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PHOTOCHEMISTRY OF 5-ARYL-2(3H)-FURANONES. A NEW ROUTE TO THE SYNTHESIS OF CHROMONES

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Abstract—The photochemistry of 5-phenyl-, 5-(2',5'-dimethoxyphenyl)-, 5-(2'-acetoxy-5'-methoxyphenyl)- and 5-(2',5'-diacetoxyphenyl)-2(3H)-furanone (**1a–d**) has been investigated. Compound **1a** yields phenyl vinyl ketone as expected. Similarly, **1b** affords the corresponding aryl vinyl ketone but, in this case, photodimerization also occurs. Irradiation of the two *o*-acetoxyaryl furanones **1c** and **1d** gives rise to the formation of chromones as the main products. This interesting result can be accounted for in terms of a photochemical opening of the lactonic ring followed by radical addition to the acetoxy group.

The photochemistry of lactones has been extensively investigated over the last few years.[1] Saturated lactones can undergo homolytic cleavage of one of the three single bonds located in the ester moiety, the predominating type of scission depending on the lactone structure.[2–5] Photochemical behaviour of unsaturated lactones is largely dependent on the double bond location. Although ring opening of α,β-unsaturated lactones is possible upon irradiation in vapour phase,[2] their condensed phase photochemistry can be related to that of the enone system, the ring remaining intact.[6–13] In contrast to this behaviour, the breaking of the lactonic O–CO bond is the main primary photoprocess in enol lactones.[14–17]

In this paper we wish to report on the photochemistry of four 5-aryl-2(3H)-furanones: **1a–d**,[18] all of which are γ-aryl substituted β,γ-unsaturated lactones. Furthermore, **1c** and **1d** possess an acetoxy group prone to undergo a photo-Fries rearrangement which would compete with the above mentioned lactone photoreactivity.

RESULTS AND DISCUSSION

Irradiation of 5-phenyl-2(3H)-furanone **1a** in ethanolic solution, under N_2, led to the expected phenyl vinyl ketone **2a**, a product previously obtained by thermolysis of the same furanone.[19] Variation of the experimental conditions produced no substantial effect upon the reaction. On the contrary, a pronounced effect was observed in the case of 5-(2',5'-dimethoxyphenyl)-2(3H)-furanone **1b**. Irradiation of a benzene solution led, as in previous case, to the expected aryl vinyl ketone **2b**. However, the irradiation of ethanolic solutions gave a more complex reaction mixture. In addition to **2b**, a new product was isolated to which the formula $C_{13}H_{18}O_4$ was assigned from the combustion analysis and mass spectrometric data (M^+ 238). This product became the major one after lengthy irradiation times. Its ^{1}H NMR spectrum-triplet centered at δ1.15 and a multiplet between δ3.00 and 4.00 corresponding to three methylene groups—clearly showed that ethanol had been added to the double bond of **2b** giving the new product 2',5'-dimethoxyphenyl-2-ethoxyethylketone **3b**. The photoinduced addition of hydroxylic solvents to the double bond of an enone is a process well substantiated in Refs. 20–23 and consequently **3b** cannot be considered as an unexpected photoproduct. More difficult to predict were the results obtained when **1b** was irradiated in benzene solution purging thoroughly with nitrogen during the photoreaction. Under these conditions, a complex mixture was obtained. Two fractions could be isolated by tlc. The one corresponding to the lowest R_f value was purified by recrystallization from benzene/hexane. The analytical data—particularly the value 440 for M^+—indicated that a photodimerization process was in the origin of the new isolated product. The IR absorption at 1780 cm^{-1} showed the presence of the lactonic ring. On the other hand, the ^{13}C NMR spectra revealed the existence of two quaternary cyclobutyl (δ91.5) and two tertiary cyclobutyl (δ43.4) equivalent carbons. An important piece of information was also obtained from the ^{1}H NMR spectrum. In the aliphatic region, this spectrum shows a signal pattern which may be attributed to two adjacent ABX systems in which the two X protons are also coupled. This fact is in better agreement with a head-to-head structure than with a head-to-tail one. On the other hand, the lower R_f value of this compound, as compared to the other isolated fraction and, consequently, its relatively higher dipolar moment[12] supports the proposed anti head-to-head configuration **4b**. The *syn*-dimer was excluded in this consideration for steric reasons.

