Photochemistry

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Photonenergy-Controlled Symmetry Breaking with Circularly Polarized Light**

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Dedicated to Professor Martin Quack on the occasion of his 65th birthday

Abstract: *Circularly polarized light (CPL) is known to be a true chiral entity capable of generating absolute molecular asymmetry. However, the degree of inducible optical activity depends on the λ of the incident CPL. Exposure of amorphous films of rac-alanine to tunable CPL led to enantiomeric excesses (ee) which not only follow the helicity but also the energy of driving electromagnetic radiation. Postirradiation analyses using enantioselective multidimensional GC revealed energy-controlled ee values of up to 4.2 %, which correlate with theoretical predictions based on newly recorded anisotropy spectra g(λ). The tunability of asymmetric photochemical induction implies that both magnitude and sign can be fully controlled by CPL. Such stereocontrol provides novel insights into the wavelength and polarization dependence of asymmetric photochemical reactions and are highly relevant for absolute asymmetric molecular synthesis and for understanding the origins of homochirality in living matter.*

Circularly polarized light (CPL) exhibits true chirality.[1] Its interaction with matter can be sensitive to molecular chirality. CPL can therefore be used to distinguish between optical isomers of a chiral molecule upon the difference in their molar extinction coefficients ($\Delta\varepsilon$) toward right-handed (r) and left-handed (l) CPL, an effect referred to as circular dichroism.[2] The absorption of CPL by chiral molecules can impart a slight bias for one of the enantiomers and lead to its preferential synthesis or destruction.[3] Such stereoselective interactions can therefore result in an *ee* value, an effect first demonstrated by Kuhn and Braun.[4] The evolution of *ee* values during a photochemical reaction as a function of time [extent of reaction (ξ)] depends upon the type of CPL-induced asymmetric transformation. There have been four different types of asymmetric CPL-induced chemical reactions classified in the literature:[3] photoequilibration, direct asymmetric photosynthesis, photoisomerization, and asymmetric photolysis. The most studied of these remains asymmetric photolysis, where an increase in *ee* value of the enantiomer with the lower extinction coefficient is observed, as the other enantiomer is preferentially photodecomposed by CPL. Moreover, asymmetric photon-induced physical processes such as CPL photoionization were recently shown to induce significant *ee* values of pure enantiomers of alanine, in a given direction of space.[5]

The chiroptical response of a molecule interacting with monochromatic CPL can be quantified by the anisotropy factor g, defined as $g = \Delta\varepsilon/\varepsilon$.[6] In molecular quantum physics g is usually approximated as $4R/D$, where R is the rotational strength and D is the dipole strength of the molecule.[7] Enantiospecific photochemistry promoted by CPL is known to depend upon the helicity of the incident light[8–10] and the extent of reaction (ξ).[11] However, how the energy-dependency, rooted in the anisotropy, affects the outcome of interactions between chiral photons and molecules has remained unexplored until now.

Herein we report on the CPL irradiation of *rac*-^{13}C-alanine in its isotropic amorphous solid state by adjusting irradiation wavelength, irradiation time, and synchrotron light polarization to show the energy-dependent regulation of CPL-induced *ee* values. Prior to the energy-selective photolysis studies, it was essential to determine the differential rates

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of excitation of L- and D-alanine enantiomers in the vacuum ultraviolet (VUV) region. VUV photons possess sufficient energy to induce direct photolysis, thus triggering stereoselective decarboxylation of *rac*-alanine. Indeed, the chiroptical response of small chiral biomolecules, such as amino acids, to UV irradiation is primarily associated with the n→π* excitation of the carboxylate group located at the stereogenic carbon atom. Previously, circular dichroism (CD) and anisotropy measurements have commonly been performed in solution, thus limiting the potentially available electronic transitions in the VUV and UV spectral region. A new experimental set-up[12] (Figure 1 a) at the synchrotron radiation facility ASTRID, in Aarhus University (Denmark), has recently allowed us to record anisotropy spectra of amino acids into the VUV spectral range.[13]

