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The detection of the precursors of the photorearranged products of 3-hydroxyflavones in selected solvents from UV-visible spectra *in situ*⁺

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Mechanistic studies relating to the photochemistry of 3-hydroxy-2-phenyl-4H-chromen-4-one (3HF) and 6-chloro-3-hydroxy-2-phenyl-4H-chromen-4-one (Cl-3HF) have been reinvestigated in selected solvents. The UV-visible spectra of the photoproduct(s) of **3HF** and **Cl-3HF** have been computed in situ via subtracting the spectra of unreacted substrates, with acetonitrile (ACN) and methanol (MeOH) as solvents. These spectra turn out to be different from the spectra of the corresponding isolated photoproducts: 3-hydroxy-3-phenyl-indan-1,2-dione and 6-chloro-3-hydroxy-3-phenyl-indan-1,2-dione (referred to as dione). Analyses of the photoproduct(s) via GC-MS show the formation of a single detectable product, *i.e.*, the corresponding dione. On the basis of some experimental observations, it is proposed that the primary photoproduct in situ is 2,3-epoxy-2-hydroxy-1-indanone (referred to as epoxide) instead of dione as reported in previous years. Earlier, epoxide has been proposed to be the intermediate in the mechanism for the formation of dione. This is the first report where the formation of epoxide has been directly detected in the selected solvents. On the other hand, both dione and epoxide (2:1) are shown to be formed with MeOH as solvent. The second important finding is that epoxide and dione interconvert in the dark, depending upon the environment. With ACN as solvent, pure dione in the dark is kinetically and partially converted to epoxide. With MeOH as solvent, epoxide is instantly and partially converted to dione until both are in equilibrium. However, a solution of dione in MeOH remains stable in the dark. The photoformation of epoxide is quantitative with ACN as solvent and it is sufficiently stable. It has been further observed that epoxide solutions of **3HF** and **Cl-3HF** in ACN are quantitatively converted into 3-phenylisobenzofuran-1(3H)-one and 6-chloro-3-phenylisobenzofuran-1(3H)-one, *i.e.*, the corresponding phthalides, through the loss of CO when kept in the dark for some days. A mechanism has been proposed where epoxide has been shown to give dione and/or phthalide via selective C-O or C-C bond cleavage in the oxiranyl ring, respectively. The selection of this cleavage depends mainly on the solvent system and the substituents in the parent flavones.

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1. Introduction

Flavonoids belong to a large group of abundant plant secondary metabolites that can be found in vascular plants such as ferns, conifers and flowering plants.^{1–3} Approximately, 4000 varieties of flavonoids have been identified and many of these are intense pigments, providing a spectrum of yellow, red and

blue colours in flowers, fruits and leaves.^{4,5} The basic flavonoids have been classified in different families depending upon the presence of several phenolic hydroxyl functionalities within the ring, including flavones and flavonols. Flavonols are characterized by the possession of a 3-hydroxypyran-4-one ring. 3-Hydroxy-2-phenyl-4H-chromen-4-one (3HF) is the simplest flavonol, and it has attracted strong interest due to its peculiar photophysical and photochemical properties. Its unique photophysical properties, involving double emission peaks attributed to an excited-state intramolecular proton transfer (ESIPT) reaction upon photo-excitation, which were discovered by Sengupta and Kasha have been widely studied.⁶⁻¹⁰ The wavelengths and intensities of the N* (the excited state of the normal form) and T* (the excited state of the tautomeric form) bands are sensitive to many physical properties of the environment. The photochemistry of 3HF has



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[†]Electronic supplementary information (ESI) available: ¹H and ¹³C{¹H} NMR, IR, and GC-MS spectra of **3HF** and **3HF phthalide**; ¹H and ¹³C{¹H} NMR, HRMS, IR, and GC-MS spectra of **Cl-3HF** and **Cl-3HF phthalide**; IR and GC-MS spectra of **3HF dione** and **Cl-3HF dione**; IR spectrum of **epoxide** in the key spectral region and GC-MS data from the photoproduct(s) of **Cl-3HF** photolysed (6 h) solution in ACN. See DOI: 10.1039/c9pp00316a

also been studied under aerobic and anaerobic conditions, and in different solvents, over a long period of time.¹¹⁻¹⁶ The different routes for its photochemical reactions proposed in the literature, *i.e.* photooxygenation and photorearrangement, and the pathways in different solvents have been well summarized.^{17,18} Many reports on the photorearrangement paths of 3HF, some of them contrasting, have been studied. Matsuura and co-workers were the first to study this photoreaction, where they identified 3-hydroxy-3-phenyl-indan-1,2-dione (dione) as the photoproduct, formed through a 2,3-epoxy-2hydroxy-1-indanone (epoxide) intermediate.¹¹ There are some papers on the mechanism of formation with dione as the major product and 3-phenylisobenzofuran-1-(3H)-one (phthalide) as the minor photoproduct of 3HF, especially with acetonitrile (ACN) as solvent.^{16,17} Phthalide has been reported to be formed as a secondary photoproduct of dione.

