Synthesis and reactions of reduced flavones

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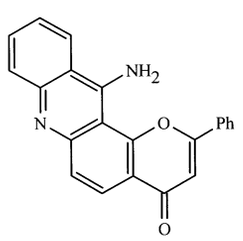
The cycloadditions of a series of 4*H*-pyran-4-ones 3c–e with electron-rich dienes 11a,b to give reduced flavones 12 is described. The subsequent reactions of these reduced flavones with HCl, trifluoroacetic anhydride, ethyl anthranilate 19a and anthranilonitrile 19b is also described.

We have recently described the synthesis of a series of pyranoacridinones, *e.g.* **1**,[1] which are potent inhibitors of the



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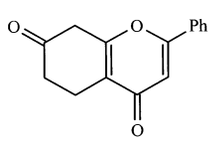

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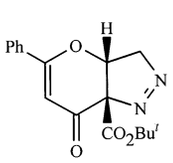

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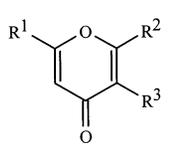

3a R^1 = Ph, R^2 = R^3 = H
3b R^1 = Ph, R^2 = CO_2Et, R^3 = H
3c R^1 = Ph, R^2 = H, R^3 = CO_2Bu^t
3d R^1 = *p*-$MeOC_6H_4$, R^2 = H, R = CO_2Bu^t
3e R^1 = Ph, R^2 = H, R^3 = CO_2Bn

spontaneous proliferation of a human-derived gastric carcinoma cell line, MKN 45, but are non-cytotoxic.[2] A key intermediate in the synthesis of these pyranoacridinones is 7-oxo-5,6,7,8-tetrahydroflavone **2** and, as part of our ongoing investigation into the biological potential of these pyranoacridinones, we have become interested in an alternative, more efficient, synthesis of reduced flavones. We have previously reported a novel method for the synthesis of reduced flavones based on the Diels–Alder reactions of 4*H*-pyran-4-ones with electron-rich dienes.[3] To date very little attention has been paid to cycloadditions of 4*H*-pyran-4-ones, in contrast to the well-documented reactivity of 4*H*-benzopyran-4-ones[4–8] or benzothiopyranones.[9] The only example of the cycloaddition of 4*H*-pyran-4-ones is a footnote by McCombie *et al.*[10] in their paper on the preparation of these compounds in which pyranone **3c** readily reacted with diazomethane in a 1,3-dipolar cycloaddition to give the adduct **4**. In this paper we describe our experimental procedures for the preparation of these ring systems, together with some observations on their chemical reactivity.

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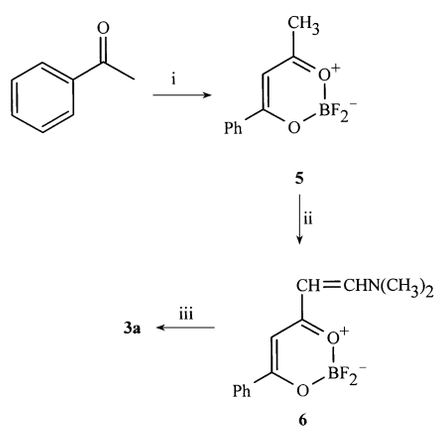
Results and discussion

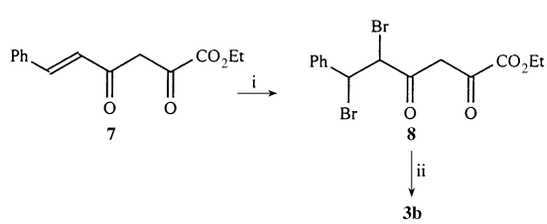
Synthesis of 4*H*-pyran-4-ones

Initially, we required a standard synthesis of a range of substituted pyranone dienophiles for the Diels–Alder reaction. After reviewing the literature the following methodologies were used, mostly with slight modifications. We have prepared the 2-phenyl-4*H*-pyran-4-one **3a** by a modification of Reynolds' method (Scheme 1).[11] The main differences in our procedure are



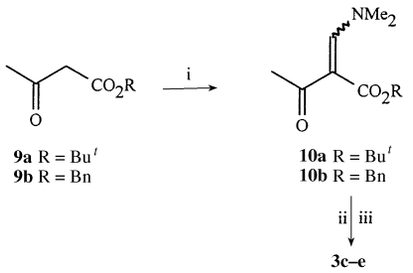
Scheme 1 *Reagents and conditions:* i, Ac_2O, $BF_3{\cdot}Et_2O$; ii, $(CH_3)_2NCH(OCH_3)_2$, DMF; iii, $HClO_4$, EtOH

the use of boron trifluoride–diethyl ether rather than gaseous boron trifluoride, and the work-up procedure in the final step (three steps, 21% overall yield). The method used first by Borsche and Peter[12] proved to be an easy route to ethyl 4-oxo-6-phenyl-4*H*-pyran-2-carboxylate **3b**, in good yield (Scheme 2).



Scheme 2 *Reagents and conditions:* i, Br_2; ii, AcOK, dry EtOH

The preparation of 6-aryl-4-oxo-4*H*-pyran-3-carboxylates **3c–e** has been described by McCombie *et al.* (Scheme 3).[10] This procedure is based on simple starting materials with two effective steps for the formation of the pyranone ring. We have altered

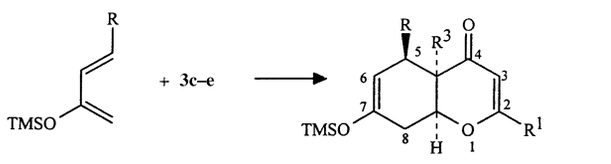


Scheme 3 *Reagents and conditions:* i, $(CH_3)_2NCH(OCH_3)_2$, 80 °C; ii, ArCOCl, $LiN(SiMe_3)_2$, −70 °C; iii, HCl, H_2O, room temp.

the method for the synthesis of the intermediate enaminone **10**; instead of using a dimethylformamide (DMF)–dimethyl sulfate adduct, the enaminone **10** was formed by simple heating of the corresponding keto ester **9** with dimethylformamide dimethyl acetal without the presence of any solvent.[13] With this modification we have prepared the pyranones **3c–3e** in 40–60% yield.

Diels–Alder reactions

The pyranone **3a** without any additional electron-withdrawing groups, and the pyranone **3b**, were unreactive towards 2-trimethylsilyloxybuta-1,3-diene **11a** and Danishefsky's diene **11b** under normal or forced (neat, 160 °C or Lewis-acid catalyst) conditions, while pyranones **3c–3e** reacted smoothly with **11b** and the reaction resulted in formation of the cycloadducts **12a–c** in good yield (Scheme 4). The addition of **3c** to 2-



11a R = H
11b R = OMe

12a R = OMe, R^1 = Ph, R^1 = CO_2Bu^t
12b R = OMe, R^1 = *p*-$MeOC_6H_4$, R^3 = CO_2Bu^t
12c R = OMe, R^1 = Ph, R^1 = CO_2Bn
12d R = H, R^1 = Ph, R^3 = CO_2Bu^t

Scheme 4

trimethylsilyloxybuta-1,3-diene **11a** under the same conditions proceeded more slowly, due to the lower reactivity of the diene, and gave the cycloadduct **12d** in poor yield (**12d** could not be isolated; the ketone **16c** was isolated in 16% overall yield, after treatment of **12d** with 0.01 M aqueous HCl–THF, followed by chromatography).

