Organolead-mediated arylation of allyl β-keto esters: selective synthesis of 2'-hydroxyisoflavones

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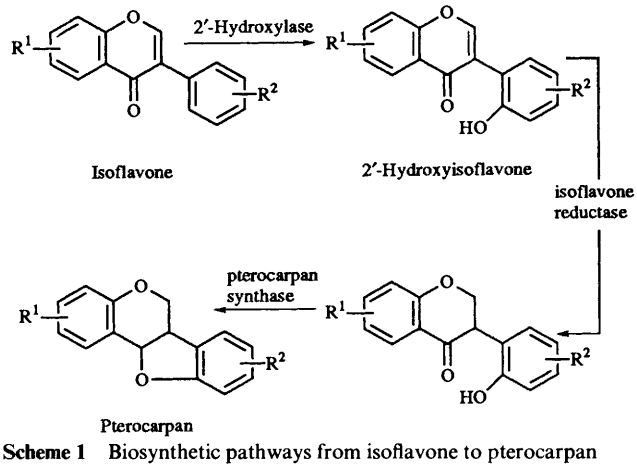
Arylation of the A-ring-unsubstituted and -substituted 3-(allyloxycarbonyl)chroman-4-ones **6–8** with [4,5-dimethoxy-2-(methoxymethoxy)phenyl]lead(IV) triacetate **5** followed by selective catalytic deallyloxycarbonylation–dehydrogenation afforded 2'-protected isoflavones in high overall yields. Acid-catalysed removal of the methoxymethyl group led to the corresponding 2'-hydroxyisoflavones.

Introduction

In contrast to the almost ubiquitous occurrence of flavonoids in higher plants, isoflavonoids have a very limited taxonomic distribution as they are mostly confined to one group of plants, the subfamily *Papilionoideae* of the *Leguminosae*.[1] Structural variations arise from the different skeletal oxidation levels and/or the presence of extra heterocyclic rings. Biosynthetically, isoflavonoids are derived from the flavonoids by a 1,2-aryl migration of the B-ring to the adjacent carbon of the heterocycle. Additional variation is conferred through elaboration of the aryl groups by secondary biosynthetic reactions (hydroxylation, methylation and prenylation) occurring after formation of the basic isoflavonoid skeleton (Scheme 1).[2] Isoflavones are the starting compounds for the formation of the other isoflavonoid classes: isoflavanones, 3-arylcoumarins, pterocarpans, rotenoids and coumestans. The range of biological activities exhibited by isoflavonoids include oestrogenic, insecticidal, piscidal and anti-microbial properties. Many of the most active compounds contain a 2'-hydroxy substituent or a fused cyclic isoprenoid moiety on the B-ring. Isoflavone and pterocarpan derivatives play an important role in the chemical defences of plants. The biological occurrence of isoflavonoids is largely constitutive, whereas pterocarpans are phytoalexins which are induced after exposure to stress, such as wounding, oxidative stress and microbe invasion.[2]

One of the most efficient methods for the synthesis of pterocarpans is based on the hydride reduction of 2'-hydroxyisoflavones, followed by cyclisation.[3] In addition, 2'-hydroxyisoflavones have been used as key intermediates in the synthesis of rotenoids.[4,5] Of the many existing synthetic routes, the thallium(III) trinitrate (TTN)-mediated oxidative rearrangement of chalcones has seen widespread application to the synthesis of isoflavones. An example of this procedure is the recent synthesis[6] of parvisoflavone B, which has been isolated from the trunk wood of *Poecilanthe parviflora*[7] and the root of *Lupinus albus*.[8] However, that method has its limitations, not the least of which is the use of stoichiometric quantities of toxic thallium(III) nitrate. Moreover, the reaction is susceptible to the nature of the substituents: in the case of a 2'-hydroxy-4',5',6'-trioxygenated chalcone, ring-A oxidation by TTN in methanol gave a quinone monoacetal.[9–11] Finally, the yields of isolated isoflavones are often low because nitric acid generated from TTN during reaction causes hydrolysis of labile acetal group[12] or the formation of unwanted nitro by-products.[13] However, this method was used recently by Hesse and co-workers in the synthesis of 2'-substituted isoflavones and the derived isoflavans.[14] All these facts show the important role played by 2'-hydroxyisoflavones and the need for general, efficient and selective methods for their synthesis.

