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# Total synthesis of the pyranocoumaronochromone lupinalbin H

Mamoalosi A. Selepe, Siegfried E. Drewes, Fanie R. van Heerden *

*School of Chemistry, University of KwaZulu-Natal, Private Bag X01, Scottsville 3209, Pietermaritzburg, South Africa*

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ABSTRACT

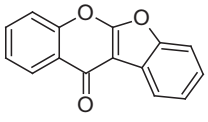
The pyranocoumaronochromone lupinalbin H was synthesized in three major steps, which involved preparation of 2′-hydroxygenistein by the Suzuki–Miyaura reaction, followed by oxidative cyclodehydrogenation into lupinalbin A. The final step was the regiospecific introduction of the dimethylpyran moiety to ring A of lupinalbin A via an aldol-type condensation with 3-methyl-2-butenal and 6π-electrocyclization.



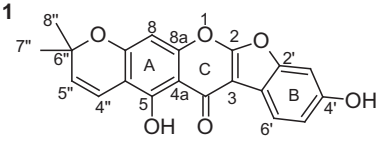
## 1. Introduction

Coumaronochromones are a subclass of isoflavonoids with general structure **1**.[1] They have been isolated from different plant genera, mostly of the Leguminosae,[1–5] although a few coumaronochromones have been reported from non-leguminous plants.[6–8] The striking feature of most naturally-occurring coumaronochromones is the presence of prenyl side chains, which in most instances are cyclized to adjacent hydroxy groups to give pyrano or furano rings.[1–3,5,7,9,10] Most pyranocoumaronochromones exhibit important biological activities, such as anthelminthic, oestrogenic, neuroprotective, antiplatelet aggregation, anti-HIV, immunosuppressive activities as well as cytotoxicity against certain cancer cell lines.[2,3,5,9–13] Despite their biological importance, the synthesis of these compounds has received little attention. Methods, which have been employed for the synthesis of the coumaronochromone nucleus are photochemical contraction of rotenoids and oxidative cyclization of 2′-hydroxyisoflavones, the latter being the strategy employed mostly.[14–16] The dimethylpyran scaffold, on the other hand, can be accessed via several synthetic approaches, which involve cycloaddition reactions of *C*-prenylated phenols, aldol-type condensation of phenols with prenal (3-methyl-2-butenal) or prenal acetal, dehydration of chromanols, Harfenist–Thom rearrangement of propargyl ethers and one-pot Wittig reactions of *o*-naphthoquinones with allyltriphenylphosphonium salts and subsequent electrocyclization.[17–20]

Despite the numerous synthetic procedures that have been developed for the dimethylpyran moiety, the regioselective introduction of the dimethylpyran system to the synthetic precursors or to the coumaronochromone core has been a major challenge in the synthesis of pyranocoumaronochromones.[14,15]



**1**




**2**

In continuation of our studies on the regioselective synthesis of pyranoisoflavonoids,[21] the present paper reports the first total synthesis of lupinalbin H (**2**) and confirmation of its structure on the basis of 1D and 2D NMR techniques. Lupinalbin H (**2**) was isolated together with other flavonoids from the methanolic extract of the roots of yellow lupin (*Lupinus luteus* cv Topaz) by Tahara et al.[22] The assignment of the structure of **2** was based mainly on comparison of its $^{1}$H NMR signals with those of related compounds and the $^{13}$C NMR data was not reported. Furthermore, the other flavonoids isolated along with it were reported to exhibit antifungal activity; however, **2** was not assayed for its activity. The lack of detailed structural characterization and bioactivity studies of lupinalbin H (**2**) can be attributed to the low quantity obtained from

* Corresponding author. Tel.: +27 33 2605886; fax: +27 33 2605009; e-mail address: vanheerdenf@ukzn.ac.za (F.R. van Heerden).