The ^{1}H NMR spectra of the cycloadducts indicate the presence of only one diastereoisomer, which is quite remarkable as the analogous process led to a 1 : 1 mixture of diastereoisomers in the benzopyranone series.[4]

We have attempted to determine the relative stereochemistry of cycloadduct **12a** by ^{1}H{^{1}H} NOE difference spectroscopy, but irradiation of the doublet for H–5 (δ 4.56) gave only a large NOE to H-6 and a medium NOE to the OMe. Irradiation of the OMe (δ 3.23) was inconclusive. The 3D structure of the cycloadduct **12a** was therefore determined by X-ray crystallography and shows that the methoxy group at C-5 and the ester group at C-4a are *trans* to one another, with the methoxy group in a pseudo-axial position (Fig. 1).

Similar observations were made when the ester-stabilised azomethine ylide **14** (generated from imine **13** in the presence of LiBr as a catalyst) acted as a 4π component in a 1,3-dipolar cycloaddition;[14] whilst **3a,b** were unreactive, in the reaction with pyranone **3d** the cycloadduct **15** was formed in good yield (Scheme 5). The configuration of cycloadduct **15** depicted was verified by ^{1}H{^{1}H} NOE difference spectroscopy, the irradiation of H-7 (δ 5.14) caused enhancement of H-7a (5%), and

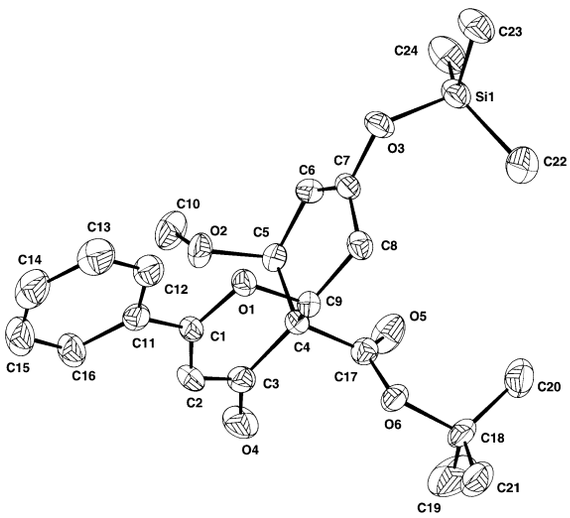
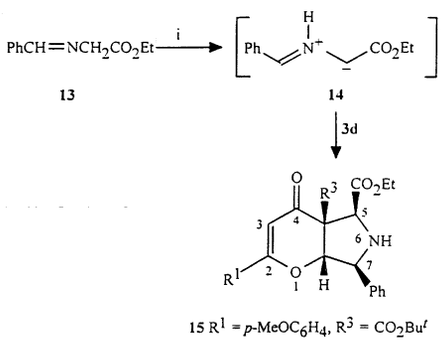


Fig. 1 X-Ray crystal structure of cycloadduct **12a**



15 R^1 = *p*-$MeOC_6H_4$, R^3 = CO_2Bu^t

Scheme 5 *Reagents and conditions:* i, LiBr, Et_3N, MeCN, room temp.

of the *ortho* protons of the 7-phenyl group (7%) whilst there was no NOE observed between H-7 and H-5.

Deprotection of Diels–Alder adducts

Treatment of the cycloadducts **12a,b** with 0.01 M HCl in THF gave the corresponding desilylated products **16a,b**. The brief treatment of **12** or **16** with trifluoroacetic anhydride (TFAA) gave the enones **17a,b** (Scheme 6). In both the treatment with hydrochloric acid and the TFAA, epimerisation of H-8a was observed to give a 1:1 mixture of diastereoisomers. This is unimportant in the synthesis of the pyranoacridinones, *e.g.* **1**, since the groups at the 4a- and 8a-positions will be lost upon aromatisation.

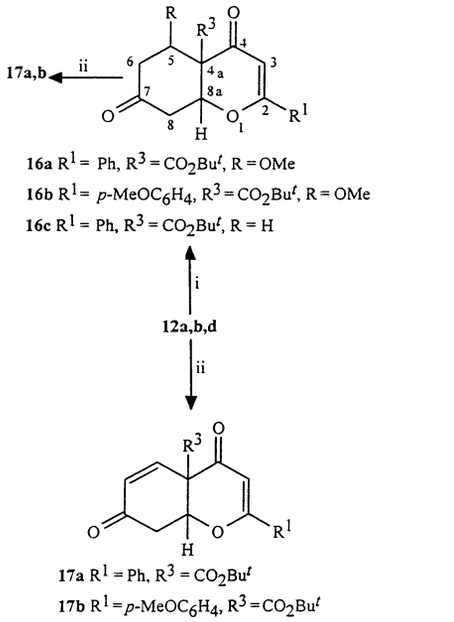
Reduction of enone 17a

To achieve the synthesis of 7-oxotetrahydroflavone **2** or an analogue the selective reduction of the 5,6-double bond of **17a** was necessary (the direct synthesis of **16c** proceeded in poor yield). Our attempts to reduce **17a** by means of PtO_2–H_2, tris(triphenylphosphine)chlororhodium(I) (ethanol, 60 °C, 40 psi‡),[15] or Red-Al–CuBr[16] were unsuccessful. In all cases only the starting material was recovered. The reduction of **17a** with Red-Al gave a complex mixture of products. The use of a large excess of $NaBH_4$ in CH_2Cl_2 solution resulted in the reduction of the 7-oxo group quantitatively and selectively, giving a mixture of diastereoisomers **18** (Scheme 7).

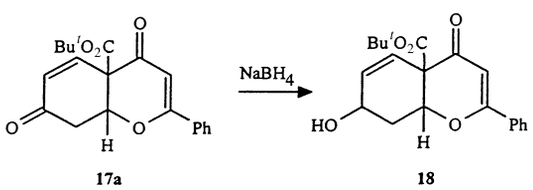
Reaction of reduced flavones with anthranilic acid derivatives

The condensation of **12a** or **12b** with the primary aromatic amines under the standard conditions for azeotropic removal

‡ 1 psi = 6894.76 Pa.

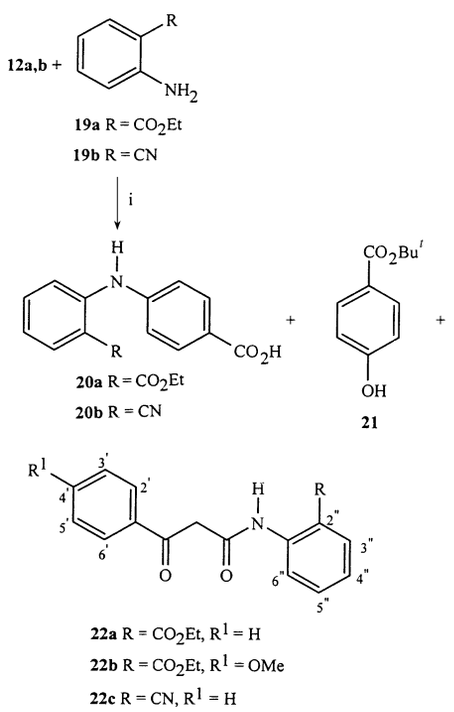


Scheme 6 *Reagents and conditions:* i, 0.01 M HCl–THF; ii, TFAA, CH_2Cl_2



Scheme 7

of water, in the presence of a catalytic amount of toluene-*p*-sulfonic acid (PTSA), resulted in an interesting degradation of the flavone ring system (**12** was deprotected immediately under the harsh conditions used) (Scheme 8). From the complex mixture of products obtained from the reaction of **12a** or **12b** with ethyl anthranilate **19a**, three were identified and at least two by-products remained unidentified (shown by TLC). The main product **20a** crystallised out from the reaction mixture after cooling in both cases. Compounds **21** (identified by comparison of spectroscopic data with literature values[17]) and **22a**, **22b** and **22c** were separated by column chromatography as minor products. The same reactivity was observed in the reaction of anthranilonitrile **19b** with **12a**. These results suggest that the reaction with the amine is not regioselective, *i.e.* unlike our earlier work with **2**[1] there is no distinction between the two carbonyl groups.