Here, we are reporting first time the detection of epoxide as the precursor for the formation of dione during the photolysis of **3HF** and 6-chloro-3-hydroxy-2-phenyl-4*H*-chromen-4-one (**Cl-3HF**), *via* computing the UV-visible spectra of the photoproduct(s) *in situ* with ACN and methanol (MeOH) as solvents. Some simple experiments carried out after this detection are likely to have significant implications for already reported mechanisms and for future studies of the photochemistry of various **3HF**-type compounds.

2. Experimental

2.1. General information

All reagents used for the preparation of 3-hydroxy-2-phenyl-4Hchromen-4-one (3HF) and 6-chloro-3-hydroxy-2-phenyl-4Hchromen-4-one (Cl-3HF) were bought from Sigma-Aldrich, USA, and were used as received without further purification. The solvents used for the photochemical reactions were of HPLC grade and were purchased from S. D. Fine and Loba Chemie. Photoreactions were carried out either in a 4 mL tightly covered quartz cuvette or in a 50 mL Pyrex glass tube. A medium pressure mercury lamp (125 W) with a built-in filter mainly emitting at around 366 nm was powered through a stabilised power supply. Although the emission band through the built-in filter is mainly centred at 366 nm, another glass filter with a cut-off of 348 nm was incorporated in between the photolysis cell and the lamp, to eliminate any low intensity emission bands below 348 nm. A special holder was used to place the photolysis cell (at a distance of 6 cm from the lamp) in front of the glass filter, so that maximum light falls on its surface. A shutter was used in between the filter and the cell to interrupt the light whenever this was desired. The photolysis cell was shielded from the heat of the lamp with a wooden screen that had a window for the filter. Most of the experiments were carried out at 20 \pm 2 °C. The progress of the reaction was monitored with a double beam UV/vis spectrophotometer (UV-1800, Shimadzu) equipped with UV-probe software and GC-MS apparatus (GCMS QP-2010 plus, Shimadzu). IR spectra were recorded using an FTIR spectrometer

(PerkinElmer, Spectrum Two). ¹H and ¹³C{¹H} NMR spectra were recorded with a Bruker Advance 400 MHz spectrometer using TMS as an internal standard. HRMS data were obtained using a XEVO G2-XS QTOF mass spectrometer with ion-source TOF MS ES+ apparatus (1.27e + 008).

2.2. General procedure for the synthesis of the substrates 3HF and Cl-3HF

A previously reported two step method was used for the synthesis of 3HF and Cl-3HF.19-21 The condensation of 0.001 moles of 2'-hydroxyacetophenone (0.12 mL) for 3HF or of 5'-chloro-2'-hydroxyacetophenone (0.170 g) for Cl-3HF and 0.001 moles (0.1 mL) of benzaldehayde was carried out in an ethanolic solution of sodium hydroxide at 5 ± 1 °C in the first step. This reaction mixture was stirred for 6-7 h, and then the ice-cold mixture was neutralised with dilute HCl to obtain the chalcone. The corresponding chalcones were further oxidised from alkaline alcoholic solution, kept as an ice-cold mixture, via the addition of 2 mL of 30% (w/v) H₂O₂ every 2 h under continuous stirring until the reaction was complete (about 8 h). Then, the final flavones were separated via neutralising the reaction mixture with dilute HCl and were crystallised from EtOH: CHCl₃ (1:1 v/v) to obtain yellow needles of both. All spectroscopic data obtained here for 3HF is identical with the reported data.²⁰ This spectroscopic data has also been obtained from Cl-3HF and is expectedly similar to that of 3HF.

3-Hydroxy-2-phenyl-4H-chromen-4-one (3HF). M.p: 171–172 °C; FTIR (neat, cm⁻¹) ν_{max} : 3196 (OH), 1604 (C=O); GC-MS retention time (t_r) = 18.25 min, m/z = 237 [M]⁺; ¹H NMR (400 MHz, DMSO-d₆) δ : 9.65 (s, OH exchangeable with D₂O), 8.23 (d, J = 7.40 Hz, 2H), 8.13 (dd, J = 8.04, 1.12 Hz, 1H), 7.82–7.76 (m, 2H), 7.60–7.56 (m, 2H), 7.53–7.46 (m, 2H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) δ : 172.9, 154.5, 145.1, 139.0, 133.7, 131.2, 129.8, 128.5, 127.6, 124.7, 124.4, 121.2, 118.4.

6-Chloro-3-hydroxy-2-phenyl-4*H***-chromen-4-one (Cl-3HF).** M.p.: 168–169 °C; FTIR (neat, cm⁻¹) ν_{max} : 3273 (OH), 3057 (C–H Ar), 1602 (C=O); GC-MS t_r = 20.40 min, m/z = 273 [M]⁺; ¹H NMR (400 MHz, CDCl₃) δ: 8.25–8.22 (m, 3H), 7.65 (dd, *J* = 8.96, 2.52 Hz, IH), 7.57–7.49 (m, 4H), 7.00 (s, OH exchangeable with D₂O); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) δ: 171.9, 153.0, 145.6, 139.2, 133.5, 130.9, 130.0, 128.9, 128.5, 127.6, 123.5, 122.4, 120.9; HRMS calcd for C₁₅H₁₀O₃Cl ([M + H]⁺): 273.0318, found: 273.0316.

