SUPPORTING INFORMATION

Halogen-bonded cocrystals of donepezil with perfluorinated diiodobenzenes

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EXPERIMENTAL DETAILS

Preparation of **dpz**

1.0 g (2.4 mmol) of donepezil hydrochloride was suspended in 20.0 mL of 96% ethanol. The precipitate was dissolved by heating, at which point 10.0 mL of concentrated ammonia solution was added. The resulting mixture was washed by distilled water, dissolved in 10.0 mL of 96% ethanol and left to crystallize overnight at room temperature.

MECHANOCHEMICAL SYNTHESES

Reaction mixtures were placed in a 10 mL stainless steel jar along with a small amount of acetonitrile (ACN) and two stainless steel balls 7 mm in diameter. The reaction mixtures were then milled for 20 minutes in a Retsch MM200 Shaker Mill operating at 25 Hz. Experimental details follow in Table S1.

Table S1. Mechanochemical synthesis parameters. $t_{milling}$ = 20 min, $\nu_{milling}$ = 25 Hz.

reactants	mole ratio	*m*(dpz) / mg	*m* or *V*(donor)	*V*(ACN) / µL	result
dpz : **13tfib**	**1 : 1**	**29.1**	**11.6 µL**	**15.0**	**powder**
	1 : 2	**19.2**	**15.3 µL**	**15.0**	**powder**
dpz : **14tfib**	**1 : 1**	**38.9**	**41.1 mg**	**25.0**	**powder**
	1 : 2	**29.1**	**30.9 mg**	**20.0**	**powder**

SOLUTION SYNTHESES

Single crystals of (**dpz**)(**13tfib**)

9.6 mg of **dpz** (25 µmol) was dissolved in 1.0 mL of acetonitrile, after which 7.7 µL of **13tfib** (21 mg, 51 µmol) was added into the solution. 2 minutes later seed crystals obtained by mechanochemical means were added into the solution and it was left then to crystallize at room temperature.

Single crystals of (**dpz**)(**14tfib**)$_2$

20.0 mg of the mechanochemical product (with stoichiometry **dpz** : **14tfib** of 1:2) was dissolved in 2.0 mL of acetone and left to crystallize at room temperature.

THERMAL ANALYSIS

DSC measurements were performed on a Mettler-Toledo DSC823^e module. The samples were placed in sealed aluminium pans (40 μL) with three holes made on the top cover, and heated in flowing nitrogen (150 mL min^{-1}) from 25 °C to 500 °C at a rate of 10 °C min^{-1}. The **ipfb** sample was heated in flowing nitrogen (150 mL min^{-1}) from 25 °C to –75 °C at a rate of 10 °C min^{-1}, held at –75 °C for 2 minutes and then heated up to 100 °C at a rate of 10 °C min^{-1} The data collection and analysis was performed using the program package STAR^e Software 15.00.[1]

POWDER X-RAY DIFFRACTION EXPERIMENTS

PXRD experiments were performed on a PHILIPS PW 1840 X-ray diffractometer with Cu*K*α1 (1.54056 Å) radiation at 40 mA and 40 kV. The scattered intensities were measured with a scintillation counter. The angular range was from 5 to 40° (2θ) with steps of 0.02 – 0.03°, and the measuring time was 0.2 – 0.5 s per step. Data collection and analysis was performed using the program package Philips X'Pert.[2]

SINGLE-CRYSTAL X-RAY DIFFRACTION EXPERIMENTS

The crystal and molecular structures of the prepared samples were determined by single crystal X-ray diffraction. Details of data collection and crystal structure refinement are listed in Table S1. Diffraction measurements were made on an Oxford Diffraction Xcalibur Kappa CCD X-ray diffractometer with graphite-monochromated MoKα (λ = 0.71073Å) radiation. The data sets were collected using the ω scan mode over the 2θ range up to 54°. Programs CrysAlis CCD and CrysAlis RED were employed for data collection, cell refinement, and data reduction.[3] The structures were solved by direct methods and refined using the SHELXS, SHELXT, and SHELXL programs, respectively.[4, 5] The structural refinement was performed on F^2 using all data. Hydrogen atoms were placed in calculated positions and treated as riding on their parent atoms. The **dpz** molecule in the (**dpz**)(**13tfib**) and (**dpz**)(**14tfib**)$_2$ cocrystals was treated as being present in both *R* and *S* enantiomer forms in the crystal structure – the positions of the relevant carbon atoms were found in the Fourier map, with their occupancy refined. All calculations were performed using the WINGX crystallographic suite of programs.[6] The molecular structures of compounds and their molecular packing projections were prepared by Mercury.[7]

