Total Synthesis of the Pyranoisoflavone Kraussianone 1 and Related Isoflavones

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

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

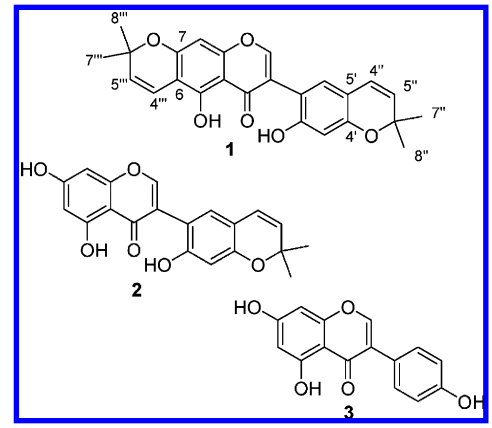
Received June 22, 2010

The first total synthesis of the pyranoisoflavone kraussianone 1 (**1**) is described. The key steps involved the Suzuki−Miyaura reaction for the construction of the isoflavone core and the regioselective formation of the dimethylpyran scaffolds to the phloroglucinol (ring A) and resorcinol (ring B) moieties of kraussianone 1 (**1**). This route also provided access to the related isoflavones eriosemaone D (**2**) and genistein (**3**) via simple structural modifications.

Kraussianone 1 (**1**) is a pyranoisoflavone that was isolated from the bark of *Eriosema kraussianum* Meisn. (Fabaceae), a plant used traditionally for the treatment of male impotence and urinary complaints in KwaZulu-Natal, South Africa.[1] Preliminary studies on the biological activity of the compounds isolated from *E. kraussianum* revealed **1** to be the most potent metabolite for the relaxation of carvenosal smooth muscle, an assay used to evaluate drugs for erectile dysfunction. In this assay, **1** showed an activity of 85% compared to sildenafil (Viagra) at 78 ng/mL.[1,2] Compound **1** further demonstrated significant hypoglycemic and secondary vasorelaxant effects.[3] Therefore, **1** serves as an ideal lead compound for the development of drugs to combat erectile dysfunction and related disorders. However, **1** awaits in-depth biochemical studies to reveal its molecular basis of action for these activities. This has been hampered by the limited supply of the compound from *E. kraussianum*, its sole natural source to date. In order to provide access to sufficient quantities of **1** for further pharmacological studies, we have developed a convenient synthetic route for the preparation of **1** and related compounds, based on the Suzuki−Miyaura reaction for the construction of the isoflavone core.[4] While the application of the Suzuki−Miyaura reaction in the synthesis of isoflavones was demonstrated more than two decades ago,[4] there are not many reports on the synthesis of isoflavones with naturally occurring substitution patterns by this method, especially those with ring A possessing a phloroglucinol moiety.[5,6] Except for the pyranoisoflavone recently synthesized as a precursor to hirtellanine A,[6] no natural pyranoisoflavones have been reported by this method. The previous synthetic procedures for pyranoisoflavones were based on the deoxybenzoin or the chalcone route, which often suffered from poor regioselectivity in the introduction of the dimethylpyran ring to the isoflavone skeleton.[7−13] We herein report the first regioselective total synthesis of kraussianone 1 (**1**), employing the Suzuki−Miyaura reaction as the key step for the construction of the isoflavone nucleus.[4] This route also gave access to a structurally related antifungal pyranoisoflavone, eriosemaone D (**2**),[14,15] whose synthesis has not been disclosed, and to an important phytoestrogen, genistein (**3**).

Results and Discussion

The retrosynthetic analysis of kraussianone 1 (**1**) is shown in Scheme 1. We envisaged that the regioselective aldol-type condensation of the pyranoisoflavone **4** with prenal and the subsequent 6π electrocyclization would give the dimethylpyran ring fused to ring A of kraussianone 1 (**1**). The isoflavone **4** would in turn be synthesized by the Suzuki−Miyaura cross-coupling of 3-iodochromone **5** and the boronic acid derivate **6**, with the requisite dimethylpyran scaffold. The latter would be prepared from readily available resorcinol (**8**) and the former from phloroacetophenone (**7**). Following this route, a number of related isoflavones can be synthesized from the same key building blocks. This has been demonstrated by the synthesis of eriosemaone D (**2**) from the kraussianone 1 precursor **4** and by the synthesis of genistein (**3**) from the 3-iodochromone **5** (*vide infra*).



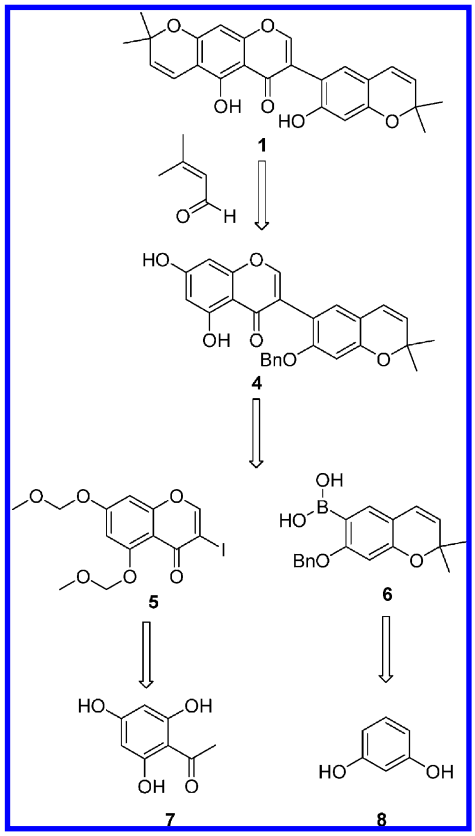
As illustrated in Scheme 2, the synthesis of the intermediate **5** commenced with regioselective protection of the hydroxy groups of phloroacetophenone (**7**) by MOMCl generated from the reaction of dimethoxymethane, AcCl, and catalytic $ZnBr_2$[16] to give **9** in 50% yield. Condensation of **9** with DMF-DMA gave the enaminoketone **10** (68%), which was cyclized in the presence of pyridine and I_2 to afford an inseparable mixture of **5** and **11** in the ratio of 50:7 (by ^{1}H NMR), giving 58% and 6% overall yields, respectively.[17−19] 3-Iodochromone **5** is thus appropriately functionalized for the ultimate conversion to an isoflavone via C−C bond formation by the Suzuki−Miyaura reaction.

Having synthesized the first key building block, **5**, the next step was to prepare its boronic acid partner, **6**. This was achieved in a sequence of steps starting from resorcinol (**8**) (Scheme 3). Thus, condensation of **8** with 3-methyl-2-butenoic acid gave chromanone **12** in 92% yield.[20] Iodination of **12** with I_2 and HIO_3 in CH_3OH/H_2O[21] gave a mixture of the targeted 6-iodochromanone **13** as the major component in 65% yield together with 8-iodochromanone **14** as a minor component. These compounds were inseparable by silica gel column chromatography. However, their purification could be effected by their different solubility properties. The 6-iodochromanone **13** was insoluble in CH_2Cl_2 and $CHCl_3$, whereas compound **14** readily dissolved in these solvents. Although compound **13** was initially obtained in moderate yields under these conditions, this method was not reproducible on a larger scale. Therefore, alternative iodinating reagents, KIO_3/KI, HIO_4/I_2, and ICl, were screened for the regioselective C-6 iodination of chromanone **12** under different conditions,[22−25] but these mostly gave the 8-iodo isomer **14** and 7-hydroxy-6,8-diiodo-2,2-dimethyl-4-chromanone (**15**). Benzyl protection of the 7-hydoxy group of

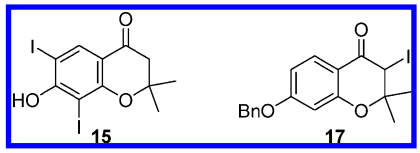
* To whom correspondence should be addressed. Tel: +27 33 2605886. Fax: +27 33 2605009. E-mail: vanheerdenf@ukzn.ac.za.

