JOC Article

Total Synthesis of Flavocommelin, a Component of the Blue Supramolecular Pigment from *Commelina communis*, on the Basis of Direct 6-*C*-Glycosylation of Flavan

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We succeeded in a first total synthesis of flavocommelin (**1**), a component of the blue supramolecular pigment, commelinin (**2**), from *Commelina communis*, by direct 6-*C*-glycosylation of the flavan **4** using perbenzylglucosyl fluoride **8** in the presence of MS 5 Å in CH_2Cl_2 and a catalytic amount of $BF_3{\cdot}Et_2O$. After 6-*C*-glycosylation of **4**, oxidation with CAN to flavanone **18** and subsequent 4′-*O*-glycosylation, promoted with a combination of $BF_3{\cdot}Et_2O$ and DTBMP, afforded diglucosylflavanone **20**. DDQ oxidation of **20** and deprotection successively gave **1**.

Introduction

A variety of *C*-glycosylflavonoids are found widely distributed in the plant kingdom.[1] The *C*-glycosides are generally linked at C-6 and/or C-8 on the A-ring of the flavonoid nucleus. Their biological activities as antioxidants,[2] flower-color-development,[3] DNA binding,[4] hypotension,[5] and ovipositional[6] and feeding[7] stimulation for insects are well-known. Carthamin, a *C*-glucosylchalcone, is practically used as a red pigment.[8] Despite the attractive biological characteristics and commercial utility, only a few synthetic methods for *C*-glycosylflavonoids have been reported.[1,9,10] In fact, the synthesis of a flavone bearing both *O*- and *C*-glucosides has hitherto never been reported.

We have focused our attention on flavocommelin (**1**), a 7-*O*-methylapigenin 6-*C*-,4′-*O*-di-*β*-D-glucoside, and one of the components of commelinin (**2**), a blue supramolecular pigment that is a metalloanthocyanin (a metal-complex anthocyanin) in *Commelina communis*.[3b] Commelinin (**2**), to our knowledge, is the most stable of the metalloanthocyanins due to the presence of *C*-glucosylflavone. Its structure has been established by X-ray crystallographic analysis[3b] and the pigment is a stoichiometric self-assembled supramolecule composed of six molecules of malonylawobanin (**3**), six molecules of **1**, and two atoms of magnesium ion (Figure 1). The components of **2** spatially self-assemble on the basis of very strict chiral molecular recognition. Recognition by self-association (itself) of **1** and **3**, and copigmentation between **1** and **3** might be caused by chiral hydrophobic $\pi-\pi$ interactions and some hydrogen bonding among the sugar residues.[3b,11] To elucidate the basis for molecular chiral recognition in the formation of commelinin (**2**), **1** and its analogues bearing various D- and/or L-glucose are necessary. We herein report the first successful synthesis of flavocommelin (**1**) using a newly developed approach for efficient *C*-glycosylation of flavan as a key reaction.

Results and Discussion

Syntheses of *C*-glycosylflavonoids have been realized on the basis of both *C*-glycosylations, Fries-type rear-

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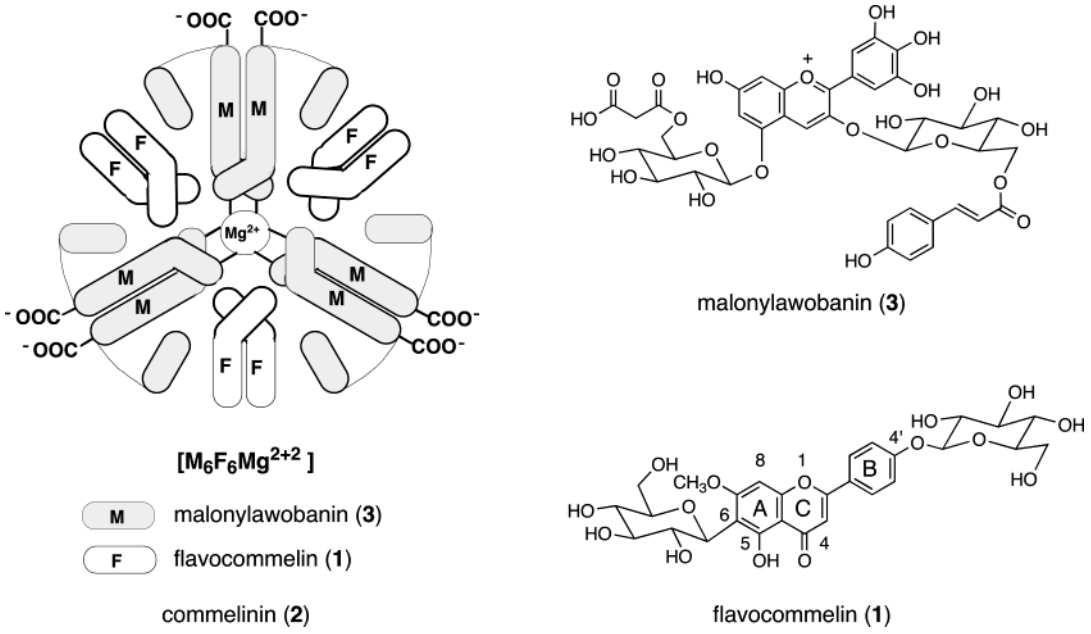
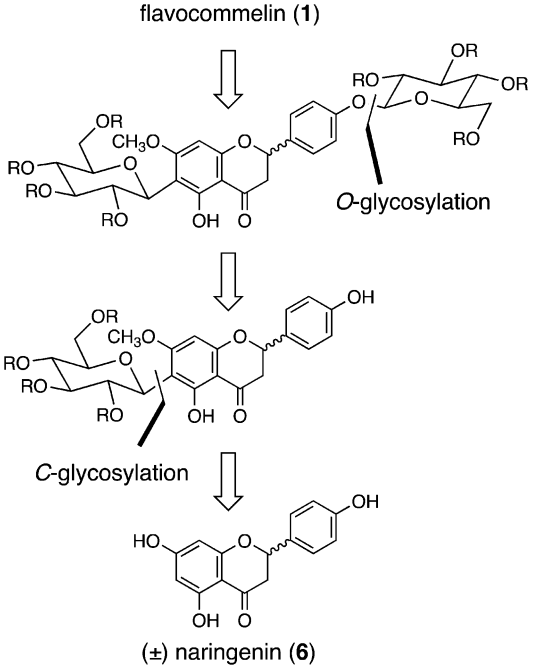


FIGURE 1. Commelinin (**2**) and the structure of its components.

SCHEME 1. Retrosynthesis of Flavocommelin (1)



rangement of *O*- to *C*-glycoside,[9] and coupling reaction between lithiated aromatic compounds and sugar derivatives.[10] Usually, with 2,4,6-trihydroxybenzene derivatives the following difficulties are encountered:[9,10] multistep selective protection of 2,4,6-trihydroxybenzene derivatives, nonregioselective cyclization to a flavone skeleton, and insufficient *C*-glycosylation.