2.3. Characterisation data of the separated photoproducts

There were two major photoproducts, dione and phthalide, formed in the photolysis of both **3HF** and **Cl-3HF** with ACN and dichloromethane as solvents. These photoproducts were separated *via* passing the photolysed samples through a silica gel column (60–120 mesh) using 5% ethylacetate in hexane (v/v) as the eluting solvent. Both diones were separated and obtained in the form of white amorphous solids, and both phthalides were in the form of grey needles. The **3HF** dione was identified *via* comparing its GC-MS, IR and UV-visible spectra with the reported data.^{11,12,15} The **Cl-3HF** dione was identified *via* comparing the GC-MS, IR and UV-visible spectra with those of the **3HF** dione. The data from both are similar, as is expected. The **3HF** phthalide was identified *via* comparing its GC-MS, UV-visible, IR, ¹H and ¹³C{¹H} NMR spectra with the reported data.^{12,17} The data from the **Cl-3HF** phthalide are also similar to those from the **3HF** phthalide.

3-Hydroxy-3-phenyl-indan-1,2-dione (3HF dione). IR (neat, cm⁻¹) ν_{max} : 3423 (OH), 3063 (C–H Ar), 1763, 1722 (C=O); GC-MS t_r = 16.58 min, m/z = 238 [M]⁺.

3-Phenylisobenzofuran-1(3*H***)-one (3HF phthalide).** IR (neat, cm⁻¹) ν_{max} : 2925, 2853 (C–H aliphatic), 1756 (C=O); GC-MS $t_r = 14.37 \text{ min}$; $m/z = 210 \text{ [M]}^+$; ¹H NMR (400 MHz, DMSO-d₆) δ : 7.93 (d, J = 7.6 Hz, 1H), 7.77 (dt, J = 7.56, 1.04 Hz, 1H), 7.64 (t, J = 7.44 Hz, 1H), 7.48–7.39 (m, 4H), 7.33–7.31 (m, 2H), 6.74 (s, 1H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) δ : 169.9, 149.9, 136.8, 134.7, 129.5, 129.0, 128.9, 126.7, 125.0, 124.5, 123.2, 81.8; twin peaks in the UV-visible spectrum at around 271 and 278 nm.

6-Chloro-3-hydroxy-3-phenyl-indan-1,2-dione (Cl-3HF dione). IR (neat, cm⁻¹) ν_{max} : 3414 (OH), 3066 (C–H Ar), 1769, 1741 (C==O); GC-MS t_r = 18.26 min, m/z = 272 [M]⁺.

6-Chloro-3-phenylisobenzofuran-1(3*H*)-one (Cl-3HF phthalide). IR (neat, cm⁻¹) ν_{max} : 2957, 2927 (C–H aliphatic), 1749 (C==O); GC-MS $t_r = 16.49$ min, m/z = 244 [M]⁺; ¹H NMR (400 MHz, DMSO-d₆) δ : 8.00 (d, J = 1.84 Hz, 1H), 7.82 (dd, J =8.16, 1.92 Hz, 1H), 7.50 (d, J = 8.24 Hz, 1H), 7.43–7.40 (m, 3H), 7.35–7.32 (m, 2H), 6.75 (s, 1H). ¹³C{¹H} NMR (125 MHz, CDCl₃) δ : 169.0, 147.8, 135.9, 134.6, 129.5, 129.1, 128.6, 128.3, 127.5, 126.9, 125.5, 124.1, 82.6; HRMS calcd for C₁₄H₁₀O₂Cl ([M + H]⁺): 245.0369, found: 245.0349; twin peaks in the UVvisible spectrum at around 284 and 292 nm.

3. Results and Discussion

3.1. The detection of 2,3-epoxy-2-hydroxy-1-indanone (epoxide) *in situ* during the photolysis of 3-hydroxy-2-phenyl-4*H*-chromen-4-one (3HF) and 6-chloro-3-hydroxy-2-phenyl-4*H*-chromen-4-one (Cl-3HF)

4 mL of **3HF** solution $(4 \times 10^{-5} \text{ M})$ with acetonitrile (ACN) as the solvent was taken in an air-tight quartz cuvette and this was photolysed for different lengths of time.

Fig. 1 shows the electronic absorption spectra of the solutions photolysed for various intervals of time. The spectral changes in this figure show that the absorbance is continuously increasing between 285 and 270 nm and decreasing between 270 and 228 nm. There are three isobestic points, at 287.4, 264.5, and 224.8 nm. The decreasing absorbance at higher wavelengths and the increasing absorbance at selected wavelengths in the UV region clearly show that reactant is disappearing and products, which absorb only at lower wavelengths in the UV region, are being formed.

