

Supplementary Information

## Spontaneous racemic resolution – towards control of molecular recognition nature

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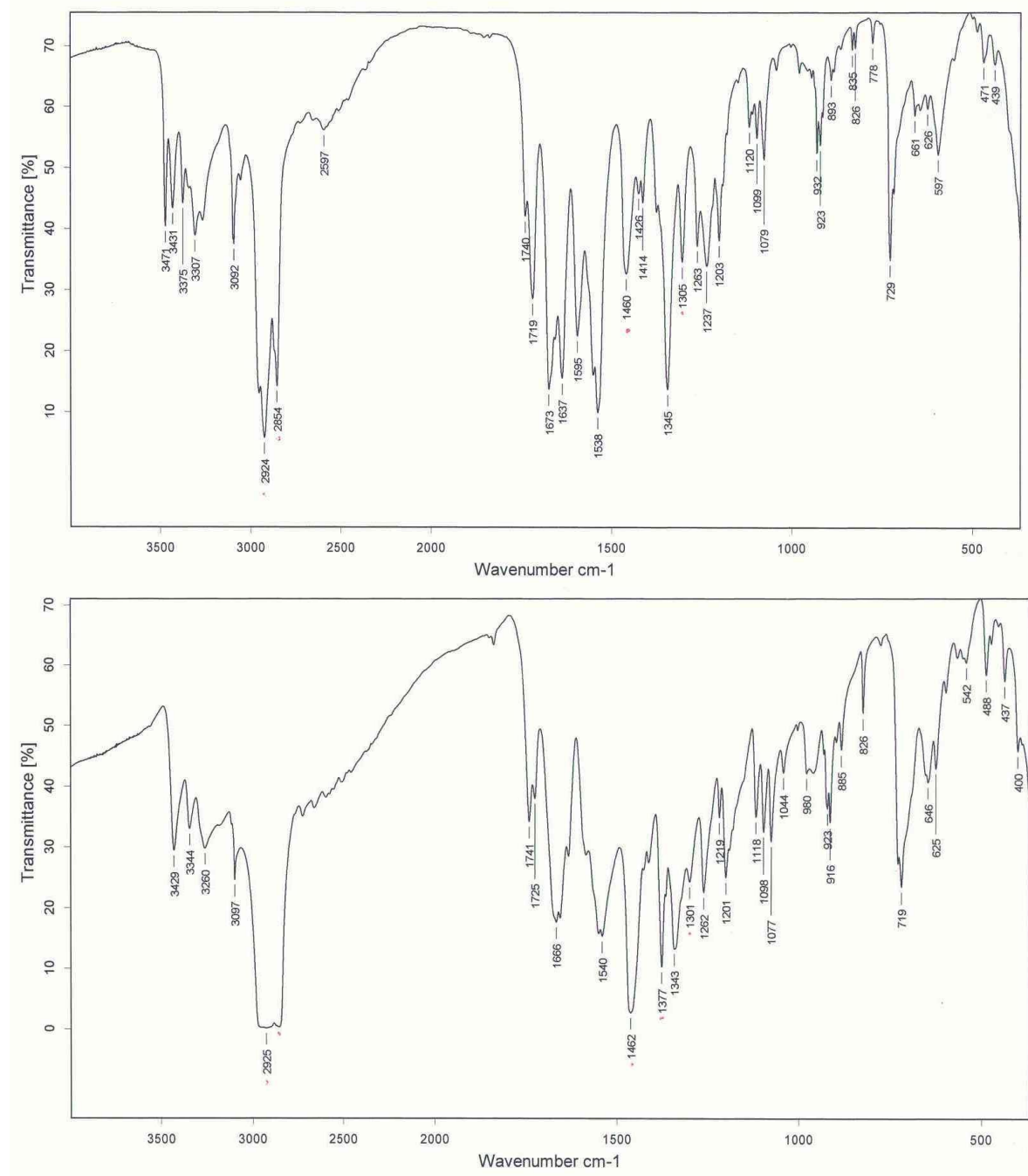
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## Experimental

### 1.1. Synthesis of *N*-(3,5-dinitrobenzoyl)asparagine

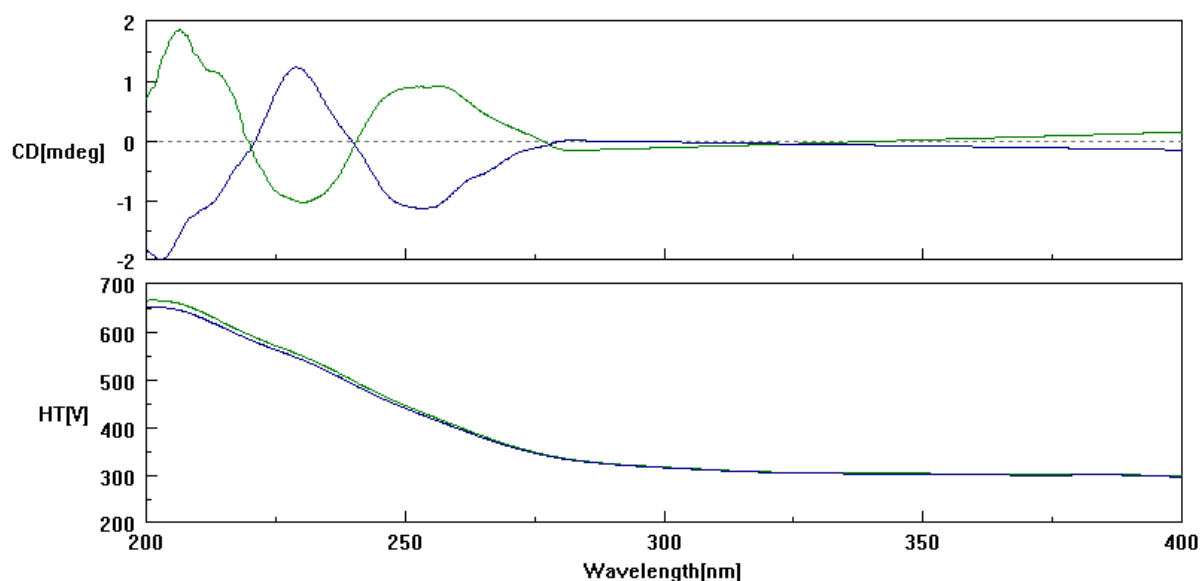
Racemic and enantiomeric *N*-(3,5-dinitrobenzoyl)asparagine were synthesized using racemic or enantiomeric asparagine, respectively, and 3,5-dinitrobenzoyl chloride (all the substrates were obtained from commercial source) and applying standard procedures described in literature [J. T. Wróbel, *Preparatyka i elementy syntezy organicznej*, PWN, Warszawa, 1983.]:

$^1\text{H}$  NMR (METHANOL- $d_4$ ):  $\delta$  9.14 (1H, *t*,  $J = 2.1$  Hz), 9.07 (2H, *d*,  $J = 2.1$  Hz), 5.00 (1H, *dd*,  $J = 5.0$  and 7.8 Hz), 2.98 (1H, *dd*,  $J = 5.0$  and 16.0 Hz), 2.89 (1H, *dd*,  $J = 8.0$  and 16.0 Hz) ( $^1\text{H}$  spectra were recorded with a Bruker Avance 500 MHz spectrometer).



**Fig. S1.** The IR spectra for racemic (upper) and chiral (lower) *N*-(3,5-dinitrobenzoyl)asparagine in nujol mull (infrared spectra were recorded with a Bruker 113v

FTIR spectrometer). The IR spectra were recorded for *N*-(3,5-dinitrobenzoyl)asparagine precipitating from ethanol solution.



**Fig. S2.** The CD spectra for aqueous solution of *N*-(3,5-dinitrobenzoyl)-D- (dark blue) and *N*-(3,5-dinitrobenzoyl)-L-asparagine (green) ( $c = 0.001$  M,  $d = 0.1$  mm)

100 mg of enantiopure (for crystallization of **DNBN-e**) or racemic (for crystallization of **DNBN-srr** and **DNBN-rac**) *N*-(3,5-dinitrobenzoyl)asparagine were dissolved by heating in 100 ml of a given solvent (water or any of the used (pure for analysis) alcohols). Since solubility of *N*-(3,5-dinitrobenzoyl)asparagine in the other solvents like nitromethane, ethyl acetate or dichloromethane is very low, crystallization using these solvents were performed from saturated solutions obtained by decanting). In further experiments (to avoid a nucleation by a given crystalline phase), basing on the dielectric constant of a given solvent, **DNBN-srr** (obtained from 2-methylpropan-1-ol solution) was used for crystallization of **DNBN-rac**, and **DNBN-rac** (obtained from water solution) was used for crystallization of **DNBN-srr**.

## 1.2. Racemic resolution of *N*-(3,5-dinitrobenzoyl)asparagine by fractional crystallization of brucinium or strychninium diastereomeric salts

Crystals of the strychninium or brucinium diastereomeric salts with *N*-(3,5-dinitrobenzoyl)asparagine were obtained during racemic resolution of *N*-(3,5-dinitrobenzoyl)asparagine by a fractional crystallization of strychninium or brucinium salts. For the racemic resolution purpose, 100 mg of brucine or strychnine (both the anhydrous resolving agents were obtained from commercial source) and equimolar amount of *N*-(3,5-dinitrobenzoyl)asparagine were dissolved in 10 ml of solvent (ethanol or methanol) and the samples were left for crystallization by solvent evaporation at room temperature. Crystals of strychninium *N*-(3,5-dinitrobenzoyl)-D-asparaginate 1.75-hydrate (**SDNBDN(1)**) precipitated from methanol solution as a first fraction of the suitable racemic resolution. A further fraction the racemic resolution is strychninium *N*-(3,5-dinitrobenzoyl)-L-asparaginate 5-hydrate (**SDNBLN(2)**). Brucinium *N*-(3,5-dinitrobenzoyl)-D-asparaginate ethanol solvate hydrate (**BDNBDN(1)**) crystallized from ethanol solution as a first fraction of the racemic resolution of *N*-(3,5-dinitrobenzoyl)asparagine and using brucine as the resolving agent. Crystals of brucinium *N*-(3,5-dinitrobenzoyl)-L-asparaginate methanol 1.2-solvate 1.5-hydrate (**BDNBLN(2)**) precipitated from methanol, which was added (10 ml) after ethanol evaporation. Brucinium *N*-(3,5-dinitrobenzoyl)-L-asparaginate methanol 2.5-solvate (**BDNBLN**)

precipitated from methanol (10 ml) solution containing equimolar amount of brucine (100 mg) and *N*-(3,5-dinitrobenzoyl)-*L*-asparaginate.