We have developed an efficient synthetic strategy to derive **1** from a flavan derivative as a presumed important intermediate based on the stepwise glycosylation of *O*- and *C*-glycosides capable of replacing D-glucose with L-glucose for preparation of chiral analogues (Scheme 1). As use of flavan **4** as a starting material avoids the abovementioned difficulties, direct *C*-glycosylation to a flavonoid nucleus would allow the concise synthesis of **1**. We have already achieved efficient *O*-glycosylation of 4′-OH of a flavone[12] using peracetylglucosyl fluoride **5** promoted with $BF_3{\cdot}Et_2O$ as a Lewis acid and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) as a Lewis base.[11,13]

Aryl *C*-glycosylation depends on the electron density of the aromatic ring[14] and protecting groups of glycosyl donors.[15] Because 1,3,5-trimethoxybenzene has a high electron density on the ring, a variety of glycosyl donors such as glycosyl imidate,[16a] pyridyl thioglycoside,[16b] glycosyl fluoride,[16c] glycosyl dinitrobenzoate,[16d] glycosyl trifluoroacetate,[16e] and glycosyl dimethylphosphinothioate[16f] in the presence of Lewis acid are applicable for *C*-glycosylation. Recently, Kumazawa reported 2,4-*O*-benzyloxy-6-hydroxyacetophenone to be *C*-glycosylated, involving Fries rearrangement.[9b,c,17]

At first we focused on (±) naringenin (**6**) having a flavanone skeleton like trihydroxyacetophenone for direct *C*-glycosylation. Attempts at glycosylation of 7,4′-*O*-dimethylnaringenin (**7b**) with 2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl fluoride (**8**), using $BF_3{\cdot}Et_2O$[17] or Cp_2-

(12) The reactivity of 4′-OH of flavone is low: (a) Harborne, J. B.; Mabry, T. J.; Mabry, H., Eds. *The Flavonoids, Part 1*; Academic Press: New York, 1975; p 166. (b) Lewis, P.; Kaltia, S.; Wähälä, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2481. (c) Du, Y.; Wei, G.; Linhardt, R. J. *Tetrahedron Lett.* **2003**, *44*, 6887.

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(14) In general the *C*-glycosylation of electron-rich aromatic compounds proceeds smoothly, while it is remarkably suppressed by substitution of electron withdrawing and/or steric hindrance groups on the aromatic ring: (a) Jaramillo, C.; Knapp, S. *Synthesis* **1994**, 1. (b) Plante, O. J.; Palmacci, E. R.; Andrade, R. B.; Seeberger, P. H. *J. Am. Chem. Soc.* **2001**, *123*, 9545. (c) Kumazawa, T.; Ishida, M.; Matsuba, S.; Sato, S.; Onodera, J.-I. *Carbohydr. Res.* **1997**, *297*, 379.

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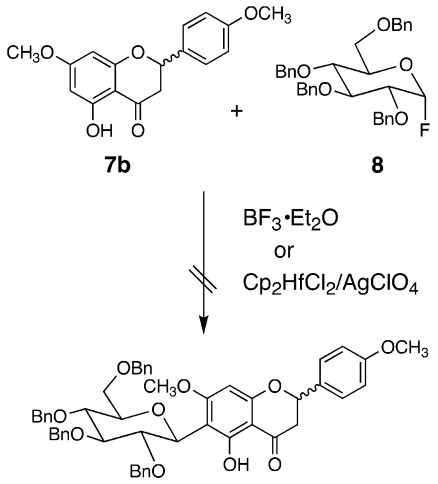
SCHEME 2. Attempted *C*-Glycosylation of Flavanone 7b

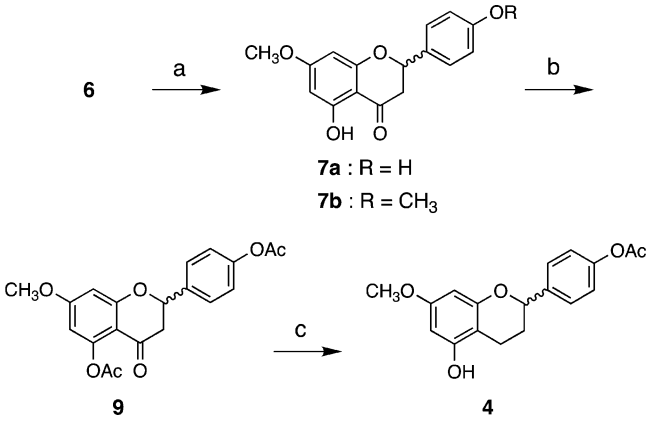


$HfCl_2/AgClO_4$,[18] however, provided no naringenin *C*-glucoside (Scheme 2). This might have been due to an electron deficiency on the A-ring of **7b** arising from the carbonyl group[19] and strong hydrogen bonding between 6-OH and the carbonyl group, suggesting that transformation of a flavanone to a flavan is necessary for *C*-glycosylation.

We assumed that flavan **4** is most suitable as an intermediate for synthesis of **1**. Regioselective methylation of commercially available (±) naringenin (**6**) with 1.5 equiv of CH_3I/K_2CO_3 in DMF at room temperature afforded the 7-*O*-methylnaringenin (**7a**) and 7,4′-*O*-dimethylnaringenin (**7b**) in 76% and 3% yields, respectively. Acetylation of **7a** with AcCl/Et_3N/DMAP in CH_2Cl_2 afforded diacetate **9** in 90% yield. Removal of the carbonyl group was carried out by reduction of **9** with 2 equiv of $NaBH_4$ in THF and H_2O at 0 °C for 30 min to give an 85% yield of the monoacetate **4** as a racemate (Scheme 3).[20] *C*-Glycosylation of the flavan **4** with glucosyl fluorides, using BF_3·Et_2O as a promoter, was investigated. Glycosylation with perbenzylglucosyl fluoride **8** and BF_3·Et_2O (100 mol %) in CH_2Cl_2 in the presence of MS 5 Å provided an inseparable diastereomeric mixture of the 6-*C*-*β*-glucoside **10**, the 8-*C*-*β*-glucoside **11**, and the 5-*O*-α- and *β*-glucosides **12a** and **12b** in 53%, 2%, and 16% yields, respectively,[21] but no *C*-α-glucoside (Table 1, entry 1). Determination of the anomeric configuration of the products was very difficult by NMR analysis because of overlapping signals for the anomeric and benzylic protons (vide infra).

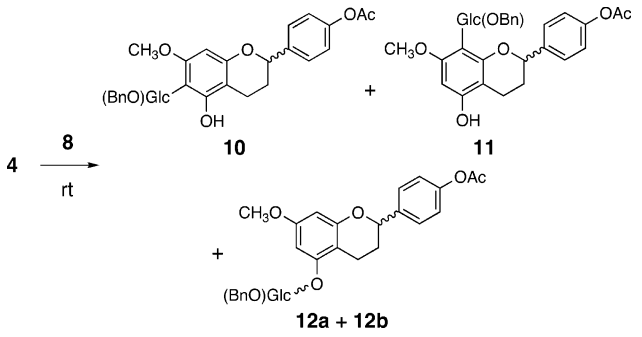
With $Cp_2HfCl_2/AgClO_4$,[18] a similar trend was observed, but yields were low (Table 1, entry 2), while using peracetylglucosyl fluoride **5**[22] promoted with BF_3·Et_2O in CH_2Cl_2 gave only a trace amount of the desired 6-*C*-*β*-glucoside **13**[23] (Table 2, entries 1 and 2). However, glycosylation of **4** with **5** promoted with a Lewis acid and a base combination of BF_3·Et_2O and DTBMP[11,13] gave predominantly the 5-*O*-*β*-glucoside (**14b**/**13** = 92/8, Table 2). These results showed that the phenolate, deprotonated with DTBMP, gives the *O*-glycoside. As a result of the screening of the reaction condition, this *C*-glycosylation could proceed smoothly with catalytic amounts (>20 mol %) of BF_3·Et_2O and the yield of the desired **10**

SCHEME 3. Synthesis of Flavan 4[a]



[a] Reagents and conditions: (a) CH_3I (1.5 equiv of **6**), K_2CO_3, DMF, rt (**7a**: R = H (76%); **7b**: R = CH_3 (3%)); (b) AcCl, Et_3N, DMAP, CH_2Cl_2, rt (90%) (from **7a**); (c) $NaBH_4$, THF/H_2O, 0 °C (85%).

