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PHOTOCHEMISTRY OF 5-(2-ACETOXYARYL)-2(3H)-FURANONES. 2. ISOLATION OF CHROMONE-3-ACETIC ACIDS AND THEIR PHOTODECARBOXYLATION TO 3-METHYLCHROMONES[1]

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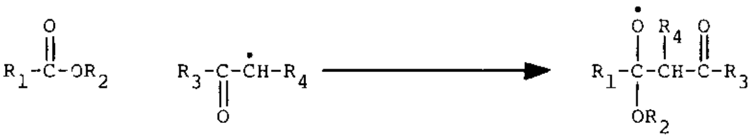
Abstract - Irradiation of the enol lactones **1a,b** in methanol led to the vinyl ketones **2a,b** and the chromones **3a,b**, while irradiation in benzene gave the vinyl ketones **2a,b** and the chromones **4a,b** and **5a,b**. The photodecarboxylation of **4a,b** to **5a,b**, analogous to that of phenylacetic acid, is very efficient. The mechanistic implications of these observations are discussed.

The photochemistry of 5-(2-acetoxyaryl)-2(3H)-furanones such as **1** follows three different pathways[1]: a) formation of [2+2] cyclobutane dimers through the styrenic double bond, b) decarbonylation to vinyl ketones[3] and c) formation of chromones. The mechanism of the latter process is not very well established, but the key step appears to be a radical addition to the carbonyl group, and the result is the formation of a C-C bond (Scheme 1).



$$R_1\text{-}\overset{\overset{O}{\|}}{C}\text{-}OR_2 \qquad R_3\text{-}\underset{\underset{O}{\|}}{C}\text{-}\overset{\bullet}{C}H\text{-}R_4 \longrightarrow R_1\text{-}\underset{OR_2}{\overset{\overset{\bullet}{O}}{C}}\text{-}\overset{R_4}{C}H\text{-}\overset{\overset{O}{\|}}{C}\text{-}R_3$$

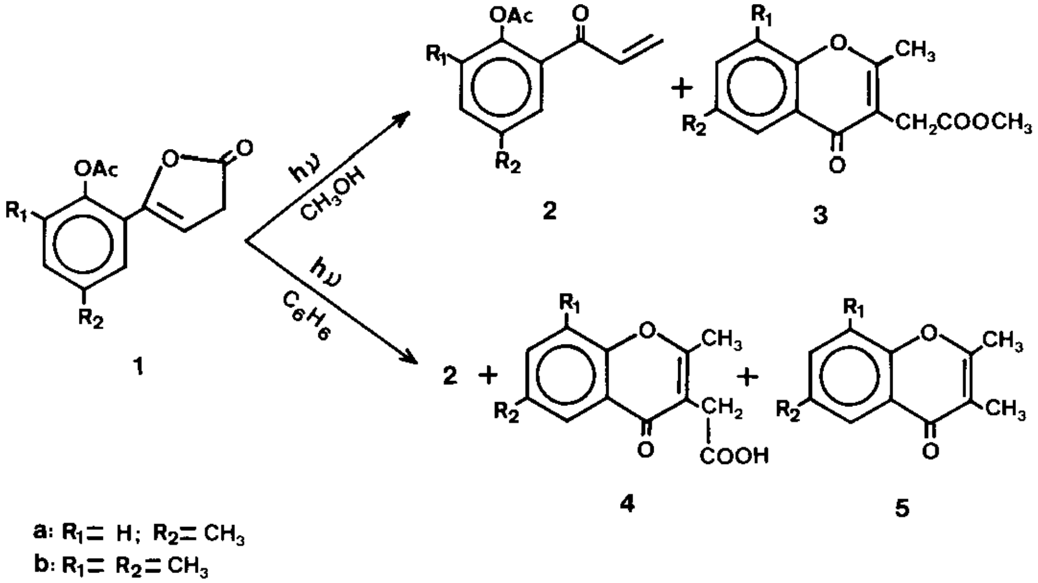
SCHEME 1

This type of process is the radical equivalent of the condensations through enolates, and might in principle be extended to a wide variety of intra- or intermolecular reactions.

