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Influence of the β-Substitution on the Photochemistry of α,2-Diacetoxystyrenes. Irradiation of Phenyl, Vinyl, and Benzyl Derivatives

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Summary. β-Substitution shows a pronounced influence on the photochemistry of α,2-diacetoxystyrenes. As in the case of the parent compound, intramolecular cyclization with participation of the neighbouring 2-acetoxy group takes place upon irradiation of the enol esters **4a–c**; however other processes are also observed, depending on the substrate. The phenyl derivative **4a** gives the *E* isomer **7a** and the phenanthrene **9**. The vinyl derivative **4b** also undergoes *cis-trans* isomerization and/or photooxidation, to afford **7b** and **10**. Finally, a 1,4-acyl migration occurs in the benzyl derivative **4c**, whereby the 1,4-diketone **12** is formed.

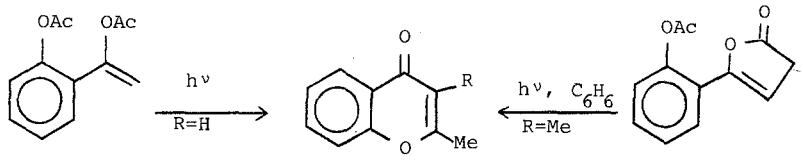
Keywords. Photolysis; α-Acetoxystyrenes; Neighbouring group participation; Chromones.

Einfluß der β-Substitution auf die Photochemie von α,2-Diacetoxystyrolen. Bestrahlung von Phenyl-, Vinyl- und Benzylderivaten

Zusammenfassung. Bei α,2-Diacetoxystyrolen haben die β-Substituenten einen deutlichen Einfluß auf das photochemische Verhalten. Wie im Fall der Stammverbindung erfolgt bei der Bestrahlung der Enolester **4a–c** intramolekulare Cyclisierung unter Einbeziehung der benachbarten 2-Acetoxygruppe; jedoch werden je nach Substrat auch andere Reaktionen beobachtet. Das Phenylderivat **4a** liefert das *E*-Isomer **7a** und das Phenanthren **9**. Das Vinylderivat **4b** erfährt ebenfalls *cis/trans*-Isomerisierung zu **7b** und/oder Photooxidation zu **10**. Beim Benzylderivat **4c** tritt eine 1,4-Acylverschiebung zum 1,4-Diketon **12** auf.

Introduction

Photolysis of enol acetates of *o*-acetoxy and *o*-(benzoyloxy)acetophenones affords benzopyran-4-ones by a mechanism probably involving an intramolecular radical addition of a benzoylmethyl radical to the carbonyl carbon of the aryl ester moiety [1–3]. Likewise, the structurally related 5-(2-acetoxyaryl)-2(3*H*)-furanones show a similar photochemical behaviour, giving rise to chromones through a parallel reaction [4], (Scheme 1).