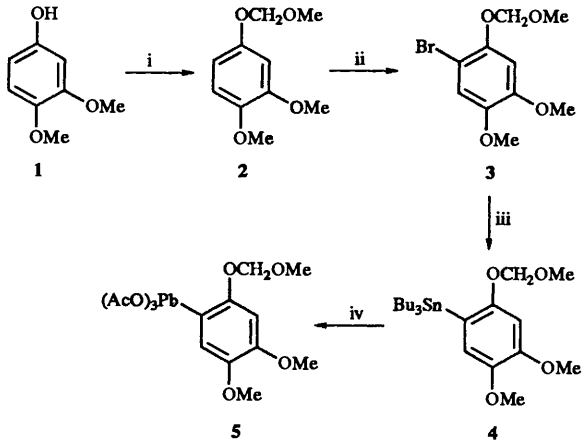


Scheme 1 Biosynthetic pathways from isoflavone to pterocarpan

Results and discussion

In a series of papers, we have recently illustrated our interest in aryllead derivatives for the synthesis of a wide range of flavonoid derivatives, such as 3-aryl-4-hydroxycoumarins,[15] neoflavonoids,[16] isoflavonoids[17,18] and biflavonoids.[19] In these studies as well as in the work of Pinhey,[20] the alkoxyphenyllead reagents were always monomethoxy- or polymethoxy-phenyl derivatives. These are not appropriate for the introduction of suitably protected phenolic moieties since selective hydrolysis of one specific methoxy group could not be performed efficiently. The adaptation of that methodology for the synthesis of 2'-hydroxyisoflavones required the preparation of an aryllead(IV) triacetate containing a conveniently protected 2'-hydroxy substituent. This is due to the fact that monohydric phenols react with lead tetraacetate to give a great variety of oxidation products, among which are *ortho*- or *para*-quinol acetates, *ortho*- or *para*-quinones and quinone diacetates.[21,22] We now report that methoxymethyl (MOM)-protected hydroxyphenyllead triacetates can be prepared and conveniently used in arylation reactions.

The methoxymethyl (MOM) group was chosen as protecting group because of its ease of insertion and selective removal[23] and because of its stability to basic conditions such as those used in the arylation reaction. The tin–lead exchange method

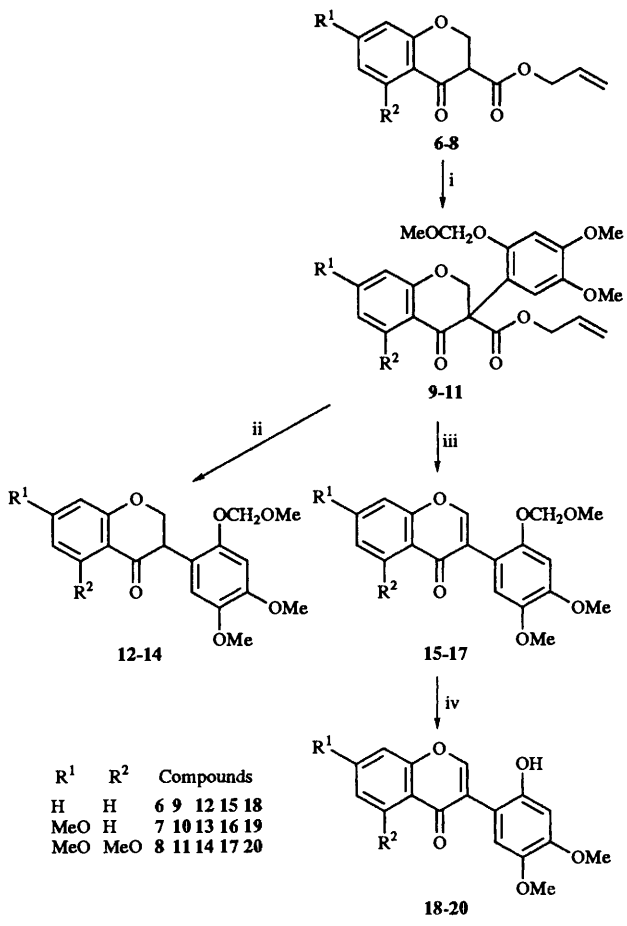


Scheme 2 *Reagents and conditions:* i, BuLi, THF, $MeOCH_2Cl$, 0 °C; ii, NBS, DMF, room temp., 14 h; iii, BuLi, THF, Bu_3SnCl, −78 °C; iv, $Pb(OAc)_4$, $Hg(OAc)_2$ (cat.), $CHCl_3$, 40 °C

was chosen for the synthesis of [4,5-dimethoxy-2-(methoxymethoxy)phenyl]lead(IV) triacetate **5** because of its complete regioselectivity and ease of product isolation.

Protection of the hydroxy group of 3,4-dimethoxyphenol **1** was performed by treatment of its lithium salt with MOM chloride. Reaction of the product **2** with *N*-bromosuccinimide (NBS) led to selective bromination on C-5. Bromine–lithium exchange followed by reaction with tributylstannyl chloride afforded the aryltin compound **4**, which was converted into the lead analogue **5** by transmetallation with lead tetraacetate. The reagent **5** was prepared in 40% overall yield from 3,4-dimethoxyphenol **1** (Scheme 2). The arylation of 3-allyloxycarbonylchroman-4-ones **6–8** with the aryllead triacetate **5** (1.1 mol equiv.) in chloroform at 40 °C in the presence of pyridine (3.3 mol equiv.) proceeded cleanly and in good yield to give the corresponding 3-allyloxycarbonyl-3-[4,5-dimethoxy-2-(methoxymethoxy)phenyl]chroman-4-ones **9–11** in 72–88% yield (Scheme 3). Oxidative deallyloxycarbonylation of esters **9–11** was performed by treatment with $Pd(OAc)_2$ in the presence of 1,2-bis(diphenylphosphanyl)ethane (DPPE) in acetonitrile under reflux for 4.5 h furnishing the corresponding isoflavones **15–17** also in good yield (78–83%). Cleavage of the MOM group was achieved by stirring of the isoflavone at room temp. in CH_2Cl_2–MeOH–HCl for 2 days and yielded the corresponding 2′-hydroxyisoflavones **18–20** in 90–98% yield. Reductive deallyloxycarbonylation of esters **9–11** was performed by treatment of the allyl esters under nitrogen with catalytic amounts of palladium(II) acetate (0.025 mol equiv.), triphenylphosphane (0.5 mol equiv.) and triethylammonium formate (2 mol equiv.) in tetrahydrofuran (THF) at room temp. for 3 days. The protected 2′-hydroxyisoflavanones **12–14** were obtained in quantitative yield. Unfortunately, when deprotection of the MOM group was performed under the conditions previously employed, decomposition predominantly occurred under these relatively strong conditions and the free isoflavanones could not be isolated pure.

