Aminolysis and Hydrolysis of Chromonyl Oxazolones and Some Condensation Reactions of 2-Methylchromone leading to Novel Chromones

By **Winton D. Jones**, jun., Merrell Research Center, Merrell-National Laboratories, Division of Richardson-Merrell, Cincinnati, Ohio, 45215, U.S.A.

The aminolysis of 4-[(4-oxo-4*H*-1-benzopyran-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-one with diethylamine gave *N*-[1-(diethylamino)-1-oxo-3-(4-oxo-4*H*-1-benzopyran-3-yl)prop-2-en-2-yl]benzamide. The hydrolysis of 2-methyl-4-[(4-oxo-4*H*-1-benzopyran-3-yl)methylene]-1,3-oxazol-5(4*H*)-one gave the α-keto-acid, which could be converted into amino-acid derivatives. Condensation of 2-methylchromone with diethyloxalate, 2-formyl-*NN*-diethylbenzamide, and 2-formylbenzoic acid gave the α-keto-acid, (*E*)-*NN*-diethyl-2-[2-(4-oxo-4*H*-1-benzopyran-2-yl)vinyl]benzamide, and (*E*)-2-[(4-oxo-4*H*-1-benzopyran-2-yl)vinyl]benzoic acid, respectively.

THE synthesis and characterization of chromone carboxylic acids have received a great deal of attention in recent years and a number of these compounds have shown potent anti-anaphylactic activity.[1-5] As part of a programme directed toward novel chromone acids, we were interested in preparing chromones in which the acid group is conjugated to the pyrone ring.[6] We report here a number of novel chromones that were prepared in this programme.

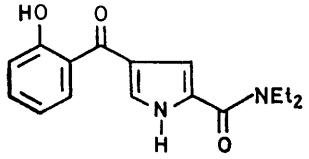
RESULTS AND DISCUSSION

Condensation of (1) with the appropriate acylamino-acid under azlactone-forming conditions[7] gave oxazolones (3), (4), and (5). Fitton *et al.*[8] reported that treatment of (3) with alcoholic sodium carbonate may give a pyrrole or an acrylic ester, the product depending on reaction conditions. We found that dropwise addition of 1 equiv. of anhydrous diethylamine at 0—20 °C to (3) in dry dioxan yielded the amide (6) in 81% yield. The amide was assigned structure (6) on the basis of spectroscopic evidence (see Experimental section).†

Hydrolysis of (4) with aqueous hydrochloric acid or preferably aqueous sulphuric acid–tetrahydrofuran gave the acid (7). Acid (7) was extremely insoluble in the common n.m.r. solvents, and its structure was assigned on the basis of subsequent transformations.‡ For example, esterification of (7) gave a compound (8), which existed exclusively in solution ($CDCl_3$) as its enolic tautomer. The enolic structure was assigned to ester (8) on the basis of its ^1H n.m.r. spectrum, which had a signal for a singlet (1 H) at δ 10.1. The i.r. ($CHCl_3$) hydroxy absorption band at 3 475 cm^{-1} added further confirmation to the structural assignment. Ester (8) was converted into the oxime (9) in 50% yield. Oxime (9) was homogeneous on t.l.c., but no attempt was made to assign the stereochemistry. The gross structure for (9) was assigned on the basis of spectral evidence (see Experimental section). Oxime (9) was reduced with zinc powder in glacial acetic acid followed by ethereal hydrochloric acid to give the amino-acid ester (10) hydrochloride in 58% yield. The ester (10) was stable indefinitely at room temperature as its hydrochloride salt. To our knowledge, compound (10) constitutes the first example of a chromone α-amino-acid derivative. Acylation of (10) with benzoyl chloride or acetic anhydride–pyridine gave (11) and (12), respectively, in good yields. Careful hydrolysis[9] of (11) with 2% aqueous potassium hydroxide at room temperature followed by acidification with hydrochloric acid gave the acylamino-acid (13) in 64% yield.