Scheme 1

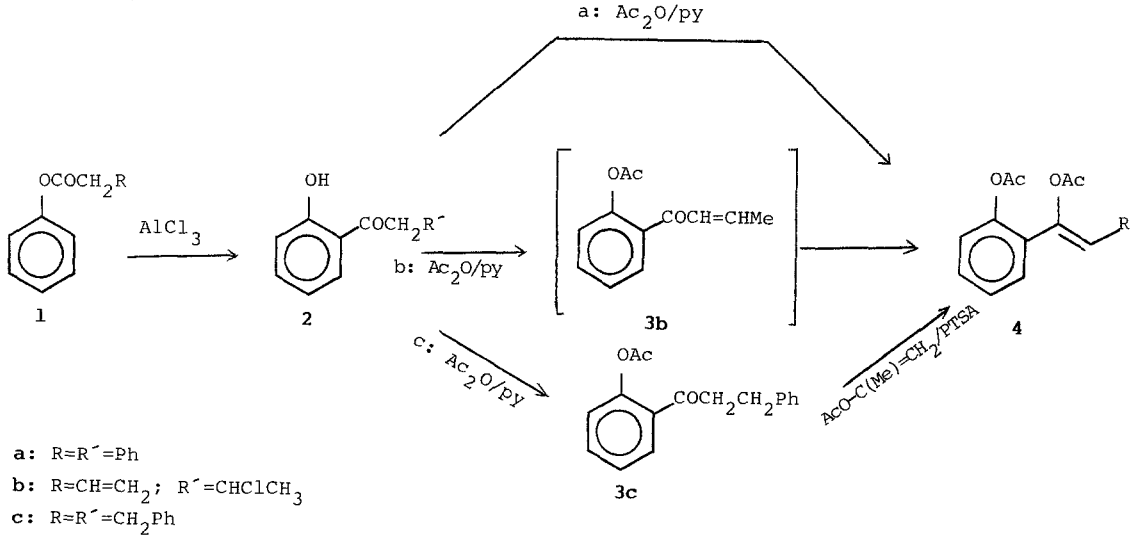
In spite of the potential application of these types of attacks to carbonyl groups by carbon centered radicals, that can be viewed as the radical counterparts of the classical reactions involving enolates, only a few scattered examples can be found in the literature [5].

The aim of the present work was to obtain further information about the influence of the structure on the photochemical reactivity of *o*-acetoxyacetophenone enol acetates, in order to get a more complete understanding of the factors governing the behaviour of radicals of the benzoylmethyl type.

In this context, we have introduced substituents at the β-position of the styrenic system which would be expected to stabilize the radical generated by homolytic O-CO bond cleavage of the enol ester, in order to establish if there is a relationship between the mesomeric stabilization of these radicals and their ability to attack the carbonyl group. On the other hand, it appeared also interesting to ascertain whether, and eventually how these structural modifications on *o*-acetoxyacetophenone enol acetates affect the normal course of the irradiation, providing alternative pathways and modifying the ordinary reactivity of these compounds [6].

Results and Discussion

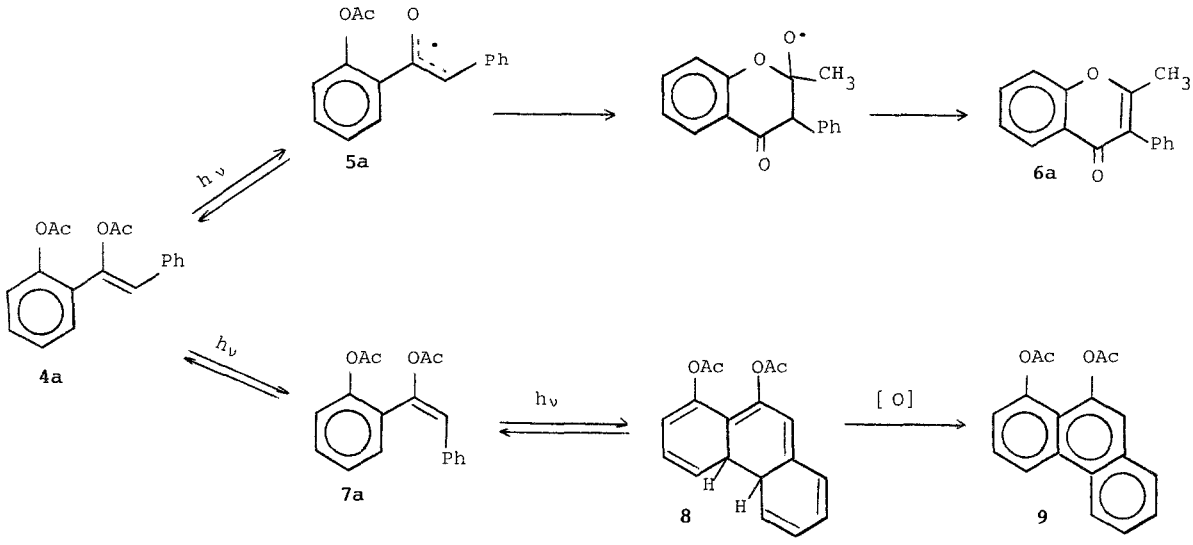
The enol acetates **4a–c** were synthesized as shown in Scheme 2. Conversion of the ketones **2a** and **2b** into the enol esters **4a** and **4b** was achieved in good yields by means of acetic anhydride in pyridine (*py*) at reflux temperature. An analogous treatment of **2c** led mainly to **3c**, and only a small amount of its enol ester **4c** was present in the reaction mixture. The latter could be efficiently prepared treating **3c** with isopropenyl acetate in the presence of catalytic amounts of *p*-toluenesulfonic acid (*PTSA*).