### 1.3. X-Ray diffraction studies (mono- and polycrystalline samples)

X-Ray data for **DNBN-rac**, **DNBN-srr** were collected on a Xcalibur PX with Onyx detector (Cu-K $\alpha$  radiation,  $\lambda = 1.54175 \text{ \AA}$ ), for **DNBN-e**, **SDNBDN(1)**, **SDNBLN(2)**, **BDNBDN(1)**, **BDNBLN(2)** – on a Xcalibur with Sapphire2 detector and **BDNBLN** – on a Xcalibur with Ruby detector (Mo-K $\alpha$  radiation;  $\lambda = 0.71073 \text{ \AA}$ ). All the data were collected at 100 K using an Oxford Cryosystem device. Data reduction and analysis were carried out with the CrysAlice 'RED' program (CrysAlis 'RED', Oxford Diffraction Ltd., Abingdon, Oxfordshire, England, 2009). The space groups were determined using the XPREP program. Structures were solved by direct methods using the SHELXS (G. M. Sheldrick, *Acta Cryst.*, 2008, **A64**, 112) or SIR2004 (M. C. Burla, R. Caliendo, M. Camalli, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori and R. Spagna, *J. Appl. Cryst.* 2005, **38**, 381) program and refined using all  $F^2$  data, as implemented by the SHELXL program. Non-hydrogen atoms were refined with anisotropic displacement parameters. In **BDNBLN(2)** and in **BDNBLN** some restraints were applied for disordered units (anions and methanol molecules). All H atoms were found in  $\Delta\rho$  maps or placed at calculated positions. Before the last cycle of refinement all H atoms were fixed and were allowed to ride on their parent atoms. The absolute structures were chosen on the basis of the known absolute configuration of strychnine (J. H. Robertson and C. A. Beevers, *Acta Crystallogr.*, 1951, **4**, 270) or brucine (F. Toda, K. Tanaka, H. Ueda and T. Oshima, *Isr. J. Chem.* 1985, **25**, 338–345.), respectively.

PXRD patterns were recorded on D8 ADVANCE with Vantec detector (Cu-K $\alpha$  radiation,  $\lambda = 1.54175 \text{ \AA}$ ).

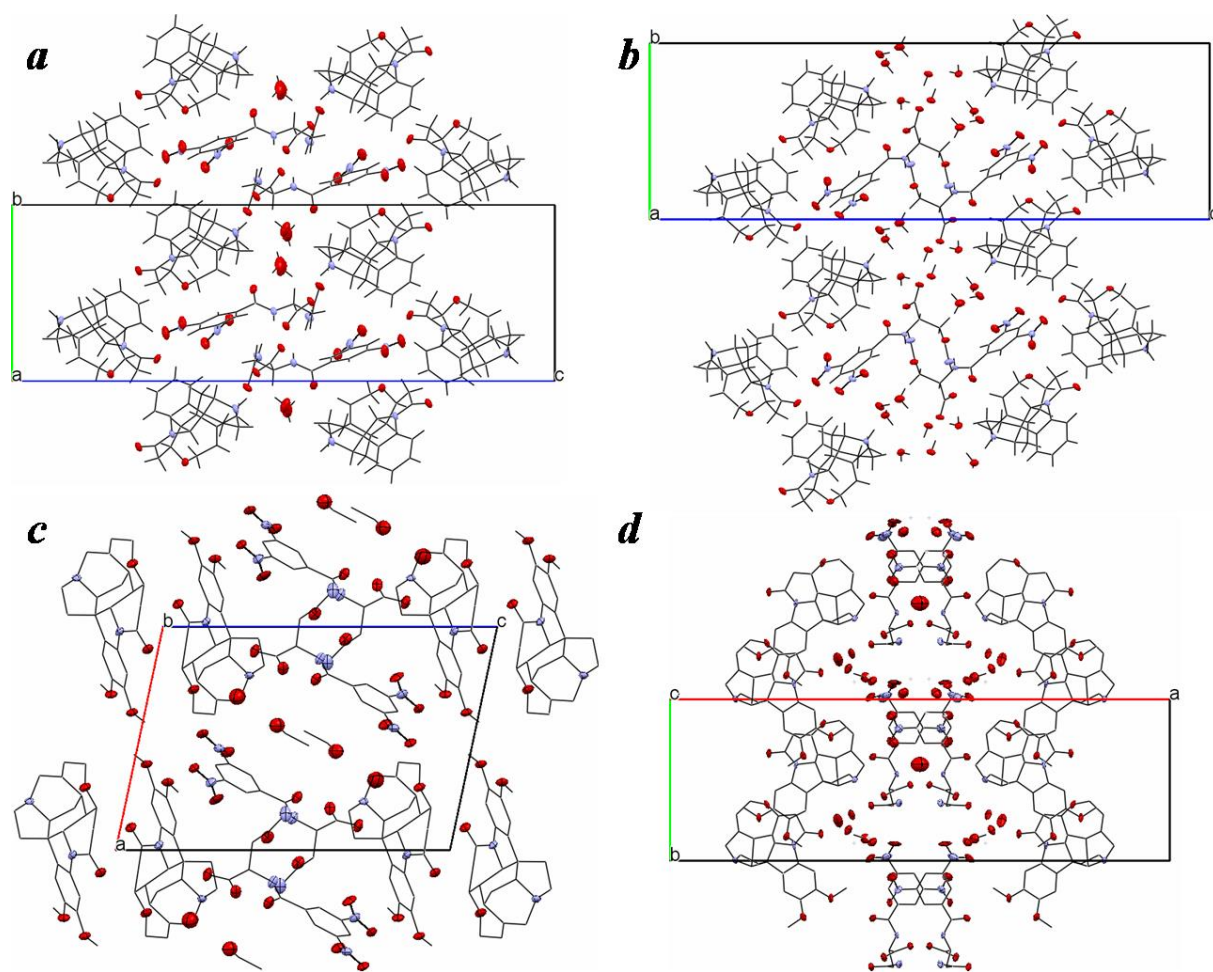
### 1.4. Thermogravimetric analysis.

