Tetrahedron Vol. 43, No. 5, pp. 999 to 1002, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00
Pergamon Journals Ltd.

NOVEL PHOTOREACTIONS OF CHROMENE DERIVATIVES. THE PHOTOLYSIS OF 4-ACETOXY-2H-CHROMENE.

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(*Received in UK* 29 *January* 1987)

Abstract - The photolysis of 4-acetoxy-2H-chromene **1a** leads to a mixture of o-acetoxyphenyl vinyl ketone **2a**, 4-chromanone **3**, chromone **4**, 3-acetoxy-4-chromanone **5**, 3-hydroxy-4-chromanone **6** and a cyclobutane dimer with anti head-to-head structure (**7**). The formation of **2a** is explained by a photochemical electrocyclic opening of the pyran ring, followed by cis-trans photoisomerization and transacylation. Compounds **3** and **4** would arise from **1a** by way of a photolytic cleavage of the acetyl-oxygen bond and subsequent disproportionation of the resulting radical **8**. The isolation of the 3-substituted chromanones **5** and **6** can be accounted for in terms of a photochemical epoxidation of **1a**. This process and the [2+2] photodimerization are unprecedented in the photochemistry of 2H-chromenes. Moreover, the photochemical epoxidation of **1a** could have biological significance.

INTRODUCTION

The photochemistry of 2H-chromenes (2H-benzo[b]pyrans) has been the subject of considerable interest in connection with the photochromic properties of the structurally related spiropyrans, whose application in the development of new imaging systems is being extensively investigated.[1,2] 2H-Chromenes undergo a photochemical ring opening to give o-quinoneallides, which can be either observed as short lived species or trapped with suitable reagents.[3-7]

Likewise, the photolysis of 4-acetoxy-2H-thiochromene (**1b**) affords the vinyl ketone **2b**, via a chromene-like ring opening, followed by irreversible migration of an acetyl group from oxygen to sulphur.[8] In this case, the introduction of an acetoxy group as substituent at C-4 provides an elegant and rather efficient system to intramolecularly trap the open-chain intermediate **9**, without altering the essential photoreactivity of this type of compounds.

The extension of this idea to the 2H-chromene series could be useful to examine the influence of the type, number and position of the substituent attached to the aromatic carbons on the photochemical reactivity of the heterocyclic ring, and would be very advantageous from the practical point of view. This led us to undertake a model study on the photolysis of 4-acetoxy-2H-chromene (**1a**).

RESULTS AND DISCUSSION

The required substrate **1a** was prepared by acetylation of the enol form of 4-chromanone with isopropenyl acetate, in the presence of p-toluenesulphonic acid.[9] Irradiation of **1a** through quartz, in hexane solution, gave rise to a variety of photoproducts.