Scheme 8 *Reagents and conditions*: i, toluene, PTSA, reflux

Experimental

Mps were determined on a Kofler hot-stage and are uncorrected. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker WM360 spectrometer at 360 and 90 MHz respectively. ^{1}H NMR coupling constants (J) are given in Hz and chemical shifts (δ) are relative to an internal standard of tetramethylsilane. Low resolution electron impact mass spectra were obtained on a Varian CH5-D spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B. IR spectra were recorded on a Perkin-Elmer 1600 series FT-IR spectrometer using sodium chloride plates. Thin layer chromatography was performed on Merck silica gel 60F_{254} and dry column flash chromatography on Merck silica gel 60H. Tetrahydrofuran was dried from sodium–benzophenone.

Crystal data for cycloadduct 12a

$C_{24}H_{32}O_6Si$, $M = 444.59$. Monoclinic, $a = 18.303(2)$, $b = 6.7340(5)$, $c = 19.987(3)$ Å, $\beta = 96.307(12)°$ (by least-squares refinement of the setting angles for 250 reflections within $\theta = 2.05$–$25.09°$), $V = 2448.2(5)$ Å^3, space group $P2_1/c$ (14), $Z = 4$, $D_m = 1.206$ g cm^{-3}, $F(000) = 952$. White crystals. Crystal dimensions 0.25 × 0.18 × 0.14 mm, μ(Mo-Kα) = 0.131 mm^{-1}.

Data collection and processing

FAST TV Area detector diffractometer following previously described procedures.[18] From the ranges scanned, 9823 data were collected ($2.05 \leq \theta \leq 25.09°$), 3687 unique ($R_{int} = 0.0699$).

Structural analysis and refinement

The structure was solved *via* direct methods (SHELX-S)[19] and refined on F_o^2 by full-matrix least-squares (SHELXL-93)[20] using all unique data corrected for Lorentz and polarisation factors to final wR (on F_o^2) and R (on F) values of 0.1015 and 0.0692 for 287 parameters (non-hydrogen atoms anisotropic; hydrogens in idealised positions with U_{iso}s tied to the U_{eq}s of the parents). The corresponding R values for data with $I > 2\sigma(I)$ are 0.0973 and 0.0433, respectively. The weighting scheme used was $w = 1/[\sigma^2(F_o^2) + (0.0467P)^2]$, where $P = [\max(F_o)^2 + 2(F_c)^2]/3$; this gave satisfactory agreement analyses. Sources of scattering factors as in ref. 20. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.§

2-Phenyl-4*H*-pyran-4-one 3a

(i) 2,2-Difluoro-6-methyl-4-phenyl-1,3,2-dioxaborinin-1-ylium-2-uide 5. Acetophenone (2.5 g, 20.8 mmol) was dissolved in acetic anhydride (4.3 g, 47.7 mmol), cooled to 5–10 °C and boron trifluoride–diethyl ether (1.6 g, 11 mmol) was added. After 2 h stirring at room temperature the reaction mixture was evaporated *in vacuo* then diluted with diethyl ether (30 cm^3). The precipitated solid was collected as yellow crystals of the benzoylacetone–boron trifluoride complex **5** (2.84 g, 65%), mp 146 °C (lit.,[11] 147–150 °C) (Found: C, 57.3; H, 4.3. $C_{10}H_9BF_2O_2$ requires C, 57.2; H, 4.3%); ν_{max}(Nujol)/cm^{-1} 1632, 1541 and

§ For details, see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/62.

779; δ_H[$(CD_3)_2SO$] 2.50 (3 H, s, CH_3), 7.28 (1 H, s, CH) and 7.60–7.90 (5 H, m, Ph); *m*/*z* 210 (M^+, 24%), 209 ($M^+ - 1$, 37), 195 (15), 191 (12), 115 (9), 105 (100), 89 (8), 77 (86), 63 (10), 51 (44) and 43 (87).

(ii) 6-(2-Dimethylaminovinyl)-2,2-difluoro-4-phenyl-1,3,2-dioxaborinin-1-ylium-2-uide 6. 2,2-Difluoro-6-methyl-4-phenyl-1,3,2-dioxaborinin-1-ylium-2-uide **5** (1.0 g, 4 mmol) was heated as a suspension in a mixture of dry *N*,*N*-dimethylformamide (2 cm^3) and *N*,*N*-dimethylformamide dimethyl acetal (0.7 cm^3, 5.3 mmol), with stirring, for 1 h at 95–100 °C. On cooling, a yellow–green solid **6** precipitated (0.57 g, 54%), mp 215 °C (lit.,[11] 215–216 °C) (Found: C, 59.0; H, 5.2; N, 5.3. $C_{13}H_{14}BF_2NO_2$ requires C, 58.9; H, 5.3; N, 5.3%); ν_{max}(Nujol)/cm^{-1} 1706, 1640, 1565, 1262 and 823; δ_H($CDCl_3$) 3.02 (3 H, s, NCH_3), 3.25 (3 H, s. NCH_3), 5.05 [1 H, d, *J* 12.0, C*H*=CHN$(CH_3)_2$], 6.13 (1 H, s, H-5), 7.41–7.52 (3 H, m, Ph), 7.93 (2 H, d, *J* 7.9, Ph) and 8.09 [1 H, d, *J* 12.0, C*H*N$(CH_3)_2$]; *m*/*z* 265 (M^+, 38%), 246 (30), 221 (41), 200 (25), 158 (27), 146 (17), 132 (28), 118 (50), 97 (62), 77 (69), 69 (93), 55 (60) and 42 (100).

(iii) 2-Phenyl-4*H*-pyran-4-one 3a. Boron complex **6** (0.3 g, 1.13 mmol) was refluxed in ethanol (10 cm^3) and 60% aqueous perchloric acid (0.5 cm^3) for 6 h. The solvent was evaporated and the residue was dissolved in water (5 cm^3) and extracted with chloroform (3 × 10 cm^3). The combined organic layers were dried over magnesium sulfate and evaporated. The resulting solid was recrystallised from ethanol to give 2-phenyl-4*H*-pyran-4-one **3a** as a white solid (0.14 g, 75%), mp 100–102 °C (lit.,[11] 101–103 °C) (Found: C; 76.6; H, 4.8. $C_{10}H_8O_2$ requires C, 76.7; H, 4.7%); ν_{max}(Nujol)/cm^{-1} 1650 (C=O), 1608, 1414, 1255, 1051, 1015, 925, 891 and 817; δ_H($CDCl_3$) 6.40 (1 H, dd, *J* 5.8 and 2.4, H-5), 6.80 (1 H, d, *J* 2.4, H-3), 7.46–7.52 (3 H, m, H-3′, -4′ and -5′), 7.75–7.78 (2 H, m, H-2′ and -6′) and 7.87 (1 H, d, *J* 5.8, H-6); *m*/*z* 172 (M^+, 54%), 144 (78), 115 (57), 102 (100), 89 (20), 77 (47), 69 (30) and 51 (52).

