

High Temperature Sublimation of α -Amino Acids: A Realistic Prebiotic Process Leading to Large Enantiomeric Excess.

Arkadii V. Tarasevych, Alexander E. Sorochinsky, Valery P. Kukhar, Jean-Claude
Guillemin*

SUPPORTING INFORMATION

Contents

Sublimation and preparation of samples for GC	S1
Yield of Sublimation	S1
Reaction pathway	S2
Chiral GC analysis	S3
Table S1. Sublimation of mixtures of L-Val and non-racemic Leu	S4

Sublimation and preparation of samples for GC.

A sample of amino acids (the amounts are indicated in the Tables 1-3 and S1) was poured at once into a 1L screw-capped Erlenmeyer flask that had been previously heated on a hot plate for 2 min (for the temperature see Tables 1,2,S1). The flask was quickly closed and the heating was maintained for another 15 min. After cooling to room temperature the sublimed material was then dissolved in 5-10 mL of 0.1 M HCl. An aliquot of the solution (90 μ L) was transferred to a 5 mL vial and diluted with water (270 μ L) and pyridine/ethanol mixture (4:1, 240 μ L). Ethyl chloroformate (ECF) (30 μ L) was added to the solution and the capped vial was vigorously shaken for ~15 s to form an N-ethoxycarbonyl-amino acid ethyl ester. The derivatives were extracted with chloroform (~1 mL containing 1% ECF) and the organic phase was separated with a pipette, passed through a pad of silica gel, then dried over Magnesium sulfate. 2,2-Dimethoxypropane (~1 mL) was added and the resulted solution was evaporated and dried in vacuo. The residue was dissolved in dry diethyl ether (~1.5 mL), transferred into a 2 mL GC vial, and a sample volume (1-3 μ L) was then injected in the GC chromatograph equipped with a chiral column.

Yield of sublimations. The yields of sublimation are strongly dependent on the temperature of sublimation and the nature of amino acids. An average of 77 % with variations of $\pm 5\%$ was observed for 30 measures taken at random in sublimations performed at 490 °C. These yields

are based on the weight of the whole product after sublimation and on the purity determined by ^1H NMR spectroscopy in D_2O with an internal reference. Not surprisingly, the yield is much better at lower temperature of sublimation ($390\text{ }^\circ\text{C}$, 95%) and smaller at a higher temperature of sublimation (530°C , ~60%).

The heating of aliphatic amino acids in standard conditions has already been reported¹⁻³ and leads to decomposition via decarboxylation, decarbonylation, dehydration and desamination reactions. Numerous low boiling products (carbon monoxide, carbon dioxide, water, aldehydes, ammonia and others) alongside with condensation products like diketopiperazines and oligopeptides have been observed. We studied several sublimed samples by ^1H NMR spectroscopy to determine the nature of the decomposition products. The spectra have revealed a number of trace signals corresponding to low boiling products among those cited above and to products of condensation. In the thermolysis of Valine by itself, for example, small amounts of isobutyraldehyde, ammonia and water were observed after condensation of the gaseous phase.

Many amino acids and particularly disubstituted derivatives like Isovaline are decomposed at more than 95 % in our experimental conditions.

Reaction pathway. In all experiments, the ee of the enantiopure did not change significantly (96 to 100% ee) except for the ee of alanine which decreased up to 86% (main text, Table 2), this latter showing unambiguously that an enantiomerization can occur during such sublimations. However, 23 % in weight on average being lost in each experiment, the results could be explained by another process resulting by a selective decomposition of one enantiomer. A protection by “self-recognition of chirality”⁴⁻¹¹ between the enantiopure and the enantiomer(s) of the racemate(s) with the same handedness could lead to the selective decomposition of the other enantiomer(s). This hypothesis is not supported by ^1H NMR spectroscopy: the ratio between amino acids is identical ($\pm 5\%$) before and after sublimation at 490°C for (L-Leu/D,L-Val), (L-Leu/D-Val) and (L-Leu/L-Val) samples. We can thus conclude in accordance with Viedma^{6,7} that enantioenrichment is a consequence of enantiomerization.

1. V. Ya. Yablokov, I. L. Smel'tsova, I. A. Zelyaev and S. V. Mitrofanova, *Rus. J. Gen. Chem.*, 2009, **79**, 1704-1706.