3.1.1. UV-visible absorption spectra of photoproduct(s) *in situ.* In a separate experiment, the photolysis product has been analysed to be 3-phenyl-3-hydroxy-1,2-indandione (dione). The UV-visible spectrum of dione shows that it does not absorb beyond 300 nm, while **3HF** has a peak at 339.4 nm and a shoulder at 354.2 nm. Therefore, it appears that in the



Fig. 1 The electronic absorption spectra of 3HF in ACN photolysed after 0, 10, 20, 30, 40, 50, and 60 min.

photolysed mixture spectra, absorbance beyond 300 nm is due to reactant only. Pure reactant spectra after various photolysis times were constructed, considering that absorbance at 355 nm of the photolysed mixture is due to reactant only. It was noticed that the so-constructed spectra of the reactant overlapped (from 330 to 390 nm) with the photolysed mixture spectra at different times. The reactant also follows the Beer-Lambert law at all wavelengths. Thereafter, the photoproduct (s) spectra were obtained through subtracting the corresponding constructed spectra at different photolysis times, and these are shown in Fig. 2. We tried this method in our earlier paper also.²²

The spectra of the photoproduct(s) shown in Fig. 2 show one shoulder at around 220.2 nm, one peak with a λ_{max} value of 280.2 nm and one hump at around 325 nm, growing as the photolysis time increases.

Similar experiments were carried out with **Cl-3HF**, and Fig. 3 shows the photoproduct(s) spectra obtained from the photolysed mixtures, as was done in the case of **3HF**.



Fig. 2 The electronic absorption spectra of the photoproduct(s) after subtracting the unreacted reactant spectra from the photolysed solution spectra of **3HF** in ACN after 10, 20, 30, 40, 50, and 60 min (*cf.* Fig. 1).



Fig. 3 The electronic absorption spectra of the photoproduct(s) after subtracting the unreacted reactant spectra from the photolysed solution spectra of **CI-3HF** in ACN after 10, 20, 30, 40, 50, and 60 min.

3.1.2. Analysis *via* **GC-MS.** 25 mL of **3HF** solution in ACN (8.40×10^{-4} M) in a Pyrex tube was photolysed for a total of 8 h. GC-MS analyses of these photolysed solutions carried out after 3, 6 and 8 h of photolysis show that the amount of a single product with a molecular mass of 238 g mol⁻¹ grows as the photolysis time increases. This product, which has the same mass but a different retention time (t_r) to the reactant, should be the photorearranged product. Representative GC-MS analysis data from photolysed solutions of **3HF** in ACN (Fig. 4a) and from a separated sample of pure dione (Fig. 4b) are given in Fig. 4.

It is clear from Fig. 4a that a single detectable product, dione, is formed during photolysis. The retention time, molecular mass and fragmentation pattern of this product are identical to pure dione (Fig. 4b). The UV-visible spectrum of dione shows two peaks at 246.7 and 291.1 nm. On the other hand, the subtracted photoproduct spectra (Fig. 2) obtained *in situ* show peaks not only at different positions than those of dione but with a minimum around λ_{245} nm, whereas dione has a maximum. This indicates that, *in situ*, there is some other product from which dione is formed during GC-MS analysis.

To look into this, conversion spectral changes were analysed *via* a set of four spectra in ACN (Fig. 5).

On comparing spectrum II with the spectrum of the separated sample of dione (spectrum IV), it is apparent that upon removing the solvent, the primary product is partly changed to dione. Spectrum IV becomes more interesting because dione formed partly in spectrum II appears to go back to the product seen in spectrum I. Obviously, during recording the GC-MS data, a stable dione product is formed from the primary product. Now the question arises; which is the primary product?

The photorearrangement of **3HF** was studied first in the 1970s by Matsuura and co-workers in benzene: isopropyl alcohol under N_2 .¹¹ The only photoproduct obtained under these conditions was dione, and they proposed the formation of this product *via* a 2,3-epoxy-2-hydroxy-1-indanone (epoxide)

intermediate from the $(\sigma^2 + \pi^2)$ cycloaddition of the substrate in its triplet state (Scheme 1).

In the same period, a similar rearrangement was reported in the photolysis of 2,6-dimethyl-3-hydroxy-4*H*-pyrane-4-one.²³ Here it was proposed that both **2** and **3** were formed, but the former could not be isolated (Scheme 2).

Matsuura and co-workers did not verify whether dione (1) is formed in one step, like that of 3, or in two steps. On the basis of these reports it can be surmised that, in our case, it is most likely that the primary product is epoxide (A).

3.2. The formation and conversion of the epoxide intermediate

3.2.1. Detection of epoxide through IR spectroscopy. It has been observed that epoxide formed in the photolysis of Cl-3HF is relatively more stable than in the case of 3HF. It has a pink colour in ACN that, upon evaporation, is immediately converted to yellow at room temperature. However, when the solvent (ACN) was distilled off at low temperature (10-12 °C) under rotary evaporation, the pink colour could be retained for some time. An attempt has been made to record its IR spectrum immediately (Fig. 6). This shows a single absorption band at 1732 cm⁻¹ in the keto group region, instead of twin bands at 1768 and 1741 cm⁻¹ due to the expected dione product. Also, the IR spectrum of epoxide is different from that of 6-chloro-3-phenylisobenzofuran-1(3H)-one (phthalide), where the bands observed due to C-H stretching at 2957, 2927 and 2872 cm^{-1} in phthalide are missing in the case of epoxide, as expected.