The TGA and DTA measurements were performed for freshly prepared polycrystalline samples (the crystalline phase was previously confirmed by the PXRD studies) on a Setaram SETSYS 16/18 instrument between 303 and 773 K with a ramp rate of  $2 \text{ Kmin}^{-1}$ . The scan was performed in flowing nitrogen (flow rate:  $1 \text{ dm}^3 \cdot \text{h}^{-1}$ )

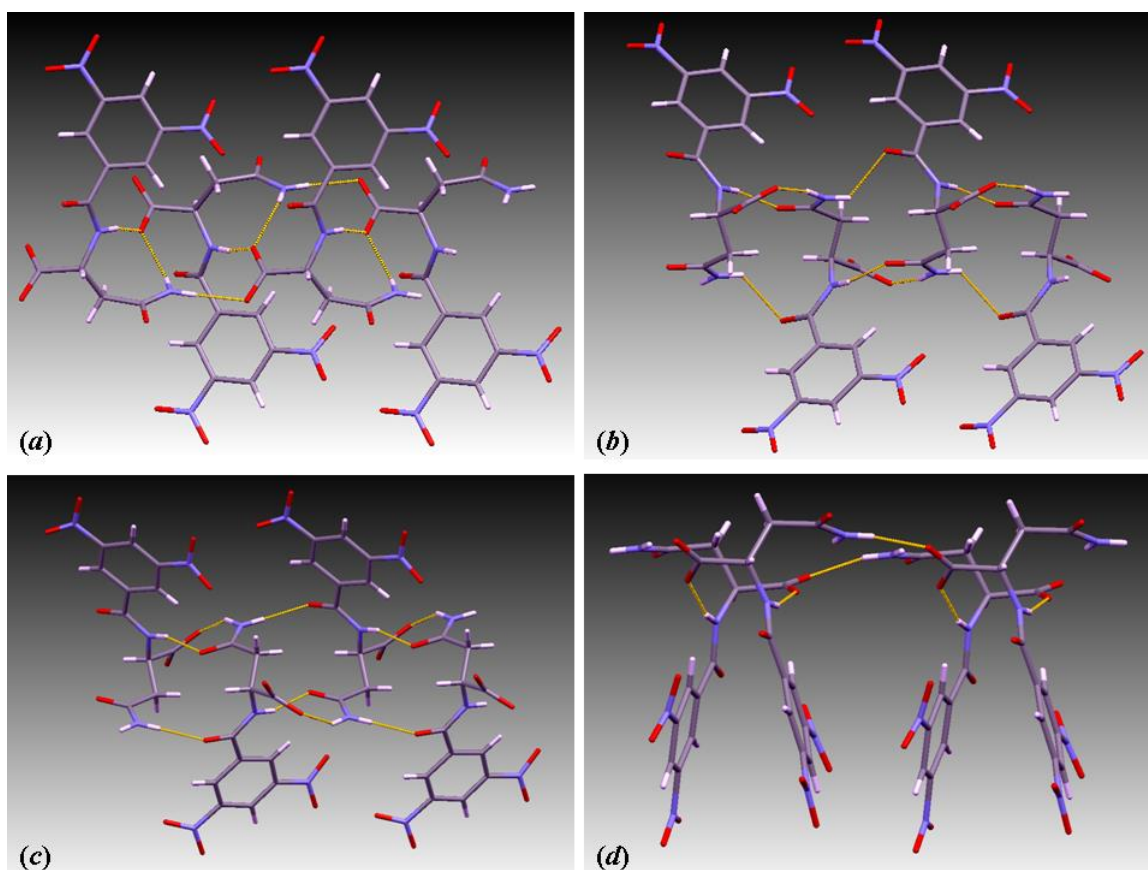
**Table S1.** Crystal data for strychninium and brucinium salts with *N*-(3,5-dinitrobenzoyl)asparagine.

	<b>SDNBDN(1)</b>	<b>SDNBLN(2)</b>	<b>BDNBDN(1)</b>	<b>BDNBLN(2)</b>	<b>BDNBLN</b>
chemical formula*	SH <sup>+</sup> N <sup>-</sup> ·1.75H <sub>2</sub> O	SH <sup>+</sup> N <sup>-</sup> ·5H <sub>2</sub> O	BH <sup>+</sup> N <sup>-</sup> ·C <sub>2</sub> H <sub>6</sub> O·H <sub>2</sub> O	BH <sup>+</sup> N <sup>-</sup> ·1.2CH <sub>4</sub> O ·1.5H <sub>2</sub> O	BH <sup>+</sup> N <sup>-</sup> ·2.5CH <sub>4</sub> O
Chemical formula weight	692.16	750.71	784.77	785.76	800.79
temperature (K)	100(2)	100(2)	100(2)	100(2)	100(2)
Cell setting, space group	orthorhombic, <i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	orthorhombic, <i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	monoclinic, <i>P</i> 2 <sub>1</sub>	monoclinic, <i>C</i> 2	triclinic, <i>P</i> 1
<i>a</i> , <i>b</i> , <i>c</i> (Å)	8.006(2) 11.184(3) 34.465(5)	7.730(2) 11.896(3) 37.812(5)	12.358(3) 8.354(2) 18.078(2)	38.752(5) 12.287(3) 7.909(2)	7.924(2) 12.140(3) 20.495(3)
<i>β</i> (°)	90.00 90.00 90.00	90.00 90.00 90.00	90 101.94(3) 90	90 100.63(3) 90	73.21(2) 79.37(2) 80.53(3)
<i>V</i> (Å <sup>3</sup> )	3086.0(12)	3477.0(13)	1826.0(7)	3701.2(14)	1842.1(8)
<i>Z</i>	4	4	2	4	2
<i>D</i> <sub>c</sub> (Mg m <sup>-3</sup> )	1.490	1.434	1.427	1.410	1.444
Crystal form, colour	plate, colorless	block, colorless	plate, orange	plate, colorless	plate, colorless
<i>R</i> [ <i>F</i> <sup>2</sup> > 2σ( <i>F</i> <sup>2</sup> )], <i>wR</i> ( <i>F</i> <sup>2</sup> ), <i>S</i>	0.068, 0.149, 1.082	0.049, 0.108, 1.038	0.077, 0.196, 1.037	0.069, 0.120, 0.871	0.063, 0.110, 0.846
CCDC	933059	933060	933061	933062	933063

