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Attrition-induced spontaneous chiral amplification of the γ polymorphic modification of glycine

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CONTENT

EXPERIMENTAL SECTION

Preparation of glycine solution

The saturated aqueous solution of glycine was obtained by intensive stirring of an excess of glycine (33 g) with sodium chloride solution (100 g/L, 110 g) during 5 hours at room temperature. An excess of crystals of glycine was removed by filtration through a Schott glass filter (Duran, grade 3, porosity 16-40 μm) using vacuum. The obtained solution was used for crystallizations under different conditions.

Crystallization without stirring

The solution of glycine prepared above was transferred to a crystallizing dish and covered with a filter paper for the protection against dust. Nucleation was observed after 3-5 days, and in 1-2 weeks single crystals of γ-Gly were formed. Using a spatula and a triangle we collected individual single crystals of γ-glycine, and the residual solution was removed from the surface of the crystals using a filter paper. The solid state measurements of circular dichroism were conducted in potassium bromide (100 ± 3 mg for each pellet) with known amount of material in the pellet (0.5 - 5 mg of Gly) in the UV range 200-300 or 200-230 nm (Table S1, entries 1-7). The crystal structure of γ polymorphic modification has been characterized by powder X-ray diffraction (Fig. S1 top, blue digram).

Crystallization under stirring

Aliquots (10 mL) of the saturated aqueous solution of glycine with sodium chloride were transferred to 25 mL flasks equipped with stir bars. Crystallization started after 3 days of an intensive stirring (~800 rpm) as a result of slow evaporation. Due to the continuous crushing of the formed crystals, the CD measurements were conducted using the formed microcrystalline powder which was separated by vacuum filtration on a glass filter and dried on air at 40°C overnight (Table S1, entries 8-18). Powder XRD are presented on Fig. S1 (top, red digram).

Crystallization under abrasive grinding conditions

γ-glycine (1.311 g, 0° CD signal, obtained as a result of crystallization without stirring) was put into the aqueous saturated solution of glycine with sodium chloride (NaCl 100 g/L, 12 mL). The mixture was stirred using a magnetic bar with the addition of a considerable amount of glass beads (soda-lime glass, 3 mm diameter, 31.3 g). For measurements, several hundreds of μL of the slurry were taken using a Pasteur pipette, the solution was removed by filtration on a Schott glass microfilter and the solid was dried up at 40°C during several hours (Table S1, entries 19-22).

Control of γ-glycine chirality under abrasive grinding conditions using enantiopure L- and D-alanine

A mixture of γ-glycine (950 mg) together with either of enantiopure alanine (L or D, 50 mg) was put into the aqueous saturated solution of glycine with sodium chloride (NaCl 100 g/L, 12 mL). The mixture was stirred using a magnetic bar with the addition of a considerable amount of glass beads (soda-lime glass, 3 mm diameter, ~30 g). The samples for CD measurements were taken as described above.

Table S1.

Entry	CD signal, specific ellipticity (mdeg/mg) at ~ 210 nm	Estimated absolute (either "+" or "-") enantiomorphous excess, %
1	~0	0
2	-34.34	49.1
3	+34.11	48.7
4	-24.06	34.4
5	-39.8	56.9
6	-40.2	57.4
7	-23.9	34.1
8	-1.61	2.3
9	+17.93	25.6
10	+1.06	1.5
11	+7.66	10.9
12	+5.57	7.9
13	+5.41	7.7
14	-3.25	4.6
15	-22.21	31.7
16	-3.3	4.7
17	~0	0
18	+3.26	4.6
19	-70	**~100**
20	+6.0	8.6
21	+4.5	6.4
22	~0	0

Measured CD signals and calculated enantiomorphous excess of *γ*-Gly samples.

a) entries 1-7, single crystal obtained without stirring;

b) entries 8-18, intensively stirred solution;

c) entries 19-22, using glass beads.

