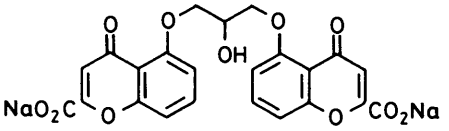
Substituted 4*H*-1-Benzopyran-4-ones (Chromones): Synthesis *via* Palladium-catalysed Coupling of their Halogeno Derivatives with Alkenes

Stephen G. Davies* and Bryan E. Mobbs
Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY
Christopher J. Goodwin
Fisons p.l.c., Pharmaceutical Division, Research and Development Laboratories, Bakewell Road, Loughborough, LE11 0RH

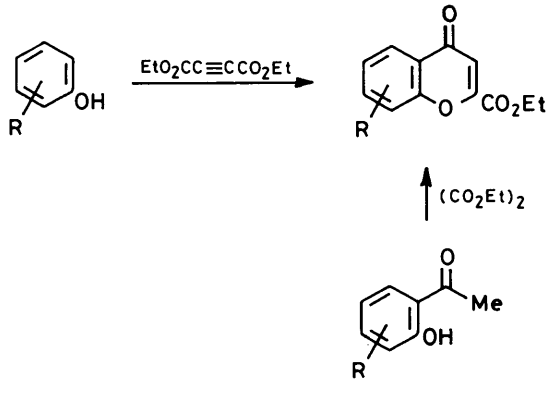
Activation of bromochromones has been achieved by Pd^0 insertion into the carbon–halogen bond. The resultant species undergo coupling with alkenes leading to vinylated chromones. Vinylation occurs regiospecifically at the original site of bromination and therefore provides a method for the clean introduction of substituents into the chromone ring system. An anomalous reaction of a dibrominated chromone leading to a ring-opened product is described.

There has been considerable interest in the 4*H*-1-benzopyran-4-one (chromone) ring system, both with regard to natural product chemistry (it forms the basis for the flavanoid family), and to the pharmacological activity of several of its derivatives.[1] Prominent in the latter area is the bis-chromone disodium 5,5′-(2-hydroxypropane-1,3-diyl)bis-(4-oxo-4*H*-1-benzopyran-2-carboxylate) (**1**), well known for its prophylactic activity against bronchial asthma.[2]



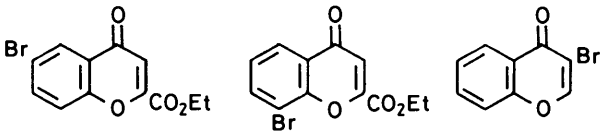
(**1**)

Unfortunately compound (**1**) is orally inactive and therefore there has been a considerable effort to find orally active analogues. Synthesis of substituted chromones is limited by the resistance of the parent ring system to electrophilic attack (due to pyrilium salt formation) and by the susceptibility of the γ-pyrone ring to undergo attack and cleavage with a variety of nucleophiles. Substituents are therefore usually introduced into an appropriate phenol or *o*-hydroxyacetophenone prior to cyclisation to the heterocycle (Scheme 1).[1]



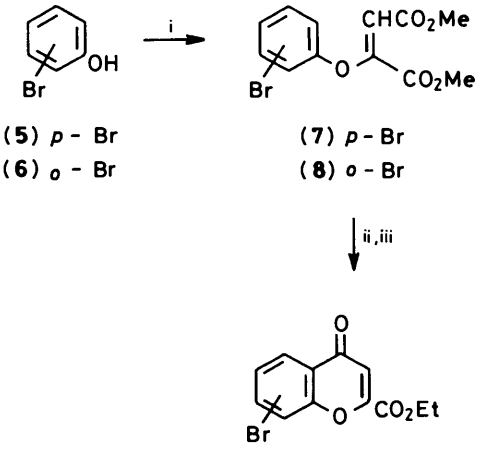
Scheme 1.

In recent years organometallic chemistry has extended the scope of the methods available to the synthetic chemist.[3] In particular, palladium(0) is known to activate aryl halides to functionalisation *via* insertion into the carbon–halogen bond, with the resultant species undergoing a number of coupling reactions. A wide range of functional groups are known to be compatible with the reaction conditions.[4] Halogenochromones might therefore serve as common precursors for the synthesis of a number of functionalised chromones – a feature not always readily achieved by traditional synthetic methods. We report here the success of this strategy using the readily available bromides (**2**), (**3**), and (**4**) as precursors.



(**2**) (**3**) (**4**)

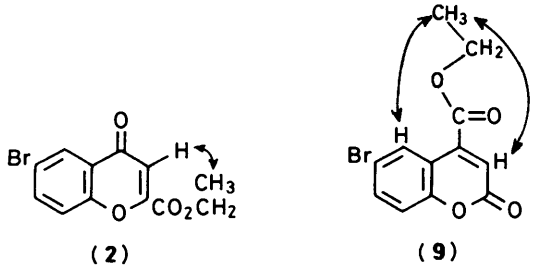
It was envisaged that the 6- and 8-bromo-2-ethoxycarbonyl-chromones (**2**) and (**3**) would be readily synthesised from the *p*- and *o*-bromophenols, (**5**) and (**6**) respectively, by the formation of the Michael adducts (**7**) and (**8**) with dimethyl acetylene-dicarboxylate and subsequent cyclisation (Scheme 2).



(**5**) *p* - Br
(**6**) *o* - Br
(**7**) *p* - Br
(**8**) *o* - Br
(**2**) 6 - Br
(**3**) 8 - Br

Scheme 2. *Reagents:* i, base, $MeO_2CC{\equiv}CCO_2Me$; ii, NaOH; iii, H^+–EtOH

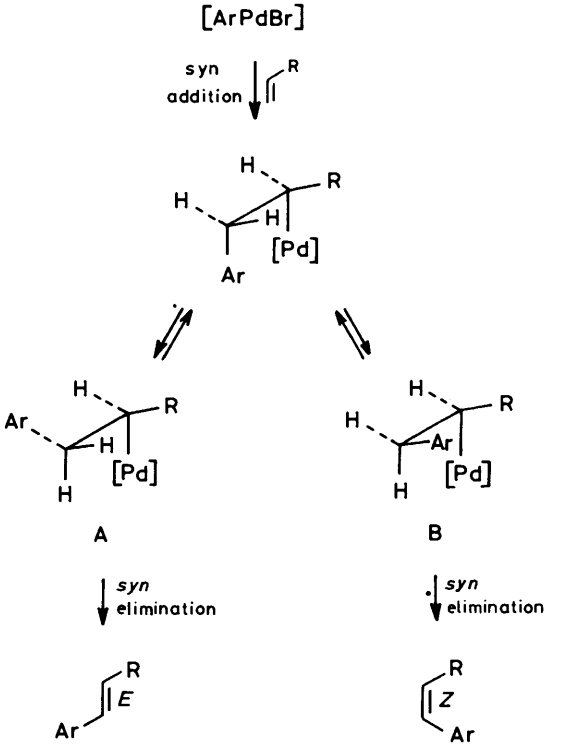
Initial attempts to synthesize the 6-bromo isomer (**2**) from *p*-bromophenol (**5**) resulted only in the isolation of a product isomeric to the desired chromone, identified as the coumarin (**9**). Structural identification of this product was achieved by two n.O.e. studies. Irradiation of the ester methyl triplet showed enhancements to both 5-H and 3-H (in addition to the ester methylene protons) whereas an authentic sample of the chromone (**2**) when similarly irradiated showed only an enhancement to 3-H. This therefore placed the ethoxycarbonyl group in the isomeric product (**9**) adjacent to 3-H and 5-H *i.e.* attached to C-4 (Scheme 3).