These results clearly indicate that arylation with aryllead triacetates can be efficiently and easily extended to the selective introduction of protected phenolic moieties, which can then be deprotected to the free hydroxy group. These conditions are suitable for the synthesis of the not-too-sensitive isoflavones, but they are too harsh for the isoflavanones. For their synthesis, a different type of protecting group should be used, which would require milder deprotection conditions. Work in this direction is now underway and will be reported in due course.



Scheme 3 *Reagents and conditions:* i, **5** (1.1 mol equiv.), pyridine (3.3 mol equiv.), $CHCl_3$, 40 °C; ii, $Pd(OAc)_2$ (0.025 mol equiv.), PPh_3 (0.5 mol equiv.), HCO_2H (2 mol equiv.), Et_3N (2.5 mol equiv.), THF, room temp., 72 h; iii, $Pd(OAc)_2$ (0.05 mol equiv.), DPPE (0.05 mol equiv.), MeCN, reflux; iv, HCl, CH_2Cl_2–MeOH

Experimental

For the general procedures, see previous papers.[17] Ether refers to diethyl ether, FC to flash column chromatography and CC to column chromatography. 3-(Allyloxycarbonyl)chroman-4-one **6**, 3-allyloxycarbonyl-7-methoxychroman-4-one **7** and 3-allyloxycarbonyl-5,7-dimethoxychroman-4-one **8** were prepared as previously reported.[17]

Preparation of 4,5-dimethoxy-2-(methoxymethoxy)phenyllead triacetate 5

(i) **1-Bromo-4,5-dimethoxy-2-(methoxymethoxy)benzene 3.** A solution of NBS (9.8 g, 0.055 mol, 1.1 mol equiv.) in dry DMF (50 cm^3) was added dropwise over a period of 1 h to a solution of 1,2-dimethoxy-4-(methoxymethoxy)benzene **2**[24] (10 g, 0.05 mol) in dry DMF (150 cm^3) under nitrogen in the dark. The solution was stirred for 14 h in the dark and was then poured onto water (200 cm^3), extracted with ether (3 × 100 cm^3) and the extract was dried (Na_2SO_4). An equal volume of light petroleum was added to the ethereal solution. The volume of the solution was reduced gradually by distillation under reduced pressure until a light cloudiness appeared. Light petroleum (~30 cm^3) was added in portions until the product precipitated. The precipitate was filtered off and the process of concentration and addition of light petroleum was repeated several times with the mother liquor. The combined precipitates were dried at the pump (11.8 g, 84%) (Note: the product was found to be sensitive to light or air and readily decomposed

over a period of 1–2 h. However, the compound could be stored as a solution in ether for up to a month with minimal decomposition); δ_H($CDCl_3$; 270 MHz) 3.55 (3 H, s, OCH_2OMe), 3.84 (3 H, s, OMe), 3.86 (3 H, s, OMe), 5.17 (2 H, s, OCH_2O), 6.79 (1 H, s, 3- or 6-H) and 7.01 (1 H, s, 6- or 3-H); δ_C($CDCl_3$; 67.80 MHz) 56.19 (OMe), 56.47 (OMe), 56.53 (OMe), 95.9 (C-1), 96.43 (OCH_2O), 102.71 (C-3), 115.83 (C-6), 144.8 (C-5), 147.8 (C-4) and 149.1 (C-2).

(ii) **Tributyl[4,5-dimethoxy-2-(methoxymethoxy)phenyl]-stannane 4.** 1-Bromo-4,5-dimethoxy-2-(methoxymethoxy)benzene **3** (9.52 g) (freshly precipitated and dried at the pump for 30 min) was dissolved in dry THF (160 cm^3) under nitrogen. The solution was cooled to −78 °C and, after 15 min, butyllithium (15 cm^3 of a 2.5 mol dm^{-3} solution in hexanes, 1.1 mol equiv.) was added dropwise. After 30 min at −78 °C the mixture was treated with a solution of tributylstannyl chloride (16.5 cm^3, 1.8 mol equiv.) in dry THF (40 cm^3) over a period of 30 min. The yellow solution was stirred for 1 h at −78 °C and poured onto water (200 cm^3). The aqueous solution was extracted with ether (3 × 50 cm^3) and the combined ethereal layers were dried (Na_2SO_4), and distilled under vacuum. The stannane **4** was obtained as a liquid after distillation (12 g, 72%), bp 141–144 °C/0.12 mbar; δ_H($CDCl_3$; 270 MHz) 0.86–1.67 (27 H, m, 3 × Bu), 3.47 (3 H, s, OCH_2OMe), 3.85 (3 H, s, OMe), 3.88 (3 H, s, OMe), 5.09 (2 H, s, OCH_2O), 6.79 (1 H, s, 3- or 6-H) and 6.85 (1 H, s, 6- or 3-H); δ_C($CDCl_3$; 67.80 MHz) 9.87 ($SnCH_2$), 13.75 (CH_2Me), 27.40 ($SnCH_2CH_2$), 29.20 (CH_2Me), 55.71 (OMe), 55.84 (OMe), 56.61 (OMe), 95.07 (OCH_2O), 98.70 (C-3), 119.39 (C-6), 119.55 (C-1), 144.16 (C-5), 150.25 (C-4) and 156.74 (C-2).