TABLE 1. Glycosylation of Flavan 4 with Perbenzylglucosyl Fluoride 8[a]



entry	promotor (mol %)	additive	solvent	yield (%)[b] 10[c]	11[c]	12a[d]	12b[e]
1	BF_3·Et_2O (100)	MS 5 Å	CH_2Cl_2	53	2	11	5
2[f]	Cp_2HfCl_2 (200)/ $AgClO_4$ (100)	MS 4 Å	CH_2Cl_2	39	6	8	6
3	BF_3·Et_2O (20)	none	CH_2Cl_2	21	1	5	2
4	BF_3·Et_2O (20)	MS 4 Å	CH_2Cl_2	39	9	9	4
5	BF_3·Et_2O (20)	MS 5 Å	CH_2Cl_2	56	7	13	6
6	BF_3·Et_2O (20)	MS 5 Å	CH_3CN	19	23	8	2
7	BF_3·Et_2O (10)	MS 5 Å	CH_2Cl_2	49	9	11	5

[a] All reactions were carried out with 2 equiv of **4** to **8** for 1.5 h. [b] The yield was determined by ^1H NMR on the basis of an isolated mixture of **10**, **11**, **12a**, and **12b**. [c] *C*-Glucosides **10** and **11** were obtained as *β*-isomers exclusively. [d] **12a** was a α-glucoside. [e] **12b** was a *β*-glucoside. [f] The reaction mixture was allowed to stand from −10 °C to rt for 1.5 h.

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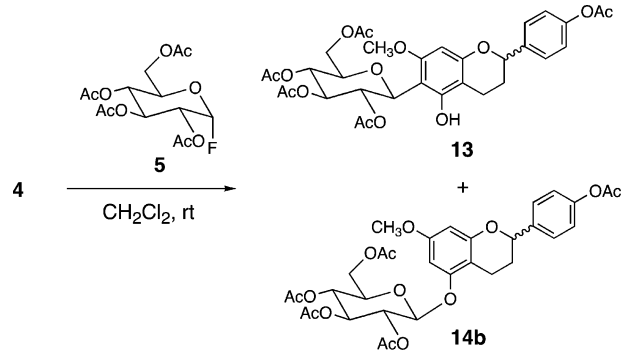
(21) All compounds **10**−**20** feature a diastereomeric mixture, arising from the stereochemistry of the C-2 position. As these were an inseparable mixture by silica gel column chromatography, ^1H NMR assignment in a diastereomeric mixture was carried out.

(22) For an example of the aryl *C*-glycosylation with peracetylated glycosyl donor: Kuribayashi, T.; Ohkawa, N.; Satoh, S. *Tetrahedron Lett.* **1998**, *39*, 4537.

(23) The regiochemistry and anomeric configuration of **13** were determined by peracetylation (see Supporting Information).

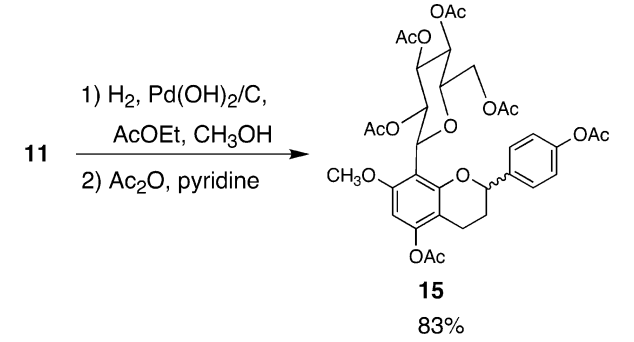
TABLE 2. Glycosylation of Flavan 4 with Peracetylglucosyl Fluoride 5



entry	condition	time (h)	yield (%)[a]	ratio (**13**/**14b**)[b,c]
1	BF_3·Et_2O (1 equiv), MS 5 Å	1.5	<1	nd[d]
2	BF_3·Et_2O (4 equiv)	1	6	94/6
3	BF_3·Et_2O (4 equiv), DTBMP	1	82	8/92

[a] Isolated yield. [b] Both *O*- and *C*-glucosides were obtained only as *β*-isomers. [c] Ratios of **13** and **14b**, inseparable by column chromatography, were determined by ^{1}H NMR. [d] nd = not determined.

SCHEME 4. Acetylation of 11

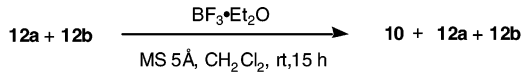


was improved to 56% (total conversion yield based on **8** was 82%) (Table 1, entry 5). In this reaction, molecular sieves (MS 5 Å) played an important role. Without MS 5 Å the yield was decreased to 29% and on changing MS 5 Å to MS 4 Å reduction to 39% was apparent (Table 1, entries 4 and 5). Therefore, MS 5 Å may be a HF-scavenger in the catalytic cycle. Change of CH_2Cl_2 to CH_3CN as the solvent altered the mole ratio of the products, the 8-*C*-*β*-glucoside **11** predominating (**10**/**11** = 19/23) (Table 1, entry 6).

To determine the anomeric configuration of **11** the corresponding acetate **15** was derived by hydrogenolysis and acetylation (83% yield, Scheme 4). As the $J_{anomeric}$ was 10.2 Hz (*δ* 5.13 Hz), **15** was a *C*-*β*-glucoside.

It is hypothesized that *C*-glycosylation of phenol involves Fries-type *O*-to-*C* rearrangement[24] via *O*-glucosides. To clarify this reaction, a mixture of the isolated *O*-glucosides (**12a** and **12b**) was treated with 20 mol % of BF_3·Et_2O in the presence of MS 5 Å in CH_2Cl_2 for 15 h at room temperature. Most of starting materials were recovered with only a trace amount of 6-*C*-glucoside **10** (Table 3, entry 1) and further addition of the catalyst up to 1 equiv gave the same result (Table 3, entry 2). Thus, this major reaction involves a different mechanism from Fries-type *O*-to-*C* rearrangement. The glucosyl cation, generated from **8** with BF_3·Et_2O, might form a *π*-complex[25] by interacting with an aromatic ring and 5-OH of **4** directly for 6-*C*-glycosylation.

TABLE 3. Attempt at *O*-to-*C* Rearrangement of the *O*-Glucosides 12a and 12b[a]



entry	BF_3·Et_2O (mol %)	yield (%)[b,c]	ratio ((**12a** + **12b**)/**10**)[d]
1	20	72	98/2
2	100	61	81/19

[a] Ratio of **12a** and **12b** as starting materials was ca. 70/30. [b] Isolated yield. [c] 8-*C*-Glucosides were not obtained. [d] Ratios were determined by ^{1}H NMR.

