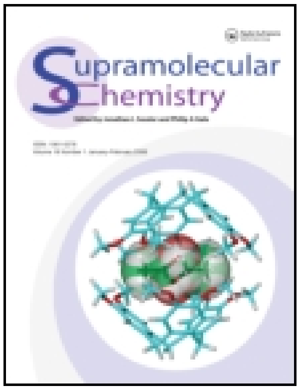

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Nanopumpkins and a sunscreen agent: the inclusion complex of cucurbituril and Tinosorb S

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Nanopumpkins and a sunscreen agent: the inclusion complex of cucurbituril and Tinosorb S

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The commercial sunscreen agent Tinosorb S (TS) is a promising oil-soluble broad spectrum UV filter. Here, we report for the first time a water-dispersible inclusion complex of TS using cucurbituril. The synthesis was carried out via a supramolecular approach in the solid state by using the high-speed vibration milling technique. The formation and the photophysical properties of the solid inclusion complex were investigated by spectroscopic techniques such as UV–vis spectrophotometry, Fourier-transform infrared and solid-state proton nuclear magnetic resonance spectroscopy as well as by thermal gravimetric analysis and X-ray diffractometry. An increase in the absorbance and a shift of the maximum absorption from 380 nm to 345 nm for the inclusion complex were observed in comparison to the precursor complex TS. The stochiometric ratio of cucurbituril and TS in the inclusion complex was found to be 2:1

Keywords: cucurbituril; Tinosorb S; inclusion complex; sunscreen agent; solvent-free process

1. Introduction

Three types of radiation can be discerned in the ultraviolet radiation (UVR) emitted by the sun: ultraviolet A (UVA) (320–400 nm), ultraviolet B (UVB) (290–320 nm) and ultraviolet C (UVC) (270–290 nm). UVA is subdivided into UVA_1 (340–400 nm) and UVA_2 (320–340 nm). The UVC radiation from the sun is blocked by the ozone layer in the stratosphere and can, therefore, not reach the surface of the earth (*1*). The UVR can induce damage such as DNA damage, skin cancer, mutations, immunosuppression, dermatoheliosis or photoageing and photodermatoses (*2*). Among them, UVB causes erythema, oedema, pigment darkening followed by delayed tanning and thickening of the epidermis and dermis, synthesis of vitamin D, photoageing, immunosuppression and photocarcinogenesis on human skin (*3*). In the human body, UVA causes oxidative reactions, which induce an increased melanin synthesis, leading to a delayed tanning response and cell membrane lipid peroxidation eventuating in cutaneous inflammation (*4*). To prevent this damage in the human body by the UVR, the use of photo-protective agents such as clothing, hats, make-up, sunglasses, window glasses, windshields and chemical UV filters is popular.

There is a great variety of chemical compounds, which have been used as UV filters or sunscreen agents; among them, 2,4,-bis-{[4-(2-ethylhexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine (commercial name: Tinosorb S, TS) (Figure 1) is a potent sunscreen agent (*1*, *5–9*). However, its insolubility in water prevents it from being used generally as a sunscreen agent especially for humans.

Cucurbituril (CB[n]), a synthetic macrocycle, can form complexes with not only easily polarisable molecules, polar compounds or ions through ion–dipole interactions and hydrogen bonding, but also with hydrophobic molecules such as fullerene [C_{60}] (*10*, *11*). Because cucurbituril exhibits only poor solubility in common organic solvents, the complexation usually is performed in strongly acidic aqueous solutions containing alkaline metal salts or as two-phase reactions between the solid cucurbituril and the dissolved or gaseous guest molecules (*12–14*).

In this study, we report the preparation of a water-dispersible inclusion complex of TS and CB[6] through the supramolecular approach using the solid-state high-speed vibration milling method towards its application as a powerful chemical UV filter (Figure 2).

2. Experimental section

2.1 Materials

Cucurbit[6]uril (CB[6]) was purchased from Merck (Schuchardt, Hohenbrunn, Germany) and was used without any further purification. TS, a slight yellowish, water-insoluble powder, was obtained from Ciba Specialty Chemical, Inc., Basel, Switzerland and was used after recrystallisation from chloroform.

