Synthesis of Flavonoid/Chromonoid-β-D-Ribofuranose Derivatives by Palladium-catalyzed Cross-coupling Reactions

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Dedication – Dedicated to the memory of Prof. Tamás Patonay.

Abstract: The synthesis of structurally novel carbohydrateflavone and -chromone derivatives with unsaturated carbon bridge has been accomplished by phosphine-free palladium catalyzed cross-coupling reaction.

Key words: cross-coupling, catalysis, palladium, Mizoroki-Heck reaction, isomerism

The class of natural occurring *C*-glycosyl flavonoids, e.g. vitexin, orientin, isovitexin, isoorientin (Figure 1) containing *C*-glucopyranosyl moiety, has recently received a great attention for organic chemists since these compounds possess wide variety of biological activities e.g. anti-inflammatory activity, antiviral activity. The antioxidant kurilensin A and B were isolated from hot-water extracts of the leaves of *Sasa kurilensis* as *C*-glycosyl flavonoids (Figure 1). What these compounds have common in that there is always one or two activating group, such as hydroxy or methoxy group, in position 5 or 7 of the flavone skeleton.

Figure 1 Natural occurring flavone *C*-glycosyl flavonoids.

The *C*-glycosyl compounds have an advantage comparing to *O*-glycosides, namely the C-C bond enzymatically is not degradable⁴ and this feature could be an attractive behavior for pharmaceutical aims. In nature only those *C*-glycosyl flavones are known in

which the aglycon is directly bonded to the carbohydrate unit in one bond distance. Scientist has no knowledge about the changes of the biological activity due to the modification of the distance between the aglycon and the sugar units since the synthesis of these compounds have not been studied yet.

In literature, the synthesis of the *C*-glycosyl flavones often starts from acetophenone derivatives which already possess the sugar moiety and usually more steps are required (e.g. Fries rearrangement or Friedel-Crafts reaction, Claisen-Schmidt condensation, Baker-Venkataraman-type rearrangement followed by oxidative ring closure)⁵⁻⁸ to obtain the target molecule. In every step, there is a chance for the degradation of the carbohydrate moiety. Although, there are a few examples for the direct *C*-glycosylation of the aglycon moiety^{9,10} but usually in these transformation the position of the carbohydrate unit is controlled by a directing group (e.g. hydroxy). On the basis of these limits, we wanted to perform a synthetic transformation in which

- a) the sugar part is introduced in the last step and
- b) its position is controlled according to our aim.

Our goal was to synthesize these molecules by utilizing our earlier acquired experiences in the field of palladium catalyzed cross-coupling reaction of oxygen containing heterocycles e. g. flavones, chromones. Namely, our group successfully developed useful methods $^{11-13a}$ for the synthesis and transformation of chromones and flavones using Mizoroki-Heck reaction and its phosphine-free version the Jeffery's conditions. 13b As a logical continuation of these results, we wished to perform the reaction of bromoflavones and -chromones with allyl ribofuranose compounds in order to prepare flavone/chromone- β -D-ribofuranose derivatives with various unsaturated linker. Moreover, the synthesis of these new types of conjugates has not been investigated up to now.

First, 6- and 7-bromoflavone (1a,b) were used as starting materials and the reactions were carried out under our optimized cross-coupling reaction condition. As terminal alkenes 1-allyl- β -D-

ribofuranose derivatives **2a** and **2b** were used in order to provide the carbohydrate unit.

Scheme 1 Reaction of 7- and 6-bromoflavones (1a,b) with 1-allyl-β-D-ribofuranose derivatives 2a,b using Jeffery's condition

Table 1 Yields of cross-coupling reaction of 6- and 7-bromoflavones (1a,b) and β -D-riboses 2a and 2b

Compound	Ribose (R)	Method	Yield
1a	OBn	Mizoroki-Heck	63% (3a)
1a	OBn	Jeffery's	89% (3a)
1a	Н	Jeffery's	68% (3b)
1b	Н	Jeffery's	75% (4b)
1b	OBn	Jefferv's	92% (4a)

Jeffery's condition: KCl, Bu₄NBr, K₂CO₃, Pd(OAc)₂, dry DMF, 100-110°C, 1-2 hrs

Mizoroki-Heck condition: Et₃N, PPh₃, Pd(OAc)₂, NMP, 100-110°C, 1-2 hrs

Initially, a Mizoroki-Heck type reaction performed with 7-bromoflavone (1a) and 1-allyl-β-Dribofuranose (2a) using Pd(OAc)₂/Ph₃P and the corresponding flavone-ribose compound 3a was obtained in 63% yield. Then under phosphine-free Jeffery's condition, the same 3a product was isolated in higher yield (89%). Therefore in all further cases the phosphine-free condition was applied (Scheme 1, Table 1). By comparing the yields of these crosscoupling reactions in case of 1-allyl-β-D-ribofuranose (2a) and 1-allyl-2-desoxy- β -D-ribofuranose (2b) derivatives, revealed furanose 2a results the products in higher yields in all cases. This result could be explained by the easier coordination of palladium in the presents of OBn group in position 2 as an oxygen donor group.

