Supplementary Material

Fast and efficient direct conversion of 2-aminopyridine into 2,3-disubstituted imidazo[1,2-a]pyridines

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1. Description of 2D NMR spectra

The NMR spectra of imidazo[1,2-*a*]pyridines **3** show a doublet for a methyl group, CH neighbour to CH_3, and a quaternary carbon at 123-125 ppm. The vinylated products **4** show characteristic signals for a terminal C=CH_2, close to *o*-protons of Ar-3 (NOESY), C_q-1 of Ar-3 (HMBC), and C_q-3 (HMBC). The spectra of compound **5e** show an additional singlet for aromatic CH, which is close to CH-5 (NOESY), *o*-protons of 4-MeOPh-2 (NOESY), and C_q-2 (HMBC); no CH-CH_3 and only one 4-methoxyphenyl group. The spectra of pyrido[1,2-a]pyrimidine **6f** show a singlet for a methyl group, an additional singlet for aromatic CH and a quaternary carbon at 65 ppm.

2-Phenyl-3-(1-phenylethyl)imidazo[1,2-*a*]pyridine (**3a).** COSY cross peaks 1.841/5.048, 6.592/7.140, 6.592/7.627, 7.140/7.679, 7.269/7.339, 7.403/7.483, 7.483/7.778; NOESY cross peaks 1.841/5.048, 1.841/7.269, 1.841/7.627, 5.048/7.778, 6.592/7.140, 6.592/7.627, 7.140/7.679, 7.269/7.339, 7.269/7.627 (weak), 7. 403/7.483, 7.483/7.778; HSQC cross peaks 1.841/16.70, 5.048/33.78, 6.592/111.56, 7.140/123.74, 7.269/126.61, 7.269/126.80, 7.339/128.81, 7.403/127.68, 7.483/128.42, 7.627/124.53, 7.679/117.78, 7.778/128.92; HMBC cross peaks 1.841/33.78, 1.841/122.96, 1.841/141.11, 5.048/16.70, 5.048/122.96, 5.048/126.80, 5.048/141.11, 5.048/143.76 (weak), 6.592/117.78, 6.592/124.53, 7.140/124.53, 7.140/144.86,

7.269/126.80, 7.339/128.81, 7.339/141.11, 7.403/128.92, 7.483/128.42, 7.483/135.02, 7.627/111.56, 7.627/117.78 (weak), 7.627/123.74, 7.627/144.86, 7.679/111.56, 7.679/144.86 (weak), 7.778/127.68, 7.778/128.92, 7.778/143.76.

2-(4-Methylphenyl)-3-(1-(4-methylphenyl)ethyl)imidazo[1,2-*a*]pyridine (**3b**). COSY cross peaks 1.691/4.889, 6.463/7.025, 6.463/7.515, 7.025/7.555, 7.174/7.555; NOESY cross peaks 1.691/4.889, 1.691/7.025, 1.691/7.515, 2.230/7.025, 2.315/7.174, 4.889/7.025, 4.889/7.515, 6.463/7.025, 6.463/7.515, 7.025/7.555, 7.174/7.555; HSQC cross peaks 1.691/16.75, 2.230/20.95, 2.315/21.29, 4.889/33.49, 6.463/111.45 (td, 1H, *J* 1.12, 6.8, C*H*-6), 7.025/123.61, 7.025/126.74, 7.025/129.52, 7.174/129.18, 7.515/124.64, 7.555/117.71, 7.555/128.82; HMBC cross peaks 1.691/33.49, 1.691/122.96, 1.691/138.12, 2.230/129.52, 2.230/136.16, 2.315/129.18, 2.315/137.43, 4.889/16.75, 4.889/122.96, 4.889/126.74 (weak), 4.889/138.12, 6.463/117.71, 6.463/124.64, 7.025/20.95, 7.025/33.49, 7.025/124.64, 7.025/126.74, 7.025/129.52, 7.025/136.16, 7.025/138.18, 7.025/144.83, 7.174/21.29, 7.174/129.18, 7.174/132.18, 7.515/123.61, 7.515/144.83, 7.555/111.45, 7.555/128.82, 7.555/137.43, 7.555/143.74.