Ethyl 4-oxo-6-phenyl-4*H*-pyran-2-carboxylate 3b

(i) Ethyl 2,4-dioxo-6-phenylhex-5-enoate 7. Compound **7** was prepared according to the literature procedure[12] as yellow crystals (76%), mp 82–83 °C (lit.,[12] 84 °C); ν_{max}(Nujol)/cm^{-1} 1725 (C=O), 1574, 1264, 1106, 982 and 778; δ_H($CDCl)_3$ 1.41 (3 H, t, *J* 7, CH_3CH_2), 3.93 (0.2 H, s, OH, enol form), 4.31 (2 H, q, *J* 7, CH_2CH_3), 6.55 (1.8 H, s, H-3, keto form), 6.67 (1 H, d, *J* 15.9, H-6), 7.40–7.44 (3 H, m, H-3′, -4′ and -5), 7.55–7.59 (2 H, m, H-2′ and -6′) and 7.74 (1 H, d, *J* 15.9, H-5); *m*/*z* 246 (M^+, 9%), 173 (100), 144 (8), 131 (62), 115 (60), 103 (74), 91 (32), 77 (84), 69 (69), 63 (24) and 51 (56).

(ii) Ethyl 5,6-dibromo-2,4-dioxo-6-phenylhexanoate 8. Compound **8** was prepared according to the literature procedure[12] as yellow crystals (90%), mp 106–107 °C (lit.,[12] 107 °C); ν_{max}(Nujol)/cm^{-1} 1748 (C=O), 1643, 1257, 1131, 1011 and 816; δ_H($CDCl_3$) 1.41 (3 H, t, *J* 7, CH_3), 3.95 (0.2 H, s, OH, enol form, 4.40 (2 H, q, *J* 7, CH_2CH_3), 4.97 (1 H, d, *J* 10.8, H-6), 5.39 (1 H, d, *J* 10.8, H-5), 6.55 (1.8 H, s, H-3, keto form) and 7.26–7.46 (5 H, *m*, Ph); *m*/*z* 407 ($M^+ + 1$, 2%), 182 (6), 173 (36), 143 (31), 131 (37), 115 (68), 103 (57), 91 (13), 77 (75), 69 (100) and 51 (42).

(iii) Ethyl 4-oxo-6-phenyl-4*H*-pyran-2-carboxylate 3b. Compound **3b** was prepared according to the literature procedure[12] as white crystals (65%), mp 127–128 °C (lit.,[12] 130 °C) (Found: C, 69.1; H, 4.9. $C_{14}H_{14}O_2$ requires C, 68.9; H, 4.9%); ν_{max}(Nujol)/cm^{-1} 1735 (C=O), 1635 (C=O), 1614, 1255, 1093, 1058, 1016, 951, 923, 893 and 861; δ_H($CDCl_3$) 1.41 (3 H, t, *J* 7, CH_3), 4.40 (2 H, q, *J* 7, CH_2CH_3), 6.87 (1 H, d, *J* 2.2, H-5), 7.12 (1 H, d, *J* 2.2, H-3), 7.27–7.55 (3 H, m, H-3′, -4′ and -5′), and 7.75–7.88 (2 H, m, H-2′ and -6′); *m*/*z* 244 (M^+, 27%), 216 (23), 188 (25), 171 (9), 144 (30), 112 (33), 102 (100), 77 (32) and 63 (24).

Synthesis of 2-(dimethylamino)methylene-3-oxobutanoates 10 —general procedure

Heating of an oxobutanoates **9** with equimolar quantities of *N*,*N*-dimethylformamide dimethyl acetal at 80 °C in the absence of solvent resulted in the formation of the desired product. The methanol generated in the reaction was removed *in vacuo* to give an oil **10**, in quantitative yield, which was used in the next step without further purification.

***tert*-Butyl 2-(dimethylamino)methylene-3-oxobutanoate 10a.** Orange oil; ν_{max}(Nujol)/cm^{-1} 2974, 2927, 1690 (C=O), 1643 (C=O), 1574, 1486, 1426, 1366, 1291, 1225, 1162, 1114, 1067, 967, 882 and 850; δ_H(60 MHz, $CDCl_3$) 1.5 (9 H, s, Bu^t), 2.3 (3 H, s, CH_3CO), 3.0 [6 H, s, $N(CH_3)_2$] and 7.5 (1 H, s, CH=); *m*/*z* 213 (M^+, 14%), 157 (10), 142 (45), 124 (78), 98 (100), 82 (18), 70 (20), 57 (58) and 43 (95).

Benzyl 2-(dimethylamino)methylene-3-oxobutanoate 10b. Red oil; ν_{max}(Nujol)/cm^{-1} 2927, 1688 (C=O), 1641 (C=O), 1578, 1422, 1362, 1283, 1215, 1187, 1114, 1050, 969, 816, 752 and 700; δ_H(60 MHz, $CDCl_3$) 2.2 (3 H, s, CH_3), 2.9 [6 H, s, $N(CH_3)_2$], 5.1 (2 H, s, CH_2), 7.3 (5 H, s, Ph) and 7.6 (1 H, s, CH=).

Preparation of 6-aryl-4-oxo-4*H*-pyran-3-carboxylates 3c, 3d and 3e

These were prepared according to the procedure described by McCombie *et al*.[10]

***tert*-Butyl 4-oxo-6-phenyl-4*H*-pyran-3-carboxylate 3c.** Pale brown solid (61%), mp 98–100 °C (lit.,[10] 99–102 °C) (Found: C, 70.4; H, 6.1. $C_{16}H_{16}O_4$ requires C, 70.6; H, 5.9%); ν_{max}(Nujol)/cm^{-1} 1705 (C=O), 1664 (C=O), 1347, 1149, 1103, 975, 908, 839 and 772; δ_H($CDCl_3$) 1.57 (9 H, s, Bu^t), 6.84 (1 H, s, H-2), 7.49 (2 H, m, H-3′ and -5′), 7.48 (1 H, m, H-4′), 7.75 (2 H, m, H-2′ and -6′) and 8.78 (1 H, s, H-5); *m*/*z* 272 (M^+, 20%), 257 (8), 217 (37), 199 (38), 171 (35), 147 (28), 144 (32), 115 (43), 95 (42), 75 (56), 69 (41), 65 (42), 51 (60) and 42 (100).