In the present work we have confirmed our preliminary studies on structurally related substrates, and, at the same time, we have got evidences in favour of the involvement of the chromoneacetic acids **4** as intermediates in the mechanism of the reactions.

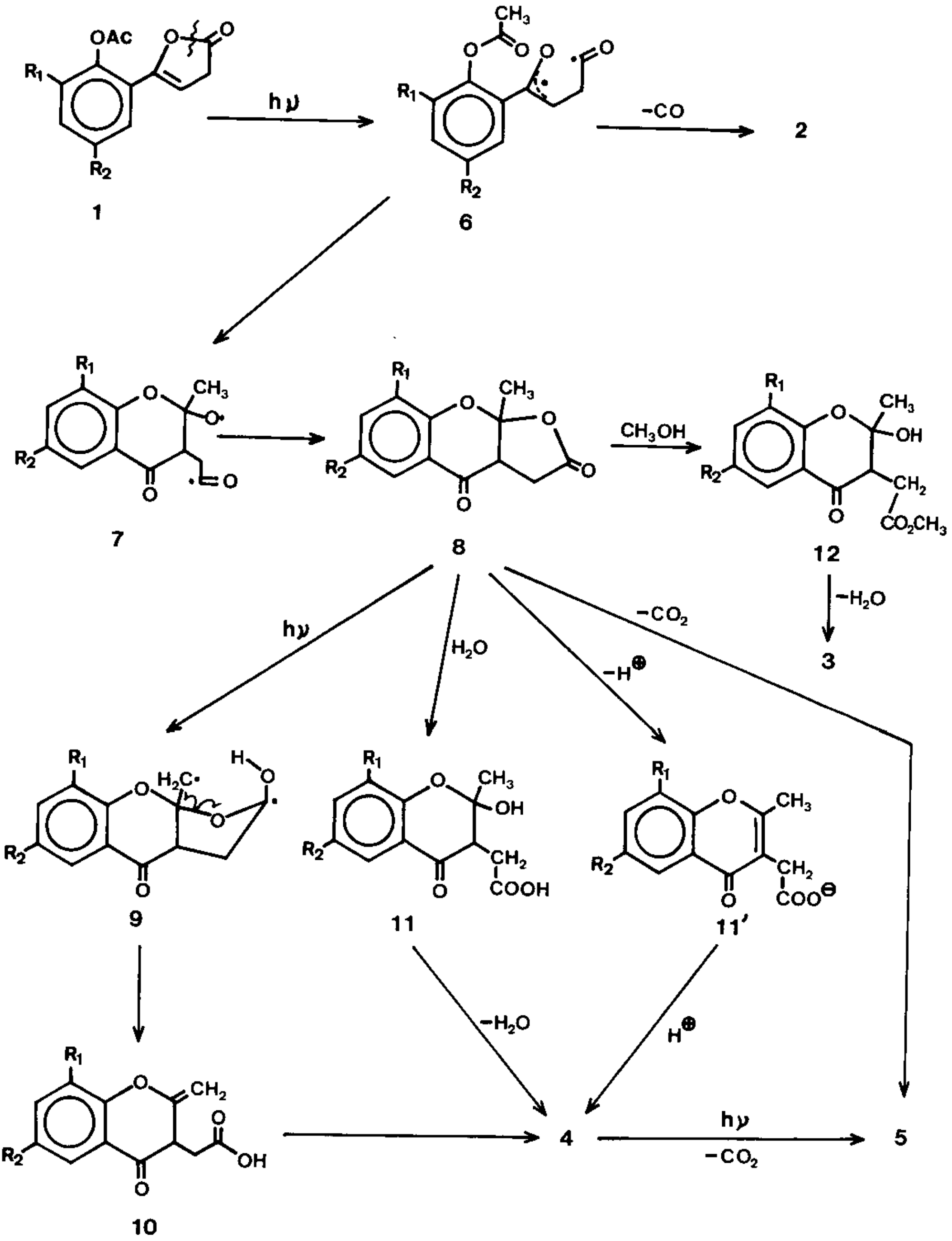
The irradiation of the lactones **1a** and **1b** in methanol led to the vinyl ketones **2a** (22%), **2b** (12%) and the chromones **3a** (16%), **3b** (23%) (Scheme 2). The yield estimated for vinyl ketones by means of ^{1}H-nmr of the crude photomixtures was nearly 60%; however the yield after purification was much lower, which is justifiable by extensive polymerization of these products during the workup.