Scheme 2 Reaction of 3-bromoflavone (5) with 1-allyl-β-D-ribofuranose derivatives 2a,b

Table 2 Yields of cross-coupling reaction of 3-bromoflavone (5) and β -D-riboses 2a and 2b

Compound	R	Product 6	Isomer product 7
2a	OBn	21%	20%
2h	Н	19%	18%

The transformation of 3-bromoflavone (5) to flavone-ribofuranose compounds **6a** and **6b** was also successful; in addition a new observation was taken. Namely, the palladium catalyzed cross-coupling reaction of 3-bromoflavone (5) and **2a** resulted in two products. The separation of these derivatives was successful and the structure elucidation was supported by 2D NMR measurements. It is revealed due to the migration of the double bond during the reaction, two isomers (**6a** and **7a**) were formed approximately in 1:1 ratio (Scheme 2, Table 2). This isomerism occurred only in case of 3-bromoflavone (**5**) and this type of phenomena can be explained by literature, ¹⁴ since in case of other allyl derivatives similar isomerism occurred in the presence of palladium.

Scheme 3 Reaction of 7- and 6-bromochromones (8a,b) with 1-allyl- β -D-ribofuranose derivatives 2a,b

In order to wider the range of the used oxygen containing heteroaromatic derivatives, bromochromones **8a,b** were reacted with 1-allyl-Dribofuranose **2a** and **2b** under Jeffery's condition. The reaction of 6-bromochromone (**8b**) with ribofuranose derivatives **2a** and **2b** provided compound **10a** and

10b in moderate yields (44%, 28%). Moreover, the reaction of 7-bromochromone (**8a**) afforded the corresponding product **9a,b** in good yields (79%, 49%) (Scheme 3, Table 3).

Table 3 Yields of cross-coupling reaction of 6- and 7-bromochromones (8a,b) and β -D-riboses 2a and 2b

Compound	Ribose (R)	Yield
8a	OBn	79 (9a)
8a	Н	49 (9b)
8b	OBn	44 (10a)
8b	Н	28 (10b)

The cross-coupling reaction of 3-boromochromone (11) was carried out only with terminal alkene 2a. Like in case of the 3-bromoflavone (5) two isomers (12a and 13a) were isolated in ~ 3:1 ratio (12a: 50%, 13a: 18% yield, respectively) (Scheme 4, Table 4).

Scheme 4 Reaction of 3-bromochromone (11) with 1-allyl- β -D-ribofuranose derivative 2a

Scheme 5 Debenzylation of 1-allyl- β -D-ribofuranose derivative 3a and 12a

Finally, the deprotection of flavone **3a** and chromone **12a** derivatives were achieved by treatment with BCl₃.Me₂S complex¹⁵ in CH₂Cl₂ at low temperature, in order to preserve the unsaturated linker (Scheme 5). This protocol afforded the products up to 77% yield.

In summary, in these transformations bromoflavones and -chromones were reacted with 1-allyl- β -Dribofuranose derivatives in the presence of palladium catalyst under phosphine-free condition, hereby providing the expected new, unknown structures in good yields. In some case the migration of the double bond was observed causing the formation of isomers, which compounds were successfully separated. These results clearly show the usefulness of this methodology in the synthesis of interesting target molecules with possible biological activity. The

biological assays of the synthetized new carbohydrateflavone and -chromone derivatives already have been started. The investigations of the synthesis of other structurally novel derivatives are also in progress with other carbohydrates bearing different unsaturated side chain.