***tert*-Butyl 4-oxo-6-(*p*-methoxyphenyl)-4*H*-pyran-3-carboxylate 3d.** Light brown solid (52%), mp 119–120 °C (Found: C, 67.5; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); ν_{max}(Nujol)/cm^{-1} 1734 (C=O), 1644 (C=O), 1621, 1604, 1574, 1512, 1399, 1310, 1296, 1251, 1235, 1178, 1160, 1077, 1034, 914, 856 and 785; δ_H($CDCl_3$) 1.54 (9 H, s, Bu^t), 3.86 (3 H, s, OMe), 6.75 (1 H, s, H-2), 6.98–7.02 (2 H, m, H-3′ and -5′), 7.67–7.72 (2 H, m, H-2′ and -6′) and 8.48 (1 H, s, H-5); *m*/*z* 302 (M^+ 60%), 287 (5), 247 (51), 229 (60), 202 (78), 174 (40), 161 (54), 146 (47), 135 (60), 115 (41), 102 (45), 89 (55), 77 (56), 69 (53), 63 (54), 57 (100), 53 (64), 43 (57) and 41 (89).

Benzyl 4-oxo-6-phenyl-4*H*-pyran-3-carboxylate 3e. Bright red solid (32%), mp 85–89 °C (Found: C, 74.5; H, 4.8. $C_{19}H_{14}O_4$ requires C, 74.5; H, 4.6%); ν_{max}(Nujol)/cm^{-1} 1706, 1655, 1622, 1395, 1342, 1294, 1266, 1154, 1108, 1025, 994, 969 and 912; δ_H($CDCl_3$) 5.35 (2 H, s, CH_2), 6.85 (1 H, s, H-3), 7.29–7.39 (3 H, m, Ar-H), 7.43–7.52 (5 H, m, Ar-H), 7.71–7.74 (2 H, m, H-2′ and -6′) and 8.58 (1 H, s, H-5); *m*/*z* 306 (M^+, 5%), 288 (3), 200 (88), 172 (100), 144 (10), 129 (22), 115 (52), 105 (71), 91 (95), 77 (96), 69 (54) and 51 (64).

Diels–Alder reactions—general procedure

The pyranone **3c–e** (7 mmol) was dissolved in anhydrous toluene (4 cm^3) and the diene **11b** (9.3 mmol) was added. The mixture was heated at 110 °C for 6 h. The residue was evaporated and recrystallised from diethyl ether–light petroleum (bp 40–60 °C) to yield the desired product **12** as a white powder.

4a-(*tert*-Butoxycarbonyl)-5-methoxy-2-phenyl-7-trimethylsilyloxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4-one 12a. White powder (1.62 g, 52%), mp 125–127 °C (Found: C, 65.0; H, 7.5. $C_{24}H_{32}O_6Si$ requires C, 64.8; H, 7.4%); ν_{max}(Nujol)/cm^{-1} 1730 (C=O), 1652 (C=O), 1598, 1571, 1334, 1251, 1216, 1187, 1162, 1077, 1017, 886 and 851; δ_H($CDCl_3$) 0.23 (9 H, s, $OSiMe_3$), 1.48 (9 H, s, Bu^t), 2.50 (1 H, dd, *J* 19 and 4.4, H-8), 2.69 (1 H, d, *J* 19, H-8), 3.23 (3 H, s, OMe), 4.56 (1 H, d, *J* 5.5, H-5), 5.27 (1 H, d, *J* 4, H-8a), 5.30 (1 H, d, *J* 5.5, H-6), 6.17 (1 H, s, H-3), 7.41 (2 H, m, H-3′ and -5′), 7.43 (1 H, m, H-4′) and 7.74 (2 H, m, H-2′ and -6′); *m*/*z* 444 (M^+, 1%), 343 (22), 223 (20), 157 (20), 141 (25), 105 (72), 89 (11), 77 (24), 73 (78) and 57 (100).

4a-(*tert*-Butoxycarbonyl)-5-methoxy-2-(4′-methoxyphenyl)-7-trimethylsilyloxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4-one 12b. White powder (1.76 g, 53%), mp 163–165 °C (Found: C, 63.3; H, 7.2. $C_{25}H_{34}O_7Si$ requires C, 63.3; H, 7.2%); ν_{max}(Nujol)/cm^{-1} 1731 (C=O), 1671 (C=O), 1594, 1569, 1510, 1426, 1350, 1307, 1254, 1237, 1218, 1189, 1121, 1080, 1030, 1000, 944, 905, 887 and 851; δ_H($CDCl_3$) 0.37 (9 H, s, $OSiMe_3$), 1.45 (9 H, s, Bu^t), 2.47 (1 H, dd, *J* 18.6 and 3.6, H-8), 2.65 (1 H, d, *J* 18.6, H-8), 3.21 (3 H, s, 5-OMe), 3.83 (3 H, s, Ar-OMe), 4.54 (1 H, d, *J* 3.6, H-5), 5.22–5.26 (2 H, m, H-8a and -6), 6.07 (1 H, s, H-3), 6.88 (2 H, d, *J* 8, H-3′ and -5′) and 7.68 (2 H, d, *J* 8, H-2′ and -6′); *m*/*z* 474 (M$^+$, 20%), 459 (5), 418 (8), 373 (75), 359 (12), 341 (13), 319 (21), 303 (12), 287 (10), 241 (10), 223 (53), 193 (22), 157 (60), 141 (55), 135 (77), 77 (51), 73 (75), 57 (100) and 41 (75).

4a-(Benzyloxycarbonyl)-5-methoxy-2-phenyl-7-trimethylsilyloxy-4a,5,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4-one 12c. White powder (1.77 g, 53%), mp 101–103 °C (Found: C, 68.1; H, 6.1. $C_{27}H_{30}O_6Si$ requires C, 67.8; H, 6.3%); ν_{max}(Nujol)/cm^{-1} 1736 (C=O), 1654 (C=O), 1602, 1572, 1345, 1292, 1257, 1229, 1196, 1092, 1074, 1051, 1022, 1004, 956, 890 and 872; δ_H($CDCl_3$) 0.30 (9 H, s, $OSiMe_3$), 2.48 (1 H, dd, *J* 18.7 and 4.5, H-8), 2.70 (1 H, d, *J* 18.7, H-8), 3.33 (3 H, s, OMe), 4.74 (1 H, d, *J* 5.3, H-5), 5.36 (2 H, s, CH_2Ph), 5.30–5.42 (2 H, m, H-6 and -8a), 6.29 (1 H, s, H-3), 7.26–7.62 (8 H, m, Ar) and 7.81–7.86 (2 H, m, H-2′ and -6′); *m*/*z* 478 (M$^+$, 9%), 463 (4), 379 (25), 343 (78), 325 (27), 317 (26), 311 (10), 271 (19), 241 (10), 223 (59), 200 (38), 172 (62), 157 (66), 141 (56), 121 (38), 115 (36), 105 (82), 91 (100), 77 (84), 73 (89), 65 (65), 59 (49) and 45 (38).