On the other hand, the irradiation of **1a** and **1b** in benzene (Scheme 2) led to very complex mixtures. After chromatography, only the vinyl ketones **2a** (12%), **2b** (10%) and the chromones **5a** (30%), **5b** (36%), could be identified, but small amounts of some acidic compounds, difficult to purify, were also isolated. We decided to assign tentatively the structures **4a** and **4b** to these acidic compounds on the basis of spectroscopic evidence.



SCHEME 2

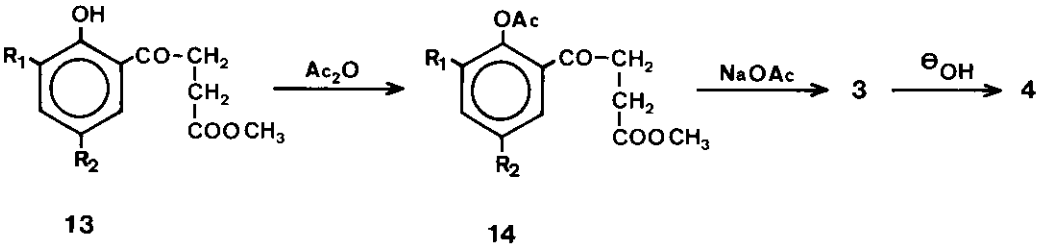
The formation of products of the type **2** and **3** by irradiation of lactones analogous to **1a** and **1b**, has been previously observed[1], and rationalized by assuming a primary photochemical cleavage of the O-CO bond, followed by decarbonylation or intramolecular radical addition (Scheme 3).



SCHEME 3

Through the intermediates **8**, not detected experimentally, one can explain all the chromone-derived products. Thus, the methyl esters **3** would be formed by solvent addition to intermediate **8** with concomitant ring opening followed by dehydration. The chromoneacetic acids **4** might be formed through three different processes: a) the Norrish type II photochemical reaction, with participation of a γ-carbonyl hydrogen[4], b) hydrolytic opening of the lactone ring by traces of moisture, followed by elimination or c) direct β-elimination, through the intermediate **11'**. Finally, the formation of tri- and tetramethylchromones **5** can be explained by direct decarboxylation of **8**[5,6] or, more probably, by decarboxylation of the chromoneacetic acids **4**, analogous to the well known photodecarboxylation of arylacetic acids[7].

In order to check this hypothesis on the origin of the chromones **5**, we decided to carry out the irradiation of their possible precursors **4**, which were independently prepared by means of the Kostanecki-Robinson[8] reaction. (Scheme 4).



a: $R_1 = H$; $R_2 = CH_3$ **b**: $R_1 = R_2 = CH_3$

c: $R_1 = H$; $R_2 = OCH_3$ **d**: $R_1 = H$; $R_2 = OAc$

e: $R_1 = H$; $R_2 = OH$

SCHEME 4

In this context, we prepared not only the chromoneacetic acids **4a** and **4b** but also the related compounds **4c** and **4d**, trying to justify previous results of our group on the photochemistry of enol lactones of the type **1**.

Using the Kostanecki-Robinson reaction, the keto esters **13** were refluxed in acetic anhydride in the presence of sodium acetate. The corresponding acetates **14** were formed after 1h, and the chromones **3** were obtained as final products after 48 h. Compounds **3a** and **3b** were identical to the products obtained by irradiation of the lactones **1a** and **1b** in methanol, while compounds **3c** and **3d** had not been previously described.