Attempts to further purify the second fraction failed. However, the similarity of its spectroscopic data with those corresponding to the product identified as **4b** suggests an isomeric mixture.

Photodimerization of enol lactones has not been reported before. Likely, γ-aryl substitution is the responsible of this kind of photoreactivity. Photodimerization of substituted styrenes is a known process,[24] that becomes very easy with electron–donor substituents.[25] Likewise, the structurally related vinylidene carbonates are known to photodimerize.[26,27] Involvement of triplet state in this photodimerization is suggested by the necessity of carrying out it in a deaerated solution. Current work is directed to elucidate this point.

Irradiation of benzene or ethanol solutions of 5-(2'-acetoxy-5'-methoxyphenyl)-2(3H)-furanone **1c** led to formation of chromones **5c** and **6c** respectively. The analytical data of the photoproducts obtained, particularly comparison of their spectroscopic properties with

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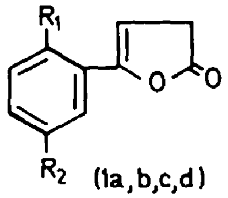
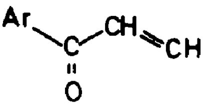
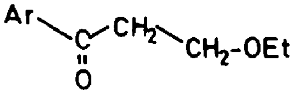


(1a,b,c,d)

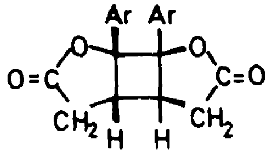
a: $R_1 = R_2 = H$
b: $R_1 = R_2 = OMe$
c: $R_1 = OAc$ $R_2 = OMe$
d: $R_1 = R_2 = OAc$



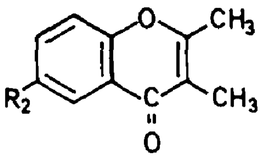
(2a,b,c)



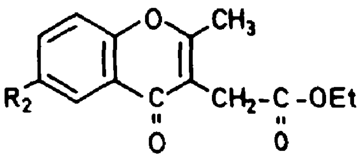
(3b)



(4b)



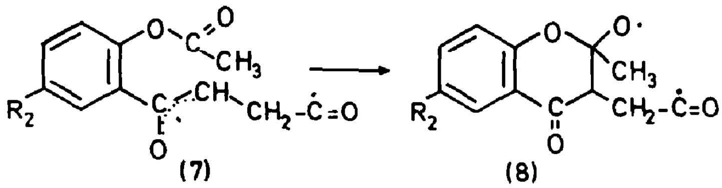
(5c,d)



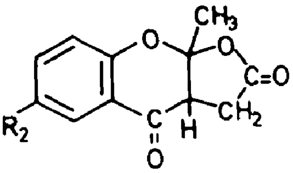
(6c,d)

those pertaining to similar compounds—UV[28], IR[29], NMR[30] and MS[31]—casts no doubt about the structural assignments. Nitrogen purging during the irradiation produced no noticeable effect on the nature of the photoproducts. Similarly, irradiation of 5-(2′,5′-diacetoxyphenyl)-2(3H)-furanone **1d** afforded the corresponding chromones **5d** and **6d**. The latter compound **6d**—the only one described before—has a m.p. in agreement with the reported value.[32] In addition to these chromones, small quantities of other products were detected but only in one case—irradiation of **1d** in ethanolic solution—it was possible to isolate and identify one of them, the expected aryl vinyl ketone **2d**. We suppose that **2c** will be also produced in the irradiation of **1c**.

Chromone formation can be rationalized by assuming that the cleavage of the lactonic O–CO bond is also the primary photochemical step in these *o*-acetoxyaryl furanones. Nevertheless, the presence of the *o*-acetoxy group wholly changes the fate of **7**, the diradical initially formed. Instead of being decarbonylated to give an aryl vinyl ketone, it transforms into diradical **8** creating in this way the chromone skeleton. This cyclization implies an internal radical addition to the ester CO group. Although this type of addition is admitted in carbonylic compounds,[33] only one report[34] has been found with regard to the CO group of an ester. Diradical **8** can be connected with the final products **5** and **6** via the common intermediate **9**, formed by internal radical collapsing of **8**.