2-(4-Fluorophenyl)-3-(1-(4-fluorophenyl)ethyl)imidazo[1,2-*a*]pyridine (**3c**). COSY cross peaks 1.800/4.900, 6.611/7.145, 6.611/7.577, 6.998/7.180, 7.145/7.673, 7.145/7.642; NOESY cross peaks 1.800/4.900, 1.800/7.180, 1.800/7.577, 4.900/7.180 (weak), 4.900/7.673, 6.611/7.145, 6.611/7.577, 6.998/7.180, 7.145/7.642, 7.145/7.673; HSQC cross peaks 1.800/17.04, 4.900/33.27, 6.611/111.92, 6.998/115.44, 6.998/115.59, 7.145/115.67, 7.145/115.81, 7.145/124.14, 7.180/128.33, 7.180/128.38, 7.577/124.39, 7.642/117.87, 7.673/130.57, 7.673/130.62; HMBC cross peaks 1.800/33.27, 1.800/122.62, 1.800/136.63, 1.800/136.65, 4.900/17.04, 4.900/115.67 (weak), 4.900/115.81 (weak), 4.900/122.62, 4.900/128.33, 4.900/128.38, 4.900/136.63, 4.900/136.65, 4.900/142.86 (weak), 6.611/117.87, 6.611/124.39, 6.998/115.67, 6.998/115.81, 6.998/136.63, 6.998/136.65, 6.998/160.80, 6.998/162.43, 7.145/115.44, 7.145/115.59, 7.145/124.39, 7.145/130.99, 7.145/131.01, 7.145/144.90, 7.145/161.81, 7.145/163.44, 7.180/33.27, 7.180/128.33, 7.180/128.38, 7.180/160.80, 7.180/162.43, 7.577/111.92, 7.577/124.14, 7.577/144.90, 7.642/111.92, 7.642/144.90 (weak), 7.673/130.57, 7.673/130.62, 7.673/142.86, 7.673/161.81, 7.673/163.44.

2-(Naphthalen-1-yl)-3-(1-(naphthalen-1-yl)ethyl)imidazo[1,2-*a*]pyridine (3d). COSY cross peaks 1.754/4.751, 6.578/7.145, 6.578/7.727, 7.145/7.697; NOESY cross peaks 1.754/4.751, 1.754/7.727, 4.751/7.727, 6.578/7.145, 6.578/7.727, 7.145/7.697; HSQC cross peaks 1.754/17.56, 4.751/34.70, 6.578/111.91, 7.145/123.97, 7.697/117.90, 7.727/124.36; HMBC cross peaks 1.754/34.70, 1.754/124.57, 1.754/139.07, 4.751/17.56, 4.751/139.07, 4.751/143.07, 6.578/117.90, 7.145/124.36, 7.145/144.81, 7.643/143.07, 7.727/123.97, 7.727/144.81.

2-(4-Methoxyphenyl)-3-(1-(4-methoxyphenyl)ethyl)imidazo[1,2-*a*]pyridine (3e). COSY cross peaks 1.774/4.928, 6.559/7.099, 6.559/7.601, 6.838/7.146, 6.991/7.668, 7.099/7.626; NOESY cross peaks 1.774/4.928, 1.774/7.146, 1.774/7.601, 3.776/6.838, 3.848/6.991, 4.928/7.146 (weak), 4.928/7.601, 6.559/7.099, 6.559/7.601, 6.838/7.146, 6.991/7.668, 7.099/7.626, 7.146/7.668, 7.146/7.601; HSQC cross peaks 1.774/16.88, 3.776/55.27, 3.848/55.33, 4.928/33.08, 6.559/111.50, 6.838/114.17, 6.991/113.95, 7.099/123.68, 7.146/127.87,

7.601/124.60, 7.626/117.58, 7.668/130.10; HMBC cross peaks 1.774/33.08, 1.774/122.73, 1.774/133.10, 3.776/158.22, 3.848/159.32, 4.928/16.88, 4.928/122.73, 4.928/127.52 (weak), 4.928/133.10, 6.559/117.58, 6.559/124.60, 6.838/114.17, 6.838/133.10, 6.838/158.22 (weak), 6.991/113.95, 6.991/127.52, 6.991/159.32 (weak), 7.099/124.60, 7.099/144.77, 7.146/33.08, 7.146/127.87, 7.146/158.22, 7.601/123.68, 7.601/144.77, 7.626/111.50, 7.668/130.10, 7.668/143.38, 7.668/159.32.