(iii) **[4,5-Dimethoxy-2-(methoxymethoxy)phenyl]lead triacetate 5.** A mixture of lead tetraacetate (4.6 g, 10.4 mmol), the stannane **4** (5 g, 10.3 mmol) and mercury(II) acetate (0.17 g, 0.53 mmol) in dry chloroform (60 cm^3) was stirred at 40 °C for 7 h. The reaction mixture was cooled, filtered through Celite, and evaporated to dryness. The residue was treated with light petroleum (20 cm^3) and the yellow precipitate was filtered off. The solid was washed with light petroleum (3 × 30 cm^3) and dried to give *title compound* **5** (4.65 g, 78%), mp 105–108 °C; δ_H($CDCl_3$; 270 MHz) 2.10 (9 H, s, 3 × OAc), 3.51 (3 H, s, OCH_2OMe), 3.90 (3 H, s, OMe), 3.91 (3 H, s, OMe), 5.18 (2 H, s, OCH_2O), 6.88 (1 H, s, 3- or 6-H) and 7.28 (1 H, s, 6- or 3-H); δ_C($CDCl_3$; 67.80 MHz) 20.37 ($OCOMe$), 56.34 (OMe), 56.50 (OMe), 56.66 (OMe), 95.86 (CH_2), 99.87 (C-3), 112.86 (C-6), 141.3 (C-5), 145.9 (C-1), 150.86 (C-4), 152.98 (C-2) and 179.69 (CO) (Found: C, 32.75; H, 3.75. $C_{16}H_{22}O_{10}Pb$ requires C, 33.05; H, 3.81%).

General procedure for arylation of 3-(allyloxycarbonyl)-chroman-4-ones 6–8

Anhydrous pyridine (3.3 mol equiv.) was added to a mixture of the appropriate 3-(allyloxycarbonyl)chroman-4-one **6**, **7** or **8** (1 mol equiv.) and [4,5-dimethoxy-2-(methoxymethoxy)-phenyl]lead triacetate **5** (1.1 mol equiv.) in dry chloroform (1 cm^3 per 0.6 mmol of substrate). The resulting mixture was stirred at 40 °C for the times specified. The reaction mixture was diluted with chloroform (50 cm^3) and washed with 6% aq. sulfuric acid (2 × 50 cm^3). The aqueous phase was extracted with chloroform (2 × 50 cm^3). The combined organic extracts were washed with water (2 × 50 cm^3), dried ($MgSO_4$), and the solvent was removed under reduced pressure to yield an oil. The 3-(allyloxycarbonyl)chroman-4-ones were isolated as specified.

Allyl 3-[4′,5′-dimethoxy-2′-(methoxymethoxy)phenyl]-4-oxochromane-3-carboxylate 9. 40 °C for 1 h, FC on silica [eluent: light petroleum–ether (2:1)], 72%, *amorphous powder* from ether–light petroleum, mp 53–55 °C; ν_{max}(KBr)/cm^{-1} 1732 and 1702; δ_H($CDCl_3$; 270 MHz) 3.45 (3 H, s, OCH_2OMe), 3.62 (3 H, s, OMe), 3.85 (3 H, s, OMe), 4.72 (2 H, m, $OCH_2CH{=}CH_2$), 4.91 (1 H, d, *J* 11.36, 2-H), 5.02 (2 H, s, OCH_2O), 5.10 (1 H, d, *J* 11.36, 2-H), 5.22 (2 H, m, $CH{=}CH_2$), 5.88 (1 H, m, $CH{=}CH_2$), 6.40 (1 H, s, 3′- or 6′-H), 6.88 (1 H, s, 6′- or 3′-H), 6.95 (1 H, d, *J* 8.43, 8-H), 7.08 (1 H, m, 6-H), 7.49 (1 H, m, 7-H) and 8.03 (1 H, dd, *J* 1.65 and 7.88, 5-H); δ_C($CDCl_3$; 67.80 MHz) 56.0 (OMe), 56.09 (OMe), 56.28 (OMe), 61.11 (C-3), 66.32 ($OCH_2CH{=}CH_2$), 71.75 (C-2), 95.81 (OCH_2O), 101.05 (C-3′), 112.37 (C-6′), 114.70 (C-1′), 117.88 (C-8), 118.70 ($CH{=}CH_2$), 120.98 (C-6), 127.70 (C-5), 131.42 ($CH{=}CH_2$), 136.03 (C-7), 143.55 (C-5′), 149.72 (C-4′), 150.03 (C-2′), 161.14 (C-9), 168.71 (CO_2allyl) and 188.767 (C-4); *m/z* 428 (M^+, 25%), 308 (8), 278 (8), 263 (10), 235 (7), 206 (30), 191 (8), 178 (17), 163 (6), 45 (100) and 41 (24) (Found: C, 64.7; H, 5.7. $C_{23}H_{24}O_8$ requires C, 64.48; H, 5.65%).