References

1. STARe Evaluation Software Version 15.00, Mettler–Toledo GmbH, 2016.
2. Philips X'Pert Data Collector 1.3e, Philips Analytical B. V. Netherlands, 2001; Philips X'Pert Graphic & Identify 1.3e Philips Analytical B. V. Netherlands, 2001; Philips X'Pert Plus 1.0, Philips Analytical B. V. Netherlands, 1999.
3. Oxford Diffraction, Oxford Diffraction Ltd., Xcalibur CCD system, CrysAlis CCD and CrysAlis RED software, Version 1.170, 2003.
4. (a) G. M. Sheldrick, *Acta Cryst. A*, 2008, **64**, 112–122; (b) G. M. Sheldrick, *Acta Cryst. C*, 2015, **71**, 3–8.
5. G. M. Sheldrick, *Acta Cryst. A*, 2015, **71**, 3–8.
6. L. J. Farrugia, *J. Appl. Cryst.*, 2012, **45**, 849–854.
7. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. v. d. Streek and P. A. Wood, *J. Appl. Crystallogr.* **2008**, 41, 466.

Table S2. Crystal data and refinement details for the prepared compounds.

	(**dpz**)(**13tfib**)	(**dpz**)(**14tfib**)$_2$
Molecular formula	$(C_{24}H_{29}NO_3)(C_6F_4I_2)$	$(C_{24}H_{29}NO_3)(C_6F_4I_2)_2$
M_r	781.34	1183.20
Crystal system	triclinic	monoclinic
Space group	$P\,\bar{1}$	$P\,2_1/c$
Crystal data:		
a / Å	9.9701(6)	26.652(3)
b / Å	12.1010(12)	15.0198(16)
c / Å	13.0835(12)	10.0293(17)
α / °	81.131(8)	90
β / °	77.847(6)	96.783(12)
γ / °	88.453(6)	90
V / Å^3	1524.6(2)	3986.7(10)
Z	2	4
D_{calc} / g cm^{-3}	1.702	1.971
λ(MoK_α) / Å	0.71073	0.71073
T / K	295	295
Crystal size / mm^3	0.49 x 0.44 x 0.05	0.47 x 0.15 x 0.10
μ / mm^{-1}	2.118	3.199
F(000)	764	2240
Refl. collected/unique	6570 / 3985	8644 / 4144
Parameters/restraints	380 / 1	488 / 0
$\Delta\rho_{max}$, $\Delta\rho_{min}$ / e Å^{-3}	0.901; –0.678	1.901; –1.334
$R[F^2 > 4\sigma(F^2)]$	0.0518	0.0697
w$R(F^2)$	0.1181	0.2034
Goodness-of-fit, S	1.005	1.054

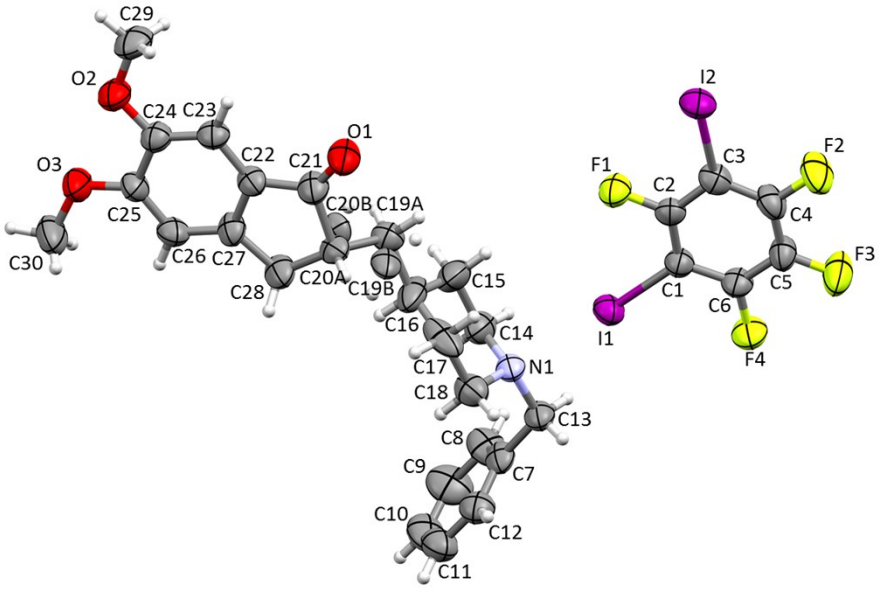

Figure S1. Molecular structure of (**dpz**)(**13tfib**) showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50 % probability level, and H atoms are shown as small spheres of arbitrary radius. The asymmetric unit of (**dpz**)(**13tfib**) contains one molecule of **dpz** and one molecule of **13tfib**.