(7) (8)



(9)

Chromanone **9** could give then chromone **6** by way of a solvolytic process, followed by elimination or, when benzene is used as the solvent, it would undergo a photodecarboxylation and rearrangement to give chromone **5**. Although this pathway seems quite plausible, there is actually no experimental evidence supporting the formation of **9**. The UV-spectra of irradiated solutions taken periodically revealed the presence of chromones at a very early stage. Thus, if **9** were the intermediate, it should be rapidly transformed into chromone. In fact, very few examples of stable chromanones with an –OR substituent in position 2 are known and these can be readily converted into chromones.[35] It is worth mentioning that an analogous, but ionic, mechanism has been put forward to explain the base-catalysed cyclization of enol-esters of *o*-acyloxyphenyl alkyl ketones to chromones.[36] Work in progress is now directed to extend the scope of this photoreaction to the latter type of compounds.

EXPERIMENTAL

Materials. The enol lactones **1a** and **1b** were prepared by Friedel–Crafts direct succinoylation of benzene and *p*-dimethoxybenzene, followed by cyclization of the resulting aroylpropionic acids by use of acetic anhydride containing a trace of sulfuric acid. Lactones **1c** and **1d** were obtained by indirect succinoylation of hydroquinone monomethyl ether and hydroquinone via a photo-Fries rearrangement followed by dehydration.[18]

Instruments. M.ps are uncorrected. UV spectra were determined in EtOH with a Perkin–Elmer 402 spectrophotometer; absorbed radiation is defined by its wavelength λ_{max} in nm and the figures in brackets are log ϵ. IR spectra were obtained for Nujol suspensions with either a Perkin–Elmer 257 or an Infracord spectrometer. ^{1}H NMR spectra were measured with either a 60 MHz Perkin–Elmer Model R-12 or a Varian XL-100-15 FT instrument. ^{13}C NMR spectra were also taken with the latter instrument. Chemical shifts are reported in ppm downfield (δ) from TMS. Unless otherwise stated, $CDCl_3$ was used for NMR work. Mass spectra were obtained with a Hitachi–Perkin–Elmer Model RMU-6MG spectrometer; the ratios *m*/*e* and the relative intensities are reported.

Irradiations

Procedure A. A soln of 100 mg of the substrate in 130 ml abs EtOH (or benzene) was placed in a cylindrical quartz cell and irradiated externally by the full light of a medium pressure 125 W mercury arc. The reaction was followed by recording periodically its UV absorption spectrum. At the completion state (24–32 hr) the spectrum remained unchanged by further irradiation.

Procedure B. When larger amounts of photoproducts were required, a 300 ml capacity conventional immersion well reactor, provided with a Pyrex (or Quartz) sleeve and a 125 W medium pressure mercury lamp was employed. The solns were purged with N_2 prior to and during the irradiation. The progress of the reaction was monitored by UV spectroscopy as in Procedure A and in general shorter irradiation times (3–4 hr) were necessary.

Isolation and purification. The irradiated solns were evaporated at reduced pressure and the residues were applied to preparative tlc plates (Kieselgel G F254 Merck) and eluted with $CHCl_3$. Oils were directly submitted to elemental analysis. Solid substances were solved in acetone (or benzene) and after addition of n-hexane were set aside to recrystallize.

Yields, analytical and spectral data

Compound **2a**.[19] Irradiation of **1a** by either procedure A or B resulted in the formation of **2a** in 41% yield. IR: $\bar{\nu}_{max}$(cm^{-1}) = 1680 (C=O); ^{1}H NMR (CCl_4): δ(ppm) = 8.10–7.40 (m, 5H, aromatic H), 7.40–5.74 (m, 3H, vinylic system); MS: *m*/*e* = 132 (M$^+$, 36), 105 (100), 77 (70).

Compound **2b**. Irradiation of **1b** in benzene by procedure A gave **2b** in 34% yield. (Found: C, 68.65, H, 6.08. $C_{11}H_{12}O_3$ requires: C, 68.73 and H, 6.29%); IR: $\bar{\nu}_{max}$(cm^{-1}) = 1660 (C=O); ^{1}H, NMR: δ(ppm) = 7.20–7.00 (m, 3H, aromatic H) 7.40–5.72 (m, 3H, vinylic system), 3.85 and 3.81 (s, s, 6H, 2 OMe); UV λ_{max}(nm) = 222 (4.0), 245 (sh), 346 (3.2); MS: *m*/*e* = 192 (M$^+$, 82), 165 (100).