Treatment of a mixture of the 6-*C*-glucoside **10** and the *O*-glucosides **12a** and **12b** with AcCl/Et_3N/DMAP acetylated only **10** to give diacetate **16** (a diastereomeric mixture), which could be readily isolated from **12a** and **12b** (Scheme 5). The $J_{anomeric}$ of **16** was 10.8 Hz (*δ* 4.70 Hz), indicating the glucoside to be in the *C*-*β*-configuration. The remaining **12a** and **12b** were hydrogenated with H_2/$Pd(OH)_2$ and acetylated to provide the pentaacetates **14a** ($J_{anomeric}$ = 2.7 Hz (*δ* 5.72, 5.73 Hz), α-glucoside) and **14b** ($J_{anomeric}$ = 8.1 Hz (*δ* 5.46 Hz), *β*-glucoside) (Scheme 6).

To oxidize **16** with CAN[26] (ceric ammonium nitrate), the benzyl ester **16** was transformed to the benzoate **17**, for which the rotamer was observed by NMR, quantitatively by hydrogenolysis,[27] and then benzoylation was accomplished with BzCl/pyridine/DMAP. **17** was oxidized with CAN[26] in AcOH/H_2O/CH_3CN at 60 °C for 30 min to the corresponding flavanone **18** in 43% yield, but DDQ[28] (2,3-dichloro-5,6-dicyano-1,4-benzoquinoe) oxidation and the other oxidations[29] failed to give the desired product. Regioselective deacetylation at 4′-OH of **18** with AcCl/CH_3OH[30] afforded the monoacetate **19** in 80% yield. **19** was glycosylated with peracetylglucosyl fluoride **5** by a combination of BF_3·Et_2O and DTBMP[11,13] in CH_2Cl_2 to give the desired di-*β*-glucoside **20** in 84% yield. Further-

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(25) (a) Olah, G. A.; Schlosberg, R. H.; Porter, R. D.; Mo, Y. K.; Kelly, D. P.; Mateescu, G. D. *J. Am. Chem. Soc.* **1972**, *94*, 2034. (b) Olah, G. A.; Kobayashi, S.; Nishimura, J. *J. Am. Chem. Soc.* **1973**, *95*, 564.

(26) For CAN oxidation of the C-4 position of chroman: (a) Kanvinde, M. N.; Kulkarni, S. A.; Paradkar, M. V. *Synth. Commun.* **1990**, *20*, 3259. (b) Bissada, S.; Lau, C. K.; Bernstein, M. A.; Dufresne, C. *Can. J. Chem.* **1994**, *72*, 1866.

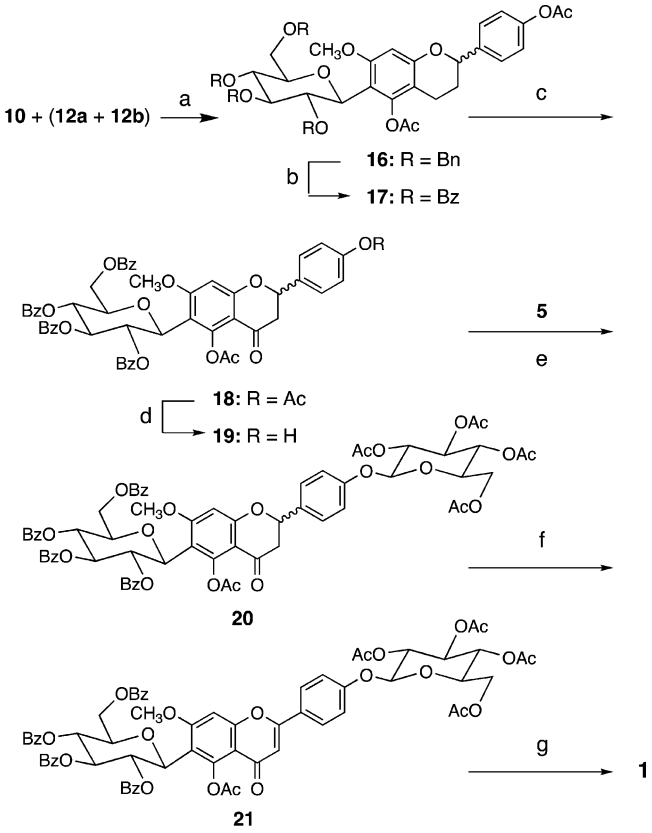
(27) For hydrogenolysis with H_2/$Pd(OH)_2$/C: Tückmantel, W.; Kozikowski, A. P.; Romanczyk, L. J., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 12073. Debenzylation of **16** with H_2 and Pd/C could not proceed and also with H_2, HCl aq, and Pd/C the yield was low (62%, 2 steps).

(28) For DDQ oxidation of the C-4 position of catechin: (a) Steenkamp, J. A.; Ferreira, D.; Roux, D. G. *Tetrahedron Lett.* **1985**, *26*, 3045. (b) Steenkamp, J. A.; Mouton, C. H. L.; Ferreira, D. *Tetrahedron Lett.* **1991**, *47*, 6705. (c) Ohmori, K.; Ohrui, H.; Suzuki, K. *Tetrahedron Lett.* **2000**, *41*, 5537.

(29) Oxidations with RuO_2/$NaIO_4$/EtOAc/H_2O,[29a] $KMnO_4$/$CuSO_4$·$5H_2O$,[29b] and MCPBA (*m*-chloroperbenzoic acid)/Air/$NaHCO_3$[29c] gave no desired compound **18**: (a) Zhang, X.; Schmitt, A. C.; Jiang, W. *Tetrahedron Lett.* **2001**, *42*, 5335. (b) Noureldin, N. A.; Zhao, D.; Lee, D. G. *J. Org. Chem.* **1997**, *62*, 8767. (c) Ma, D.; Xia, C.; Tian, H. *Tetrahedron Lett.* **1999**, *40*, 8915.

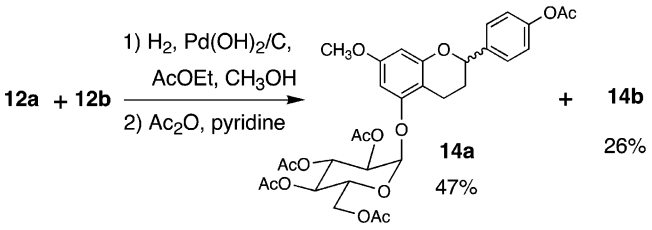
(30) Byramova, N.; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1983**, *124*, C8.

SCHEME 5. Synthesis of Flavocommelin (1)[a]



[a] Reagents and conditions: (a) AcCl, Et_3N, DMAP, CH_2Cl_2, rt (**16**: 69%; recovered **12a** and **12b**: 24%); (b) H_2, $Pd(OH)_2$/C, AcOEt/CH_3OH, rt and then BzCl, pyridine, DMAP, rt (95%, 2 steps); (c) CAN, AcOH/CH_3CN/H_2O, 60 °C (43%); (d) AcCl/CH_3OH, $CHCl_3$, rt (80%); (e) BF_3·Et_2O, DTBMP, CH_2Cl_2, rt (84%); (f) DDQ, PhCl, 140 °C (84%); (g) KOH, MeOH/THF, rt (90%).

SCHEME 6. Acetylation of the *O*-Glucosides 12a and 12b



more, DDQ dehydrogenation of **20** with DDQ in PhCl at 140 °C afforded a single compound, flavone **21**, in 83% yield, but under previously described conditions[11,13b,31] (110 °C in 1,4-dioxane) production of **21** was only minor. Finally deprotection of flavone **21** with KOH/CH_3OH gave flavocommelin (**1**) in 90% yield (12 steps, 6.2% overall yield). Synthetic **1** proved identical with an authentic sample of the natural occurring component with ^{1}H NMR and optical rotation.[32]

(31) For DDQ dehydration of flavanone with 1,4-dioxane as a solvent: Shanker, C. G.; Mallaiah, B. V.; Srimannarayana, G. *Synthesis* **1983**, 310.