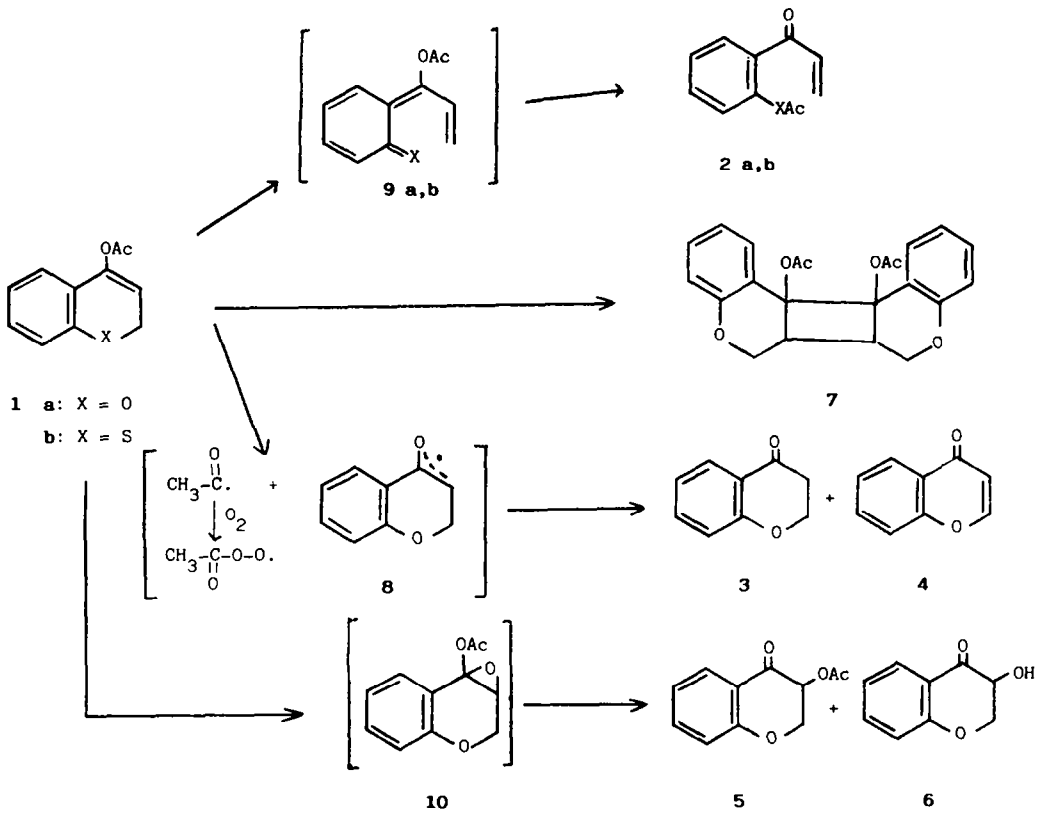
As expected, o-acetoxyphenyl vinyl ketone (**2a**)[10] was present in the photolysis mixture, although the yield (4%) was markedly lower than that found for the analogous transformation of 4-acetoxy-2H-thiochromene (**1b**) into the corresponding vinyl ketone **2b**. The isolation of **2a** is a proof for the occurrence of an electrocyclic opening of the pyran ring of **1a**, and hence for the involvement of the o-quinoneallide **9** as intermediate. We think that the conversion of this intermediate into the vinyl ketone **2a** takes place via cis-trans photoisomerization of the exocyclic carbon-carbon double bond, followed by a thermal intramolecular transacylation similar to those reported in the literature for related systems.[11-13] This seems more probable than the suggested photochemical 1,5-acyl migration leading from **1a** to **2a**,[8] which is scarcely documented.[14]

Two further products isolated from the photolysis mixture were 4-chromanone (**3**) (6%) and chromone (**4**) (4%), probably formed by disproportionation of the radical intermediate **8**, generated in turn by initial homolysis of the carbonyl-oxygen bond. Therefore, **3** and **4** can be considered "normal" products of the photochemical behavior of the chromene **1a** as an enol ester.[15]

3-Acetoxy-4-chromanone (**5**)[16] (9%) and 3-hydroxy-4-chromanone (**6**)[10] (6%) were also photoproducts of **1a**. The formation of **5** can be accounted for as occurring via the epoxide **10** (not isolated), through a rearrangement involving 1,3-migration of the acetyl group and opening of the oxirane ring. Compound **6** would be formed from **5** by hydrolysis of the ester moiety, either under the reaction conditions or during the workup. In order to verify if an epoxidation of the double bond between C-3 and C-4 could be the origin of the 3-substituted chromanones **5** and **6**, we performed the independent reaction of 4-acetoxy-2H-chromene (**1a**) with m-chloroperbenzoic acid. The only isolated products were **5** and **6**, a fact which supports our hypothesis on the formation of these compounds.[17]

The course of the photochemical epoxidation of 4-acetoxy-2H-chromene (**1a**) could be explained as indicated in the scheme. The acetyl radical formed after homolysis of the carbonyl-oxygen bond of the enol ester might react with the air oxygen to give an acetylperoxy radical. This new reactive species would be capable of inducing an epoxidation of the chromene double bond. Reasonably similar processes have been recently reported in the literature.[18]

The major photoproduct (28%) was an anti head-to-head dimer (**7**) whose structure was assigned on the basis of the following data: i) the elemental composition was the same as that of the starting chromene **1a**, as revealed by the combustion analysis, ii) in spite of the low intensity of the molecular peak (M^+ 380), it was easy to identify the peaks corresponding to $M^+ - (42+42)$ and $M^+ - (42+43)$, indicative of the existence of two acetyl groups, iii) the IR spectrum showed a single carbonyl absorption at 1745 cm^{-1}, as expected for a saturated ester, iv) the ^{1}H-NMR spectrum exhibited a set of signals consisting of an AB-like system centered at δ = 4.4 ppm, very weakly coupled with a singlet-like signal at δ = 2.8 ppm, assignable to the protons of the heterocyclic ring; in addition, the spectrum presented a rather shielded (δ = 1.7 ppm) singlet for the acetoxy group and a characteristic multiplet for the aromatic protons and v) the ^{13}C-NMR spectrum was also in agreement with structure **7**.