A custom-built ultrahigh vacuum (UHV) sublimation-condensation chamber was used to deposit amorphous films of enantiopure L- and D-alanine onto VUV optical windows with defined film thicknesses. The noncrystalline, amorphous, solid state and isotropic orientation of alanine in the condensed form has been confirmed by electron diffraction. Scanning electron microscope images show no regularities such as alignments of adjacent molecules in the external structures (see Figure S1 in the Supporting Information). Moreover, the zwitterionic structure of condensed alanine has been verified by the characteristic NH_3^+, $\nu_{as}COO^-$, and ν_sCOO^- vibration modes.[14] Anisotropy spectra of these isotropic amorphous films have been recorded between $\lambda =$ 130 and 300 nm. The obtained spectra of L- and D-alanine (Figure 2 a,b), which have each been constructed from multiple single-enantiomer measurements (see Figure S2), are almost perfect mirror images of each other, and significantly larger average chiroptical responses are observed for the amorphous films relative to solution measurements. Both the sign and the magnitude of the anisotropy (g) clearly depend on the wavelength of the CPL. Based on these anisotropy spectra, the optimal photon energies to study the energy-dependent chiral selection of asymmetric photochemistry were determined to be 6.19 and 6.74 eV. These bands have been respectively assigned to the electronic n→π* transition in the carboxylate anion mixed with the n(COO^-)→σ*(N-H) transition and the first π→π* transition.[15]

In addition to our experiments, we have studied theoretically the anisotropy factor g as a function of the wavelength (λ) for zwitterionic L- and D-alanine. Upon averaging over twelve molecular geometries sampling the low-energy landscape of the isolated molecule, we found that the main feature of the anisotropy spectra can be predicted by time-dependent density functional theory (see Figure S3). Other significant features are much better reproduced by the g-curve corresponding to geometries with the plane of the carboxylate group rotated by 60° with respect to the equilibrium geometry of the isolated molecule. This result suggests that, in the amorphous film, this geometry might be the dominant conformation (see the Supporting Information).

The anisotropy spectra furthermore allow the quantitative prediction of inducible *ee* value into a racemic sample by enantioselective photolysis at a given extent of reaction (ξ). Theoretical characteristics of asymmetric photodecomposition were first considered by Kuhn and Knopf[16] and detailed kinetic aspects were later given by Kagan and co-workers.[11] We generalized the kinetic resolution of CPL-induced decomposition for amino acids in the low g limit and found that the *ee* value as function of g and ξ becomes[13]

$$ee \geq (1-(1-\xi)^{g/2}) \times 100\,\%. \qquad (1)$$

Throughout a photolytic process, while the optical purity of alanine approaches 100 % the amount of enantioenriched substrate to be quantified approaches zero. This dichotomy was first observed by Kagan and co-workers[11] in the partial photodecomposition of camphor, and more recently by Meierhenrich and co-workers[9,17] in the asymmetric photochemistry of the amino acid [^{12}C]leucine. The predicted

