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Isotopic labelling of quercetin 3-glucoside

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Abstract—The potentially important dietary antioxidant, quercetin 3-*O*-β-D-glucoside, has been ^{13}C-labelled at C-2 of the flavonoid unit by synthesis in 15% yield over five steps from [^{13}C]carbon dioxide. The route is appropriate for radiochemical synthesis. Formation of the protected 3-glucosylated flavonol appears to result from [1,7]-sigmatropic rearrangement with migration of a benzyl group followed by cyclisation. A free 5-OH results even when a phosphazene superbase is used.

1. Introduction

The flavonol quercetin[1] **1** is a polyphenolic plant secondary metabolite (Fig. 1), and its *O*-glycosides are found in high concentrations in onions, broccoli, apples, red wine and tea.[2] Epidemiological studies have linked the consumption of diets rich in the polyphenolic compounds produced by plants with a range of health benefits. Quercetin in particular reduces the risk of lung cancer.[3] It has been argued that these health benefits arise from the ability of the various polyphenolics to act as biological antioxidants, scavenging reactive oxygen species within the body. Indeed, quercetin is a more effective antioxidant than vitamin E in vitro, reacting 4.5 times more rapidly with oxygen-centred radicals, and quenching more than three oxygen-centred radicals per flavonol molecule.[4,5] However, while a compound's ability to scavenge radicals is a useful predictor of whether it will act as a food antioxidant, preventing rancidity, it is not sufficient evidence for a role as a biological antioxidant, reducing oxidative damage within the body. Vital to this latter role is the compound's bioavailability.[6,7] In a similar vein, a huge range of biological activities have been demonstrated for quercetin in vitro, but most studies have not even considered whether quercetin, consumed as its glycoside derivatives in the quantities found in the diet, can reach cells in sufficient concentration to elicit the effects observed in vitro.[7,8]

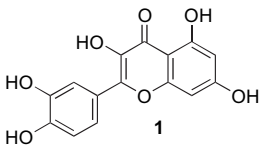

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Figure 1. Quecetin.

In order to understand the absorption, metabolism, distribution and excretion of a compound, it is necessary to identify accurately and quantify the compound and all its metabolites in the various parts of the body. In a recent study,[9,10] we prepared [2-^{14}C]quercetin 4′-glucoside, following our route to [2-^{13}C]quercetin 4′-glucoside,[11] and used it in a feeding study in rats. This was followed by analysis with reversed-phase HPLC with on-line radioactivity detection and ion-trap mass spectrometry capable of performing data dependent MS–MS studies.[12] Radioactivity allowed the location and quantification of quercetin-4′-glucoside-derived material in different tissues (93.6% of ingested radioactivity recovered). The HPLC then separated the metabolites, the radioactivity allowing identification and quantification of those derived from quercetin-4′-glucoside, and MS–MS allowing structural determination so that the HPLC peak assignment was unambiguous. The ion-trap method allowed almost all contributors to HPLC peaks to be identified. In this way we identified 17 different metabolites of the parent flavonol glycoside.[9]

The differential absorption of dietary flavonol glycosides and aglycones is currently attracting a good deal of attention. The parent flavonol, the type of sugar attached, and the position of glycosylation all appear to affect absorption. Indeed, some experiments indicate that lactase phlorizin hydrolase (LPH) hydrolyses quercetin-3-glucoside prior to absorption,[13,14] but that quercetin-4′-glucoside is actively transported by the intestinal sodium-dependent glucose

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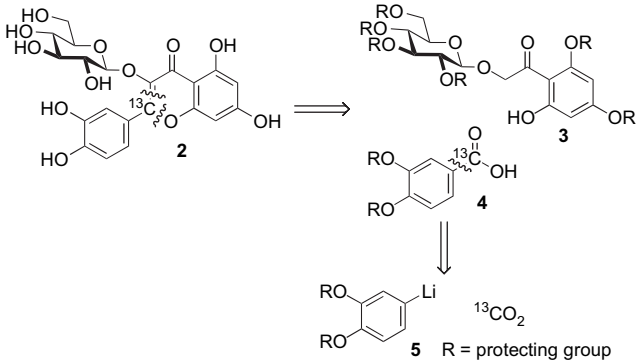
transporter (SGLT1).[15] Other experiments, however, seem to show that these two glucosides interact similarly with SGLT[16] and/or LPH,[17] but that other polyphenols and their glycosides do not. Our synthesis of [2-^{13}C]quercetin-4′-*O*-β-D-glucoside had provided a general route that should be applicable to all flavon-3-ols glycosylated on the B-ring, but did not allow the preparation of 3-*O*-glycosides. The latter are important not only as dietary components themselves, but also as synthetic precursors of dietary anthocyanins[18] (which are invariably glycosylated at the 3-position to enhance stability) and 3-*O*-glucuronides,[19] considered to be important metabolites. Here we report the synthesis of [2-^{13}C]quercetin 3-*O*-β-D-glucoside in a way that should be easy to adapt to ^{14}C-labelling and provides a paradigm for the labelling of other flavonol 3-glycosides:[20,21] the label is introduced from carbon dioxide generated from barium carbonate (barium [^{14}C]carbonate is one of the cheapest sources of carbon-14), and labelling within the flavonoid unit avoids any possibility of loss of radioactivity by exchange under physiological conditions. Labelling using chemical synthesis, rather than biosynthesis,[22] ensures the production of a single compound labelled at a specific site with a controlled amount of the isotope used.

2. Results and discussion

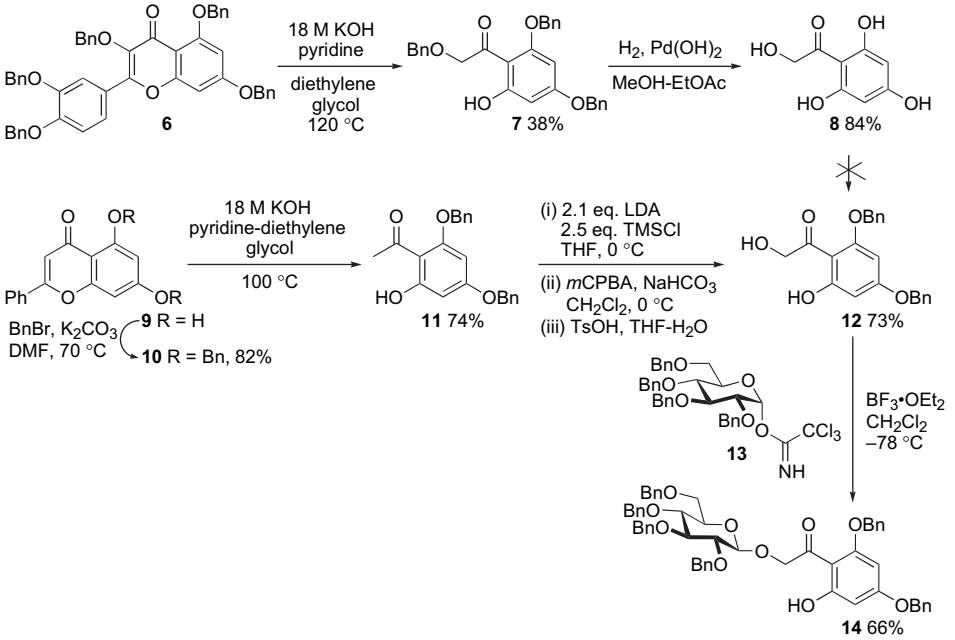
Retrosynthetic analysis of [2-^{13}C]quercetin 3-*O*-β-D-glucoside **2** (Scheme 1) revealed that the key intermediates in the synthesis would be a glycosylated acetophenone **3** with one free phenolic hydroxy group and a labelled carboxylic acid **4**, which would be easily prepared by reaction of an aryllithium **5** with [^{13}C]carbon dioxide. Initially we decided on *O*-benzyl protection, as hydrogenolysis of these groups is known not to affect the flavonoid core or glycosidic links.