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References

- Ishikura, K. T.; Nukaya, H. Jpn. Kokai Tokkyo Koho, 2002, 194828
- (2) Nagai, T.; Miyaichi, Y.; Tomimori, T.; Suzuki, Y.; Yamada, H. Chem. Pharm. Bull. 1990, 38, 1329-1332
- (3) Hasegawa, T.; Tanaka, A.; Hosoda, A.; Takano, F.; Ohta, T. Phytochemistry. 2008, 69(6), 1419-1424
- Maurice Jay, "C-Glycosylflavonoids," in "The Flavonoids; Advances in Research Since 1986," ed by J. B. Harborne, Chapman and Hall, London (1993), Chap. 3, pp. 57-93
- (5) Kumazawa, T.; Kimura, T.; Matsuba, S.; Sato, S.; Onodera, J. Carbohydr. Res, 2001, 334(3), 183-193
- (6) Sato, S.; Akiya, T.; Nishizawa, H.; Suzuki, T. Carbohydr. Res., 2006, 341, 964-970
- (7) Mahling, J.-A.; Jung K.-H.; Schmidt, R. R. Liebigs Ann. Chem., 1995, 461-466
- (8) Kumazawa, T.; Minatogawa, T.; Matsuba, S.; Sato, S.; Onodera, J. Carbohydr. Res. 2000, 329(3), 507-513
- (9) Sato, S.; Koide, T. Carbohydr. Res. 2010, 345, 1825-1830
- (10) Santos, R.G. X.; Bordado, J.C.; Rauter, A.P. Eur J Org Chem, 2013, 8, 1441-1447
- (11) Vasas, A.; Patonay, T.; Kónya, K.; Silva, A.M.S.; Cavaleiro, J.A.S. Austr. J. Chem. 2011, 64, 647-657
- (12) Patonay, T.; Pazurik, I.; Ábrahám, A. Austr. J. Chem. 2013, 66, 647-654
- (13) (a) Fekete, Sz., Patonay, T., Silva, A. M. S., Cavaleiro, J.
 A. S. ARKIVOC, 2012, v, 210-225. (b) Jeffery, T. Tetrahedron, 1996, 52, 10113-30
- (14) (a) Harrod, J. F.; Chalk, A. J., J. Am. Chem. Soc., 1964, 86(9), 1776–1779; (b) Lim, H. J.; Smith, C. R.; Babu, T. V. R., J. Org. Chem. 2009, 74(12), 4565-4572
- (15) Congreve, M. S.; Davison, E. C.; Fuhry, M. A. M.; Holmes, A. B.; Payne, A. N.; Robinson, R. A.; Ward, S. E. Synlett, 1993, 663-664
- (16) General procedures, experimental and analytical data of selected compounds:

General procedure for the synthesis of flavone-ribose derivatives by Mizoroki-Heck reaction

Condition A (Jeffery's condition): A stirred, preheated mixture of bromoflavone (1a,b) (75 mg, 0.249 mmol), 3-(2,3,5-tribenzyloxy-β-D-ribofuranozyl)-prop-1-ene (2a) (0.249 mmol, 1.0 equiv) or 3-(3,5-dibenzyloxy-β-D-ribofuranozyl)-prop-1-ene (2b) (0.249 mmol, 1.0 equiv), potassium carbonate (52 mg, 0.375 mmol, 1.5 equiv), potassium chloride (19 mg, 0.250 mmol, 1.0 equiv), tetrabutylammonium bromide (162 mg, 0.500 mmol, 2.0 equiv) and palladium acetate (4 mg, 0.015 mmol, 6 mol%) in dry DMF (5 mL) was heated at 110 °C for 2

hours under nitrogen atmosphere. The mixture was cooled then silica gel was added to the mixture and the solvent was evaporated under reduced pressure. Then it was purified by column chromatography to obtain the pure product.

Condition B (classic Mizoroki-Heck condition): A stirred, preheated mixture of bromoflavone (1a,b) (75 mg, 0.249 mmol), 3-(2,3,5-tribenzyloxy-β-D-ribofuranozyl)-prop-1-ene (2a) (0.249 mmol, 1.0 equiv), triethylamine (39 μL, 0.274 mmol, 1.1 equiv), triphenylphosphine (7 mg, 0.025 mmol, 10%) and palladium acetate (4 mg, 0.015 mmol, 6 mol%) in dry DMF (5 mL) was heated at 110 °C for 2 hours under nitrogen atmosphere. The mixture was cooled then silica gel was added to the mixture and the solvent was evaporated under reduced pressure. Then it was purified by column chromatography to obtain the pure product.

7-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydro-furan-2-yl)prop-1-enyl)-2-phenyl-4H-chromen-4-one (3a)

Condition A: 147 mg (89%), mp 126-127 °C, white crystal Condition B: 104 mg (63%), mp 126-127 °C, white crystal

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 2.45-2.63 (m, 2H), 3.52 (m, 2H), 3.66 (t, J = 6.1 Hz, 1H), 3.93 (t, J = 4.6 Hz, 1H), 4.21 (m, 2H), 4.42-4.64 (m, 6H), 6.44 (s, 2H), 6.80 (s, 1H), 7.29 (m, 15H), 7.39 (s, 1H), 7.52 (m, 3H), 7.90 (m, 2H), 8.10 (d, J = 8.2 Hz, 1H).