2-(4-Phenyl)-3-(1-(4-phenyl)vinyl)imidazo[1,2-*a*]pyridine (4a). COSY cross peaks 5.580/6.170, 6.653/7.177, 6.653/7.634, 7.177/7.685, 7.264/7.333, 7.333/7.387, 7.333/7.934; NOESY cross peaks 5.580/6.170, 6.170/7.387, 6.653/7.177, 6.653/7.634, 7.177/7.685, 7.264/7.333, 7.333/7.387, 7.333/7.934; HSQC cross peaks 5.580/121.42, 6.170/121.42, 6.653/112.24, 7.177/124.71, 7.264/127.63, 7.333/128.32, 7.333/128.78, 7.333/129.067.387/126.17, 7.634/124.28, 7.685/117.35, 7.934/127.88; HMBC cross peaks 5.580/120.12, 5.580/137.58, 6.170/120.12, 6.170/137.58, 6.653/117.35, 6.653/124.28, 7.177/124.28, 7.177/144.81, 7.264/127.88, 7.333/128.32, 7.333/128.78, 7.333/129.06, 7.333/133.93, 7.333/137.58, 7.387/126.17, 7.387/128.78, 7.387/137.58, 7.634/112.24, 7.634/124.71, 7.634/144.81, 7.685/112.24, 7.685/144.81 (weak), 7.934/127.88, 7.934/143.37.

2-(4-Methoxyphenyl)-3-(1-(4-methoxyphenyl)vinyl)imidazo[1,2-*a*]pyridine (4e). COSY cross peaks 5.485/6.087, 6.660/7.174, 6.660/7.668, 6.863/7.330, 6.898/7.903, 7.174/7.668; NOESY cross peaks 3.809/6.863, 3.824/6.898, 5.485/6.087, 6.087/7.330, 6.660/7.174, 6.660/7.668, 6.863/7.330, 6.898/7.903, 7.174/7.668; HSQC cross peaks 3.809/55.23, 3.824/55.33, 5.485/119.10, 6.087/119.10, 6.660/111.99, 6.863/114.37, 6.898/113.76, 7.174/124.41, 7.330/127.48, 7.668/124.23, 7.668/117.12, 7.903/129.06; HMBC cross peaks 3.809/160.08, 3.824/159.20, 5.485/119.54, 5.485/130.11, 5.485/137.17 (weak), 6.087/119.54, 6.087/130.11, 6.087/137.17 (weak), 6.660/117.12, 6.660/124.23, 6.863/114.37, 6.863/130.11, 6.863/160.08 (weak), 6.898/113.76, 6.898/126.75, 6.898/159.20 (weak), 7.174/124.23, 7.174/144.80, 7.330/127.48, 7.330/137.17, 7.330/160.08, 7.668/111.99, 7.668/124.41, 7.668/144.80, 7.903/129.06, 7.903/143.12, 7.903/159.20.

2-(4-Nitrophenyl)-3-(1-(4-nitrophenyl)vinyl)imidazo[1,2-*a*]pyridine (4f). COSY cross peaks 6.821/7.316, 6.821/7.738, 7.316/7.728, 7.528/8.193, 8.039/8.176; NOESY cross peaks 5.889/6.473, 5.889/7.738, 5.889/8.039 (weak), 6.473/7.528, 6.473/8.039 (weak), 6.821/7.316, 6.821/7.738, 7.316/7.728, 7.528/8.193, 8.039/8.176; HSQC cross peaks 5.889/125.69, 6.473/125.69, 6.821/113.56, 7.316/126.23, 7.528/126.96, 7.728/117.95, 7.738/123.90, 8.039/128.22, 8.176/123.83, 8.193/124.54; HMBC cross peaks 5.889/120.34, 5.889/135.76 (weak), 5.889/143.35, 6.473/120.34, 6.473/135.76 (weak), 6.473/143.35, 6.821/117.95, 6.821/123.90, 7.316/123.90, 7.316/145.45, 7.528/126.96, 7.528/135.76, 7.528/148.08, 7.728/113.56, 7.728/145.45 (weak), 7.738/126.23, 7.738/145.45 (weak), 8.039/123.83 (weak), 8.039/128.22, 8.039/141.17, 8.039/147.10, 8.176/123.83, 8.176/128.22 (weak), 8.176/139.99, 8.176/147.10, 8.193/124.54, 8.193/143.35, 8.193/148.08.