Scheme 2

The easier formation of **4a, b** compared with **4c** can be understood taking into consideration the stabilization gained through additional conjugation of the enolic double bond with the phenyl ring or the vinyl moiety in **4a** and **4b**, respectively. It is also remarkable that the one-pot formation of **4b** must involve three different processes, i.e., dehydrochlorination, phenolic O-acetylation, and enolic O-acetylation. The fact that 1-(2-acetoxyphenyl)-2-buten-1-one (**3b**) could be isolated from the reaction mixture at early stages of the acetylation indicates that, at least in part, dehydrohalogenation takes place before enol acetylation to afford the α,β-unsaturated ketone **3b**, which is an intermediate in the formation of **4b**.

Photolysis of **4a** led to 2-methylisoflavone (**6a**) (20%) and 1,10-diacetoxyphenanthrene (**9**) (40%). The formation of **9** is not surprising since compound **4a** is in fact a diacetoxystilbene. It is known that stilbenes undergo upon irradiation a *cis-trans* isomerization followed by a [6]-electrocyclic ring closure to give dihydrophenanthrenes which may be converted back to *cis*-stilbenes or may be oxidized to phenanthrenes [7, 8]. On the other hand, the isoflavone **6a** is the expected product considering **4a** as an *o*-acetoxyacetophenone enol ester (Scheme 3).