4a-(*tert*-Butoxycarbonyl)-2-phenyl-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*b*]pyran-4,7-dione 16c. Pyranone **3c** (0.3 g, 1.10 mmol) was dissolved in toluene (1 cm^3) and diene **11a** (0.93 g, 6.5 mmol) was added. The mixture was heated at 110 °C for 24 h. The residue was treated with 0.01 M HCl–THF (5 cm^3), then washed with saturated aqueous sodium hydrogen carbonate (2 cm^3), dried ($MgSO_4$) and the solvent evaporated. Purification by flash column chromatography gave a white powder **16c** (62 mg, 18%), mp 157–158 °C (Found: C, 70.1; H, 6.9. $C_{20}H_{22}O_5$ requires C, 70.2; H, 6.8%); ν_{max}(Nujol)/cm^{-1} 1732 (C=O), 1726 (C=O), 1660 (C=O), 1595, 1573, 1341, 1296, 1272, 1249, 1151, 1083, 1046, 982 and 842; δ_H($CDCl_3$) 1.54 (9 H, s, Bu^t), 2.13–2.18 (1 H, m), 2.51–2.53 (2 H, m), 2.62–2.69 (2 H, m), 3.00 (1 H, ddd, *J* 15.8, 3.9 and 2.0), 5.39 (1 H, d, *J* 3.4, H-5), 6.07 (1 H, s, H-3), 7.43–7.54 (3 H, m, H-3′, -4′ and -5′) and 7.74 (2 H, d, H-2′ and -6′); *m*/*z* 342 (M$^+$, 18%), 286 (3), 269 (9), 241 (23), 199 (23), 196 (52), 147 (64), 140 (71), 123 (63), 112 (57), 105 (87), 91 (22), 81 (86), 77 (63), 69 (88), 57 (92) and 41 (100).

***tert*-Butyl 5-ethoxycarbonyl-2-(4′-methoxyphenyl)-4-oxo-7-phenyl-4,4a,5,6,7,7a-hexahydropyrano[2,3-*c*]pyrrole-4a-carboxylate 15.** To a solution of pyranone **3d** (0.1 g, 0.33 mmol) and imine **13** (0.07 g, 0.36 mmol) in acetonitrile (10 cm^3), triethylamine (0.035 g, 0.35 mmol) and lithium bromide (0.04 g, 0.46 mmol) were added. The reaction mixture was stirred for 8 h at room temperature, then was poured into saturated aqueous ammonium chloride (6 cm^3). The mixture was extracted with diethyl ether (10 cm^3) and the organic layer was dried ($MgSO_4$), evaporated and the residue was purified by flash chromatography on silica, eluting with light petroleum–ethyl acetate (1:1), to give the title compound **15** as a yellow powder (80 mg, 49%), mp 111 °C (Found: C, 68.3; H, 6.1: N, 2.9. $C_{28}H_{30}NO_7$ requires C, 68.3; H, 6.1: N 2.9%); ν_{max}(Nujol)/cm^{-1} 1688 (C=O), 1606 (C=O), 1585, 1536, 1510, 1308, 1254, 1192, 1176, 1114, 1090, 1022, 998, 913, 866, 837, 798, 775 and 698; δ_H($CDCl_3$) 1.32 (2 H, t, *J* 7, CH_3CH_2), 1.51 (9 H, s, Bu^t) 3.85 (3 H, s, MeO), 4.26 (2 H, q, *J* 7, CH_2), 5.01 (1 H, d, *J* 5.7, H-7a), 5.14 (1 H, t, *J* 5.5, H-7), 5.27 (1 H, d, *J* 3.7, H-5), 6.53 (1 H, s, H-3), 6.87–6.91 (2 H, m, H-3′ and -5′), 7.17–7.28 (5 H, m, Ph) and 7.85–7.88 (2 H, m, H-2′ and -6′); δ_C($CDCl_3$) 13.6 (Me), 27.5 (3 × Me), 45.4 (CH_2), 55.0 (C-5), 55.5 (MeO), 58.4 (C-7), 66.4 (C-7a), 82.9 (C-4a), 101.9 (C-3). 113.9 (C-3′ and -5′), 126.4 (C-2″ and -6″), 128.0 (C-1′), 128.6 (C-2′ and -6′), 129.5 (C-4″), 130.9 (C-3″ and -5″), 141.2 (C-1″), 163.5 (C-4′), 165.8 (C-2), 170.7 (C=O), 171.8 (C=O) and 192.2 (C-4); *m*/*z* 493 (M$^+$ + 1, 2%), 437 (2), 332 (5), 144 (8), 135 (10), 116 (9), 77 (24), 68 (18), 57 (100) and 41 (43).

Desilylation of Diels–Alder adducts—general procedure

The tetrahydroflavone **12** (0.23 mmol) was dissolved in THF (5 cm^3) and 36% aqueous HCl (1 drop) was added. The reaction mixture was stirred for 44 h then saturated aqueous sodium hydrogen carbonate (1 cm^3) was added. The organic layer was separated, dried ($MgSO_4$) and evaporated *in vacuo*. Recrystallisation from light petroleum gave the desired product **16**.

4a-(*tert*-Butoxycarbonyl)-5-methoxy-2-phenyl-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*b*]pyran-4,7-dione 16a. White powder (90 mg, 82%), mp 150–151 °C (Found: C, 67.8; H, 6.6. $C_{21}H_{24}O_6$ requires C, 67.7; H, 6.5%); ν_{max}(Nujol)/cm^{-1} 1722 (C=O), 1656 (C=O), 1602, 1574, 1246, 1156, 1095, 1056, 1023, 978, 878 and 842; δ_H($CDCl_3$) 1.52 (9 H, s, Bu^t) 2.66 (1 H, dd, *J* 4.3 and 15.6, H-8), 2.85 (2 H, d, *J* 3.2, H-6), 3.04 (1 H, dd, *J* 15.6 and 2.9, H-8), 3.19 (3 H, s, OMe), 4.47–4.50 (1 H, m, H-5), 5.48–5.53 (1 H, m, H-8a), 6.18 (1 H, s, H-3), 7.40–7.50 (3 H, m, H-3′, -4′ and -5′) and 7.70–7.74 (2 H, m, H-2′ and -6′); *m*/*z* 372 (M$^+$, 16%), 315 (47), 299 (11), 286 (8), 271 (35), 257 (11), 241 (29), 230 (19), 217 (40), 199 (37), 177 (38) 170 (53), 153 (62), 147 (57), 138 (51), 125 (48), 105 (59), 102 (53), 95 (67), 85 (68), 77 (40), 68 (100), 57 (53), 53 (68) and 41 (65).

4a-(*tert*-Butoxycarbonyl)-5-methoxy-2-(4′-methoxyphenyl)-4a,5,6,7,8,8a-hexahydro-4*H*-benzo[*b*]pyran-4,7-dione 16b. White powder (54 mg, 58%), mp 139–40 °C (Found: C, 65.9: H, 6.7. $C_{22}H_{26}O_7$ requires C, 65.7; H, 6.5%); ν_{max}(Nujol)/cm^{-1} 1734 (C=O), 1645 (C=O), 1594, 1588, 1510, 1426, 1346, 1296, 1260, 1238, 1207, 1178, 1113, 1081, 1059, 1031, 979 and 878; δ_H($CDCl_3$) 1.47 (9 H, s, Bu^t), 2.65 (1 H, dd, *J* 15.5 and 4.2, H-8), 2.85 (2 H, d, *J* 3.3, H-6), 3.02 (1 H, br d, *J* 15.7, H-8), 3.18 (3 H, s, 5-OMe), 3.86 (3 H, s, 4′-OMe), 4.48–4.49 (1 H, m, H-5), 5.48–5.52 (1 H, m, H-8a), 6.10 (1 H, s, H-3), 6.92 (2 H, d, H-3′ and -5′) and 7.62 (2 H, d, H-2′ and -6′); δ_C($CDCl_3$) 27.9 (3 × CH_3), 43.2 (C-8), 43.4 (C-6), 55.5 (4′-MeO), 58.6 (C-5), 58.3 (CMe_3), 80.5 (C-8a), 81.6 (5-MeO), 83.6 (C-4a), 101.5 (C-3), 114.3 (C-3′ and -5′), 124.4 (C-1′), 128.7 (C-2′ and -6′), 162.8 (C-4′), 167.8 (C-2), 170.8 (CO_2Bu^t), 189.2 (C-4) and 204.5 (C-7); *m*/*z* 402 (M$^+$, 41%), 370 (10), 345 (37), 329 (13), 301 (13), 271 (30), 247 (25), 229 (21), 216 (11), 207 (20), 176 (100), 153 (17), 135 (68), 121 (49), 107 (32), 92 (37), 85 (52), 77 (53), 67 (41), 57 (40) and 42 (50).