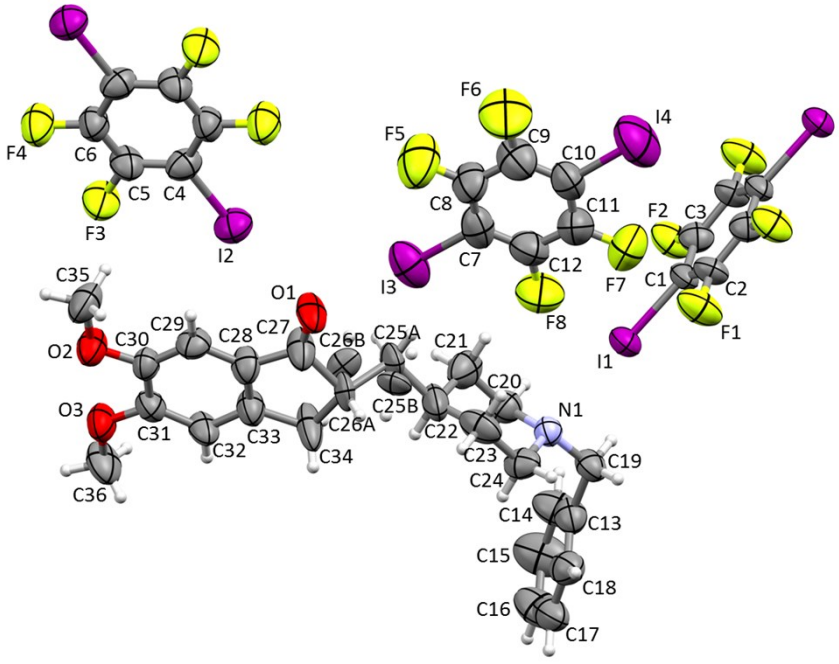

Figure S2. Molecular structure of (**dpz**)(**14tfib**)$_2$ showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50 % probability level, and H atoms are shown as small spheres of arbitrary radius. The asymmetric unit of (**dpz**)(**14tfib**)$_2$ contains one molecule of **dpz** and one full and two symmetrically inequivalent halves of **14tfib** molecules.