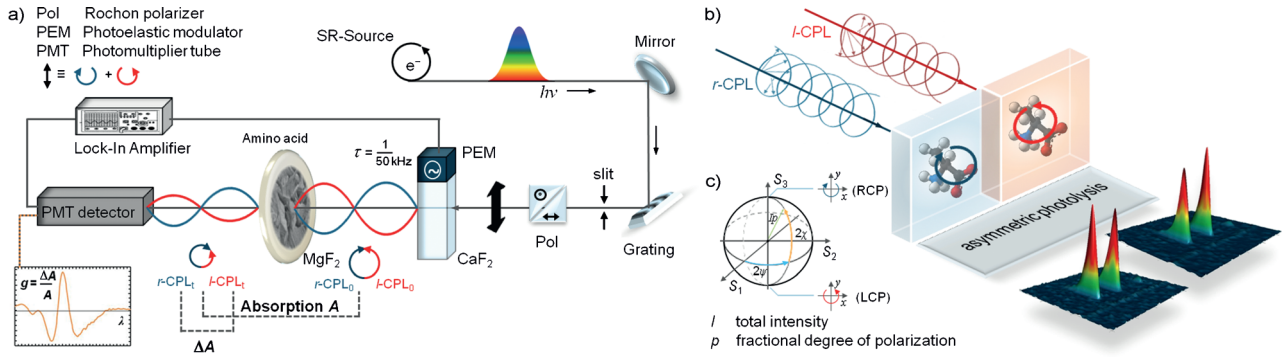

Figure 1. Outline of anisotropy spectroscopy and energy-tunable asymmetric photolysis. a) Experimental set-up for recording anisotropy spectra of amino acid enantiomers condensed in form of isotropic amorphous films on VUV-MgF_2 optical windows in the VUV and UV spectral range using a synchrotron radiation (SR) source. The PEM converts monochromatic SR into alternating *l*- and *r*-circularly polarized light (CPL). Both the differential absorption ΔA of alternating *l*- and *r*-CPL by optically active amino acid enantiomers and the sample absorbance A is recorded simultaneously to obtain anisotropy spectra $g(\lambda) = \Delta A/A$. b) Photolytic induction of *ee* values into amino acids in the amorphous solid state as a function of CPL energy and circular polarization. c) Energy-tunable and tailored elliptical polarization as defined by its Stokes parameters (S_1, S_2, and S_3, where Ip, 2χ, and 2ψ are the spherical coordinates) are provided by the HU640 undulator at the DESIRS beamline on the SOLEIL storage ring. Postirradiation detection of enantiomeric enrichment is carried out by multidimensional gas chromatography.

