Synthesis utilising the β-Carbonyl System. Part 5.[1] A Synthesis directed towards the Fungal Xanthone Bikaverin

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2-[3-(1-Oxo-3-aminobut-2-enyl)-7-methoxy-5-methyl-4-oxo-4*H*-benzopyran-2-ylmethyl]dioxolans, (7a and b), with an ethoxycarbonylmethyl or methyl substituent on the 2-position, have been synthesised starting with three precursors corresponding to β-tetra-, β-tri-, and β-di-carbonyl compounds. Acid treatment of the 2-ethoxycarbonylmethyl compound (7a) afforded ethyl 3-(1-hydroxy-6-methoxy-3,8-dimethyl-9-oxoxanthen-2-yl)-3-oxopropanoate (13a) as the major product together with three minor products, including ethyl 2-acetyl-1-hydroxy-6-methoxy-8-methyl-9-oxoxanthen-3-ylacetate (11); whereas the 2-methyl compound (7b) yielded 2-acetyl-1-hydroxy-6-methoxy-3,8-dimethylxanthen-9-one (13b), exclusively. The structures of (13a) and (17) were confirmed by ^{13}C n.m.r. spectroscopy using the long-range selective proton-decoupling (LSPD) method. Formation of (13a) from (7a) is explained in terms of a Wessely–Moser rearrangement of the intermediary benzopyranone (9a) or the xanthone (10a) under mild acidic conditions. Base-catalysed cyclisation of the xanthone-3-acetate (11) gave 8,10,11-trihydroxy-3-methoxy-1-methyl-12*H*-benzo[*b*]xanthen-12-one (20) in excellent yield.

THE modes of cyclisation of β-polyketonic precursors to give certain phenols or oxygen heterocycles related to natural products have been investigated extensively by several schools.[2] We report here an attempt to synthesise bikaverin,[3] a fungal metabolite having a benzo[*b*]-xanthen skeleton, which seems to be derived in a straightforward way from a β-nonacarbonyl precursor.[4]

RESULTS AND DISCUSSION

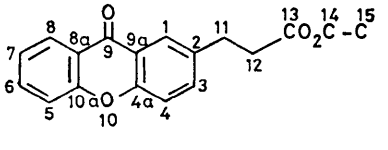
Since no detailed biogenetic information on the sequence of forming the benzo[*b*]xanthen ring had been obtained,[5] we intended, at first, to construct the A, B, C, and D rings in that order. To this end we began with three synthons, *o*-orsellinic acid [6] (1), acetonedicarboxylic acid (2), and 3,5-dimethylisoxazole (3), the corresponding equivalents of β-tetra-, β-tri-, and β-di-carbonyl systems, respectively.

Condensation of 1 equiv. of the sodioethyl salicylate (1a) with 2 equiv. of the anion (3a) [7] in tetrahydrofuran gave the isoxazolylmethyl ketone (4) in 63% yield. Compound (4) was converted into the sodium salt and allowed to react with (2a) [8] at room temperature giving, after chromatographic separation, the dihydrobenzopyranone (5a) [9] and the benzopyranone (6a) in 42 and 28% yields, respectively. The former was readily dehydrated to the latter on treatment with cold dilute hydrochloric acid without cleavage of the acetal group. Hydrogenolysis of (6a) in ethanol over platinum oxide afforded the benzopyranone ester (7a) in 95% yield. Its structure was identified by the presence of a vinyl proton signal at δ 5.43 in the n.m.r. spectrum. Subsequent hydrolysis of (7a) was effected by use of aqueous oxalic acid at room temperature, giving the diketobenzopyranone ester (8a) in 55.8% yield.

On the other hand, hydrolysis of (7a) at reflux temperature afforded, after purification by column chromatography, four products (A, B, C, and D). Of these, A, B, and C (yields 67, 5, and 1.2%, respectively), proved to be isomeric xanthone esters from a consideration of their elemental analyses and spectral data. Product D, obtained in 7% yield, was an acetylxanthone with a hydroxy-substituent at the 1-position [δ_H 14.01 (1 H, s)],

^{13}C N.m.r. data for (13a) and (17) (solvent $CDCl_3$; p.p.m. from $SiMe_4$)