Scheme 1. Retrosynthetic analysis of [^{13}C]quercetin 3-glucoside.

In our first approach to glycosylated acetophenone **14** (Scheme 2), fully benzylated quercetin **6** was fragmented to give acetophenone **7** as we had previously reported.[11] Hydrogenation removed all protection, yielding tetraol **8**. Unfortunately attempts to selectively benzylate the phenoxides generated from acetophenone **8** under basic conditions led to a range of products including *C*-benzylated adducts. This is not surprising as the aromatic C–H's that appear at δ_H 5.82 ppm in the ^{1}H NMR spectrum were 95% exchanged for deuterium when acetophenone **8** was heated overnight in D4-methanol (*C*–D appears as a 1:1:1 triplet, *J* 96 Hz, at 95.91 ppm in the ^{13}C NMR spectrum).

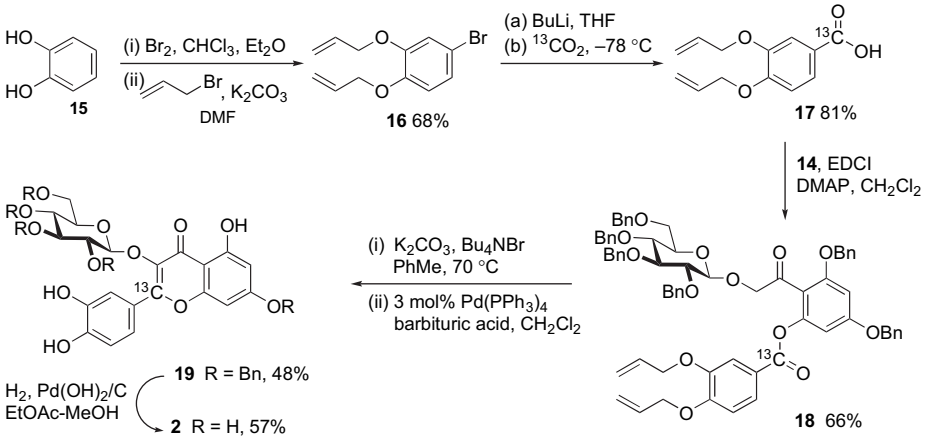
An alternative approach was then investigated. The readily available flavone, chrysin **9**, was benzylated and the resulting flavone **10** fragmented to give acetophenone **11**. Although direct dibenzylation of 2,4,6-trihydroxyacetophenone is possible,[23] we found that reaction under a variety of conditions gave rise to *C*-benzylated and mono-*O*-benzylated by-products that were difficult to remove. The α-hydroxy group was then introduced through Rubottom oxidation[24,25] of the silyl enol ether derived from acetophenone **11**, the phenolic hydroxy group being transiently protected as a TMS ether. The α-hydroxy group of the resulting acetophenone **12** was then glucosylated regioselectively,



Scheme 2. Preparation of acetophenone coupling partner.

without affecting the phenolic hydroxy, and with good β-selectivity using Schmidt's imidate[26,27] **13**. Pure β-anomer **14** was obtained following a single recrystallisation and the stereochemistry was confirmed by the presence of a doublet of *J* 7.6 Hz at 4.34 ppm in the ^{1}H NMR spectrum.

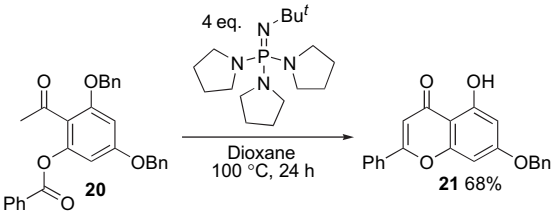
The carboxylic acid coupling partner to acetophenone **14** was synthesised from catechol **15** (Scheme 3). Bromination



Scheme 3. Synthesis of [^{13}C]quercetin 3-*O*-β-D-glucoside.

and double allylation gave aryl bromide **16**, which was lithiated and reacted with $^{13}CO_2$, freshly generated from barium [^{13}C]carbonate using the procedure and apparatus described by Kratzel and Billek,[28] to give carboxylic acid **17** (this and all later steps were tested unlabelled first). Acetophenone **14** and carboxylic acid **17** were then coupled using a water-soluble coupling agent, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, EDCI. Cyclisation of the resulting ester **18** proceeded with loss of the 5-benzyl group, and palladium-catalysed removal of the allyl protecting groups then gave a triol **19** that could be purified. A mixed protecting group strategy was employed because purification had proved too problematic when only benzyl groups were employed, and lithiation–carboxylation of 3,4-dibenzyloxy-1-iodobenzene had proceeded in only 24% yield, probably due to poor solubility of the lithiated species. Global debenzylation of triol **19** completed the synthesis of [2-^{13}C]quercetin 3-*O*-β-D-glucoside **2** in 15% overall yield from barium [^{13}C]carbonate.

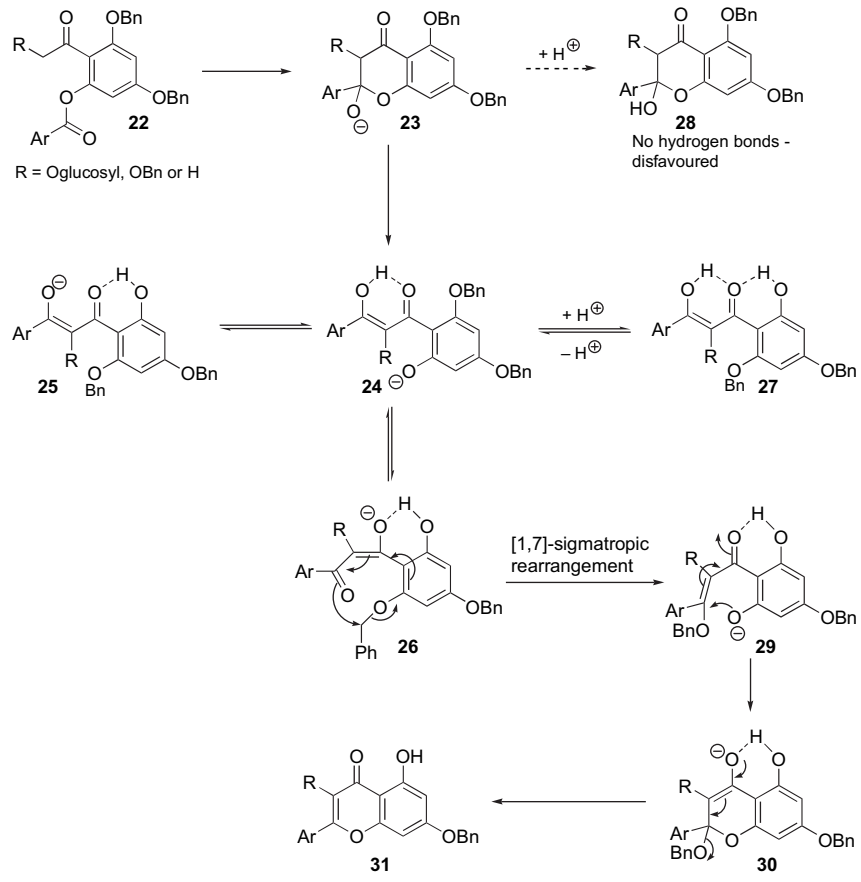
The debenzylation to produce a flavonoid with a free 5-OH by cyclisation–dehydration of ester **18** appeared mechanistically interesting and was examined briefly. A similar debenzylation had occurred in our earlier synthesis of labelled quercetin-4′-glucoside.[11] Benzoate **20** derived from acetophenone **11** was used as a model substrate (Scheme 4). One