By saponification, **3** were easily converted into **4**. Compound **3d**, after saponification, led to the acid **4e** which was acetylated by treatment with acetic anhydride giving **4d**. Compounds **4a** and **4b** were identical to the products obtained by irradiation of the lactones **1a** and **1b** in benzene, thereby having been confirmed the tentative structure.

According to the results previously found for phenylacetic acid and some heterocyclic analogues, irradiation of the chromoneacetic acids **4a**,**4b**,**4c** and **4d** in benzene under nitrogen produced quantitatively the compounds **5a**,**5b**,**5c** and **5d**, whose spectroscopic and physical properties matched with those of the compounds obtained from the irradiation of the corresponding lactones 1.

In summary, in the course of the photolysis of enol lactones **1** the chromoneacetic acids **4** are formed. Since these compounds undergo a highly efficient photodecarboxylation, this process can be the source of the chromones 5, also isolated from the irradiations of enol lactones 1.

EXPERIMENTAL

Melting points are uncorrected. Combustion analyses were performed at the Instituto de Química Orgánica of CSIC (Madrid). Ir spectra were determined in CCl_4 solutions with a Perkin-Elmer 577 spectrophotometer; absorptions ($\bar{\nu}$, cm^{-1}) are given only for the main bands. ^{1}H-Nmr spectra were measured with a Hitachi Perkin-Elmer R-24-B instrument, using CCl_4 or $CDCl_3$ as solvent; chemical shifts are reported in ppm downfield (δ) from TMS.

Irradiation of the Lactones 1

A solution of 500 mg of the lactone **1** in 300 ml of methanol or benzene was irradiated at room temperature under nitrogen for 50 min, with a 125W medium pressure mercury lamp immersed inside a quartz immersion well photoreactor. The photoproducts were isolated, after removal of the solvent, by column chromatography on silica gel using hexane:ethyl ether (1/1,v/v) as eluent. Then, the different fractions were purified by thick layer chromatography, on silica gel (2 mm), using hexane:ethyl acetate (4/1,v/v) as eluent.

Alternative Synthesis of the Chromoneacetic Acids **4**

A mixture of the keto ester **13** (2g) and sodium acetate (2g) in 25 ml of acetic anhydride was refluxed during 1 h. After this time, 5 ml of the resulting solution was poured into water, precipitating the corresponding acetate **14**, which was filtered and then purified by recrystallization. The remaining was refluxed during 48 h, and then poured into water. The resulting suspension was filtered to give the corresponding chromone (**3**). One g of the latter was treated with 20 ml of 5% aqueous NaOH under magnetic stirring during 5 min. After this time, the mixture was neutralized with an aqueous solution of HCl (35%) and the resulting suspension was filtered affording **4** in quantitative yield. The final purification was done by recrystallization.

(*A mixture of* **4e** *(500 mg) with 10 ml of acetic anhydride and* 2 drops of sulfuric acid was refluxed 45 min and then poured into water to give **4d**, which was purified by recrystallization).

Irradiation of the Chromones **4**

A solution of 1g of the chromone **4** in 300 ml of benzene was irradiated at room temperature under nitrogen for 15 min, with a 125 W medium pressure mercury lamp immersed inside a quartz immersion well photoreactor. After this time the solvent was evaporated to give quantitatively the decarboxylated chromones **5**, whose purification was done by recrystallization.

Products

2-Acetoxy-5-methylphenyl Vinyl Ketone (**2a**), colourless oil, ir 1780, 1680, ^{1}H-nmr 7.05-6.50 (m, 3H, Ar$\underline{H}$), 6.90-5.50 (AMX, J_{trans}=15, J_{cis}=9, J_{gem}=3, 3H, C$\underline{H}$=C$\underline{H}_2$), 2.30 (s, 3H, C$\underline{H}_3$), 2.10 (s, 3H, OCOC$\underline{H}_3$).