The first projected synthesis of the 2-substituted acid (20) was envisioned as proceeding through the oxazolone. However, the literature procedure for preparation of the requisite intermediate chromone-2-carbaldehyde was a tedious three-step procedure starting with 2-methylchromone (14).[10-12] It was expected that (14) could serve as a direct precursor to ester (19) through conversion into the anion and condensation with diethyl oxalate. Ester (19) could then be hydrolysed to the desired acid (20). Heilbron *et al.*[13] have shown that (14) could be successfully condensed with benzaldehyde in the presence of sodium methoxide to give the styryl compound. We investigated this reaction and found that magnesium methoxide in methanol gave slightly higher yields. We also found the reaction to be applicable to

† Careful attention to experimental detail is required since addition of greater than stoicheiometric quantities of amine coupled with elevated temperatures gives another product. For example, heating (3) with an excess of anhydrous diethylamine in dry tetrahydrofuran gave a product isolated in 65% yield and tentatively identified as the pyrrole:



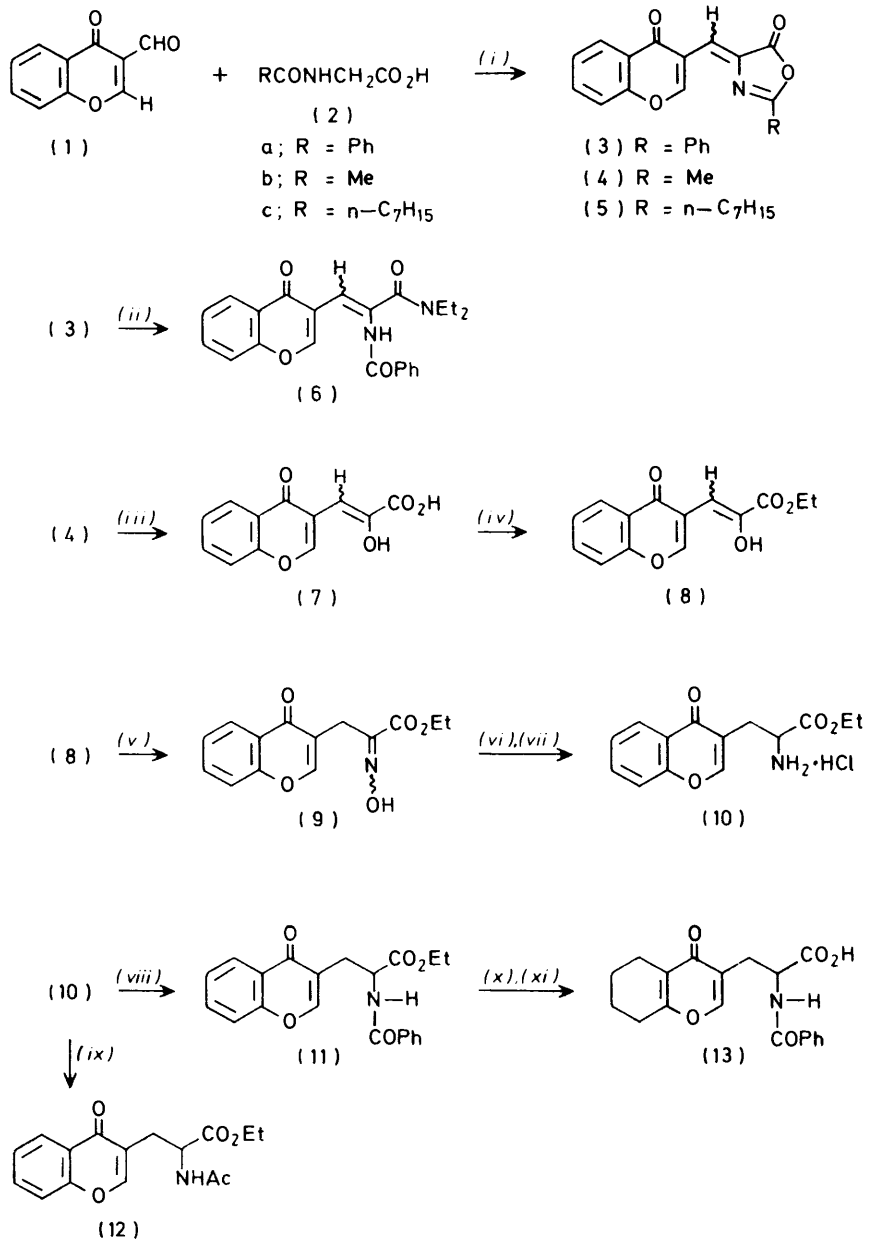
Additional support for the structural assignment of (6) was provided by a comparison of the ^{13}C n.m.r. spectra of the pyrrole and (6). The chemical shift of the pyrone carbonyl at δ 177.5 was consistent with that reported characteristic for the pyrone carbonyl in the literature (I. W. J. Still, N. Plavac, D. M. McKinnon, and M. S. Chauhan, *Can. J. Chem.*, 1976, **54**, 280).