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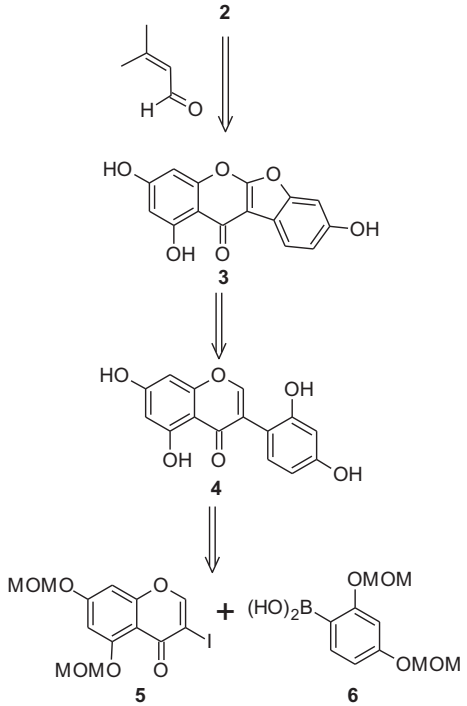
the plant source.[22] Therefore, our aim was to develop a synthetic route that can readily give access to **2** in a good yield, to confirm its structure unambiguously and provide material for future biological studies.

With this synthesis we hope to demonstrate the usefulness of the Suzuki–Miyaura reaction in the synthesis of isoflavonoids. Previous methods for the synthesis of this class of compounds were based mainly on chalcones and deoxybenzoins as intermediates.[14,16] However, the chalcone route depends on the use of the highly toxic thallium trinitrate whereas the deoxybenzoin route employs harsh reaction conditions.

## 2. Results and discussion

Scheme 1 shows the retrosynthetic analysis of lupinalbin H (**2**). Lupinalbin H (**2**) was planned to be synthesized by the regiospecific condensation of lupinalbin A (**3**)[23,24] with prenal. Compound **3** could be prepared by oxidative cyclization of 2′-hydroxygenistein (**4**),[25,26] which could readily be accessed by the Suzuki–Miyaura reaction of 3-iodochromone **5**[21] and boronic acid **6**.[27] The synthesis of the penultimate precursor **3** from 2′-hydroxyisoflavones has been reported previously.[14,16] However, the former syntheses were based on the deoxybenzoin and the chalcone routes for the construction of the isoflavone core.[14,16]




**Scheme 1.** Retrosynthetic analysis of lupinalbin H (**2**).

The synthesis of intermediate **5** was described in a previous paper.[21] Vasselin et al.[28] reported that with the widely used benzyl protecting group, the 3-iodobenzopyran-4-one could not be prepared and therefore we opted for methoxymethyl as protecting group in the synthesis of **5**. Boronic acid **6**[27] was prepared from commercially available resorcinol (**7**), as illustrated in Scheme 2. Protection of **7** with MOMCl, prepared in situ from the readily available dimethoxymethane and acetyl chloride,[29] rendered methoxymethyl ether **8** (60%),[30] which was regioselectively iodinated at C-4 by $I_2$ in the presence of $CH_3CO_2Ag$ to give an aryl iodide **9** in 95% yield.[31] In our previous investigation, we demonstrated the successful regioselective iodination of a chromanone containing resorcinol moiety using $CF_3CO_2Ag$ and $I_2$.[21] $CH_3CO_2Ag$ gave comparable results in the present case. Other readily available silver salts ($AgNO_3$ and $Ag_2SO_4$) were tested for C-4 iodination of **8**, but rendered **9** in low yields when $CHCl_3$ was used as the solvent and in moderate yields in EtOH (Table 1).[32,33] The aryl iodide **9** was converted into boronic acid **6** by lithium–iodine exchange, followed by immediate in situ nucleophilic attack of the generated aryl lithium species on triisopropyl borate and hydrolysis of the resulting boronate ester with $NH_4Cl$ in a one-pot reaction.[34,35]

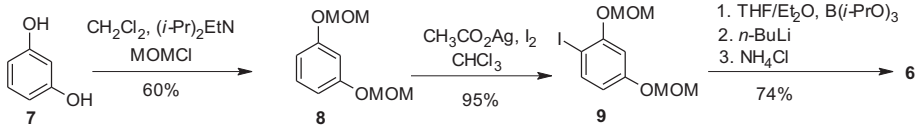
**Table 1**
Preparation of aryl iodide **9** by iodination of **8** with $I_2$ and silver salts[a]

| Silver salt | Solvent | Time (h) | Yields[b] (%) |
|---|---|---|---|
| $AgNO_3$ | $CHCl_3$ | 5 | 40 |
| $Ag_2SO_4$[c] | $CHCl_3$ | 5 | 35 |
| $AgNO_3$ | EtOH | 1 | 62 |
| $Ag_2SO_4$[c] | EtOH | 1 | 58 |
| $CH_3CO_2Ag$ | $CHCl_3$ | 5 | 95 |