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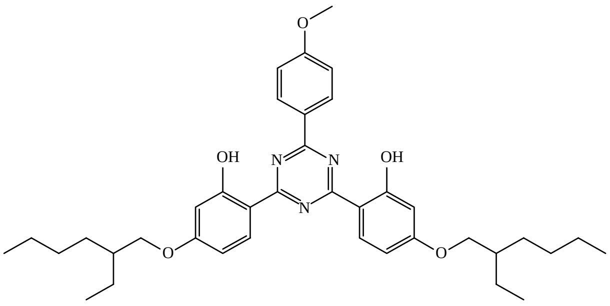

Figure 1. Structural formula of 2,4,-bis-{[4-(2-ethylhexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine (Tinosorb S, TS).

2.2 Computation

In order to calculate the optimum molecular ratio and to visualise the formation of the inclusion complex between CB[6] and TS, molecular modelling was performed under non-aqueous conditions (Spartan` 04, Wavefunction, Inc., Irvine, CA, USA).

2.3 Preparation of the inclusion complex

The inclusion complex was prepared in 3:1 molar ratio of CB[6] powder (152 mg, 1.5 mmol) and TS powder (32 mg, 0.5 mmol) by high-speed vibration milling in a solvent-free process (Mixer Mill, Type MM200, Retsch, Germany) at 1800 rpm for 3 h at ambient temperature. After milling, the inside temperature of the capsule was observed to be 47°C. Then, 500 ml of deionised (DI) (Milli-Q grade) water was added to the obtained light yellowish crude solid and the mixture was centrifuged (3000 rpm for 5 min; VS5000N, Vision) in order to remove unreacted reactants. Afterwards, the solution was freeze-dried (Freeze Dry System, Labconco) and the inclusion complex was obtained in solid form (Yield: 69 mg, 38%).

2.4 Characterisation

2.4.1 Fourier-transform infrared spectroscopy

A FT-IR 460 plus spectrometer (JASCO Inc., Easton, MD, USA) was used to obtain the IR spectra. The sample was placed in a sample holder. The IR spectra of CB[6], TS and the inclusion complex were measured from dried samples as dried potassium bromide pellets. Spectra acquisitions were performed directly on the samples with the application of 20 scans at a resolution of $4\,\mathrm{cm}^{-1}$ over the range of $4000 \sim 400\,\mathrm{cm}^{-1}$.

2.4.2 Solid-state nuclear magnetic resonance spectroscopy

Solid-state ^{1}H NMR spectroscopy was performed with a Unity NOVA 600 (Varian, 600 MHz) spectrometer.

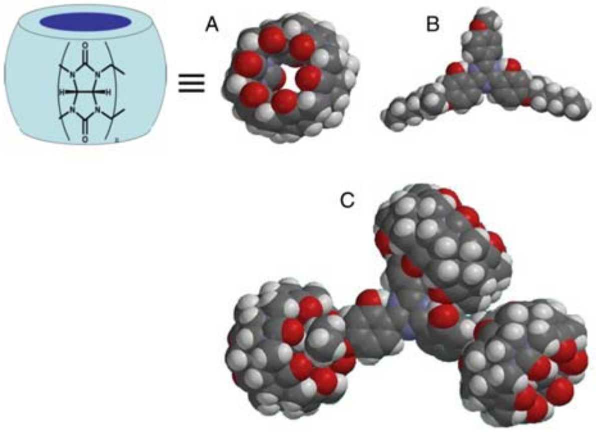

Figure 2. Energy-minimised models of cucurbituril (A), TS (B) and the inclusion complex (C) of both precursors (software: Spartan` 04).

2.4.3 X-ray diffraction study

The X-ray powder diffraction patterns of CB[6], TS and the inclusion complex were obtained at room temperature with a wide angle goniometer (Rigaku, model RINT2000) equipped with copper as the anode material, using a voltage of 40 kV and a current of 40 mA. The diffractograms were recorded in the 2θ angle range between 10° and 40°, and the process parameters were set at a scan step size of 0.02 (2θ) and a scan step time of 0.5 s.