‡ Treatment of (7) with hydroxylamine hydrochloride gave a product whose elemental analysis, melting point, and spectral data were identical to those reported in the literature for 4-oxo-4*H*-1-benzopyran-3-acetonitrile (S. Klutchko, M. P. Cohen, J. Shavel, jun., and M. von Strandtmann, *J. Heterocyclic Chem.*, 1974, **11**, 183).

benzaldehydes substituted in the *ortho* position with a carboxy or a carboxamide function.

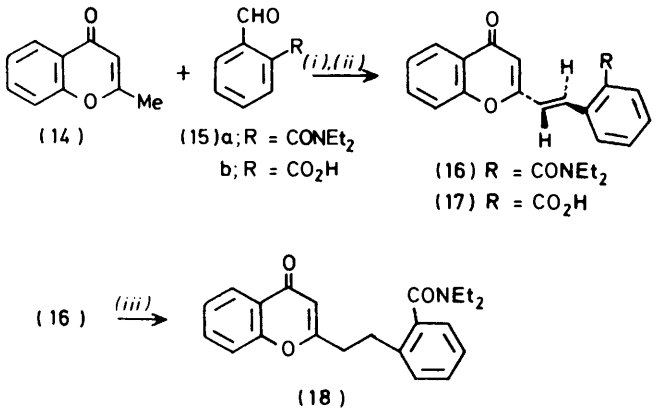
For example, styryl compounds (16) and (17) were prepared in this manner in yields of 33 and 31%, respectively.

Compound (17) was potentially important biologically since it contained an acid function conjugated to the pyrone nucleus.[2] The styryl chromones (16) and (17) were assigned the expected *trans* configuration on the basis of their ^{1}H n.m.r. spectra, which had a signal for a doublet (1 H) at δ *ca.* 6.8 (J 17 Hz). Catalytic hydrogenation of (16) with 10% palladium–charcoal in acetic acid selectively reduced the disubstituted double bond to give amide (18). Effects to improve the yield of (16) with lithium di-isopropylamide as the condensation reagent in tetrahydrofuran, or tetrahydrofuran–hexamethylphosphoramide were unsuccessful. Attempts to condense (14) with diethyl oxalate with magnesium methoxide were unsuccessful. However, conversion of (14) to its anion with lithium di-isopropylamide in hexamethylphosphoramide (1 equiv.)–tetrahydrofuran at −30 °C followed by addition of diethyl oxalate at 0—20 °C gave the ester (19). The ^{1}H n.m.r. spectrum of (19) [δ (TFA–$CDCl_3$) 8.4 (1 H, m, H-5), 8.1—7.4 (4 H, m, aromatic and vinyl), 6.6 (1 H, s, 3-H), 4.6 (2 H, q, J 7.0



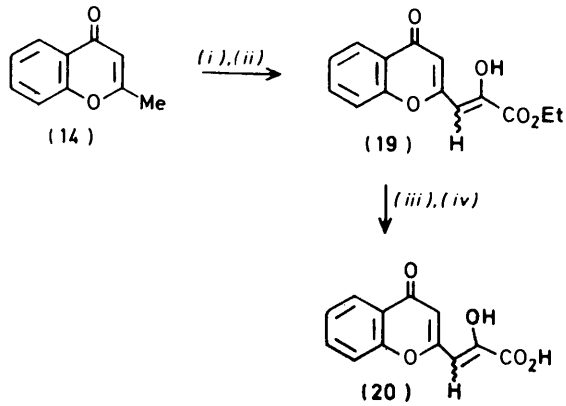
SCHEME 1 (*i*) NaOAc–Ac_2O; (*ii*) $HNEt_2$–dioxan; (*iii*) 12% HCl; (*iv*) EtOH, H_2SO_4; (*v*) NH_2OH–pyridine–EtOH; (*vi*) Zn–HOAc; (*vii*) Et_2O–HCl; (*viii*) PhCOCl–pyridine; (*ix*) Ac_2O–pyridine; (*x*) 2% KOH; (*xi*) HCl

Hz, CH_2), and 1.5 (3 H, t, *J* 7.0 Hz, Me)] indicated that in this solvent system the compound exists exclusively as the enolic tautomer (19). To the best of our knowledge



SCHEME 2 (*i*) $Mg(OMe)_2$–MeOH; (*ii*) HOAc–HCl; (*iii*) H_2–Pd/C–HOAc

this is the first example of a condensation between 2-methylchromone and an ester. Treatment of (19) with 2.0% aqueous potassium hydroxide at room temperature followed by acidification gave the desired acid (20). The



SCHEME 3 (*i*) LDA–HMPA (1 equiv.)–THF; (*ii*) $(CO_2Et)_2$; (*iii*) 2.0% KOH; (*iv*) HCl

^1H n.m.r. of (20) indicated that it also existed as the enol tautomer in $[^2H_6]$DMSO.