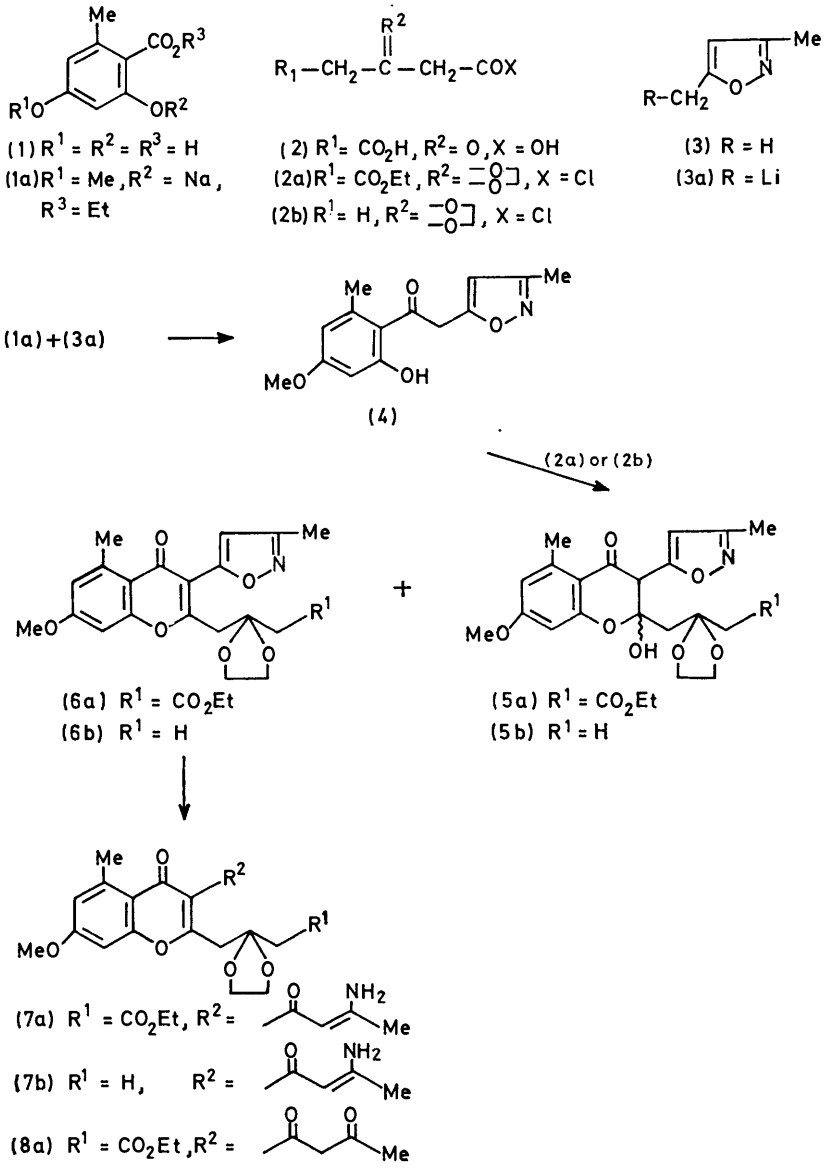
	δ[$^nJ_{CH}$/Hz] (17)	(13a)
C-1 [a]	157.2 d, [^3J 3.7]	161.7 d, [^2J 4.9]
C-2	132.6 d, [^3J 7.4]	121.1 [b]
C-3	141.4 q, [^2J 6.1]	141.8 q, [^2J 6.1]
C-4	114.7 dq, [^1J 163.8, ^3J 5.5]	108.8 dq, [^1J 163.8, ^3J 5.5]
C-4a	156.7 d, [^2J 3.1]	156.0 d, [^2J 3.1]
C-5	98.1 dd, [^1J 163.6, ^3J 4.9]	98.5 dd, [^1J 164.2, ^3J 4.3]
C-6	163.1 q, [^3J 4.3]	164 2 q, [^3J 4.3]
C-7	115.5 ddq, [^1J 161.0, ^3J 5 5, ^3J 4.9]	116.0 ddq, [^1J 161.0, ^3J 5.5, ^3J 4.9]
C-8	143.6 q, [^2J 6.1]	143.5 q, [^2J 6.1]
C-8a	115.2 [b]	112.5 [b]
C-9	176.5 s	182.7 s
C-9a	114.7 d, [^3J 3.7]	106.4 dd, [^3J 5.5, ^3J 4.3]
C-10a	158.2 d, [^2J 3.1]	159.1 d, [^2J 3.1]
C-11	204.4 q, [^2J 6.1]	195.9 t, [^2J 6.1]
C-12	32.5 q, [^1J 128.0]	50.5 t, [^1J 131.6]
C-13		168 0 [b]
C-14		61.0 tq, [^1J 148.5, ^2J 4.3]
C-15		14.1 qt, [^1J 127.0, ^2J 1.4—2.4]
1-OMe	63.4 q, [^1J 145.6]	
3-Me	19.6 qd, [^1J 128.0, ^3J 5.2]	21.8 qd, [^1J 129.4, ^3J 5.5]
6-OMe	55.6 q, [^1J 144.9]	55.7 q, [^1J 145.6]
8-Me	23.6 qd, [^1J 128.7, ^3J 6.6]	23.4 qd, [^1J 129.4, ^3J 6.1]

[a] 

[b] The multiplicity of these signals was not clear.

which was also formed, in quantitative yield, directly from A on treatment with hydrochloric acid.

For the cyclisation of the intermediate triketo-benzopyranone ester (9a), three different modes were possible, *i.e.* C_{α}–$C_{\gamma'}$, C_{β}–$C_{\beta'}$, and C_{γ}–$C_{\alpha'}$, giving (10a), (11), and (12), respectively. Although structure (10a) was thought to be most likely for the major product A in view of its



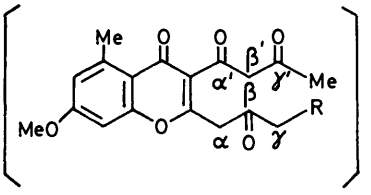
easy decarboxylation, typical of β-ketoesters, the ^{13}C n.m.r. study rather indicated that product A was the xanthone-2-ketoester (13a). The numbering system and the ^{13}C n.m.r. data of compound (13a) are given in the Table.