10.1021/np100407n
Published on Web 08/18/2010

Scheme 1. Retrosynthetic Analysis of Kraussianone 1 (**1**)



chromanone **12** and subsequent iodination of the resulting benzyloxychromanone **16** with HIO_3/I_2[21] resulted in the formation of 7-benzyloxy-3-iodo-2,2-dimethyl-4-chromanone (**17**).

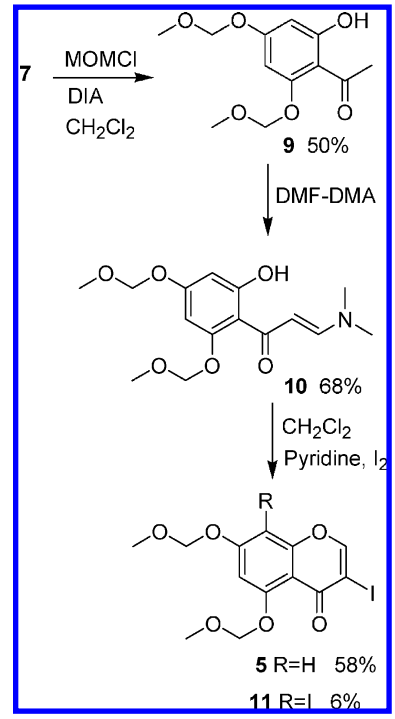


Eventually, the targeted C-6-iodinated chromanone was successfully synthesized by treatment of the $CHCl_3$ solution of 7-benzyloxy-2,2-dimethyl-4-chromanone (**16**) with CF_3CO_2Ag and I_2 at room temperature.[26] This reaction gave 7-benzyloxy-6-iodo-2,2-dimethyl-4-chromanone (**18**) as the sole product in 94% yield. Reduction of **18** with $NaBH_4$ and subsequent dehydration proceeded smoothly to afford the iodochromene **20** in 96% overall yield.[27,28]

We envisioned that the boronic acid **6** could be synthesized from **20** by lithium−iodine exchange with *n*-BuLi, followed by treatment of the phenyllithium with triisopropyl borate and hydrolysis of the resulting boronate ester.[29] The viability of this method was tested on *p*-methoxymethylphenyl iodide (**21**) (Scheme 4), synthesized by protection of the hydroxy group of *p*-iodophenol as the methoxymethyl ether.[16] A solution of phenyl iodide **21** in THF was therefore sequentially treated with *n*-BuLi, triisopropyl borate, and NH_4Cl in one pot. Following this procedure, a small amount of the targeted boronic acid **22** was obtained plus appreciable quantities of the deiodinated material. It was evident from these results that the lithium−iodine exchange occurred rapidly as expected and that the generated aryllithium was very unstable.

Optimum results were obtained by changing the solvent system to THF/Et_2O (1:2) and the sequence in which the reagents were added, by employing the "*in situ* quench" procedure developed by Li and co-workers.[30] Accordingly, the boronic acid **22** was prepared in a one-pot sequence that involved addition of *n*-BuLi to a solution of aryl iodide **21** and triisopropyl borate in THF/Et_2O (1:2), followed

Scheme 2. Synthesis of 3-Iodochromone **5**



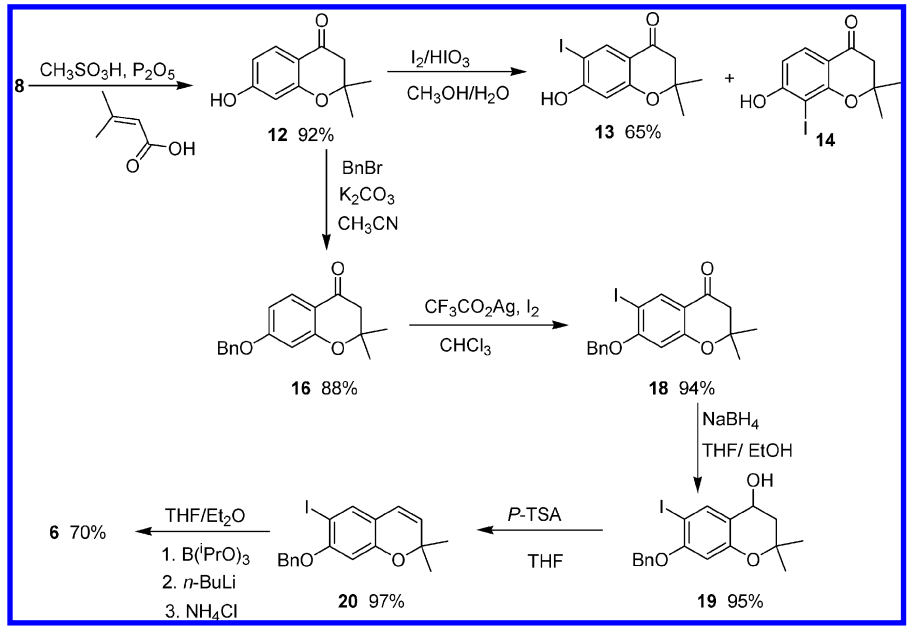
by the hydrolysis of the boronate ester with an NH_4Cl solution (Scheme 4). The improvement observed with this procedure may be attributed to the immediate *in situ* quench of the generated phenyllithium with triisopropyl borate, thus preventing side reactions of the phenyllithium.[30] These optimized reaction conditions were subsequently employed for the synthesis of the boronic acid **6** in 70% yield from iodochromene **20**, as shown in Scheme 3.

The Suzuki−Miyaura cross-coupling of 3-iodochromone **5** with boronic acid **6** using a heterogeneous Pd(C) catalyst[19,31] and subsequent cleavage of the MOM protecting groups with HCl furnished the pyranoisoflavone **4** in 72% yield. Base-catalyzed condensation of the pyranoisoflavone **4** with prenal[32] gave the benzyl derivative of kraussianone 1, **23** (74% yield), which was finally deprotected with BCl_3[13] to afford kraussianone 1 (**1**) in 69% yield (Scheme 5).

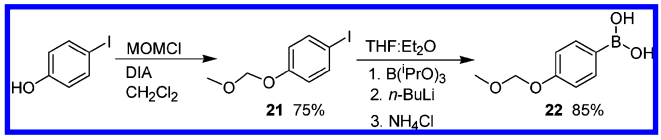
Having successfully synthesized kraussianone 1 (**1**), we took advantage of the available materials and the optimized reaction conditions to synthesize genistein (**3**) and eriosemaone D (**2**). Eriosemaone D (**2**) was isolated from *E. tuberosum* A.Rich,[14,15] but its total synthesis has not been disclosed. The synthesis of genistein (**2**) by the Suzuki−Miyaura reaction has also not been published. As shown in Scheme 5, genistein (**3**) was synthesized in 66% yield over two steps, by coupling the boronic acid **22** to 3-iodochromone **5**,[19,31] followed by removal of MOM protecting groups under similar conditions to those employed for **4**. Eriosemaone D (**2**) on the other hand was synthesized by benzyl deprotection of the pyranoisoflavone **4** with BCl_3.[13] The physical properties and the spectroscopic data of all the synthesized compounds were in agreement with those of the isolated natural compounds. This represents the first total synthesis of kraussianone 1 (**1**) and eriosemaone D (**2**) and the first synthesis of genistein using the Suzuki−Miyaura reaction.