Methoxy group elimination—general procedure

The tetrahydroflavone (0.23 mmol) was dissolved in dichloromethane (3 cm^3) and TFAA (1 drop) was added. The reaction mixture was stirred for 30 min then saturated aqueous sodium hydrogen carbonate (1 cm^3) was added. The organic layer was separated, dried ($MgSO_4$) and evaporated *in vacuo*. Recrystallisation from light petroleum gave the desired product **17.**

4a-(*tert*-Butoxycarbonyl)-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4,7-dione 17a. White powder (61 mg, 78%), mp 135–137 °C (Found: C, 70.5; H, 5.9. $C_{20}H_{20}O_5$ requires C, 70.6; H, 5.9%); ν_{max}(Nujol)/cm^{-1} 1731 (C=O), 1687 (C=O), 1660 (C=O), 1601, 1571, 1334, 1294, 1272, 1252, 1151, 1103, 1062, 1028, 1007, 991 and 834; δ_H($CDCl_3$) 1.52 (9 H, s, Bu^t), 2.73 (1 H, dd, *J* 17.2 and 2.6, H-8), 3.12 (1 H, dd, *J* 17.2 and 3.9, H-8), 5.48–5.50 (1 H, m, H-8a), 6.18 (1 H, s, H-3), 6.24 (1 H, d, *J* 10.1, H-6), 6.64 (1 H, d, *J* 10.1, H-5), 7.42–7.54 (3 H, m, H-3′, -4′ and -5′) and 7.70–7.73 (2 H, m, H-2′ and -6′); δ_C($CDCl_3$) 27.8 (3 × CH_3), 40.0 (C-8), 58.7 (CMe_3), 81.6 (C-8a), 84.3 (C-4a), 102.8 (C-3), 126.6 (C-2′ and -6′), 128.8 (C-3′ and -5′), 131.4 (C-4′), 131.8 (C-1′), 132.4 (C-7), 140.6 (C-5), 166.1 (C-2), 170 (CO_2Bu^t), 187.2 (C-4) and 193.3 (C-7); *m*/*z* 341 (M$^+$ + 1, 18%), 340 (M$^+$, 7), 315 (15), 215 (38), 267 (20), 241 (21), 211 (19), 194 (28), 183 (13), 165 (13), 153 (24), 147 (57),

138 (58), 128 (29), 121 (61), 110 (33), 105 (80), 93 (48), 81 (76), 76 (91), 65 (55), 63 (65), 51 (71) and 42 (100).

4a-(*tert*-Butoxycarbonyl)-2-(4′-methoxyphenyl)-4a,7,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4,7-dione 17b. White powder (42 mg, 49%), mp 128 °C (Found: C, 68.1; H, 6.1. $C_{20}H_{22}O_5$ requires C, 68.1; H, 6.0%); ν_{max}(Nujol)/cm^{-1} 1726 (C=O), 1686 (C=O), 1661 (C=O), 1606, 1588, 1565, 1511, 1425, 1326, 1312, 1299, 1272, 1239, 1183, 1155, 1120, 1102, 1064, 1036, 1004 and 898; δ_H($CDCl_3$), 1.52 (9 H, s, Bu^t), 2.71 (1 H, dd, *J* 17.2 and 2.6, H-8), 3.10 (1 H, dd, *J* 17.2 and 4.1, H-8), 3.86 (3 H, s, OMe), 5.45–5.47 (1 H, m, H-8a), 6.10 (1 H, s, H-3), 6.23 (1 H, d, *J* 10.1, H-6), 6.64 (1 H, m, H-5), 6.92 (2 H, d, H-3′ and -5) and 7.67 (2 H, d, H-2′ and -6′); δ_C($CDCl_3$) 27.9 (3 × CH_3), 40.2 (C-8), 55.6 (OMe), 58.8 (CMe_3), 78.7 (C-8a), 84.3 (C-4a), 100.3 (C-3), 114.3 (C-3′ and -5′), 123.7 (C-1′), 128.7 (C-2′ and -6′), 130.7 (C-6), 141.0 (C-5), 163.3 (C-4′), 166.5 (C-2), 170.1 (CO_2Bu^t), 187.0 (C-4) and 193.7 (C-7); *m*/*z* 370 (M$^+$, 36%), 355 (3), 315 (5), 297 (27), 270 (8), 240 (10), 194 (10), 176 (88), 149 (11), 135 (100), 121 (76), 107 (56), 92 (72), 77 (71), 69 (75), 65 (78), 57 (78), 43 (63) and 41 (80).

4a-(*tert*-Butoxycarbonyl)-7-hydroxy-2-phenyl-4a,7,8,8a-tetrahydro-4*H*-benzo[*b*]pyran-4-one 18. Pyranone **17a** (0.17 g, 0.5 mmol) was dissolved in dry dichloromethane (10 cm^3) and sodium borohydride (0.19 g, 5 mmol) and silica gel (1.0 g) were added. The reaction mixture was stirred for 24 h, then filtered, washed with water (3 cm^3), dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography on silica, eluting with light petroleum–ethyl acetate (2:1), to give **18** as a colourless oil (0.16 g, 94%) (Found: C, 69.9; H, 6.7. $C_{20}H_{22}O_5$ requires C, 70.2; H, 6.5%); ν_{max}(Nujol)/cm^{-1} 3431 (OH), 2977, 2932, 1729 (C=O), 1659 (C=O), 1603, 1573, 1494, 1450, 1392, 1389, 1343, 1256, 1156, 1057, 982, 913 and 843; δ_H($CDCl_3$) 1.52 (9 H, s, Bu^t), 1.99–2.06 (2 H, m, H-8), 2.59–2.65 (1 H, m, H-7), 4.25 (1 H, br s, OH), 5.32–5.33 (1 H, m, H-8a), 5.72 (1 H, d, *J* 9.9, H-5), 6.12 (1 H, s, H-3), 6.18 (1 H, dd, *J* 9.9 and 4.0, H-6), 7.42–7.55 (3 H, m, H-3′, -4′ and -5′) and 7.72–7.75 (2 H, m, H-2′ and -6′); *m*/*z* 345 (M$^+$, 3%), 287 (5), 268 (8), 167 (8), 147 (47), 139 (27), 123 (28), 105 (54), 95 (28), 77 (60), 69 (45), 57 (100), 43 (52) and 41 (80).