All the carbon signals except those of the xanthone framework were readily distinguished by multiplicities in the gated-1 spectrum,[10] by comparison of the chemical-shift values with those of known xanthones,[5,11] and by $^{13}C\{^1H\}$ selective decoupling.[12] For the signals due to the tertiary and quaternary carbons, the long-range selective proton-decoupling (LSPD) [12] technique was effectively used. Thus, a doublet signal at 161.7 p.p.m. (^2J 4.9 Hz) was assigned to C-1 because it collapsed to a singlet upon irradiation at the frequency of the 1-OH proton, or on addition of D_2O. The rather simple splitting pattern of this signal suggested the quaternary character of C-2. This decoupling also changed a doublet of doublets signal at 106.4 p.p.m. to a doublet (^3J 5.5 Hz), attributed to C-9a. A signal assigned to C-2 appeared at 121.1 p.p.m. as a multiplet, which simplified upon irradiation at the frequency of either H-4 or H-3-Me. The C-4 signal, a doublet of quartets at 108.8 p.p.m., changed to a doublet (^1J 163.8 Hz) upon decoupling of H-3-Me, and the quartet of doublets due to 3-Me changed to a quartet upon decoupling H-4.

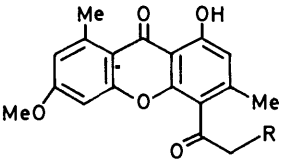
Compound (13a) also reacted with diazomethane

giving a complex mixture, from which the 1-hydroxyxanthone-β-methoxyacrylate (14) was isolated in 77% yield, accompanied by the 1-methoxyxanthone-2-ketoester (15); methyl iodide in acetone in the presence of potassium carbonate afforded predominantly the 1-hydroxyxanthone-α-methyl-β-ketoester (16).

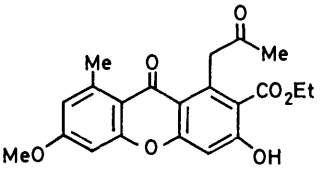
The formation of the abnormal product (13a) is explained in terms of Wessely–Moser type rearrangement [13] of the benzopyranone (8a) or the xanthone (10a) [produced initially from (8a)], during hydrolysis and simultaneous cyclisation with aqueous acid in mild conditions.



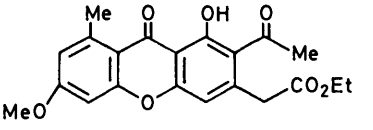
(9a) R = CO_2Et
(9b) R = H



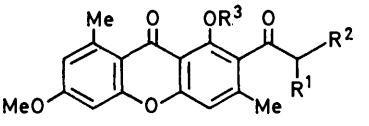
(10a) R = CO_2Et
(10b) R = H



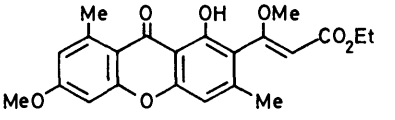
(12)



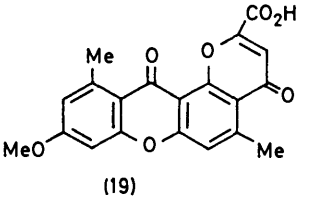
(11)



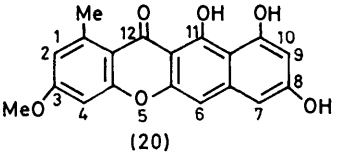
(13a) R^1 = H, R^2 = CO_2Et, R^3 = H
(13b) R^1 = R^2 = R^3 = H
(15) R^1 = H, R^2 = CO_2Et, R^3 = Me
(16) R^1 = Me, R^2 = CO_2Et, R^3 = H
(17) R^1 = R^2 = H, R^3 = Me
(18) R^1 = H, R^2 = CO—CO_2Et, R^3 = H



(14)



(19)



(20)

The product D was, therefore, suggested to be the 2-acetyl-1-xanthone (13b) instead of the 4-acetyl-1-xanthone (10b). To prove this, D was converted into the 1-methoxy-2-acetylxanthone (17) * by methylation with methyl iodide and potassium carbonate in dimethylformamide, and the ^{13}C n.m.r. spectrum of (17) was recorded. The assignment of all the carbon signals, obtained by correlation with that of (13a), is given in the Table. The signals due to C-4, C-5, and C-7 were readily recognised by selective proton decoupling, based on the ^1H n.m.r. spectrum in which the H-4 signal appeared separately from the overlapping singlets due to H-5 and H-7. A signal at 156.7 p.p.m. changed from a doublet (^1J 3.1 Hz) to a sharp singlet upon decoupling of H-4, and was assigned to C-4a. The resonance at 114.7 p.p.m., a doublet of quartets (^1J 163.8, ^3J 5.5 Hz), changed to a doublet upon decoupling of 3-CH_3, and was, therefore, assigned to C-4.