Scheme 4. Phosphazene superbase-induced rearrangement.

possibility was that nucleophilic attack by bromide had removed the benzyl group, but when the neutral phosphazene P1 superbase[29,30] was used instead of K_2CO_3 and tetrabutylammonium bromide, ester **20** also cyclised to give monobenzylated chrysin **21**. This excludes the involvement of bromide, but raises the possibility that mono-debenzylation occurred after formation of dibenzylated chrysin as a result of nucleophilic attack by hydroxide generated from water produced in the reaction. However, dibenzylated chrysin **10** was isolated unchanged after treatment under the cyclisation conditions with 1 equiv of water added. Thus, debenzylation must have occurred prior to cyclisation.

A plausible mechanism for the debenzylation–cyclisation of esters **22** is shown in Scheme 5. Such reactions are known to begin with Baker–Venkataraman rearrangement[31] to give 1,3-diketones **27**, which will exist predominantly in their enol form in non-polar solvents. The hydrogen bonding in keto-enol **27** with Ar=Ph and R=H, which was isolated from fragmentation of dibenzylated chrysin **10**, is evident from its crystal structure (Fig. 2), and its ^{1}H NMR spectrum in $CDCl_3$ shows an enolic proton at 15.64 ppm and a chelated phenolic proton at 13.68 ppm. Cyclic alkoxides **23** are intermediates in the Baker–Venkataraman rearrangement and open to give the tautomeric enolates **24**–**26**, which are in equilibrium with each other and diketones **27** (depending on the strength of the base employed). Protonation of the cyclic alkoxides **23** to give cyclic hemiacetals **28**, which would be intermediates in the formation of fully benzylated flavonoids, is less favourable since no intramolecular hydrogen bonding is possible. We suggest that [1,7]-sigmatropic rearrangement[32] of ketones **26** involving migration of a benzyl group, generates phenoxides **29** (such a rearrangement is symmetry allowed if helical geometry allows antarafacial transfer of the benzyl group). The resulting phenoxides **29** would cyclise easily to give enolates **30** as the α,β-unsaturated ketone is made more reactive by hydrogen bonding. Bois et al.[33] and Rama Rao et al.[34] have previously noted the importance of a free *ortho*-hydroxy group in accelerating cyclisations of this sort. Elimination of benzyloxide would then give flavonoids **31**. It is noteworthy that benzyl esters were produced as side products under most conditions employed to cyclise aryl esters **22** (R≠H) to give flavon-3-ol derivatives **31**, and these are presumably formed by transesterification of



Scheme 5. Proposed mechanism of rearrangement–cyclisation.

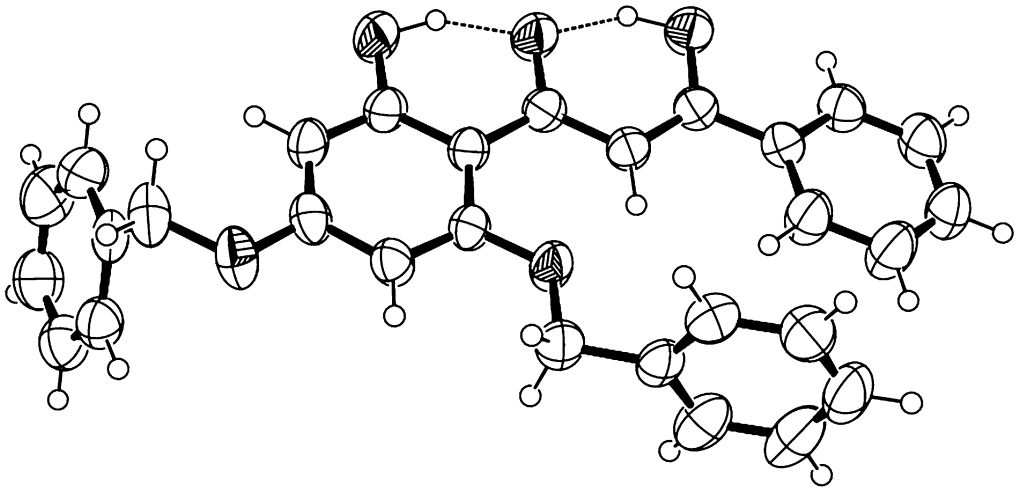


Figure 2. Crystal structure of keto-enol **27** (Ar=Ph, R=H).

the starting aryl esters **22** with benzyloxide produced during the reaction.

3. Conclusion

In summary, we have provided a useful method for the isotopic labelling of the important dietary flavonoid, quercetin 3-*O*-β-D-glucoside, and the route should be easy to adapt for the synthesis of other flavonoid 3-*O*-glycosides. We have also briefly explored the unexpected debenzylation reaction that occurs in the flavonoid-forming step, and propose a [1,7]-sigmatropic rearrangement to account for this.

4. Experimental

^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX/400 spectrometer operating at 400 and 100 MHz, respectively. All coupling constants are measured in Hertz.

DEPT was used to assign the signals in the ^{13}C NMR spectra as C, CH, CH_2 or CH_3. The entire labelling sequence was first checked with unlabelled material (data not presented), and the ^{13}C NMR spectra of unlabelled material were used to identify coupling in the ^{13}C NMR spectra of labelled material. Mass spectra (MS) were recorded on a Jeol JMS700 (MStation) spectrometer. Infra-red (IR) spectra were obtained on a Perkin–Elmer 983 spectrophotometer. A Golden Gate™ attachment that uses a type IIa diamond as a single reflection element was used in some cases so that the IR spectrum of the compound (solid or liquid) could be directly detected without any sample preparation. Column chromatography was carried out on silica gel, 70–230 mesh, or neutral alumina (Brockmann grade III). Tetrahydrofuran and diethyl ether were dried over sodium and benzophenone, and dichloromethane was dried over calcium hydride. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 297713. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.1. [2-^{13}C]Quercetin 3-*O*-β-D-glucoside 2