(32) Natural flavocommelin (**1**) was obtained according to Takeda's method.[32a] (a) Takeda, K.; Mitsui, S.; Hayashi, K. *Bot. Mag. Tokyo* **1966**, *79*, 578. (b) Goto, T.; Yoshida, K.; Yoshikane, M.; Kondo, T. *Tetrahedron Lett.* **1990**, *31*, 713. (c) Ohsawa, Y.; Ohba, S.; Kosemura, S.; Yamamura, S.; Nakagawa, A.; Yoshida, K.; Kondo, T. *Acta Crystallogr.* **1994**, *C50*, 645.

Conclusion

We have succeeded in the first total synthesis of flavocommelin (**1**) by *C*-glycosylation of flavan. This first direct *C*-glycosylation of a flavonoid nucleus provides a promising methodology for synthesis of other natural occurring potential *O*- and *C*-glycosyl flavonoids. Preparation of chiral analogues of flavocommelin (**1**) having a variety of sugars is now in progress to facilitate studies of the flower-color-development of commelinin (**2**).

Experimental Section

7-*O*-Methylnaringenin (7a) and 7,4′-*O*-Dimethylnaringenin (7b). To a solution of naringenin (**6**) (1.634 g, 6 mmol) and K_2CO_3 (0.829 g, 6 mmol) in DMF (20 mL) was added CH_3I (0.56 mL, 9 mmol) at room temperature. The solution was stirred for 12 h and then quenched by addition of saturated aqueous NH_4Cl and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo. The crude product was purified by flash column chromatography (hexane−AcOEt 2:1) to afford **7a** (1.300 g, 76%) and **7b** (56 mg, 3%) as white solids.

Data for **7a**: mp 144−143 °C; IR (KBr) 3241, 1642, 1520, 1459, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.77 (1H, dd, J = 17.2, 3.0 Hz), 3.07 (1H, dd, J = 17.2, 13.1 Hz), 3.79 (3H, s, OCH_3), 5.06 (1H, s, OH), 5.34 (1H, dd, J = 13.1, 3.0 Hz), 6.03 (1H, d, J = 2.2 Hz), 6.05 (1H, d, J = 2.2 Hz), 6.86 (2H, d, J = 8.5 Hz), 7.31 (2H, d, J = 8.5 Hz), 11.99 (1H, s, OH); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 43.3, 55.7, 79.0, 94.2, 95.1, 103.1, 115.6, 127.9, 130.5, 156.0, 162.7, 164.0, 167.8, 195.8; HRMS (EI) calcd for $C_{16}H_{14}O_5$ $[M]^+$ 286.0841, found 286.0854.

Data for **7b**: mp 114−115 °C; IR (KBr) 2950, 1630, 1307, 1212, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.77 (1H, dd, J = 17.2, 3.0 Hz), 3.08 (1H, dd, J = 17.2, 13.2 Hz), 3.78 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 5.34 (1H, dd, J = 13.2, 3.0 Hz), 6.02 (1H, d, J = 2.1 Hz), 6.05 (1H, d, J = 2.1 Hz), 6.93 (2H, d, J = 8.5 Hz), 7.36 (2H, d, J = 8.5 Hz), 12.01 (1H, s, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 43.2, 55.3, 55.6, 79.0, 94.2, 95.1, 103.1, 114.2, 127.7, 130.4, 160.0, 162.9, 164.1, 167.9, 196.0; HRMS (EI) calcd for $C_{17}H_{16}O_5$ $[M]^+$ 300.0998, found 300.1009.

5,4′-Diacetoxy-7-methoxyflavanone (9). To a solution of **7a** (3.722 g, 13 mmol), Et_3N (14.5 mL, 104 mmol), and DMAP (1.588 g, 13 mmol) in CH_2Cl_2 (80 mL) was added AcCl (7.4 mL, 104 mmol) at room temperature. The solution was stirred for 15 h at room temperature, diluted with AcOEt, and washed with 1 N HCl. After neutralization with saturated aqueous $NaHCO_3$, the organic layer was dried over anhydrous $MgSO_4$ and evaporated in vacuo. The resulting crude product was purified by flash column chromatography (hexane−AcOEt 3:2) to afford **9** (4.315 g, 90%) as a white solid: mp 103−104 °C; IR (KBr) 2954, 1768, 1621, 1444, 1189 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.30 (3H, s, OAc), 2.37 (3H, s, OAc), 2.71 (1H, dd, J = 16.6, 3.0 Hz), 2.98 (1H, dd, J = 16.6, 13.5 Hz), 3.81 (3H, s, OCH_3), 5.44 (1H, dd, J = 13.5, 3.0 Hz), 6.27 (1H, d, J = 2.6 Hz), 6.41 (1H, d, J = 2.6 Hz), 7.14 (2H, d, J = 8.5 Hz), 7.45 (2H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 21.1, 45.0, 55.8, 78.9, 99.4, 104.7, 107.8, 121.9, 127.2, 135.8, 150.7, 151.6, 163.8, 165.2, 169.0, 169.2, 188.2; HRMS (FAB) calcd for $C_{20}H_{19}O_7$ $[M + H]^+$ 371.1131, found 371.1132.

4′-Acetoxy-5-hydroxy-7-methoxyflavan (4). To a solution of **9** (2.103 g, 5.1 mmol) in THF (18 mL) and H_2O (9 mL) was added $NaBH_4$ (386 mg, 10.2 mmol) at 0 °C. The solution was stirred for 30 min at 0 °C then quenched by addition of saturated aqueous NH_4Cl and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo. The crude product was purified by flash column chromatography (hexane−AcOEt 2:1) to afford **4** (1.356 g, 85%) as a white solid: mp 169−170 °C; IR (KBr) 3374, 2960, 1747, 1629, 1198 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.9−2.1 (1H, m), 2.2−2.3 (1H, m), 2.29 (3H, s, OAc), 2.6−2.7 (2H, m),

3.71 (3H, s, OCH_3), 4.78 (1H, s, OH), 4.98 (1H, dd, J = 10.3, 2.4 Hz), 6.00 (1H, d, J = 2.3 Hz), 6.10 (1H, d, J = 2.3 Hz), 7.09 (2H, d, J = 8.6 Hz), 7.41 (2H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 19.0, 21.2, 29.5, 55.3, 77.1, 94.2, 94.8, 101.8, 121.5, 127.1, 139.0, 150.1, 154.4, 156.4, 159.1, 169.4; HRMS (FAB) calcd for $C_{18}H_{18}O_5$ $[M + H]^+$ 314.1154, found 314.1145.