The photolysis of **3HF** has also been carried with methanol (MeOH) as solvent, in a similar fashion to that of with ACN experiments. Fig. 7 shows the photoproduct(s) spectra obtained *in situ via* subtracting the unreacted **3HF** from the photolysed solution.

There are two λ_{max} values at around 245 and 290 nm, which are close to those obtained from the spectrum of pure dione in MeOH (Fig. 5). However, the finer details of these spectra have been compared with pure dione in MeOH and epoxide in ACN. It is observed that these subtracted spectra correspond to mixtures of epoxide and dione. The ratio of the concentration of dione to epoxide is about 2. Clearly, this result is different from the results obtained in ACN (Fig. 2). As explained above, the primary product in ACN is epoxide; it appears that in MeOH, the primarily formed epoxide is instantly partially converted to dione. In another experiment, the effects of adding MeOH to a solution of epoxide in ACN were studied. A solution (30 mL) of **3HF** with ACN as solvent $(0.7 \times 10^{-6} \text{ M})$ was photolysed for 110 min. The UV spectrum of the photolysed solution shown in Fig. 8 shows epoxide only, *i.e.*, the reactant appears to be quantitatively converted into the product (epoxide). When MeOH was added to this photolysed solution, the initial UV spectrum instantly changed and shows two shoulders at about 246 and 295 nm, which correspond to the absorption bands of dione. This shows that upon adding MeOH, epoxide is instantly partially changed to dione. This supports the above-mentioned photolysis results with MeOH as solvent.

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Fig. 4 GC-MS analysis of the photoproduct(s) of **3HF**: (a) photolysed solution (6 h) of **3HF** with ACN as solvent (top panel). Second and third panels are for the first component and fourth and fifth panels are for second component of top panel; and (b) a separated sample of **3HF** dione.

M. Kubinyi and co-workers in recent reports have carried out theoretical studies on photoreactions of **3HF**.¹⁸ They have suggested the formation of an intermediate with a 1-indanone skeleton (**B**) instead of an epoxide intermediate in the photorearrangement reaction of **3HF** to form dione (Scheme 3). However, the stability of the intermediate in ACN as reported in the present work suggests that it cannot be a biradical (**B**) rather than epoxide, as suggested by M. Kubinyi and co-workers. However, they admit that epoxide may be formed *via*

another route involving $T_1\mathchar`-S_0$ conical intersection, which they have not studied.

3.2.2. The interconversion of epoxide and dione. As suggested by the results of Fig. 5, epoxide formed during the photolysis of **3HF** is reversibly changed into dione. Therefore, the stability of dione was studied with ACN as solvent. It has been observed that the electronic absorption spectrum of dione changes continuously, even if it is kept in the dark, as shown in Fig. 9a. The changes in the spectra, *i.e.*, the decreas-

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Fig. 5 The electronic absorption spectra of photolysed samples of **3HF** under various conditions and of dione: (I) a freshly photolysed solution; (II) after evaporating ACN from solution (I) and then adding the same amount of ACN; (III) when solution (II) was kept overnight; and (IV) the spectrum of a separated sample of **3HF** dione.



Scheme 1 The photorearrangement of 3HF as proposed by Matsuura et al.



Scheme 2 The photoreaction of 2,6-dimethyl-3-hydroxy-4*H*-pyrane-4-one in MeOH.



Fig. 6 The IR spectrum of 4-chloro-2,3-epoxy-2-hydroxy-1-indanone (epoxide).



Fig. 7 The electronic absorption spectra of the photoproduct(s) after subtracting the unreacted reactant from photolysed solutions of **3HF** in MeOH after 10, 20, 30, 40, and 50 min.



Fig. 8 The effect of adding MeOH into a solution of the primary photoproduct (epoxide) in ACN: (a) is the photolysed solution spectrum of **3HF** in ACN and (b) is the spectrum of (a) after MeOH (0.5 mL to a total of 4 mL of (a)) was added.



Scheme 3 The structure of intermediate B proposed by M. Kubinyi *et al.* from theoretical studies.

ing absorbance at around 245 nm and the increasing absorbance at around 280 nm, suggest that dione is kinetically converting to epoxide. Unchanged dione spectra over time could be constructed (Fig. 9b), and upon subtracting these spectra from the corresponding spectra in Fig. 9a, the converted product spectra (Fig. 9c) are obtained. These spectra are identical to those of epoxide as observed for the product formed

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Fig. 9 (a) The changing spectra of dione in the dark with ACN as solvent, (b) the spectra of unchanged dione after different time intervals, and (c) the remaining spectra upon subtracting the spectra of (b) from the corresponding spectra of (a).

in situ. This conversion is also temperature dependent. Similar results are also obtained with **Cl-3HF**. However, there are no changes in the dione spectra of **3HF** with MeOH as solvent. Detailed kinetics studies of these processes are being carried out and they will be reported later on.