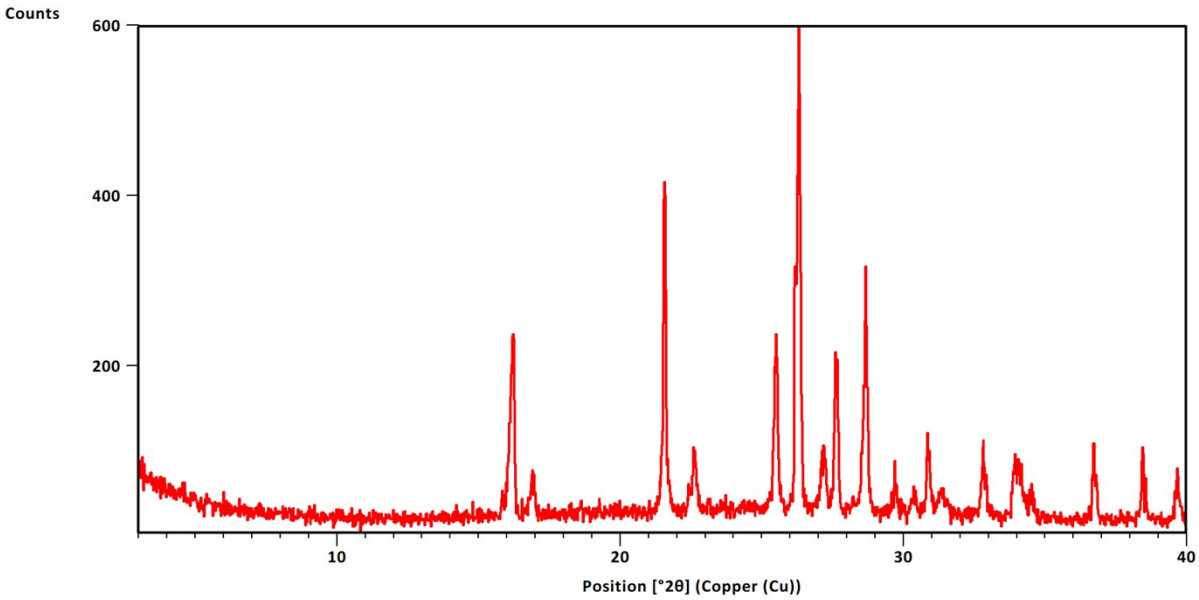

Figure S3. PXRD pattern of **14tfib**.

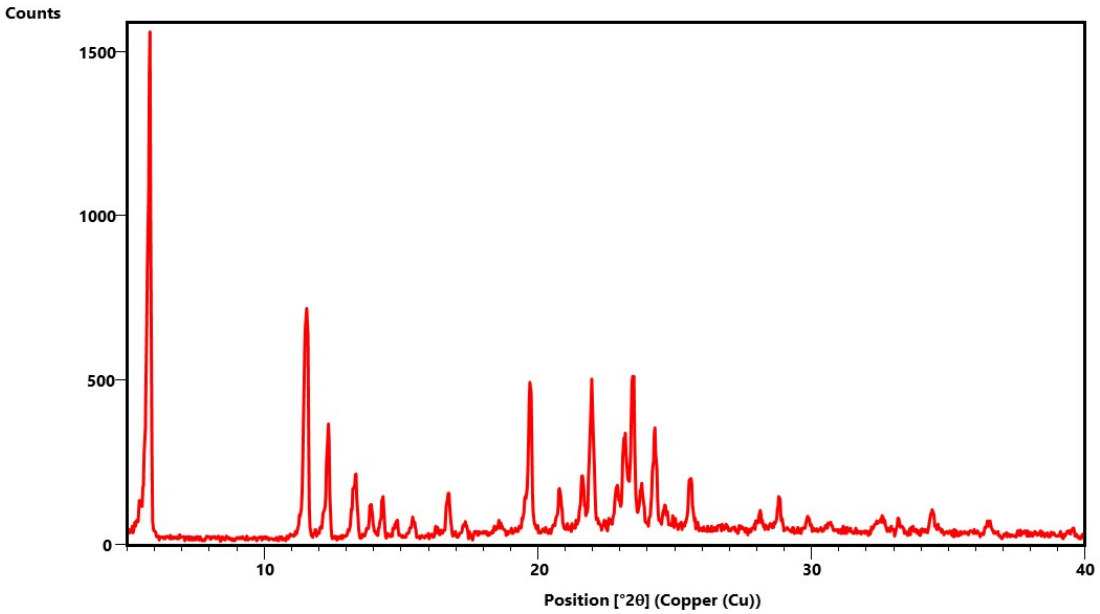

Figure S4. PXRD pattern of **dpz**.