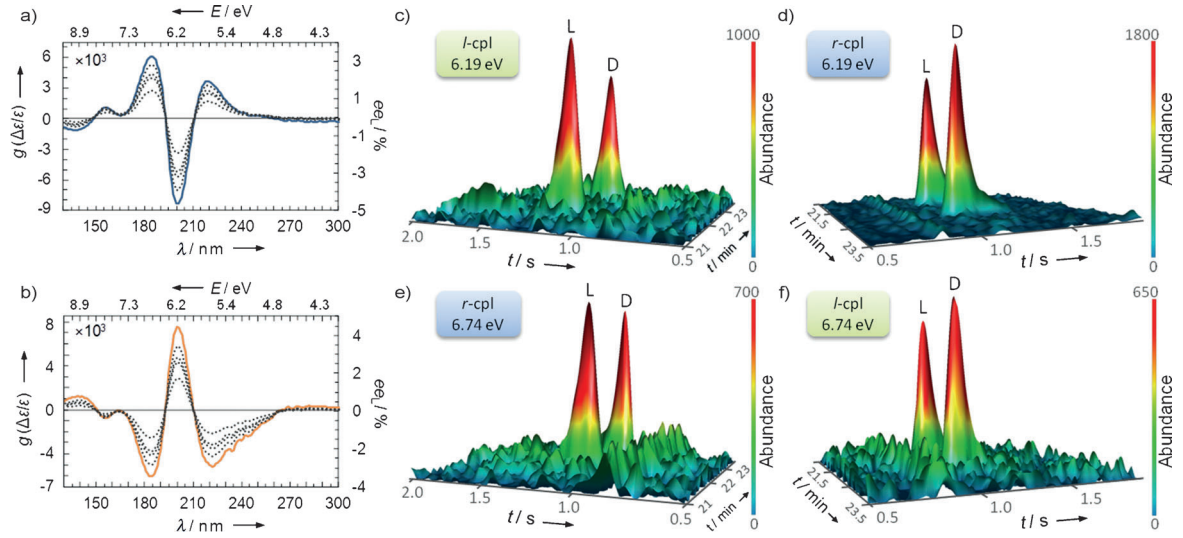

Figure 2. Energy- and polarization-dependent CPL-induced symmetry breaking. a,b) Anisotropy spectra $g(\lambda)$ in the vacuum UV and UV spectral range of enantiopure L-Ala (a) and D-Ala (b) (thick lines) condensed as isotropic amorphous films. Dotted lines represent the predicted corresponding L-enantiomeric excesses (ee_L) induced by either *l*- or *r*-CPL as a function of g and ξ of 0.9999, 0.9995, 0.999, and 0.99. c–f) Close-up of the multidimensional enantioselective gas chromatographic resolution of [^{13}C]alanine enantiomers, derivatized as *N*-ethoxycarbonyl heptafluorobutyl esters, after irradiation with CPL differing polarization and photon energies for 5 h. Amorphous films of *rac*-[^{13}C]alanine were irradiated at anisotropy the extrema 6.19 eV (200 nm) with *l*-CPL, thus resulting in an *ee* value for L-[^{13}C]alanine (c) and *r*-CPL, thus producing an equivalent *ee* value but for D-[^{13}C]alanine (d). According to the anisotropy spectra of alanine (a, b), irradiation of amorphous *rac*-[^{13}C]alanine films at a photon energy of 6.74 eV (184 nm) with e) *r*-CPL and f) *l*-CPL yielded reversed magnitudes of induced *ee* values thus with the opposite helicity of incident light as compared to the anisotropy band at 6.19 eV.

ee values, which can be photochemically induced into *rac*-alanine as a function of g for a selected ξ, are depicted as dotted lines in Figures 2 a,b.

The experimental energy-selective asymmetric photolysis of solid-state alanine was investigated using intense and quasiperfect circularly polarized synchrotron radiation (CPSR) emitted by the undulator feeding the DESIRS[18] VUV beamline at the SOLEIL facility. Absolute circular polarization rates on the sample were above 97%, as measured by an in situ polarimeter.[19] Solid films of *rac*-[^{13}C]alanine were irradiated individually with *r*- and *l*-CPSR. ^{13}C-labeled samples were used to exclude any biological bias in the enantioselective postirradiation analyses. Ten isotropic amorphous *rac*-alanine films of 300 nm thickness were therefore prepared prior to irradiation by sublimating D,L-[^{13}C]alanine using the UHV sublimation-condensation chamber.

After stereoselective decarboxylation by CPSR, the remaining alanine residues were stored under stable dry conditions on their MgF_2 windows to be analyzed by multidimensional gas chromatography coupled to time-of-flight mass spectrometry (GC × GC-TOFMS). Both irradiated and non-irradiated [^{13}C]alanine films were extracted at a clean-bench and analyzed as their *N*-ethoxycarbonyl heptafluorobutyl ester (ECHFBE) derivatives by GC × GC-TOFMS. All samples were alternately injected at least five times to accurately determine photolysis rates and CPL-induced *ee* values with reliable statistical error bars. The atomic mass unit 118 was used for identification and volume-peak quantification of [^{13}C]alanine enantiomers based on time-of-flight mass spectrometric detection. In total, a set of ten samples was analyzed, as summarized in Table 1: two of these are reference samples that were not irradiated to calculate the photolysis rates (see Figure S4). Moreover, a blank sample was prepared and analyzed under same analytical conditions to investigate any biological or laboratory ^{13}C-sources (see Figure S5).

On Beamline DESIRS, amorphous films of *rac*-[^{13}C]alanine were first irradiated at 6.19 eV for 5 hours with *l*-CPSR, thus yielding an ee_L value of 4.19% in sample A1 (Figure 2 c). Sample A2 was irradiated with identical photon-energy for the same irradiation time but with *r*-CPSR, and its photolytic degradation proceeded to the same extent of reaction but resulted in a reversal in the sign of the induced ee_L value of −4.22% in the remaining residue (Figure 2 d). Samples A3 and A4 were each irradiated respectively at 6.19 eV for 2.5 hours with *l*- and *r*-CPSR. Decreasing the irradiation time from 5 to 2.5 hours decreased the number of chiral photons absorbed by the racemic substrate and, consequently, lower optical purities are observed (see Table 1 and Figure S6 a,b). Samples B1–B4 were all irradiated at 6.74 eV and, similar to samples A1–A4, the sign and absolute magnitude of the induced *ee* value follow the helicity of incident CPSR and the number of photons absorbed, as measured by the extent of reaction (ξ; see Figure 2 e,f and Figure S4 c,d). However, at 6.74 eV, *l*-CPSR was found to yield an ee_L value of −3.12% (Figure 2 f) while *r*-CPSR was found to induce an ee_L value of 3.15% after 5 hours of irradiation (Figure 2 e), that is, mirroring the results found for 6.19 eV. These experimental data demonstrate for the first time that changing the energy of a given handedness of CP light from 6.19 eV to 6.74 eV switches the sign of the *ee* value

Table 1: Experimental and predicted enantiomeric excesses (ee_L) induced by asymmetric photolysis of racemic [^{13}C]alanine as function of irradiation wavelength (λ), helicity, irradiation time, and extent of reaction (ξ).