SH<sup>+</sup> = C<sub>21</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub>, BH<sup>+</sup> = C<sub>23</sub>H<sub>27</sub>N<sub>2</sub>O<sub>4</sub>, N<sup>-</sup> = C<sub>11</sub>H<sub>9</sub>N<sub>4</sub>O<sub>8</sub>



**Fig. S3.** Packing of a) strychninium *N*-(3,5-dinitrobenzoyl)-*D*-asparaginate 1.75-hydrate, b) strychninium *N*-(3,5-dinitrobenzoyl)-*L*-asparaginate pentahydrate, c) brucinium *N*-(3,5-dinitrobenzoyl)-*D*-asparaginate ethanol solvate hydrate and d) brucinium *N*-(3,5-dinitrobenzoyl)-*L*-asparaginate methanol 1.25-solvate 1.5-hydrate.

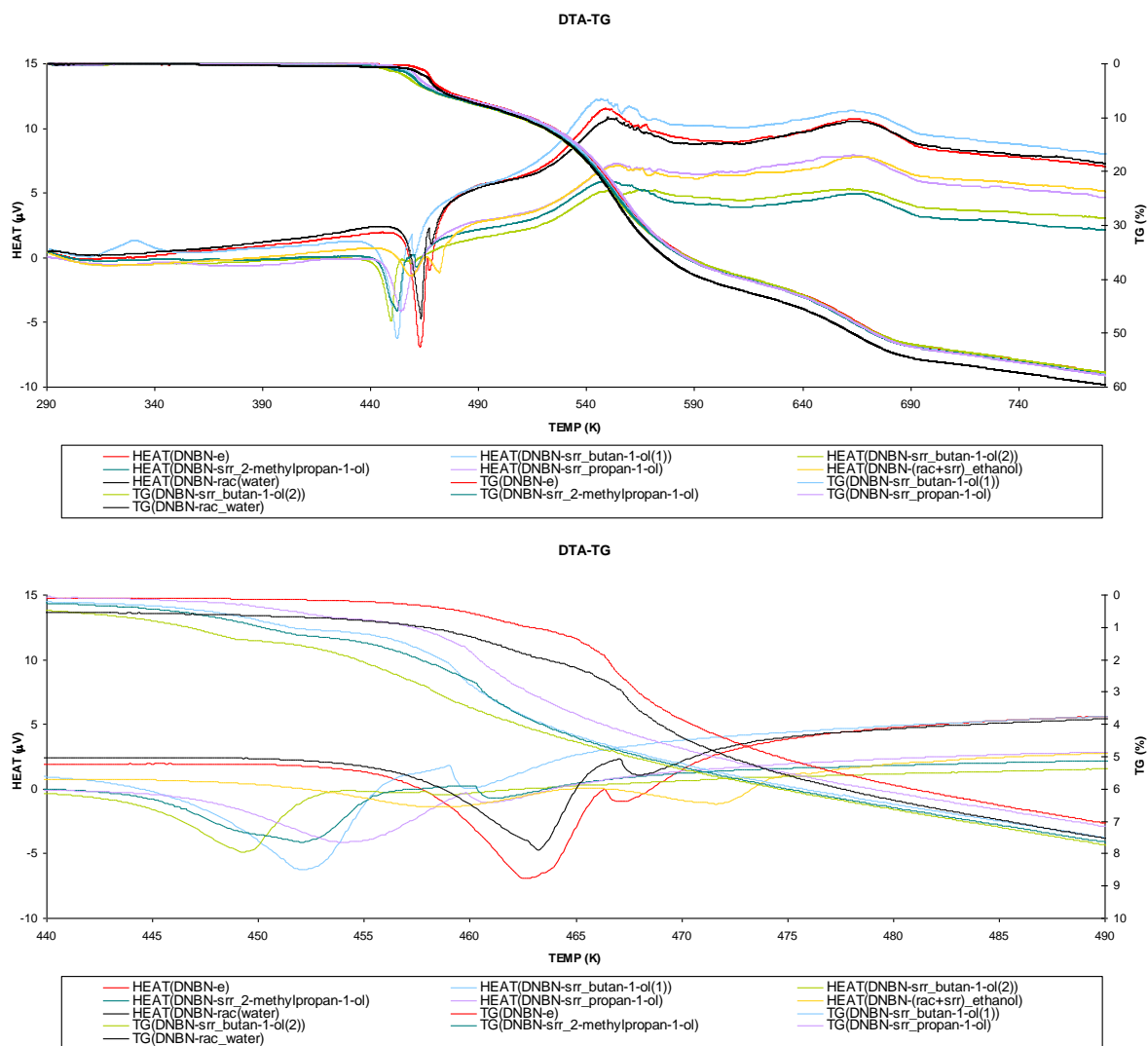


**Fig. S4.** Hydrogen bonded *N*-(3,5-dinitrobenzoyl)-D-asparaginate anions in the first ((a) and (c)) and *N*-(3,5-dinitrobenzoyl)-L-asparaginate anions in the following fractions ((b) and (d)) obtained during racemic resolution of *N*-(3,5-dinitrobenzoyl)asparagine by using strychnine ((a) and (b)) and brucine ((c) and (d)).