2.4.4 Thermal gravity analysis

Thermal gravity analysis (TGA) was carried out using TGA 2950 (TA Instruments). The decomposition was studied by heating the samples in a nitrogen atmosphere from 25 to 800°C at a rate of 10°C/min.

2.4.5 UV–vis spectrophotometry

To demonstrate the UV protection of the inclusion complex on a glass surface (thickness: 0.15 mm, size: $22 \times 40\,\mathrm{mm}^2$, Paul Marienfeld GmbH & Co., Lauda-Königshofen, Germany), a typical experiment was performed as follows: in order to ensure the cleanness of the glass surface, it was cleaned appropriately before the experiment (it was sonicated in acetone for 10 min and dried in the oven at 65°C. Then, it was sonicated in ethanol for 10 min and dried in the oven at 65°C. Afterwards, it was sonicated in DI-water for 1 h and dried in the oven at 65°C.These processes were performed twice). The coating and the spreading of the dispersed inclusion complex in the aqueous solution and TS in ethanol (it is not water dispersible) onto the glass surface were performed by drop casting. In both cases, the concentration of TS was kept constant (6.4 mM, 4.37×10^{13} atom/mm^2). After drying the treated glass

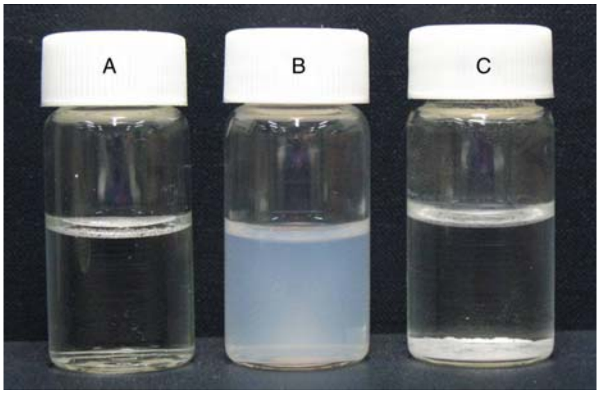

Figure 3. Comparison of the dispersions in water: (A) TS accumulated in the upper layer, (B) the inclusion complex of cucurbituril and TS and (C) cucurbit[6]uril precipitated at the bottom.

surface at room temperature, the UV protection efficiency was measured by UV–vis spectrophotometry (CARY 1E, Varian, Inc., Palo Alto, CA, USA).

3. Results and discussion

The preparation of the water-dispersible complex between TS and cucurbituril was carried out by using a solid-state reaction. The inclusion complex was obtained from a precursor mixture in a 3:1 molar ratio of CB[6] and TS at room temperature. A good dispersion of the sample prepared in water was obtained (Figure 3). Because of the intrinsic structural properties of TS, which were designed for a high UV absorbance, it is not soluble in water without any additives such as surfactants. CB[6] also shows only a poor solubility in water. In contrast, the inclusion complex was found to be well dispersible in water. A maximum concentration of 2.1 wt% [21 mg/10 ml] was observed for the dispersed inclusion complex in water.

Computer calculations using the AM1 theoretical model incorporated into the Spartan program were performed to obtain the energy-minimised model of the inclusion complex between CB[6] and TS in the absence of water (Figure 2). In this computation, the inclusion complex was found to be formed in a way that the hydrophobic cavity of CB[6] and two aliphatic side chains and the methoxy group of the TS interacted via van der Waals forces in a 3:1 molar ratio (CB[6]: TS).

Figure 4 shows the FT-IR spectra of CB[6], TS and the inclusion complex. It was found that the inclusion complex contains both CB[6] and TS. From the spectra, it was observed that the bands at 2870 and 2927 cm^{-1} (two aliphatic side chains in TS) were shifted to 2872 and 2930 cm^{-1}, respectively, in the inclusion complex and this result complements the computer calculation (*15*, *16*).