It is worth mentioning that the abnormal shielding of the acetoxy group in the ^{1}H-NMR spectrum was very useful in assessing an anti head-to-head arrangement of the two monomeric units. A Dreiding model of the compound shows that the acetoxy group is in the shielding region of the neighbouring aromatic ring, thus justifying the observed chemical shift.

In summary, we have observed a variety of processes in the photolysis of 4-acetoxy-2H-chromene (**1a**). To our knowledge, the formation of cyclobutane dimers and the epoxidation of the double bond are unprecedented in the photochemistry of 2H-chromenes. It is noteworthy that the precocenes and related 2H-chromenes with antijuvenile hormone activity are thought to act via a ractive 3,4-epoxide, which cause selective cellular necrosis on the corpora allata of sensitive insects.[19] In this context the photochemical epoxidation of the chromene **1a** could have biological significance, since photolysis has been recognised as one of the main factors determining the fate and, in a number of cases, the mode of action of pesticides in the environment.[20]

EXPERIMENTAL

General. M.ps were determined with a Büchi 510 apparatus and are uncorrected. Ir-spectra were obtained in CCl_4 solns with a Perkin-Elmer Model 781 spectrometer; $\bar{\nu}_{max}$ (cm^{-1}) is given only for the carbonyl absorption bands. ^{1}H-nmr spectra were measured in CCl_4 with a 60-MHz Varian 360 EM instrument; chemical shifts are reported in δ(ppm) values, using TMS as internal standard. The ^{13}C-nmr spectrum of was recorded with a Bruker WP 80 SY spectrometer; the signals are reported in δ(ppm) referenced to TMS. Mass spectra was determined using a VG ZAB-2F spectrometer; the ratio m/e and the relative intensities are indicated for the significant peaks. The combustion analysis was performed at the Instituto de Química Bio-Orgánica of C.S.I.C. in Barcelona. Isolation and purification were done by flash column chromatography on silica gel

Merck 60, 70-230 mesh, using hexane as eluent and a Waters isocratic h.p.l.c. equipment provided of a semipreparative microporasil™ column, using hexane-ethyl acetate as eluent.

4-Acetoxy-2H-chromene was prepared heating 1 g (5.26 mmol) of 4-chromanone with 25 ml of isopropenyl acetate and 100 mg (0.58 mmol) of p-toluenesulphonic acid, under continuous removing of the resulting acetone by distillation, as described in reference 9.

Irradiation of **1a**. A soln of 500 mg of the substrate in 300 ml of distilled hexane was placed in an immersion well photoreactor, provided with a quartz sleeve and a 125 W medium pressure Hg lamp, and irradiated for 6 h. After this time, the resulting soln was concentrated in vacuo and the mixture submitted to chromatography. The following products were isolated: 1-(2-acetoxyphenyl)propenone **2a** (20 mg, 4%); 4-chromanone **3** (25 mg, 6%); chromone **4** (15 mg, 4%); 3-acetoxy-4-chromanone **5** (50 mg, 9%); 3-hydroxy-4-chromanone **6** (25 mg, 6%); anti-7,8-diacethoxydibenzo[ei]-4,11-dioxatricyclo[6.4.0.0^{2,7}]dodecane **7** (40 mg, 28%), m.p 206-208 °C, analysis: C 69.19 H 5.01% (Calcd. for $C_{22}H_{20}O_6$ C 69.47 H 5.30%), ir 1745 (ester), ^{1}H-nmr: δ =7.63-6.82 (m, 4H, ArH), 4.53 (d, J=11 Hz, 1H, H at C-2), 4.21 (d, J=11 Hz, 1H, H at C-2), 2.78 (s, 1H, H at C-3), 1.72 (s, 3H, $COCH_3$); ^{13}C-nmr: δ=168.65, 154.40, 129.46, 129.22, 120.80, 117.72, 62.88, 38.32, 20.89; M/S: m/e=380 (0.1), 296 (3), 295 (8), 277 (1), 262 (6), 236 (4), 201 (10), 191 (10), 190 (77), 189 (13), 148 (100), 147 (94).

Epoxidation of **1a**. 190 mg (1.1 mmol) of m-chloroperbenzoic acid were added to a soln of 190 mg (1 mmol) of **1a** in 25 ml of CH_2Cl_2 and the mixture stirred for 5 h. After this time, the resulting soln was washed with 5% aqueous NaOH, then with water, dried with anhydrous Na_2SO_4 and the solvent removed in vacuo. The residue was submitted to purification, affording 3-acetoxy-4-chromanone **5** (115 mg, 55%) and 3-hydroxy-4-chromanone **6** (40 mg, 25%).

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