2-Acetoxy-3,5-dimethylphenyl Vinyl Ketone (**2b**), colourless oil, ir 1765, 1670, ^{1}H-nmr 7.18 (m, 2H, Ar$\underline{H}$), 7.10-5.71 (AMX, J_{trans}=15, J_{cis}=9, J_{gem}=3, 3H, C$\underline{H}$=C$\underline{H}_2$), 2.37 and 2.30 (s and s, 6H, 2xC$\underline{H}_3$), 2.20 (s, 3H, OCOC$\underline{H}_3$).

3-Methoxycarbonylmethyl-2,6-dimethylchromone (**3a**), recrystallized from cyclohexane, colourless crystal mp 85-86°C, Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73; Found: C, 68.51; H, 5.73%, ir 1750, 1655, ^{1}H-nmr 7.65 (d, J<2, 5-Ar$\underline{H}$), 7.25-6.90 (m, 2H, Ar$\underline{H}$), 3.55 (s, 3H, COOC$\underline{H}_3$), 3.35 (s, 2H, C$\underline{H}_2$), 2.35 and 2.30 (s and s, 6H, 2xC$\underline{H}_3$).

3-Methoxycarbonylmethyl-2,6,8-trimethylchromone (**3b**), recrystallized from hexane, colourless crystal mp 112-117°C, Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20; Found: C, 69.44; H, 6.39%, ir 1750, 1655, ^{1}H-nmr 7.70 (d, J<2, 5-Ar$\underline{H}$), 7.15 (d, J<2, 7-Ar$\underline{H}$), 3.65 (s, 3H, COOC$\underline{H}_3$), 3.55 (s, 2H, C$\underline{H}_2$), 2.38 and 2.30 (s and s, 6H and 3H, 3xC$\underline{H}_3$).

6-Methoxy-3-methoxycarbonylmethyl-2-methylchromone (**3c**), recrystallized from cyclohexane, colourless crystal mp 92-95°C, Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5. 38; Found: C, 63.76; H, 5.00%, ir 1750, 1650, ^{1}H-nmr 7.40-7.00 (m, 3H, Ar$\underline{H}$), 3.70 (s, 3H, OC$\underline{H}_3$), 3.65 (s, 3H, COOC$\underline{H}_3$), 3.50 (s, 2H, C$\underline{H}_2$), 2.35 (s, 3H, C$\underline{H}_3$).

6-Acetoxy-3-methoxycarbonylmethyl-2-methylchromone (**3d**), recrystallized from hexane, colourless crystal mp 120-123°C, Anal. Calcd for $C_{15}H_{14}O_6$: C, 62.07; H, 4.86; Found: C, 61.70; H, 4.77%, ir 1780, 1750, 1655, ^{1}H-nmr 7.80 (m, 5-Ar$\underline{H}$), 7.40-7.20 (m, 2H, Ar$\underline{H}$), 3.70 (s, 3H, COOC$\underline{H}_3$), 3.55 (s, 2H, C$\underline{H}_2$), 2.40 (s, 3H, C$\underline{H}_3$), 2.30 (m, 3H, OCOC$\underline{H}_3$).

3-Hydroxycarbonylmethyl-2,6-dimethylchromone (**4a**), recrystallized from acetone, colourless crystal mp 189-194°C, Anal. Calcd for: $C_{13}H_{12}O_4$: C, 67.24; H, 5. 17; Found: C, 67.75; H, 4.76%, ir 1720, 1650, ^{1}H-nmr 8.05 (d, J<2, 1H, 5-Ar$\underline{H}$), 7.60-7.25 (m, 2H, 7,8-Ar$\underline{H}$), 3.65 (s, 2H, C$\underline{H}_2$), 2.50 and 2.45 (s and s, 6H, 2xC$\underline{H}_3$).

3-Hydroxycarbonylmethyl-2,6,8-trimethylchromone (**4b**), recrystallized from acetone:CCl_4 (1/1), colourless crystal mp 189-194°C, Anal. Calcd for. $C_{14}H_{14}O_4$: C, 68.28; H, 5. 73; Found: C, 67.80; H, 5.77%, ir 1730, 1645, ^{1}H-nmr 7.90 (d, J<2, 1H, 5-Ar$\underline{H}$), 7.35 (d, J<2, 7-Ar$\underline{H}$), 3.65 (s, 2H, C$\underline{H}_2$), 2.50, 2.45 and 2.40 (s,s and s, 9H, 3xC$\underline{H}_3$).