Scheme 3. N.O.e. enhancements for the isomers (**2**) and (**9**)

This novel product (**9**) presumably arose from initial *C*- rather than *O*-alkylation of the bromophenol followed by subsequent cyclisation. The ratio of *C*:*O* alkylation for ambident substrates is frequently influenced by the base and solvent system employed and a different combination can substantially alter the product ratio.[5] In this case changing the reagent from Triton B in ethanol to tetrabutylammonium fluoride in isopropyl alcohol resulted in the isolation of the Michael adduct (**7**) in good yield (70%), which was then converted into the 6-bromochromone (**2**) as originally outlined (Scheme 2). The 8-bromo isomer (**3**) was prepared analogously from *o*-bromophenol (**6**) in 56% overall yield. The remaining required precursor, 3-bromochromone (**4**) was prepared from *o*-hydroxyacetophenone by the method of Gammill.[6]

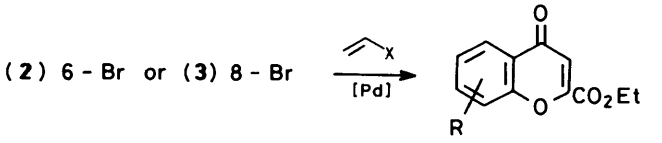
Heating a DMF solution of the 6-bromochromone (**2**) with methyl acrylate, triethylamine, and a catalytic quantity of bis(triphenylphosphine)palladium dichloride afforded the vinylated chromone (**10**) in 61% yield (Table). Of the two possible product isomers (alkene with *E* or *Z* geometry) only one was observed, the coupling constant of 16 Hz between the two alkenic protons clearly indicating the *E*-isomer. The use of acrylonitrile as a substrate led to the vinylated chromone (**11**) as a 3:1 mixture of the *E* and *Z* stereoisomers. The accepted mechanism for this vinylation involves a *syn* pericyclic addition of an aryl–palladium species to the alkene followed by a *syn* pericyclic elimination of a palladium hydride species to give the coupled product.[7] The two alkene isomers originate from the two possible transition states A and B available to the adduct from which a *syn* elimination can occur (Scheme 4).



Scheme 4.

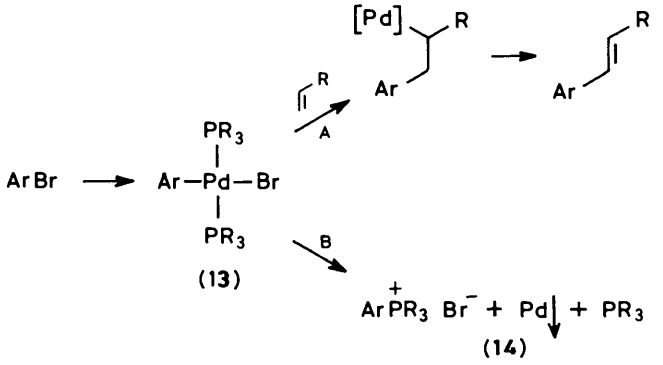
Transition state B is of higher energy due to the steric repulsion between the eclipsed substituents and this is reflected in the observed product ratio in favour of the *E*-alkene isomer. The exclusive formation of the *E* isomer of (**10**), for R = CO_2Me (and Ph *vide infra*) compared with a mixture for (**11**), R = CN, indicates the considerably greater steric bulk of the methyl ester (and phenyl) substituent compared to the linear nitrile.

Table. Vinylation of bromochromones



Substrate	X	Product	R	Yield (%)	*E*:*Z*
(**2**)	CO_2Me	(**10**)	6-CH=CHCO$_2$Me	61	*E* only
(**2**)	CN	(**11**)	6-CH=CHCN	55	3:1
(**3**)	CO_2Me	(**12**)	8-CH=CHCO$_2$Me	76	*E* only
(**3**)	CN	(**15**)	8-CH=CHCN	60	8:1
(**2**)	Ph	(**16**)	6-CH=CHPh	67	*E* only
(**3**)	Ph	(**17**)	8-CH=CHPh	65	*E* only
(**2**)	$CH(OEt)_2$	(**18**)	6-CH$_2$CH$_2$CO$_2$Et	47	
(**3**)	$CH(OEt)_2$	(**19**)	8-CH$_2$CH$_2$CO$_2$Et	39	

Initial attempts to vinylate the 8-bromo isomer (**3**) with methyl acrylate again using bis(triphenylphosphine)palladium dichloride as the catalyst resulted in incomplete reaction giving a mixture of recovered starting material and the product (**12**). This was attributed to a known side-reaction involving phosphonium salt formation which removes the ligand required to stabilise the catalyst.[8] Consumption of the triarylphosphine results in the palladium precipitating from solution and the reaction ceases. Phosphonium salt formation by pericyclic elimination from the initial organopalladium complex (Scheme 5, path B) competes with the addition of the complex (**13**) to the



Scheme 5.

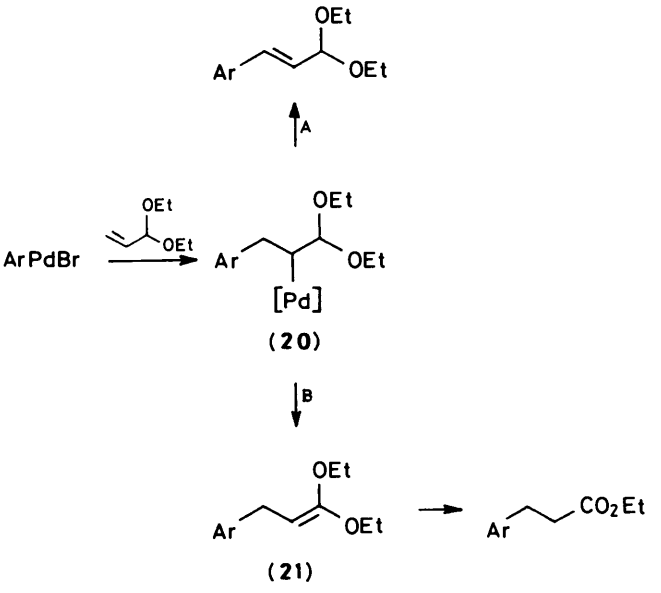
alkene (path A) and is likely to predominate either if the alkene is relatively unreactive or if the formation of the salt (**14**) is unusually facile.

The suppression of this side-reaction requires a phosphine that is slow to quaternise but still functions efficiently as a ligand for the palladium catalyst. A study of a variety of phosphines has revealed that *o*-alkylated triarylphosphines are significantly less reactive towards quaternisation but still perform as well as triphenylphosphine as ligands for palladium.[8] The use of a mixture of palladium acetate and tri-*o*-tolylphosphine under identical conditions led to the complete reaction of (**3**) and formation of the chromone (**12**) in 76% isolated yield. This mixture was therefore adopted as the standard catalyst for all subsequent reactions.

Under these conditions the 8-bromochromone (**3**) was coupled with acrylonitrile to give the vinylated chromone (**15**), as an 8:1 mixture of *E*:*Z* stereoisomers. Both bromochromone isomers (**2**) and (**3**) coupled readily to styrene to give the adducts (**16**) and (**17**) respectively, exclusively as the *E*-stereoisomers.

α,β-Unsaturated aldehydes undergo ready polymerisation upon heating and are therefore incompatible with the reaction conditions required for chromone vinylation. However, protection as their acetals renders them sufficiently stable to be used as substrates in the reaction. Heating acrylaldehyde diethyl acetal with either of the bromochromone isomers (**2**) or (**3**) under the standard conditions gave a mixture of products from which the major component was separated by chromatography. These products lacked any vinyl proton signals and were identified as the esters (**18**) and (**19**) respectively. The formation of saturated esters from the vinylation of protected acrylaldehydes has been reported[8] and is rationalised by considering the elimination of the palladium hydride species from the intermediate (**20**) after the addition of the arylpalladium species to the acrylaldehyde (Scheme 6).