Similar processes have been reported in the rearrangement of an oxiranyl carbinyl radical (C) into an allyloxy radical (D) *via* C–O bond cleavage and/or in the formation of E *via* C–C bond cleavage, depending upon the natures of R_3 and R_4 (Scheme 4).²⁴

Evidence for reversibility between C and D has been reported in different cases. The mechanistic and kinetic aspects of this mechanism have been widely studied.²⁵⁻²⁹

S. Tommasini and co-workers have studied the photoreactions of **3HF** with ACN as solvent.¹⁴ They analysed the photolysed solutions after selected irradiation times *via* reversedphase liquid chromatography. Multistep gradient elution was carried out using MeOH/H₂O (with 10% glacial acetic acid) as solvent. The amounts of a number of products are shown in the chromatogram to grow with increasing irradiation time. The absorption spectra of four products appearing at different retention times have been recorded but no interpretation of these spectra has been made. With the help of our findings here, these results can be easily analysed. First, two of these spectra should be due to dione and two should be due to epoxide. Under the solvent system conditions used, the epoxide formed in the primary reaction is partly converted to dione, along with the formation of many side products.

3.2.3. The formation of 3-phenylisobenzofuran-1(3*H*)-one (3HF phthalide) and 6-chloro-3-phenylisobenzofuran-1-(3*H*)-one (Cl-3HF phthalide). There are a number of reports on the photochemical reactions of 3HF under aerobic and anaerobic

conditions, and in different solvent systems.¹¹⁻¹⁶ A common feature is that dione is the photorearranged product, along with the formation of phthalide. Phthalide has been shown to be formed from dione following long-term photolysis. Here, after the detection of epoxide as the primary product, it has been observed that phthalide is formed directly from epoxide instead of through dione. As explained above, dione in ACN is converted to epoxide kinetically. It has been found that if epoxide solutions of both 3HF and Cl-3HF in ACN are kept in the dark for some days, the corresponding epoxides are quantitatively converted to the corresponding phthalides. Phthalides have been identified via their ¹H NMR, ¹³C{¹H} NMR, IR, GC-MS and UV-visible spectra. It has also been verified that a solution of dione in MeOH remains stable when placed in the dark, unlike with ACN as solvent (see the above discussion). It is neither converted to epoxide nor decomposed to phthalide, as revealed by the UV-visible spectrum and GC-MS data. On the basis of the above-mentioned observations, results, and detection of epoxide as the primary product, the following basic steps shown in Scheme 5 are proposed.

The formation of epoxide has been earlier suggested to occur *via* ($\sigma^2 + \pi^2$) cycloaddition of the substrate in its triplet state.¹¹ In the present work, we have inferred that the formation, stability and further conversion of epoxide into dione, phthalide and other minor products depend mainly upon the solvent system and the substrate structure. The role of ACN in the formation of epoxide and the interconversion of dione in this solvent appears to be significant.

In a report by R. Diller and co-workers, they obtained mid-IR vibrational spectra of **3HF** excited states in solution using acetonitrile-d₃.³⁰ On the basis of vibrational frequencies, structural information about the intermediate states was obtained.



Scheme 4 The reversibility and modes of the ring opening of the oxiranyl carbinyl radical (C).



Scheme 5 The proposed steps for the formation of dione and phthalide in ACN from the epoxide formed by the photolysis of **3HF**.

It was predicted that **3HF** has two structures in the ground state: one possessing intact intramolecular hydrogen bonds, and another in the form of a **3HF**-ACN aggregate with inserted ACN. Aggregation weakens the intramolecular hydrogen bonding in **3HF**. It has also been reported that a small proportion of **3HF** exists in the anionic form.³¹ The anionic form proportion is relatively higher with MeOH as solvent, compared to ACN. The formation, stability, *etc.* of epoxide in ACN could be due to these properties of **3HF**, *i.e.* special kinds of solute-solvent interactions.

The quality of **3HF** photoreactions also depends upon the substitution at the phenyl ring in the second position. In a report on the photoreactions of 4'-diethylamino-3-hydroxy-flavone, it was found that it was oxidised into *O*-4-diethyl-aminobenzoyl salicylic acid differently from **3HF**, which undergoes photorearrangement with ACN as solvent.¹⁶

We have also reported the photoreactions of 2-(furan-2-yl)-3-hydroxy-4*H*-chromen-4-one (FHC) and 3-hydroxy-2-(thiophene2-yl)-4*H*-chromen-4-one (THC) with ACN as solvent.²² In those cases, it was observed that the photochemical reactions of two similar looking flavones, FHC and THC, are different in the same solvent (ACN), while the same flavone behaves differently in different solvents. FHC in aerated ACN gives a dimer (an oxidised product) and its dione upon photolysis, while in de-oxygenated ACN, its dione and phthalide are formed. In the case of THC, only dimer is formed in aerated ACN. It has been explained that this kind of flavone behaviour is because of complexity added by excited state intramolecular charge transfer (ESICT) to the already complex behaviour resulting from ESIPT reactions in excited states.