Powder Debye-Scherrer diagram

The powder XRD diffractograms of (i) commercially available glycine (black), (ii) ground crystals obtained by slow growing from NaCl aqueous solution according to the above described method (red) and (iii) crystals formed under the same conditions but applying intensive stirring (blue) are shown on Figure S1. It is interesting to note that the commercially available sample of glycine (Aldrich), that was used for the obtaining of *γ* form, alongside with the kinetically favorable *α* modification contained *γ*-Gly as well (Figure S1, top).

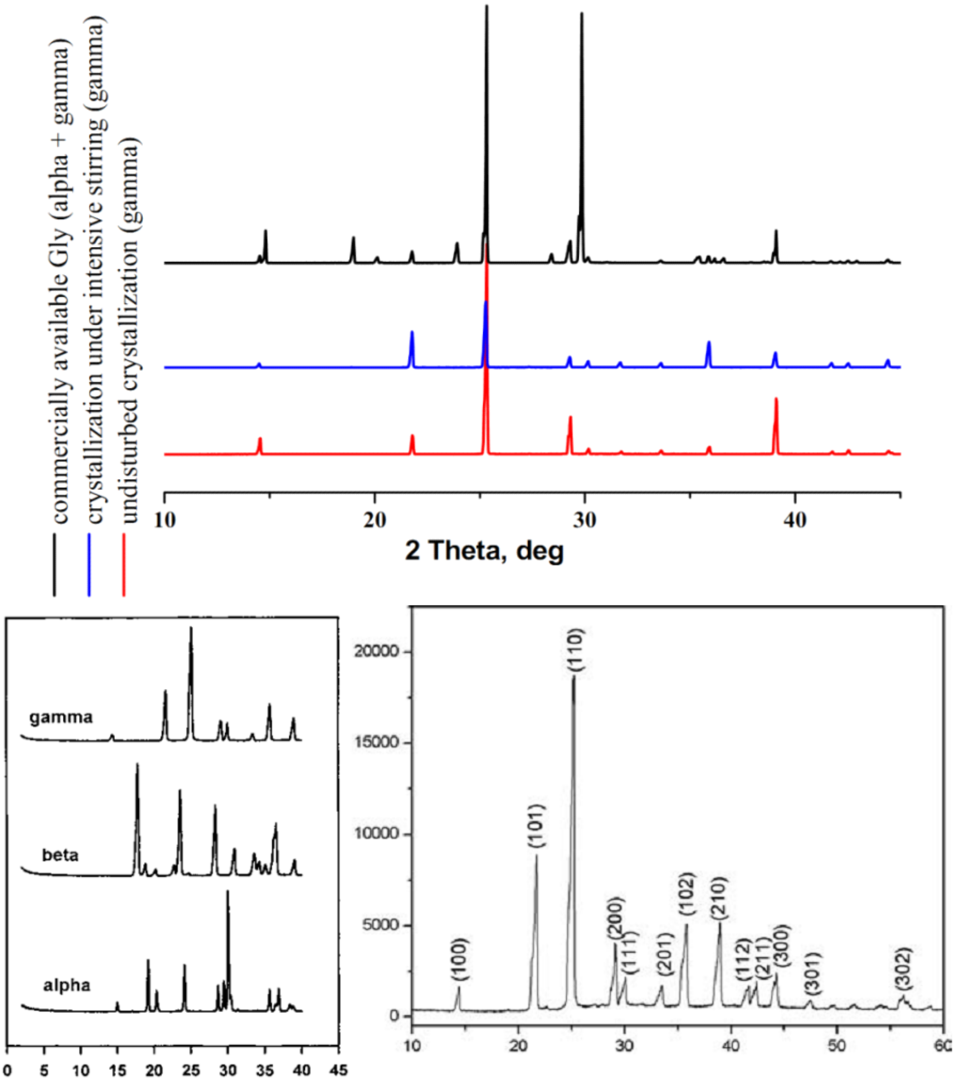

Fig. S1 Powder X-ray diffractograms of *α*, *β* and *γ*-Gly: our experimental data (top); literature data: bottom left (*α*, *β*, *γ*)[1] and right (*γ*)[2]