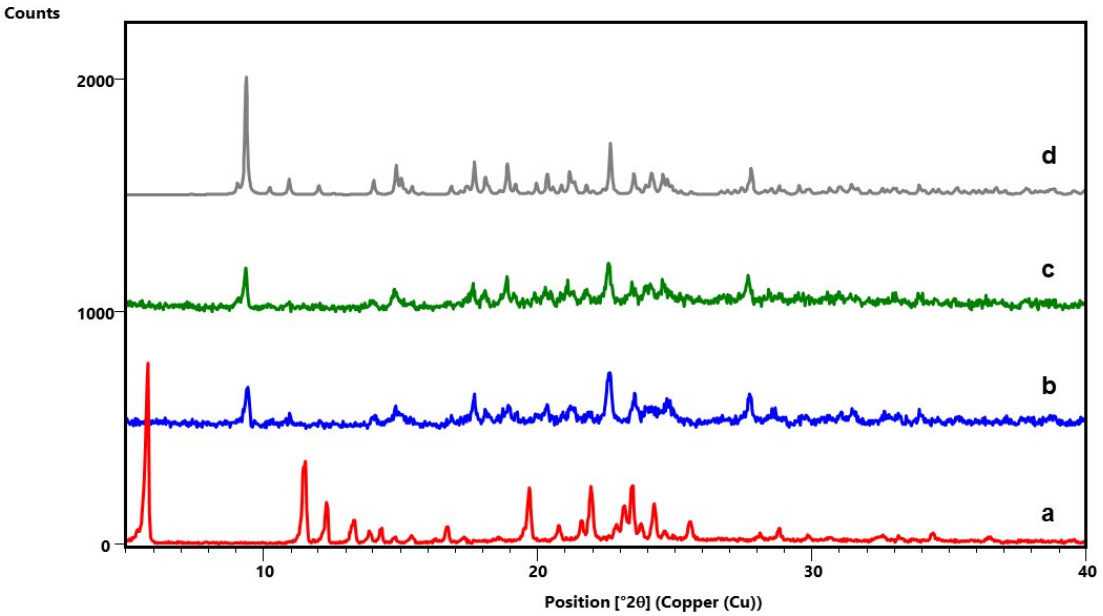

Figure S5. PXRD patterns of: a) **dpz**, b) product obtained by grinding **dpz** and **13tfib** in a 1:1 stoichiometric ratio, c) product obtained by grinding **dpz** and **13tfib** in a 1:2 stoichiometric ratio, d) calculated pattern from (**dpz**)(**13tfib**) single crystal data.

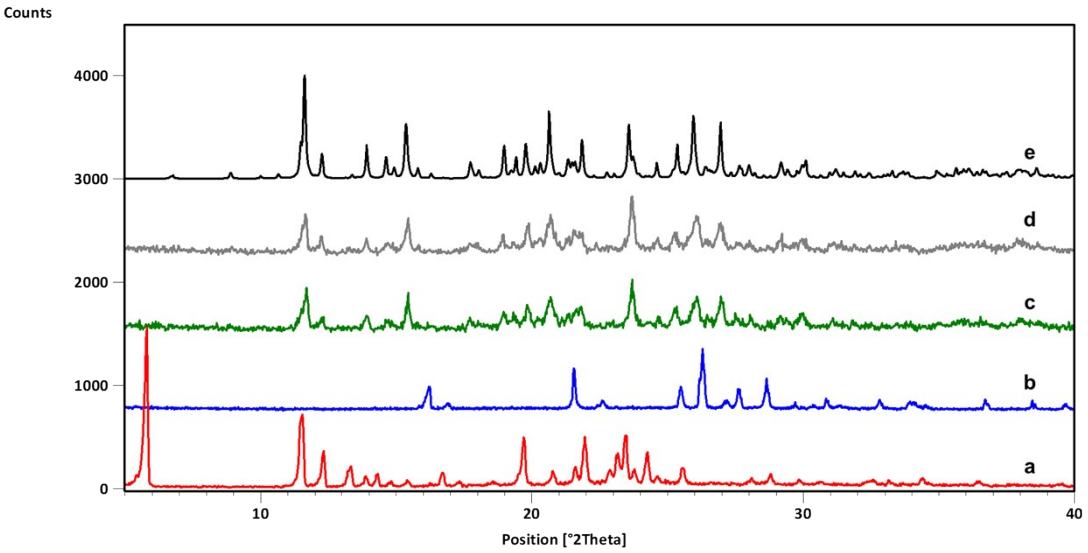

Figure S6. PXRD patterns of: a) **dpz**, b) **14tfib**, c) product obtained by grinding **dpz** and **14tfib** in a 1:1 stoichiometric ratio, d) product obtained by grinding **dpz** and **14tfib** in a 1:2 stoichiometric ratio, e) calculated pattern from (**dpz**)(**14tfib**)$_2$ single crystal data.