Compound **3b**. Irradiation of **1b** in EtOH by procedure A during 24 hr afforded **3b** in 20% yield. (Found: C, 65.29, H, 7.35. Calc. for $C_{13}H_{18}O_4$: C, 65.52 and H, 7.61%). IR: $\bar{\nu}_{max}$(cm^{-1}) = 1670 (C=O); ^{1}H NMR: δ(ppm) = 7.30 – 6.90 (m, 3H, aromatic H), 3.90 (s, 3H, 5′-OCH_3), 3.80 (s, 3H, 2′-OCH_3) 4.00–3.00 (m, 6H, 3 × CH_2), 1.15 (t, 3H, CH_3); UV: λ_{max}(nm) = 221 (4.0), 248 (3.6); 333 (3.3); MS: *m*/*e* = 238 (M$^+$, 14), 192 (23), 165 (100).

Photodimers. Irradiation of 200 mg **1b** in benzene by procedure B using a Pyrex immersion well, followed by removal of the solvent, left a residue that solidified on standing. The crude material was chromatographed on silica gel as above indicated, giving mainly two fractions: A and B (R_fA < R_{fB}). Recrystallization of fraction A from benzene-n-hexane afforded a pure product assigned as **4b** (35% yield), m.p. 230–233°. (Found: C, 65.16; H, 5.59. Calc. for $C_{24}H_{24}O_8$: C, 65.44, H, 5.49%). IR: ν_{max}(cm^{-1}) = 1780 (C=O, lactone); ^{1}H NMR: δ(ppm) = 7.20 – 6.80 (m, 6H, aromatic H), 3.82 and 3.68 (s, s, 12H, 4 × OCH_3), 3.41 (d, broad, 2H, $J \simeq 8$ Hz, 2 × CH), 3.00–2.50 (m, 4H, 2 × CH_2, $J_{AB} \simeq$ 17 Hz); ^{13}C NMR δ(ppm) 175.9 (COO), 153.0 and 151.7 (aromatic C-2′ and C-5′), 124.0 (aromatic C-1′), 116.3, 115.2 and 111.7 (aromatic C-3′, C-4′ and C-6′), 91.5 (quaternary cyclobutyl C), 55.8 and 55.3 (2′ and 5′-OCH_3), 43.4 (tertiary cyclobutyl C) and 36.0 (CH_2). The off-resonance experiment showed the following respective multiplicities: s, s, s, s, d, d, d, s, q, q, d, t.; UV λ_{max}(nm) = 230, 300; MS: *m*/*e* = 440 (M$^+$, 1), 396 (13), 352 (13), 220 (M$^+$/2, 100). No further purification could be made with fraction B (23% yield) that showed very closely related spectra: IR: λ_{max}(cm^{-1}) = 1770 (C=O, lactone); ^{1}H NMR: δ(ppm) = 7.30 – 6.60 (m, 6H, aromatic H), 3.65, 3.64, 3.63 and 3.62 (s, s, s, s, 12H, 4 × OCH_3), 3.50 – 2.05 (m, 6H, 2 × CH_2 + 2 cyclobutanic H); MS: *m*/*e* = 440 (M$^-$, 0.1), 396 (17), 352 (24), 220 (M$^+$/2, 100).

2,3-*Dimethyl*-6-*methoxy chromone* **5c**. Irradiation of 200 mg **1c** in benzene by procedure B using a Pyrex sleeve gave **5c** in 30% yield, m.p. 82°. (Found: C, 70.36, H, 5.85. $C_{12}H_{12}O_3$ requires: C, 70.57 and H, 5.92%). IR: $\bar{\nu}_{max}$(cm^{-1}) = 1630 (C=O, chromone); ^{1}H NMR: δ(ppm) = 7.50 – 7.10 (m, 3H, aromatic H), 3.79 (s, 3H, OCH_3), 2.30 (broad singlet, 3H, CH_3 in position 2), 1.96 (broad singlet, 3H, CH_3 in position 3); UV λ_{max}(nm) = 235–242 (4.3), 268–278 (3.7), 322 (3.8); MS: *m*/*e* = 204 (M$^+$, 100), 203 (44), 189 (11), 175 (11), 174 (22), 161 (11), 151 (44), 150 (11).