2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine (5e). COSY cross peaks 6.748/7.152, 6.748/8.081, 6.988/7.901, 7.152/7.620; NOESY cross peaks 3.862/6.988, 6.748/7.152,

6.748/8.081, 6.988/7.901, 7.152/7.620, 7.764/7.901, 7.764/8.081; HSQC cross peaks 3.862/55.33, 6.748/112.25, 6.988/114.15, 7.152/124.47, 7.620/117.28, 7.764/107.26, 7.901/127.30, 8.081/125.49; HMBC cross peaks 3.862/159.58, 6.748/117.28, 6.748/125.49, 6.988/114.15, 6.988/127.30, 6.988/159.58, 7.152/125.49, 7.152/145.63, 7.620/107.26 (weak), 7.620/112.25, 7.620/145.63, 7.764/145.72, 7.901/107.26 (weak), 7.901/126.50 (weak), 7.901/127.30, 7.901/145.72, 7.901/159.58, 8.081/112.25, 8.081/124.47, 8.081/145.63.

4-Methyl-2,4-bis(4-nitrophenyl)-4*H*-pyrido[1,2-*a*]pyrimidine (6f). COSY cross peaks 6.039/6.743, 6.039/6.962, 6.723/6.962, 7.636/8.173, 7.834/8.093; NOESY cross peaks 2.111/5.106, 2.111/6.743, 2.111/7.636, 5.106/7.636 (weak), 5.106/7.834, 6.039/6.743, 6.039/6.962, 6.723/6.962, 7.636/8.173, 7.834/8.093; HSQC cross peaks 2.111/29.32, 5.106/105.05, 6.039/110.05, 6.723/124.83, 6.743/133.47, 6.962/134.71, 7.636/127.35, 7.834/126.39, 8.093/123.44, 8.173/124.16; HMBC cross peaks 2.111/64.90, 2.111/105.05, 2.111/152.87, 5.106/29.32, 5.106/64.90, 5.106/144.89, 5.106/152.87 (weak), 6.039/124.83, 6.039/133.47, 6.723/110.05, 6.743/134.71, 6.743/151.48, 6.962/133.47, 6.962/151.48, 7.636/127.35, 7.636/147.33, 7.834/126.39, 7.834/140.11, 7.834/147.41, 8.093/123.44, 8.093/144.89, 8.093/147.41 (weak), 8.173/124.16, 8.173/147.33 (weak), 8.173/152.87.

2. Crystallography

2-Phenyl-3-(1-phenylethyl)imidazo[1,2-*a*]pyridine (**3a).** Crystals of **3a** were obtained from a CH_2Cl_2/heptane solution. An *ORTEP* view of the molecule is reported on Figure 2 together with the atomic labeling scheme. Selected bond lengths [Å]: C11–N12 1.312(6), C21–N22 1.330(6), N12–C13 1.346(6), N22–C23 1.382(6), C13–C14 1.358(7), C23–C24 1.397(6), C116–C117 1.544(6), C216–C217 1.551(6), C14–C116 1.516(6), C24–C216 1.502(6). Compound **3a** crystallizes in the monoclinic centrosymmetric *P* $2_1/c$ space group, with two independent molecules in the asymmetric unit (Table S1). Both R and S enantiomers are present in the crystals as seen on Figure S1. The majority of bond lengths and angles are comparable in the two independent molecules. The ring systems are nearly planar with respective rmsd of (0.0122, 0.0114), (0.0095, 0.0041) and (0.0051, 0.0049) for the imidazo[1,2-*a*]pyridine, 2-phenyl and the 3-phenyl substituents in the two molecules. The angles between the mean planes of the imidazole/2-phenyl and imidazole/3-phenyl rings are also similar in the two molecules: 39.1(2)^o, 42.8(2)^o and 79.9(2)^o, 86.2(2)^o, respectively. The crystal packing does not show hydrogen bonding or weak interactions. The lack of such interaction, usually associated with the stabilization of the crystal structure, is probably responsible for the difficulties in the obtainment of single crystals. The main structural dissimilarity between the two molecules in the ASU relates to the positioning of the phenyl from the substituent at the 3 position, which is clearly demonstrated by the overlay of the two molecules shown on Figure 3a. Thus, the angle between the mean planes of the imidazole and 3-phenyl moiety in the two molecules is 79.9(2)^o and 86.2(2)^o, respectively. Even slighter differences are observed for the 2-phenyl moiety in the two molecules; the angle between the imidazo[1,2-*a*]pyridine and 2-phenyl mean planes is 39.1(2)^o and 42.8(2)^o.

