-z (*xvii*) x, 1/2-y,1/2+z (*xviii*) 1-x,1/2+y,3/2-z where A= acceptor and D= donor.

Figure S1: a) Ladder–like lattice structure in **G7K**. b) Herringbone–like lattice structure in **G9K** (hydrogens, water molecules removed for clarity).

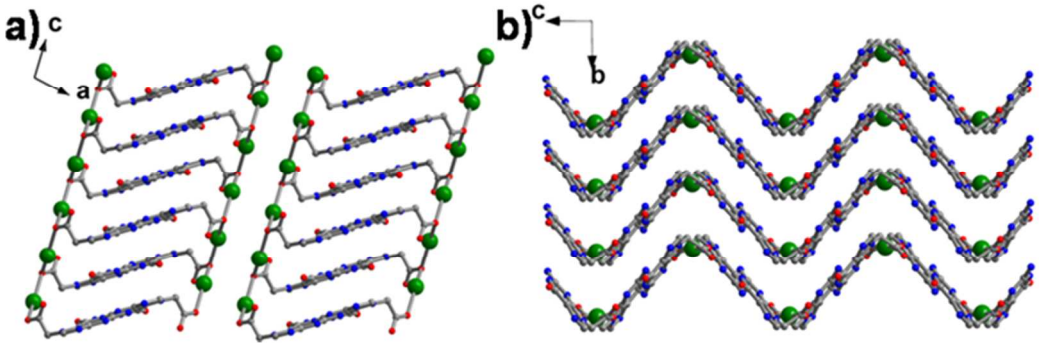


Figure S2: π—π interactions (Å) in a) **G7K** b) **G9K**.

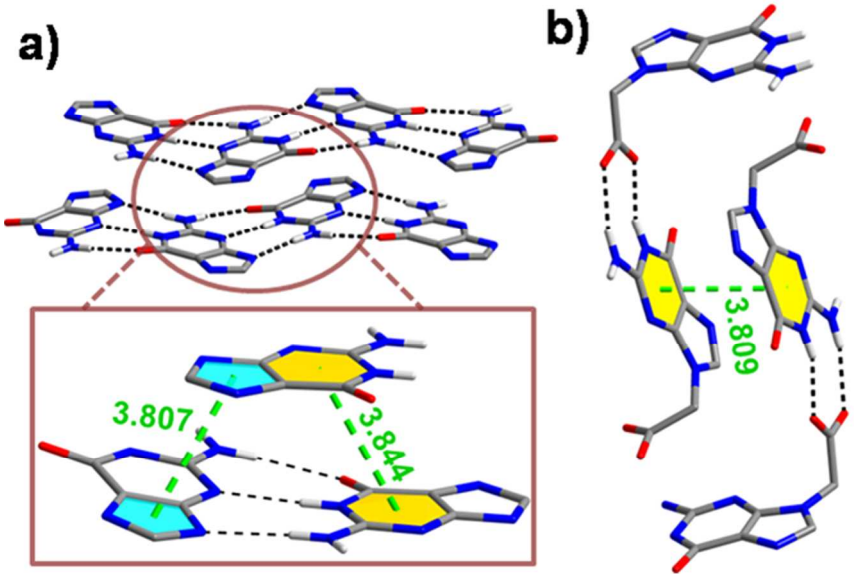


Figure S3: a) Hydrogen bonding interactions (Å) between K–bound water molecules and O6 of guanine in **G7K**. b) Hydrogen bonding interactions (Å) between K–bound water molecules and O1 of guanine in **G7K**.