Twenty percent palladium hydroxide on carbon (184 mg) was added to a stirring suspension of partly benzyl protected flavonol **19** (597 mg, 652 μmol) in 1:1 EtOAc–MeOH (10 mL) under an atmosphere of hydrogen. The suspension was stirred for 6 h at rt. The suspension was filtered through a plug of Celite eluting with MeOH. The filtrate was concentrated under vacuum and the resulting solid was recrystallised from MeOH–water (1:1) to give the quercetin 3-glucoside **2** as a green solid (174 mg, 57%), mp 224–226 °C. $[\alpha]_D^{22}$ –12.9 (*c* 1.0, MeOH). ν_{max}(Golden Gate)/cm^{-1}: 3170 (OH), 1653 (C═O), 1602 (C═O). δ_H (400 MHz; CD_3OD): 3.10–3.66 (6H, m, H-2″, 3″, 4″, 5″ and 6″), 5.14 (1H, d, *J* 7.4 Hz, H-1″), 6.08 (1H, d, *J* 2.1 Hz, H-6 or H-8), 6.27 (1H, d, *J* 2.1 Hz, H-6 or H-8), 6.76 (1H, d, *J* 8.4 Hz, H-5′), 7.47 (1H, ddd, J 2.1, 3.8 and 8.4 Hz, H-6′), 7.61 (1H, dd, *J* 2.1 and 3.9 Hz, H-2′). δ_C (100 MHz, MeOD-d_4): 62.53 (CH_2), 71.17 (CH), 75.70 (CH), 78.07 (CH), 78.32 (CH), 94.71 (CH, d, *J* 3 Hz), 99.86 (CH), 104.35 (CH), 105.64 (C), 115.97 (CH, d, *J* 5 Hz), 117.57 (CH, d, *J* 2 Hz), 122.94 (CH, d, *J* 68 Hz), 123.36 (C), 135.58 (C, d, *J* 89 Hz), 145.83 (C, d, *J* 6 Hz), 149.81 (C), 158.64 (C), 158.99 (^{13}C-label), 162.95 (C), 165.92 (C), 179.43 (C, d, *J* 6 Hz). *m/z* (FAB): 466 [(M+H)$^+$, 44%], 304 (84), 74 (100). HRMS: 466.1069. $^{12}C_{20}\,^{13}CH_{21}O_{12}$ requires (M+H)$^+$ 466.1063. HPLC Gradient reverse phase HPLC (Phenomonex Max RP C12 250× 4.6 mm×5 μm), solvent A 1% aqueous formic acid–Solvent B acetonitrile, 1.0 mL/min 5–40% B gradient over 60 min, *t*=26.64 min, showed 95% purity by peak area measurement (Absorbance wavelengths 200–600 nm, photodiode array detector). Spectral data in good agreement with literature for unlabelled compound.[19]

4.2. 3,5,7,3′,4′-Pentabenzyloxyflavone 6 and 2-hydroxy-ω,4,6-tribenzyloxyacetophenone 7

The syntheses of these compounds have already been reported.[11]

4.3. 1-(2′,4′,6′-Trihydroxyphenyl)-2-hydroxyethanone 8

Twenty percent palladium hydroxide on carbon (400 mg) was added to a suspension of phenol **7** (4.00 g, 8.8 mmol) in methanol–ethyl acetate (1:1, 20 mL) under an atmosphere of hydrogen. The suspension was then stirred overnight. The resulting solution was filtered through a pad of Celite, which was subsequently washed with methanol (30 mL). The solution concentrated under vacuum and the resulting solid recrystallised from ethanol to yield phenol **8** as an amorphous solid (1.36 g, 84%), mp decomp >225 °C. Lit.: 224 °C.[35] R_f [silica, EtOAc–hexane (7:3)] 0.19. ν_{max}(nujol)/cm^{-1}: 3380 (OH), 3299 (OH), 3153 (OH), 1650 (C═O). δ_H (400 MHz: DMSO-d_6): 4.60 (2H, s, CH_2), 4.73 (1H, broad s, CH_2OH), 5.82 (2H, s, H-3′, H-5′), 10.4 (1H, broad s, OH), 12.1 (2H, broad s, OH). δ_C (100 MHz: DMSO-d_6): 68.27 (CH_2), 94.91 (CH), 102.30 (C), 164.40 (C), 165.35 (C), 203.85 (C). *m/z* (EI) 184 (M$^{+\bullet}$, 18%), 153 (100), 69 (10). HRMS: 184.0372 $C_8H_8O_5$ requires (M$^+$), 184.0371. Microanalysis: C, 52.32; H, 4.62%. $C_8H_8O_5$ requires C, 52.17; H, 4.35%.

4.4. 5,7-Dibenzyloxyflavone 10

Benzyl bromide (46.8 mL, 394 mmol, 4.0 equiv) and K_2CO_3 (54.3 g, 394 mmol, 4.0 equiv) were added to a stirring solution of chrysin (25.00 g, 98.5 mmol) in DMF (150 mL). The resulting suspension was stirred at 70 °C for 4 d under a nitrogen atmosphere. After cooling, the solution was acidified to pH 1 with 1 M HCl and extracted into EtOAc (250 mL). The solution was allowed to stir for 10 min before the resulting precipitate was filtered off and washed with 50 mL of EtOAc to give flavone **10** as an off white solid pure enough for the next step (35.15 g, 82%). A sample was recrystallised from EtOAc–$CHCl_3$ for characterisation purposes, mp 165–167 °C. R_f [silica, EtOAc–hexane (7:3)] 0.52. δ_H (400 MHz: $CHCl_3$): 5.05 (2H, s, OCH_2), 5.16 (2H, s, OCH_2), 6.44 (1H, d, *J* 1.7 Hz, H-6), 6.59 (1H, d, *J* 1.7 Hz, H-8), 6.61 (1H, s, H-3), 7.19–7.81 (15H, m, Ar-H). δ_C (100 MHz: $CHCl_3$): 70.29 (CH_2), 70.48 (CH_2), 94.06 (CH), 98.18 (CH), 108.91 (CH), 109.70 (C), 125.75 (CH), 126.38 (CH), 127.44 (CH), 128.25 (CH), 128.40 (CH), 128.58 (CH), 128.74 (CH), 130.00 (CH), 131.35 (C), 135.35 (C), 136.29 (C), 159.49 (C), 159.56 (C), 160. 41 (C), 162.77 (C), 177.05 (C). *m/z* (EI): 434 (M$^{+\bullet}$, 10%), 91 (100). HRMS: 434.1518. $C_{29}H_{22}O_4$ requires (M$^+$) 434.1515. Microanalysis: C, 80.16; H, 5.13%. $C_{29}H_{22}O_4$ requires C, 80.17; H, 5.10%.

4.5. 2,4-Dibenzyloxy-6-hydroxyacetophenone 11

Diethylene glycol (170 mL) was added slowly to a stirring mixture of flavone 10 (39.6 g, 91.4 mmol) in pyridine (150 mL) and 18 M KOH (150 mL). The solution was heated at 120 °C for 4 h. After cooling, the solution was acidified to pH 1 with 4 M HCl and the precipitate filtered off. The solid was washed with water then extracted into EtOAc (300 mL). The organics were washed with saturated $NaHCO_3$ solution (3×400 mL) then dried over magnesium sulfate and concentrated under vacuum. The resulting solid was recrystallised from MeOH to give acetophenone **11**

as off white prisms (23.4 g, 74%), mp 108–109 °C. Lit.:110–111 °C.[36] R_f [silica, EtOAc–hexane (7:3)] 0.73. ν_{max}(nujol)/cm^{-1}: 1615 (C=O). δ_H (400 MHz: $CDCl_3$): 2.54 (3H, s, CH_3), 5.049 (2H, s, $ArOCH_2$), 5.053 (2H, s, $ArOCH_2$), 6.09 (1H, d, *J* 2.4 Hz, H-3), 6.15 (1H, d, *J* 2.4 Hz, H-5), 7.32–7.40 (10H, m, Ar-H), 14.02 (1H, s, OH). δ_C (100 MHz: $CDCl_3$): 33.26 (CH_3), 70.19 (CH_2), 71.05 (CH_2), 92.29 (CH), 94.69 (CH), 106.28 (C), 127.59 (CH), 127.93 (CH), 128.30 (CH), 128.37 (CH), 128.41 (C), 128.66 (CH), 128.69 (CH), 135.56 (C), 135.81 (C), 161.90 (C), 165.03 (C), 167.51 (C), 203.13 (C). *m/z* (EI): 348 ($M^{+\bullet}$, 15%), 306 (7), 91 (100). HRMS: 348.1361. $C_{22}H_{20}O_4$ requires (M^+), 348.1361. Microanalysis: C, 75.90; H, 5.75%. $C_{22}H_{20}O_4$ requires C 75.86, H 5.75%. ^{1}H NMR agrees with literature.[37,38]