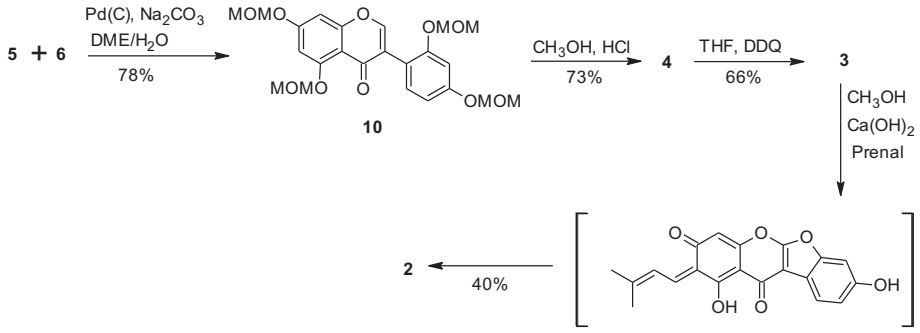
[a] Silver salt (1.2 equiv), 1.1 equiv $I_2$.
[b] Isolated yields.
[c] $Ag_2SO_4$ (0.6 equiv), 1.1 equiv $I_2$.

Having successfully synthesized the boronic acid **6**, the next step involved coupling of **6** with 3-iodochromone **5**[21] in the presence of 10% Pd(C) to give an isoflavone **10** (Scheme 3).[36] Cleavage of the MOM protecting groups of **10** under acidic conditions and subsequent oxidation of 2′-hydroxygenistein (**4**) with DDQ afforded the phytoestrogen lupinalbin A (**3**)[16] in a 66% yield.[14] The last step was regioselective introduction of the dimethylpyran scaffold to the phloroglucinol moiety of lupinalbin A (**3**) to give lupinalbin H (**2**). This was planned to be achieved by base-catalyzed coupling of **3** with prenal, which proceeds via aldol-type reaction and 6π-electrocylization.[18] Thus, treatment of the methanolic solution of **3** with $Ca(OH)_2$ and prenal (2.5 equiv) rendered lupinalbin H (**2**) in 40% yield and 35% of **3** was recovered.[37] Addition of a large excess of prenal (5 equiv) effected complete consumption of **3** as observed on TLC but required tedious chromatographic isolation of the targeted product from the reaction mixture due to side products resulting from the polymerization of prenal.

Lupinalbin A (**3**) has four nucleophilic sites at positions 6, 8, 3′ and 5′, which can condense with prenal to give multiple products. As anticipated, the reaction favoured the more nucleophilic phloroglucinol moiety (ring A) rather than the resorcinol moiety (ring B). Nevertheless, three possible regioisomers can result from condensation of prenal with ring A of **3**, i.e., the targeted linear isomer **2** and two angular isomers **11** and **12**. From the $^1H$ NMR results, it could be readily deduced that the isomer **12** was not