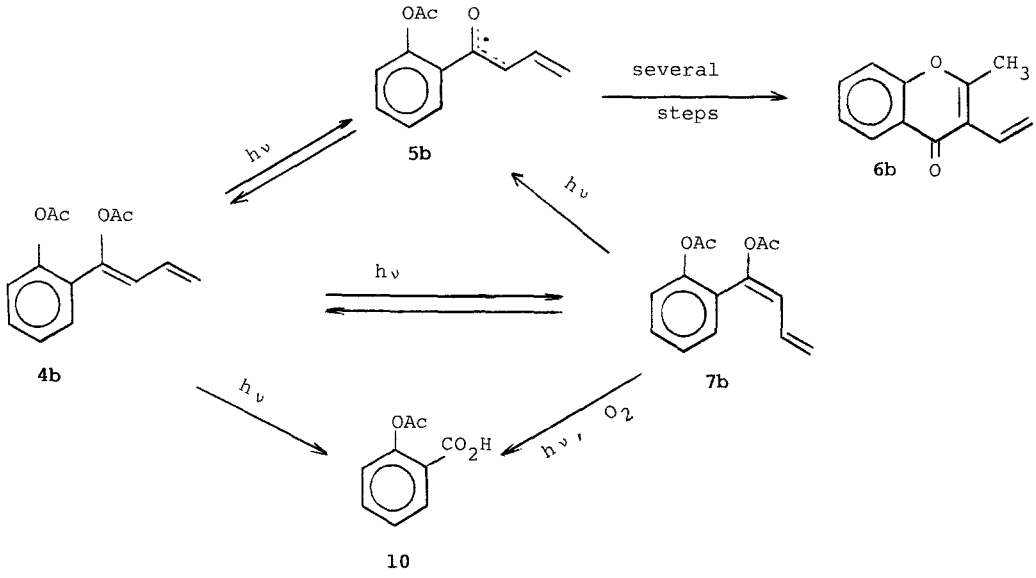
Scheme 3

Since the formation of the phenanthrene **9** requires the presence of air oxygen as oxidant, and this process is competitive with the cyclization to the isoflavone **6a**, a second irradiation of **4a** was carried out purging continuously the reaction mixture with argon in order to determine if the yield of isoflavone **6a** increases under these favourable conditions.

As expected, in accordance to the normal photochemical behaviour of stilbenes above described, the result was a substantial decrease in the yield of phenanthrene **9** (15%), and the presence of the (*E*)-diacetoxystylbene **7a** as the main product (23%), besides recovering of some unreacted starting material **4a** (11%). The most interesting fact is that the yield of 2-methylisoflavone (**6a**) did not show any appreciable increase under these experimental conditions, which is somewhat surprising, specially if it is considered that the *E* isomer **7a** is also a potential precursor

for **6a**. This might be due to steric hindrance, that makes it difficult for the *E*-isomer to reach the conformation from which cyclization to **6a** must occur. It is also possible that the *E* isomer undergoes a thermally reversible [6]-electrocyclic ring closure to the dihydrophenanthrene **8**, which could act as a "hidden" photochemical process deactivating the excited state of **7a**.

Irradiation of the β-vinyl derivative **4b** afforded the *E*-isomer **7b** (30%), 2-methyl-3-vinylchromone (**6b**) (7%), and *o*-acetoxybenzoic acid (**10**) (23%), besides unreacted starting material **4b** (15%). Longer irradiation times led to a progressive consumption of **4b** and **7b**, and a corresponding increase in the amount of **10**. It is significant that, at long times, the chromone **6b** underwent extensive polymerization, so that it could not be detected in the photolysis mixture after 6 hours. This lack of stability of the vinylchromone **6b** under the photolysis conditions would explain the low yield obtained for this compound, in spite of the fact that the homolytic O-CO bond cleavage of the enol ester moiety would be favoured by the stability of the mesomeric allylic radical **5b** (Scheme 4).