In agreement with the assigned structure of (13b), the oxalylxanthone (18), derived from (13b) by condensation with diethyl oxalate and sodium ethoxide in ethanol, cyclised to the pyrano[2,3-*a*]xanthone-carboxylic acid (19) when refluxed with a mixture of hydrochloric and acetic acids.[14]

The minor product B was assigned as the 1-hydroxy-2-acetylxanthone-3-acetate (11) on the basis of its u.v.

* This compound almost quantitatively regenerated (13b) upon treatment with boron tribromide in dichloromethane.

spectrum, which was closely similar to those of the 1-hydroxy-2-acetylxanthone (13b) in acidic and alkaline solution.

Although the least abundant product C could not be assigned unambiguously on account of lack of material, it was believed to be the 1-acetonylxanthone (12) on the basis of its ^{1}H n.m.r. spectrum which showed a characteristic signal at δ_H 7.46, due to a hydroxy-group at a position other than that *peri* to the xanthone 9-carbonyl group.

We also synthesised the enamino-ketobenzopyranone (7b) by a similar method to that used for (7a), starting with (4) and 2-methyl-1,3-dioxolan-2-ylacetyl chloride (2b),[15] *via* the dihydro-benzopyranone (5b) and the benzopyranone (6b). Cyclisation of (7b) with 85% phosphoric acid at ambient temperature gave (13b) as the sole product (69% yield).

Attempted cyclisation of (11) with sodium ethoxide in ethanol [16] afforded the expected benzo[*a*]xanthone (20) in 81% yield as red crystals. Its molecular ion at *m/e* 338, and the ^{1}H n.m.r. spectrum which lacked the signals due to either a methyl ketone or an ester function, supported the structure shown. An investigation of the tautomerism of (20) is now in progress.

EXPERIMENTAL

Unless otherwise stated, i.r. spectra were recorded with a JASCO IR-E spectrometer for Nujol mulls, and ^{1}H n.m.r. spectra with a JEOL JNM-ME-60 spectrometer for solutions in $CDCl_3$ with $SiMe_4$ as internal standard. ^{13}C N.m.r. spectra were recorded with a JEOL FX-100 FT spectrometer at 25.05 MHz. LSPD measurements were made with the low-power irradiation unit. Conditions for Fourier-transform measurement were as follows; spectral width, 6 kHz; data points, 16 000; precision of *J* values, ±0.4 Hz; power level for LSPD ($\gamma H_2/2\pi$), 14 Hz. All extracts were dried over anhydrous sodium sulphate, and solvents were removed with a rotary evaporator.

2-Hydroxy-4-methoxy-6-methylphenyl 3-Methylisoxazol-5-ylmethyl Ketone (4).—A solution of n-butyl-lithium (82.5 ml, 8.5% n-hexane solution) was added at −60 to −50 °C to a solution of 3,5-dimethylisoxazole (10.1 g) in anhydrous tetrahydrofuran (100 ml). After stirring for 20 min, a solution of the sodium salt (1a) prepared from ethyl 4-methoxy-6-methylsalicylate (10.5 g) and sodium hydride (1.80 g, 66% dispersion in oil) in anhydrous tetrahydrofuran (50 ml) was added dropwise, and the mixture was kept at the same temperature for 3.5 h. Acetic acid (7.2 ml) was added to the reaction mixture and the solvent was removed. The residue was dissolved in water (100 ml) and the aqueous solution was, after shaking with ether, acidified with 10% hydrochloric acid. Separated oil was taken up in ethyl acetate and the solution was washed with aqueous sodium bicarbonate and dried. After evaporation of the solvent, the residue was purified by column chromatography [silica gel; ethyl acetate–n-hexane (1 : 1)] to give (4) (8.2 g, 63% yield) as colourless needles, m.p. 94.5—95.5 °C (isopropyl ether) (Found: C, 64.4; H, 5.9; N, 5.5. $C_{14}H_{15}NO_4$ requires C, 64.3; H, 5.7; N, 5.3%); $\nu_{max.}$ 3 140, 3 090, and 1 610 cm^{-1}; δ_H 2.26 (3 H, s), 2.43 (3 H, s), 3.71 (3 H, s), 4.29 (2 H, s), 6.02 (1 H, s), and 6.16 (2 H, s); *m/e* 261 (M^+).