**Scheme 2.** Synthesis of boronic acid **6**.




**Scheme 3.** Total synthesis of lupinalbin H (**2**).

formed due to the appearance of a signal characteristic for a hydrogen-bonded OH at $\delta_H$ 13.38 (1H, OH-5). Furthermore, in the $^1$H NMR spectrum was present four aromatic protons, which gave an ABX spin system for ring B protons at $\delta_H$ 7.82 (1H, d, $J$=8.3 Hz, H-6′), 7.14 (1H, d, $J$=2.0 Hz, H-3′), 7.02 (1H, dd, $J$=2.0 and 8.3 Hz, H-5′),and a one-proton singlet for the ring A proton at $\delta_H$ 6.54 (H-8). The dimethylpyran protons displayed a singlet integrating for six protons at $\delta_H$ 1.48 (2× $CH_3$) and two one-proton doublets for the olefinic protons at $\delta_H$ 6.70 ($J$=10.0 Hz, H-4″) and 5.79 (1H, d, $J$=10.0 Hz, H-5″). These $^1$H NMR results were in agreement with those reported in the literature for **2**.[22] The $^{13}$C NMR spectrum displayed 19 carbon resonances, which were identified as two methyl carbons overlapping at $\delta_C$ 27.3, six methine carbons at $\delta_c$ 128.6, 121.3, 114.6, 113.6, 98.5 and 95.3 and 12 quaternary carbons at $\delta_C$ 178.6, 164.7, 158.5, 157.0, 156.4, 154.0, 150.4, 114.0, 105.9, 104.0, 97.5 and 80.0 by DEPT and HSQC experiments. From the HMBC spectrum, the olefinic proton at $\delta_H$ 6.70 (H-4″) displayed correlations to carbon signals at $\delta_C$ 80.0 (C, C-6″), 105.9 (C, C-6), 157.0 (C, C-5) and 158.5 (C, C-7) and the aromatic proton at $\delta_H$ 6.54 (H-8) showed connections to carbon resonances at $\delta_C$ 104.0 (C, C-4a), 105.9 (C, C-6), 154.0 (C, C-8a) and 158.5 (C, C-7) (Fig. 1). From these correlations, it was confirmed that the dimethylpyran ring was attached to C-6 and OH-7, giving the targeted product **2** and not the angular isomer **11**. The assignments of the quaternary carbons on ring B were also based on HMBC correlations. The proton at $\delta_H$ 7.82 (H-6′) displayed correlations to carbon signals at $\delta_C$ 97.5 (C, C-3), 150.4 (C, C-2′) and 156.4 (C, C-4′), whereas H-5′ ($\delta_H$ 7.02) showed correlations to carbons at $\delta_C$ 114.0 (C, C-1′) and 156.4 (C, C-4′), and the proton at $\delta_H$ 7.14 (H-3′) showed correlations to signals at $\delta_C$ 114.0 (C, C-1′), 150.4 (C, C-2′) and 156.4 (C, C-4′) (Fig. 1). The structure of **2** was confirmed by HRMS-ESI, which gave an $m/z$ peak of 349.0710 $[M-H]^-$, in agreement with the calculated molecular weight of 349.0712 for $C_{20}H_{13}O_6$.

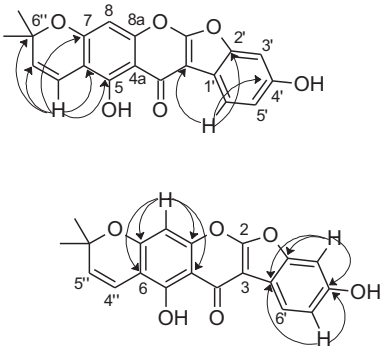
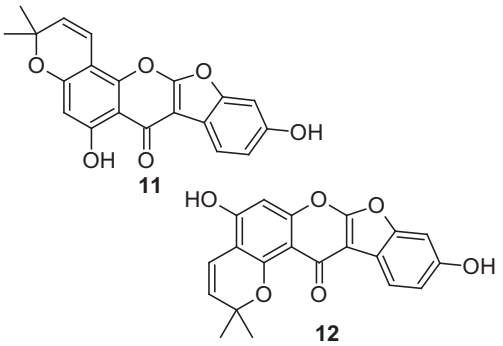



**Fig. 1.** Key HMBC correlations of (**2**).




## 3. Conclusion

In conclusion, lupinalbin H (**2**) has been successfully synthesized by a highly convergent route. The synthesis featured the Suzuki–Miyaura coupling reaction for the construction of the isoflavone nucleus in good yields, and a highly regioselective introduction of the dimethylpyran scaffold to the coumaronochromone core. Furthermore, it gave access to other naturally-occurring phytoestrogens, 2′-hydroxygenistein (**4**) and lupinabin A (**3**). Owing to the potential pharmacological properties of the pyranocoumaronochromones, the development of the practical synthetic route described herein for lupinalbin H (**2**) represents a significant advance towards the synthesis of other structurally related compounds and exploration of their biological properties.