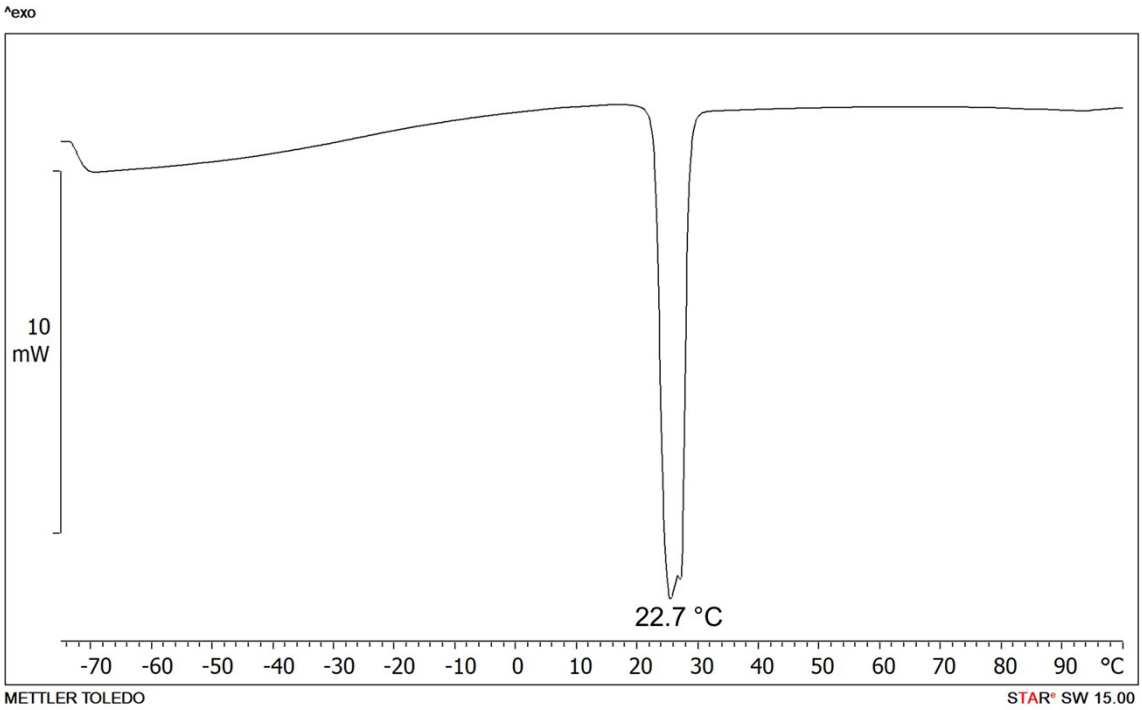

Figure S7. Heating segment of the DSC curve of **13tfib**.

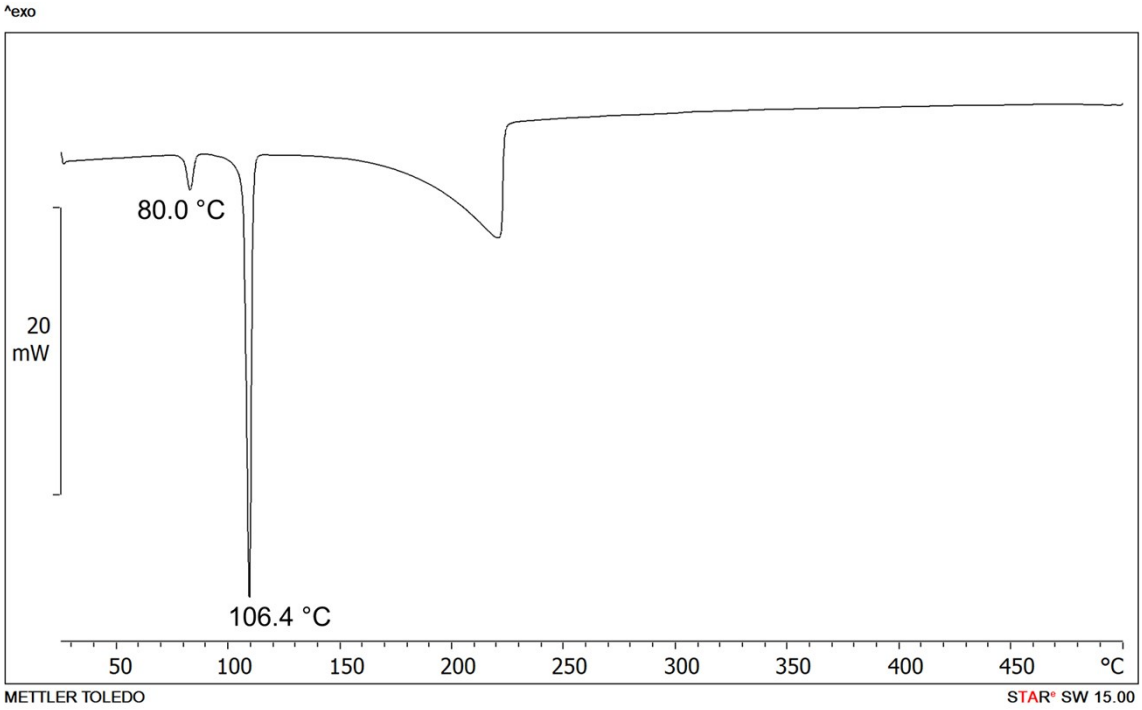

Figure S8. DSC curve of **14tfib**.