2. V. A. Yablokov, I. L. Smel'tsova, and V. I. Faerman, *Rus. J. Gen. Chem.*, 2013, **83**, 476-480.

3. J. Li, Z. Wang, X. Yang, L. Hu, Y. Liu and C. Wang, *Thermochimica Acta*, 2006, **447**, 147-153.
4. S. Kojo, H. Uchino, M. Yoshimura and K. Tanaka, *Chem. Commun.*, 2004, 2146-2147.
5. V. Tarasevych, A. E. Sorochinsky, V. P. Kukhar and J.-C. Guillemin, *Orig. Life Evol. Biosph.*, 2013, **43**, 129-135.
6. C. Viedma, W. L. Noorduin, J. E. Ortiz, T. de Torres and P. Cintas, *Chem. Comm.*, 2011, **47**, 671-673.
7. C. Viedma, J.E. Ortiz, T. de Torres and P. Cintas, *Chem. Comm.*, 2012, **48**, 3623-3625.
8. Y. Hayashi, M. Matsuzawa, J. Yamaguchi, S. Yonehara, Y. Matsumoto, M. Shoji, D. Hashizume and H. Koshino, *Angew. Chem. Int. Ed.* 2006, **45**, 4593-4597.
9. M. Klussmann, H. Iwamura, S. P. Mathew, D. H. Wells, Jr., U. Pandya, A. Armstrong and D. G. Blackmond, *Nature* 2006, **441**, 621-623.
10. J. E. Hein, E. Tse and D. G. Blackmond, *Nature Chem.*, 2011, **3**, 704-706.
11. S. Kojo and K. Tanaka, *Chem. Comm.* 2001, 1980-1981.

Chiral GC analysis

GC capillary CHIRALDEX™ G-TA column (L x I.D. 30 m x 0.25 mm, d_f 0.12 μm – film thickness) at Shimadzu GC-2014 was used for the analysis of enantiomeric composition of derivatized sublimates of aliphatic amino acids.

Conditions for the analysis of N-ethoxycarbonyl-amino acid ethyl ester (alanine, 2-aminobutyric acid, iso-leucine, leucine, nor-leucine, nor-valine, valine, tert-leucine), total time of the program 126.33 min. Carrier gas He, flow control mode – linear velocity, pressure 145.9 kPa, total flow 22.3 mL/min, column flow 1.76 mL/min, linear velocity 40.0 cm/sec, purge flow 3.0 mL/min. Column conditions: 90°C for 3 min; 0.6 °C/min up to 120 °C, hold time 20 min; 0.6 °C/min up to 140 °C, without hold time; 2 °C/min up to 160 °C, hold time 10 min at this temperature.

Retention times (min), measured D/L ratio for commercially available racemates: Ala 37.88 (L), 34.44 (D), D/L 1.0032; Leu 59.06 (L), 55.56 (D), D/L 1.017; Val 47.58 (L), 45.28 (D), D/L 1.0024; isoLeu 59.83 (L), 54.08 (D), 1.0855; norLeu 70.16 (L), 65.35 (D), 0.9650; tertLeu 46.74 (L); norVal 58.34 (L), 52.09 (D), 0.9928; 2-Aba 47.49 (L), 42.04 (D), 1.0086.

Table S1. Sublimation of mixtures of L-Val and non-racemic Leu.^a

Entry	1 st series (490°C)		2 nd series (530°C)	
	Starting mixture (ee %)	Sublimed mixture (ee %)	Starting mixture (ee %)	Sublimed mixture (ee %)
1	87.2 (D)	81.4 (D)	42 (D)	0
2	77.4 (D)	71.3 (D)	30 (D)	16.2 (L)
3	69.3 (D)	60.8 (D)	10 (D)	27.0 (L)
4	61.4 (D)	47.9 (D)		
5	40.1 (D)	19.8 (D)		
6	23.1 (D)	9.0 (L)		
7	0	28.0 (L)		
8	18.1 (L)	46.3 (L)		
9	63.9 (L)	75.9 (L)		
10	89.6 (L)	92.8 (L)		
11	100 (L)	100 (L)		

^a Mechanical mixtures, prepared by careful grinding of enantiopure L-Val and D- or L-Leu and DL-Leu. Amounts: 100 mg of L-Val (1 equiv.), 28 mg of non-racemic Leu (0.25 equiv.). Time of sublimation: 15 min., ee of Leu.