Allyl 3-[4′,5′-dimethoxy-2′-(methoxymethoxy)phenyl]-7-methoxy-4-oxochromane-3-carboxylate 10. 40 °C for 2 h, FC on silica [eluent: light petroleum–ether (1:1)], 83%, *plates* from ether–light petroleum, mp 91–93 °C; ν_{max}(KBr)/cm^{-1} 1723 and 1692; δ_H($CDCl_3$; 270 MHz) 3.46 (3 H, s, OCH_2OMe), 3.82 (3 H, s, OMe), 3.85 (3 H, s, OMe), 3.89 (3 H, s, OMe), 4.71 (2 H, m, CO_2CH_2), 4.91 (1 H, d, *J* 11.36, 2-H), 5.03 (2 H, s, OCH_2O), 5.08 (1 H, d, *J* 11.36, 2-H), 5.23 (2 H, m, $CH{=}CH_2$), 5.89 (1 H, m, $CH{=}CH_2$), 6.37 (1 H, d, *J* 2.38, 8-H), 6.39 (1 H, s, 3′- or 6′-H), 6.63 (1 H, dd, *J* 2.38 and 8.8, 6-H), 6.87 (1 H, s, 6′- or 3′-H) and 7.97 (1 H, d, *J* 8.98, 5-H); δ_C($CDCl_3$; 67.80 MHz) 55.65 (OMe), 55.98 (OMe), 56.09 (OMe), 56.28 (OMe), 60.76 (C-3), 66.17 (CO_2CH_2), 71.97 (C-2), 95.83 (OCH_2O), 100.54 (C-8), 101.0 (C-3′), 110.65 (C-6), 112.53 (C-6′), 114.70 (C-10), 115.30 (C-1′), 118.62 ($CH{=}CH_2$), 129.41 (C-5), 131.53 ($CH{=}CH_2$), 143.52 (C-5′), 149.62 (C-4′), 150.06 (C-2′), 163.19 (C-9), 166.07 (C-7), 168.86 (CO_2allyl) and 187.43 (C-4); *m/z* 458 (M^+, 11%), 308 (14), 276 (7), 263 (10), 235 (7), 206 (20), 191 (9), 178 (16), 163 (7), 151 (6), 122 (3), 107 (7), 45 (100) and 41 (30) (Found: C, 62.95; H, 5.7. $C_{24}H_{26}O_9$ requires C, 62.88; H, 5.72%).

Allyl 3-[4′,5′-dimethoxy-2′-(methoxymethoxy)phenyl]-5,7-dimethoxy-4-oxochromane-3-carboxylate 11. 40 °C for 3 h, FC on silica [eluent: ether–light petroleum (7:1)], 88% as a gum; ν_{max}(KBr)/cm^{-1} 1728 and 1678; δ_H($CDCl_3$; 270 MHz) 3.47 (3 H, s, OCH_2OMe), 3.61 (3 H, s, OMe), 3.79 (3 H, s, OMe), 3.85 (3 H, s, OMe), 3.90 (3 H, s, OMe), 4.68 (2 H, m, $OCH_2CH{=}CH_2$), 4.87 (1 H, d, *J* 11.35, 2-H), 5.05 (1 H, s, OCH_2O), 5.06 (1 H, s, OCH_2O), 5.09 (1 H, d, *J* 11.36, 2-H), 5.22 (2 H, m, $CH{=}CH_2$), 5.90 (1 H, m, $CH{=}CH_2$), 5.98 (1 H, d, *J* 2.2, 6- or 8-H), 6.10 (1 H, d, *J* 2.38, 8- or 6-H), 6.43 (1 H, s, 3′- or 6′-H) and 6.85 (1 H, s, 6′- or 3′-H); δ_C($CDCl_3$; 67.80 MHz) 55.84 (OMe), 55.93 (OMe), 56.06 (OMe), 56.19 (OMe), 56.38 (OMe), 61.07 (C-3), 65.87 (CO_2CH_2), 71.13 (C-2), 93.04 (C-6 or -8), 93.18 (C-8 or -6), 95.78 (CH_2), 100.76 (C-3′), 105.85 (C-10), 113.02 (C-6′), 115.63 (C-1′), 118.24 ($CH{=}CH_2$), 131.86 ($CH{=}CH_2$), 143.28 (C-5′), 149.46 (C-4′), 150.33 (C-2′), 162.55 (C-9), 164.41 (C-5), 165.95 (C-7), 169.17 (CO_2allyl) and 186.18 (C-4); *m/z* 488 (M^+, 9%), 308 (76), 276 (25), 263 (10), 250 (12), 235 (20), 225 (35), 206 (35), 191 (20), 178 (26), 163 (13), 137 (12), 45 (100) and 41 (27).

