Configuration of a single centre determines chirality of supramolecular carotenoid self-assembly

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Abstract—Card-pack and head-to-tail types of self-assembly are formed upon aqueous dilution of capsantholon 6′-epimers dissolved in water-miscible organic solvents. Slow transformation of head-to-tail assembly into card-pack type is observed. Induced supramolecular chirality is seen upon addition of achiral β-carotene, as judged from the increased intensity of exciton signal detected in circular dichroism spectra. © 2001 Elsevier Science Ltd. All rights reserved.

Hydrophobic molecules stack together in aqueous-organic solvents.[1] The UV spectra detect the aggregation of molecules possessing chromophores[2] owing to the distinct character of the absorption band exhibited by the aggregate as compared with the monomer. Aggregates of chiral chromophores may give rise to an exciton signal appearing in the CD spectrum.[3,4] The transfer of excitation energy between molecules has been observed in carotenoid aggregates[5] and interpreted on the basis of the molecular exciton model.[6] According to the spectral changes, blue-shifted UV spectra are indicative of card-pack stacking, while red-shift in the UV–vis range demonstrates head-to-tail association.[7] Hydrogen bonding between aggregated molecules was suggested to be responsible for the formation of card-pack assemblies,[8] but the role of other structural features that influence the type of stacking remained largely unknown. Since nature applies the self-assembly of molecules for economic synthesis and facile formation of biological systems,[9] it is of interest to understand how the structure of monomers govern the building of supramolecular structures. Here, we report an example of the decisive role of a single centre of asymmetry in defining the type of aggregate. In addition, we demonstrate chiral induction of an achiral molecule by the influence of the supramolecular chirality of a carotenoid self-assembly.
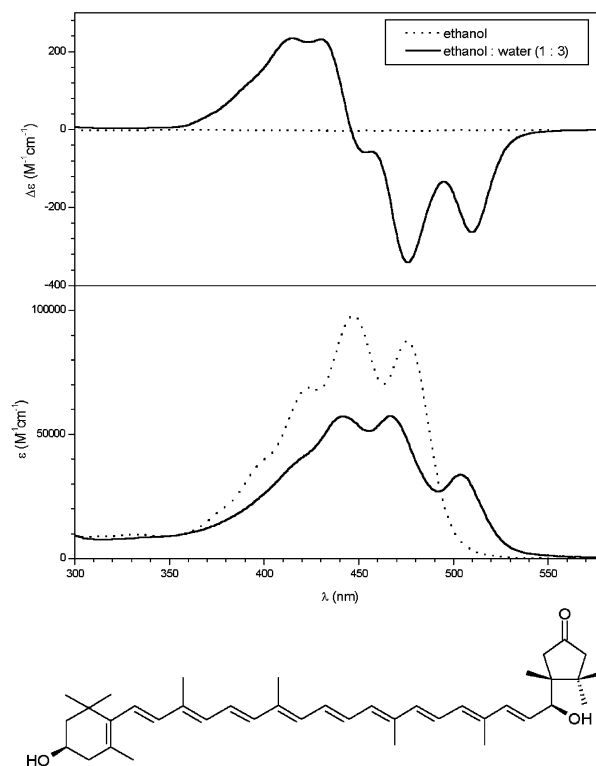
Figure 1. UV–vis and CD spectra of 6′*S*-capsanthol-3′-on; in ethanol: $c = 3.4 \times 10^{-5}$ M; $l = 0.2$ cm; in ethanol/water: $c = 2.5 \times 10^{-5}$ M; $l = 0.5$ cm. UV–vis [· · ·]: 424; 446; 475; [—]: 441; 467; 504; CD [—]: 415; 430; 475; 509.

In order to gain insight into the influence of molecular chirality on the structure of a supramolecular aggregate, we sought a model containing a stereogenic centre neighbouring the polyene chain. The major carotenoid component of ripe *Capsicum annuum* (red paprika), capsanthin[10] ((all-*E*,3*R*,3′*S*,5′*R*)-3,3′-dihydroxy-β,κ-carotene-6′-one) contains an oxo-function at the required position. Oxidation[11] and subsequent reduction[12] of capsanthin yields the 6′*R*-, and 6′*S*-epimers of capsanthol-3′-on ((all-*E*,3*R*)-3,6′-dihydroxy-5′*R*-β,κ-caroten-3′-ones) that served for the above purpose.