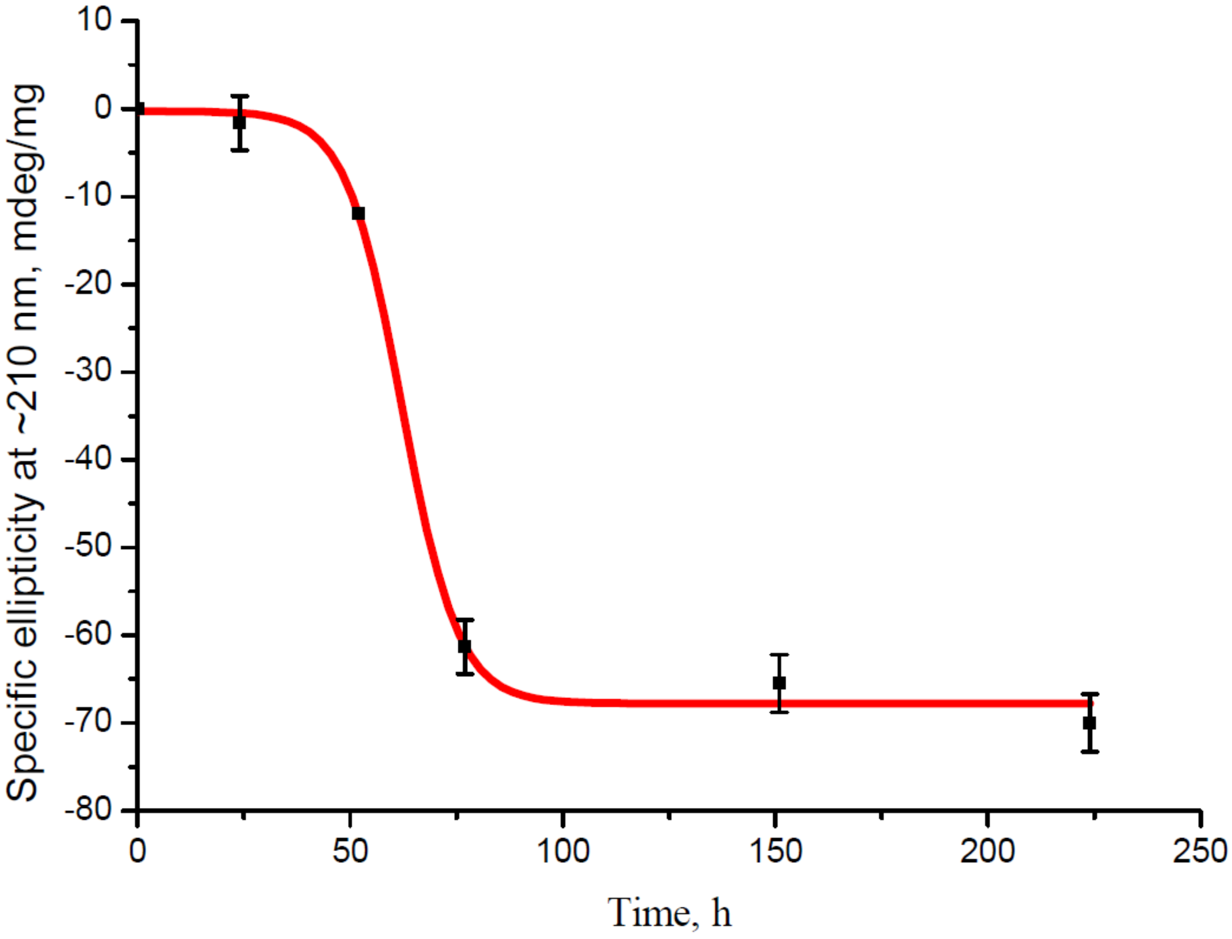

Fig. S2 The evolution of optical activity in the *γ*-Gly crystalline phase as a result attrition-enhanced grinding using glass beads.