3-Hydroxycarbonylmethyl-6-methoxy-2-methylchromone (**4c**), ir 1745, 1645, ^{1}H-nmr 7.40-7.10 (m, 3H, Ar$\underline{H}$), 3.75 (s, 3H, OC$\underline{H}_3$), 3.45 (s, 2H, C$\underline{H}_2$), 2.30 (s, 3H, C$\underline{H}_3$).

6-Acetoxy-3-hydroxycarbonylmethyl-2-methylchromone (**4d**), recrystallized from acetone, colourless crystal mp 162-169°C, Anal. Calcd for: $C_{14}O_{12}O_6$: C, 60.87; H, 4.38; Found: C, 61.17; H, 4.74%, ir 1750, 1645, ^{1}H-nmr 7.50-7.00 (m, 3H, Ar$\underline{H}$), 3.50 (s, 2H, C$\underline{H}_2$), 2.35 (s, 3H, C$\underline{H}_3$), 2.00 (s, 3H, OCOC$\underline{H}_3$).

6-Hydroxy-3-hydroxycarbonylmethyl-2-methylchromone (**4e**), recrystallized from acetone, colourless crystal mp 235-243°C, Anal. Calcd for: $C_{12}H_{10}O_5$: C, 61.54; H, 4.30; Found: C, 61.36; H, 4.96%, ir 1730, 1645, ^{1}H-nmr 7.50-7.10 (m, 3H, ArH), 3.60 (s, 2H, CH_2), 2.40 (s, 3H, CH_3).

2,3,6-Trimethylchromone (**5a**), recrystallized from petroleum ether, colourless crystal mp 100-102°C (lit.[9,10] 105-106°C), ir 1640, ^{1}H-nmr 7.70 (d, J<2, 5-ArH), 7.15-6.90 (m, 2H, ArH), 2.40 and 2.30 (s and s, 6H, 2xCH_3), 1.90 (s, 3H, C_3-CH_3).

2,3,6,8-Tetramethylchromone (**5b**), recrystallized from hexane, colourless crystal mp 132-138°C, Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.81; H, 7.15%, ir 1650, ^{1}H-nmr 8.80 (d, J<2, 5-ArH), 7.25 (d, J<2, 7-ArH), 2.40 (s, 9H, 3xCH_3), 2.05 (s, 3H, C_3-CH_3).

6-Methoxy-2,3-dimethylchromone (**5c**), recrystallized from petroleum ether, mp 82°C (lit.[1] 82°C), ir 1640, ^{1}H-nmr 7.50-7.10 (m, 3H, ArH), 3.79 (s, 3H, OCH_3), 2.30 (s, 3H, C_2-CH_3), 2.00 (s, 3H, C_3-CH_3).

6-Acetoxy-2,3-dimethylchromone (**5d**), recrystallized from hexane, mp 136-137°C (lit.[10] 139°C), ir 1750, 1630, ^{1}H-nmr 8.00-7.40 (m, 3H, ArH), 2.45 (s, 3H, C_2-CH_3), 2.35 (s, 3H, $OCOCH_3$), 2.09 (s, 3H, C_3-CH_3).

Methyl 4-(2-Hydroxy-5-methylphenyl)-4-oxobutanoate (**13a**) recrystallized from water, colourless crystal mp 52-53°C, Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.71; H, 6.34%, ir 1755, 1660, ^{1}H-nmr 11. 44 (s, 1H, chelated OH), 7.24 (d, J<2, 6-ArH), 7.00 (dd, J=8, J<2, 4-ArH), 6.55 (d, J=8, 3-ArH), 3.51 (s, 3H, $COOCH_3$), 3.11 (t, J=6, 2H, $ArCOCH_2$), 2.53 (t, J=6, 2H, CH_2COOCH_3), 2.20 (s, 3H, CH_3).