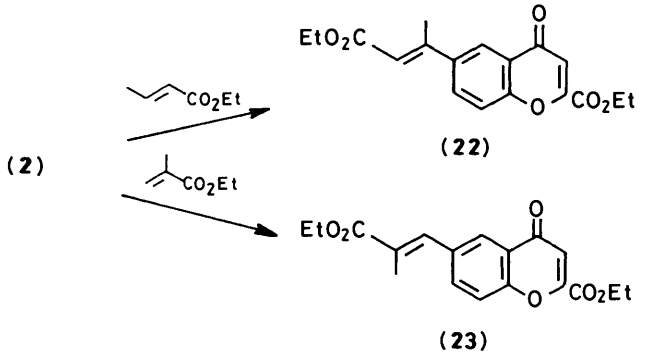
The intermediate (**20**) contains two hydrogens β to the palladium and therefore two possible modes of palladium hydride elimination exist. From the observed products (**18**) and (**19**), path B must predominate leading to the ketene acetal (**21**)



Scheme 6.

which is hydrolysed to the saturated ester during the work-up.

Ethyl crotonate and methyl methacrylate were two substrates used to examine the reactivity of disubstituted alkenes. Each underwent coupling to the 6-bromochromone (**2**) to give the vinylated products (**22**) and (**23**) (Scheme 7). In each case the alkene stereochemistry was determined as *E* by n.O.e. experiments, irradiation of the methyl group resulting in enhancements of 5-H and 7-H but not of the vinyl proton.

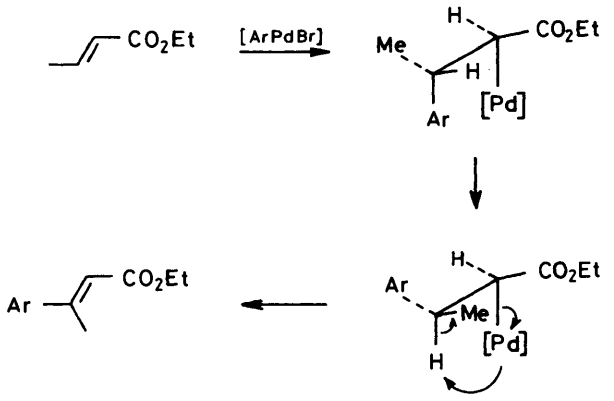


Scheme 7.

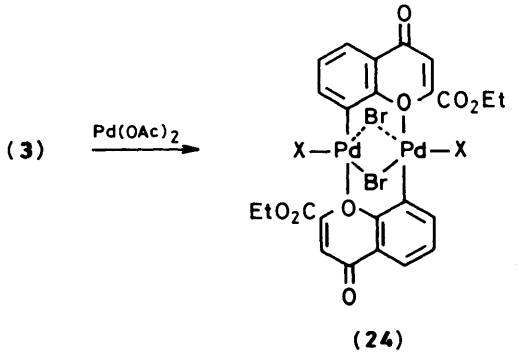
The formation of the *E*-isomer of product (**22**) supports the generally accepted mechanism for the reaction as involving a *syn* addition and a *syn* elimination.[7] Following the initial *syn* addition of the arylpalladium species to the alkene, a *syn* elimination of a palladium hydride species (which requires a rotation to occur in the intermediate) results in the original relationship between the two alkene substituents being reversed. (Scheme 8).

The 8-bromo isomer (**3**) was found to be unreactive to both of these disubstituted alkenes, no vinylated product being isolated. This lack of reactivity may have been due to the formation of a stable palladium dimer species, such as the complex (**24**), after it had undergone insertion into the carbon–bromine bond (Scheme 9).

Disubstituted alkenes are generally less reactive under the



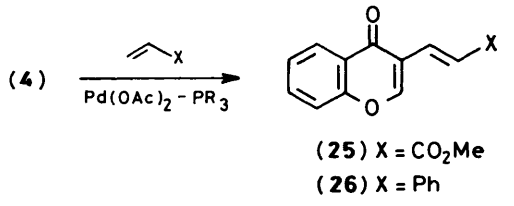
Scheme 8.



Scheme 9.

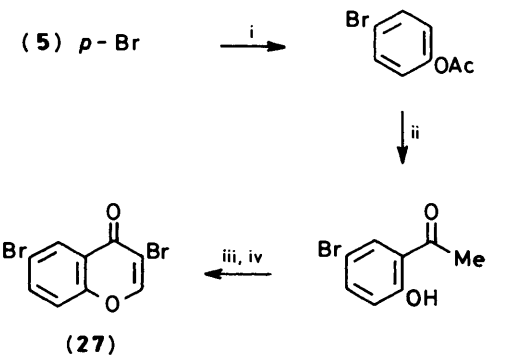
usual conditions for this coupling reaction than the corresponding mono-substituted compounds owing to steric inhibition.[9] Should the chromone (**3**) form the stable complex (**24**), the reduction in alkene reactivity on moving from mono- to di-substituted alkenes could be sufficient to suppress the coupling reaction. The same problem is not found with the 6-bromo isomer (**2**) since there is no adjacent chelating group.

Vinylation of the third chromone precursor, 3-bromochromone (**4**) with methyl acrylate and styrene was similarly found to give high yields of the products (**25**) and (**26**), with exclusively *E*-alkene stereochemistry (Scheme 10).



Scheme 10.

The ease with which 3-bromochromone (**4**) underwent vinylation suggested the possibility of combining this with the similar reactivity of the 6-bromochromone (**2**). Vinylation of a dibromochromone should result in the simultaneous coupling of an alkene to the chromone system at two different sites. The required 3,6-dibromochromone (**27**) was synthesized by an analogous method to that used to prepare 3-bromochromone (**4**) (Scheme 11).

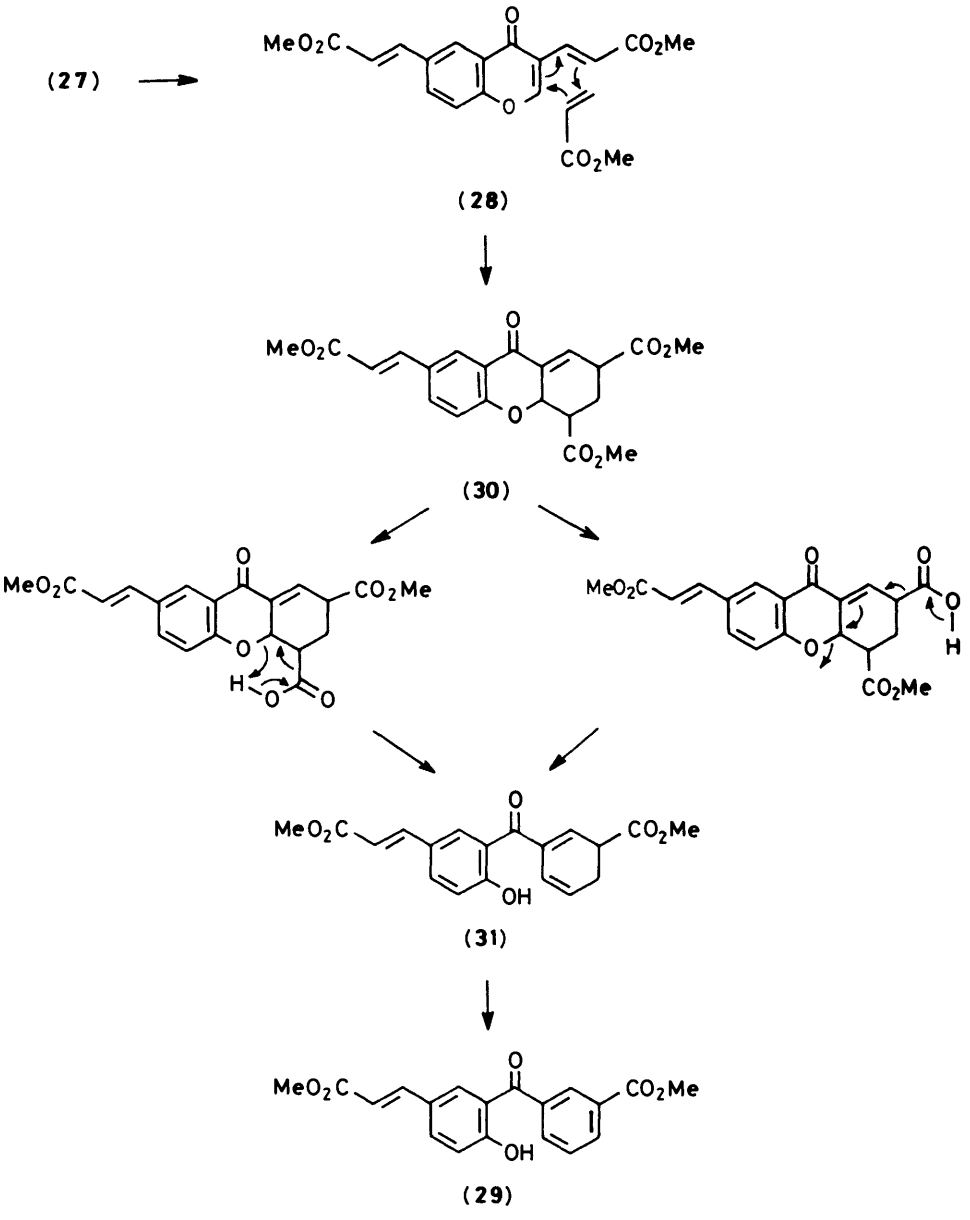


Scheme 11. *Reagents:* i, Ac_2O–Py; ii, $AlCl_3$, heat; iii, $Me_2NCH(OMe)_2$; iv, Br_2