General procedure for deallyloxycarbonylation of 3-allyloxycarbonyl-3-arylchroman-4-ones 9–11

A solution of the appropriate 3-allyloxycarbonyl-3-arylchroman-4-one (1 mol equiv.), palladium(II) acetate (0.025 mol equiv.), triphenylphosphine (0.5 mol equiv.), formic acid (2 mol equiv.) and triethylamine (2.5 mol equiv.) in dry THF (6 cm^3 per mmol of substrate) was stirred under nitrogen for 3 days. The mixture was then filtered through a short silica column and eluted with chloroform. The eluate was evaporated to yield an oil, which was purified as specified.

4′,5′-Dimethoxy-2′-(methoxymethoxy)isoflavanone 12. CC on silica [eluent: ether–light petroleum (3:1)], 98%, *amorphous powder* from absolute ethanol–light petroleum, mp 89–92 °C;

δ_H($CDCl_3$; 270 MHz) 3.45 (3 H, s, OCH_2OMe), 3.80 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.31 (1 H, *J* 12.55 and 5.6, 3-H), 4.54 (1 H, dd, *J* 12.55 and 5.7, 2-H equatorial), 4.65 (1 H, dd, *J* 12.55 and 11, 2-H axial), 5.07 (2 H, s, OCH_2O), 6.66 (1 H, s, 3'- or 6'-H), 6.83 (1 H, s, 6'- or 3'-H), 7.0–7.09 (2 H, m, 6- and 8-H), 7.50 (1 H, m, 7-H) and 7.98 (1 H, dd, *J* 7.88 and 1.65, 5-H); δ_C($CDCl_3$; 67.80 MHz) 48.47 (C-3), 56.04 (OMe), 56.11 (OMe), 56.42 (OMe), 70.8 (C-2), 95.68 (OCH_2O), 100.95 (C-3'), 113.48 (C-6'), 115.12 (C-10), 117.84 (C-8), 121.43 (C-6), 121.48 (C-1'), 127.6 (C-5), 135.73 (C-7), 144.12 (C-5'), 149.34 (C-2' or -4'), 149.75 (C-4' or -2'), 161.82 (C-9) and 192.54 (C-4); *m/z* 344 (M^+, 52%), 299 (100), 283 (8), 206 (9), 194 (11), 179 (35), 151 (28), 121 (27), 92 (25) and 77 (10) (Found: C, 66.3; H, 5.8. $C_{19}H_{20}O_6$ requires C, 66.27; H, 5.85%).

4',5',7-Trimethoxy-2'-(methoxymethoxy)isoflavanone 13. FC on silica [eluent: ether–light petroleum (10:1)], 97%, *amorphous powder* from absolute ethanol, mp 91–93 °C; δ_H($CDCl_3$; 270 MHz) 3.46 (3 H, s, OCH_2OMe), 3.80 (3 H, s, OMe), 3.86 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.26 (1 H, dd, *J* 12.1 and 5.7, 3-H), 4.51 (1 H, dd, *J* 11 and 5.7, 2-H equatorial), 4.62 (1 H, m, 2-H axial), 5.08 (2 H, s, OCH_2O), 6.45 (1 H, d, *J* 2.38, 8-H), 6.61 (1 H, m, 6-H), 6.65 (1 H, s, 3'- or 6'-H), 6.82 (1 H, s, 6'- or 3'-H) and 7.92 (1 H, d, *J* 8.8, 5-H); δ_C($CDCl_3$; 67.80 MHz) 47.9 (C-3), 55.65 (OMe), 56.04 (OMe), 56.11 (OMe), 56.42 (OMe), 71.18 (C-2), 95.75 (OCH_2O), 100.71 (C-8 or -3'), 100.97 (C-3' or -8), 109.9 (C-6), 113.43 (C-6'), 115.41 (C-10), 129.33 (C-5), 144.09 (C-5'), 149.23 (C-2' or -4'), 149.8 (C-4' or -2'), 163.76 (C-9), 165.79 (C-7) and 191.32 (C-4) (C-1' could not be detected) (Found: C, 64.2; H, 5.8. $C_{20}H_{22}O_7$ requires C, 64.16; H, 5.92%).

4',5,5',7-Tetramethoxy-2'-(methoxymethoxy)isoflavanone 14. FC on silica (eluent: ether), 95%, *amorphous powder* from absolute ethanol–light petroleum, mp 111–112 °C; δ_H($CDCl_3$; 270 MHz) 3.47 (3 H, s, OCH_2OMe), 3.78 (3 H, s, OMe), 3.84 (3 H, s, OMe), 3.85 (3 H, s, OMe), 3.87 (3 H, s, OMe), 4.27 (1 H, dd, *J* 11.2 and 5.5, 3-H), 4.47 (1 H, dd, *J* 10.8 and 5.5, 2-H equatorial), 4.55 (1 H, m, 2-H axial), 5.09 (2 H, s, OCH_2O), 6.10 (2 H, br s, 6- and 8-H), 6.65 (1 H, s, 3'- or 6'-H) and 6.80 (1 H, s, 6'- or 3'-H); δ_C($CDCl_3$; 67.80 MHz) 47.94 (C-3), 55.58 (OMe), 55.76 (OMe), 56.03 (OMe), 56.11 (OMe), 56.45 (OMe), 70.77 (C-2), 93.03 (C-6 or -8), 93.28 (C-8 or -6), 95.98 (OCH_2O), 101.0 (C-3'), 106.6 (C-10), 113.3 (C-6'), 116.28 (C-1'), 144.0 (C-5'), 148.99 (C-2' or -4'), 149.84 (C-4' or -2'), 162.59 (C-9), 165.23 (C-5), 165.65 (C-7) and 189.96 (C-4); *m/z* 404 (M^+, 51%), 359 (16), 331 (22), 224 (63), 192 (64), 179 (36), 151 (29), 137 (15), 121 (12) and 45 (100) (Found: C, 62.2; H, 6.0. $C_{21}H_{24}O_8$ requires C, 62.37; H, 5.98%).