EXPERIMENTAL

Melting points were determined in open capillaries with a Thomas-Hoover apparatus. The i.r. and u.v. spectra were obtained on Perkin-Elmer 521 and Perkin-Elmer 350 recording spectrometers, respectively. U.v. spectra were run in 95% ethanol unless otherwise indicated. N.m.r. spectra were obtained on a Varian A60A spectrometer. Mass spectra were obtained on a Finnigan 1015 quadrupole mass spectrometer.

N-(1-Octanoyl)glycine (2c).—To a stirred solution of glycine (15.0 g, 0.2 mol) in 10% sodium hydroxide (200 ml) at room temperature was added octanoyl chloride (32.4 g, 0.2 mol) dropwise. The mixture was stirred for 1 h at ambient temperature and was then neutralized with glacial acetic acid. The resulting precipitate when recrystallized from ethanol gave the product (18.5 g), m.p. 105—106 °C. The compound was not further characterized.

2-Methyl-4-[(4-oxo-4H-1-benzopyran-3-yl)methylene]-1,3-oxazol-5(4H)-one (4).—A mixture of chromone-3-carbaldehyde (1) [14] (17.4 g, 0.1 mol), acetylglycine (Aldrich) (2b) (7.51 g, 0.10 mol), and anhydrous sodium acetate (8.2 g, 0.10 mol) was heated and stirred in acetic anhydride (50 ml) on a steam-bath. The heterogeneous mixture cleared almost at once. The solution turned red and at the end of 15 min a yellow solid precipitated. The solution was allowed to cool to room temperature, and was then diluted with water (150 ml) while cooling in an ice-bath. The resulting suspension was poured into water (350 ml) and the precipitated solid removed by filtration. Recrystallization from dioxan–heptane gave (4) (11.5 g, 45%), m.p. 167—169 °C. Two recrystallizations gave an analytical sample of (4), m.p. 181.5—183 °C (Found: C, 65.65; H, 3.55; N, 5.4. $C_{14}H_9NO_4$ requires C, 65.88; H, 3.55; N, 5.48%); $\nu_{max.}$ (KBr) 1 800, 1 770 (oxazolone CO) and 1 640 cm^{-1} (chromone CO); δ ($[^2H_6]$DMSO) 9.4 (1 H, s, 2-H),[5] 8.2 (1 H, m, 5-H), 7.95—7.2 (4 H, m, aromatic and vinyl), and 2.4 (3 H, s, Me); $\lambda_{max.}$ 335 nm (ε 10 001).

2-Heptyl-4-[(4-oxo-4H-1-benzopyran-3-yl)methylene]-1,3-oxazol-5(4H)-one (5).—A mixture of chromone-3-carboxaldehyde (1) (15.7 g, 0.09 mol), *N*-(1-octanoyl)glycine (2c) (17.8 g, 0.09 mol), and anhydrous sodium acetate (8.4 g, 0.10 mol) in acetic anhydride (50 ml) was treated as above. Recrystallization from chloroform–heptane gave 8.0 g (26%), m.p. 118—119 °C. A second recrystallization from ethyl acetate gave an analytical sample of (5), m.p. 118—119 °C (Found: C, 70.75; H, 6.25; N, 4.1. $C_{20}H_{21}NO_4$ requires C, 70.78; H, 6.24; N, 4.13%); $\nu_{max.}$ (KBr) 1 800, 1 760, and 1 645 cm^{-1}; δ ($CDCl_3$) 9.5 (1 H, s, 2-H), 8.25 (1 H, m, 5-H), 7.75—7.30 (4 H, m, aromatic and vinyl), 2.8—2.5 (2 H, m, CH_2), 2.0—1.0 (10 H, m, $5CH_2$), and 0.92 (3 H, s, Me); $\lambda_{max.}$ 337 nm (ε 19 900).

