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Supporting information for:

The effects of molecular flexibility and substituents on conformational polymorphism in a series of 2,5-diamino-3,6-dicyanopyrazine dyes with highly flexible groups

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Table S1-S6.

Figure S1.

Table legends

Table S1. Solvent combinations for solvent diffusion method for crystallisation.

Table S2. Conformational similarities in all observed molecular conformations. The similarity was determined by RMSD calculated using the Molecule Overlay module of Mercury 3.3. RMSD is the root mean square deviation of distance between two molecular structures. The calculation was performed using the modified molecular conformations in which the terminal substituent on the benzyl group in each molecular conformation was converted to a hydrogen atom. RMSD values lower than 1 Å in this table are highlighted. These low values indicated that these pairs exhibited molecular similarity.

Table S3. List of compounds with the same refcode in the search for compounds containing the target fragment in the CSD. The structural similarity was evaluated using the Crystal Packing Similarity module of Mercury 3.3. The number of matched molecules was set as the number of molecules in common between the two crystal structures [19]. The size of the compared molecule cluster in the two structures was 15 molecules. RMSD is the root mean square deviation of distance between two crystal structures. PXRD is the powder pattern similarity. The two parameters for geometric tolerances were 20%.

Table S4. Incidences of polymorphism in the compounds with the target fragment in the CSD. Polymorph occurrence was altered by the type of covalent bond between *Z* and *X* in the target fragment (Fig. 3).

Table S5. Short contacts in all observed crystal structures.

Table S6. Lattice energy[a] of all forms, and total crystal energy[b] in the polymorphs of derivatives **2** and **3**.

Figure legend

Figure S1. DSC traces of the crystal forms in the derivatives **1**–**5**. (a) **1O**, (b) **2R** and **2Y**, (c) **3R** and **3Y**, (d) **4Y**, and (e) **5O**.

Table S1. Solvent combinations for solvent diffusion method for crystallisation.

1O	$CHCl_3$/*n*-hexane	**3R**	$CHCl_3$/*n*-hexane
2Y	THF/methanol	**3RV**	Benzene/*n*-hexane
2R	THF/methanol	**4Y**	1,4-dioxane/methanol
3Y	$CHCl_3$/ethanol	**4O**	Benzene[a]
3YO	$CHCl_3$/ethanol	**5O**	$CHCl_3$[a]
3O	Benzene[a]		

[a] Slow evaporation at room temperature.

Table S2. Conformational similarities in all observed molecular conformations. The similarity was determined by RMSD calculated using the Molecule Overlay module of Mercury 3.3. RMSD is the root mean square deviation of distance between two molecular structures. The calculation was performed using the modified molecular conformations in which the terminal substituent on the benzyl group in each molecular conformation was converted to a hydrogen atom. RMSD values lower than 1 Å in this table are highlighted. These low values indicated that these pairs exhibited molecular similarity.

RMSD/Å	**2Y**	**2R**	**3Y**	**3YO**	**3R**	**4Y**	**5O**
1O	1.0565	1.3476	1.060	1.5879	1.3535	1.0404	1.0620
2Y	-	1.4171	0.0688	1.4729	1.3970	0.1334	0.2439
2R	-	-	1.4375	1.2088	0.5252	1.3971	1.4111
3Y	-	-	-	1.4845	1.4147	0.1431	0.2283
3YO	-	-	-	-	1.4135	1.4711	1.3574
3R	-	-	-	-	-	1.4013	1.3765
4Y	-	-	-	-	-	-	0.3354

Table S3. List of compounds with the same refcode in the search for compounds containing the target fragment in the CSD. The structural similarity was evaluated using the Crystal Packing Similarity module of Mercury 3.3. The number of matched molecules was set as the number of molecules in common between the two crystal structures [19]. The size of the compared molecule cluster in the two structures was 15 molecules. RMSD is the root mean square deviation of distance between two crystal structures. PXRD is the powder pattern similarity. The two parameters for geometric tolerances were 20%.