General procedure for deallyloxycarbonylation–dehydrogenation of 3-allyloxycarbonyl-3-arylchroman-4-ones 9–11

A solution of the appropriate 3-allyloxycarbonyl-3-arylchroman-4-one (1 mmol) in anhydrous acetonitrile (10 cm^3) was added dropwise to a boiling solution of palladium(II) acetate (0.05 mmol) and DPPE (0.05 mmol) in anhydrous acetonitrile (30 cm^3) under nitrogen over a period of 30 min. The mixture was refluxed for 4 h under nitrogen and was then concentrated to ~ 5 cm^3. The mixture was filtered through a short silica column and eluted with chloroform. The solvent was removed under reduced pressure to yield a solid, which was purified as specified.

4',5'-Dimethoxy-2'-(methoxymethoxy)isoflavone 15. CC on silica [eluent: ether–light petroleum (3:1)], 83%, *amorphous powder* from absolute ethanol, mp 104–105 °C; ν_{max}(KBr)/cm^{-1} 1643; δ_H($CDCl_3$; 270 MHz) 3.43 (3 H, s, OCH_2OMe), 3.86 (3 H, s, OMe), 3.91 (3 H, s, OMe), 5.08 (2 H, s, OCH_2O), 6.89 (1 H, s, 3'- or 6'-H), 6.90 (1 H, s, 6'- or 3'-H), 7.43 (1 H, m, 6-H), 7.49 (1 H, m, 8-H), 7.69 (1 H, m, 7-H), 8.03 (1 H, s, 2-H) and 8.30 (1 H, dd, *J* 1.69 and 7.87, 5-H); δ_C($CDCl_3$; 67.80 MHz) 56.96 (OMe), 56.99 (OMe), 57.24 (OMe), 97.28 (CH_2), 102.53 (C-3'), 114.11 (C-10), 115.22 (C-6'), 118.95 (C-8), 123.13 (C-3), 125.40 (C-1'), 125.99 (C-6), 127.22 (C-5), 134.34 (C-7), 144.95 (C-5'), 150.66 (C-2' and -4'), 155.43 (C-2), 157.10 (C-9) and 177.13 (C-4); *m/z* 342 (M^+, 72%), 297 (100), 282 (10), 281 (25) and 266 (20) (Found: C, 66.75; H, 5.3. $C_{19}H_{18}O_6$ requires C, 66.66; H, 5.3%).

4',5',7-Trimethoxy-2'-(methoxymethoxy)isoflavone 16. FC on silica [eluent: ether], 82%, *amorphous powder* from absolute ethanol, mp 134–135 °C; ν_{max}(KBr)/cm^{-1} 1632; δ_H($CDCl_3$; 270 MHz) 3.43 (3 H, s, OCH_2OMe), 3.86 (3 H, s, OMe), 3.90 (3 H, s, OMe), 3.91 (3 H, s, OMe), 5.07 (2 H, s, OCH_2O), 6.86 (1 H, d, *J* 2.38, 8-H), 6.88 (1 H, s, 3'- or 6'-H), 6.90 (1 H, s, 6'- or 3'-H), 6.99 (1 H, m, 6-H), 7.94 (1 H, s, 2-H) and 8.19 (1 H, d, *J* 8.79, 5-H); δ_C($CDCl_3$; 67.80 MHz) 55.82 (OMe), 56.07 (OMe), 56.11 (OMe), 56.34 (OMe), 96.46 (CH_2), 100.16 (C-8), 101.76 (C-3'), 113.43 (C-10), 114.13 (C-6 and -6'), 118.40 (C-3), 122.05 (C-1'), 127.70 (C-5), 144.07 (C-5'), 149.69 (C-4'), 149.76 (C-2'), 154.10 (C-2), 157.94 (C-9), 163.91 (C-7) and 175.67 (C-4); *m/z* 372 (M^+, 80%), 357 (10), 341 (10), 327 (100), 311 (27), 299 (30), 296 (18) and 281 (5) (Found: C, 64.75; H, 5.5. $C_{20}H_{20}O_7$ requires C, 64.51; H, 5.41%).