N-[1-(Diethylamino)-1-oxo-3-(4-oxo-4H-1-benzopyran-3-yl)prop-2-en-2-yl]benzamide (6).—To a stirred suspension of 4-[(4-oxo-4*H*-1-benzopyran-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-one (3) [8] (44.1 g, 0.139 mol) in dry dioxan (1 500 ml) cooled in an ice-bath diethylamine (10.3 g, 0.141 mol) was added dropwise. At the end of 1 h a solid had precipitated. The mixture was stirred for an additional hour and the solid was collected on a Buchner funnel to yield 44 g (81%) of a white solid, m.p. 181—183 °C. Recrystallization from methanol–water gave an analytical sample of (6), m.p. 181—183 °C (Found: C, 70.65; H, 5.85; N, 7.15. $C_{33}H_{22}N_2O_4$ requires C, 70.75; H, 5.68; N, 7.18%); $\nu_{max.}$ (KBr) 1 670 and 1 650 cm^{-1} (amide CO), and 1 630 cm^{-1} (chromone CO); $\lambda_{max.}$ 307 nm (ε 6 005); δ ($CDCl_3$) 8.3—8.0 (5 H, m, aromatic and 2-H),[5] 7.6—7.3 (6 H, m, aromatic and amide), 5.4 (1 H, s, vinyl H), 3.5 (4 H, q, *J* 7.0 Hz, 2 × CH_2), and 1.2 (6 H, br t, 2 × Me).

2-Hydroxy-3-(4-oxo-4H-1-benzopyran-3-yl)prop-2-enoic Acid (7).—To a stirred solution of 2-methyl-4-[(4-oxo-4*H*-benzopyran-3-yl)methylene]-1,3-oxazol-5(4*H*)-one (4) (3.0 g, 0.012 mol) in tetrahydrofuran (500 ml) was added 12.0% hydrochloric acid (30 ml). The resulting tan suspension was heated and stirred overnight at reflux. Upon cooling and concentration a yellow solid precipitated (2.5 g, 80%). Recrystallization from methanol–water gave an analytical sample of (7), m.p. 187—189 °C (Found: C, 62.3; H, 3.45. $C_{12}H_8O_5$ requires C, 62.07; H, 3.47%); $\nu_{max.}$ (KBr) 1 700, 1 640, and 1 610 cm^{-1}; $\lambda_{max.}$ 300(sh) (ε 3 904) and 305 nm (4 120).

Ethyl 2-*Hydroxy*-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*prop*-2-*enoate* (8).—A stirred mixture of the above acid (7) (7.0 g, 0.03 mol), sulphuric acid (10.0 ml), and anhydrous ethanol (100 ml) was heated and stirred at reflux overnight. The reaction mixture was concentrated on a rotary evaporator and the resulting oil was extracted into ether. The ether solution was washed with 5.0% sodium hydrogencarbonate and brine, and was then concentrated *in vacuo* to yield 3.5 g (45%) of a solid. Recrystallization from ethanol–water gave (5) (2.0 g), m.p. 117.5—119 °C (Found: C, 64.45; H, 4.35. $C_{14}H_{12}O_5$ requires C, 64.61; H, 4.65%); $\nu_{max.}$ (CH_3Cl_3) 3 475 (enolic OH), 1 715, 1 705 (ester CO), and 1 645 cm^{-1} (chromone CO); δ ($CDCl_3$) 10.11 (1 H, s, enol H), 8.4 (1 H, s, 2-H), 8.3 (1 H, m, 5-H), 8.0—7.3 (3 H, 6-H, 7-H, 8-H), 6.5 (1 H, s, vinyl H), 4.4 (2 H, q, *J* 7.0 Hz, CH_2), and 1.4 (3 H, t, *J* 7.0 Hz, Me).