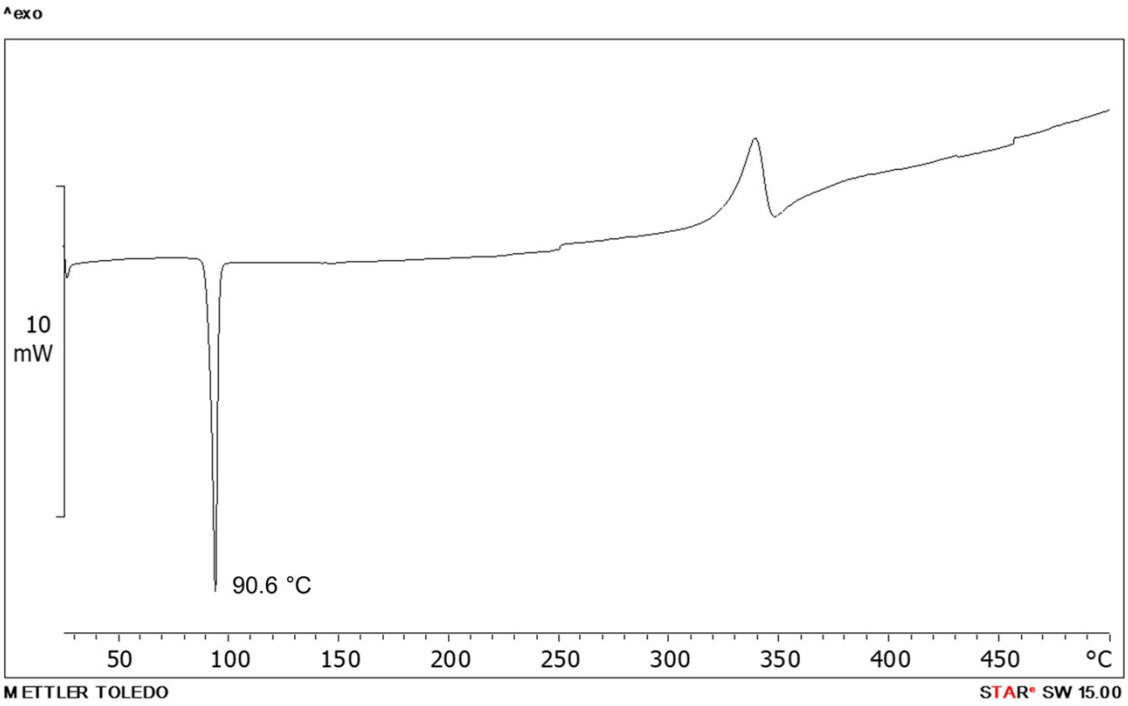

Figure S9. DSC curve of **dpz**.