Refcode	Number of matched molecule	RMSD/Å	PXRD similarity	Occurrence of polymorph
DICGED vs DICGED01	1	0.355	0.92	polymorphs
ICUBAL vs ICUBAL01	3	0.889	0.924	polymorphs
NUPJOX vs NUPJOX01	15	0.017	1	No polymorph
NUPJOX01 vs NUPJOX02	8	1.229	0.934	polymorphs
TIBGAN vs TIBGAN01	4	0.572	0.948	polymorphs
IMUQEM vs IMUQEM01	3	0.993	0.998	polymorphs
ESAHUB vs ESAHUB01	15	0.094	0.996	No polymorph
KEGVAV vs KEGVAV01	15	0	1	No polymorph
NALWUS vs NALWUS02	15	0.174	0.990	No polymorph
NANSUR vs NANSUR01	15	0.043	0.999	No polymorph
NODQAY vs NODQAY01[a]	-	-	-	No polymorph
TBENZA vs TBENZA02	15	0.123	0.995	No polymorph
EBULES vs EBULES01	15	0.072	0.996	No polymorph
UDEVUU vs UDEVUU01	15	0	1	No polymorph
VEXRIZ vs VEXRIZ01	15	0.071	0.997	No polymorph
VUKBAE vs VUKBAE01[b]	-	-	-	No polymorph
ZAWSUL vs ZAWSUL01	15	0.030	0.998	No polymorph
JUKTEO vs JUKTEO01	15	0.013	1	No polymorph

[a] The comparison between these structures could not be performed because the crystal structures were disordered. The lattice parameters between these structures are equal; thus, the relationship between these structures was considered non-polymorphic.
[b] The comparison between these structures could not be performed. In VUKBAE, hydrogens were not present, while the position of hydrogen was fixed in VUKBAE01. The lattice parameters between these structures are quite similar; thus, the relationship between these structures was considered non-polymorphic.

Table S4. Incidences of polymorphism in the compounds with the target fragment in the CSD. Polymorph occurrence was altered by the type of covalent bond between *Z* and *X* in the target fragment (Fig. 3).

	Covalent bond between *Z* and *X*		
	Single bond	Non-aromatic double bond[a]	Aromatic double bond
Number of polymorphic compounds[b]	3 (1%)	0 (0%)	2 (6%)
Total compounds	285	63	33

[a] The double bonds in this group excluded aromatic double bonds.
[b] The value in parentheses is the incidence of polymorphism.

Table S5. Short contacts in all observed crystal structures.

	Packing structures	Interactions	Distance (d/D)[a]	θ[b]	Symmetry operation
1O	Intra-1D column	C-H_{ph2}···N_{CN}	2.560/3.618(3)	163.6	x, ±1+y, z
	Inter-1D column	C- H_{CH2}···π_{ph}	2.745/3.673	143.0	x, 1-y, ±1/2+z
		C-H_{ph4}···C_{ph3}	2.827/3.820(5)	151.5	x, 1-y, ±1/2+z
		C-H_{ph4}··· H_{ph3}-C	2.116/3.956(6)	125.7/153.9	x, -y, ±1/2+z
		C-H_{ph4}···C_{ph3}	2.890/3.956(6)	166.3	x, -y, ±1/2+z
		C-H_{ph3}···H_{ph3}-C	2.226/4.180(6)	163.5/144.5	x, 2-y, ±1/2+z
		C-H_{ph4}··· H_{ph4}-C	2.387/4.004(6)	125.7/125.7	-x, y, 1/2-z
		C-H_{CH2}···C_{ph3}	2.768/3.783(5)	155.0	-x, 1-y, -z
		C-H_{ph3}···π_{ph}	2.688/3.653	147.5	-x, 1-y, -z
		C-H_{ph4}···C_{ph3}	2.768/3.803(8)	158.7	1/2-x, ±1/2+y, 1/2-z
2Y	Inter-1D column	C-H_{ph3}···N_{CN}	2.478/3.419(3)	143.9	x, 1-y, ±1/2+z
		C-H_{Me}··· H_{Me}-C	2.166/3.858(3)	129.4/129.4	1-x, y, 2.5-z
		C-H_{ph2}···H_{ph2}-H	2.181/4.075(3)	138.4/138.4	1-x, 1-y, 2-z
2R	Intra-1D column	C-H_{ph2}···N_{CN}	2.638/3.488(8)	134.4	±1+x, y, z
		C-H_{ph2}···N_{CN}	2.538/3.485(8)	144.7	±1-x, 1-y, 1-z
		C-H_{Me}···C_{ph2}	2.881/3.665(8)	128.9	±1+x, y, z
		C-H_{Me}···C_{ph3}	2.862/3.782(9)	142.2	±1+x, y, z
	Inter-1D column	C-H_{Me}···H_{ph3}-C	2.133/3.92(1)	127.6/167.8	-1+x, y,1+z 1+x, y, -1+z
		C-H_{Me}···N_{CN}	2.732/3.566(9)	133.2	x, y, ±1+z
		C-H_{Me}···C_{ph3}	2.892/3.98(1)	173.3	-1+x, 1/2-y, 1/2+z 1+x, 1/2-y, -1/2+z
3Y	Inter-1D column	C-H_{ph3}···N_{CN}	2.500/3.371(3)	136.1	x, 1-y, ±1/2+z
		C-H_{ph2}···H_{ph2}-C	2.204/4.091(4)	138.0/138.0	-x, 1-y, 1-z
		C-Cl···H_{CH2}	2.879/3.921(3)	160.2	-x, -y, 1-z
3YO	Intra-1D column	C-H_{ph2}···N_{CN}	2.723/3.780(5)	163.6	-1+x, y, z
	Inter-1D	C-Cl···N_{CN}	-/3.181(3)	169.6(1)	±1.5+x, 1/2-y, 1/2+z