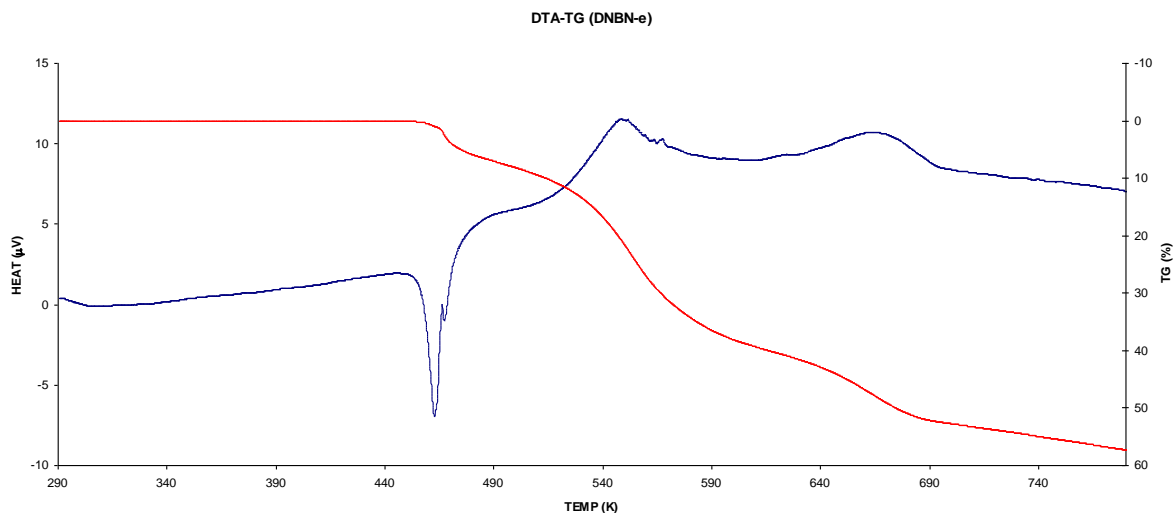
**Table S2.** Geometry of hydrogen bonds in **DNBN-rac**, **DNBN-e** and **DNBN-ssr**.

DNBN-rac			DNBN-e			DNBN-ssr		
DHA	D...A	∠ DHA	DHA	D...A	∠ DHA	DHA	D...A	∠ DHA
O1-H1C...O3 <sup>i</sup>	2.633(6)	169	O1-H1C...O3 <sup>i</sup>	2.596(3)	176	O1-H1C...O3 <sup>i</sup>	2.590(6)	176
N1-H1A...O1 <sup>ii</sup>	3.275(7)	129	N1-H1A...O2 <sup>ii</sup>	3.017(3)	142	N1-H1A...O2 <sup>ii</sup>	3.024(7)	143
N1-H1A...O4 <sup>iii</sup>	2.987(7)	126	N1-H1B...O4 <sup>iii</sup>	2.986(3)	162	N1-H1B...O4 <sup>iii</sup>	2.979(7)	163
N1-H1B...O6 <sup>iv</sup>	2.964(8)	153	N2-H2B...O3 <sup>iii</sup>	2.852(3)	157	N2-H2A...O3 <sup>iii</sup>	2.845(7)	157
N2-H2A...O3 <sup>v</sup>	2.904(8)	151						
C11-H11A...O2 <sup>iii</sup>	3.255(7)	161						

**Symmetry codes for DNBN-rac:** (i)  $x+1, -y+3/2, z+1/2$ ; (ii)  $x-1, -y+3/2, z-1/2$ ; (iii)  $x, -y+3/2, z-1/2$ ; (iv)  $-x+3, y-1/2, -z+1/2$ ; (v)  $5x+1, y, z$ ; **DNBN-e:** (i)  $-x+1, y+1/2, -z+1/2$ ; (ii)  $-x+2, y-1/2, -z+1/2$ ; (iii)  $-x+2, y+1/2, -z+1/2$ ; **DNBN-ssr:** (i)  $-x+1, y+1/2, -z+1/2$ ; (ii)  $-x, y-1/2, -z+1/2$ ; (iii)  $-x, y+1/2, -z+1/2$

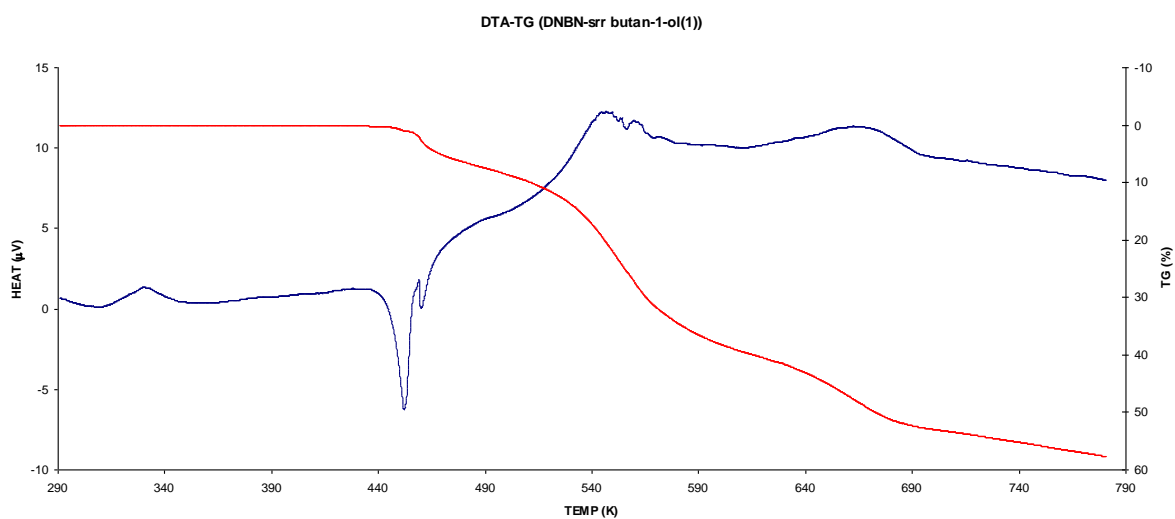


**Fig. S5.** DTA-TG curves showing a comparison of stability of enantiomer (**DNBN-e**), conglomerate (**DNBN-srr**) and racemate (**DNBN-rac**) of *N*-(3,5-dinitrobenzoyl)asparagine (**DNBN-(rac+srr)** represents a mixture of two forms **DNBN-rac** and **DNBN-srr**; number in parenthesis indicates succeeding recrystallizations)