In conclusion, kraussianone 1 (**1**) and the structurally related isoflavones eriosemaone D (**2**) and genistein (**3**) have been successfully synthesized by employing the Suzuki−Miyauara reaction as the key step. The successful synthesis of kraussianone 1 (**1**), via a route that readily gives entry to analogues, will allow for further investigations of its pharmacological properties and structure−activity relationship studies.

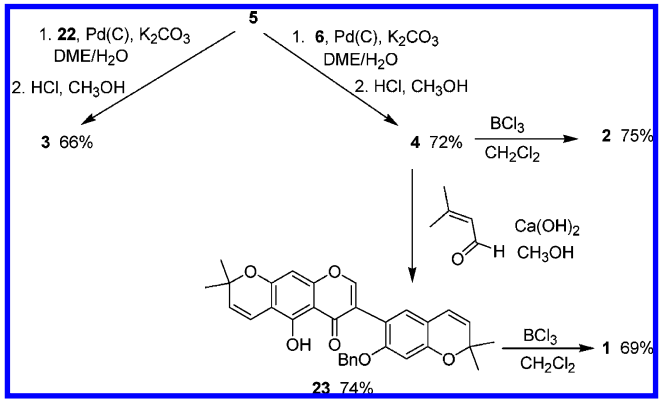
Scheme 3. Synthesis of Boronic Acid **6**



Scheme 4. Model Reaction for Synthesis of Boronic Acid



Scheme 5. Synthesis of Kraussianone 1 (**1**), Eriosemaone D (**2**), and Genistein (**3**)



Experimental Section

General Experimental Procedures. Abbreviations: DIA, diisopropylamine; DMF-DMA, *N*,*N*-dimethylformamide dimethylacetal; Hex, hexanes (bp 68−70 °C); *p*-TSA, *p*-toluenesulfonic acid. Hex used for chromatographic purifications was distilled prior to use. Anhydrous CH_2Cl_2, CH_3CN, THF, and Et_2O were obtained from Innovative Technologies (Newburyport, MA) Pure-Solv 800 solvent purification system. Reagents used for syntheses were purchased from Fluka, Sigma-Aldrich, or Merck and were used without further purification unless otherwise stated. 2′,4′,6′-Trihydroxyacetophenone monohydrate was dried in an oven at 90 °C for 24 h prior to use. Reactions were monitored by TLC. The TLC was performed on Merck silica gel plates (60 F_{254}) and visualized under UV light (254 nm). 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 the volume ratio 1:1:18, respectively. Column chromatography was performed using Merck Kieselgel 60 (230−400 mesh). Centrifugal chromatography was performed on a Harrison Research Chromatotron model 7924T on glass plates coated with Merck silica gel with particle size 0.040−0.063 mm, 2−4 mm thick.

The melting points were measured on a Reichert electrothermal melting point apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer spectrophotometer, and NMR spectra on a Bruker AVANCE DPX_{400} spectrometer. ^{11}B NMR spectra were referenced against an external standard of neat $BF_3 \cdot OEt_2$ containing a capillary tube of acetone-d_6 for deuterium lock. The chemical shifts from ^1H NMR and ^{13}C NMR spectra are reported in parts per million relative to the residual protonated or deuterated solvents peaks ($CDCl_3$: δ_H 7.26, δ_C 77.0 and DMSO-d_6: δ_H 2.50, δ_C 39.5). The spin multiplicities are given as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), br (broad), or m (multiplet). The mass spectra were recorded on a Thermo Finnigan GC-MS ion trap using electron-impact ionization or on a time-of-flight Waters LCT Premier MS using electrospray ionization in the positive or negative mode.

2′-Hydroxy-4′,6′-dimethoxymethoxyacetophenone (9). Catalytic $ZnBr_2$ was dissolved in dimethoxymethane (2.62 mL, 29.74 mmol) under an N_2 atmosphere, and then AcCl (2.12 mL, 29.74 mmol) was added dropwise to the stirred solution. The solution was stirred for an additional 2 h at room temperature and transferred via a cannula to an ice-cold solution of the predried phloroacetophenone (**7**) (2.0 g, 11.89 mmol) and DIA (3.6 mL, 23.59 mmol) in CH_2Cl_2 (100 mL) under an N_2 atmosphere. The mixture was stirred for 3 h, diluted with saturated NH_4Cl solution (40 mL), and stirred for an additional 15 min. The two phases were partitioned, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were washed with brine (3 × 100 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to give a yellow oil, which was purified by column chromatography using Hex/EtOAc (7:3) as eluent to afford **9** as a colorless oil (1.53 g, 50%): IR (neat) ν_{max} 3100, 2925, 1618 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 13.68 (1H, s, OH), 6.26 (1H, d, J = 2.4 Hz, H-3′), 6.24 (1H, d, J = 2.4 Hz, H-5′), 5.25 (2H, s, OCH_2O), 5.16 (2H, s, OCH_2O), 3.52 (3H, s, OCH_3), 3.47 (3H, s, OCH_3), 2.65 (3H, s, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.1 (C, C-1), 167.3 (C, C-2′), 163.3 (C, C-4′), 160.5 (C, C-6′), 107.3 (C, C-1′), 97.3 (CH, C-3′), 94.5 (CH, C-5′), 94.0 (CH_2, 2 × OCH_2O), 56.7 (CH_3, OCH_3), 56.4 (CH_3, OCH_3), 32.9 (CH_3, −$COCH_3$); EIMS *m*/*z* 225 (10%), 209 (29), 207 (100), 191 (22), 44 (40), 40 (62).

3-(*N*,*N*-Dimethylamino)-1-(2′-hydroxy-4′,6′-dimethoxymethoxyphenyl)propenone (10). DMF-DMA (0.29 mL, 2.19 mmol) was added to **9** (0.28 g, 1.09 mmol) at 95 °C. The mixture was stirred at the same temperature for 1.5 h. The volatiles in the orange oil were evaporated on a rotary evaporator, and the crude solid was subjected to flash chromatography using Hex/EtOAc (1:1) as eluent. Evaporation of the solvent gave **10** as a yellow oil, which solidified upon cooling (0.23 g, 68%). The solid was recrystallized to give yellow needle-like crystals (1:1 Hex/Et_2O): mp 85−86 °C; IR (KBr) ν_{max} 3445, 3163, 2913, 1606, 1233 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 15.08 (1H, s, OH-2′), 7.92 (1H, d, J = 12.0 Hz, H-3), 6.29 (1H, d, J = 12.0 Hz, H-2), 6.26 (1H,

d, J = 2.4 Hz, H-3′), 6.17 (1H, d, J = 2.4 Hz, H-5′), 5.20 (2H, s, OCH_2O), 5.14 (2H, s, OCH_2O), 3.51 (3H, s, OCH_3), 3.46 (3H, s, OCH_3), 3.13 (3H, brs, $N(CH_3)_2$), 2.94 (3H, brs, $N(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 190.6 (C, C-1), 166.9 (C, C-2′), 161.3 (C, C-4′), 158.9 (C, C-6′), 154.4 (CH, C-3), 107.1 (C, C-1′), 97.9 (CH, C-3′), 97.0 (CH, C-2), 95.2 (CH_2, OCH_2O), 94.5(CH, C-5′), 94.1 (CH_2, OCH_2O), 56.7 (CH_3, OCH_3), 56.3 (CH_3, OCH_3), 45.5 (CH_3, $N(CH_3)_2$), 37.2 (CH_3, $N(CH_3)_2$); HRMS-ES m/z $[M + Na]^+$ 334.1267 (calcd for $C_{15}H_{21}NO_6Na$ 334.1267).