4.6. 1-(2′,4′-Dibenzyloxy-6′-hydroxyphenyl)-2-hydroxyethanone 12

A solution of ketone **11** (10.0 g, 28.7 mmol) in dry THF (30 mL) was added to a solution of LDA (2.1 equiv) in dry THF (100 mL), under N_2, at 0 °C over 10 min. The solution was stirred at 0 °C for 30 min after which point chlorotrimethylsilane (9.0 mL, 71.8 mmol, 2.5 equiv) was added slowly, the solution was then stirred for a further 30 min at 0 °C. After this time, the reaction mixture was quenched with aqueous $NaHCO_3$ (100 mL) and extracted into ether (300 mL). The aqueous layer was re-extracted with ether (200 mL). The combined organic layers were washed with H_2O (2×300 mL) and dried over sodium sulfate and concentrated under vacuum. The whole washing process was performed as quickly as possible to minimise the risk of hydrolysing the silyl enol ether. The crude silyl enol ether was dissolved in CH_2Cl_2 (100 mL) and $NaHCO_3$ (3.61 g, 43.0 mmol, 1.5 equiv) was added. The solution was cooled 0 °C and *m*CPBA (70–75%, 7.45 g, 43.0 mmol, 1.5 equiv) was added slowly. The reaction mixture was allowed to stir at 0 °C for 1.5 h. After this time, the yellow cloudy solution was diluted with CH_2Cl_2 (200 mL) and washed with saturated $NaHCO_3$ (2×300 mL) and H_2O (2×300 mL) and concentrated under vacuum. The product was dissolved in 4:1 THF–H_2O (150 mL) and 2.5 g of *para*-toluenesulfonic acid was added, the solution was then stirred at rt for 30 min. The product was extracted into Et_2O (400 mL), washed with saturated $NaHCO_3$ (2×300 mL) and H_2O (2×300 mL), dried over magnesium sulfate and concentrated under vacuum. The crude product was recrystallised from EtOAc–hexanes (3:7) to give ketone **12** as an amorphous solid (7.61 g, 73%), mp 105–107 °C. ν_{max}(nujol)/cm^{-1}: 3451 (OH), 1636 cm^{-1} (C=O). δ_H (400 MHz: $CDCl_3$): 3.71 (1H, t, *J* 4.8 Hz, OH), 4.62 (2H, d, *J* 4.8 Hz, CH_2OH), 5.04 (2H, s, OCH_2), 5.06 (2H, s, OCH_2), 6.10 (1H, d, *J* 2.2 Hz, H-3′), 6.19 (1H, d, *J* 2.2 Hz, H-5′), 7.32–7.42 (10H, m, Ar-H), 13.2 (1H, s, Ar-OH). δ_C (100 MHz: $CDCl_3$): 68.83 (CH_2), 70.40 (CH_2), 71.31 (CH_2), 92.45 (CH), 94.92 (CH), 103.63 (C), 127.60 (CH), 128.14 (CH), 128.42 (CH), 128.72 (CH), 128.75 (CH), 128.88 (CH), 134.89 (C), 135.57 (C), 162.212 (C), 166.02 (C), 167.23 (C), 201.90 (C). *m/z* (CI): 365 [(M+H)$^+$, 100%], 347 (25), 333 (22), 307 (20), 91 (70). HRMS: 365.1389. $C_{22}H_{21}O_5$ requires (M+H)$^+$ 365.1386. Microanalysis: C, 72.38; H, 5.66%. $C_{22}H_{20}O_5$ requires C, 72.51%; H, 5.53%.

4.7. 1-(2′,4′-Dibenzyloxy-6′-hydroxyphenyl)-2-(2″,3″,4″,6″-tetra-*O*-benzyl-β-D-glucopyranosyloxy)ethanone 14

Boron trifluoride diethyl etherate (0.33 mL, 2.6 mmol, 0.3 equiv) was added dropwise to a solution of phenol **12** (3.14 g, 8.6 mmol) and *O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)trichloroacetimidate **13** (6.50 g, 9.5 mmol, 1.1 equiv, prepared) in dry CH_2Cl_2 (40 mL) at −78 °C, under an atmosphere of nitrogen. The solution was stirred for 1 h at −78 °C and then quenched with aqueous $NaHCO_3$ (75 mL). The solution was diluted with CH_2Cl_2 (250 mL) and washed with brine (2×300 mL), dried over magnesium sulfate and concentrated under vacuum. The solid was recrystallised from EtOAc–pet. ether to give *glucoside* **14** as an amorphous solid (4.98 g, 66%), mp 118–119 °C. R_f (silica, ether) 0.68. ν_{max}(nujol)/cm^{-1}: 1633 (C=O), 1604 (Ar), 1583 (Ar). δ_H (400 MHz: $CDCl_3$): 3.29–3.72 (6H, m, H-2″, 3″, 4″, 5″, 6″), 4.34 (1H, d, *J* 7.6 Hz, H-1″), 4.48 (1H, d, *J* 12.4 Hz, $ArOCH_AH_B$), 4.52 (1H, d, *J* 10.8 Hz, $ArOCH_CH_D$), 4.56 (1H, d, *J* 12.0 Hz, $ArOCH_AH_B$), 4.74 (1H, d, *J* 18.4 Hz, $ArOCH_EH_F$), 4.75 (1H, d, *J* 12.0 Hz, $ArOCH_GH_H$), 4.77 (1H, d, *J* 11.2 Hz, $ArOCH_IH_J$), 4.81 (1H, d, *J* 10.8 Hz, $ArOCH_CH_D$), 4.96 (1H, d, *J* 10.8 Hz, $ArOCH_IH_J$), 4.97 (1H, d, *J* 18.4 Hz, $ArOCH_EH_F$), 4.99 (2H, s, $ArOCH_2$), 5.12 (2H, s, $ArOCH_2$), 5.14 (1H, d, *J* 10.8 Hz, $ArOCH_GH_H$), 6.08 (1H, d, *J* 2.2 Hz, H-5′), 6.20 (1H, d, *J* 2.1 Hz, H-3′), 7.15–7.40 (30H, m, Ar-H), 13.7 (1H, s, Ar-OH). δ_C (100 MHz: $CDCl_3$): 68.76 (CH_2), 70.33 (CH_2), 71.22 (CH_2), 73.48 (CH_2), 74.23 (CH_2), 74.71 (CH_2), 74.84 (CH), 75.06 (CH_2), 75.66 (CH_2), 77.62 (CH), 81.90 (CH), 84.45 (CH), 92.25 (CH), 95.04 (CH), 103.15 (CH), 104.54 (C), 127.52 (CH), 127.53 (CH), 127.58 (CH), 127.61 (CH), 127.71 (CH), 127.75 (CH), 127.85 (CH), 127.04 (CH), 128.18 (CH), 128.28 (CH), 128.33 (CH), 128.37 (CH), 128.56 (CH), 128.71 (CH), 128.75 (CH), 135.14 (C), 136.26 (C), 138.10 (C), 138.19 (C), 138.48 (C), 138.66 (C), 161.59 (C), 165.33 (C), 167.46 (C), 199.39 (C). *m/z* (FAB): 909.6 [(M+Na)$^+$, 100%], 439.3 (30), 91.5 (82%). HRMS: 909.3611. $C_{56}H_{54}O_{10}Na$ requires (M+Na)$^+$, 909.3614. Microanalysis: C, 75.91; H, 6.12%. $C_{56}H_{54}O_{10}$ requires C, 75.83%; H, 6.14%. $[\alpha]_D^{19}$ −5.0 (*c* 140 mg mL^{-1}, $CHCl_3$).