In ethanol, the main absorption band of 6′*S*-capsanthol-3′-on in the visible region is assigned to the electronic transition from the ^1A_g ground state to the ^1B_u excited state of conjugated π-electrons; the spectrum becomes red-shifted and widened upon aqueous dilution (Fig. 1). The spacing in the UV spectrum between neighbouring maxima/shoulders is consistent with the superposition of 0-0, 0-1, 0-2, etc. vibrational levels on the electronic excitation.[5] The circular dichroism spectrum of 6′*S*-capsanthol-3′-on is very weak in ethanol indicating that the chiral perturbation of the polyene chromophore even by the 6′-centre is not substantial. However, the CD-spectrum dramatically changes in aqueous ethanol displaying broad and structured negative–positive Cotton bands. Splitting of the CD curve corresponds to a typical exciton signal of left-handed chirality (Fig. 1). All these spectral changes indicate the formation of a head-to-tail type aggregate in which the individual molecules are positioned in a chiral arrangement and retain their vibrational freedom.

The UV–vis spectrum of 6′*R*-capsanthol-3′-on in ethanol is not different from that of its epimer, but aqueous dilution reduces the structured part of the absorption curve and produces a sharp blue-shifted peak (Fig. 2). Contrary to the 6′*S*-epimer, the spectrum of 6′*R*-capsanthol-3′-on is time-dependent in aqueous ethanol displaying the elimination of the vibrationally structured band as well as a large increase of the blue-shifted peak after an hour. The circular dichroism spectrum is again very weak in ethanol. Upon aqueous dilution, however, a left-handed exciton splitting about twice as intense as that of 6′*S*-capsanthol-3′-on appears immediately that roughly doubles in an hour. Simultaneously, the initial long-wavelength structured band disappears. The amplitude (A) of split Cotton effects $\Delta\varepsilon^{389} - \Delta\varepsilon^{372} = -1672$ is the largest we know about in the field of carotenoid self-assemblies. Since the A value is negative, it indicates the interaction of the transition dipole moments to be left-handed. The angle between neighbouring molecules provides the chiral character of the supramolecular assembly. These spectral characteristics refer to the initial simultaneous formation of right-handed head-to-tail and left-handed card-pack types of aggregates, of which the former slowly transforms to the latter. Since both UV–vis and CD final spectra only contain the exciton peak blue-shifted by about 100 nm, the electronic excitation in the card-pack assembly corresponds to a single transition to the perturbed excited state independent of the vibrations of individual

molecules (Fig. 2). The spectra demonstrate that the molecules stack together more tightly in the card-pack aggregate. The spontaneous transformation of the head-to-tail assembly to the card-pack one is consistent with the increased stability of the latter.

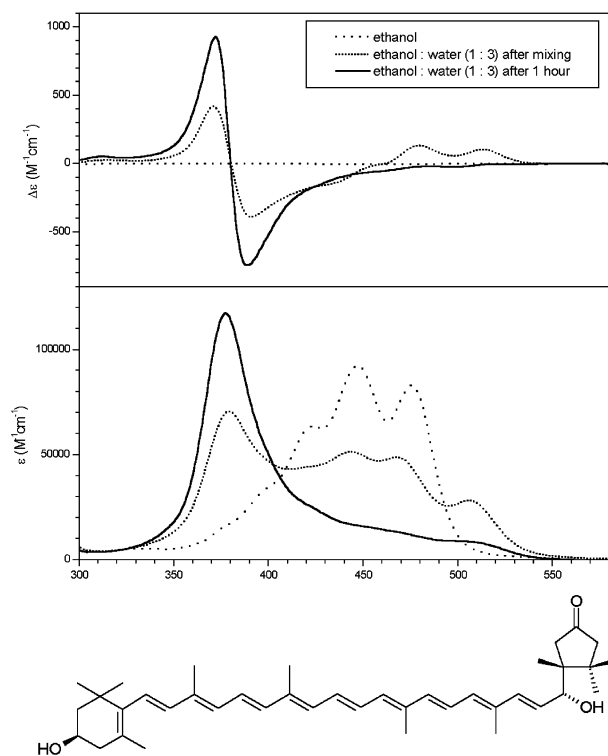In the lack of any centre of asymmetry, β-carotene is achiral. Its UV–vis spectrum in acetone is similar to