3-Iodo-5,7-dimethoxymethoxychromone (5). To a solution of propenone **10** (0.12 g, 0.38 mmol) in CH_2Cl_2 (20 mL) was added pyridine (0.06 mL, 0.74 mmol) followed by I_2 (0.11 g, 0.44 mmol). The resulting solution was stirred at room temperature for 12 h. The reaction was quenched with a saturated $Na_2S_2O_3$ solution (10 mL), and the two phases were partitioned. The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The organic layers were combined, washed with H_2O (15 mL) and brine (15 mL), and dried over anhydrous $MgSO_4$. The solvent was evaporated to give a yellow solid. The crude product was purified on a chromatotron using Hex/EtOAc (7:3) as eluent. The solvent was evaporated to afford a cream-white solid (94 mg), which was identified (^{1}H NMR) as a mixture of **5** and **11** in the ratio 50:7, respectively. Therefore, the percentage yield of compound **5** was 58%: IR (KBr) ν_{max} 3179, 3099, 3058, 2958, 2904, 1622, 1445, 1275, 1140, 1036, 921, 844 cm^1; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (1H, s, H-2), 6.75 (1H, d, J = 2.3 Hz, H-8), 6.71 (1H, d, J = 2.3 Hz, H-6), 5.29 (2H, s, OCH_2O), 5.22 (2H, s, OCH_2O), 3.54 (3H, s, OCH_3), 3.49 (3H, s, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2 (C, C-4), 161.5 (C, C-7), 159.2 (C, C-5), 158.3 (C, C-8a), 155.6 (CH, C-2), 108.8 (C, C-4a), 102.1 (CH, C-6), 96.8 (CH, C-8), 95.5 (CH_2, OCH_2O), 94.4 (CH_2, OCH_2O), 89.4 (C, C-3), 56.7 (CH_3, OCH_3), 56.5 (CH_3, OCH_3); HRMS-ES m/z $[M + Na]^+$ 392.9834 (calcd for $C_{13}H_{14}O_6NaI$ 392.9835).

7-Hydroxy-2,2-dimethyl-4-chromanone (12). Resorcinol (**8**) (1.0 g, 9.1 mmol) and 3-methyl-2-butenoic acid (0.91 g, 9.1 mmol) were added simultaneously under N_2 to a stirred mixture of CH_3SO_3H (14.5 mL, 218.2 mmol) and P_2O_5 (0.7 g, 5.1 mmol) at 70 °C. The reaction mixture was stirred at the same temperature for 30 min, cooled to room temperature, and poured into ice−water (150 mL). The aqueous phase was extracted with Et_2O (3 × 25 mL), and the combined organic extracts were washed with H_2O (2 × 50 mL) and brine (25 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to afford a yellow solid. The solid was purified by flash chromatography using Hex/EtOAc (3:2) as mobile phase to give chromanone **12** as a light yellow solid (1.61 g, 92%). Recrystallization of the solid afforded white crystals (9:1 CH_2Cl_2/Et_2O): mp 170.0−171.5 °C (lit.[20] 172−174 °C); IR (KBr) ν_{max} 3129, 2967, 2837, 1578, 1252, 1169, 1126, 854 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.58 (1H, d, J = 8.4 Hz, H-5), 6.43 (1H, dd, J = 1.9 and 8.4 Hz, H-6), 6.24 (1H, d, J = 1.9 Hz, H-8), 2.65 (2H, s, H-3), 1.36 (6H, s, 2 × CH_3); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 190.1 (C, C-4), 164.7 (C, C-7), 161.4 (C, C-8a), 127.9 (CH, C-5), 112.8 (C, C-4a), 109.8 (CH, C-6), 102.8 (CH, C-8), 79.3 (C, C-2), 47.8 (CH_2, C-3), 26.2 (2 × CH_3); HRMS-ES m/z $[M + Na]^+$ 215.0687 (calcd for $C_{11}H_{12}O_3Na$ 215.0684).

7-Hydroxy-6-iodo-2,2-dimethyl-4-chromanone (13). A solution of chromanone **12** (0.15 g, 0.78 mmol), HIO_3 (0.03 g, 0.17 mmol), and I_2 (0.08 g, 0.32 mmol) in CH_3OH/H_2O (3:1, 10 mL) was heated to 85 °C for 12 h. The CH_3OH was evaporated to give a yellow residue, which was diluted with EtOAc (20 mL) and H_2O (25 mL). The two phases were partitioned, and the aqueous phase was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed with saturated $Na_2S_2O_3$ solution (20 mL), H_2O (40 mL), and brine (30 mL) and dried over anhydrous $MgSO_4$. Evaporation of solvent gave a yellow solid, which was washed with hot CH_2Cl_2, cooled, and filtered. The residue was recrystallized from CH_2Cl_2/EtOAc (8:2) to give pure **13** (0.16 g, 65%). The mother liquor, which contained mostly 7-hydroxy-8-iodo-2,2-dimethyl-4-chromanone (**14**), was evaporated to give a yellow solid (49 mg). Compound **13** had mp 195−197 °C; IR (KBr) ν_{max} 2978, 2922, 2702, 1641, 1563, 1327, 1259, 849 cm^1; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.96 (1H, s, H-5), 6.40 (1H, s, H-8), 2.67 (2H, s, H-3), 1.36 (6H, s, 2 × CH_3); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 189.2 (C, C-4), 163.1 (C, C-7), 161.1 (C, C-8a), 136.3 (CH, C-5), 114.9 (C, C-4a), 102.8 (CH, C-8), 79.8 (C, C-2), 76.4 (C, C-6), 47.4 (CH_2, C-3), 26.1 (2 × CH_3); HRMS-ES m/z $[M + Na]^+$ 340.9656 (calcd for $C_{11}H_{11}O_3NaI$ 340.9651).