Heating 3,6-dibromochromone (**27**) with methyl acrylate and the standard catalyst gave the expected *E,E*-diacrylated chromone (**28**) and a minor product methyl 4-hydroxy-3-(3-methoxycarbonylbenzoyl)cinnamate (**29**). The most likely source of (**29**) would be *via* addition of an excess of methyl acrylate to product (**28**) followed by demethoxycarbonylation. A probable mechanism (Scheme 12) for the formation of the minor product (**29**) therefore involves an initial Diels–Alder addition of an excess of methyl acrylate to the diacrylate product (**28**) to produce (**30**). The indicated orientation of this addition is the more likely from the polarisation of the diene and the dieneophile and furthermore subsequent loss of either ester group leads to the same product (**31**). Monoester hydrolysis (of either ester) followed by decarboxylation with concomitant ring opening would generate (**31**) and finally dehydrogenation, presumably effected by palladium in the reaction mixture, gives the observed product (**29**).

Experimental

All palladium(II)-catalysed reactions were carried out in a glass Fischer–Porter pressure bottle (a small-scale glass pressure apparatus) under a nitrogen atmosphere. Dichloromethane was distilled from calcium hydride under nitrogen. DMF was heated (100 °C) over calcium sulphate for 4 h and then distilled under reduced pressure (41 °C, 0.1 mmHg) from a small quantity of fresh calcium sulphate. Hexane refers to that fraction of light petroleum of boiling point range 67—70 °C. Other solvents were used as supplied. All solutions after extraction from aqueous solution were dried over $MgSO_4$ and solvent removal or evaporation was carried out under reduced pressure. Bis(triphenylphosphine)palladium chloride was prepared by adding triphenylphosphine (2.4 equiv.) to a solution of palladium chloride in DMF at 140 °C, cooling and collecting the resultant yellow precipitate. T.l.c. was performed on aluminium sheets precoated with silica gel (Merck Kieselgel 60 F_{254}). Column chromatography was performed on silica gel (Merck Kieselgel 60 H). Infra red spectra were recorded (as Nujol mulls unless otherwise stated) on a Perkin-Elmer 297 instrument and were calibrated against polystyrene, 1601 cm^{-1}. ^1H N.m.r. spectra were obtained, in deuteriochloroform unless otherwise stated, on a Bruker WH 300 (300 MHz) instrument. Those spectra at 60 MHz were obtained on a Hitachi–Perkin-Elmer R24B instrument and were referenced to internal tetramethylsilane. All chemical shifts are quoted as δ values. ^{13}C N.m.r. spectra were recorded on a Bruker AM 250 (62.89 MHz) instrument, in deuteriochloroform. Quoted chemical shifts are from the broad-band decoupled spectrum, assignments are from the off-resonance spectrum. Mass spectra were obtained on a V.G. Micromass VG ZAB IF instrument using electron impact techniques unless otherwise stated. Melting points were



Scheme 12.

recorded on a Kofler block and are uncorrected. Elemental microanalyses were carried out by Dr. F. B. Strauss, and the microanalysis services of the University of Manchester and of Fisons Pharmaceuticals Division.

Ethyl 6-*Bromo*-2-*oxo*-2H-1-*benzopyran*-4-*carboxylate* (**9**): *Attempted Preparation of Ethyl* 6-*Bromo*-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**2**).—A solution of *p*-bromophenol (**5**) (43.25 g, 0.25 mol), dimethyl acetylenedicarboxylate (36 g, 0.25 mol), and benzyltrimethylammonium hydroxide (40% solution in methanol; 1 ml) in ethanol (100 ml) was heated under reflux (15 min). Cooling failed to produce the expected precipitate, so heating was continued (45 min). Subsequent cooling followed by solvent evaporation gave a viscous purple oil. This oil was dissolved in 50% aqueous ethanol (100 ml), sodium hydroxide (9 g, 0.23 mol) was added, and the mixture was heated under reflux (1 h). Solvent evaporation gave a viscous yellow oil which was dissolved in ethanol (270 ml), concentrated H_2SO_4 (45 ml) was added, and the mixture heated under reflux (1 h). On being cooled cream needles crystallised from the mixture; these were collected and dried to give ethyl 6-bromo-2-oxo-2*H*-1-benzopyran-4-carboxylate (**9**) (15.25 g, 21%), m.p. 122—125 °C (Found: C, 48.8; H, 2.9. $C_{12}H_9BrO_4$ requires C, 48.5; H, 3.05%); $\nu_{max.}$ 3 100w (ArH), 1 740s (ester), 1 720s (lactone), and 1 595w cm^{-1}; δ 8.49 (1 H, d, *J* 2 Hz, 5-H), 7.65, 7.24 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.00 (1 H, s, 3-H), 4.47 (2 H, q, *J* 7 Hz, CH_2Me), 1.45 (3 H, t, *J* 7 Hz, CH_2Me); irradiation of the methyl group at δ_H 1.45 gave n.O.e.s of 3.3% (CH_2), 0.8% (3-H), and 0.6% (5-H); *m/z* 296 [M^+ (^{79}Br)] and 298 [M^+ (^{81}Br)].

Ethyl 6-*Bromo*-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**2**).—*p*-Bromophenol (**5**) (8.65 g, 50 mmol) was added to a solution of dimethyl acetylenedicarboxylate (7.2 g, 50 mmol) and tetrabutylammonium fluoride (1 crystal) in isopropyl alcohol (20 ml) and the mixture was stirred (20 °C; 19 h). Further dimethyl acetylenedicarboxylate (0.72 g, 5 mmol) was added when t.l.c. indicated incomplete reaction and the reaction

mixture was heated under reflux (100 °C; 15 min). On being cooled the 3-aryloxypropenoic ester (**7**) crystallised from the reaction mixture. This was collected and dried *in vacuo* (50 °C, 15 mmHg) to give a mixture of dimethyl 4-bromophenoxymaleate and fumarate (**7**) (11.06 g, 70%), δ(60 MHz) 7.50—7.30 (2 H, m, ArH), 6.95—6.70 (2 H, m, ArH), 6.60 (1 H, s, fumarate =C*H*CO_2Me), 5.20 (1 H, s, maleate =C*H*-CO_2Me), 3.70 (3 H, s, OMe), and 3.65 (3 H, s, OMe).