4′-Acetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-5-hydroxy-7-methoxyflavan (10), 4′-Acetoxy-8-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-5-hydroxy-7-methoxyflavan (11), 4′-Acetoxy-5-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-5-hydroxy-7-methoxyflavan (12a), and 4′-Acetoxy-5-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-5-hydroxy-7-methoxyflavan (12b). To a solution of **4** (189 mg, 0.6 mmol), **8** (163 mg, 0.3 mmol), and MS 5 Å (0.9 g) in CH_2Cl_2 (5 mL) was added BF_3·Et_2O (7.6 μL, 0.06 mmol) at room temperature. The solution was stirred for 90 min at room temperature then quenched by addition of saturated aqueous $NaHCO_3$ and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo. The crude product was purified by flash column chromatography (hexane−AcOEt 5:2 and then 3:2) to afford a mixture of **10**, **12a**, and **12b** (187 mg, 74%, **10**:**12a**:**12b** = 75:17:8) and **11** (17 mg, 7%) as white foams. All **10**−**12** products were inseparable diastereomeric mixtures (1:1), with rotamers observed by ^{1}H NMR.

Data for **11**: IR (KBr) 3424, 1759, 1609, 1200, 1066 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.75−2.00 (1H, m), 2.10−2.17 (1H, m), 2.28 (3H, s, OAc), 2.52−2.69 (2H, m), 3.45−3.90 and 4.10−5.12 (16H, m), 3.62 and 3.71 (3H, s, OCH_3), 5.96 (0.4H, s, H-6), 6.02 (0.6H, s, H-6), 6.80−7.55 (24H, m); HRMS (FAB) calcd for $C_{52}H_{53}O_{10}$ $[M + H]^+$ 837.3639, found 837.3633.

4′-Acetoxy-5-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-7-methoxyflavan (14a) and 4′-Acetoxy-5-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-7-methoxyflavan (14b) (from 12a and 12b). To a solution of a mixture of **12a** and **12b** (84 mg, 0.1 mmol) in CH_3OH (2 mL) and AcOEt (2 mL) was added 20 wt % of $Pd(OH)_2$/C (7 mg). The solution was stirred under 1 atm of H_2 for 3.5 h at room temperature. The catalyst was then removed by filtration through Celite followed by washing with CH_3OH. The filtrate was concentrated in vacuo to afford the debenzylated product. To a solution of this crude product in pyridine (0.5 mL) was added Ac_2O (0.5 mL) at room temperature. After being stirred for 24 h, the reaction mixture was diluted with AcOEt and washed with 1 N HCl. After neutralization with saturated aqueous $NaHCO_3$, the organic layer was dried over anhydrous $MgSO_4$. After evaporation, the resulting crude product was purified by thin-layer chromatography (hexane−AcOEt 1:1) affording **14a** (31 mg, 47%) and **14b** (17 mg, 26%) as amorphous material. The products **14a** and **14b** were an inseparable mixture of diastereomers (1:1), respectively.

Data for **14a**: IR (KBr) 2958, 1755, 1223, 1147, 1042 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 1.90−2.00 (1H, br), 1.96 (1.5H, s, OAc), 1.97 (1.5H, s, OAc), 1.99 (6H, s, OAc), 2.00 (1.5H, s, OAc), 2.04 (1.5H, s, OAc), 2.19−2.25 (1H, br), 2.26 (3H, s, OAc), 2.67−2.73 (2H, m), 3.67 (3H, s, OCH_3), 3.99−4.22 (3H, m), 5.03−5.10 (3H, m), 5.50 (1H, t, J = 9.8 Hz), 5.72 (0.5H, d, J = 2.7 Hz, H-1″), 5.73 (0.5H, d, J = 2.7 Hz, H-1″), 6.20 (0.5H, d, J = 2.6 Hz), 6.21 (0.5H, d, J = 2.6 Hz), 6.31 (0.5H, d, J = 2.6 Hz), 6.32 (0.5H, d, J = 2.6 Hz), 7.14 (2H, d, J = 8.5 Hz), 7.47 (2H, d, J = 8.5 Hz); HRMS (FAB) calcd for $C_{32}H_{37}O_{14}$ $[M + H]^+$ 645.2183, found 645.2194.

Data for **14b**: IR (KBr) 2939, 1754, 1219, 1141, 1048 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 1.84−1.95 (1H, m), 1.96 (1.5H, s, OAc), 1.97 (1.5H, s, OAc), 1.98 (1.5H, s, OAc), 2.00 (3H, s, OAc), 2.01 (1.5H, s, OAc), 2.02 (1.5H, s, OAc), 2.04 (1.5H, s, OAc), 2.11−2.18 (1H, m), 2.26 (3H, s, OAc), 2.37−2.55 (2H, m), 3.68 (3H, s, OCH_3), 4.06 (0.5H, dd, J = 12.3, 2.8 Hz), 4.07 (0.5H, dd, J = 12.3, 2.8 Hz), 4.18 (0.5H, dd, J = 12.3, 5.9 Hz), 4.19 (0.5 H, dd, J = 12.3, 5.9 Hz), 4.25−4.29 (1H, m), 4.96 (0.5H, t, J = 9.8 Hz), 4.97 (0.5H, t, J = 9.8 Hz), 5.03 (0.5H, dd, J = 10.3, 2.0 Hz), 5.05 (0.5H, dd, J = 10.3, 2.0 Hz), 5.07 (0.5H, dd, J = 9.8, 8.1 Hz), 5.08 (0.5H, dd, J = 9.8, 8.1 Hz), 5.40 (0.5H, t, J = 9.8 Hz), 5.41 (0.5H, t, J = 9.8 Hz), 5.46 (1H, d, J = 8.1 Hz, H-1″), 6.19 (1H, d, J = 2.2 Hz), 6.25 (0.5H, d, J = 2.2 Hz), 6.26 (0.5H, d, J = 2.2 Hz), 7.13 (2H, d, J = 8.8 Hz), 7.44 (1H, d, J = 8.8 Hz), 7.45 (1H, d, J = 8.8 Hz); HRMS (FAB) calcd for $C_{32}H_{37}O_{14}$ $[M + H]^+$ 645.2183, found 645.2180.

5,4′-Diacetoxy-8-*C*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-7-methoxyflavan (15). To a solution of a mixture of **11** (50 mg, 0.06 mmol) in CH_3OH (1 mL) and AcOEt (1 mL) was added 20 wt % of $Pd(OH)_2$/C (8 mg). The solution was stirred under 1 atm of H_2 for 4 h at room temperature. The catalyst was then removed by filtration through Celite followed by washing with CH_3OH. The filtrate was concentrated in vacuo to afford the debenzylated product. To a solution of this crude product and DMAP (7.3 mg, 0.06 mmol) in pyridine (1 mL) was added Ac_2O (1 mL) at room temperature. After being stirred for 14 h, the reaction mixture was diluted with AcOEt and washed with 1 N HCl. After neutralization with saturated aqueous $NaHCO_3$, the organic layer was dried over anhydrous $MgSO_4$. After evaporation, the resulting crude product was purified by thin-layer chromatography (hexane−AcOEt 1:1) affording **15** (34 mg, 83%) as an amorphous material. The product was an inseparable diastereomeric mixture (1:1), with rotamers observed by ^{1}H NMR: IR (KBr) 2941, 1755, 1619, 1371, 1222 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 1.65−2.00 (12H, m, OAc), 2.15−2.50 (3H, m), 2.24−2.29 (6H, m, OAc), 2.56−2.64 (1H, m), 3.70, 3.72, 3.73, and 3.74 (3H, s, OCH_3), 3.92−4.14 (3H, m), 4.89−4.95 (1H, m), 5.08 and 5.10 (1H, br s), 5.13 (1H, d, J = 10.2 Hz, H-1″), 5.22−5.33 (1H, m), 6.34 and 6.45 (1H, s), 7.13−7.19 (2H, m), 7.45, 7.48, 7.64, and 7.68 (2H, d, J = 8.4 Hz); HRMS (FAB) calcd for $C_{34}H_{39}O_{15}$ $[M + H]^+$ 687.2289, found 687.2277.