4.8. 1-Bromo-3,4-diallyloxybenzene 16

Commercially available catechol **15** (20.0 g, 182 mmol, 1 equiv) was dissolved in a mixture of chloroform–diethyl ether (2:1, 150 mL) that was cooled to 0 °C and stirred under argon. Bromine (9.3 mL, 182 mmol, 1 equiv) dissolved in chloroform (200 mL) was added dropwise to the catechol solution over a period of 2 h, the resulting solution was then stirred for another 30 min. The reaction mixture was quenched by adding saturated sodium thiosulfate (400 mL). The organic layer was collected, and the aqueous layer was extracted with EtOAc (300 mL). Both organic fractions were combined, dried ($MgSO_4$) and concentrated to give 3-bromocatechol as an intermediate. The intermediate was dissolved into DMF (300 mL), and the solution was put under argon. K_2CO_3 (55.0 g, 400 mmol, 2.2 equiv) and allyl bromide (35.0 mL, 400 mmol, 2.2 equiv) were added and the resulting suspension was stirred for 20 h at rt. The reaction mixture was then acidified to pH 1 with 1 M HCl. The solution was then extracted with diethyl ether

(300 mL) and the aqueous layer was re-extracted with diethyl ether (150 mL). The combined organic layers were washed with H_2O (2×100 mL), 1 M KOH (200 mL) and brine (100 mL), before the ether layer was dried ($MgSO_4$) and concentrated. Flash chromatography (silica) eluting with cyclohexane–EtOAc (30:1) gave 1-bromo-3,4-diallyloxybenzene **16** as a yellow oil (32.6 g, 68%). R_f [silica, pet. ether–EtOAc (8:1)] 0.83. ν_{max}(nujol)/cm^{-1}: 1586 (Ar), 1495 cm^{-1} (Ar). δ_H (400 MHz; $CDCl_3$): 4.50–4.54 (4H, m, 2×OCH_2), 5.22–5.27 (2H, m, 2×CH_AH$_B$=CH), 5.38–5.42 (2H, m, 2×CH$_A$$H_B$=CH), 5.98–6.05 (2H, m, 2×CH$_A$H$_B$=C*H*), 6.71 (1H, d, *J* 8.4 Hz, H-5), 6.96 (1H, dd, *J* 2.3 and 8.0 Hz, H-6), 6.97 (1H, d, *J* 2.3 Hz, H-2). δ_C (100 MHz, $CDCl_3$): 69.53 (CH_2), 69.65 (CH_2), 112.62 (C), 114.93 (CH), 116.81 (CH), 117.34 (CH_2), 117.49 (CH_2), 123.08 (CH), 132.74 (CH), 133.01 (CH), 147.38 (C), 148.93 (C). *m*/*z* (EI): 270 [M$^{+\bullet}$ (^{81}Br), 22%], 268 [M$^{+\bullet}$ (^{79}Br), 22], 229 [M$^{+\bullet}$(^{81}Br)-$^{\bullet}$C$_3$H$_5$, 22], 227 [M$^{+\bullet}$(^{79}Br)-$^{\bullet}$C$_3$H$_5$, 22], 41 ($^{+}$C$_3$H$_5$, 100). HRMS: 270.0079 and 268.0096. $C_{12}H_{13}O_2{}^{81}Br$ requires M$^+$, 270.0079, $C_{12}H_{13}O_2{}^{79}Br$ requires M$^+$, 268.0099. Microanalysis: C, 53.95; H, 4.99%. $C_{12}H_{13}O_2Br$ requires C, 53.55; H, 4.89%.

4.9. 3,4-Diallyloxy[*carboxy*-^{13}C]benzoic acid 17

Carboxylation of the aryl bromide **16** was carried out using the apparatus described by Kratzel and Billek[28] and a variation of their method. *n*-Butyllithium (4.7 mL, 2.1 M in hexane, 9.9 mmol, 2.0 equiv) was added to a stirred solution of 3,4-diallyloxy-1-bromobenzene **16** (2.69 g, 10.0 mmol, 2 equiv) in dry THF (20 mL) at −78 °C under nitrogen. After 3 min, the reaction mixture was cooled to −198 °C. When the solution was frozen the whole system was put under vacuum. The system was sealed from vacuum and [^{13}C]carbon dioxide was generated by adding an excess of concentrated sulfuric acid (10 mL) dropwise onto powdered [^{13}C] barium carbonate (0.99 g, 5.0 mmol, 1 equiv) in a separate reaction vessel in the same system. The carbon dioxide evolved condensed onto the frozen THF solution of aryllithium. After 20 min the THF solution was allowed to warm up to –78 °C and the reaction mixture was stirred for 40 min. The entire system was filled with nitrogen and reaction mixture was quenched by the addition of HCl (1M, 10 mL). The solution was extracted into EtOAc (2×100 mL) and the combined organic extracts were washed with brine (2×200 mL). The combined organic layers were extracted with 2 M NaOH (2×250 mL). The resulting aqueous layer was acidified with 1 M HCl and then extracted into EtOAc (2×200 mL). The combined extracts were dried over $MgSO_4$ and concentrated to give acid **17** as a powder (956 mg, 81%). R_f [silica, pet. ether–EtOAc (1:1)] 0.56. ν_{max}(Golden Gate)/cm^{-1}: 1638 (C=O), 1581 (Ar). δ_H (400 MHz: $CDCl_3$): 4.66–4.70 (4H, m, 2×OCH_2), 5.30–5.34 (2H, m, 2×CH_AH$_B$=CH), 5.42–5.48 (2H, 2×CH$_A$$H_B$=CH), 6.04–6.15 (2H, m, 2×CH$_A$H$_B$=C*H*), 6.95 (1H, dd, *J* 0.9 and 8.5 Hz, H-5), 7.62 (1H, dd 2.0 and 4.3 Hz, H-2), 7.74 (1H, ddd 2.0, 4.1 and 8.5 Hz, H-6). δ_C (100 MHz: $CDCl_3$): 69.63 (CH_2), 69.84 (CH_2), 112.34 (CH, d, *J* 5.6 Hz), 114.86 (CH, d, *J* 3.2 Hz), 118.08 (CH_2), 118.18 (CH_2), 121.72 (C, d, *J* 74.8 Hz, C-1), 124.63 (CH, d, *J* 2.6 Hz), 132.53 (CH), 132.85 (CH), 147.90 (C, d, *J* 5.3 Hz), 153.22 (C), 171.89 (^{13}C-label). *m*/*z* (EI): 235 (M$^{+\bullet}$, 78%), 194 (M$^{+\bullet}$-$^{\bullet}$C$_3$H$_5$, 32), 41 ($^{+}$C$_3$H$_5$, 100%). HRMS: 235.0926, $^{12}C_{12}{}^{13}CH_{14}O_4$ requires 235.0926.