2-(4-Phenyl)-3-(1-(4-phenyl)vinyl)imidazo[1,2-*a*]pyridine (4a). Compound **4a** crystallizes from heptane in the monoclinic centrosymmetric *P* $2_1/c$ space group, with two independent molecules in the asymmetric unit (Table S1). An *ORTEP* view of the molecule is reported on Figure 4 together with the atomic labeling scheme. Selected bond lengths [Å]: C11–N12 1.333(3), N12–C13 1.375(3), C13–C14 1.376(3), C13–C110 1.474(3), C21–N22 1.327(3), N22–C23 1.379(3), C23–C24 1.369(3), C23–C210 1.477(3). The majority of bond lengths and angles are comparable in the two independent molecules. The ring systems are nearly planar with respective rmsd of (0.0106, 0.0125), (0.0012, 0.0012) and (0.0054, 0.0067) for the imidazo[1,2-*a*]pyridine, 2-phenyl and the 3-phenyl substituents in the two molecules. The angles between the mean planes of the imidazole/3-phenyl rings are also similar in the two molecules: 84.2(2)^o and 77.9(2)^o, respectively. On the other hand the angle between the mean planes of the imidazole/2-phenyl rings is quite different 16.2(2)^o, 46.6(2)^o. Similarly to **3a** the crystal packing (Figure 3b) does not show hydrogen bonding or weak interactions. As in **3a**, the dissimilarity between the two molecules in the ASU of **4a** is associated to the rotation of the phenyl along C13-C110/C23-C210 (Figure 3b). The rotation of the phenyl ring C-C bond is 63.31^o and thus "obliges" the existence of two molecules per ASU (Figure S2).

2-(4-Methoxyphenyl)imidazo[1,2-*a*]pyridine (5e). Crystals of **5e**, suitable for single crystal X-ray analysis (Table S1), were obtained by slow evaporation from $CHCl_3$/ethyl acetate solution. An *ORTEP* view of the molecule is reported on Figure 5 together with the atomic labeling scheme. Selected bond lengths [Å]: C1–N2 1.329(3), N2–C3 1.374(3), C3–C4 1.377(3), C3–C10 1.468(3). Compound **5e** crystallizes in the orthorhombic noncentrosymmetric *Pna2*$_1$ space group, with one independent molecule in the asymmetric unit. The noncentrosymmetry is due to the packing of the molecules as no chiral centers are present. The majority of bond lengths and angles are comparable with those of compound **3a**. The ring systems are nearly planar with respective rmsd of 0.0102 and 0.0084 Å for imidazo[1,2-*a*]pyridine and 2-phenyl. The angle between the mean planes of the imidazole/2-phenyl ring is 12.5(4)^o while in **3a** the values ranged between 39^o and 43^o. The crystal packing of the molecules of **5e** does not show typical hydrogen bonds however, weak C-H…..π interactions can be detected. The main structural dissimilarity between compounds **3a** and **5e** relates to the positioning of the 2-phenyl with respect to the imidazo[1,2-*a*]pyridine one (Figure 3a).

Table S1. Crystal data for **3a**, **4a** and **5e**

Compound	**3a**	**4a**	**5e**
Formula	$C_{21}H_{18}N_2$	$C_{21}H_{16}N_2$	$C_{14}H_{12}N_2O_1$
MW	298.37	296.365	224.26
Crystal system	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_1/c$	$P2_1/c$	$Pna2_1$
a [Å]	25.370(4)	9.6379(6)	6.3186(4)
b [Å]	6.0454(11)	8.3186(7)	7.1021(5)
c [Å]	21.181(2)	40.816(2)	24.4768(14)
α, β, γ [°]	90/87.341(11)/90	90/103.038(6)/90	90/90/90
V [Å^3]	3245.1(8)	3188.1(4)	1098.4(2)
Z	4	4	4
F_{000}	1264	1248	472
$D_{calculated}$ [Mg m^{-3}]	1.221	1.235	1.356
Crystal size, [mm]	0.15x0.14x0.12	0.24x0.22x0.24	0.35x0.25x0.25
Reflections collected/unique	11281/5731	14219/6442	3617/1837
Reflections observed [$I > 2\sigma(I)$]	2182	3445	1661
Parameters	419	415	155
R indices [$F^2 > 2\sigma(F^2)$], *R1//wR*	0.044/0.056	0.062/0.12	0.040/0.103
R indices [F^2, all data], *R/ wR1*	0.030/0.082	0.13/0.15	0.047/0.096