5,4′-Diacetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-7-methoxyflavan (16). To a solution of a mixture of **10**, **12a**, and **12b** (1.623 g, 1.94 mmol), Et_3N (1.62 mL, 11.64 mmol), and DMAP (0.237 g, 1.94 mmol) in CH_2Cl_2 (40 mL) was added AcCl (0.83 mL, 11.64 mmol) at 0 °C. The solution was stirred for 1.5 h at room temperature, diluted with AcOEt, and washed with 1 N HCl. After neutralization with saturated aqueous $NaHCO_3$, the organic layer was dried over anhydrous $MgSO_4$. After evaporation, the resulting crude product was purified by flash column chromatography (hexane−AcOEt 5:2) to afford **16** (1.170 g, 69%) as a white foam and recovered **12a** and **12b** (0.410 g, 24%). The product **16** was an inseparable mixture of diastereomers (1:1), with rotamers observed by ^{1}H NMR.

Data for **16**: IR (KBr) 2924, 1770, 1625, 1196, 1870 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.92−2.04 (1H, m), 2.07 and 2.08 (3H, s, OAc), 2.14−2.16 (1H, m), 2.29 (3H, s, OAc), 2.42−2.62 (2H, m), 3.44−3.46 (1H, br), 3.73 and 3.74 (3H, s, OCH_3), 3.66−3.83 and 4.04−4.14 (6H, m), 4.45−4.55 (3H, m), 4.70 (1H, d, J = 10.8 Hz, H-1″), 4.85−5.04 (5H, m), 6.41 and 6.40 (1H, s), 6.96−7.43 (24H, m); HRMS (FAB) calcd for $C_{54}H_{54}O_{11}$ $[M + Na]^+$ 878.3666, found 878.3676.

Data for the mixture of **12a** and **12b**: IR (KBr) 2921, 1758, 1620, 1497, 1023 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.89−2.01 (2H, m), 2.07−2.17 (2H, m), 2.29 (6H, s, OAc), 2.58−2.97 (4H, m), 3.58−3.90 and 4.41−5.03 (36.6H, m), 4.12 (0.35H, t, J = 9.3 Hz, for **12a**), 4.13 (0.35H, t, J = 9.3 Hz, for **12a**), 5.47 (0.35H, d, J = 3.3 Hz, for **12a**, H-1″), 5.51 (0.35H, d, J = 3.3 Hz, for **12a**, H-1″), 6.18 (1.4H, d, J = 2.5 Hz, for **12a**), 6.20 (0.6H, d, J = 2.5 Hz, for **12b**), 6.31 (0.3H, d, J = 2.5 Hz, for **12b**), 6.32 (0.3 H, d, J = 2.5 Hz, for **12b**), 6.36 (0.7H, d, J = 2.5 Hz, for **12a**), 6.37 (0.7H, d, J = 2.5 Hz, for **12a**), 7.07−7.43 (48H, m); HRMS (FAB) calcd for $C_{52}H_{53}O_{10}$ $[M + H]^+$ 837.3639, found 837.3633.

5,4′-Diacetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-7-methoxyflavan (17). To a solution of a mixture of **16** (770 mg, 0.876 mmol) in CH_3OH (4 mL) and AcOEt (4 mL) was added 20 wt % of $Pd(OH)_2$/C (62 mg). The solution was stirred under 1 atm of H_2 for 1.5 h at room temperature,

then the catalyst was removed by filtration through Celite followed by washing with CH_3OH. The filtrate was concentrated in vacuo to afford the debenzylated product. To a solution of this crude product and DMAP (107 mg, 0.876 mmol) in pyridine (3 mL) was added BzCl (2.0 mL, 17.520 mmol) at 60 °C. After being stirred for 1 h, the reaction mixture was diluted with AcOEt and washed with 1 N HCl. After neutralization with saturated aqueous $NaHCO_3$, the organic layer was dried over anhydrous $MgSO_4$. After evaporation, the resulting crude product was purified by flash column chromatography (hexane−AcOEt 5:3) affording **17** (778 mg, 95%) as a white foam. The products **17** were an inseparable mixture of diastereomers (1:1), with rotamers observed by ^{1}H NMR: IR (KBr) 2942, 1771, 1732, 1268, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.88−1.96 (1H, br), 2.05−2.15 (1H, br), 2.27 and 2.30 (6H, s, OAc), 2.40−2.70 (2H, br), 3.67 (3H, br s, OCH_3), 4.20 (1H, br s), 4.44 (1H, dd, J = 12.3, 4.5 Hz), 4.60 (1H, br d, J = 12.3 Hz), 4.93 and 4.90 (1H, d, J = 10.6, H-1″; signals of rotamer were overlapped), 5.40 (0.7H, br s), 5.76 (1H, t, J = 9.8 Hz), 5.95 (1H, br t, J = 9.3 Hz), 6.02 (0.3H, br s), 6.18 (1H, br s), 7.04−7.50 and 7.75−7.97 (25H, m); HRMS (FAB) calcd for $C_{54}H_{47}O_{15}$ [M + H]$^+$ 935.2915, found 935.2929.

5,4′-Diacetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzoyl-*β*-D-glucopyranosyl)-7-methoxyflavanone (18). To a solution of **17** (232 mg, 0.248 mmol) in CH_3CN (2 mL), AcOH (2 mL), and H_2O (1 mL) was added CAN (816 mg, 1.488 mmol) at room temperature. The solution was stirred for 30 min at 50 °C then quenched by addition of saturated aqueous $NaHCO_3$ and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo, and purified by flash column chromatography (hexane−AcOEt 5:4) to afford **18** (100 mg, 43%) as a white foam. The product **18** was an inseparable mixture of diastereomers (1:1), with rotamers observed by ^{1}H NMR: IR (KBr) 2950, 1734, 1615, 1266, 1067 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.28 (3H, s, OAc), 2.34 and 2.44 (3H, br s, OAc), 2.56 (1H, br), 2.96 (1H, br), 3.71 and 3.89 (3H, br s, OCH_3), 4.18 (1H, br s), 4.41 (1H, br s), 4.61 (1H, br s), 5.05 and 5.38 (2H, br, H-2, 1″), 5.76 (1H, t, J = 9.8 Hz), 5.94 (1H, br s), 6.22 (1H, br s), 6.06 and 6.39 (1H, br s), 7.10 (1H, d, J = 8.5 Hz), 7.11 (1H, d, J = 8.5 Hz), 7.39 (2H, d, J = 8.5 Hz), 7.10−7.55 and 7.74−8.01 (20H, m); HRMS (FAB) calcd for $C_{54}H_{44}O_{16}Na$ [M + Na]$^+$ 971.2527, found 971.2531.