Methyl 4-(2-Hydroxy-3,5-dimethylphenyl)-4-oxobutanoate (**13b**), recrystallized from water, colourless crystal mp 60-65°C, Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.10; H 6.78. Found: C, 66.08; H, 6.88%, ir 1750, 1650, ^{1}H-nmr 11.65 (s, 1H, chelated OH), 7.25 (d, J<2, 6-ArH), 7.00 (d, J<2, 4-ArH), 3.65 (s, 3H, $COOCH_3$), 3.25 (t, J=6, 2H, $ArCOCH_2$), 2.65 (t, J=6 2H, CH_2COOCH_3), 2.23 and 2.17 (s and s, 2x3H, 2xCH_3).

Methyl 4-(2-Hydroxy-5-methoxyphenyl)-4-oxobutanoate (**13c**),[11] colourless oil, Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.49; H, 5.92. Found: C, 60.28; H,6.07%, ir 1750, 1640, ^{1}H-nmr 11.70 (s, 1H, chelated OH), 7.30-7.00 (m, 3H, ArH), 3.83 (s, 3H, OCH_3), 3.70 (s, 3H, $COOCH_3$), 3. 38 (t, J=6, 2H, $ArCOCH_2$), 2.82 (t, J=6, 2H, CH_2COOCH_3).

Methyl 4-(2-Acetoxy-5-methylphenyl)-4-oxobutanoate (**14a**), recrystallized from petroleum ether, colourless crystal mp 62-65°C, Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.06, Found: C, 63.49; H, 5.88%, ir 1780, 1750, 1700, ^{1}H-nmr 7.45 (d, J<2, 6-ArH), 7.20 (dd, J=6, J<2, 4-ArH), 6.80 (d, J=6, 3-ArH), 3.60 (s, 3H, $COOCH_3$), 3.05 (t, J=7, 2H, $ArCOCH_2$), 2.55 (t, J=7, 2H, CH_2COOCH_3), 2.35 (s, 3H, Ar-CH_3), 2.25 (s, 3H, $OCOCH_3$).

Methyl 4-(2-Acetoxy-3,5-dimethylphenyl)-4-oxobutanoate (**14b**), recrystallized from petroleum ether, colourless crystal mp 71-72°C, Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.47, Found: C, 64.30; H, 6.16%, ir 1780, 1750, 1700, ^{1}H-nmr 7.20 (d, J<2, 6-ArH), 6.95 (d, J<2, 4-ArH), 3.05 (s, 3H, $COOCH_3$), 3.00 (t, J=6, 2H, $ArCOCH_2$), 2.50 (t, J=6, 2H, CH_2COOCH_3), 2.25, 2.20 and 2.05 (s,s and s, 9H, 3xCH_3).

Methyl 4-(2-Acetoxy-5-methoxyphenyl)-4-oxobutanoate (**14c**), colourless oil, ir 1770, 1740, 1700, ^{1}H-nmr 7.30-6.90 (m, 3H, ArH), 3.75 (s, 3H, OCH_3), 3.60 (s, 3H, $COOCH_3$), 3.10 (t, J=6, 2H, $ArCOCH_2$), 2.60 (t, J=6, 2H, CH_2COOCH_3), 2.25 (s, 3H, $OCOCH_3$).

Methyl 4-(2,5-Diacetoxyphenyl)-4-oxobutanoate (**14d**), recrystallized from hexane, colourless crystal mp 75-78°C, Anal. Calcd for $C_{15}H_{16}O_7$: C, 58.44; H, 5.23, Found: C, 58.34; H, 5.17%, ir 1780, 1750, 1710, ^{1}H-nmr 7.45-6.80 (m, 3H, ArH), 3.65 (s, 3H, $COOCH_3$), 3.05 (t, J=6, 2H, $ArCOCH_2$), 2.60 (t, J=6, 2H, CH_2COOCH_3), 2.28 and 2.23 (s and s, 6H, 2x$OCOCH_3$).

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