## 4. Experimental procedures

### 4.1. General

All moisture-sensitive reactions were performed using dried anhydrous solvents in oven-dried glassware under an atmosphere of $N_2$. Hexanes (Hex) used for chromatographic purifications was distilled prior to use. Reactions were monitored by TLC, performed on silica gel plates (60 $F_{254}$) and visualized under UV light. Alternatively, detection of spots on the TLC was achieved by heating with a heat gun after treatment with a solution of anisaldehyde in concentrated $H_2SO_4$ and EtOH prepared in volume ratios 1:1:18, respectively. Column chromatographic purifications were effected using silica gel (60 Å, 230–400 mesh). Centrifugal chromatography (chromatotron) was performed on glass plates coated with silica gel with particle size 0.040–0.063 mm, 2–4 mm thick. $^1$H, $^{11}$B, $^{13}$C NMR spectra were recorded on 400 or 500 MHz spectrometer. DEPT and 2D NMR (COSY, HSQC and HMBC) were used for assignments of individual protons and carbons resonances. $^{11}$B NMR spectra were referenced against an external standard of neat $BF_3$.$OEt_2$ containing a capillary tube of acetone-$d_6$ for deuterium

lock. The chemical shifts from $^1$H NMR and $^{13}$C NMR spectra are reported in parts per million relative to the residual protonated or deuterated solvents peaks ($CDCl_3$: $\delta_H$ 7.26, $\delta_c$ 77.0; $CD_3OD$: $\delta_H$ 3.31, $\delta_c$ 49.0 and acetone-$d_6$: $\delta_H$ 2.05, $\delta_c$ 205.1). The mass spectra were recorded on a time-of-flight mass spectrometer using electrospray ionisation in the positive or negative mode. IR spectra were recorded with FT-IR spectrophotometer.

### 4.2. Synthesis

*4.2.1. 1,3-Dimethoxymethoxybenzene (**8**)*[30]. Catalytic $ZnBr_2$ was dissolved in dimethoxymethane (16.0 mL, 0.182 mol) under nitrogen atmosphere, and then acetyl chloride (12.9 mL, 0.182 mol) was added dropwise to the stirred solution. The solution was stirred for an additional 2 h at rt then transferred via a cannula to the ice-cold solution of resorcinol (**7**) (5.00 g, 45.4 mmol) and ($i$-Pr)$_2$EtN (23.3 mL, 0.136 mol) in $CH_2Cl_2$ (100 mL) under a nitrogen atmosphere. The mixture was stirred for 3 h, diluted with saturated $NH_4Cl$ solution and stirred for an additional 15 min. The two phases were partitioned and the aqueous phase was extracted with $CH_2Cl_2$. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was evaporated to give a yellow oil, which was purified by column chromatography using Hex/EtOAc (9:1) to give **8** as a colorless oil (5.4 g, 60%): IR (neat) $\nu_{max}$ 2955, 2902, 2827, 1768, 1591, 1487, 1219, 1138, 1004, 772 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.19 (1H, t, $J$=8.3 Hz, H-5), 6.75 (1H, t, $J$=2.3 Hz, H-2), 6.71 (2H, dd, $J$=2.3 and 8.3 Hz, H-4 and H-6), 5.16 (4H, s, 2× $OCH_2O$), 3.48 (6H, s, 2× $OCH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 158.3 (2× C, C-1 and C-3), 129.9 (CH, C-5), 109.6 (2× CH, C-4 and C-6), 105.0 (CH, C-2), 94.5 (2× $OCH_2O$), 55.9 (2× $OCH_3$); LRMS-ESI $m/z$ [M]$^+$ 198.1.