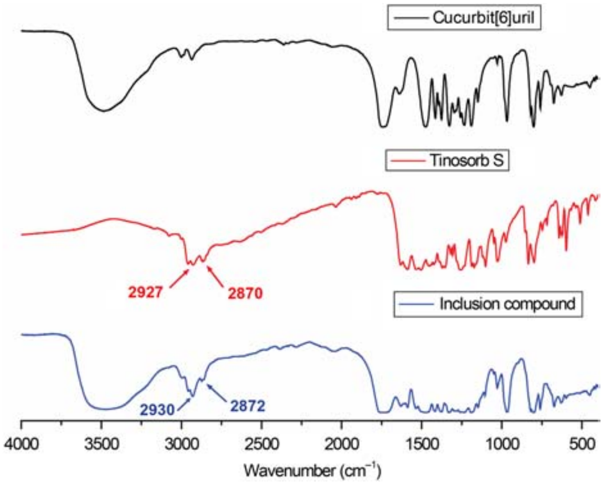

Figure 4. FT-IR spectra of educts and the product.

A further confirmation was obtained by the solid-state ^{1}H NMR spectra (Figure 5). The peaks of CB[6] at 5.92 and 4.31 ppm were shifted to 5.68 and 3.93 ppm, respectively, in the inclusion complex. This is in accord with the literature and can be considered as a normal shift of the inclusion complex (*17*). The peak of aliphatic side chains in TS at 0.92 ppm was shifted to 1.16 ppm in the inclusion complex, which is an abnormal shift of inclusion complexes. The portal carboxyl groups in CB[6], which have a high electronegativity, are responsible for the down-field shifts of the peaks of the aliphatic side chain. Strong electronegative groups can reduce the local diamagnetic shielding (*17*, *18*).

The X-ray diffractogram pattern (Figures 6 and 7) of the product shows that the inclusion complex has neither the typical 2θ values of CB[6] nor those of TS. After

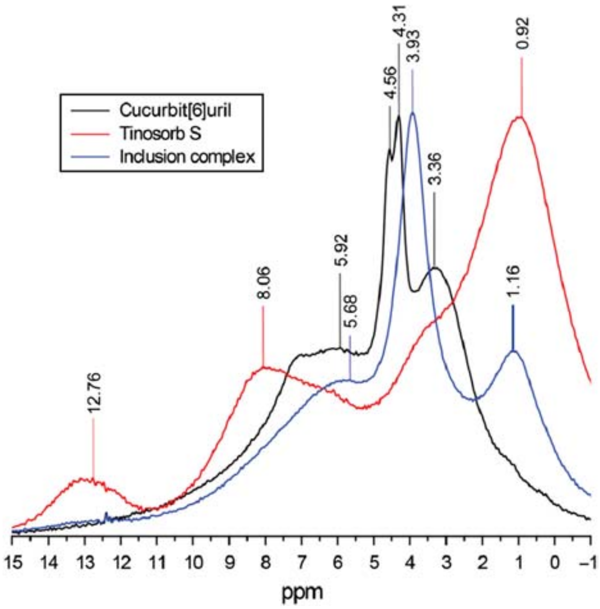

Figure 5. Solid-state NMR spectra of educts and the product.

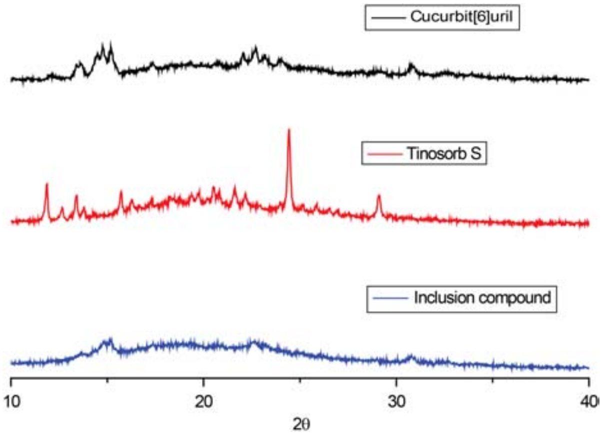

Figure 6. X-ray diffractograms of educts and the product.

complexation, a total suppression of the crystalline structure of TS took place.