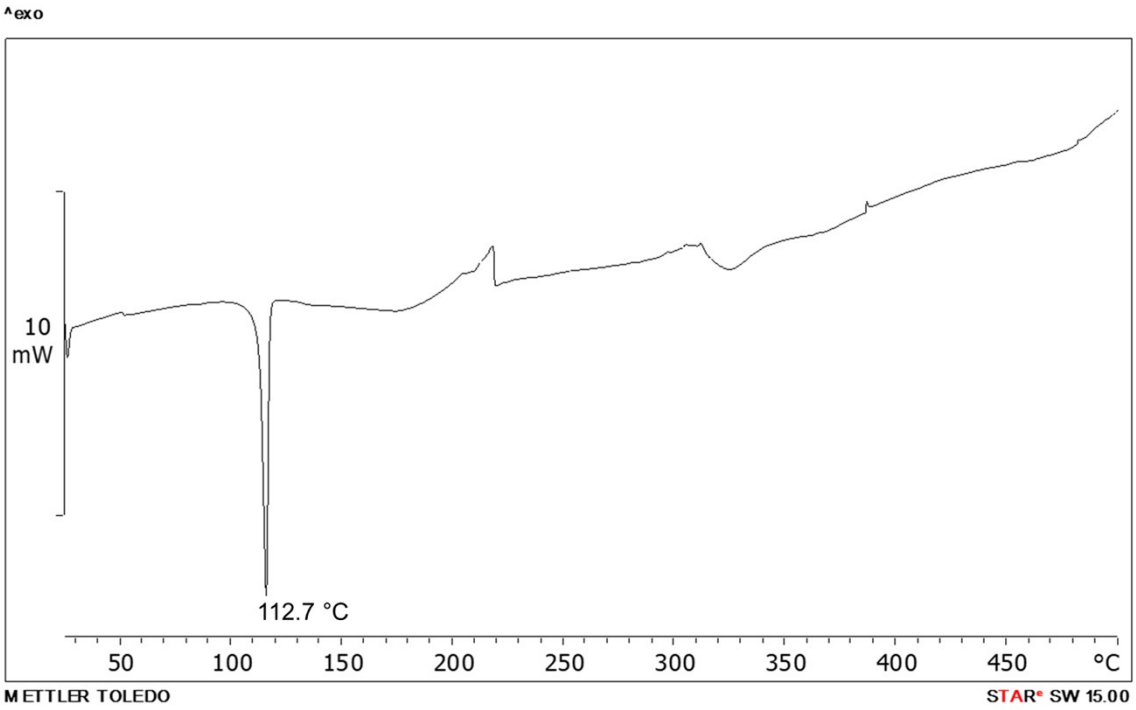

Figure S10. DSC curve of (**dpz**)(**13tfib**).

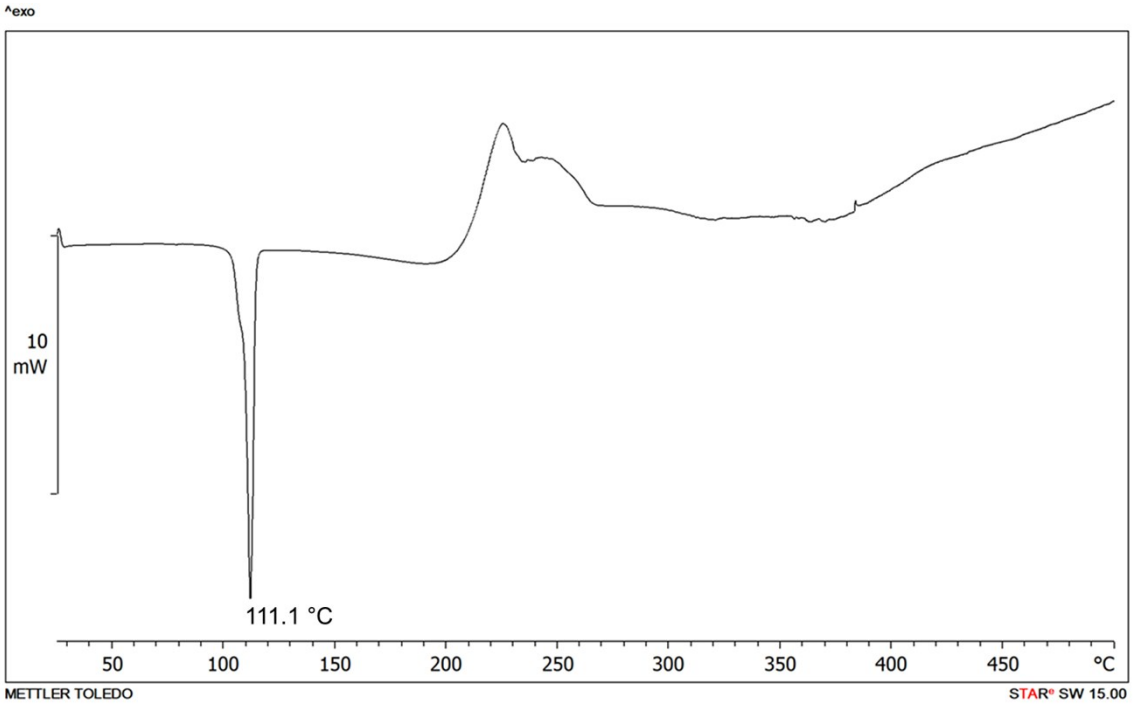

Figure S11. DSC curve of (**dpz**)(**14tfib**)$_2$.