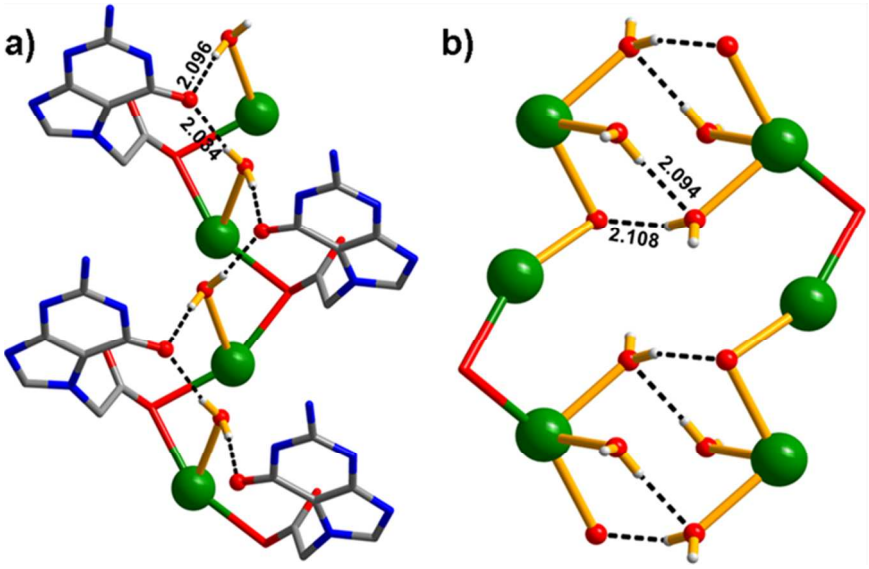


Figure S4: a) Hydrogen bonding interactions (Å) between K–bound water molecules and O6 of guanine in **G9K**. b) Hydrogen bonding interactions (Å) between water molecules and guanine in **G9K**.

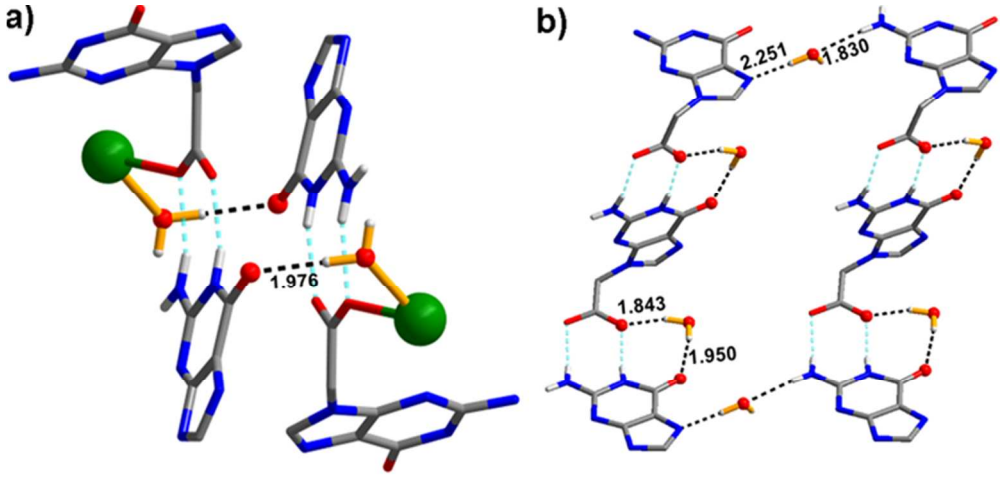


Figure S5: a) Ladder–like lattice structure in **G7Na** (hydrogens, some of water molecules removed for clarity). b) π—π interactions (Å) in **G7Na**.

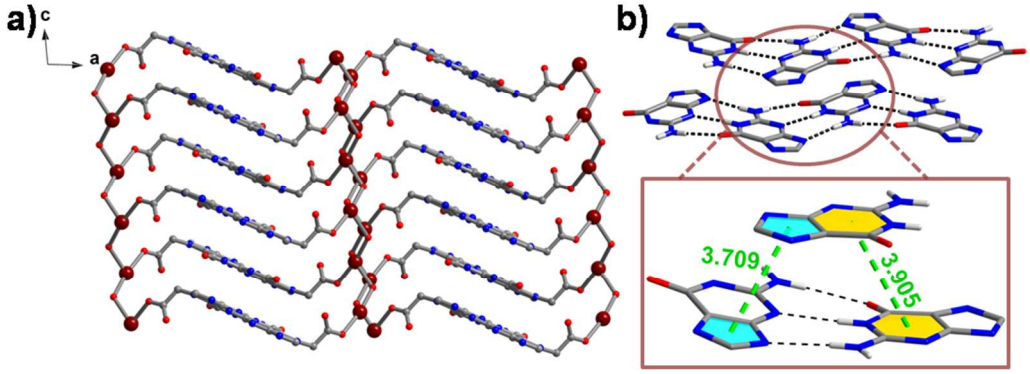


Figure S6: a) Water and carboxylate oxygens (sky blue balls) involvement in potassium ions connection in **G7K**. b) Water oxygens involvement in sodium ions connection in **G7Na**.