[^{13}C]alanine sample	E_{photon} [eV]/λ [nm]	Circular polarization	Irradiation [h]	Extent of reaction ξ [%]	ee_L [%][a] (n)[b]	ee_L [%][c]
blank 1[d]	–	–	–	–	0.08 ± [e] 0.15 (7)	–
blank 2[d]	–	–	–	–	0.05 ± 0.19 (10)	–
A1	6.19/200	*l*-CPSR[f]	5.0	99.95	4.19 ± 0.14 (6)	3.10
A2	6.19/200	*r*-CPSR	5.0	99.97	−4.22 ± 0.21 (5)	−3.42
A3	6.19/200	*l*-CPSR	2.5	99.56	0.57 ± 0.17 (9)	2.22
A4	6.19/200	*r*-CPSR	2.5	99.66	−1.11 ± 0.16 (9)	−2.38
B1	6.74/184	*l*-CPSR	5.0	99.93	−3.12 ± 0.34 (5)	−2.24
B2	6.74/184	*r*-CPSR	5.0	99.96	3.15 ± 0.30 (4)	2.36
B3	6.74/184	*l*-CPSR	2.5	99.89	−2.88 ± 0.28 (7)	−2.10
B4	6.74/184	*r*-CPSR	2.5	99.80	1.58 ± 0.15 (9)	1.88

[a] Experimentally determined by enantioselective GC×GC-TOFMS. [b] Number of replicate analyses. [c] Predicted ee_L value based on the anisotropy factor g and achieved extent of reaction ξ; $ee = (1-(1-\xi)^{g/2}) \times 100\,\%$. [d] Non-irradiated sample: control and reference sample to calculate photolysis rate ξ. [e] ± gives standard deviation 1 σ of multiple injections n. [f] Circularly polarized synchrotron radiation.

induced by asymmetric irradiation of amino acids. Moreover, the *ee* value identified in sample A2 is the largest degree of an *ee* value ever induced by CP light in amino acids. Given the second dimension of the chromatograms, the alanine enantiomers were not only "base surface"-separated but were also separated from both the solvent and the column bleeding (Figure 2 and see Figures S4 and S6). The GC × GC instrument[20] used for these studies therefore considerably improved the sensitivity and precision of experimentally determined *ee* values as compared to conventional one-dimensional separation techniques. Consequently, photolysis rates of up to 99.97 % carrying the photochemical reaction to high optical purities but low levels of residual alanine were reached.

Given the detection of CPL in star-forming regions[21] and the identification of amino acids from meteorite samples which possess higher *ee* values of the naturally occurring L-enantiomeric form,[22] it is reasonable to postulate that interstellar asymmetric photochemistry could have introduced initial chiral biases into key biomolecular building blocks. Once in place, this sense of chirality may have perpetuated throughout autocatalytic enhancement and ultimately afforded the homochiral biopolymers present in life on earth today. As such, the results reported here support a photochemical origin for life's asymmetry as induced by interstellar CPL, however, under restrictive initial radiation conditions, considering the wavelength dependence of the initial chiral bias. The European Space Agency's Rosetta mission may provide insight into the CPL-induced origins of biomolecular chirality by in situ analyses of a variety of chiral organic molecules including amino acids[23] after soft landing on a cometary nucleus in November 2014.[24]

In summary, the present study demonstrates the energy- and polarization-controllable symmetry breaking in amorphous films of *rac*-alanine using CPSR. The anisotropy spectra of alanine into the VUV spectral region proved essential for determining the optimal wavelengths for CPL-induced enantiomer enrichment. We hope these results spark further experimental and theoretical efforts in the study of asymmetric photochemical reactions of individual chiral molecules to pave the way for efficient polarized-light-induced absolute asymmetric molecular synthesis.

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