Furthermore, the results of the present work suggest that phthalide is formed *via* the decomposition of epoxide, instead of dione as reported earlier.^{12,17} It is proposed that the formation of dione from epoxide takes place *via* C–O bond cleavage, and the formation of phthalide takes place *via* the C–C bond cleavage of the oxiranyl ring of epoxide along the same lines as suggested in the case of oxiranyl carbinyl radical C (Scheme 4).²⁴ These selective bond cleavages depend upon the nature of the substituents in the rings of the substrate and, most importantly, on the nature of the solvent in which the

epoxide is kept. The conversion of epoxide into dione with MeOH as solvent is favoured because of the hydroxyl group in MeOH, which helps in the transfer of H from OH to the O atom of the oxiranyl ring of epoxide during C–O bond cleavage.

The detection of epoxide as the primary product, especially in ACN, here will definitely help in explaining the mechanisms of the photorearrangement reactions of **3HF**-type molecules that have already been studied or are being studied.

4. Conclusions

Epoxide as a precursor for the formation of dione has been detected in the photorearrangements of **3HF** and **Cl-3HF** from the photoproduct spectra *in situ*. It has been found that epoxide and dione are interconvertible, depending upon the environment. Phthalide has been shown to be formed from epoxide in the solution phase in the dark instead of from the secondary photolysis of dione, in contrast to some reports from previous years. Thus, it can be said that epoxide is the photoproduct in the photorearrangement reactions of **3HF** molecules, at least in the selected solvents. To date, in all reports from previous years, dione and phthalide have been reported as the photoproducts in these reactions; however, they actually appear to be formed from the epoxide photoproduct in the dark, especially with ACN as solvent.

Conflicts of interest

The authors have no competing interests to declare.

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References

- 1 G. D. Carlo, N. Mascolo, A. A. Izzo and F. Capasso, Flavonoids: Old and new aspects of a class of natural therapeutic drugs, *Life Sci.*, 1999, **65**, 337–353.
- 2 L. Rackova, S. Firakova, D. Kostalova, M. Stefek, E. Sturdik and M. Majekova, Oxidation of liposomal membrane suppressed by flavonoids: Quantitative structure-activity relationship, *Bioorg. Med. Chem.*, 2005, **13**, 6477–6484.
- 3 E. Middleton, C. Kandaswami and T. C. Theoharides, The effects of plant flavonoids on mammalian cells:

Implications for inflammation, heart disease, and cancer, *Pharmacol. Rev.*, 2000, **52**, 673–751.

- 4 R. J. Nijveldt, E. van Nood, D. E. van Hoorn, P. G. Boelens, K. van Norren and P. A. van Leeuwen, Flavonoids: a review of probable mechanisms of action and potential applications, *Am. J. Clin. Nutr.*, 2001, **74**, 418–425.
- 5 J. B. Harborne and C. A. Williams, Advances in flavonoid research since 1992, *Phytochemistry*, 2000, 55, 481–504.
- 6 P. K. Sengupta and M. Kasha, Excited state proton transfer spectroscopy of 3-hydroxyflavone and quercetin, *Chem. Phys. Lett.*, 1979, **68**, 382–385.
- 7 A. J. G. Strandjord, D. E. Smith and P. F. Barbara, Structural Effects on the Proton-Transfer Kinetics of 3-Hydroxyflavones, *J. Phys. Chem.*, 1985, **89**, 2362–2366.
- 8 S. Protti and A. Mezzetti, Any colour you like. Excited state and ground state proton transfer in flavonols and applications, *Photochemistry*, 2012, **40**, 295–322.
- 9 V. I. Tomin, A. P. Demchenko and P. T. Chou, Thermodynamic vs. kinetic control of excited-state proton transfer reactions, *J. Photochem. Photobiol.*, *C*, 2015, **22**, 1–18.
- 10 A. C. Sedgwick, L. Wu, H. H. Han, S. D. Bull, X. P. He, T. D. James, J. L. Sessler, B. Z. Tang, H. Tian and J. Yoon, Excited-state intramolecular proton-transfer (ESIPT) based fluorescence sensors and imaging agents, *Chem. Soc. Rev.*, 2018, 47, 8842–8880.
- 11 T. Matsuura, T. Takemoto and R. Nakashima, Photoinduced Reactions—LXXI*1: Photorearrangement of 3-hydroxyflavones to 3-Aryl-3-hydroxy-1,2-indandiones, *Tetrahedron*, 1973, **29**, 3337–3340.
- 12 I. Yokoe, K. Higuchi, Y. Shirataki and M. Komatsu, Photochemistry of Flavonoids. III. Photorearrangement of Flavonols, *Chem. Pharm. Bull.*, 1981, **29**, 894–898.
- 13 W. E. Brewer, S. L. Studer, M. Standiford and P. T. Chou, Dynamics of the Triplet State and the Reverse Proton Transfer of 3-hydroxyflavone, *J. Phys. Chem.*, 1989, **93**, 6088–6094.
- 14 M. L. Calabro, S. Tommasini, D. Raneri, P. Donato, P. Ficarra and R. Ficarra, Selective reversed-phase liquid chromatography method for the kinetic investigation of 3-hydroxyflavone photostability, *J. Chromatogr. B*, 2004, 800, 245–251.
- 15 S. Protti, A. Mezzetti, C. Lapouge and J. P. Cornard, Photochemistry of metal complexes of 3-hydroxyflavone: towards a better understanding of the influence of solar light on the metal-soil organic matter interactions, *Photochem. Photobiol. Sci.*, 2008, 7, 109–119.
- 16 Z. Szakacs, M. Bojtar, L. Drahos, D. Hessz, M. Kallay, T. Vidoczy, I. Bitter and M. Kubinyi, The kinetics and mechanism of photooxygenation of 4'-diethylamino-3-hydroxyflavone, *Photochem. Photobiol. Sci.*, 2016, **15**, 219–227.
- 17 S. Protti and A. Mezzetti, Solvent effects on the photophysics and photoreactivity of 3-hydroxyflavone: A combined spectroscopic and kinetic study, *J. Mol. Liq.*, 2015, **205**, 110–114.