4.10. 1-[2′-(3″,4″-Dialloxy[*carbonyl*-^{13}C]benzoyloxy)-4′,6′-dibenzyloxyphenol]-2-(2‴,3‴,4‴,6‴-*tetra*-*O*-benzyl-β-D-glucopyranosyloxy)ethanone 18

EDCI (0.76 g, 4.0 mmol, 1.6 equiv) was added to a solution of the labelled benzoic acid **17** (0.64 g, 2.7 mmol, 1.1 equiv), phenol **14** (2.19 g, 2.47 mmol, 1 equiv) and DMAP (0.30 g, 2.5 mmol, 1 equiv) in dry DCM (25 mL) under an atmosphere of nitrogen. The solution was stirred for 24 h at rt, then diluted with DCM (100 mL) and washed with water (2×100 mL) and brine (2×100 mL), dried over $MgSO_4$ and concentrated to give the crude ester as an oil. Flash column chromatography (silica) eluting with hexane–EtOAc (4:1) gave labelled ester **18** as yellow oil (1.81 g, 66%). R_f [silica, pet. ether–EtOAc (4:1)] 0.52. ν_{max}(Golden Gate)/cm^{-1}: 1688 (C=O), 1607 cm^{-1} (Ar). δ_H (400 MHz: $CDCl_3$): 3.18 (1H, dt, *J* 2.4 and 9.6 Hz, H-5‴), 3.40–3.63 (5H, m, H-2‴, 3‴, 4‴, and 6‴), 4.30 (1H, d, *J* 7.4 Hz, H-1‴), 4.44 (1H, d, *J* 12.2 Hz, OCH_2Ph), 4.49 (1H, d, *J* 10.9 Hz, OCH_2Ph), 4.52–4.59 (6H, m, 2×OCH_2CHCH_2, 2×OC*H*HPh), 4.66 (1H, d, *J* 17.0 Hz, OCH_2CO), 4.70 (1H, d, *J* 11.0 Hz, OCH_2Ph), 4.78 (1H, d, *J* 10.8 Hz, OCH_2Ph), 4.81 (1H, d, *J* 17.2 Hz, OCH_2CO), 4.88 (1H, d, *J* 10.9 Hz, OCH_2Ph), 4.93 (1H, d, *J* 11.1 Hz, OCH_2Ph), 4.97 (2H, s, OCH_2Ph), 5.02 (2H, s OCH_2Ph), 5.24–5.30 (2H, m, 2×CH_AH$_B$=CH), 5.38–5.42 (2H, m, 2×CH$_A$$H_B$=CH), 6.00–6.09 (2H, m, 2×CH$_A$H$_B$=C*H*), 6.46 (1H, d, *J* 2.2 Hz, H-5′), 6.53 (1H, d, *J* 2.1 Hz, H-3′), 6.82 (1H, dd, *J* 1.0 and 8.6 Hz, H-5″), 7.13–7.40 (30 H, m, ArH), 7.61 (1H, dd, *J* 2.0 and 4.4 Hz, H-2″), 7.74 (1H, ddd, *J* 2.0, 4.2 and 8.5 Hz, H-6″). δ_C (100 MHz: $CDCl_3$): 68.64 (CH_2), 69.52 (CH_2), 69.72 (CH_2), 70.40 (CH_2), 70.99 (CH_2), 73.37 (CH_2), 74.25 (CH_2), 74.38 (CH_2), 74.74 (CH), 74.86 (CH_2), 75.58 (CH_2), 77.51 (CH), 81.84 (CH), 84.42 (CH), 98.20 (CH), 101.75 (CH), 103.40 (CH), 112.42 (CH, d, *J* 5.7 Hz, C-5″), 114.84 (CH, d, *J* 3.1 Hz, C-2″), 114.91 (C), 117.95 (CH_2), 118.02 (CH_2), 121.39 (C, d, *J* 79.7 Hz, C-1″), 124.71 (CH, d, *J* 2.3 Hz, C-6″), 127.28 (CH), 127.47 (CH), 127.48 (CH), 127.57 (CH), 127.62 (CH), 127.70 (CH), 127.83 (CH), 127.87 (CH), 128.08 (CH), 128.26 (CH), 128.29 (CH), 128.32 (CH), 128.38 (CH), 128.66 (CH), 128.71 (CH), 132.52 (CH), 132.81 (CH), 135.65 (C), 135.85 (C), 138.17 (C), 138.25 (C), 138.66 (C), 138.69 (C), 148.02 (C, d, *J* 6.0 Hz, C-3″), 150.66 (C, d, *J* 7.3 Hz, C-2′), 153.13 (C), 158.41 (C), 161.64 (C), 164.48 (C=O, ^{13}C-label), 197.16 (C=O). *m*/*z* (FAB): 1126.6 [(M+Na)$^+$, 10%], 218 (46), 93 (100). HRMS: 1126.4438, $^{12}C_{68}{}^{13}CH_{66}O_{13}Na$ requires (M+Na)$^+$, 1126.4435.

4.11. 3-(2″,3″,4″,6″-*tetra*-*O*-Benzyl-β-D-glucopyranosyloxy)-7-benzyloxy-3′,4′,5-trihydroxy[2-^{13}C]flavonol 19

The labelled ester **18** (1.58 g, 1.43 mmol, 1 equiv) was stirred in toluene (20 mL) under argon. K_2CO_3 (0.79 g, 5.7 mmol, 4 equiv) was added followed by tetrabutylammonium bromide (0.69 g, 2.2 mmol, 1.5 equiv) and the mixture was heated at 70 °C for 23 h. After the mixture was cooled down, toluene was evaporated in vacuo. The solid was dissolved in DCM (100 mL) and washed with water (2×100 mL) and brine (2×100 mL) and concentrated. The

crude mono-deprotected labelled flavonol was dissolved in DCM (10 mL) and the solution degassed with argon for 20 min. $Pd(PPh_3)_4$ (50 mg, 0.043 mmol, 3 mol%) and barbituric acid (1.34 g, 8.58 mmol, 6 equiv) were added and the solution was stirred for 2 h at rt under argon. After this time, the solvent was removed in vacuo and the resulting solid was dissolved into EtOAc (100 mL). The organic solution was washed with satd $NaHCO_3$ (3×300 mL), dried ($MgSO_4$) and concentrated to give a brown/black oil. Column chromatography (silica, hexane–EtOAc, 2:1) gave flavonol **19** as a pale yellow oil (637 mg, 48%), R_f [SiO_2, pet. ether–EtOAc (4:1)] 0.26. ν_{max}(Golden Gate)/cm^{-1}: 1652 (C═O), 1593 cm^{-1} (C═O). δ_H (400 MHz: $CDCl_3$): 3.42–3.44 (1H, m, H-5″), 3.58–3.80 (5H, m, H-2″, 3″, 4″ and 6″), 4.28 (1H, d, *J* 12.1 Hz, OCH_2Ph), 4.34 (1H, d, *J* 12.0 Hz, OCH_2Ph), 4.50 (1H, d, *J* 10.9 Hz, OCH_2Ph), 4.75 (1H, d, *J* 12.5 Hz, OCH_2Ph), 4.78 (1H, d, *J* 11.1 Hz, OCH_2Ph), 4.79 (1H, d, *J* 10.9 Hz, OCH_2Ph), 4.96 (1H, d, *J* 11.1 Hz, OCH_2Ph), 5.06 (1H, d, *J* 13.1 Hz, OCH_2Ph), 5.08 (2H, s, OCH_2Ph), 5.58 (1H, d, *J* 7.0 Hz, H-1″), 6.41 (1H, d, *J* 2.0 Hz, H-6 or H-8), 6.45 (1H, d, *J* 2.0 Hz, H-6 or H-8), 6.84 (1H, d, *J* 8.5 Hz, H-5′), 7.10–7.42 (25H, m, Ar-H), 7.52 (1H, ddd, *J* 8.5, 3.8, and 2.0 Hz, H-6′), 7.91 (1H, dd, *J* 2.0 and 3.8 Hz, H-2′), 12.51 (1H, s, OH). *m/z* (FAB): 916.7 [$(M+H)^+$, 3%]. 808.6 [$(M+H)^+-HOCH_2Ph$, 1], 393.3 [$(M+H)^+-C_{34}H_{35}O_5$, 4], 364.3 [$(M+H)^+$-$C_{35}H_{36}O_6$, 3], 91.5 ($^+C_7H_7$, 100). HRMS: 938.3224, $^{12}C_{55}{}^{13}CH_{50}O_{12}Na$ requires $(M+Na)^+$, 938.3234.