The UV–vis spectroscopic study (Figure 8) shows that not only the absorption maximum ($\lambda_{\max}$) was shifted from 380 nm to 345 nm, but the absorbance was also increased almost by a factor of 2 due to the complexation effect with the carbonyl groups of CB[6] in the inclusion complex in comparison to TS. It is to be mentioned that in both cases the concentration of TS was kept constant.

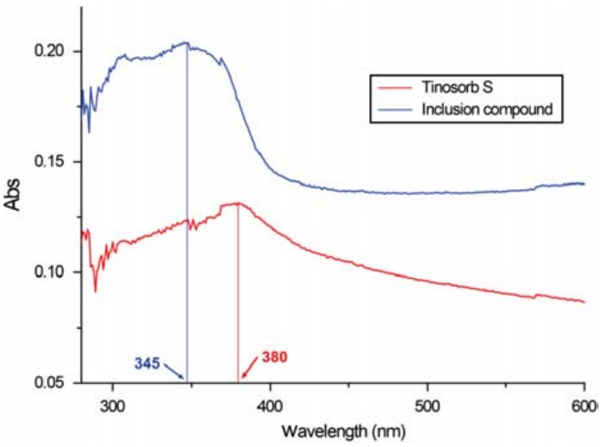

Figure 8. UV–vis absorption of TS and the inclusion complex with cucurbituril on a glass surface.