- 18 Z. Szakacs, M. Kallay and M. Kubinyi, Theoretical study on the photooxygenation and photorearrangement reactions of 3-hydroxyflavone, *RSC Adv.*, 2017, 7, 32185–32192.
- 19 M. Wera, V. G. Pivovarenko, A. Sikorski, T. Lis and and J. Blazejowski, 2-(Furan-2-yl)-3-hydroxy-4H-chromen-4-one, *Acta Cryst. E*, 2011, 67, 0266.
- 20 D. Zhang, X. Ji, R. Gao, H. Wang, S. Meng, Z. Zhong, Y. Li, J. Jiang and Z. Li, Synthesis and antiviral activities of a novel class of thioflavone and flavonoid analogues, *Acta Pharm. Sin. B*, 2012, 2, 575–580.
- 21 M. Bansal and R. Kaur, Electromeric effect of substitution at 6th position in 2-(Furan-2-yl)-3-hydroxy-4*H*-chromen-4one (FHC) on the absorption and emission spectra, *J. Chem. Sci.*, 2015, **12**7, 405–412.
- 22 K. Kaur, R. Kaur, J. Tomar and M. Bansal, Photoreactions of 2-(furan-2-yl)-3-hydroxy-4*H*-chromen-4-one and 3-hydroxy-2-(thiophene-2-yl)-4*H*-chromen-4-one using cyclohexane and acetonitrile as solvents, *Photochem. Photobiol. Sci.*, 2017, **16**, 1311–1319.
- 23 M. Shiozaki and T. Hiraoka, Photochemistry of β -hydroxy- γ -pyrone. A new synthesis of 3-methylcyclopent-2-en-2-ol-1one from Maltol, *Tetrahedron Lett.*, 1972, **46**, 4655–4658.
- 24 J. Amaudrut and O. Wiest, Epoxide Formation by Ring Closure of the Cinnamyloxy Radical, *Org. Lett.*, 2000, **2**, 1251–1254 (and the references cited there in).
- 25 F. E. Ziegler and A. K. Petersen, Tandem Fragmentation of Cyclopropylcarbinyl/Oxiranylcarbinyl Radicals. On the Reversibility of Oxiranylcarbinyl/Allyloxyl Radical Formation, J. Org. Chem., 1994, **59**, 2707–2714.
- 26 D. J. Pasto, F. Cottard and C. Picconatto, The C_3H_5O Radical System. Formation and Reactions of the Allyloxy and Oxiranylmethyl Radicals Generated by the Photolysis of the Allyl and 4,5-Epoxy-2-methyl-2-pentyl 4-nitrobenzenesulfenates, *J. Org. Chem.*, 1994, **59**, 7172–7177.
- 27 F. E. Ziegler and A. K. Petersen, Allyloxy Radicals are Formed Reversibly from Oxiranylcarbinyl Radicals: A Kinetic Study, *J. Org. Chem.*, 1995, **60**, 2666–2667.
- 28 D. J. Pasto, Ab *Initio*, Theoretical Studies on the Ring-Opening Modes of the Oxiranyl-, Aziridinyl-, Oxaziridinyl-, and Thiaranylmethyl Radical Systems, *J. Org. Chem.*, 1996, 61, 252–256.
- 29 V. Krishnamurthy and V. H. Rawal, Kinetics of the Oxiranylcarbinyl Radical Rearrangement, *J. Org. Chem.*, 1997, **62**, 1572–1573.
- 30 K. Chevalier, M. M. N. Wolf, A. Funk, M. Andres, M. Gerhards and R. Diller, Transient IR spectroscopy and ab initio calculations on ESIPT in 3-hydroxyflavone solvated in acetonitrile, *Phys. Chem. Chem. Phys.*, 2012, **14**, 15007–15020.
- 31 R. Kaur, K. Kaur and M. Bansal, Comparative Studies in the Fluorescence and Excitation Spectra of 3-hydroxyflavone and 2(2'-heteroaryl)-3-hydroxy-4*H*-chromen-4-ones, *J. Appl. Spectrosc.*, 2017, **84**, 219–225 (and the references cited there in).