7-Benzyloxy-2,2-dimethyl-4-chromanone (16). K_2CO_3 (2.16 g, 15.63 mmol) and BnBr (1.2 mL, 10.42 mmol) were added under N_2 to a stirred solution of chromanone **12** (1.00 g, 5.21 mmol) in dry CH_3CN (30 mL). The reaction mixture was refluxed for 8 h under N_2. The mixture was cooled to room temperature, acidified with 2 M HCl (40 mL), and extracted with EtOAc (3 × 20 mL). The organic extracts were combined and washed with H_2O (25 mL) and brine (25 mL), then dried over anhydrous $MgSO_4$. The solvent was removed with a rotary evaporator and the crude product purified on a chromatotron using a Hex/EtOAc (7:3) solvent mixture. The product **16** was obtained as white crystals after evaporation of the solvent and recrystallization from Hex (1.30 g, 88%): mp 55−56 °C; IR (KBr) ν_{max} 3324, 2982, 2964, 2890, 1672, 1604, 1441, 1319, 1258, 1164, 1000, 988, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (1H, d, J = 8.4 Hz, H-5), 7.32−7.43 (5H, m, PhCH_2), 6.62 (1H, dd, J = 1.9 and 8.4 Hz, H-6), 6.46 (1H, d, J = 1.9 Hz, H-8), 5.08 (2H, s, PhCH_2), 2.66 (2H, s, H-3), 1.45 (6H, s, 2 × CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 191.2 (C, C-4), 165.7 (C, C-7), 161.8 (C, C-8a), 136.2 (PhCH$_2$), 128.7 (PhCH_2), 128.3 (CH, C-5), 128.2 (PhCH$_2$), 127.5 (PhCH_2), 113.1 (C, C-4a), 109.8 (CH, C-6), 102.2 (CH, C-8), 79.6 (C, C-2), 70.2 (CH_2, PhCH_2), 48.6 (CH_2, C-3), 26.7 (2 × CH_3); HRMS-ES m/z $[M + Na]^+$ 305.1149 (calcd for $C_{18}H_{18}O_3Na$ 305.1154).

7-Benzyloxy-6-iodo-2,2-dimethyl-4-chromanone (18). CF_3CO_2Ag (94 mg, 0.426 mmol) was added to a solution of **16** (100 mg, 0.355 mmol) in $CHCl_3$ (10 mL). The mixture was stirred for 5 min, and then a solution of I_2 (90 mg, 0.355 mmol) in $CHCl_3$ (20 mL) was added dropwise to the stirred suspension. The resulting mixture was stirred at room temperature for 12 h. The solution was filtered to remove the AgI, and the filtrate was washed with $Na_2S_2O_3$ solution (10%, 30 mL), $NaHCO_3$ solution (5%, 30 mL), H_2O (50 mL), and brine (30 mL). The organic phase was dried over anhydrous $MgSO_4$, and the solvent was evaporated to give a cream-white solid. The solid was purified by flash chromatography using Hex/EtOAc (6:4) as eluent to afford iodochromanone **18** as a white solid (136 mg, 94%). Recrystallization of the solid from CH_3OH gave colorless needles: mp 128−130 °C; IR (KBr) ν_{max} 2983, 1661, 1583, 1262 cm^1; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (1H, s, H-5), 7.48 (2H, d, J = 7.5 Hz, PhCH_2), 7.41 (2H, t, J = 7.5 Hz, PhCH_2), 7.34 (1H, t, J = 7.3 Hz, PhCH_2), 6.40 (1H, s, H-8), 5.14 (2H, s, PhCH_2), 2.65 (2H, s, H-3), 1.44 (6H, s, 2 × CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.2 (C, C-4), 162.8 (C, C-7), 162.1 (C, C-8a), 137.3 (CH, C-5), 135.6 (PhCH$_2$), 128.7 (PhCH_2), 128.2 (PhCH_2), 127.0 (PhCH_2), 116.0 (C, C-4a), 101.3 (CH, C-8), 80.1 (C, C-2), 77.2 (C, C-6), 71.1 (CH_2, PhCH_2), 48.2 (CH_2, C-3), 26.6 (2 × CH_3); HRMS-ES m/z $[M + Na]^+$ 431.0118 (calcd for $C_{18}H_{17}O_3NaI$ 431.0120).

7-Benzyloxy-6-iodo-2,2-dimethyl-4-chromanol (19). To a solution of **18** (0.295 g, 1.05 mmol) in THF (5 mL) was added $NaBH_4$ (0.20 g, 5.25 mmol) in EtOH (20 mL). The resulting solution was refluxed for 3 h. The reaction mixture was cooled to room temperature, quenched with saturated NH_4Cl solution (40 mL), and extracted with EtOAc (3 × 20 mL). The organic phases were combined, washed with saturated $NaHCO_3$ solution (20 mL), brine (20 mL), and H_2O (20 mL), and dried over anhydrous $MgSO_4$. The organic layer was concentrated, and the product was purified by flash chromatography using a Hex/EtOAc (1:1) solvent system to afford chromanol **19** as a colorless oil (0.282 g, 95%), which eventually solidified. The solid was recrystallized from Hex/Et_2O (3:2) to give white crystals: mp 90−92 °C; IR (KBr) ν_{max} 3782, 3467, 2982, 2929, 1579, 1460, 1278, 1163, 1129, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83 (1H, s, H-5), 7.49 (2H, d, J = 7.5 Hz, PhCH_2), 7.39 (2H, t, J = 7.6 Hz, PhCH_2), 7.32 (1H, t, J = 7.3 Hz, PhCH_2), 6.36 (1H, s, H-8), 5.07 (2H, s, PhCH_2), 4.75 (1H, brq, J = 7.5 Hz, H-4), 2.17 (1H, brd, J = 7.3 Hz, OH-4), 2.10 (1H, dd, J = 6.0 and 13.6 Hz, H-3b), 1.80 (1H, dd, J = 8.5 and 13.6 Hz, H-3a), 1.43 (3H, s, CH_3), 1.30 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8 (C, C-7), 154.9 (C, C-8a), 138.0 (CH, C-5), 136.6 (PhCH$_2$), 128.5 (PhCH$_2$), 127.9 (PhCH$_2$), 127.0 (PhCH$_2$), 119.5 (C, C-4a), 101.8 (CH, C-8), 76.2 (C, C-2), 75.2 (C, C-6), 70.8 (CH_2, PhCH_2), 62.9 (C, C-4), 42.6 (CH, C-3), 28.8 (CH_3), 25.9 (CH_3); HRMS-ES m/z $[M + Na]^+$ 433.0280 (calcd for $C_{18}H_{19}O_3NaI$ 433.0277).

7-Benzyloxy-6-iodo-2,2-dimethylchromene (20). *p*-TSA (0.012 g, 0.058 mmol) was added to a solution of chromanol **19** (0.12 g, 0.29 mmol) in THF (15 mL) under N_2. The resulting solution was refluxed under N_2 for 2 h. A NaOH solution (10%, 15 mL) was added to the cooled reaction mixture, and the mixture was extracted with Et_2O (3 × 15 mL). The combined organic extracts were washed with H_2O (40 mL) and brine solution (30 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded a colorless oil, which solidified upon cooling. The solid was successively recrystallized from Hex and

CH_3OH to give iodochromene **20** as white fluffy crystals (0.112 g, 97%): mp 63−65 °C; IR (KBr) ν_{max} 3032, 2972, 2924, 1713, 1602, 1480, 1454, 1358, 1158, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49 (2H, d, J = 7.3 Hz, PhCH_2), 7.40 (2H, t, J = 7.3 Hz, PhCH_2), 7.37 (1H, s, H-5), 7.32 (1H, t, J = 7.2 Hz, PhCH_2), 6.41 (1H, s, H-8), 6.22 (1H, d, J = 9.9 Hz, H-4), 5.48 (1H, d, J = 9.9 Hz, H-3), 5.10 (2H, s, PhCH_2), 1.42 (6H, s, 2 × CH_3); ^{13}C NMR ($CDCl_3$,100 MHz) δ 157.9 (C, C-7), 154.6 (C, C-8a), 136.5 (PhCH_2), 136.0 (CH, C-5), 128.7 (CH, C-3), 128.5 (PhCH_2), 127.9 (PhCH_2), 127.0 (PhCH_2), 120.9 (CH, C-4), 117.0 (C, C-4a), 102.0 (CH, C-8), 76.8 (C, C-2), 74.8 (C, C-6), 70.9 (CH_2, PhCH_2), 28.0 (2 × CH_3); HRMS-ES m/z $[M + Na]^+$ 415.0176 (calcd for $C_{18}H_{17}O_2NaI$ 415.0171).