*4.2.2. 1-Iodo-2,4-dimethoxymethoxybenzene (**9**).* $CH_3CO_2Ag$ (5.10 g, 30.3 mmol) was added to a solution of **8** (5.00 g, 25.2 mmol) in $CHCl_3$ (50 mL). The mixture was stirred for 5 min, and then a solution of $I_2$ (7.04 g, 27.7 mmol) in $CHCl_3$ (150 mL) was added dropwise to the stirred suspension. The resulting mixture was stirred at rt for 5 h and filtered to remove the AgI. The filtrate was washed with 10% $Na_2S_2O_3$ solution, 5% $NaHCO_3$ solution, $H_2O$ and brine. The organic phase was dried over anhydrous $MgSO_4$ and the solvent evaporated to give a colourless oil. The oil was purified by flash chromatography using Hex/EtOAc (9:1) to afford the iodinated compound **9** as a colorless oil (7.76 g, 95%): IR (neat) $\nu_{max}$ 2956, 2902, 2826, 1716, 1577, 1567, 1474, 1219, 1149, 982, 772 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.62 (1H, d, $J$=8.5 Hz, H-6), 6.80 (1H, d, $J$=2.5 Hz, H-3), 6.53 (1H, dd, $J$=2.5 and 8.5 Hz, H-5), 5.21 (2H, s, $OCH_2O$), 5.13 (2H, s, $OCH_2O$), 3.50 (3H, s, $OCH_3$), 3.46 (3H, s, $OCH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 158.7 (C, C-4), 156.7 (C, C-2), 139.2 (CH, C-6), 111.4 (CH, C-5), 104.4 (CH, C-3), 95.0 ($CH_2$, $OCH_2O$), 94.5 ($CH_2$, $OCH_2O$), 77.4 (C, C-1), 56.4 ($CH_3$, $OCH_3$), 56.0 ($CH_3$, $OCH_3$); HRMS-ESI $m/z$ [M+Na]$^+$ calcd for $C_{10}H_{13}INaO_4$ 346.9756, found 346.9754.

*4.2.3. 2,4-Dimethoxymethoxyphenylboronic acid (**6**)*[27]. Triisopropyl borate (10.7 mL, 46.3 mmol) was added to the stirred solution of aryl iodide **9** (5.00 g, 15.4 mmol) in THF/$Et_2O$ (1:2, 100 mL) under $N_2$. The solution was cooled to −100 °C using liquid $N_2$ and $CH_3OH$ bath, and then $n$-BuLi (14.5 mL of a 1.6 M solution in hexanes, 23.2 mmol) was added slowly with stirring. After 1 h of stirring at the temperature below −78 °C, saturated $NH_4Cl$ solution was added. The solution was stirred for an additional 1 h at rt and the two phases partitioned. The aqueous phase was extracted with $Et_2O$. The combined organic phases were washed with $H_2O$ and brine, and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure to give an orange oil. Purification of the oil by column chromatography (8:2 Hex/EtOAc) and evaporation of the solvent afforded the boronic acid **6** as an orange soild (2.76 g, 74%): IR (neat) $\nu_{max}$ 3385, 2957, 1726, 1603, 1142, 993 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.79 (1H, d, $J$=8.4 Hz, H-6), 6.80 (1H, d, $J$=2.0 Hz, H-3), 6.76 (1H, dd, $J$=2.0 and 8.4 Hz, H-5), 6.68 (2H, br s, $B(OH)_2$), 5.27 (2H, s, $OCH_2O$), 5.19 (2H, s, $OCH_2O$), 3.50 (3H, s, $OCH_3$), 3.47 (3H, s, $OCH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 163.5 (C, C-2), 160.9 (C, C-4), 137.8 (CH, C-6), 109.3 (CH, C-5), 102.1 (CH, C-3), 94.6 ($OCH_2O$), 94.0 ($OCH_2O$), 56.4 ($OCH_3$), 56.0 ($OCH_3$), (C-1 signal not observed); $^{11}$B NMR ($CDCl_3$, 128 MHz) $\delta_B$ 28.55.