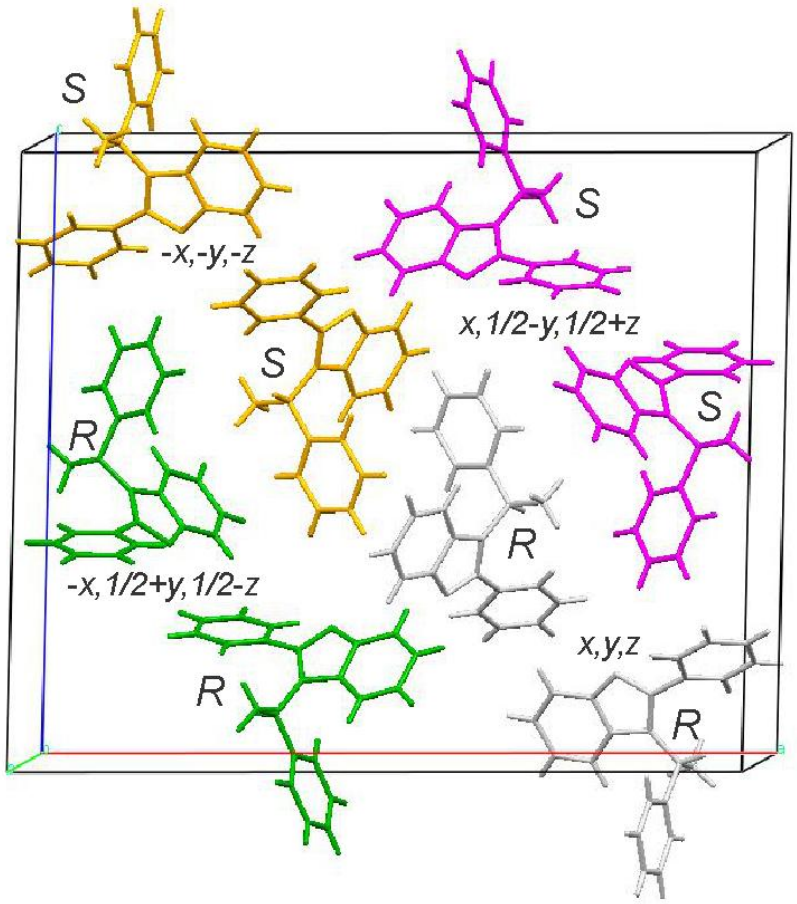

Figure S1. Crystal packing of **3a**. The R and S stereo centers are shown along with the symmetry operations for generating the molecules.

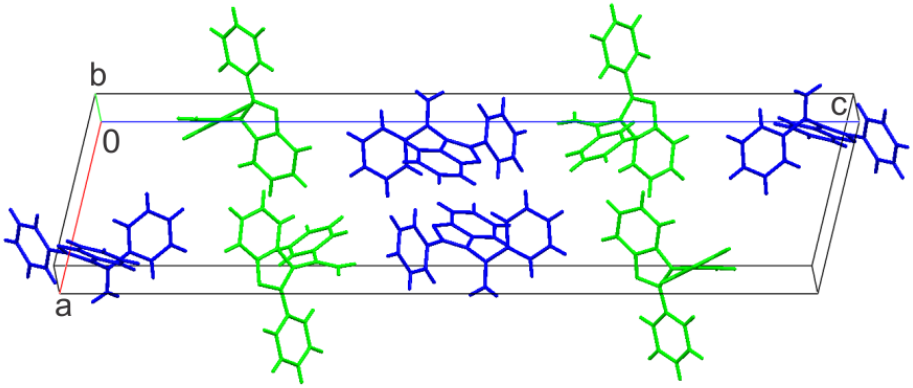

Figure S2. Crystal packing of **4a**.