	column	C-H $_{ph3}$···C$_{py}$	2.864/3.787(4)	142.5	-1/2+*x*, 1/2-*y*, 1/2+*z*, 1/2+*x*, 1/2-*y*, -1/2+*z*
		C-H $_{ph3}$···C$_{CN}$	2.844/3.605(4)	127.0	-1/2+*x*, 1/2-*y*, 1/2+*z*, 1/2+*x*, 1/2-*y*, -1/2+*z*
		C-H $_{ph3}$···N$_{py}$	2.508/3.567(3)	163.8	-1/2+*x*, 1/2-*y*, 1/2+*z*, 1/2+*x*, 1/2-*y*, -1/2+*z*
		C-H$_{ph3}$···π_{ph}	2.581/3.657	169.38	1/2+*x*, 1/2-*y*, 1/2+*z*, -1/2+*x*, 1/2-*y*, -1/2+*z*
3R	Inter-1D column	C-H$_{ph2}$···Cl	2.714/3.650(2)	143.8	1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{CH2}$···N$_{CN}$	2.586/3.373(2)	128.5	-1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{ph3}$···Cl	2.884/3.774(3)	139.1	-1/2-*x*, -1/2+*y*, -1/2-*z*
		C$_{CN}$···Cl	-/3.418	83.7(1)/107.97(9)	1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{ph3}$···N$_{CN}$	2.531/3.562(4)	157.7	1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{ph3}$···H$_{ph2}$-C	2.373/4.279(4)	145.3/141.8	-1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{ph3}$···H$_{CN2}$-C	2.317/3.894(3)	124.0/116.4	-1/2-*x*, ±1/2+*y*, -1/2-*z*
		C-H$_{ph2}$···Cl	2.913/3.700(3)	129.3	-1-*x*, 1-*y*, -*z*
		C-H$_{ph2}$···π_{ph}	2.794/3.792	152.3	-*x*, 1-*y*, -*z*
4Y	Inter-1D column	C-H$_{ph3}$···N$_{CN}$	2.371/3.371(8)	151.9	-1/2+*x*, -1/2-*y*, 1/2+*z*, 1/2+*x*, -1/2-*y*, -1/2+*z*
		C-H$_{ph3}$···C$_{ph3}$	2.900/3.927(8)	157.4	1.5-*x*, ±1/2+*y*, 1/2-*z*
		C-H$_{ph3}$···Br	2.974/3.949(6)	149.2	1.5-*x*, ±1/2+*y*, 1/2-*z*
		C-H$_{CH2}$···Br	2.973/3.987(6)	155.0	1.5-*x*, ±1/2+*y*, 1/2-*z*
5O	Intra-1D column	C-N$_{CN}$···C$_{CN}$	-/3.242	81.4(2)/82.9(3)	1/2-*x*, 1.5-*y*, -*z*
		C- H$_{ph}$··· H$_{ph}$-C	2.352/4.071(5)	124.0/133.0	*x*, ±1+*y*, *z*
	Inter-1D column	C-H$_{ph}$···N$_{CN}$	2.562/3.427(5)	135.8	*x*, 1-*y*, -1/2+*z*
		C-H$_{CH2}$···C$_{ph}$	2.837/3.661(5)	132.4	1/2-*x*, ±1/2+*y*, 1/2-*z*
		C-H$_{CH2}$···C$_{ph}$	2.722/3.670(5)	145.4	1/2-*x*, ±1/2+*y*, 1/2-*z*
		C- H$_{ph}$··· C$_{ph}$	2.760/3.631(6)	136.8	*x*, -*y*, ±1/2+*z*
		C- H$_{ph}$··· H$_{ph}$-C	2.260/3.942(7)	114.0/171.3	*x*, -1-*y*, ±1/2+*z*
		C- H$_{ph}$··· C$_{ph}$	2.880/3.942(7)	165.0	*x*, -1-*y*, ±1/2+*z*

	$C\text{-}H_{ph}\cdots C_{ph}$	2.778/3.730(5)	146.0	*-x*, *-y*, *-z*
	$C\text{-}H_{ph}\cdots C_{ph}$	2.621/3.613(4)	151.1	*-x*, *-y*, *-z*