Condensation of (4) *with* (2a).—To a solution of the sodium salt of (4) [from (4) (4.7 g) and sodium hydride (1.1 g, 66% dispersion in oil)] in monoglyme (100 ml) was added a solution of (2a) (5.7 g) in monoglyme (50 ml) at 0—3 °C and stirring was continued at the same temperature for 4 h. Acetic acid (0.35 ml) was added to the reaction mixture and the solvent was distilled off. Usual work-up of the residue with ethyl acetate gave a crude product, which was purified by column chromatography on silica gel [ether–n-hexane (3 : 1)]. The first fraction gave *ethyl* 2-[2-*hydroxy*-7-*methoxy*-5-*methyl*-3-(3-*methylisoxazol*-5-*yl*)-4-*oxo*-3,4-*dihydro*-2H-*benzopyran*-2-*ylmethyl*]-1,3-*dioxolan*-2-*ylacetate* (5a) (3.5 g, 42%) as colourless prisms, m.p. 121—122 °C (ethyl acetate) (Found: C, 60.0; H, 5.6; N, 5.4. $C_{23}H_{27}NO_9$ requires C, 59.8; H, 5.7; N, 5.3%), $\nu_{max.}$ 3 430, 1 740, 1 692, and 1 658 cm^{-1}; δ_H 1.28 (3 H, t, *J* 7 Hz), 2.35 (3 H, s), 2.60 (3 H, s), 3.86 (3 H, s), 4.05 (4 H, s), and 4.18 (2 H, q, *J* 7 Hz). The second fraction gave *ethyl* 2-[7-*methoxy*-5-*methyl*-3-(3-*methylisoxazol*-5-*yl*)-4-*oxo*-4H-*benzopyran*-2-*ylmethyl*]-1,3-*dioxolan*-2-*ylacetate* (6a) (2.2 g, 28%) as colourless needles, m.p 132—133 °C (ethyl acetate) (Found: C, 62.4; H, 6.0; N, 3.4. $C_{23}H_{25}NO_8$ requires C, 62.3; H, 5.7; N, 3.2); $\nu_{max.}$ 1 730, 1 667, 1 640, and 1 623 cm^{-1}; δ_H 1.25 (3 H, t, *J* 7 Hz), 2.35 (3 H, s), 2.80 (5 H, s), 3.52 (2 H, s), 3.88 (7 H, s), 4.17 (2 H, q, *J* 7 Hz), and 6.72 (3 H, s).

Dehydration of (5a).—To a solution of (5a) (3.0 g) in ethanol (100 ml) was added 7% ethanolic hydrochloric acid (50 ml) and the solution was kept at 18—21 °C for 16 h. After addition of solid sodium hydrogencarbonate (10 g), the solvent was evaporated and the residue was taken up in ether. Evaporation of the ether left the solid, which was recrystallised from ethyl acetate to give (6a) (2.1 g, 73%) as colourless needles, m.p. 132—133 °C.

Ethyl 2-[3-(3-*Amino*-1-*oxobut*-2-*enyl*)-7-*methoxy*-5-*methyl*-4-*oxo*-4H-*benzopyran*-2-*ylmethyl*]-1,3-*dioxolan*-2-*ylacetate* (7a).—A solution of (6a) (2.0 g) in ethanol (250 ml) was shaken with platinum oxide (0.30 g) in a hydrogen atmosphere at 1 atm (hydrogen uptake 1.1 mol equiv.). After removal of the catalyst, the solvent was evaporated to give crude (7a). Recrystallisation gave colourless prisms (1.90 g, 95%), m.p. 151—152 °C (benzene–ethyl acetate) (Found: C, 61.8; H, 6.2; N, 3.2. $C_{23}H_{27}NO_8$ requires C, 62.0; H, 6.1; N, 3.1%); $\nu_{max.}$ 3 310, 3 160, 1 740, and 1 640 cm^{-1}; δ_H 1.45 (3 H, t, *J* 7 Hz), 2.18 (3 H, s), 2.94 (3 H, s), 3.03 (2 H, s), 3.43 (2 H, s), 4.04 (4 H, s), 4.13 (3 H, s), 4.35 (2 H, q, *J* 7 Hz), 5.43 (1 H, s), and 6.84 (2 H, s).

Cyclisation of (7a).—A solution of (7a) (5.7 g) and 10% aqueous oxalic acid (80 ml) in ethanol (80 ml) was refluxed for 3.5 h. The solvent was evaporated and the residue was taken up in ethyl acetate. Evaporation of the solvent left a red oil, which was purified by column chromatography on silica gel. Elution with ethyl acetate–n-hexane (1 : 1) gave *ethyl* 3-(1-*hydroxy*-6-*methoxy*-3,8-*dimethyl*-9-*oxoxanthen*-2-*yl*)-3-*oxopropionate* (13a) (3.3 g, 67.1%), m.p. 123—124 °C (ethanol) (Found: C, 65.4; H, 5.3. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.2%); $\nu_{max.}$ 1 742, 1 722, 1 685, 1 675, and 1 620 cm^{-1}; δ_H 1.20 (3 H, t, *J* 7 Hz), 2.41 (3 H, s), 2.74 (3 H, s), 3.85 (3 H, s), 4.00 (2 H, s), 4.11 (2 H, q, *J* 7 Hz), 6.58 (3 H, s), and 14.05 (1 H, s). From the second fraction, 2-*acetyl*-1-*hydroxy*-6-*methoxy*-3,8-*dimethylxanthen*-9-*one* (13b) (0.28 g, 7.4%) was isolated as pale yellow needles, m.p. 181—182 °C (ethyl acetate) (Found: C, 68.9; H, 5.2. $C_{18}H_{16}O_5$ requires C, 69.2; H, 5.1%); $\nu_{max.}$ 1 673, 1 640, and 1 610 cm^{-1}; δ_H 2.38 (3 H, s), 2.62 (3 H, s), 2.82 (3 H, s), 3.90 (3 H, s), 6.67 (3 H, s), and 13.83 (1 H, s); *m/e* 312 (M^+). The third fraction afforded *ethyl* 2-*acetyl*-1-*hydroxy*-6-*methoxy*-8-*methyl*-9-*oxoxanthen*-3-*ylacetate* (11) (0.23 g, 4.7%) as yellow needles, m.p. 155—158 °C (ethanol) (Found: C, 65.8; H, 5.0.