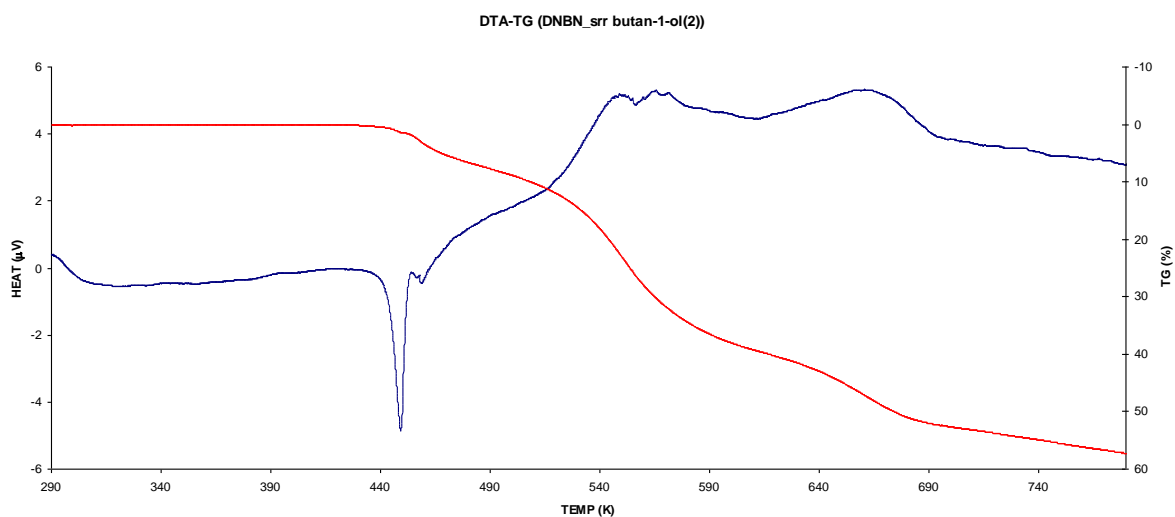




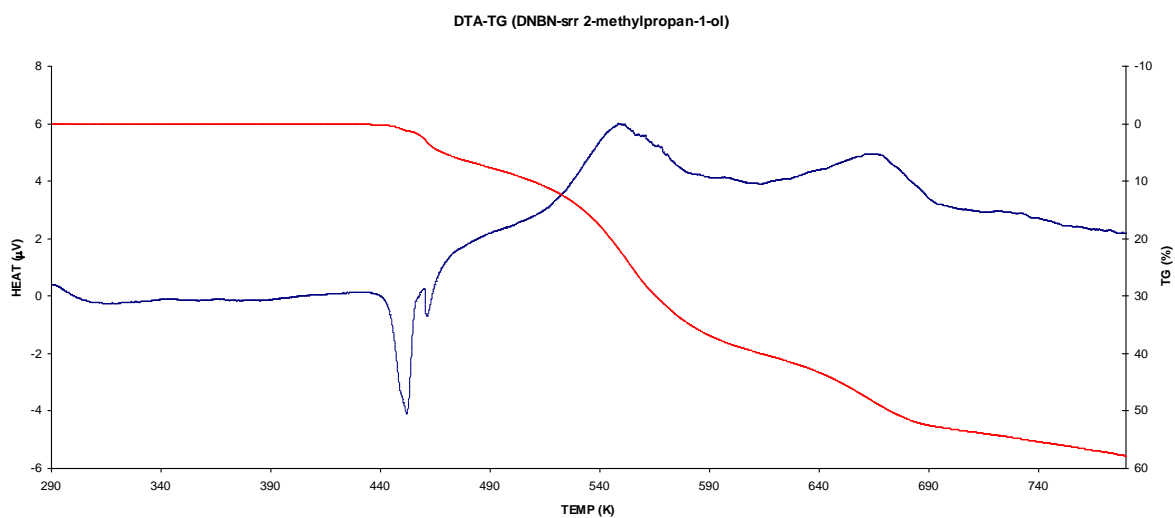
**Fig. S6.** DTA-TG curves for DNBN-e.