7-Benzyloxy-2,2-dimethylchromene-6-boronic acid (6). Triisopropyl borate (1.8 mL, 7.65 mmol) was added to a stirred solution of **20** (1.0 g, 2.55 mmol) in THF/Et_2O (1:2, 75 mL) under N_2. The solution was cooled to −100 °C using a liquid N_2 and CH_3OH bath, and then *n*-BuLi (2.4 mL of a 1.6 M solution in hexanes) was added slowly with stirring. After 1 h of stirring at a temperature below −78 °C, saturated NH_4Cl solution was added (50 mL). The solution was stirred for an additional 1 h at room temperature, and the aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with H_2O (2 × 60 mL) and brine (60 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated to give a white solid, which was purified by column chromatography using Hex/EtOAc (4:1) as the mobile phase. Evaporation of the solvent gave boronic acid **6** as a fluffy white solid (0.55 g, 70%): IR (KBr) ν_{max} 3367, 3027, 2969, 2928, 1643, 1607, 1567, 1449 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.47 (1H, s, H-5), 7.36−7.42 (5H, m, PhCH_2), 6.46 (1H, s, H-8), 6.32 (1H, d, J = 10.1 Hz, H-4), 5.54 (2H, s, $B(OH)_2$), 5.49 (1H, d, J = 10.1 Hz, H-3), 5.08 (2H, s, PhCH_2), 1.44 (6H, s, 2 × CH_3); ^{13}C NMR ($CDCl_3$,100 MHz) δ 165.6 (C, C-7), 157.4 (C, C-8a), 135.8 (PhCH_2), 134.8 (CH, C-5), 128.9 (PhCH_2), 128.6 (PhCH_2), 127.9 (C, C-3), 127.8 (PhCH_2), 121.8 (CH, C-4), 114.9 (C, C-4a), 100.1 (CH, C-8), 77.1 (C, C-2), 70.9 (CH_2, PhCH_2), 28.3 (2 × CH_3) (C-6 signal not observed); ^{11}B NMR ($CDCl_3$, 128 MHz) δ_B 28.74.

2′-Benzyloxy-5,7-dihydroxy-6″,6″-dimethylpyrano[2″,3″:4′,5′]isoflavone (4). To a solution of **5** (0.5 g, 1.28 mmol) in DME/H_2O (1:1, 60 mL) were added K_2CO_3 (0.52 g, 3.82 mmol), boronic acid **6** (0.55 g, 1.77 mmol), and 10% Pd(0)/C (68 mg, 5 mol %). The reaction mixture was stirred at 40−45 °C for 12 h. The catalyst was filtered and washed with Et_2O and H_2O. The organic solvents were evaporated, and the crude product was diluted with CH_3OH (25 mL) and HCl (3 M, 10 mL). The resulting solution was stirred at 50 °C for 18 h. CH_3OH was evaporated, and the reaction mixture was diluted with CH_2Cl_2 (15 mL) and H_2O (10 mL). The two phases were partitioned, and the aqueous phase was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic phases were washed with $NaHCO_3$ solution (10%, 50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried over anhydrous $MgSO_4$. Evaporation of the solvent with a rotary evaporator gave a yellow oil, which was subjected to column chromatography using Hex/EtOAc (3:2) as eluent. The solvent was evaporated to give **4** as a yellowish oil, which solidified upon cooling (0.41 g, 72%). Recrystallization of the solid from Hex/Et_2O (1:1) gave white crystals: mp 93−95 °C; IR (KBr) ν_{max} 3255, 2974, 2929, 1650, 1615, 1497, 1277, 1151, 1038, 832, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 12.79 (1H, s, OH-5), 7.77 (1H, s, H-2), 7.22−7.34 (5H, m, PhCH_2), 6.92 (1H, s, H-6′), 6.50 (1H, s, H-3′), 6.23 (1H, d, J = 9.8 Hz, H-4″), 6.21 (1H, d, J = 2.2 Hz, H-8), 6.19 (1H, d, J = 2.2 Hz, H-6), 5.44 (1H, d, J = 9.8 Hz, H-5″), 5.03 (2H, s, PhCH_2), 1.40 (6H, s, H-7″ and H-8″); ^{13}C NMR ($CDCl_3$,100 MHz) δ 181.0 (C, C-4), 163.0 (C, C-7), 162.5 (C, C-5), 158.0 (C, C-8a), 157.5 (C, C-2′), 154.8 (C, C-4′), 154.6 (CH, C-2), 136.6 (PhCH_2), 129.2 (CH, C-6′), 128.5 (PhCH_2), 128.2 (CH, C-5″), 127.9 (PhCH_2), 127.3 (PhCH_2), 121.5 (CH, C-4″), 120.8 (C, C-3), 114.6 (C, C-5′), 112.0 (C, C-1′), 105.8 (C, C-4a), 101.8 (CH, C-3′), 99.6 (CH, C-6), 94.1 (CH, C-8), 76.8 (C, C-6″), 70.9 (CH_2, PhCH_2), 28.2 (2 × CH_3, C-7″ and C-8″); HRMS-ES m/z $[M + Na]^+$ 465.1312 (calcd for $C_{27}H_{22}O_6Na$ 465.1314).

2′-*O*-Benzylkraussianone 1 (23). 3-Methyl-2-butenal (0.18 mL, 1.85 mmol) was added under an N_2 atmosphere to a stirred mixture of $Ca(OH)_2$ (55 mg, 0.74 mmol) and **4** (82 mg, 0.185 mmol) in CH_3OH (10 mL). The mixture was stirred for 3 days at room temperature. CH_3OH was evaporated, and the reaction mixture was diluted with EtOAc (15 mL) and H_2O (20 mL). The two phases were partitioned, and the aqueous phase was extracted with EtOAc (2 × 15 mL). The organic layers were combined, washed with 1 M HCl (40 mL), H_2O (40 mL), and brine (40 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by column chromatography gave **23** as a yellowish oil (70 mg, 74%): IR (KBr) ν_{max} 3422, 3034, 2974, 2927, 1651,1615, 1496, 1463, 1287, 1146, 1058, 828, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 13.22 (1H, s, OH-5), 7.79 (1H, s, H-2), 7.27−7.34 (5H, m, PhCH_2), 6.96 (1H, s, H-6′), 6.73 (1H, d, J = 10.0 Hz, H-4‴), 6.52 (1H, s, H-3′), 6.31 (1H, s, H-8), 6.28 (1H, d, J = 9.8 Hz, H-4″), 5.61 (1H, d, J = 10.0 Hz, H-5‴), 5.49 (1H, d, J = 9.8 Hz, H-5″), 5.04 (2H, s, PhCH_2), 1.47 (6H, s, H-7‴ and H-8‴), 1.44 (6H, s, H-7″ and H-8″); ^{13}C NMR ($CDCl_3$,100 MHz) δ 180.9 (C, C-4), 159.3 (C, C-7), 157.5 (CH, C-2′), 157.3 (C, C-8a), 156.9 (C, C-5), 154.7 (C, C-4′), 154.4 (CH, C-2), 136.8 (PhCH_2), 129.1 (CH, C-6′), 128.5 (PhCH_2), 128.1 (CH, C-5″), 128.0 (CH, C-5‴), 127.8 (PhCH_2), 127.2 (PhCH_2), 121.6 (CH, C-4″), 120.6 (C, C-3), 115.6 (CH, C-4‴), 114.5 (C, C-5′), 112.2 (C, C-1′), 106.2 (C, C-4a), 105.5 (C, C-6), 101.8 (CH, C-3′), 94.8 (CH, C-8), 77.9 (C, C-6‴), 76.8 (C, C-6″), 70.8 (CH_2, PhCH_2), 28.3 (2 × CH_3, C-7‴ and C-8‴), 28.2 (2 × CH_3, C-7″ and C-8″); HRMS-ES m/z $[M + Na]^+$ 531.1782 (calcd for $C_{32}H_{28}O_6Na$ 531.1784).