Ethyl 2-(*Hydroxyimino*)-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)-*propanoate* (9).—A mixture of the above ester (8) (5.60 g, 0.021 mol), hydroxylamine hydrochloride (1.75 g, 0.025 mol), and pyridine (20 ml) was stirred and heated in ethanol (100 ml) overnight. The resulting homogeneous solution was allowed to cool to room temperature, and was then concentrated on a rotary evaporator. The resulting oil was dissolved in dichloromethane, and washed with water and brine. The organic layer was separated, dried ($MgSO_4$), and filtered. The filtrate was concentrated *in vacuo* to give a tan solid (3.0 g, 51%), m.p. 143—145 °C. Recrystallization from dichloromethane–hexane gave an analytical sample of (9), m.p. 144.5—146 °C (Found: C, 60.7; H, 4.55; N, 5.0. $C_{14}H_{13}NO_5$ requires C, 61.09; H, 4.76; N, 5.09%); $\nu_{max.}$ (KBr) 1 710 (broad ester CO), and 1 640 cm^{-1} (chromone CO); $\lambda_{max.}$ 300(sh) (ε 6 938), and 307 nm (6 991); δ ([$^2H_6$]-DMSO) 8.2 (1 H, s, 2-H), 8.1 (1 H, m, 5-H), 7.9—7.3 (3 H, m, 6-H, 7-H, 8-H), 4.2 (2 H, q, *J* 7.0 Hz, CH_2), 3.7 (2 H, s, CH_2), and 1.3 (3 H, t, *J* 7.0 Hz, Me).

Ethyl 2-*Amino*-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*propanoate Hydrochloride* (10).—To a stirred solution of the above ester (9) (3.00 g, 0.011 mol) and carbon tetrachloride (2.0 ml) in acetic acid (150 ml) was added zinc dust (5.0 g, 0.076 mol) in divided portions. The mixture began to effervesce after a short induction period. An additional 5.0 g of zinc and 2.0 ml of carbon tetrachloride was added and the reaction mixture was chilled in an ice-bath. After effervescence ceased, the reaction mixture was stirred for 2 h at room temperature, and the reaction mixture was then filtered through Celite. The filter cake was washed thoroughly with ethyl acetate (350 ml) and water (150 ml). The filtrate was then neutralized with solid potassium carbonate to pH 8.0. The organic layer was separated, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to a light yellow oil which was then dissolved in dry ether. Addition of ethereal hydrochloric acid precipitated a gummy yellow solid which when recrystallized from ethanol–acetonitrile gave (10) (1.9 g, 58%), m.p. 191—193 °C (Found: C, 56.35; H, 5.4; N, 4.55. $C_{14}H_{15}NO_4$·HCl requires C, 56.47; H, 5.42; N, 4.70%); $\nu_{max.}$ 1 740 (broad ester CO) and 1 640 cm^{-1} (chromone CO); $\lambda_{max.}$ 302 (ε 6 880) and 307 nm (6 882); δ (D_2O) 8.3 (1 H, s, 2-H), 8.0 (1 H, dd, *J* 9.0 and 3.0 Hz, 5-H), 7.9—7.4 (3 H, m, 6-H, 7-H, 8-H), 4.5 (1 H, t, *J* 7.0 Hz, CH), 4.3 (2 H, q, *J* 7.0 Hz, OCH_2), 2.9 (2 H, d, *J* 7.0 Hz, CH_2), and 1.2 (3 H, t, *J* 7.0 Hz, Me).

Ethyl 2-(*Benzoylamino*)-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)-*propanoate* (11).—To a stirred solution of the above ester (10) (12.0 g, 0.04 mol) in dry pyridine (100 ml) was added benzoyl chloride (14.5 g, 0.10 mol). The reaction mixture was stirred at room temperature for several hours and was then concentrated and poured into a two-phase dichloromethane–water mixture. The dichloromethane layer was separated, washed with water and brine, and dried ($MgSO_4$). Evaporation of solvent gave a solid, recrystallization of which from ethanol–water gave (11) (10.96 g, 75%), m.p. 135—136 °C (Found: C, 69.25; G, 5.3; N, 3.75. $C_{21}H_{19}NO_5$ requires C, 69.03; H, 5.34; N, 3.83%); $\lambda_{max.}$ 300(sh) (ε 7 168) and 305 nm (7 192).

Ethyl 2-(*Acetylamino*)-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*propanoate* (12).—In a similar manner to that above, (10) (6.00 g, 0.02 mol) and acetic anhydride (5.41 g, 0.053 mol) in pyridine (50 ml) were allowed to react. Recrystallization of the crude solid (5.9 g) from ethanol–water gave an analytical sample of (12), m.p. 123—124 °C (Found: C, 63.1; H, 5.75; N, 4.65. $C_{16}H_{17}NO_5$ requires C, 63.35; H, 5.65; N, 4.62%); δ ($CDCl_3$) 8.2 (1 H, dd, *J* 7.0 Hz, 3.0 Hz, 5-H), 8.1 (1 H, s, 2-H), 7.8—7.2 (3 H, m, 6-H, 7-H, and 8-H), 4.8—4.5 (1 H, m, CH), 4.2 (2 H, q, *J* 7.0 Hz, OCH_2), 3.0 (2 H, d, *J* 7.0 Hz, CH_2), 2.0 (3 H, s, Me), and 1.2 (3 H, t, *J* 7.0 Hz, Me).