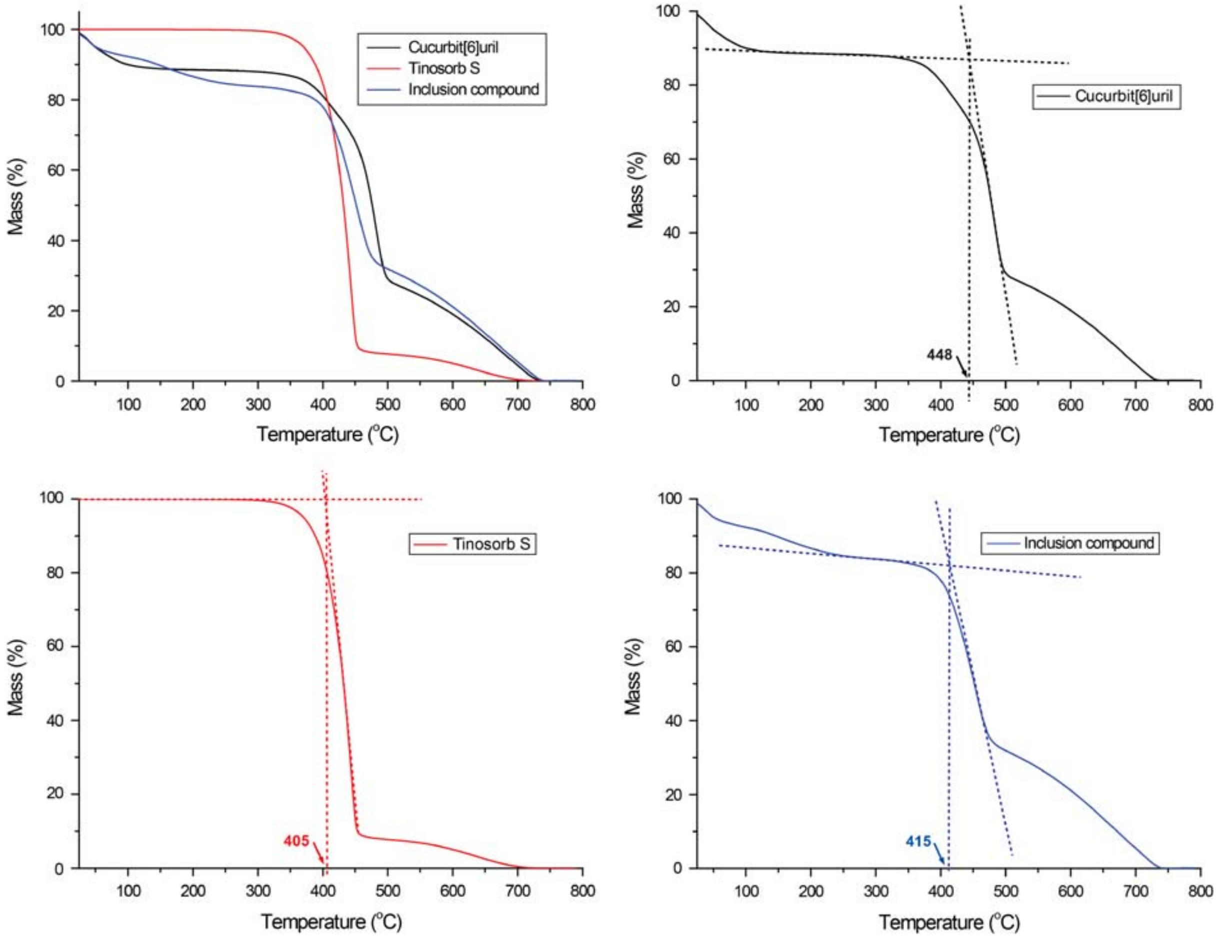

Figure 7. Thermal gravimetric analysis data.

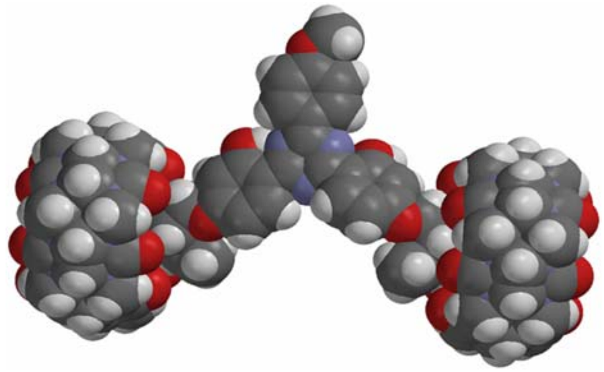

Figure 9. The inclusion complex model based on the experimental result – 2:1 stochiometric ratio of CB[6] and TS.

The TGA of the inclusion complex in nitrogen atmosphere was studied in comparison with CB[6] and TS (Figure 7). The first step of the mass loss in the thermogravimetric curves of the inclusion complex and CB[6], which began at < 100°C, can be ascribed to the total loss of the crystallisation of water in CB[6]. Decomposition of TS began at approximately 405°C, whereas the decomposition of both the inclusion complex and CB[6] after the water loss did not start below 415°C due to the destruction of CB[6] molecule. Therefore, the decomposition temperature of the inclusion complex was increased by at least 10°C upon inclusion. The encapsulated TS molecule did not undergo any decomposition while the host remained intact (*16*, *19–23*). Even though the TGA data indicate the formation of the inclusion complex, it is very difficult to elucidate the stochiometric ratio of CB[6] and TS in the product. Analytical calculations revealed that a 2:1 stochiometric ratio of CB[6] and TS in the inclusion complex was obtained. These data were measured from the unreacted TS present in the precipitate, which contained unreacted TS and CB[6], after decantation of the dispersion of the inclusion complex. From the energy-minimised computer calculation, it was shown that a 3:1 molar ratio of CB[6] and TS is possible in the inclusion complex, where the cavity of two CB[6] units were involved in the complex formation with two alkyl side chains of TS and another one with the methoxy substituent of TS. The inclusion formation with the methoxy group of TS is not as strong as the alkyl side chains (see Figure 2). Overall, a 2:1 stochiometric ratio of CB[6] and TS was found in the inclusion complex, which is also in good agreement with the infrared and ^{1}H NMR spectroscopic analytical data. The 2:1 stochiometric ratio model is described in Figure 9.

4. Conclusions

The preparation of a water-dispersible inclusion complex of CB[6] and TS is reported for the first time. A stochiometric ratio of 2:1 of CB[6] and TS was found in the inclusion complex. The UV absorbance of the inclusion complex increased by a factor of 2 compared to that of free TS on a glass surface, demonstrating the applicability of using it as an enhanced chemical UV filter.

Acknowledgements

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