*4.2.4. 2′,4′,5,7-Tetramethoxymethoxyisoflavone (**10**).* To a solution of 3-iodochromone **5** (1.20 g, 3.06 mmol) in 1:1 DME/$H_2O$ (50 mL) were added 10% Pd/C (0.160 g, 5 mol %), $Na_2CO_3$ (0.970 g, 9.18 mmol) and phenylboronic acid **6** (1.11 g, 4.59 mmol). The resulting mixture was stirred at 40–45 °C overnight. The catalyst was filtered and washed with water and EtOAc. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with water, brine and dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude product was purified by silica gel column chromatography using Hex/EtOAc (7:3) to afford an isoflavone **10** (1.1 g, 78%) as a yellow oil: IR (neat) $\nu_{max}$ 2905, 2828, 1647, 1609, 1570, 1256, 1150, 999, 918 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.75 (1H, s, H-2), 7.22 (1H, d, $J$=8.5 Hz, H-6′), 6.88 (1H, d, $J$=2.3 Hz, H-3′), 6.76–6.72 (3H, m, H-6, H-8, H-5′), 5.27 (2H, s, $OCH_2O$), 5.23 (2H, s, $OCH_2O$), 5.17 (2H, s, $OCH_2O$), 5.10 (2H, s, $OCH_2O$), 3.52 (3H, s, $OCH_3$), 3.50 (3H, s, $OCH_3$), 3.47 (3H, s, $OCH_3$), 3.41 (3H, s, $OCH_3$); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 174.9 (C, C-4), 160.9 (C, C-7), 159.4 (C, C-8a), 158.5 (C, C-5), 158.4 (C, C-4′), 156.2 (C, C-2′), 151.8 (CH, C-2), 132.4 (CH, C-6′), 123.1 (C, C-3), 115.5 (C, C-1′), 111.5 (C, C-4a), 108.9 (CH, C-5′), 104.1 (CH, C-3′), 102.4 (CH, C-6), 97.3 (CH, C-8), 95.8 ($CH_2$, $OCH_2O$), 95.1 ($CH_2$, $OCH_2O$), 94.5 ($CH_2$, $OCH_2O$), 94.3 ($CH_2$, $OCH_2O$), 56.5 ($CH_3$, $OCH_3$), 56.4 ($CH_3$, $OCH_3$), 56.1 ($CH_3$, $OCH_3$), 56.0 ($CH_3$, $OCH_3$); HRMS-ESI $m/z$ [M+Na]$^+$ calcd for $C_{23}H_{26}NaO_{10}$ 485.1424, found 485.1415.

*4.2.5. 2′,4′,5,7-Tetrahydroxyisoflavone (**4**)*[25,26]. HCl (3 M, 15 mL) was added to a solution of **10** (1.00 g, 2.16 mmol) in $CH_3OH$ (30 mL) and stirred at 50 °C for 12 h. $CH_3OH$ was evaporated and the reaction mixture was extracted with EtOAc. The combined organic phases were washed with $H_2O$ and brine. The organic layer was dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure to give a yellow solid. Purification of the solid by column chromatography using Hex/EtOAc (1:1) afforded **4** as a pale yellow solid (0.45 g, 73%): recrystallization of **4** from Hex/EtOAc (1:4) gave pale yellow needles. Mp 268.4–270.1 °C (lit.[26] mp 272.0 °C); IR (neat) $\nu_{max}$ 3319, 1652, 1613, 1502, 1254, 1171 cm$^{-1}$; $^1$H NMR ($CD_3OD$, 400 MHz) $\delta$ 8.00 (1H, s, H-2), 7.04 (1H, d, $J$=8.2 Hz, H-6′), 6.40 (1H, d, $J$=2.3 Hz, H-3′), 6.37 (1H, dd, $J$=2.3 and 8.2 Hz, H-5′), 6.36 (1H, d, $J$=2.3 Hz, H-8), 6.23 (1H, d, $J$=2.3 Hz, H-6); $^{13}$C NMR ($CD_3OD$, 100 MHz) $\delta$ 182.7 (C, C-4), 166.2 (C, C-7), 163.7 (C, C-5), 160.2 (C, C-4′), 159.8 (C, C-8a), 157.8 (C, C-2′), 156.7 (CH, C-2), 133.2 (CH, C-6′), 122.6 (C, C-3), 110.9 (C, C-1′), 108.2 (CH, C-5′), 106.2 (C, C-4a), 104.4 (CH, C-3′), 100.3 (CH, C-6), 94.9 (CH, C-8), HRMS-ESI $m/z$ [M−H]$^-$ calcd for $C_{15}H_9O_6$ 285.0399, found 285.0399.

*4.2.6. Lupinalbin A (**3**)*[23]. DDQ (79.0 mg, 0.349 mmol) was added under $N_2$ to a solution of **4** (100 mg, 0.35 mmol) in THF (20 mL). The reaction mixture was heated to 60 °C with stirring for 15 min. Additional DDQ (79.0 mg, 0.349 mmol) was added to the mixture and stirring was continued at the same temperature for 30 min. The solvent was evaporated and the crude mixture purified by column chromatography using Hex/EtOAc as eluent to give coumaronochromone **3** (66 mg, 66%) as a white solid: **3** was recrystallized from Hex/EtOAc (1:4) to afford white needle-like crystals, which