2-(*Benzoylamino*)-3-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*propanoic* (13).—A suspension of the above ester (11) (6.46 g, 0.018 mol) was stirred overnight at room temperature in 2.0% aqueous potassium hydroxide (500 ml) and the resulting yellow solution was filtered through Celite. Acidification of the filtrate gave an oil which solidified on standing overnight and recrystallization from ethanol–water gave (13) (5.42 g, 89%), m.p. 199—201 °C (Found: C, 67.55; H, 4.55; N, 4.4. $C_{19}H_{15}NO_5$ requires C, 67.65; H, 4.48; N, 4.15%); $\lambda_{max.}$ 305 (ε 33 108).

2-*Formyl*-NN-*diethylbenzamide* (15a).—A mixture of 2-formylbenzoic acid (Aldrich) (25.0 g, 0.160 mol) and pyridine (1.0 ml) in thionyl chloride (100 ml) was stirred and heated until solution was achieved. Excess of thionyl chloride was removed on a rotary evaporator and the resulting yellow oil was dissolved in dry tetrahydrofuran. To this tetrahydrofuran solution was added diethylamine (50 ml). The reaction mixture was filtered and the filtrate concentrated *in vacuo* to yield a yellow oil (25.0 g); δ ($CDCl_3$) 9.95 (1 H, s, CHO), 7.98—7.1 (4 H, m, aromatic), 3.6 (2 H, q, *J* 7.0 Hz, CH_2), 3.1 (2 H, q, *J* 7.0 Hz, CH_2), 1.3 (3 H, t, *J* 7.0 Hz, Me), and 1.0 (3 H, t, *J* 7.0 Hz, Me). The compound was not further characterized.

(E)-NN-*Diethyl*-2-[2-(4-*oxo*-4H-1-*benzopyran*-2-*yl*)*vinyl*]-*benzamide* (16).—To a solution of magnesium methoxide (24.2 g magnesium in 1 000 ml methanol) was added 2-methylchromone (14) [15] (64.0 g, 0.40 mol) at room temperature under nitrogen, followed by dropwise addition of 2-formyl-*NN*-diethylbenzamide (15a) (81.0 g, 0.40 mol). The resulting mixture was refluxed and stirred for 4 h, then allowed to cool to room temperature and neutralized with glacial acetic acid. The solution was then filtered, the filtrate was concentrated *in vacuo*, and the resulting residue was dissolved in a two-phase water–dichloromethane solution. The dichloromethane layer was separated and washed with 5% sodium hydrogencarbonate, water, and brine. The dichloromethane layer was concentrated *in vacuo* and the resulting oil triturated with ether. The ether was decanted off and the resulting gummy solid was recrystallized (methanol–water) to yield 45.9 g (33%) of a tan solid, m.p. 140—147 °C. One more recrystallization gave an analytical sample of (16), m.p. 159—160 °C (Found: C, 76.1; H, 6.05; N, 3.95. $C_{22}H_{21}NO_3$ requires C, 76.06; H, 6.09; N, 4.03%); δ ($CDCl_3$) 8.2 (1 H, m, aromatic), 8.0—

7.2 (8 H, m, aromatic and vinyl H), 6.8 (1 H, d, *J* 17.0 Hz, vinyl H), 6.3 (1 H, s, 3-H), 3.7 (2 H, q, *J* 7.0 Hz, CH_2), 3.1 (2 H, q, *J* 7.0 Hz, CH_2), 1.4 (3 H, t, *J* 7.0 Hz, Me), and 1.0 (3 H, t, *J* 7.0 Hz, Me); $\nu_{max.}$ (KBr) 1 645, 1 635, and 1 620 cm^{-1}; $\lambda_{max.}$ 327 nm (ε 32 800).