3-*Carbethoxymethyl*-6-*methoxy*-2-*methyl chromone* **6c**. Irradiation of **1c** in EtOH by prodecure A gave **6c** in 54% yield, m.p. 111°. (Found: C, 65.08; H, 5.97. Calc. for $C_{15}H_{16}O_5$: C, 65.20 and H, 5.83%). IR: $\bar{\nu}_{max}$(cm^{-1}) = 1725 (C=O, ester), 1635 (C=O, chromone); ^{1}H NMR: δ(ppm) = 7.50 – 7.10 (m, 3H, aromatic H), 4.06 (q, 2H, $O\underline{CH_2}CH_3$), 3.76 (s, 3H, OCH_3), 3.49 (s, 2H, CH_2COO), 2.30 (s, 3H, CH_3 in position 2), 1.16 (t, 3H, $OCH_2\underline{CH_3}$); UV: λ_{max}(nm) = 242 (4.3), 265–275 (3.6), 322 (3.7); MS: *m*/*e* = 276 (M$^-$, 45), 231 (31), 230 (97), 219 (14), 203 (31), 202 (100), 175 (14), 151 (20).

6-*Acetoxy*-2,3-*dimethyl chromone* **5d**.[32] Irradiation of **1d** in benzene by procedure A during 80 hr afforded **5d** in 24% yield, m.p. 136–137° (lit. 139°). (Found: C, 67.04, H, 5.27. Calc. for $C_{13}H_{12}O_4$: C, 67.23 and H, 5.20%). IR: $\bar{\nu}_{max}$(cm^{-1}) = 1750 (C=O, ester), 1630 (C=O, chromone); ^{1}H NMR: (ppm) = 8.00 – 7.40 (m, 3H, aromatic H), 2.45 (broad singlet, 3H, CH_3 in position 2), 2.35 (s, 3H, CH_3COO), 2.09 (broad singlet, 3H, CH_3 in position 3); UV λ_{max}(nm) = 232 (4.3), 262–271 (3.7), 305 (3.8); MS: *m*/*e* = 232 (M$^+$).

6-*Acetoxy*-3-*carbethoxymethyl*-2-*methyl chromone* **6d**. Irradiation of **1d** in EtOH by procedure A during 24 hr followed by removal of the solvent left a residue that was separated in two fractions by preparative tlc as above indicated. Recrystallization of the more polar fraction in the usual way gave **6d** in 13% yield. (Found: C, 62.95, H, 5.40. Calc. for $C_{16}H_{16}O_6$: C, 63.15 and H, 5.30%). IR: $\bar{\nu}_{max}$(cm^{-1}) = 1750 (C=O, acetate), 1725 (C=O, aliphatic ester 1625 (C=O, chromone); ^{1}H NMR: δ(ppm) = 8.10 – 7.50 (m, 3H, aromatic H), 4.23 (q, 2H, $O\underline{CH_2}CH_3$), 3.64 (s, 2H,

CH_2COO), 2.47 (s, 3H, CH_3 in position 2), 2.36 (s, 3H, CH_3COO), 1.29 (t, 3H, OCH_2CH_3); UV: λ_{max}(nm) = 230 (4.3), 260–267 (3.7), 303 (3.8); MS: *m/e* = 304 (M^+, 10), 262 (52), 259 (11), 232 (6), 231 (10), 216 (100), 190 (56), 189 (54), 188 (25), 137 (21).

2′,5′-Diacetoxyphenyl vinyl ketone **2d**. The less polar fraction (9%) showed spectra consistent with the structure of **2d**. IR: $\tilde{\nu}_{max}$(cm^{-1}) = 1760 (C=O, ester), 1665 (C=O, ketone); ^{1}H NMR: δ(ppm) = 7.50 − 7.20 (m, 3H, aromatic H), 7.10 − 5.95 (m, 3H, vinylic system), 2.35 and 2.31 (s, s, 6H, 2 × CH_3COO); UV: λ_{max}(nm) = 218 (4.1) 245 (3.8).

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