$C_{21}H_{20}O_7$ requires C, 65.6; H, 5.2%); $\nu_{max.}$ 1 730, 1 723, 1 685, 1 675, and 1 660—1 610 (br) cm^{-1}; δ_H 1.25 (3 H, t, *J* 7.5 Hz), 2.64 (3 H, s), 2.74 (3 H, s), 3.80 (2 H, s), 3.85 (3 H, s), 4.20 (2 H, q, *J* 7.5 Hz), 6.62 (3 H, s), and 14.04 (1 H, s). The final fraction gave *ethyl* 1-*acetonyl*-3-*hydroxy*-6-*methoxy*-8-*methyl*-9-*oxoxanthen*-2-*carboxylate* (12) (0.06 g, 1.2%) as pale yellow needles, m.p. 184—185 °C (ethanol) (Found: C, 65.1; H, 5.3. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.2%); $\nu_{max.}$ 1 731, 1 718, 1 670, 1 662, 1 633, and 1 620 cm^{-1}; δ_H [$CDCl_3$–$(CD_3)_2SO$] 1.27 (3 H, t, *J* 7.5 Hz), 2.38 (3 H, s), 2.66 (3 H, s), 3.70 (2 H, s), 3.89 (3 H, s), and 4.22 (2 H, q, *J* 7.5 Hz).

Ethyl 2-[3-(1,3-*dioxobutyl*)-7-*methoxy*-5-*methyl*-4-*oxo*-4H-*benzopyran*-2-*ylmethyl*]-1,3-*dioxolan*-2-*ylacetate* (8a).—To a solution of 10% aqueous oxalic acid (10 ml) and ethanol (10 ml) was added (7a) (1.1 g) and the mixture was stirred at 16—21 °C for 3 h. The solvent was evaporated below 40 °C and the residue was taken up in chloroform. Removal of the solvent gave a white residue, which was purified by t.l.c. on silica gel [ether–n-hexane (5 : 1)] to give (8a) (0.56 g, 49.1%) as colourless needles, m.p. 129 °C (ethanol) (Found: C, 61.6; H, 5.7. $C_{23}H_{26}O_9$ requires C, 61.8; H, 5.8%); $\nu_{max.}$ 1 718, 1 655—1 610(br), and 1 580 cm^{-1}; δ_H 1.28 (3 H, t, *J* 7.5 Hz), 2.36 (3 H, s), 2.82 (3 H, s), 2.83 (2 H, s), 3.54 (2 H, s), 3.91 (3 H, s), 3.95 (4 H, s), 4.19 (2 H, q, *J* 7.5 Hz), and 6.76 (2 H, s); *m/e* 446 (M^+).

Condensation of (4) *with* (2b).—By using the same procedure as described in the condensation ot (4) with (2a), (4) was allowed to react with (2b) to give, after chromatographic separation, 2-[2-*hydroxy*-7-*methoxy*-5-*methyl*-3-(3-*methylisoxazol*-5-*yl*)-4-*oxo*-2,3-*dihydro*-4H-*benzopyran*-2-*ylmethyl*]-2-*methyl*-1,3-*dioxolan* (5b) (27.9%) as colourless prisms, m.p. 121—122 °C (ethanol) (Found: C, 61.8; H, 6.2; N, 3.6. $C_{20}H_{23}NO_3$ requires C, 61.6; H, 5.9; N, 3.6%); $\nu_{max.}$ 3 380, 1 673, and 1 608 cm^{-1}; δ_H 1.60 (3 H, s), 2.30 (3 H, s), 2.55 (3 H, s), 3.80 (3 H, s), 3.95 (4 H, s), 6.15 (1 H, s), 6.16 (1 H, s, exchangeable), 6.25 (1 H, d, *J* 1.5 Hz), and 6.35 (1 H, d, *J* 1.5 Hz); *m/e* 389 (M^+). The second fraction gave 2-*methyl*-2-[7-*methoxy*-5-*methyl*-3-(3-*methylisoxazol*-5-*yl*)-4-*oxo*-4H-*benzopyran*-2-*ylmethyl*]-1,3-*dioxolan* (6b) (63.7%) (Found: C, 64.6; H, 5.7; N, 4.0. $C_{20}H_{21}NO_6$ requires C, 64.6; H, 5.7; N, 3.7%) as colourless needles (ethanol), m.p. 143—144 °C (decomp.); $\nu_{max.}$ 1 650, 1 618, 1 592, and 1 570 cm^{-1}; δ_H 1.45 (3 H, s), 2.35 (3 H, s), 2.82 (3 H, s), 3.33 (2 H, s), 3.90 (3 H, s), 3.92 (4 H, s), and 6.75 (3 H, s); *m/e* 371 (M^+).