Figure 2. UV–vis and CD spectra of 6′*R*-capsanthol-3′-on; in ethanol: $c = 5.6 \times 10^{-5}$ M; $l = 0.2$ cm; in ethanol/water: $c = 2.5 \times 10^{-5}$ M; $l = 0.5$ cm. UV–vis [· ·]: 423; 447; 475.5; [·····]: 379; 443; 467; 505; [—]: 377; CD [·····]: 371; 391; 478; 512; [—]: 372; 388.
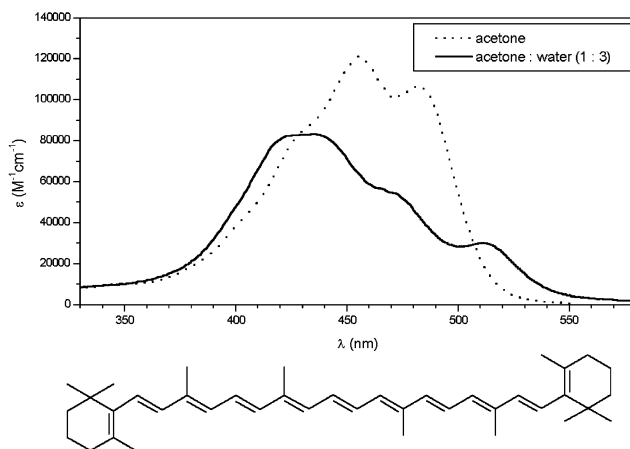

Figure 3. UV–vis spectra of β-carotene; in acetone: $c = 1.2 \times 10^{-5}$ M; $l = 0.5$ cm; in acetone/water: $c = 1.2 \times 10^{-5}$ M; $l = 0.5$ cm. UV–vis [· ·]: 455; 480; [—]: 434; 511.

those in ethanol shown above. Upon aqueous dilution, it widens showing both red and blue shifts as signs of forming aggregates of different types (Fig. 3). Since no chiral element influences the aggregation of β-carotene, its assembly is formed as a haystack without measurable supramolecular chirality. Addition of β-carotene to 6′S-capsanthol-3′-on modifies both the UV–vis and CD spectra; while the former is blue-shifted with vibrational spacing retained, the latter clearly indicates that β-carotene contributes to the supramolecular chirality of the head-to-tail assembly formed by 6′S-capsanthol-3′-on. The CD peaks at long and shortest wavelengths became more intense indicating that even the weaker supramolecular organisation is able to induce chirality of an achiral molecule (Fig. 4).

Since no basic difference is seen in the ability of intermolecular hydrogen bond formation[8] between the two epimers, it does not appear to be the prerequisite of card-pack assemblies. In order to interpret the difference between the types of assemblies formed by capsanthol-3′-on 6′-epimers, a grid search by the MMFF94 force field was performed so as to have a potential energy profile depending on the torsion angle, $\tau_{5'-6'-7'-8'}$. Three minima were found roughly 120 degrees apart. For 6′S-capsanthol-3′-on the minima were equienergetic, while one of the minima for 6′R-capsanthol-3′-on at −60 degrees was found to be deeper by 3 kcal/mol than the other two. It seems to be the main reason why the head-to-tail aggregate of this epimer transforms into a card-pack assembly in contrast to 6′S-capsanthol-3′-on having energy-minima of equal energy.

Acknowledgements

Figure 4. Influence of β-carotene ($c = 1.3 \times 10^{-5}$ M) on the UV–vis and CD spectra of 6′S-capsanthol-3′-on (in both media: $c = 1.3 \times 10^{-5}$ M; $l = 0.5$ cm). UV–vis [· · ·]: 424; 449; 476; [·····]: 443; 467; 504; [—]: 437; 502; CD [·····]: 432; 448; 475; 509; [—]: 412; 475; 509.

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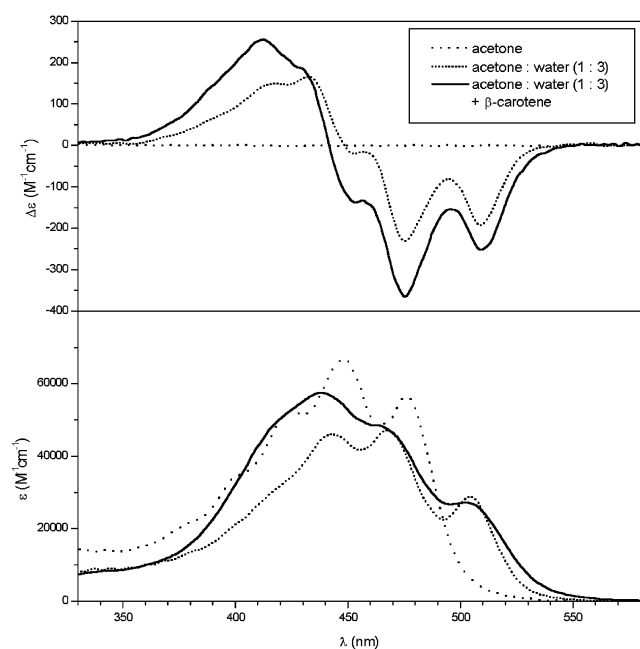12. Deli, J.; Ősz, E.; Visy, J.; Zsila, F.; Simonyi, M.; Tóth, G. *Helv. Chim. Acta* **2001**, *84*, 263–270.