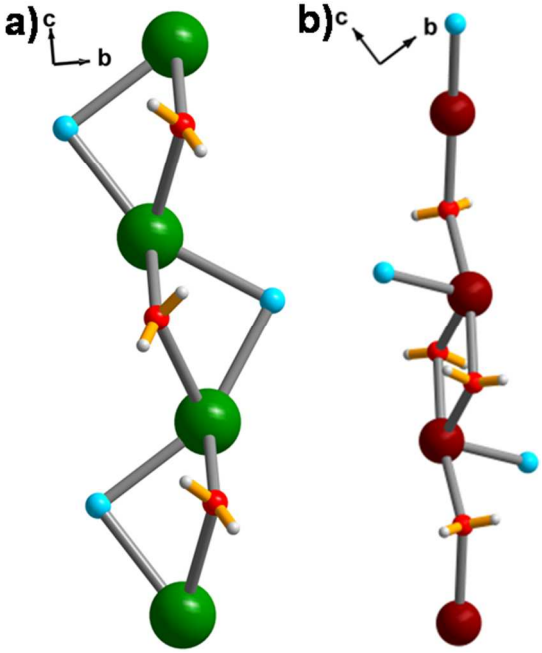


Figure S7: a) Potassium ion geometry in **G7K**. b) Sodium ion geometry in **G7Na**. (sky blue balls-carboxylate oxygens)

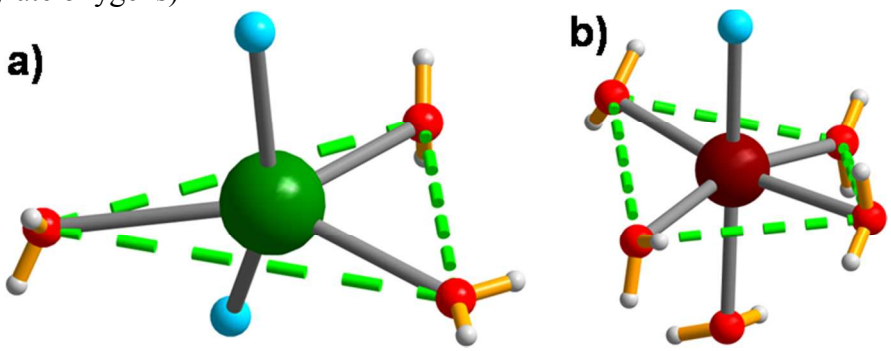


Figure S8: a) STM image (I_t = 1.22 nA, V_t = 0.2 V) of **G7K** (scale 2.9×2.93 nm). b) Crystal lattice of **G7K** when viewed along *c*–axis. c) Diameter–height profile along the dotted line in the panel [a], distance between parallel rows (highlighted in red ellipses) = ~0.05 nm. d) Distance of H1W1 (blue balls) from adjacent plane passing through potassium ions = 0.0519 nm.