Dehydration of (5b).—In the same way as for the dehydration of (5a), (5b) was converted into (6b) in 84% yield.

2-[3-(3-*Amino*-1-*oxobut*-2-*enyl*)-7-*methoxy*-5-*methyl*-4-*oxo*-4H-*benzopyran*-2-*ylmethyl*]-2-*methyl*-1,3-*dioxolan* (7b).—In the same way as for the catalytic hydrogenation of (6a), (6b) was hydrogenated to give (7b) (89.6%) (Found: C, 64.5; H, 6.3; N, 3.8. $C_{20}H_{23}NO_6$ requires C, 64.3; H, 6.2; N, 3.7%) as colourless prisms, m.p. 203—205 °C; $\nu_{max.}$ 3 380, 1 640, and 1 610 cm^{-1}; δ_H 1.52 (3 H, s), 2.03 (3 H, s), 2.82 (3 H, s), 3.15 (2 H, s), 3.90 (3 H, s), 3.96 (4 H, s), 5.36 (1 H, s), and 6.73 (2 H, s); *m/e* 373 (M^+).

2-*Acetyl*-1-*hydroxy*-6-*methoxy*-3,8-*dimethylxanthen*-9-*one* (13b).—A solution of the enamino-ketone (7b) (3.89 g) in 75% phosphoric acid (80 ml) was stirred at 60—70 °C for 9 h. The reaction mixture was then poured into ice–water and the separated crystals were filtered off, dried, and recrystallised from ethanol to give (13b) (2.25 g, 69.3%) as colourless needles, m.p. 181—182 °C.

Ethyl 3-(1-*Hydroxy*-6-*methoxy*-3,8-*dimethyl*-9-*oxoxanthen*-2-*yl*)-*methyl*-3-*oxopropanoate* (16).—A mixture of (13a) (0.20 g), methyl iodide (0.11 g), and anhydrous potassium carbonate (0.1 g) in acetone (30 ml) was stirred at 20—25 °C for 20 h, then at 50 °C for 3 h. The solvent was removed and the residue was extracted with chloroform after addition of water (30 ml). The extract was dried, evaporated, and the residue purified by preparative t.l.c. on silica gel [n-hexane–ethyl acetate (10 : 1)]. Elution of the yellow band (R_F 0.68) gave (16) (0.123 g, 59.3%) (Found: C, 66.4; H, 5.7. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.5%) as yellow needles, m.p. 129—131 °C (ethyl acetate); $\nu_{max.}$ 3 400, 1 743, and 1 682 cm^{-1}; δ_H 1.16 (3 H, t, *J* 7.5 Hz), 1.46 (3 H, d, *J* 7.0 Hz), 2.36 (3 H, s), 2.77 (3 H, s), 3.83 (3 H, s), 4.05 (2 H, q, *J* 7.5 Hz), 4.46 (1 H, q, *J* 7.0 Hz), 6.57 (3 H, m), and 14.02 (1 H, s); *m/e* 398 (M^+).

Methylation of (13a) *with Diazomethane.*—To a solution of (13a) (0.725 g) in tetrahydrofuran (80 ml) and ethanol (10 ml) was added, while stirring at 0—5 °C, a solution of ethereal diazomethane [from nitrosomethylurea (0.5 g) and 40% potassium hydroxide (2.5 ml)] and the reaction mixture was kept at this temperature for 3 d. The solvent was evaporated and the residue was purified by preparative t.l.c. using silica gel [benzene–ethyl acetate (12 : 1)]. Many bands developed. The band at R_F 0.6 gave the starting material (0.18 g). From the band at R_P 0.30 *ethyl* 3-(1-*hydroxy*-6-*methoxy*-3,8-*dimethyl*-9-*oxoxanthen*-2-*yl*)-3-*methoxyacrylate* (14) (0.577 g, 77.0%) (Found: C, 66.2; H, 5.7. $C_{22}H_{22}O_7$ requires C, 66.30; H, 5.5%) was obtained as pale yellow needles, m.p. 183—184 °C (ethyl acetate); $\nu_{max.}$ 1 715, 1 648, 1 637, and 1 610 cm^{-1}; δ_H 1.27 (3 H, t, *J* 7 Hz), 2.35 (3 H, s), 2.76 (3 H, s), 3.55 (3 H, s), 3.85 (3 H, s), 4.14 (2 H, q, *J* 7 Hz), 4.95 (1 H, s), 6.53—6.70 (3 H), and 13.44 (1 H, s); *m/e* 398 (M^+). The band of lowest R_F gave *ethyl* 3-(1,6-*dimethoxy*-3,8-*dimethyl*-9-*oxoxanthen*-2-*yl*)-3-*oxopropanoate* (15) (0.09 g, 12.0%) as colourless needles, m.p. 158—160 °C (ethanol) (Found: C, 66.2; H, 5.7. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.6%); δ_H 1.26 (3 H, t, *J* 7 Hz), 2.61 (3 H, s), 2.82 (3 H, s), 3.74 (2 H, s), 3.92 (3 H, s), 3.87 (3 H, s), 4.15 (2 H, q, *J* 7 Hz), 6.65 (2 H, s), and 7.05 (1 H, s); *m/e* 398 (M^+).