Reaction of reduced flavones 12 with anthranilic acid derivatives 19—general procedure

Tetrahydroflavone **12** (0.4 mmol) and anthranilonitrile **19b** (0.4 mmol) or ethyl anthranilate **19a** (0.4 mmol) were dissolved in toluene (10 cm^3) and PTSA (5–10 mg) was added. The reaction mixture was refluxed for 3 h, then was cooled, diluted with diethyl ether (15 cm^3) and methanol (3 cm^3) and extracted with 5% aqueous sodium hydrogen carbonate (4 cm^3). The organic layer was separated, dried ($MgSO_4$), evaporated under reduced pressure and triturated with diethyl ether to give a white powder **20**. The residue was separated by column chromatography on silica, eluting with light petroleum–ethyl acetate (1:1), to give the products **21** and **22**.

4-(2′-Ethoxycarbonylanilino)benzoic acid 20a. From tetrahydroflavone **12a** and ethyl anthranilate **19a**. White–green powder (56 mg, 49%), mp 198–200 °C (Found: C, 67.3; H, 5.4; N, 4.9. $C_{16}H_{15}NO_2$ requires C, 67.4; H, 5.3; N, 4.9%); ν_{max}(Nujol)/cm^{-1} 3291 (NH), 1686 (C=O), 1682 (C=O), 1594, 1569, 1529, 1509, 1421, 1310, 1294, 1261, 1237, 1178, 1161, 1114, 1087, 1016, 929 and 867; δ_H[$(CD_3)_2SO$] 1.29 (3 H, t, *J* 7, CH_3), 4.28 (2 H, q, *J* 7, CH_2), 6.97 (1 H, t, *J* 7.9, H-4′), 7.22 (2 H, d, *J* 8.5, H-3 and -5), 7.44–7.53 (2 H, m, H-5′ and -6′), 7.84 (2 H, d, *J* 8.5, H-2 and -6), 7.91 (1 H, d, *J* 7.9, H-3′), 9.41 (1 H, s, NH) and 12.56 (1 H, br s, CO_2H); *m*/*z* 285 (M$^+$, 100)%), 239 (77), 221 (41), 195 (84), 167 (84), 139 (43), 115 (15), 97 (15), 92 (64), 77 (48), 65 (71), 51 (52), 45 (82) and 43 (53).

***N*-(2″-Ethoxycarbonylphenyl)-3-oxo-3-phenylpropionamide 22a.** From tetrahydroflavone **12a** and ethyl anthranilate **19a**. Colourless oil (21 mg, 17%) (HRMS: calc. for $C_{18}H_{17}NO_4$, 311.1158. Found *M*, 311.1158); ν_{max}(Nujol)/cm^{-1} 1689 (C=O), 1635, 1609, 1589, 1576, 1537, 1492, 1299, 1262, 1190, 1146, 1093, 1021, 993, 886 and 791; δ_H($CDCl_3$) 1.41 (3 H, t, *J* 7, CH_3), 4.30 (1 H, s, H-2, keto form), 4.43 (2 H, q, *J* 7, CH_2CH$_3$), 6.64 (1 H, t, H-4″), 7.26–7.62 (4 H, m, H-3′, -4′, -5′ and -5″), 7.82 (1 H, d, *J* 7.1, H-6″), 8.04–8.08 (2 H, m, H-2′ and -6′), 8.67–8.74 (1 H, m, H-3″), 11.54 (1 H, s, NH) and 14.02 (1 H, s, OH, enol form); *m*/*z* 311 (M$^+$, 99%), 266 (10), 238 (10), 192 (22), 165 (99), 146 (72), 137 (48), 132 (35), 119 (99), 105 (78), 92 (57), 77 (100), 69 (70), 64 (69), 51 (62) and 41 (43).

***N*-(2″-Ethoxycarbonylphenyl)-3-oxo-3-(4′-methoxyphenyl)-propionamide 22b.** From tetrahydroflavone **12b** and ethyl anthranilate **19a**. White powder (30 mg, 22%), mp 110–111 °C (Found: C, 66.8; H, 5.7; N, 4.1. $C_{19}H_{19}NO_5$ requires C, 66.8; H, 5.6; N, 4.1%); ν_{max}(Nujol)/cm^{-1} 1688 (C=O), 1606, 1583, 1538, 1510, 1308, 1297, 1254, 1192, 1176, 1144, 1114, 1090, 1022, 998 and 914; δ_H($CDCl_3$) 1.29 (3 H, t, *J* 7, CH_3), 3.9 (3 H, s, CH_3), 4.19 (2 H, s, H-2, keto form), 4.30 (2 H, q, *J* 7, CH_2CH$_3$), 7.05 (2 H, d, *J* 8.8, H-3′ and -5′), 7.20 (1 H, t, H-4″), 7.58 (1 H, t, H-5″), 7.90 (1 H, dd, *J* 1.5 and 7.9, H-6″), 7.99 (2 H, d, *J* 8.9, H-2′ and -6′) and 8.22 (1 H, d, *J* 8.2, H-3″); *m*/*z* 341 (M$^+$, 61%), 285 (22), 239 (8), 195 (31), 177 (13), 165 (97), 150 (93), 135 (100), 119 (92), 107 (27), 92 (81), 77 (50), 65 (50) and 51 (20).

4-(2′-Cyanoanilino)benzoic acid 20b. From tetrahydroflavone **12b** and anthranilonitrile **19b**. White powder (62 mg, 65%), mp 182 °C (Found: C, 70.5; H, 4.2; N, 11.8. $C_{14}H_{10}N_2O_2$ requires C, 70.6; H, 4.2; N, 11.8%); ν_{max}(Nujol)/cm^{-1} 3326 (NH), 2222 (CN), 1686 (C=O), 1596, 1521, 1316, 1286, 1255, 1207, 1170, 1034, 1010, 937 and 845; δ_H[$(CD_3)_2SO$] 7.05 (2 H, d, *J* 7.9, H-3 and -5), 7.07 (1 H, t, *J* 7.8, H-4′), 7.49 (1 H, t, *J* 7.8, H-5), 7.54 (1 H, d, *J* 8.0, H-6′), 7.59 (1 H, d, *J* 7.8, H-3′), 7.79 (2 H, d, *J* 7.9, H-2, -6) and 8.76 (1 H, s, NH); *m*/*z* 238 (M$^+$, 48%), 220 (47), 192 (52), 166 (37), 136 (38), 105 (57), 91 (91), 75 (74), 63 (58) and 50 (100).

***N*-(2″-Cyanophenyl)-3-oxo-3-phenylproprionamide 22c.** From tetrahydroflavone **12a** and anthranilonitrile **19b**. Red crystals (27 mg, 28%), mp 129 °C (Found: C, 72.4; H, 4.8; N, 10.5. $C_{16}H_{12}N_2O_4$ requires C, 72.4; H, 4.9; N, 10.6%); ν_{max}(Nujol)/cm^{-1} 3271, 2229 (CN), 1697, 1669, 1581 and 1540; δ_H($CDCl_3$) 4.20 (2 H, s, H-2), 7.21 (1 H, m, H-4″), 7.46–7.66 (5 H, m, H-3′, -4′, -5′, -5″ and -6″), 8.06 (2 H, m, H-2′ and -6′), 8.40 (1 H, d, *J* 8.5, H-3″) and 11.34 (1 H, br s, NH); *m*/*z* 264 (M$^+$, 50%), 241 (30), 236 (32), 147 (57), 105 (80), 102 (53), 89 (40), 75 (100), 69 (95), 50 (89) and 43 (57).

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