The dimethyl esters (**7**) (10.88 g, 34 mmol) were dissolved in 50% aqueous ethanol (40 ml), sodium hydroxide (2.68 g, 67 mmol) was added, and the reaction mixture was heated under reflux (1 h). Acidification with concentrated HCl followed by solvent evaporation gave a yellow solid which was recrystallised from aqueous ethanol to give the diacid as a yellow powder (7.41 g, 75%). This was dissolved, with warming, in concentrated H_2SO_4 (15 ml) and the solution was added dropwise to refluxing ethanol (100 ml). The resulting clear orange solution was then heated under reflux (for a further 30 min) during which time crystallisation began. The reaction mixture was cooled until crystallisation was complete. Collection of this product followed by recrystallisation from aqueous ethanol gave ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) as fine white needles (6.20 g, 43% overall), m.p. 142—144 °C (lit.,[10] 144—145 °C); $\nu_{max.}$ 3 060w (ArH), 1 735s (ester), 1 650s (pyrone carbonyl), and 1 610m, and 1 600m cm^{-1}; δ 8.33 (1 H, d, *J* 2 Hz, 5-H), 7.83 and 7.53 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.13 (1 H, s, 3-H), 4.48 (2 H, q, *J* 7 Hz, CH_2Me), 1.44 (3 H, t, *J* 7 Hz, CH_2*Me*) [lit.,[10] δ 8.28 (1 H, d, *J* 2.5 Hz, 5-H), 7.85 (1 H, dd, *J* 9, 2.5 Hz, 7-H) 7.52 (1 H, d, *J* 9 Hz, 9-H), and 7.11 (1 H, s, 3-H)]; irradiation of the methyl group at δ_H 1.44 gave n.O.e.s of 3.6% (CH_2) and 1.6% (3-H); *m/z* 296 [M^+ (^{79}Br)] and 298 [M^+(^{81}Br)].

Ethyl 8-*Bromo*-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**3**).—*o*-Bromophenol (**6**) (15 g, 87 mmol) was treated under conditions analogous to the synthesis of ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) from *p*-bromophenol (**5**), to give the title compound (**3**) as fine white needles (14.4 g, 56% overall), m.p. 125—126 °C (Found: C, 48.4; H, 3.1. $C_{12}H_9BrO_4$ requires C, 48.5; H, 3.05%); $\nu_{max.}$ 3 090w (ArH), 1 735s (ester), 1 658s (pyrone carbonyl), and 1 620m and 1 595m cm^{-1}; δ 8.12 (1 H, dd, *J* 2, 8 Hz, ArH), 7.95 (1 H, dd, *J* 2, 8 Hz, ArH), 7.32 (1 H, t, *J* 8 Hz, 6-H), 7.13 (1 H, s, 3-H), 4.47 (2 H, q, *J* 7 Hz, CH_2Me), and 1.44 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 296 [M^+(^{79}Br)] and 298 [M^+(^{81}Br)].

General Chromone Vinylation Procedure.—The bromochromone (1.0 g, 3.4 mmol), triethylamine (0.53 ml, 3.8 mmol), the alkene, and the catalyst were added to DMF (4 ml) in a Fischer–Porter bottle. The vessel was degassed by repeatedly pressurising and venting the apparatus. Finally, the vessel was placed under nitrogen pressure (3 atm) and the reaction mixture heated (120 °C, 5 h). The warm reaction mixture was poured into aqueous sodium hydrogen carbonate (35 ml) and the resulting precipitate was collected and dried. Column chromatography [eluting with methanol–dichloromethane (2:98)] gave triarylphosphine followed by the vinylated chromone. Recrystallisation of the vinylated chromone from dichloromethane–hexane, including treatment with decolourising charcoal, gave in each case analytically pure material.

Ethyl 6-[(E)-2-*Methoxycarbonylethenyl*]-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**10**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with methyl acrylate (0.35 ml, 3.9 mmol) and bis(triphenylphosphine)palladium chloride (47 mg; 2 mol %) to give the title compound (**10**) as a white crystalline powder (62 mg, 61%), m.p. 205—206 °C (Found: C, 63.8; H, 4.7. $C_{16}H_{14}O_6$ requires C, 63.6; H, 4.7%); $\nu_{max.}$ 3 060w (ArH), 1 735s (ester), 1 700s (α,β-unsaturated ester), and 1 660br cm^{-3} (pyrone carbonyl); δ 8.31 (1 H, d, *J* 2 Hz, 5-H), 7.88, 7.64 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.74 (1 H, d, *J* 16 Hz, alkene-H, 7.13 (1 H, s, 3-H), 6.53 (1 H, d, *J* 16 Hz, alkene-H), 4.48 (2 H, q, *J* 7 Hz, CH_2Me), 3.83 (3 H, s, OMe), and 1.45 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 302 (M^+).

Ethyl 6-(2-*Cyanoethenyl*)-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**11**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with acrylonitrile (0.25 ml, 3.8 mmol) and bis(triphenylphosphine)palladium chloride (47 mg, 2 mol %) to give the title compound (**11**), an off-white powder, as a 3:1 mixture of *E*:*Z* isomers (505 mg, 55%), m.p. 190—200 °C (Found: C, 67.0; H, 4.1; N, 5.1. $C_{15}H_{11}NO_4$ requires C, 67.0; H, 4.1; N, 5.2%); $\nu_{max.}$ 2 215w (nitrile), 1 745s (ester), and 1 660s cm^{-1} (pyrone carbonyl); δ(major *E*-isomer) 8.27 (1 H, d, *J* 2 Hz, 5-H), 7.83, 7.69 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.48 (1 H, d, *J* 16 Hz, alkene-H), 7.15 (1 H, s, 3-H), 6.02 (1 H, d, *J* 16 Hz, alkene-H), 4.49 (2 H, q, *J* 7 Hz, CH_2Me), 1.46 (3 H, t, *J* 7 Hz, CH_2*Me*); δ(minor *Z*-isomer) 8.51 (1 H, dd, *J* 2, 8 Hz, 7-H), 8.31 (1 H, d, *J* 2 Hz, 5-H), 7.72 (1 H, d, *J* 11 Hz, alkene-H), 7.23 (1 H, s, 3-H), 5.63 (1 H, d, *J* 11 Hz, alkene-H), and ethyl ester and 8-H resonances identical with the *E*-isomer; *m/z* 269 [M^+, 12% (*Z*-isomer)] and 269 [M^+ 88, (*E*-isomer)].

Ethyl 8-[(E)-2-*Methoxycarbonylethenyl*]-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**12**).—Ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) was heated with methyl acrylate (0.35 ml, 3.9 mmol) and bis(triphenylphosphine)palladium chloride (47 mg, 2 mol %) to give a mixture of the title compound (**12**) and unchanged ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) by t.l.c. The use of palladium acetate (15 mg; 2 mol %) and tri-*o*-tolylphosphine (123 mg, 12 mol %) as the catalyst mixture gave (**12**) as white fluffy needles (770 mg, 76%), m.p. 157—158 °C (Found: C, 63.8; H, 4.7. $C_{16}H_{14}O_6$ requires C, 63.6; H, 4.7%); $\nu_{max.}$ 3 080w (ArH), 1 735s (ester), 1 720s (α,β-unsaturated ester), and 1 670s cm^{-1} (pyrone carbonyl); δ 8.22 (1 H, dd, *J* 2, 8 Hz, ArH), 7.98 (1 H, d, *J* 16 Hz, alkene-H), 7.88 (1 H, dd, *J* 2, 8 Hz, ArH), 7.47 (1 H, t, *J* 8 Hz, 6-H), 7.16 (1 H, s, 3-H), 7.08 (1 H, d, *J* 16 Hz, alkene-H), 4.51 (2 H, q, *J* 7 Hz, CH_2Me), 3.86 (3 H, s, OMe), and 1.49 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 302 (M^+).