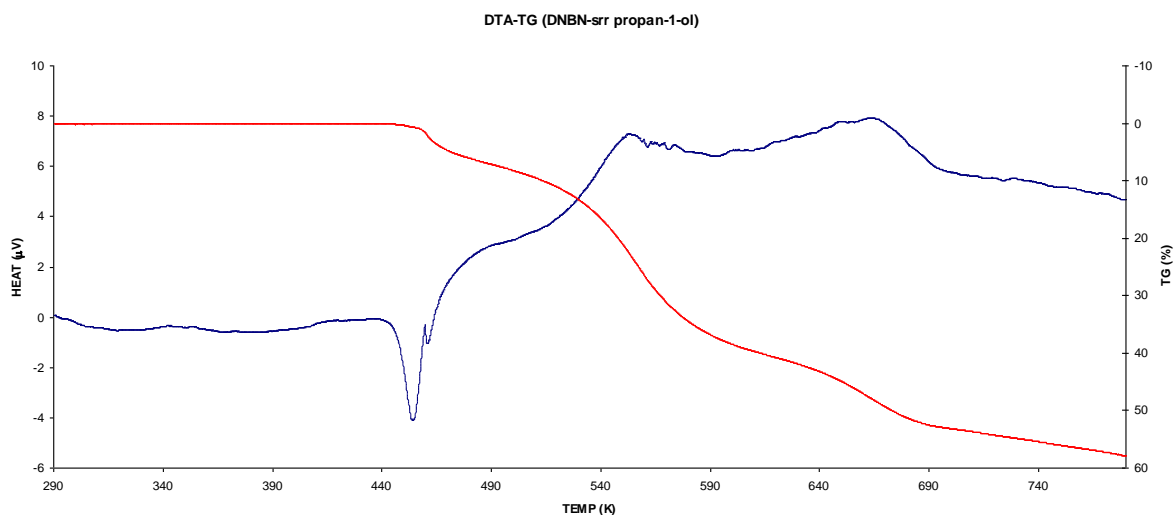
**Fig. S7.** DTA-TG curves for DNBN-srr precipitating from butan-1-ol solution.



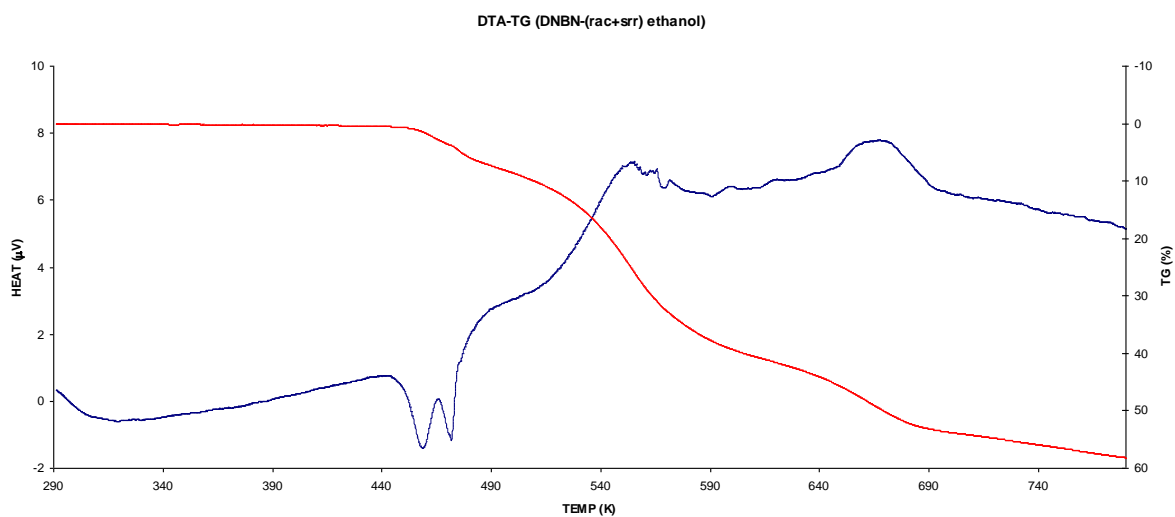
**Fig. S8.** DTA-TG curves for DNBN-srr recrystallized from butan-1-ol solution.



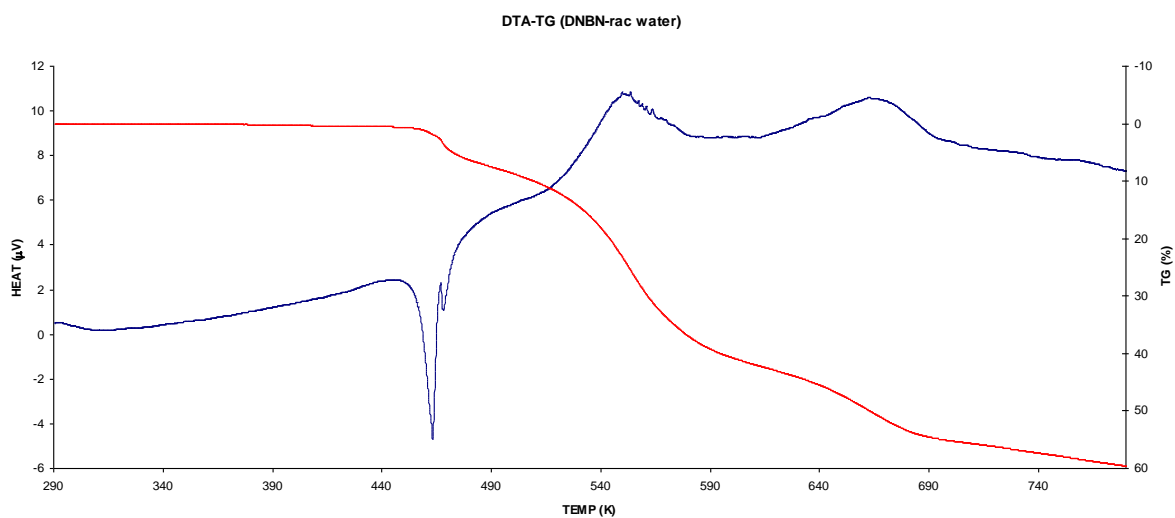
**Fig. S9.** DTA-TG curves for DNBN-srr precipitating from 2-methylpropan-1-ol solution.



**Fig. S10.** DTA-TG curves for DNBN-srr precipitating from propan-1-ol solution.



**Fig. S11.** DTA-TG curves for a mixture of DNBN-rac and DNBN-srr precipitating from ethanol solution.



**Fig. S12.** DTA-TG curves for DNBN-rac precipitating aqueous solution.