decomposed at 278.4–280.0 °C (lit.[14] mp >300 °C); IR (neat) $\nu_{max}$ 3327, 3101, 2922, 1622, 1436, 1029, 822 $cm^{-1}$; $^1H$ NMR ($CD_3OD$, 400 MHz) $\delta$ 7.75 (1H, d, $J$=8.4 Hz, H-6′), 6.99 (1H, d, $J$=1.9 Hz, H-3′), 6.89 (1H, dd, $J$=1.9 and 8.4 Hz, H-5′), 6.46 (1H, d, $J$=2.0 Hz, H-8), 6.27 (1H, d, $J$=2.0 Hz, H-6); $^{13}C$ NMR ($CD_3OD$, 100 MHz) $\delta$ 180.0 (C, C-4), 166.2 (C, C-2), 165.2 (C, C-7), 164.0 (C, C-5), 157.8 (C, C-4′), 156.6 (C, C-8a), 151.9 (C, C-2′), 122.5 (CH, C-6′), 115.2 (CH, C-5′), 114.7 (C, C-1′), 104.5 (C, C-4a), 100.9 (CH, C-6), 99.5 (C, C-3), 98.7 (CH, C-3′), 95.8 (CH, C-8); HRMS-ESI $m/z$ $[M-H]^-$ calcd for $C_{15}H_7O_6$ 283.0243, found 283.0239.

*4.2.7. Lupinalbin H (**2**)*[22]. To a solution of **3** (40.0 mg, 0.141 mmol) in $CH_3OH$ (15 mL) was added $Ca(OH)_2$ (21.0 mg, 0.282 mmol) followed by prenal (0.03 mL, 0.353 mmol). The mixture was stirred under an $N_2$ atmosphere for 3 days at rt. $CH_3OH$ was evaporated and the reaction mixture was diluted with EtOAc and 1 M HCl. The two phases were partitioned and the aqueous phase was back-extracted with EtOAc. The combined organic extracts were washed with $H_2O$ and brine and dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude product purified by column chromatography using Hex/EtOAc/acetone (6:1:1), followed by centrifugal chromatography using $CH_2Cl_2$ to give **2** as a cream white solid (20 mg, 40%) and lupinalbin A (**3**) (14 mg, 35%) was recovered. Recrystalization of **2** from $CH_3OH$ gave cream white crystals, which decomposed at 245.5–247.2 °C (lit.[22] mp 248–250 °C); IR (neat) $\nu_{max}$ 3501, 3230, 2923, 2853, 1729, 1640, 1594, 1456, 1393, 1116, 811 $cm^{-1}$; $^1H$ NMR (acetone-$d_6$, 500 MHz) $\delta$ 13.38 (1H, s, OH-5), 8.98 (1H, br s, OH-4′), 7.82 (1H, d, $J$=8.3 Hz, H-6′), 7.14 (1H, d, $J$=2.0 Hz, H-3′), 7.02 (1H, dd, $J$=2.0 and 8.3 Hz, H-5′), 6.70 (1H, d, $J$=10.0 Hz, H-4″), 6.54 (1H, s, H-8), 5.79 (1H, d, $J$=10.0 Hz, H-5″), 1.48 (6H, s, H-7″ and H-8″); $^{13}C$ NMR (acetone-$d_6$, 125 MHz) $\delta$ 178.6 (C, C-4), 164.7 (C, C-2), 158.5 (C, C-7), 157.0 (C, C-5), 156.4 (C, C-4′), 154.0 (C, C-8a), 150.4 (C, C-2′), 128.6 (CH, C-5″), 121.3 (CH, C-6′), 114.6 (CH, C-4″), 114.0 (C, C-1′), 113.6 (CH, C-5′), 105.9 (C, C-6), 104.0 (C, C-4a), 98.5 (CH, C-3′), 97.5 (C, C-3), 95.3 (CH, C-8), 80.0 (C, C-6″), 27.3 (2× $CH_3$, C-7″ and C-8″); HRMS-ESI $m/z$ $[M-H]^-$ calcd for $C_{20}H_{13}O_6$ 349.0712, found 349.0710.

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## Supplementary data

Copies of $^1H$ and $^{13}C$ NMR spectra of **8**, **9**, **6**, **10**, **4**, **3** and lupinalbin H (**2**) as well as copies of HSQC and HMBC NMR spectra of **2**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.09.042.

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