4.12. 2-Benzoyloxy-4,6-dibenzyloxyacetophenone 20

Benzoyl chloride (4.00 mL, 34.9 mmol, 2.4 equiv) was added to a solution of acetophenone **11** in pyridine (20 mL). The solution was stirred at rt under an atmosphere of nitrogen overnight. The solution was then extracted into EtOAc and washed with 1 M HCl (3×250 mL), dried over magnesium sulfate and concentrated under vacuum. The resulting solid was then recrystallised from Et_2O–hexane (1:1) to give ester **20** as an amorphous solid (4.45 g, 72%), mp 105–106 °C. R_f [silica, EtOAc–hexane (7:3)] 0.67. ν_{max}(nujol)/cm^{-1}: 1730 (C═O of ester), 1693 (C═O). δ_H (400 MHz: $CDCl_3$): 2.47 (3H, s, CH_3), 5.03 (2H, s, $ArOCH_2$), 5.08 (2H, s, $ArOCH_2$), 6.48 (1H, d, *J* 2.2 Hz, H-5), 6.54 (1H, d, *J* 2.2 Hz, H-3), 7.24–7.39 (10H, m, Ar-H), 7.47–7.51 (2H, m, H-3′,5′), 7.60–7.64 (1H, m, H-4′), 8.13–8.15 (2H, m, H-2′,6′). δ_C (100 MHz: $CDCl_3$): 32.03 (CH_3), 70.43 (CH_2), 70.94 (CH_2), 98.52 (CH), 101.38 (CH), 117.90 (C), 127.42 (CH),127.59 (CH), 128.24 (CH), 128.30 (CH), 128.54 (CH), 128.68 (CH), 129.147 (C), 130.26 (CH), 133.63 (CH), 135.79 (C), 135.93 (C), 149.72 (C), 158.17 (C), 158.21 (C), 165.00 (C), 199.21 (C). *m/z* (EI): 452 ($M^{+\bullet}$, 5%), 347 (10), 91 (100). HRMS: 452.1623. $C_{29}H_{24}O_5$ requires M^+, 452.1624. Microanalysis: C, 76.84; H, 5.41%. $C_{29}H_{24}O_5$ requires C 76.98, H 5.35%.

4.13. 7-Benzyloxy-5-hydroxyflavone 21

tert-Butylimino-tri(pyrrolidino)phosphorane[29] (0.57 mL, 1.9 mmol, 4.0 equiv) was added to a solution of ester **20** in dry 1,4-dioxane (2 mL). The reaction mixture was heated at 100 °C under N_2 for 24 h. After cooling, the reaction mixture was extracted into EtOAc (50 mL) and washed with H_2O (3×200 mL). The organic layer was dried over magnesium sulfate and concentrated under vacuum. The crude product was recrystallised from ^{i}PrOH to give flavone **21** as an amorphous solid (92 mg, 61%), mp 177–178 °C. R_f (silica, Et_2O) 0.76. δ_H (400 MHz: $CDCl_3$): 5.05 (2H, s, OCH_2), 6.36 (1H, d, *J* 2.2 Hz, H-6), 6.48 (1H, d, *J* 2.2 Hz, H-8), 6.57 (1H, s, H-3), 7.25–7.49 (8H, m, Ar-H), 7.77–7.80 (2H, m, H-2,6′), 12.65 (1H, broad s, OH). δ_C (100 MHz: $CDCl_3$): 70.39 (CH_2), 93.45 (CH), 98.90 (CH), 105.81 (CH), 126. 23 (CH), 127.45 (CH), 128. 34 (CH), 128.71 (CH), 129.03 (CH), 131.20 (C), 131.81 (CH), 135.68 (C), 157.68 (C), 162.12 (C), 163. 95 (C), 164.59 (C), 182.41 (C), *m/z* (EI): 344 ($M^{+\bullet}$, 70%), 91 (100). HRMS: 344.1045. $C_{22}H_{16}O_4$ requires M^+, 344.1049. Found: C, 76.76; H, 4.67%. $C_{22}H_{16}O_4$ requires C, 76.73; H 4.68%. Literature NMR spectroscopy data which was run in DMSO-d_6 is in close agreement.[39]

4.14. 1-(4′,6′-Dibenzyloxy-2′-hydroxyphenyl)-3-hydroxy-3-phenylpropenone 27

Diethylene glycol (50 mL) was added slowly to a stirring mixture of flavone **10** (12.64 g, 29.0 mmol) in pyridine (50 mL) and 18 M KOH (50 mL). The solution was heated at 100 °C for 2 h. After cooling, the solution was acidified to pH 1 with 1 M HCl and extracted into EtOAc (2× 300mL). The organics were washed with H_2O (3× 400 mL) and 1M HCl (2×400 mL). The EtOAc layer was dried over magnesium sulfate and concentrated under vacuum. The resulting solid was recrystallised from MeOH to give dibenzoylmethane **27** as yellow needles (3.91 g, 39%), mp 131–133 °C.). R_f [silica, EtOAc–hexane (7:3)] 0.73. ν_{max}(nujol)/cm^{-1}: 3170 (OH), 1610 (C═O), 1571 (C═C). δ_H (400 MHz: $CDCl_3$): Keto-enol form: 5.01 (2H, s, OCH_2), 5.07 (2H, s, OCH_2), 6.18 (1H, d, *J* 2.3 Hz, H-3′), 6.21 (1H, d, *J* 2.3 Hz, H-5′), 7.10–7.68 (16 H, m, Ar-H, C═CHCO), 13.68 (1H, s, Ar-OH), 15.64 (1H, s, OH). δ_C (100 MHz: $CDCl_3$): Keto-enol form: 70.18 (CH_2), 71.38 (CH_2), 92.54 (CH), 95.22 (CH), 97.93 (CH), 104.45 (C), 126.48 (CH), 127.64 (CH), 128.31 (CH), 128.36 (CH), 128.68 (CH), 128.72 (CH), 128.92 (CH), 129.15 (CH), 131.51 (CH), 133.90 (C), 135.60 (C), 135.86 (C), 161.07 (C), 164.52 (C), 167.36 (C), 175.76 (C), 193.43 (C). *m/z* (EI): 452.1 ($M^{+\bullet}$, 5%), 434.1 (40), 345.1 (5), 91.1 (100). HRMS: 452.1630. $C_{29}H_{24}O_5$ requires M^+, 452.1624. Microanalysis: C, 76.84; H, 5.39%. $C_{29}H_{24}O_5$ requires C 76.98, H 5.35%.

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