2-[2-(4-*Oxo*-4H-1-*benzopyran*-2-*yl*)*vinyl*]*benzoic Acid* (17).—To a stirred solution of magnesium (2.42 g, 0.10 mol) in methanol (200 ml) at room temperature under argon were added 2-methylchromone (14) (6.40 g, 0.040 mol) and 2-formylbenzoic acid (15b) (Aldrich) (6.00 g, 0.040 mol). The solution was then heated and stirred at reflux for 4 h. The resulting tan solution was neutralized with acetic acid, the methanol was removed *in vacuo*, and the resulting gum was extracted with ether (400 ml) and 5.0% hydrochloric acid (100 ml). The insoluble residue was removed by filtration giving 3.60 g (31%), m.p. 154—156 °C; recrystallization from ethanol–water gave an analytical sample of (17), m.p. 156—159 °C (Found: C, 73.85; H, 4.15%; M^+, 292. $C_{18}H_{12}O_4$ requires C, 73.97; H, 4.14%; *M*, 292).

NN-*Diethyl*-2-[2-(4-*oxo*-4H-1-*benzopyran*-2-*yl*)*ethyl*]*benzamide* (18).—(*E*)-*NN*-diethyl-2-[2-(4-oxo-4*H*-1-benzopyran-2-yl)vinyl]benzamide (16) (13.4 g, 0.039 mol) in acetic acid (150 ml) was hydrogenated over 10% palladium–charcoal (.75 g) at room temperature in a Parr shaker. The catalyst was removed by filtration, and the resulting yellow solution was concentrated *in vacuo* to a yellow oil (13.0 g). Trituation of the oil gave a yellow waxy solid, recrystallization of which from ethyl acetate–heptane gave (18) (5.9 g, 43%), m.p. 83—84 °C (Found: C, 75.65; H, 6.65; N, 3.8. $C_{22}H_{23}NO_3$ requires C, 75.62; H, 6.63; N, 4.01%); $\lambda_{max.}$ 296 (ε 7 885) and 302(sh) nm (7 436); δ 8.2 (1 H, m, aromatic), 7.7—7.2 (7 H, m, aromatic), 6.2 (1 H, s, 2-H), 3.8—2.9 (8 H, m, 4 × CH_2), and 1.5—0.9 (6 H, m, 2 × Me).

Ethyl 2-*Hydroxy*-3-(4-*oxo*-4H-1-*benzopyran*-2-*yl*)*prop*-2-*enoate* (19).—To a stirred solution of lithium di-isopropylamide (0.05 mol) and hexamethylphosphoramide (9.0 ml) in dry tetrahydrofuran at −30 °C under argon was added 2-methylchromone (14) (7.2 g, 0.045 mol) in tetrahydrofuran. The reaction mixture gradually became dark red. The reaction mixture was allowed to warm to −10 °C and then diethyl oxalate (8.06 g, 0.05 mol) was added. The mixture was allowed to warm to room temperature and stirred for 1 h, during this time the colour became lighter and a solid precipitated. The reaction was quenched with saturated ammonium chloride solution, and to the resulting two-phase solution was added acetic acid (5.0 ml). The resulting brown mixture was poured into a mixture of ether (300 ml) and water (500 ml), and the resulting yellow solid was collected by filtration and allowed to air-dry. Recrystallization from ethanol (800 ml) gave (19) (6.3 g, 56%), m.p. 197—199 °C (Found: C, 64.7; H, 4.95. $C_{14}H_{12}O_5$ requires C, 64.61; H, 4.65%); δ (TFA–$CDCl_3$) 8.4 (1 H, m, 5-H), 8.1—7.4 (4 H, m, aromatic and vinyl), 6.6 (1 H, s, 3-H), 4.6 (2 H, q, *J* 7.0 Hz, OCH_2), and 1.5 (3 H, t, *J* 7.0 Hz, Me).

2-*Hydroxy*-3-(4-*oxo*-4H-1-*benzopyran*-2-*yl*)*prop*-2-*enoic Acid* (20).—A heterogeneous mixture of the above ester (19) (2.7 g, 0.10 mol) was stirred in 2% potassium hydroxide (150 ml) at room temperature for 1 h, during which time the solution became homogeneous and turned red. The solution was filtered through Celite and the filtrate was acidified. A fine solid, which precipitated on cooling, was collected, washed well with ether, and air-dried to give a crude solid (1.94 g, 79%), m.p. 201—210 °C. Recrystallization from methanol–water gave an analytical sample of (20), m.p. 215—217 °C (Found: C, 61.85; H, 3.7%; M^+, 232. $C_{12}H_8O_5$, requires C, 62.07; H, 3.47%; *M*, 232); δ ([$^2H_6$]-DMSO) 8.3—7.3 (m, 5 H, aromatic, acid, enol), 7.0 (1 H, s, vinyl), and 6.2 (1 H, s, 3-H).

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