UVA Chemical Filters:

A Systematic Study

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Abstract

Sunscreens are a popular and effective method of protecting against the damaging effects of solar radiation including skin cancer and immune system suppression. Chemical sunscreen filters achieve this by absorbing ultraviolet radiation and can be classified as UVB (280 – 320 nm) or UVA (320 – 400 nm) sunscreens depending on the wavelengths in which they absorb energy. An efficient sunscreen must afford protection against both UVB and UVA. The majority of chemical filters approved for use worldwide are UVB absorbers and the few UVA filters approved provide minimal UVA protection or show only moderate photostability. For example, the enol form of the \( \beta \)-diketone, BMDBM (I), absorbs strongly in the UVA region but is prone to photodegradation via the keto form (II).

\[
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\]

The purpose of the research presented has been to investigate methods aimed at improving sunscreen protection against wavelengths in the UVA region. The first approach involves adaptation of the commonly used sunscreen filter, BMDBM, to enhance its effectiveness as a UVA sunscreen filter. The emphasis has been on improving the photostability and absorption properties whilst maintaining the chemical identity of the sunscreen. This can be achieved by chelation of either Zn(II) or Al(III) by the enol form (I) of BMDBM. The results of a systematic study including potentiometric titration, spectroscopic analysis and laser flash photolysis studies are presented.

A second approach has been the encapsulation of the \( \beta \)-diketone, BMDBM, in cyclodextrins. Cyclodextrins are cyclic oligosaccharides having a hydrophobic central cavity. The interest in cyclodextrins comes from their ability to encapsulate other molecules (guest) within their annuli to form host-guest complexes held by non-covalent forces. The formation of such inclusion complexes often results in the modification of the guest characteristics. The inclusion complexes formed between BMDBM and either \( \beta \)-
cyclodextrin (βCD) or hydroxypropyl-β-cyclodextrin (HPβCD) has been characterized by $^1$H and $^1$H ROESY NMR spectroscopic methods.

The further method aimed at improving UVA protection has involved exploring the use of theoretical methods as a tool in the design of potentially new sunscreens. In particular, the ability of the SAC-CI method to represent the trends and properties important to the photochemistry of a series of known β-diketones has been investigated. This information can then be used to complement experimental methods in the design of candidate sunscreen filters having the desired properties.
Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Jacqueline F. Cawthray

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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>I</td>
<td>ionic strength</td>
</tr>
<tr>
<td>[ ]</td>
<td>concentration (mol dm(^{-3}))</td>
</tr>
<tr>
<td>Å</td>
<td>Ångström (10(^{-10}) m)</td>
</tr>
<tr>
<td>ACAC</td>
<td>2,4-pentanedione</td>
</tr>
<tr>
<td>BA</td>
<td>1-phenyl-1,3-butanedione</td>
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<tr>
<td>BMDBM</td>
<td>4-tert-butyl-4’-methoxydibenzoylmethane, tradenames: avobenzone, Parsol(^{®}) 1789</td>
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<tr>
<td>BMDBM(^{-})</td>
<td>β-diketone anion of BMDBM</td>
</tr>
<tr>
<td>CD</td>
<td>cyclodextrin</td>
</tr>
<tr>
<td>CE</td>
<td>chelated enol</td>
</tr>
<tr>
<td>DBM</td>
<td>1,3-diphenyl-1,3-propanedione</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulphoxide</td>
</tr>
<tr>
<td>f</td>
<td>oscillator strength</td>
</tr>
<tr>
<td>HEPES</td>
<td>N-2-hydroxyethylpiperazine-N’-2-ethanesulphonic acid</td>
</tr>
<tr>
<td>HF</td>
<td>Hartree-Fock</td>
</tr>
<tr>
<td>HPβCD</td>
<td>2-hydroxypropyl-β-cyclodextrin</td>
</tr>
<tr>
<td>IMHB</td>
<td>intramolecular hydrogen bond</td>
</tr>
<tr>
<td>IMPT</td>
<td>intramolecular proton transfer</td>
</tr>
<tr>
<td>IndolePh</td>
<td>1-(1H-indol-6-yl)-3-phenyl-1,3-propanedione</td>
</tr>
<tr>
<td>K</td>
<td>keto</td>
</tr>
<tr>
<td>LFP</td>
<td>laser flash photolysis</td>
</tr>
<tr>
<td>M(^{2+})</td>
<td>divalent metal ion</td>
</tr>
<tr>
<td>MO</td>
<td>molecular orbital</td>
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<tr>
<td>NapPh</td>
<td>1-(2-naphthyl)-3-phenyl-1,3-propanedione</td>
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<tr>
<td>NCE</td>
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</tr>
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<td>OMC</td>
<td>2-ethylhexyl-4-methoxycinnamate, octyl methoxycinnamate, octinoxate</td>
</tr>
<tr>
<td>PES</td>
<td>potential energy surface</td>
</tr>
<tr>
<td>RAHB</td>
<td>resonance-assisted hydrogen bonding</td>
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<tr>
<td>RHF</td>
<td>restricted Hartree-Fock</td>
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<tr>
<td>SAC</td>
<td>symmetry-adapted cluster</td>
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<tr>
<td>SAC-CI</td>
<td>symmetry-adapted cluster-configuration interaction</td>
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<tr>
<td>TEAOH</td>
<td>tetraethyl ammonium hydroxide</td>
</tr>
<tr>
<td>Acronym</td>
<td>Definition</td>
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<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration</td>
</tr>
<tr>
<td>UV-AI</td>
<td>ultraviolet AI radiation (340 - 400 nm)</td>
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<td>UV-AII</td>
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<td>UV-B</td>
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<td>ZPE</td>
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<tr>
<td>βCD</td>
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<tr>
<td>8-oxo-dG</td>
<td>8-oxo-7,8-dihydro-2´-deoxyguanosine</td>
</tr>
<tr>
<td>$\lambda_{\text{max}}$</td>
<td>wavelength of maximum absorption</td>
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