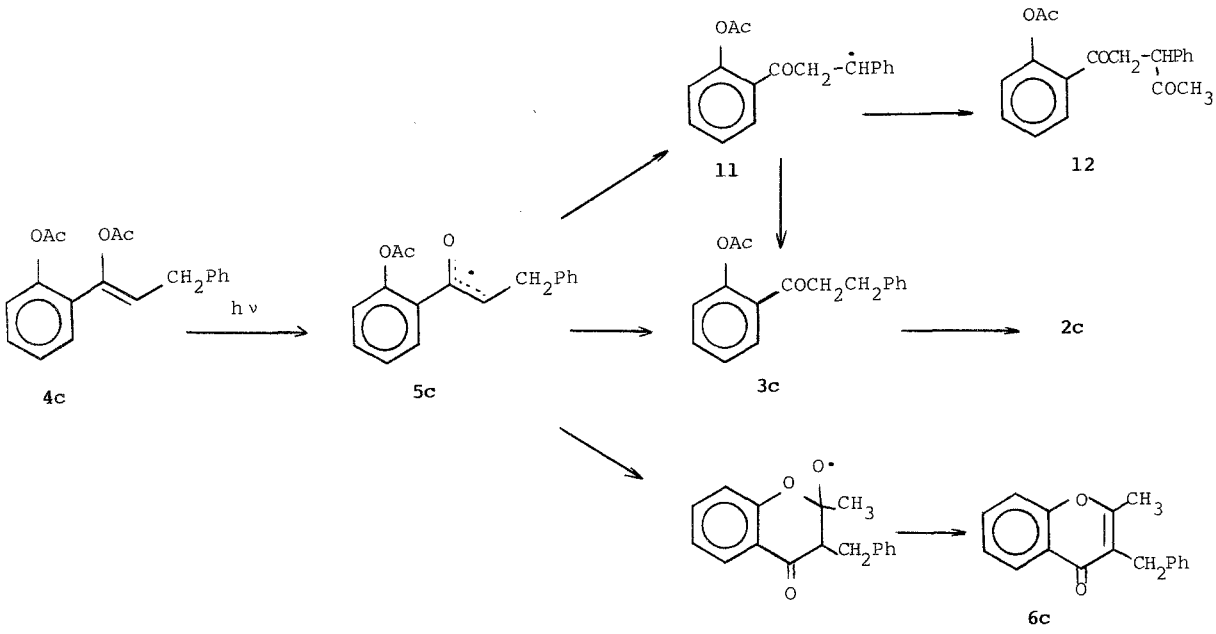


Scheme 4

The formation of acetylsalicyclic acid (**10**) could be due to photooxidation of the enolic double bond of **4b**, for which there are reasonably related examples in the literature [9, 10].

Finally, irradiation of the benzyl derivative **4c** led to 3-benzyl-2-methylchromone (**6c**) (24%), together with the 1,4-pentanedione **12** (16%) and the 3-phenylpropiophenones **2c** (30%) and **3c** (6%). The diketone **12** is a product involving a formal 1,4-migration of the acetyl group in **4c**, and its formation is in sharp contrast with the general behaviour of enol esters, which generally undergo a photochemical 1,3-acyl shift [11, 12] (Scheme 5).

These results may be rationalized in terms of a primary cleavage of the enol acetate carbonyl-oxygen bond. The resulting intermediate **5c** might undergo intramolecular radical addition involving the carbonyl group of the phenyl ester



Scheme 5

moiety to give the chromone **6c** or, alternatively, a 1,2-hydrogen migration [13] to generate the benzylic radical **11**, which could further undergo a recombination with the acetyl radical to afford the 1,4-pentanedione **12**. An additional mechanistic possibility for the latter process would be hydrogen transfer to the oxygen of the enoxy radical moiety in **5c**, leading in this way to the same intermediate **11**. Finally, **3c** could arise from the primary benzoylmethyl **5c** or the benzylic radical **11** by hydrogen abstraction from the medium, and the little amount of **2c** could be formed from **3c** by a photochemical deacetylation similar to those observed in related *o*-acetoxyphenyl ketones [1, 3].

In conclusion, the present work shows that the substitution pattern at the β-position of α,2-diacetoxystyrenes plays an important role in their photochemical behaviour, partially modifying the course of their reactions and dramatically affecting the observed product distribution. Finally, although intramolecular cyclization with participation of the neighbouring 2-acetoxy group was a general process observed in the irradiation of the enol esters **4a–c**, the yields of chromones **6a–c** ranging from 7 to 24% do not seem to be in accordance with the expectations, taking into account the stability of the radical intermediates **5**, which are actually the attacking species. The lack of a more explicit correlation can be attributed to the complexity of the processes involved.

Experimental

IR spectra were obtained in CCl_4 solutions with a Perkin-Elmer 851 spectrometer; wave number absorptions (cm^{-1}) are given only for the significant bands. ^{1}H-NMR spectra were measured in CCl_4 with a 60-MHz Varian 360 EM instrument; chemical shifts are reported as δ values (ppm), using Me_4Si as internal standard; coupling constants are given in Hz. MS were recorded with a GC/MS Hewlett-Packard 5988 A spectrometer; *m/e* ratio and their relative abundances in percentages (in

brackets) are given only for the main peaks. Elemental analyses were performed at the Instituto de Química Bio-Orgánica of the C.S.I.C. in Barcelona. Isolation and purification were done by flash column chromatography on silica gel Merck 60, 70–230 mesh, using a 5:1 mixture of hexane/ether as eluent and a Waters isocratic HPLC apparatus equipped with a semipreparative Microporasil™ column, using mixtures of hexane and ethyl acetate as eluent. For previously described compounds physical and spectroscopic data were in good agreement with the literature values. Yields are related to isolated material.