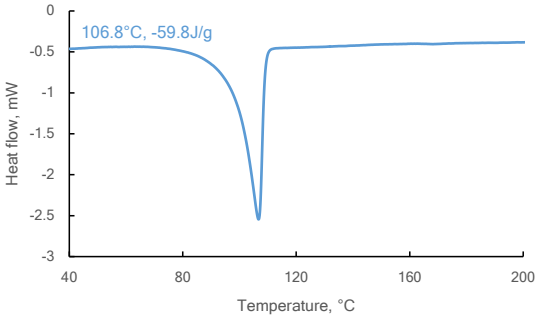
[a] *d* represents the H···A distance (Å), and *D* represents the D···A distance (Å).
[b] θ represents the D-H···A angle (°).
H_{phn} is a hydrogen atom of the phenyl ring or naphthyl ring and n is the position on the phenyl ring. For example, H_{ph4} represents the hydrogen in the 4-position of the phenyl ring. C_{phn} is a carbon atom of the phenyl ring and n is the position on the phenyl ring.
H_{CH2} is the hydrogen atoms of the methylene group, N_{CN} is the nitrogen atom of a cyano group, and N_{py} is a nitrogen atom of the pyrazine ring. π_{ph} represents the centre of the phenyl ring. H_{Me} is the hydrogen atoms of the methyl groups in derivative **2**.

Table S6. Lattice energy[a] of all forms, and total crystal energy[b] in the polymorphs of derivatives **2** and **3**.

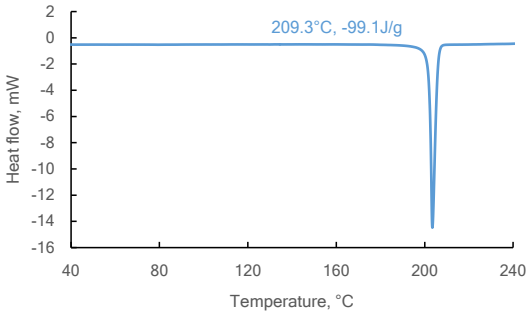
	Lattice energy [kcal/mol]	Relative conformational energy[c] [kcal/mol]	Total energy[b] [kcal/mol]
1O	−45.1	-	-
2Y	−51.4	0.00	−51.4
2R	−53.8	15.8	−38.0
3Y	−52.8	1.27	−51.5
3YO	−48.3	0.00	−48.3
3R	−51.4	1.28	−50.1
4Y	−57.9	-	-
5O	−67.5	-	-

[a] Lattice energy was calculated using the AA-CLP model.
[b] Total energy was estimated from the sum of the lattice energy and the relative conformational energy.
[c] Relative conformational energy was an energy difference from the conformational energy of the lowest-energy forms.

Figure S1. DSC traces of the crystal forms in the derivatives **1–5**. (a) **1O**, (b) **2R** and **2Y**, (c) **3R** and **3Y**, (d) **4Y**, and (e) **5O**.



(a)



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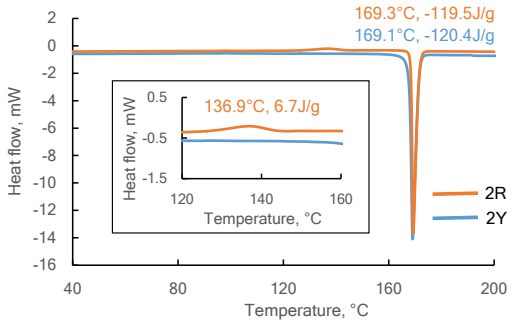

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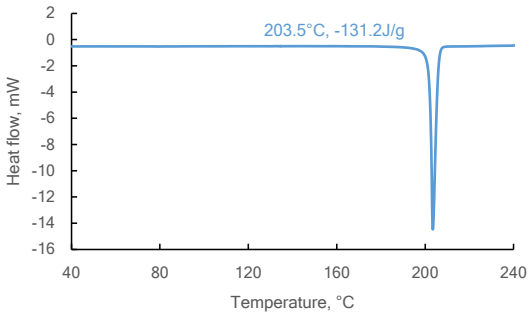

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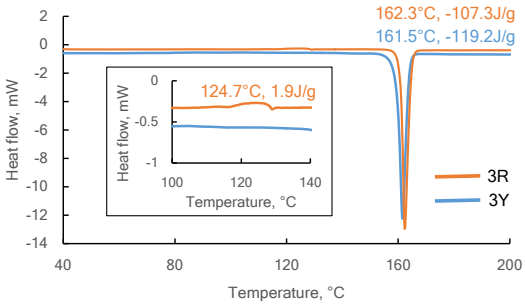

(c)