X-ray Crystallographic Study

Single crystal data collection were performed at 200 K with a SuperNova Agilent diffractometer with Cu-Kα radiation (α = 1.54184 Å). Reflections were indexed, Lorentz-polarization corrected and integrated by the Crysalis program.[3] Structure determinations were performed by direct methods with the program SIR2002,[4] that revealed all the non hydrogen atoms. SHELXL program[5] was used to refine the structures by full-matrix least-squares based on *F*2. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were found with Fourier Difference map. Flack x parameter for absolute configuration is determined using 150 quotients [(I+)-(I-)]/[(I+)+(I-)].[6]

Atomic scattering factors for all atoms were taken from International Tables for X-ray Crystallography.[7] Details of crystal data and structural refinements are given in Tables S2-S5. CCDC reference numbers 1037456, 1037459, 1037299, 1037358 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retreving.html or from the Cambridge Crystallographic Data Center, 12 union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk.

Table S2. Crystal data and structure refinement for gly_d_Cu_200k (CCDC1037456).

Identification code	shelx
Empirical formula	$C_2H_5NO_2$
Formula weight	75.07
Temperature	200(2) K
Wavelength	1.54184 A
Crystal system, space group	Trigonal, *P*3_1
Unit cell dimensions	a = 7.0047(2) A alpha = 90 deg. b = 7.0047(2) A beta = 90 deg. c = 5.4772(3) A gamma = 120 deg.
Volume	232.738(18) A^3
Z, Calculated density	3, 1.607 Mg/m^3
Absorption coefficient	1.243 mm^-1
F(000)	120
Crystal size	0.319 x 0.074 x 0.066 mm
Theta range for data collection	7.301 to 49.723 deg.
Limiting indices	-6<=h<=6, -6<=k<=6, -5<=l<=5
Reflections collected / unique	1610 / 309 [R(int) = 0.0451]
Completeness to theta = 67.684	56.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.52487
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	309 / 1 / 47
Goodness-of-fit on F^2	1.229
Final R indices [I>2sigma(I)]	R1 = 0.0770, wR2 = 0.2202
R indices (all data)	R1 = 0.0770, wR2 = 0.2202
Absolute structure parameter	-0.1(4)
Extinction coefficient	0.25(9)
Largest diff. peak and hole	0.480 and -0.413 e.A^-3

Table S3. Crystal data and structure refinement for gly_f_cu_200k (CCDC 1037459).

Identification code	shelx
Empirical formula	$C_2H_5NO_2$
Formula weight	75.07
Temperature	200(2) K
Wavelength	1.54184 A
Crystal system, space group	Trigonal, *P*3_1
Unit cell dimensions	a = 7.0055(3) A alpha = 90 deg. b = 7.0055(3) A beta = 90 deg. c = 5.4774(2) A gamma = 120 deg.
Volume	232.80(2) A^3
Z, Calculated density	3, 1.606 Mg/m^3
Absorption coefficient	1.242 mm^-1
F(000)	120
Crystal size	0.251 x 0.220 x 0.056 mm
Theta range for data collection	7.300 to 49.717 deg.
Limiting indices	-6<=h<=6, -6<=k<=6, -5<=l<=5
Reflections collected / unique	1674 / 316 [R(int) = 0.0353]
Completeness to theta = 67.684	56.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.46934
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	316 / 1 / 47
Goodness-of-fit on F^2	1.146
Final R indices [I>2sigma(I)]	R1 = 0.0210, wR2 = 0.0547
R indices (all data)	R1 = 0.0212, wR2 = 0.0550
Absolute structure parameter	-0.2(3)
Extinction coefficient	0.172(19)
Largest diff. peak and hole	0.115 and -0.088 e.A^-3

Table S4. Crystal data and structure refinement for gly_g_cu_200k (CCDC 1037299).