Preparation of the Enol Acetates 4 a–c

Phenyl Esters **1 a–c**. Acyl chlorides were synthesized by treating the corresponding carboxylic acid (21.2 mmol) with $SOCl_2$ (21.2 mmol) in $CHCl_3$ (50 ml) at reflux temperature for 2 h. Then, the solvent was eliminated in vacuo to remove the unreacted $SOCl_2$ and the crude chloride was stirred overnight with phenol (2.0 g, 21.2 mmol) in $CHCl_3$ (50 ml). The reaction mixture was concentrated and submitted to purification. The yields obtained were: **1 a** [14]: 94%; **1 b**: 96%; **1 c** [15]: 78%.

o-Hydroxyaryl Ketones **2 a–c**. Fries rearrangement of the phenyl esters was performed by heating a mixture of **1** (12.0 mmol) and $AlCl_3$ (2.0 g, 15.0 mmol) between 80 and 130°C for 1 h. After this time, the crude was cooled to room temperature, concentrated hydrochloric acid (10 ml) was added and then water (100 ml). The organic phase was extracted thoroughly with CH_2Cl_2, washed with water, and dried with anhydrous Na_2SO_4. After removal of the solvent the residue was submitted to purification to give the ketones **2** with the following yields: **2 a** [16]: 72%; **2 b**: 38%; **2 c** [17]: 84%.

Enol Acetates **4 a, b**. A mixture of the *o*-hydroxyaryl ketone **2** (5 mmol), acetic anhydride (10 ml) and pyridine (15 ml) was boiled for 1 h, then poured into ice/water (100 ml), and extracted with CH_2Cl_2. The organic phase was washed successively with 5% aqueous HCl, 5% aqueous $NaHCO_3$, and finally with water. After drying with anhydrous Na_2SO_4, the solvent was eliminated and the crude submitted to chromatography, giving rise to the enol acetates **4 a, b**. Yields: **4 a**: 95%; **4 b**: 61%.

Enol Acetate **4 c**. The above treatment of **2 c** afforded almost quantitatively the *o*-acetoxyaryl ketone **3 c**. Longer reaction times (5 h) led only to a small amount of the enol ester **4 c** (15% measured by ^{1}H-NMR). Enol acetylation was accomplished by heating together **3 c** (5 mmol) with isopropenyl acetate (12.5 ml, 125 mmol) and *p*-toluenesulfonic acid (100 mg) at about 90°C, following the procedure described in Ref. [3]. The yield of **4 c** was 78%.

Irradiation Procedure

A solution of 500 mg of the enol ester **4** in 450 ml of freshly distilled hexane was irradiated for 2 h at room temperature with a 125 W medium pressure mercury lamp inside a quartz immersion well photoreactor. After removal of the solvent, the photolysis residue was submitted to purification.

Spectroscopic and Analytical Data of the New Compounds

Phenyl 3-butenoate (**1 b**).

IR 1755 (C=O), 1630 (C=C). ^{1}H-NMR 7.49–6.82 (m, 5H, *Ar*-H), 6.34–5.61 (m, 1H, C*H*=CH_2), 5.44–4.93 (m, 2H, CH=C*H*$_2$), 3.20 (broad d, J=7, 2H, $COCH_2$) Anal. calcd. for $C_{10}H_{10}O_2$: C 74.06, H 6.22; found: C 73.45, H 6.19%.

3-Chloro-1-(2-hydroxyphenyl)-1-butanone (**2 b**).