5-Acetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzoyl-*β*-D-glucopyranosyl)-4′-hydroxy-7-methoxyflavanone (19). To a solution of **18** (256 mg, 0.27 mmol) in $CHCl_3$ was added a mixed solution[33] of AcCl (0.2 mL) and CH_3OH (4 mL) at room temperature. The solution was stirred for 2 h at room temperature, then quenched by addition of saturated aqueous $NaHCO_3$ and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo, and purified by flash column chromatography (hexane−AcOEt 1:1) to afford **19** (197 mg, 80%) as a white foam. The product **19** was an inseparable mixture of diastereomers (1:1), with rotamers observed by ^{1}H NMR: IR (KBr) 2950, 1735, 1616, 1267, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.45 and 2.35 (3H, br s, OAc), 2.56 (1H, br d, J = 16.4 Hz), 2.91 (1H, br t, J = 15.3 Hz), 3.68 and 3.84 (3H, br s, OCH_3), 4.18 (1H, br s), 4.41 (1H, br s), 4.64 (1H, br s), 5.05 and 5.37 (1H, br d, J = 8.6 Hz, H-1″), 5.25 (1H, br t, J = 12.0 Hz), 5.71 and 5.68 (1H, br s, OH), 5.77 (1H, t, J = 9.8 Hz), 5.96 (1H, br s), 6.06 and 6.34 (1H, br s), 6.18 (1H, br s), 6.76 (2H, dd, J = 8.6, 2.0 Hz), 7.19 (2H, dd, J = 8.6, 2.2 Hz), 7.20−7.50 amd 7.70−8.02 (20H, m); HRMS (FAB) calcd for $C_{52}H_{42}O_{15}Na$ [M + Na]$^+$ 929.2421, found 929.2419.

5-Acetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzoyl-*β*-D-glucopyranosyl)-4′-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-7-methoxyflavanone (20). To a solution of acetylglucosyl fluoride **5** (14.0 mg, 0.04 mmol), **19** (18.0 mg, 0.02 mmol), and DTBMP in CH_2Cl_2 (1 mL) was added BF_3·Et_2O (20 μL, 0.16 mmol) at room temperature. The solution was stirred for 1 h at room temperature then quenched by addition of saturated aqueous $NaHCO_3$ and extracted with AcOEt. The combined extracts were dried over anhydrous $MgSO_4$ and evaporated in vacuo. The crude product was purified by flash column chromatography (hexane−AcOEt 1:1) to afford **20** (20.7 mg, 84%) as white foam. The product **20** was an inseparable mixture of diastereomers (1:1), with rotamers observed by ^{1}H NMR: IR (KBr) 2966, 1736, 1615, 1264, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.01 (3H, s, OAc), 2.02 (3H, s, OAc), 2.03 (3H, s, OAc), 2.05 (3H, s, OAc), 2.34 and 2.44 (3H, br s, OAc), 2.61 (1H, br d, J = 16.9 Hz), 2.77−2.99 (1H, br), 3.70 and 3.88 (3H, br s, OCH_3), 3.83 (1H, dd, J = 9.8, 5.4, 2.2 Hz), 4.15 (1H, dd, J = 12.2, 2.2 Hz), 4.26 (1H, dd, J = 12.2, 5.4 Hz), 4.41 (1H, br s), 4.62 (1H, br s), 5.06 (1H, d, J = 7.4 Hz, H-1‴), 5.14 (1H, t, J = 9.8 Hz), 5.25 (1H, dd, J = 9.8, 7.4 Hz), 5.28 (1H, t, J = 9.8 Hz), 5.35 (2H, br, H-2, 1″), 5.76 (1H, t, J = 9.8 Hz), 5.94 (1H, br s), 6.05 and 6.38 (1H, br s), 6.20 (1H, br s), 6.99 (2H, d, J = 8.5 Hz), 7.31 (2H, d, J = 8.5 Hz), 7.20−7.55 and 7.70−8.05 (20H, m); HRMS (FAB) calcd for $C_{66}H_{60}O_{24}Na$ [M + Na]$^+$ 1259.3372, found 1259.3346.

5-Acetoxy-6-*C*-(2,3,4,6-tetra-*O*-benzoyl-*β*-D-glucopyranosyl)-4′-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-7-methoxyflavone (21). A solution of **20** (136 mg, 0.11 mmol) and DDQ (122 mg, 0.44 mmol) in PhCl (5 mL) was refluxed for 13 h at 140 °C. After concentration in vacuo, the reaction mixture was purified by thin-layer chromatography (hexane−AcOEt 1:2) to afford **21** (109 mg, 83%) as a foam. $[\alpha]^{24}_D$ −48.9 (c 0.3, $CHCl_3$); IR (KBr) 2938, 1735, 1605, 1233, 1094 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 1.97, 2.00, and 2.01 (3H, s, OAc), 3.90 and 3.91 (3H, s, OCH_3), 4.07 (1H, dd, J = 12.3, 2.2 Hz), 4.19 (1H, dd, J = 12.3, 5.3 Hz), 4.30 (1H, ddd, J = 9.5, 5.3, 2.2 Hz), 4.41−4.59 (3H, m), 5.02 (1H, t, J = 9.5 Hz), 5.09 (1H, dd, J = 9.5, 8.1 Hz), 5.41 (1H, dd, J = 9.5 Hz), 5.58 (1H, br d, J = 9.5, H-1″), 5.69 (1H, t, J = 9.5 Hz), 5.75 (1H, d, J = 8.1 Hz, H-1‴), 6.02 and 6.05 (1H, t, J = 9.5 Hz), 6.20 and 6.31 (1H, t, J = 9.5 Hz), 6.82 and 6.87 (1H, s), 6.95 and 7.00 (1H, s), 7.14 (2H, d, J = 8.4 Hz), 7.33−8.02 (20H, m), 8.05 (2H, d, J = 8.4 Hz), 13.60 and 13.67 (1H, s, OH); HRMS (FAB) calcd for $C_{64}H_{57}O_{23}$ [M + H]$^+$ 1193.3291, found 1193.3274.

Flavocommelin (1). To a solution of **21** (31.0 mg, 26 μmol) in a mixture of THF (1 mL) and CH_3OH (1 mL) was added KOH (0.2 mL, 0.5 mol/L of CH_3OH solution) at room temperature. After being stirred for 16 h, the reaction mixture was neutralized with Dowex 50W-8X (H^+), filtered, and evaporated in vacuo. The residue was recrystallized from H_2O and CH_3CN to afford **1** (14.2 mg, 90%), with rotamers observed by ^{1}H NMR: mp 209−210 °C [natural: mp 209−210 °C]; $[\alpha]^{25}_D$ −57.6 (c 0.3, H_2O) [natural: $[\alpha]^{24}_D$ −57.7 (c 0.3, H_2O)]; IR (KBr) 3418, 2926, 1654, 1244, 1204 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 3.03−3.47 (10H, m), 3.68−3.70 (2H, m), 3.86 and 3.89 (3H, s, OCH_3), 3.96−4.00 (0.5H, m), 4.15−4.19 (0.5H, m), 4.57 (0.5H, d, J = 9.6 Hz, H-1″), 4.59 (0.5H, d, J = 9.6 Hz, H-1″), 5.04 (1H, d, J = 7.2 Hz, H-1‴), 6.88 (0.5H, s), 6.89 (0.5H, s), 6.98 (0.5H, s), 7.00 (0.5H, s), 7.19 (2H, d, J = 8.4 Hz), 8.09 (2H, d, J = 8.4 Hz), 13.41 (0.5H, s), 13.43 (0.5H, s); HRMS (FAB) calcd for $C_{28}H_{33}O_{15}$ [M + H]$^+$ 609.1819, found 609.1814.

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Supporting Information Available: Copies of ^{1}H NMR spectra of all new compounds and natural **1** and experimental details of acetylation of **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(33) This mixed solution was prepared according to the following procedure. To CH_3OH (4 mL) was added AcCl (0.2 mL) dropwise at 0 °C and this solution was stirred for 15 min at 0 °C.