Kraussianone 1 (1). BCl_3 (0.5 mL, 1 M in heptane) was added to a solution of **23** (50 mg, 0.1 mmol) in CH_2Cl_2 (5 mL) cooled to −80 °C. The mixture was stirred under N_2 at a temperature below −68 °C for 30 min. The reaction was quenched with H_2O and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with H_2O (20 mL) and brine (20 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a yellow oil, which was purified on a chromatotron using CH_2Cl_2 to give **1** (24 mg, 69%) as a yellow solid. The solid was recrystallized from Hex/CH_3OH (4:1): mp 186−188 °C (lit.[1] 185−187 °C); IR (KBr) ν_{max} 3336, 2975, 2872, 1649, 1615, 1460, 1132, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 12.55 (1H, s, OH-5), 8.27 (1H, s, OH-2′), 7.73 (1H, s, H-2), 6.75 (1H, s, H-6′), 6.74 (1H, d, J = 10.0 Hz, H-4‴), 6.53 (1H, s, H-3′), 6.40 (1H, s, H-8), 6.28 (1H, d, J = 9.8 Hz, H-4″), 5.65 (1H, d, J = 10.0 Hz, H-5‴), 5.52 (1H, d, J = 9.8 Hz, H-5″), 1.49 (6H, s, H-7‴ and H-8‴), 1.44 (6H, s, H-7″ and H-8″); ^{13}C NMR ($CDCl_3$,100 MHz) δ 182.0 (C, C-4), 160.4 (C, C-7), 157.2 (CH, C-2′), 157.1 (C-8a), 156.4 (C, C-5), 155.7 (C, C-4′), 154.7 (CH, C-2), 128.8 (CH, C-5″), 128.6 (CH, C-5‴), 127.1 (CH, C-6′), 123.1 (C, C-3), 121.3 (CH, C-4″), 115.28 (CH and C, C-4‴ and C-5′), 112.1 (C, C-1′), 107.3 (CH, C-3′), 106.1 (C, C-6), 105.5 (C, C-4a), 95.0 (CH, C-8), 78.5 (C, C-6‴), 77.2 (C, C-6″), 28.4 (2 × CH_3, C-7‴ and C-8‴), 28.2 (2 × CH_3, C-7″ and C-8″); HRMS-ES m/z $[M + Na]^+$ 441.1317 (calcd for $C_{25}H_{22}O_6Na$ 441.1314).

Eriosemaone D (2). Compound **4** (10 mg, 0.023 mmol) was debenzylated under similar conditions to those applied for **1**, and the product was purified on a chromatotron to give **2** as a yellow solid (6 mg, 75%): ^1H NMR ($CDCl_3$, 400 MHz) δ 12.32 (1H, s, OH-5), 8.21 (1H, brs, OH-7 or OH-2), 7.96 (1H, s, H-2), 6.76 (1H, s, H-6′), 6.53 (1H, s, H-3′), 6.44 (1H, d, J = 2.3 Hz, H-8), 6.37 (1H, d, J = 2.3 Hz, H-6), 6.27 (1H, d, J = 9.8 Hz, H-4″), 5.53 (1H, d, J = 9.8 Hz, H-5″), 1.44 (6H, s, H-7″ and H-8″); LRMS-ES m/z $[M - H]^+$ 351.0.

4-Methoxymethoxy-1-iodobenzene (21). AcCl (1.94 mL, 27.27 mmol) was added dropwise to the stirred solution of dimethoxymethane (2.40 mL, 27.27 mmol) and catalytic $ZnBr_2$ under N_2. The solution was stirred for an additional 2 h at room temperature and transferred via a cannula to an ice-cold solution of 4-iodophenol (2.0 g, 9.09 mmol) and DIA (4.16 mL, 27.27 mmol) in CH_2Cl_2 (100 mL) under an N_2 atmosphere. The mixture was stirred for 4 h, diluted with saturated NH_4Cl solution (40 mL), and stirred for an additional 15 min. The two phases were partitioned, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were washed with brine (3 × 100 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the product was purified with column chromatography using Hex/EtOAc (8:2) to afford **21** as a colorless oil (1.8 g, 75%): IR (neat) ν_{max} 2954, 2901, 2825, 1585, 1483, 1231, 1147, 987, 818 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 (2H, d, J = 9.0 Hz, H-2 and H-6), 6.82 (2H, d, J = 9.0 Hz, H-3 and H-5), 5.14 (2H, s, OCH_2O), 3.46 (3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.0 (C, C-4), 138.2 (CH, C-2 and C-6), 118.5 (CH, C-3 and C-5), 94.3 (CH_2, OCH_2O), 84.3 (C, C-1), 55.9 (CH_3, OCH_3).

4-Methoxymethoxyphenylboronic acid (22). Triisopropyl borate (2.21 mL, 9.47 mmol) was added in one portion to the stirred solution of iodobenzene **21** (1.0 g, 3.79 mmol) in THF/Et_2O (60 mL, 1:2) under N_2. The solution was cooled to −100 °C using a liquid N_2 and CH_3OH bath, and then *n*-BuLi (3.79 mL of a 1.5 M solution in hexanes) was

added with stirring over 5 min. After 1 h of stirring at a temperature below −78 °C, a saturated NH_4Cl (30 mL) solution was added. The mixture was stirred for an additional 1 h, and the two phases were partitioned. The aqueous phase was extracted with Et_2O (2 × 20 mL). The organic phases were combined, washed with H_2O (40 mL) and brine (40 mL), and dried over anhydrous $MgSO_4$. The solvent was evaporated to give a white solid, which was subjected to column chromatography using Hex/EtOAc (4:1) as the mobile phase. The solvent was evaporated to give boronic acid **22** as a white solid (0.59 g, 85%): IR (KBr) ν_{max} 3436, 3359, 1651, 1606, 1235, 1016, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.16 (2H, d, J = 8.6 Hz, H-2 and H-6), 7.15 (2H, d, J = 8.6 Hz, H-3 and H-5), 5.27 (2H, s, OCH_2O), 3.52 (3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.9 (C, C-4), 137.5 (CH, C-2 and C-6), 115.6 (CH, C-3 and C-5), 94.1 (CH_2, OCH_2O), 56.1 (CH_3, OCH_3) (C-1 signal not observed); ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.52.