Ethyl 8-(2-*Cyanoethenyl*)-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**15**).—Ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) was heated with acrylonitrile (0.25 ml, 3.8 mmol), palladium acetate (15 mg, 2 mol %) and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give the title compound (**15**), a white powder, as an 8:1 mixture of *E*:*Z* isomers (545 mg, 60%), m.p. 123—126 °C (Found: C, 66.85; H, 4.4; N, 5.2. $C_{15}H_{11}NO_4$ requires C, 66.9; H, 4.1; N, 5.2%); $\nu_{max.}$ 2 215w (nitrile), 1 745s (ester), and 1 660br cm^{-1} (pyrone carbonyl); δ(major *E*-isomer) 8.24 (1 H, dd, *J* 2, 8 Hz, ArH), 7.81 (1 H, dd, *J* 2, 8 Hz, ArH), 7.64 (1 H, d, *J* 16 Hz, alkene-H), 7.50 (1 H, t, *J* 8 Hz, 6-H), 7.15 (1 H, s, 3-H), 6.66 (1 H, d, *J* 16 Hz, alkene-H), 4.51 (2 H, q, *J* 7 Hz, CH_2Me), 1.47 (3 H, t, *J* Hz, CH_2*Me*); δ(minor *Z*-isomer) 8.57—8.52 (1 H, m, ArH), 8.29—8.21 (1 H, m, ArH), 7.85—7.78 (1 H, m), 7.58—7.50 (1 H, m), 7.13 (1 H, d, 3-H), 5.76 (1 H, d, *J* 11 Hz, alkene-H), and ester resonances identical to the *E*-isomer; *m/z* 269 [M^+, 11% (*Z*-isomer)] and 269 [M^+, 87 (*E*-isomer)].

Ethyl 4-*Oxo*-6-(E)-*styryl*-4H-1-*benzopyran*-2-*carboxylate* (**16**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with styrene (0.45 ml, 3.9 mmol), palladium acetate (15 mg; 2 mol %), and tri-*o*-tolylphosphine (82 mg; 8 mol %) to give the title compound (**16**) as fine pale yellow needles (720 mg, 67%), m.p. 194—195 °C (Found: C, 75.1; H, 5.2. $C_{20}H_{16}O_4$ requires C, 75.0; H, 5.0%); $\nu_{max.}$ 1 745s (ester), 1 650s

(pyrone carbonyl), and 1 610m cm^{-1}; δ 8.24 (1 H, d, *J* 2 Hz, 5-H), 7.89, 7.62 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.51 (2 H, d, *J* 7 Hz, ArH), 7.40—7.28 (3 H, m, Ph), 7.19, 7.13 (2 H, AB system, J_{AB} 16 Hz, alkene-H), 7.11 (1 H, s, 3-H), 4.45 (2 H, q, *J* 7 Hz, CH_2Me), and 1.43 (3 H, t, *J* 7 Hz, CH_2*Me*); δ $^{13}C\{^1H\}$ 178.2 (C), 160.4 (C), 155.2 (C), 152.0 (C), 136.5 (C), 135.4 (C), 132.5 (CH), 130.8 (CH), 128.7 (CH), 128.1 (CH), 126.6 (CH), 126.3 (CH), 124.5 (C), 122.8 (CH), 119.1 (CH), 114.6 (CH), 62.9 (CH_2), and 14.1 (Me); *m/z* 320 (M^+).

Ethyl 4-*Oxo*-8-(E)-*styryl*-4H-1-*benzopyran*-2-*carboxylate* (**17**).—Ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) was heated with styrene (0.5 ml, 4.4 mmol), palladium acetate (15 mg, 2 mol %), and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give the title compound (**17**) as pale yellow needles (705 mg, 65%), m.p. 141—142 °C (Found: C, 75.2; H, 5.1. $C_{20}H_{16}O_4$ requires C, 75.0; H, 5.0%); $\nu_{max.}$ 3 080w (ArH), 1 730s (ester), 1 660s (pyrone carbonyl), and 1 590m and 1 580m cm^{-1}; δ 8.07 (1 H, d, *J* 2 Hz, ArH), 7.94 (1 H, dd, *J* 8, 2 Hz, ArH), 7.57 and 7.47 (2 H, AB system, J_{AB} 16 Hz, alkene-H), 7.60—7.55 (2 H, m, Ph), 7.45—7.29 (4 H, m, Ph and 6-H), 7.13 (1 H, s, 3-H), 4.48 (2 H, q, *J* 7 Hz, CH_2Me), 1.47 (3 H, t, *J* 7 Hz, CH_2*Me*); δ $^{13}C\{^1H\}$ 178.2 (C), 160.3 (C), 152.9 (C), 151.8 (C), 136.9 (C), 132.8 (CH), 131.5 (CH), 128.7 (CH), 128.2 (CH), 127.9 (C), 126.7 (CH), 125.5 (CH), 124.7 (C), 124.3 (CH), 120.6 (CH), 114.3 (CH), 62.8 (CH_2), and 14.0 (Me); *m/z* 320 (M^+).

Ethyl (2-*Ethoxycarbonyl*-4-*oxo*-4H-1-*benzopyran*-6-*yl*)*propanoate* (**18**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with acrylaldehyde diethyl acetal (0.58 ml, 3.8 mmol), palladium acetate (15 mg, 2 mol %), and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give initially a dark red oil. Extraction with dichloromethane (3 × 30 ml) followed by solvent evaporation gave a dark residue. This was purified according to the general procedure to give the title compound (**18**) as white fluffy needles (500 mg, 47%), m.p. 81—82 °C (Found: C, 64.4; H, 5.7. $C_{17}H_{18}O_6$ requires C, 64.1; H, 5.7%); $\nu_{max.}$ 3 060w (ArH), 1 725s (ester), 1 665s (pyrone carbonyl), and 1 625 m and 1 613 m cm^{-1}; δ 8.02 (1 H, d, *J* 2 Hz, 5-H), 7.61 and 7.55 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.10 (1 H, s, 3-H). 4.47 (2 H, q, *J* 7 Hz, CH_2Me), 4.13 (2 H, q, *J* 7 Hz, CH_2Me), 3.07 (2 H, t, *J* 6 Hz, CH_2), 2.69 (2 H, t, *J* 6 Hz, CH_2), 1.44 (3 H, t, *J* 7 Hz, CH_2*Me*), and 1.24 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 318 (M^+).

Ethyl (2-*Ethoxycarbonyl*-4-*oxo*-4H-1-*benzopyran*-8-*yl*)*propanoate* (**19**).—Ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) was heated with acrylaldehyde diethyl acetal (0.60 ml, 3.9 mmol), palladium acetate (15 mg, 2 mol %), and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give, after an analogous work-up to that described for (**18**), the title compound (**19**) as cream rods (420 mg, 39%), m.p. 67—68 °C (Found: C, 64.0; H, 5.45. $C_{17}H_{18}O_6$ requires C, 64.1; H, 5.7%); $\nu_{max.}$ 3 060w (ArH), 1 743s and 1 725s (ester), 1 650 (pyrone carbonyl), and 1 610m, 1 600m and 1 585m cm^{-1}; δ 8.05 (1 H, dd, *J* 2, 8 Hz, ArH), 7.62 (1 H, dd, *J* 8, 2 Hz, ArH), 7.36 (1 H, t, *J* 8 Hz, 6-H), 7.10 (1 H, s, 3-H), 4.46 (2 H, q, *J* 7 Hz, CH_2CH_3), 4.11 (2 H, q, *J* 7 Hz, CH_2CH_3), 3.26 (2 H, t, *J* 6 Hz, CH_2), 2.81 (2 H, t, *J* 6 Hz, CH_2), 1.44 (3 H, t, *J* 7 Hz, CH_2*Me*), and 1.21 (3 H, t, *J* 7 Hz, CH_2*Me*); *m/z* 318 (M^+).

Ethyl 6-[(E)-3-*Ethoxycarbonylprop*-2-*enyl*]-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**22**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with ethyl crotonate (0.50 ml, 4.0 mmol), palladium acetate (15 mg, 2 mol %) and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give the title compound (**22**) as white needles (340 mg, 31%), m.p. 124—125 °C (Found: C, 65.6; H, 5.6. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.5%); $\nu_{max.}$ 3 055m (ArH), 1 738s, 1 720s (ester), 1 665s (pyrone carbonyl), and 1 630m and 1 610m cm^{-1}; δ 8.27 (1 H, d, *J* 2 Hz, 5-H), 7.84 and 7.60 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.11 (1 H, s, 3-H), 6.20 (1 H, q, *J* 1.5 Hz, vinyl-H), 4.45 (2 H, q, *J* 7 Hz, CH_2Me), 4.21 (2 H, q, *J* 7 Hz, CH_2Me), 2.60 (3 H, d, *J* 1.5 Hz, Me), 1.42 (3 H, t, *J* 7 Hz, CH_2*Me*), and 1.30 (3 H, t, *J* 7 Hz, CH_2*Me*); irradiation of the vinyl proton at δ_H 6.20 gave n.O.e.s of 9% (7-H) and 8.8% (5-H); irradiation of the methyl doublet at δ_H 2.60 gave n.O.e.s of 6% (7-H) and 15% (H-5); *m/z* 330 (M^+).