Identification code	shelx
Empirical formula	$C_2H_5NO_2$
Formula weight	75.07
Temperature	200(2) K
Wavelength	1.54184 A
Crystal system, space group	Trigonal, *P*3_1
Unit cell dimensions	a = 7.0051(3) A alpha = 90 deg. b = 7.0051(3) A beta = 90 deg. c = 5.4758(2) A gamma = 120 deg.
Volume	232.71(2) A^3
Z, Calculated density	3, 1.607 Mg/m^3
Absorption coefficient	1.243 mm^-1
F(000)	120
Crystal size	0.247 x 0.214 x 0.116 mm
Theta range for data collection	7.301 to 49.725 deg.
Limiting indices	-6<=h<=6, -6<=k<=6, -5<=l<=5
Reflections collected / unique	1687 / 316 [R(int) = 0.0302]
Completeness to theta = 67.684	56.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.66047
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	316 / 1 / 47
Goodness-of-fit on F^2	0.668
Final R indices [I>2sigma(I)]	R1 = 0.0269, wR2 = 0.0724
R indices (all data)	R1 = 0.0269, wR2 = 0.0724
Absolute structure parameter	0.1(4)
Extinction coefficient	0.19(2)
Largest diff. peak and hole	0.108 and -0.128 e.A^-3

Table S5. Crystal data and structure refinement for gly_h_cu_200k (CCDC 1037358).

Identification code	shelx
Empirical formula	$C_2H_5NO_2$
Formula weight	75.07
Temperature	200(2) K
Wavelength	1.54184 A
Crystal system, space group	Trigonal, *P*3_1
Unit cell dimensions	a = 7.0045(3) A alpha = 90 deg. b = 7.0045(3) A beta = 90 deg. c = 5.4789(3) A gamma = 120 deg.
Volume	232.80(2) A^3
Z, Calculated density	3, 1.606 Mg/m^3
Absorption coefficient	1.242 mm^-1
F(000)	120
Crystal size	0.229 x 0.084 x 0.068 mm
Theta range for data collection	7.301 to 49.718 deg.
Limiting indices	-6<=h<=6, -6<=k<=6, -5<=l<=5
Reflections collected / unique	1728 / 305 [R(int) = 0.0336]
Completeness to theta = 67.684	56.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.55530
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	305 / 1 / 47
Goodness-of-fit on F^2	1.229
Final R indices [I>2sigma(I)]	R1 = 0.0181, wR2 = 0.0522
R indices (all data)	R1 = 0.0184, wR2 = 0.0526
Absolute structure parameter	0.1(4)
Extinction coefficient	0.085(12)
Largest diff. peak and hole	0.087 and -0.079 e.A^-3

Comments on X-ray analyses

The four samples are presumably enantiomorphs of the same handedness ($P3_1$) because the indexation of data gives a result between 95 and 98%. The opposite configuration ($P3_2$) have been tested and the results are:

gly_d_Cu_200k (CCDC 1037456) : 0.8(3)
gly_h_cu_200k (CCDC 1037358) : 1.1(3)
gly_g_cu_200k (CCDC 1037299) : 0.9(4)
gly_f_cu_200k (CCDC 1037459) : 0.9(3)

The large uncertainty of the Flack parameters (determined with only 150 quotients) is probably due to a lack of resolution since the resolution cannot be below 0.772 with the used diffractometer and Cu source.

Two versions of PLATON, 2005 and 2014, have been used. The results are the following:

gly_d_Cu_200k (CCDC 1037456)

- 2014 : BASF 0.16 and -1-10 0 1 0 0 0 -1 ; the corresponding refinement with TWIN and BASF instructions do not give significantly different results.
- 2005 : "floating point stack fault"

gly_h_cu_200k (CCDC 1037358)

- 2014 : "too few obs.GT.fcalc"
- BASF : 0.0

gly_g_cu_200k (CCDC 1037299)

- 2014 : "no twin law detected"
- 2005 : "floating point stack fault"

gly_f_cu_200k (CCDC 1037459)

- 2014 : "too few obs.GT.fcalc"
- 2005 : "floating point stack fault"

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