Genistein (3). 4-Methoxymethoxyphenylboronic acid (**22**) (42 mg, 0.23 mmol), K_2CO_3 (51 mg, 0.37 mmol), and catalytic 10% Pd/C were added to a solution of 3-iodochromone **5** (50 mg, 0.13 mmol) in DME (2 mL) and H_2O (2 mL). The resulting mixture was stirred at 40−45 °C for 12 h. The catalyst was filtered and washed with H_2O and Et_2O. The organic solvents were evaporated, and the crude product was diluted in CH_3OH (10 mL) and HCl (3 M, 5 mL). The resulting solution was refluxed for 30 min. CH_3OH was evaporated, and the aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with H_2O (30 mL) and brine (30 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the crude product was purified by column chromatography using Hex/EtOAc (3:2) and recrystallized from EtOH to give the isoflavone **3** as a yellow solid (23 mg, 66%): mp 300−303 °C (lit.[33] 301−302 °C); IR (KBr) ν_{max} 3434, 3181, 3069, 2922, 1652, 1621, 1176, 809, 784 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 12.93 (1H, s, OH-5), 9.65 (1H, brs, OH-4′), 8.29 (1H, s, H-2), 7.36 (2H, d, J = 8.8 Hz, H-2′ and H-6′), 6.81 (2H, d, J = 8.8 Hz, H-3′ and H-5′), 6.38 (1H, d, J = 2.1 Hz, H-6), 6.22 (1H, d, J = 2.1 Hz, H-8); ^{13}C NMR (DMSO-d_6, 100 MHz,) δ 182.3 (C, C-4), 166.0 (C, C-7), 163.9 (C, C-5), 159.8 (C, C-4′), 158.9 (C, C-8a), 154.8 (CH, C-2), 131.2 (CH, C-2′ and C-6′), 124.8 (C, C-1′), 123.3 (C, C-3), 116.8 (CH, C-3′ and C-5′), 106.3 (C, C-4a), 100.1 (CH, C-6), 94.8 (CH, C-8); HRMS-ES (m/z) $[M - H]^-$ 269.0452 (calcd for $C_{15}H_9O_5$ 269.0450).

Acknowledgment. We are grateful to the National Research Foundation (South Africa) for financial assistance.

Supporting Information Available: Copies of NMR spectra of kraussianone 1 (**1**), eriosemaone D (**2**), genistein (**3**), and synthetic intermediates **4**, **5**, **6**, **10**, **13**, **18**, **19**, **20**, and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Drewes, S. E.; Horn, M. M.; Munro, O. Q.; Dhlamini, J. T. B.; Meyer, J. J. M.; Rakuambo, N. C. *Phytochemistry* **2002**, *59*, 739–747.
(2) Drewes, S. E.; Horn, M. M.; Khan, F.; Munro, O. Q.; Dhlamini, J. T. B.; Rakuambo, C.; Marion Meyer, J. J. *Phytochemistry* **2004**, *65*, 1955–1961.
(3) Ojewole, J. A. O.; Drewes, S. E.; Khan, F. *Phytochemistry* **2006**, *67*, 610–617.
(4) Hoshino, Y.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3008–3010.
(5) Wei, G.; Yu, B. *Eur. J. Org. Chem.* **2008**, 3156–3163.
(6) Zheng, S.-Y.; Shen, Z.-W. *Tetrahedron Lett.* **2010**, *51*, 2883–2887.
(7) Jain, A. C.; Jain, S. M. *Tetrahedron* **1972**, *28*, 5063–5067.
(8) Jain, A. C.; Sharma, B. N. *J. Org. Chem.* **1974**, *39*, 2215–2217.
(9) Jain, A. C.; Kumar, A.; Gupta, R. C. *J. Chem. Soc., Perkin Trans. 1* **1979**, 279–282.
(10) Rao, K. S. R. M.; Iyer, C. S. R.; Iyer, P. R. *Tetrahedron* **1987**, *43*, 3015–3019.
(11) Tsukayama, M.; Horie, T.; Iguchi, Y.; Nakayama, M. *Chem. Pharm. Bull.* **1988**, *36*, 592–600.
(12) Tsukayama, M.; Kawamura, Y.; Tamaki, H.; Kubo, T.; Horie, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 826–832.
(13) Tsukayama, M.; Kawamura, Y.; Tamaki, H.; Horie, T. *Chem. Pharm. Bull.* **1991**, *39*, 1704–1706.
(14) Hostettmann, K.; Marston, A. *Pure Appl. Chem.* **1994**, *66*, 2231–2234.
(15) Ma, W. G.; Fuzzati, N.; Li, Q. S.; Yang, C. R.; Stoeckli-Evans, H.; Hostettmann, K. *Phytochemistry* **1995**, *39*, 1049–1061.
(16) Berliner, M.; Belecki, K. *Org. Synth.* **2007**, *84*, 102.
(17) Gammill, B. R. *Synthesis* **1979**, 901–903.
(18) Hong, R.; Feng, J.; Hoen, R.; Lin, G.-Q. *Tetrahedron* **2001**, *57*, 8685–8689.
(19) Felpin, F.-X.; Lory, C.; Sow, H.; Acherar, S. *Tetrahedron* **2007**, *63*, 3010–3016.
(20) Camps, F.; Coll, J.; Messeguer, A.; Pericas, M. A.; Ricart, S. *Synthesis* **1980**, 725–728.
(21) Mujahidin, D.; Doye, S. *Eur. J. Org. Chem.* **2005**, 2689–2693.
(22) Adimurthy, S.; Ramachandraiah, G.; Ghosh, P. K.; Bedekar, A. V. *Tetrahedron Lett.* **2003**, *44*, 5099–5101.
(23) Aslam, S. N.; Stevenson, P. C.; Phythian, S. J.; Veitch, N. C.; Hall, D. R. *Tetrahedron* **2006**, *62*, 4214–4226.
(24) Hossain, M. M.; Tokuoka, T.; Yamashita, K.; Kawamura, Y.; Tsukayama, M. *Synth. Commun.* **2006**, *36*, 1201–1211.
(25) Weitl, F. L. *J. Org. Chem.* **1976**, *41*, 2044–2045.
(26) Haszeldine, R. N.; Sharpe, A. G. *J. Chem. Soc.* **1952**, 993–1001.
(27) Lichtenfels, A. R.; Coelho, A. L.; Costa, R. R. *J. Chem. Soc., Perkin Trans. 1* **1995**, 949–951.
(28) Lim, J.; Kim, H.-I.; Kim, H. H.; Ahn, K.-S.; Han, H. *Tetrahedron Lett.* **2001**, *42*, 4001–4003.
(29) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316–1319.
(30) Li, W.; Nelson, D. P.; Jensen, M. S.; Hoerrner, R. S.; Cai, D.; Larsen, R. D.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 5394–5397.
(31) Felpin, F.-X. *J. Org. Chem.* **2005**, *70*, 8575–8578.
(32) Mondal, M.; Puranik, G. V.; Argade, N. P. *J. Org. Chem.* **2006**, *71*, 4992–4995.
(33) Bradbury, R. B. *J. Chem. Soc.* **1951**, 3447–3449.

NP100407N