IR 1630 (C=O). ^{1}H-NMR 11.89 (s, 1H, O*H*), 7.86–6.67 (m, 4H, *Ar*-H), 4.87–4.32 (m, 1H, CHCl), 3.57–3.24 (ABM, 2H, CH_2), 1.64 (d, J=6, 3H, CH_3). MS 200 (2), 198 (7), 163 (24), 121 (100), 93 (15). Anal. calcd. for $C_{10}H_{11}ClO_2$: C 60.46, H 5.58, Cl 17.85; found: C 59.88, H 5.23, Cl 17.15%.

1-(2-Acetoxyphenyl)-2-buten-1-one (**3b**).

IR 1750 (C=O, ester), 1660 (C=O, ketone), 1640 (C=C). ^{1}H-NMR 7.73–6.27 (m, 6H, *Ar*-H+CH=CH), 2.23 (s, 3H, $OCOCH_3$), 1.96 (d, 3H, $J=6$, $=C-CH_3$. MS 204 (1), 189 (10), 162 (5), 161 (7), 147 (100), 121 (15), 93 (5), 69 (9), 65 (10), 43 (34). Anal. calcd. for $C_{12}H_{12}O_3$: C 70.58, H 5.92; found C 70.48, H 6.05%.

1-(2-Acetoxyphenyl)-3-phenyl-1-propanone (**3c**).

IR 1760 (C=O, ester), 1685 (C=O, ketone). ^{1}H-NMR 7.90–6.91 (m, 4H, C_6H_4), 7.27 (broad s, 5H, C_6H_5), 3.32–2.74 (m, 4H, CH_2-CH_2), 2.20 (s, 3H, CH_3). MS 268 (5), 253 (22), 225 (33), 207 (10), 147 (10), 121 (98), 104 (10), 91 (26), 77 (21), 43 (100). Anal. calcd. for $C_{17}H_{16}O_3$: C 76.10, H 6.01; found: C 75.99, H 5.76%.

(Z)-1-Acetoxy-1-(2-acetoxyphenyl)-2-phenylethene (**4a**).

IR 1775 (C=O). ^{1}H-NMR 7.67–6.74 (m, 9H, *Ar*-H), 6.23 (s, 1H, CH-Ph), 2.19 (s, 3H, *Ar*-$OCOCH_3$), 2.06 (s, 3H, C=C-$OCOCH_3$). MS 296 (1), 254 (11), 212 (21), 121 (71), 119 (97), 117 (100), 82 (2), 43 (22). Anal. calcd. for $C_{18}H_{16}O_4$: C 72.96, H 5.44; found: C 73.08, H 5.76%.

(Z)-1-Acetoxy-1-(2-acetoxyphenyl)-1,3-butadiene (**4b**).

IR 1760 (C=O), 1655 (C=C). ^{1}H-NMR 7.58–6.80 (m, 4H, *Ar*-H), 6.77–5.97 (m, 2H, CH-CH=CH_2), 5.56–4.97 (m, 2H, CH_2), 2.16 (s, 3H, *Ar*-$OCOCH_3$), 2.03 (s, 3H, C=C-$OCOCH_3$). MS 246 (2), 204 (24), 162 (41), 161 (15), 147 (28), 145 (10), 144 (25), 121 (25), 115 (10), 43 (100). Anal. calcd. for $C_{14}H_{14}O_4$: C 68.28, H 5.73; found: C 67.74, H 5.50%).

(Z)-1-Acetoxy-1-(2-acetoxyphenyl)-3-phenylpropene (**4c**).

IR 1750 (C=O). ^{1}H-NMR 7.58–6.80 (m, 4H, C_6H_4), 7.24 (broad s, 5H, C_6H_5) 5.59 (t, $J=8$, 1H, CH-CH_2), 3.41 (d, $J=8$, 2H, CH_2), 2.03+2.01 (s+s, 6H, $2\times CH_3$). MS 310 (1), 267 (10), 226 (13), 225 (13), 208 (33), 207 (22), 121 (56), 91 (20), 77 (10), 43 (100). Anal. calcd. for $C_{19}H_{18}O_4$: C 73.53, H 5.85; found: C 73.37, H 5.61%.