Ethyl 4-(1-*Hydroxy*-6-*methoxy*-3,8-*dimethyl*-9-*oxoxanthen*-2-*yl*)-*dioxobutanoate* (18).—A mixture of (13b) (1.25 g), diethyl oxalate (20 ml), and sodium ethoxide (2.72 g) in ethanol (100 ml) was refluxed for 8 h and the solvent was then evaporated. The residue was treated with water, acidified with 10% hydrochloric acid, and extracted with chloroform. The extracts were washed with water, dried, and evaporated to give a solid, which was recrystallised from chloroform to yield (18) (1.15 g, 69.6%) as pale yellow needles, m.p. 183—184 °C (decomp.) (Found: C, 64.28; H, 4.68. $C_{22}H_{20}O_8$ requires C, 64.07; H, 4.89%); $\nu_{max.}$ 1 735 cm^{-1}; δ_H 1.40 (3 H, t, *J* 7.0 Hz), 2.48 (3 H, s), 2.80 (3 H, s), 3.95 (3 H, s), and 4.42 (2 H, q, *J* 7.0 Hz); *m/e* 412 (M^+).

9-*Methoxy*-5,11-*dimethyl*-4,12-*dioxo*-4,12-*dihydropyrano*-[2,3-a]*xanthen*-2-*carboxylic Acid* (19).—A mixture of (18) (0.435 g), 36% hydrochloric acid (2 ml), and acetic acid (7 ml) was refluxed for 1.5 h. After cooling, the crystals which separated were filtered off, washed with water, and dried. Recrystallisation of the crude product from dimethyl sulphoxide gave (19) (0.30 g, 74.1%) as colourless fine needles, m.p. 287 °C (decomp.) (Found: C, 62.5; H, 4.2. $C_{20}H_{14}O_7 \cdot H_2O$ requires C, 62.4; H, 4.3%); $\nu_{max.}$ 1 715, 1 680, and 1 620 cm^{-1}; *m/e* 384 (M^+).

2-*Acetyl*-1,6-*dimethoxy*-3,8-*dimethylxanthen*-9-*one* (17).—A mixture of (13b) (0.936 g), anhydrous potassium carbonate (0.69 g), and methyl iodide (0.64 g) in dimethylformamide (200 ml) was stirred at room temperature for 36 h. The reaction mixture was poured into ice–water and the separated oil was extracted with chloroform. After the usual work-up, the solvent was evaporated to give crude (17) (0.895 g, 91.5%), which was recrystallised from ethanol as colourless needles, m.p. 154—155 °C (Found: C, 69.8; H, 5.8. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.6%); $\nu_{max.}$ 1 680, 1 650, 1 620, and 1 600 cm^{-1}; δ_H 2.33 (3 H, s), 2.57 (3 H, s), 2.86 (3 H, s), 3.90 (3 H, s), 3.93 (3 H, s), 6.70 (2 H, s), and 7.03 (1 H, s).

Demethylation of (17) *with Boron Trichloride*.—A solution of (17) (0.326 g) and boron trichloride (0.351 g) in dichloromethane (20 ml) was allowed to stand at 10—15 °C for 22 h. After evaporation of the solvent, the residue was extracted with chloroform. The extract was washed with aqueous sodium hydrogencarbonate, dried, and the solvent was removed. The residue was recrystallised from ethyl acetate to give (13b) (0.19 g, 60.5%), m.p. 181—182 °C, which was identical with an authentic specimen by mixed melting point, and spectral comparisons.

8,10,11-*Trihydroxy*-3-*methoxy*-1-*methylbenzo*[b]*xanthen*-12-*one* (20).—A solution of (11) (0.08 g) in anhydrous ethanol (90 ml) was added, under nitrogen atmosphere, to a sodium ethoxide solution [from ethanol (10 ml) and sodium (0.014 g)] and the mixture was refluxed for 2.5 h. After cooling, the reaction mixture was acidified with acetic acid and the solvent was removed. After trituration of the residue with a mixture of water and ether, the solid was filtered off and recrystallised from ethanol to give (20) as red needles (0.05 g, 80.9%), m.p. 270—275 °C (decomp.); $\nu_{max.}$ 3 390, 1 650, 1 645, 1 610, and 1 595 cm^{-1}; $\lambda_{max.}$ (EtOH) 229, 254, 279 (sh), 300, 335, and 351 nm; $\lambda_{max.}$ (alkaline EtOH) 249, 281, 302, and 318 nm; *m/e* 338 (M^+), 309, and 295.

We thank Dr. T. Ohishi (Institute of Physical and Chemical Research) for his helpful discussions and suggestions in this work, and Professor Emeritus S. Sugasawa (Tokyo University) and Dr. S. Saito (director of this laboratory) for encouragement.

[9/391 *Received*, 12*th March*, 1979]

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