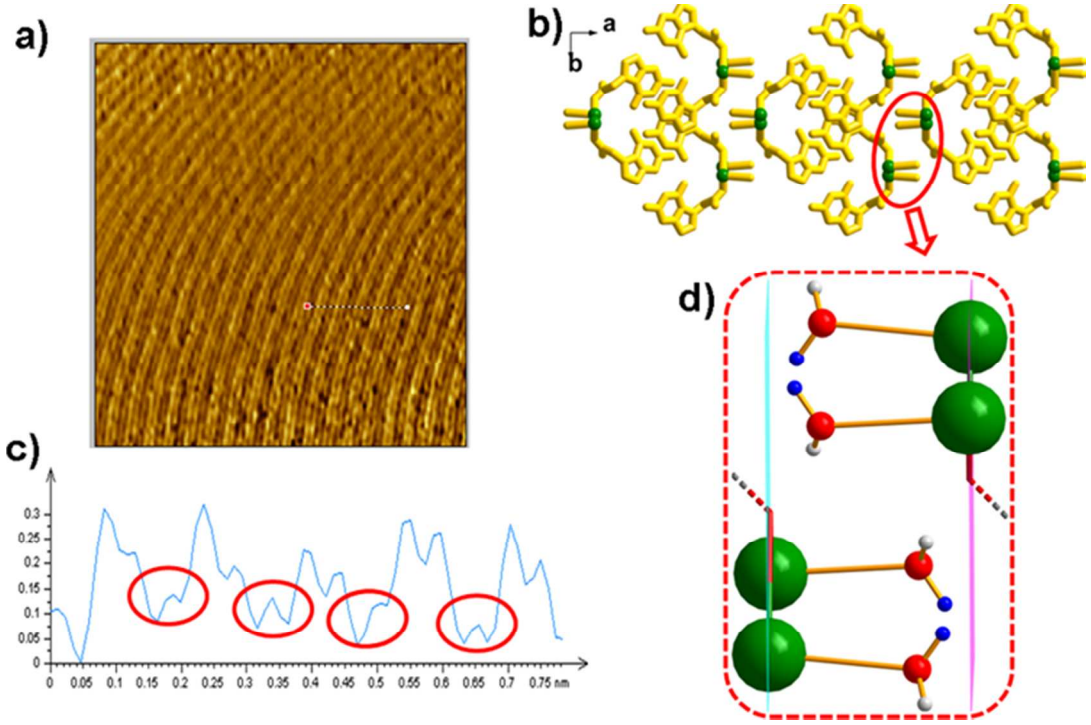


Figure S9: (a & c) STM images (I_t = 1.22 nA, V_t = 0.2 V) of **G9K** (scale 2.97×2.97 nm in [a], scale 0.88×0.6 nm in [c]). b) Diameter–height profile along the dotted line in the panel [a]. d) Magnified STM image of highlighted area in [c].

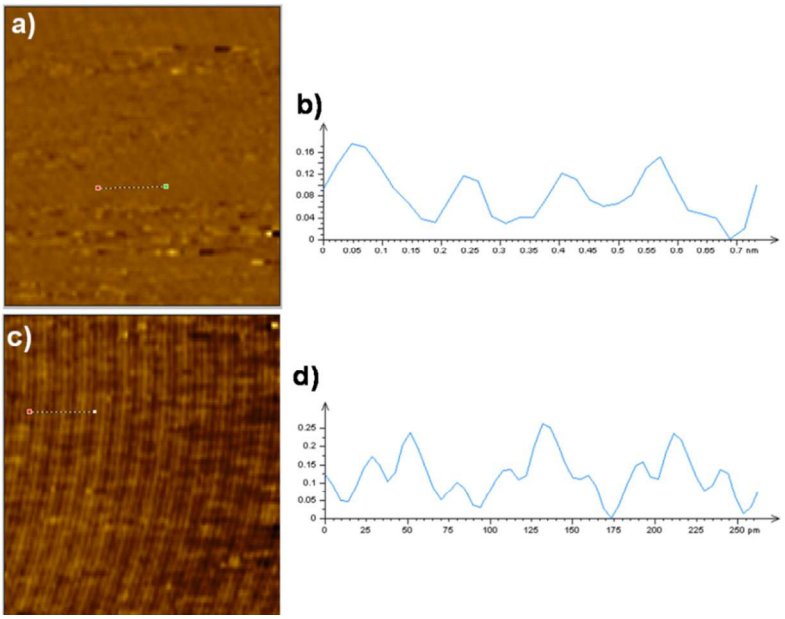


Figure S10: a) Possible correlation between magnified STM image and lattice structure when viewed along *c*–axis in **G7K**. b) Possible correlation between magnified STM image and lattice structure when viewed along *b*–axis in **G9K**.