4',5,5',7-Tetramethoxy-2'-(methoxymethoxy)isoflavone 17. FC on silica [eluent: ethyl acetate], 78%, *amorphous powder* from absolute ethanol, mp 200–204 °C; ν_{max}(KBr)/cm^{-1} 1645; δ_H($CDCl_3$; 270 MHz) 3.42 (3 H, s, OCH_2OMe), 3.85 (3 H, s, OMe), 3.89 (3 H, s, OMe), 3.90 (3 H, s, OMe), 3.93 (3 H, s, OMe), 5.04 (2 H, s, OCH_2O), 6.37 (1 H, d, *J* 2.39, 6- or 8-H), 6.46 (1 H, d, *J* 2.38, 8- or 6-H), 6.84 (1 H, s, 3'- or 6'-H), 6.91 (1 H, s, 6'- or 3'-H) and 7.79 (1 H, s, 2-H); δ_C($CDCl_3$; 67.80 MHz) 55.73 (OMe), 56.03 (OMe), 56.12 (OMe), 56.34 (OMe), 56.41 (OMe), 92.58 (C-8), 96.14 (C-6), 96.65 (CH_2), 101.74 (C-3'), 110.06 (C-10), 113.67 (C-3), 114.76 (C-6'), 122.62 (C-1'), 143.96 (C-5'), 149.42 (C-4'), 149.64 (C-2'), 152.26 (C-2), 159.90 (C-9), 161.37 (C-5), 163.78 (C-7) and 175.25 (C-4); *m/z* 402 (M^+, 100%), 387 (11), 371 (10), 357 (55), 342 (8), 341 (56), 329 (83) and 301 (18) (Found: C, 62.8; H, 5.5. $C_{21}H_{22}O_8$ requires C, 62.68; H, 5.51%).

Hydrolysis of 4',5'-dimethoxy-2'-(methoxymethoxy)-isoflavones—general procedure

The appropriate 4',5'-dimethoxy-2'-(methoxymethoxy)isoflavone was dissolved in methanol–dichloromethane (1:1; 10 cm^3), and hydrochloric acid (5 cm^3 of 5 mol dm^{-3}) was added. The solution was stirred for 48 h and then the precipitate of the corresponding 4',5'-dimethoxy-2'-hydroxyisoflavone was filtered off. The filtrate was extracted with chloroform (3 × 30 cm^3) to yield a second crop of the product on evaporation.

2'-Hydroxy-4',5'-dimethoxyisoflavone 18. 94%, *amorphous yellow powder* from absolute ethanol, mp 182–183 °C; ν_{max}(KBr)/cm^{-1} 1630; δ_H($CDCl_3$; 270 MHz) 3.86 (3 H, s, OMe), 3.90 (3 H, s, OMe), 6.67 (1 H, s, 3'- or 6'-H), 6.68 (1 H, s, 6'- or 3'-H), 7.51 (1 H, m, 6-H), 7.56 (1 H, m, 8-H), 7.77 (1 H, m, 7-H), 8.18 (1 H, s, 2-H), 8.35 (1 H, m, 5-H) and 8.59 (1 H, s, OH); δ_C($CDCl_3$; 67.80 MHz) 55.93 (OMe), 56.80 (OMe), 103.77 (C-3'), 110.68 (C-10), 112.85 (C-6'), 117.99 (C-8), 123.16 (C-3), 125.01 (C-1'), 125.91 (C-6), 126.43 (C-5), 134.47 (C-7), 143.29 (C-5'), 151.08 (C-2'), 151.22 (C-4'), 155.51 (C-2), 155.89 (C-9) and 179.11 (C-4) (Found: C, 68.0; H, 4.8. $C_{17}H_{14}O_5$ requires C, 68.45; H, 4.73%).

2'-Hydroxy-4',5',7-trimethoxyisoflavone 19. 90%, yellow rods from absolute ethanol, mp 200–202 °C (lit.,[25] 203–204 °C); δ_H($CDCl_3$; 270 MHz) 3.86 (3 H, s, OMe), 3.90 (3 H, s, OMe), 3.95 (3 H, s, OMe), 6.66 (1 H, s, 3'- or 6'-H), 6.68 (1 H, s, 6'- or 3'-H), 6.92 (1 H, d, *J* 2.4, 8-H), 7.07 (1 H, dd, *J* 2.4 and 9, 6-H), 8.08 (1 H, s, 2-H), 8.25 (1 H, d, *J* 9, 5-H) and 8.84 (1 H, s, OH).

2'-Hydroxy-4',5,5',7-tetramethoxyisoflavone 20. 98%, *needles* from absolute ethanol, mp 225–226 °C; ν_{max}(KBr)/cm^{-1} 1628;

δ_H($CDCl_3$; 270 MHz) 3.85 (3 H, s, OMe), 3.88 (3 H, s, OMe), 3.92 (3 H, s, OMe), 3.98 (3 H, s, OMe), 6.44 (1 H, d, *J* 2.44, 6- or 8-H), 6.52 (1 H, d, *J* 2.44, 8- or 6-H), 6.59 (1 H, s, 3'- or 6'-H), 6.67 (1 H, s, 6'- or 3'-H), 7.88 (1 H, s, 2-H) and 9.0 (1 H, br s, OH); δ_C($CDCl_3$; 67.80 MHz) 55.91 (OMe), 55.92 (OMe), 56.58 (OMe), 56.87 (OMe), 92.29 (C-8), 96.90 (C-6), 103.53 (C-3'), 108.85 (C-10), 111.09 (C-3), 113.42 (C-6'), 126.09 (C-1'), 142.94 (C-5'), 151.08 (C-2' or -4'), 151.35 (C-4' or -2'), 152.80 (C-2), 159.67 (C-9), 161.33 (C-5), 164.72 (C-7) and 178.56 (C-4) (Found: C, 63.4; H, 5.1. $C_{19}H_{18}O_7$ requires C, 63.68; H, 5.06%).

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