Ethyl 6-[(E)-2-*methoxycarbonylprop*-1-*enyl*]-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**23**).—Ethyl 6-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**2**) was heated with methyl methacrylate (0.41 ml, 3.8 mmol), palladium acetate (15 mg, 2 mol %), and tri-*o*-tolylphosphine (123 mg, 12 mol %) to give the title compound (**23**) as white needles (305 mg, 29%), m.p. 139—140 °C (Found: C, 64.3; H, 5.1. $C_{17}H_{16}O_6$ requires C, 64.55; H, 5.1%); $\nu_{max.}$ 3 060m (ArH), 1 740s (ester), 1 710s (α,β-unsaturated ester), 1 665s (pyrone carbonyl), and 1 610m cm^{-1}; δ 8.22 (1 H, d, *J* 2 Hz, 5-H), 7.73 (1 H, s, alkene-H), 7.75 and 7.65 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.15 (1 H, s, 3-H), 4.48 (2 H, q, *J* 7 Hz, CH_2Me), 3.85 (3 H, s, OMe), 2.18 (3 H, s, Me), and 1.46 (3 H, t, *J* 7 Hz, CH_2*Me*); irradiation of the methyl group at δ_H 2.18 gave n.O.e.s of 3.4% (7-H) and 7.1% (5-H); *m/z* 316 (M^+).

Attempted Vinylation of Ethyl 8-*Bromo*-4-*oxo*-4H-1-*benzopyran*-2-*carboxylate* (**3**) *with Ethyl Crotonate and Methyl Methacrylate*.—Ethyl 8-bromo-4-oxo-4*H*-1-benzopyran-2-carboxylate (**3**) was heated with palladium acetate (15 mg, 2 mol %), tri-*o*-tolylphosphine (123 mg, 12 mol %), and either ethyl crotonate (0.50 ml, 4 mmol) or methyl methacrylate (0.41 ml, 3.8 mmol). In each case only the recovery of the bromochromone (**3**) was observed.

3-*Bromo*-4H-1-*benzopyran*-4-*one*[6] (**4**).—*o*-Hydroxyacetophenone (4.0 g, 29 mmol) was added to dimethylformamide dimethyl acetal (5.25 g, 44 mmol) and the mixture was heated (90 °C; 2 h). Cooling followed by evaporation of the mixture gave a light brown residue which was chromatographed (ethyl acetate) to give the vinylogous amide as a bright yellow solid (4.38 g, 78%). To an ice-cold solution of this material (2.3 g, 12 mmol) in chloroform (20 ml) was added dropwise a solution of bromine (1.92 g, 12 mmol) in chloroform (10 ml), and the mixture was stirred (5 min). The reaction mixture was warmed, the solvent evaporated, and the residue chromatographed (5% ethyl acetate in chloroform) to give a cream solid. This was recrystallised from dichloromethane–hexane to give 3-bromo-4*H*-1-benzopyran-4-one (**4**) as cream needles (2.04 g, 59% overall; lit.,[6] 78%), m.p. 95—99 °C (lit.,[6] 93—94 °C); $\nu_{max.}$ 3 060m (ArH), 1 648s (pyrone carbonyl), and 1 610s, 1 600s, and 1 560m cm^{-1} [lit.,[6] 3 060 (C–H), 1 665 (C=O), 1 615, 1 600, 1 560, 1 370, and 1 075 cm^{-1} (C–O)]; δ 8.26 (1 H, dd, *J* 2, 8 Hz, 5-H), 8.24 (1 H, s, 2-H), 7.74—7.69 (1 H, m, ArH), and 7.50—7.43 (2 H, m, ArH) [lit.,[6] δ 8.25 (1 H, s, 2-H), 8.30—8.10 (1 H, m), and 7.90—7.25 (3 H, m)]; *m/z* 224 [M^+(^{79}Br)] and 226 [M^+(^{81}Br)].

(E)-*Methyl* 3-(4-*Oxo*-4H-1-*benzopyran*-3-*yl*)*propenoate* (**25**).—3-Bromo-4*H*-1-benzopyran-4-one (**4**) (500 mg, 2.2 mmol) was added to a mixture of methyl acrylate (0.30 ml, 3.3 mmol), triethylamine (0.45 ml, 3.2 mmol), palladium acetate (10 mg, 2 mol %), and triphenylphosphine (23 mg, 4 mol %) in DMF (2 ml) in a Fischer–Porter bottle. The reaction mixture was degassed and heated (120 °C; 6 h). Work-up as above gave (*E*)-methyl 3-(4-oxo-4*H*-1-benzopyran-3-yl)propenoate (**25**) as white needles (300 mg, 59%), m.p. 139—140 °C (Found: C, 67.6; H, 4.3. $C_{13}H_{10}O_4$ requires C, 67.8; H, 4.4%); $\nu_{max.}$ 3 060w

(ArH), 1 725s (α,β-unsaturated ester), 1 660s (pyrone carbonyl), and 1 612s and 1 560m cm^{-1}; δ 8.24 (1 H, dd, *J* 2, 8 Hz, 5-H), 8.16 (2 H, s, 2-H), 7.74—7.62 (1 H, m, ArH), 7.52—7.43 (2 H, m, ArH), 7.40, 7.26 (2 H, AB system, J_{AB} 16 Hz, alkene-H), and 3.78 (3 H, s, OMe); δ $^{13}C\{^1H\}$ 175.6 (C), 167.6 (C), 157.3 (CH), 155.3 (C), 135.5 (CH), 133.9 (CH), 126.1 (CH), 125.7 (CH), 124.0 (C), 121.6 (CH), 119.1 (CH), 118.0 (CH), and 51.5 (Me); *m/z* 230 (M^+).

3-(E)-*Styryl*-4H-1-*benzopyran*-4-*one* (**26**).—3-Bromo-4*H*-1-benzopyran-4-one (**4**) (500 mg, 2.2 mmol) was added to a mixture of styrene (0.30 ml, 2.6 mmol), palladium acetate (10 mg, 2 mol %), tri-*o*-tolylphosphine (81 mg, 12 mol %), and triethylamine (0.40 ml, 2.9 mmol) in DMF (3 ml) in a Fischer–Porter bottle. The mixture was degassed and heated (100 °C, 5 h). An analogous work-up gave recovered starting material (**4**) (50 mg, 10%) and 3-(E)-*styryl*-4H-1-*benzopyran*-4-*one* (**26**) as white needles (370 mg, 75% based on recovered starting material), m.p. 170—171 °C (Found: C, 82.3; H, 4.8. $C_{17}H_{12}O_2$ requires C, 82.2; H, 4.9%); $\nu_{max.}$ 1 640s (pyrone carbonyl), and 1 620s and 1 610s cm^{-1}; δ 8.27 (1 H, dd, *J* 2, 8 Hz, 5-H), 8.07 (1 H, s, 2-H), 7.67—7.60 (1 H, m), 7.58 (1 H, d, *J* 16 Hz, alkene-H), 7.49—7.18 (7 H, m), and 6.94 (1 H, d, *J* 16 Hz, alkene-H); *m/z* 248 (M^+).

3,6-*Dibromo*-4H-1-*benzopyran*-4-*one* (**27**).—*p*-Bromophenol, (**5**) (10.0 g, 58 mmol) was added to a mixture of acetic anhydride (25 ml, 265 mmol) and pyridine (22 ml, 272 mmol) and the mixture was heated (100 °C; 2 h). The cooled reaction mixture was poured into water (150 ml), acidified with dilute aqueous acid, and extracted with diethyl ether (3 × 100 ml). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (3 × 50 ml), dried, and the solvent was evaporated to give *O*-acetyl-*p*-bromophenol as a colourless oil (12.07 g, 97%), $\nu_{max.}$ 1 770s (ester) and 1 590w cm^{-1}; δ(60 MHz) 7.65—7.40 (2 H, m, ArH), 7.15—6.90 (2 H, m, ArH), and 2.25 (3 H, s, COMe).