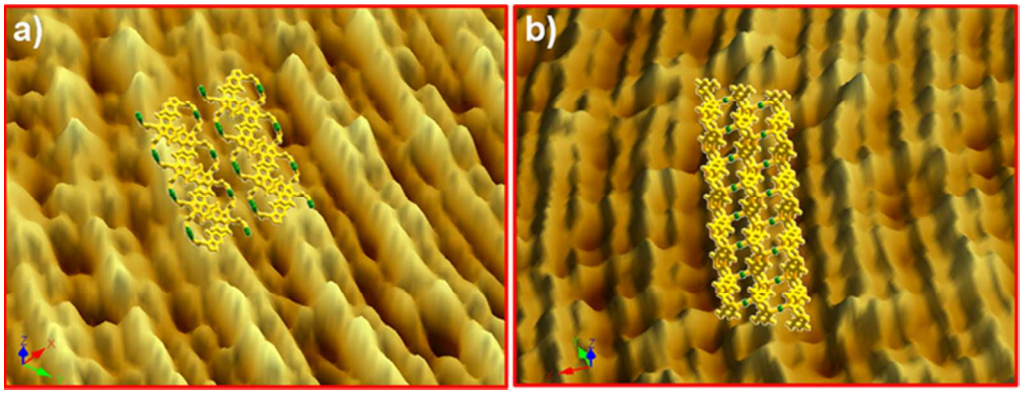
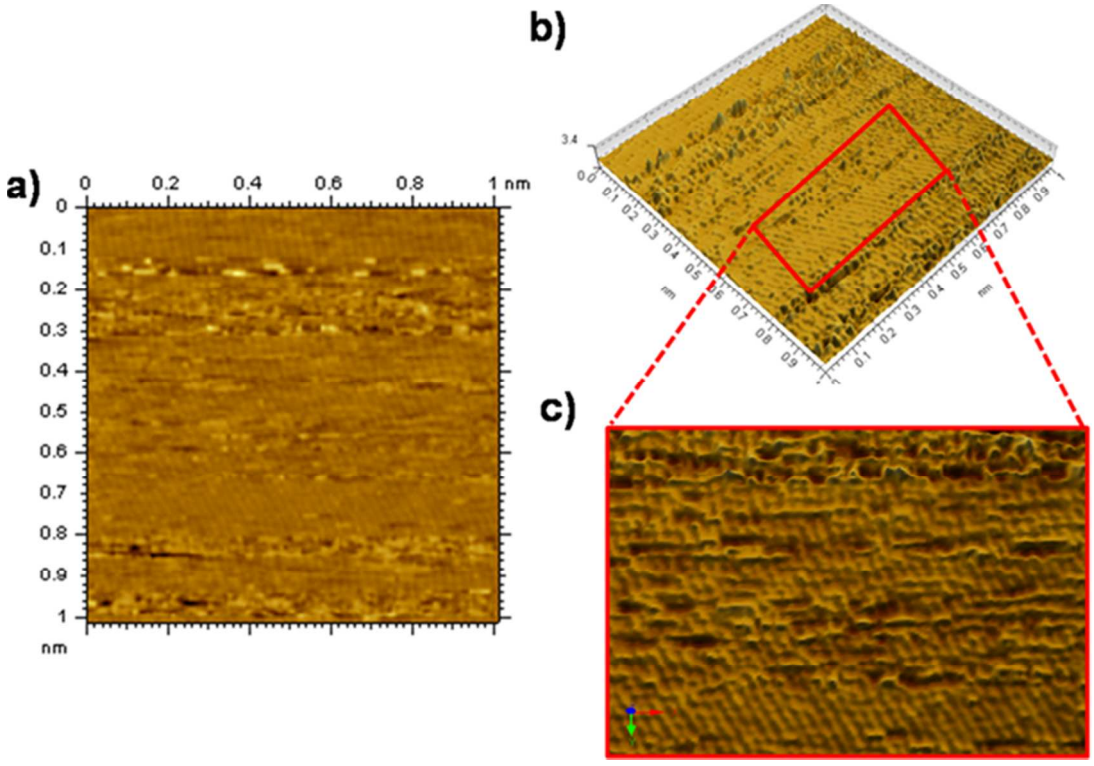


Figure S11: a) STM image (I_t = 1.22 nA, V_t = 0.2 V) of Au(111) surface used. b) 3D view of panel [a]. c) Magnified image of highlighted region in panel [b].



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