2-Methyl-3-vinylchromone (**6b**).

M.p. 83–85°C. IR 1640 (C=O). ^{1}H-NMR 8.23 (dd, $J_{orto}=8$, $J_{meta}=2$, 1H, H at C-5), 7.72–6.97 (m, 3H, Hs at C-6, C-7, and C-8), 6.30 (m, 1H, CH=CH_2), 5.66–5.30 (m, 2H, CH=CH_2), 2.50 (s, 3H, CH_3). Anal. calcd. for $C_{12}H_{10}O_2$: C 77.40, H 5.41; found: C 76.87, H 5.76%.

2-Methyl-3-(phenylmethyl)chromone (**6c**).

IR 1620 (C=O). ^{1}H-NMR 8.18 (dd, $J_{orto}=7$, $J_{meta}=2$, 1H, H at C-5), 7.73–6.97 (m, 3H, Hs at C-6, C-7, and C-8), 7.18 (broad s, 5H, C_6H_5), 3.85 (s, 2H, CH_2), 2.36 (s, 3H, CH_3). MS 250 (100), 249 (71), 235 (21), 233 (12), 167 (16), 121 (27), 76 (21), 55 (34), 51 (32), 43 (66), 41 (66). Anal. calcd. for $C_{17}H_{14}O_2$: C 81.58, H 5.64; found: C 81.75, H 6.04%.

(E)-1-Acetoxy-1-(2-acetoxyphenyl)-2-phenylethene (**7a**).

IR 1755 (C=O). ^{1}H-NMR 7.53–6.77 (m, 9H, *Ar*-H), 6.40 (s, 1H, CH-*Ph*), 2.16 (s, 3H, *Ar*-$OCOCH_3$), 1.89 (s, 3H, C=C-$OCOCH_3$). Anal. calcd. for $C_{18}H_{16}O_4$: C 72.96, H 5.44; found: C 72.73, H 5.63%.

(E)-1-Acetoxy-1-(2-acetoxyphenyl)-1,3-butadiene (**7b**).

IR 1760 (C=O), 1640 (C=C). ^{1}H-NMR 7.54–6.83 (m, 4H, *Ar*-H), 6.37–5.70 (m, 2H, CH-CH=CH_2), 5.54–4.86 (m, 2H, CH=CH_2), 2.20 (s, 3H, *Ar*-OCOCH_3), 1.86 (s, 3H, C=C-OCOCH_3). Anal. calcd. for $C_{14}H_{14}O_4$: C 68.28, H 5.73; found: C 67.56, H 5.65%.

1,10-Diacetoxyphenanthrene (**9**).

IR 1760 (C=O). ^{1}H-NMR 8.58 (d, 1H, J = 8, H at C-9), 7.96–6.98 (m, 7H, *Ar*-H), 2.31 (s, 6H, 2×CH_3). MS 294 (13), 252 (13), 210 (100), 181 (14), 152 (19), 43 (34). Anal. calcd. for $C_{18}H_{14}O_4$: C 73.46, H 4.79; found: C 73.38, H 4.66%.

1-(2-Acetoxyphenyl)-3-phenyl-1,4-pentanedione (**12**).

IR 1750 (C=O, ester), 1710 (C=O, $COCH_3$), 1690 (C=O, *Ar*CO). ^{1}H-NMR 7.97–6.73 (m, 4H, *Ar*-H), 7.21 (s, 5H, *Ph*-H), 4.50 (t, J=7, 1H, CH), 3.18 (d, J, 2H, CH_2), 2.24 (s, 3H, $OCOCH_3$), 2.04 (s, 3H, $CHCOCH_3$). MS 310 (1), 268 (2), 225 (20), 133 (15), 121 (45), 43 (100).

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