O-Acetyl-*p*-bromophenol (12.07 g, 56 mmol) was added to aluminium trichloride (11.25 g, 84 mmol) and the mixture was heated (150 °C; 3 h). Water (150 ml) was added slowly to the cooled reaction mixture and the resulting solution was extracted with diethyl ether (3 × 100 ml). The combined organic fractions were dried and the solvent evaporated to give an orange oil. Distillation under reduced pressure gave a pale yellow solid which was recrystallised from aqueous ethanol to give 5-bromo-2-hydroxyacetophenone (7.50 g, 62%), $\nu_{max.}$ 1 645s cm^{-1} (carbonyl); δ(60 MHz) 7.80 (1 H, d, *J* 2 Hz, 6-H), 7.70—7.35 (1 H, m, ArH), 6.95—6.75 (1 H, m, ArH), and 2.55 (3 H, s, COMe).

5-Bromo-2-hydroxyacetophenone (1.0 g, 4.7 mmol) was added to dimethylformamide dimethyl acetal (0.83 g, 7.0 mmol) and the mixture was heated (100 °C; 2 h). Cooling of the mixture followed by evaporation gave a red–orange solid which was chromatographed (10% hexane in ethyl acetate) to give a yellow solid (1.0 g). This solid was dissolved in chloroform (10 ml), cooled (0 °C), and treated dropwise with a solution of bromine (0.60 g, 3.8 mmol) in chloroform (10 ml). The mixture was stirred (5 min), warmed to room temperature, and the solvent was evaporated. Chromatography (5% ethyl acetate in chloroform) gave 3,6-dibromo-4*H*-1-benzopyran-4-one (**27**) as a pale yellow powder (860 mg, 36% overall), m.p. 137—138 °C; $\nu_{max.}$ 1 655s (pyrone carbonyl) and 1 600m, and 1 550m cm^{-1}; δ(60 MHz) 8.35 (1 H, d, *J* 2 Hz, 5-H), 8.20 (1 H, s, 2-H), 7.80 and 7.35 (2 H, ABX system, J_{AB} 9 Hz, J_{BX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H); *m/z* (i.b.e.i.) 302 [M^+, 50% ($^{79}Br^{79}Br$)], 304 [M^+, 100 ($^{79}Br^{81}Br$)], and 306 [M^+, 50 ($^{81}Br^{81}Br$ 50%)].

Coupling of 3,6-*Dibromo*-4H-1-*benzopyran*-4-*one* (**27**) *with Methyl Acrylate:* 3,6-Dibromo-4*H*-1-benzopyran-4-one (**27**) (1.0 g, 3.3 mmol) was added to a mixture of methyl acrylate (0.68 ml, 7.5 mmol), triethylamine (1.06 ml, 7.6 mmol), palladium acetate (30 mg, 4 mol %), and tri-*o*-tolylphosphine (248 mg, 24 mol %) in DMF (4 ml) in a Fischer–Porter bottle. The vessel was degassed and heated (120 °C; 2 h). After work-up as above two products were isolated; (*E,E*)-dimethyl 3,3′-(4-oxo-4*H*-1-benzopyran-3,6-diyl)bispropenoate (**28**) as a white powder (420 mg, 41%) and methyl 3-{2-hydroxy-5-[(*E*)-2-methoxycarbonylethanyl]benzoyl}benzoate (**29**) as a pale yellow powder (85 mg, 8%).

Compound (**28**) had m.p. 210—215 °C (Found: C, 64.65; H, 4.4. $C_{17}H_{14}O_6$ requires C, 65.0; H, 4.5%); $\nu_{max.}$ 1 725s (α,β-unsaturated ester), 1 655s (pyrone carbonyl), and 1 610m and 1 560w cm^{-1}; δ 8.41 (1 H, d, *J* 2 Hz, 5-H), 8.13 (1 H, s, 2-H), 7.85 and 7.51 (2 H, ABX system, J_{AB} 8 Hz, J_{AX} 2 Hz, J_{BX} 0 Hz, 7-H and 8-H), 7.77 (1 H, d, *J* 16 Hz, alkene-H), 7.41 and 7.31 (2 H, AB system, J_{AB} 16 Hz, alkene-H), 6.55 (1 H, d, *J* 16 Hz, alkene-H), 3.85 (3 H, s, OMe), and 3.82 (3 H, s, OMe); *m/z* 314 (M^+).

Compound (**29**) had m.p. 125—126 °C; $\nu_{max.}$ 1 735s (ester), 1 625s (diaryl ketone), and 1 580w cm^{-1}; δ 12.16 (1 H, s, OH), 8.38—8.31 (2 H, m), 7.93—7.87 (1 H, m), 7.82—7.79 (1 H, m), 7.71—7.65 (2 H, m), 7.58 (1 H, d, *J* 16 Hz, alkene-H), 7.15 (1 H, d, *J* 8 Hz), 6.26 (1 H, d, *J* 16 Hz, alkene-H), 4.00 (3 H, s, OMe), and 3.81 (3 H, s, OMe); δ ([$^2H_6$]acetone; aromatic region) 8.37 (1 H, t, *J* 1.5 Hz, 2′-H), 8.30 (1 H, dt, *J* 8 Hz, *J* 1.5 Hz, 6′- or 4′-H) 8.06 (1 H, dt, *J* 8 Hz, *J* 1.5 Hz, 4′- or 6′-H), 8.01 (1 H, dd, *J* 2, 8 Hz, 6-H), 7.91 (1 H, d, *J* 2 Hz, 2-H), 7.76 (1 H, t, *J* 8 Hz, 5′-H), 7.62 (1 H, d, *J* 16 Hz, alkene-H), and 7.15 (1 H, d, *J* 8 Hz, 5-H); δ $^{13}C\{^1H\}$ 200.2 (C), 167.2 (C), 165.9 (C), 164.9 (C), 143.2 (CH), 137.6 (C), 134.9 (CH), 133.8 (CH),. 133.1 (CH), 133.0 (CH), 130.9 (C), 130.0 (CH), 128.8 (CH), 125.6 (C), 119.5 (CH), 118.8 (C), 116.6 (CH), 52.5 (CH_3), and 51.7 (Me); *m/z* 340 (M^+) and 205 ($M^+ - C_6H_4CO_2Me$) (Found: M^+, 340.0946. $C_{19}H_{16}O_6$ requires *M*, 340.0947).

Acknowledgements

We thank the S.E.R.C. and Fisons p.l.c., Pharmaceutical Division for a CASE award (to B. E. M.).

References

1 G. P. Ellis, 'Chromenes, Chromanones and Chromones,' Wiley, New York, 1977.
2 J. L. Suschitzky, *Chem. Br.*, 1985, 554.
3 S. G. Davies, 'Organotransition Metal Chemistry, Applications to Organic Synthesis,' Pergamon Press, Oxford, 1982.
4 R. F. Heck, *Org. React.*, 1982, **27**, 345; R. F. Heck, 'Palladium Reagents in Organic Syntheses,' Academic Press, London, 1985.
5 L. M. Jackman, and B. C. Lange, *Tetrahedron*, 1977, **33**, 2737.
6 R. B. Gammill, *Synthesis*, 1979, 901.
7 R. F. Heck, *Acc. Chem. Res.*, 1979, **12**, 146.
8 R. F. Heck, *Ann. N.Y. Acad. Sci.*, 1977, **295**, 201.
9 R. F. Heck, *J. Am. Chem. Soc.*, 1968, **90**, 5518.
10 G. Barker and G. P. Ellis, *J. Chem. Soc. C*, 1970, 2609.

Received 13*th November* 1986; *Paper* 6/2178