¹³C NMR (90 MHz, CDCl₃): δ (ppm) = 36.7, 70.3, 71.7, 72.0, 73.3, 79.8, 80.0, 81.6, 107.6, 114.9, 122.5, 123.1, 125.6, 126.2, 127.4, 127.6, 127.7, 128.0, 128.1, 128.3, 128.9, 130.5, 130.7, 131.4, 131.8, 137.7, 138.0, 143.2, 156.5, 163.2, 178.1.

IR (v_{max}, cm^{-1}) : 2922, 2903, 2856, 1639, 1624, 1450, 1372, 1101, 697.

Anal. Calcd for $C_{44}H_{40}O_6$: C, 79.50; H, 6.06. Found: C, 79.54; H, 6.10.

6-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-2-phenyl-4H-chromen-4-one (4a)

Condition A: 152 mg (92%), mp 89-90 °C, white crystal

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 2.52-2.59 (m, 2H), 3.52 (m, 2H), 3.66 (t, J = 5.8 Hz, 1H), 3.91 (t, J = 4.6 Hz, 1H), 4.15-4.22 (m, 2H), 4.43-4.62 (m, 6H), 6.25-6.34 (m, 1H), 6.37-6.48 (m, 1H), 6.79 (s, 1H), 7.28 (m, 15H), 7.43 (t, J = 6.6 Hz, 1H), 7.50 (m, 4H), 7.59 (d, J = 6.6 Hz, 1H), 7.90 (m, 2H), 8.08 (s, 1H).

 13 C NMR (90 MHz, CDCl₃): δ (ppm) = 36.7, 70.2, 71.7, 71.9, 73.3, 77.1, 79.8, 80.1, 81.3, 107.3, 118.1, 122.6, 123.7, 126.1, 127.4, 127.6, 127.6, 127.7, 127.9, 128.2, 128.7, 128.9, 130.5, 131.0, 131.4, 131.6, 134.7, 137.6, 137.7, 138.7, 155.2, 163.1, 178.2.

IR (v_{max} , cm⁻¹): 3029, 2875, 1639, 1614, 1451, 1360, 1097, 731, 697;

Anal. Calcd for $C_{44}H_{40}O_6$: C, 79.50; H, 6.06. Found: C, 79.55; H, 6.08.

6-((E)-3-((2S,4S,5R)-4-(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-2-phenyl-4H-chromen-4-one (4b)

Condition A: 104 mg (75%), mp 82-83 °C, white crystal

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 1.67-1.80 (m, 2H), 2.43-2.61 (m, 2H), 3.46-3.59 (m, 2H), 4.00-4.04 (m, 1H), 4.15-

4.17 (m, 1H), 4.23-4.29 (m, 1H), 4.50 (s, 2H), 4.56 (s, 2H), 6.29-6.36 (m, 1H), 6.49-6.53 (d, J = 16.1 Hz, 1H), 6.79 (s, 1H), 7.31 (m, 8H), 7.48 (m, 4H), 7.67 (d, J = 8.7 Hz, 1H), 7.89 (m, 2H), 8.12 (d, J = 7.2 Hz, 1H).

¹³C NMR (90 MHz, CDCl₃): δ (ppm) = 37.6, 38.6, 70.9, 73.3, 73.3, 78.1, 81.0, 83.5, 107.3, 118.1, 122.5, 123.7, 126.1, 127.5, 128.1, 128.2, 128.7, 128.9, 130.4, 131.2, 131.5, 131.6, 134.8, 138.0, 138.1, 155.2, 163.1, 178.3.

IR (v_{max}, cm^{-1}) : 3059, 3030, 2902, 2876, 1650, 1615, 1453, 1360, 1097, 741, 698;

Anal. Calcd for $C_{37}H_{34}O_5$: C, 79.55; H, 6.13; H, 6.06. Found: C, 79.57; H, 6.09.

3-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-2phenyl-4H-chromen-4-one (6a)

Condition A: 40%, oil.

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 2.33-2.43 (m, 2H), 3.52 (m, 2H), 3.69 (t, J = 5.4 Hz, 1H), 3.87 (t, J = 5.2 Hz, 1H), 4.15 (m, 2H), 4.48-4.57 (m, 6H), 6.10 (d, J = 15.8 Hz, 1H), 6.91 (m, 1H), 7.24 (m, 15H), 7.44 (m, 6H), 7.64 (m, 2H), 8.26 (d, J = 7.6 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) = 28.7, 70.5, 72.2, 73.4, 77.8, 177.9, 81.4, 81.5, 81.9, 118.0, 119.6, 123.0, 124.9, 128.5, 127.6, 127.7, 127.9, 128.1, 128.3, 128.4, 128.6, 129.9, 130.4, 131.4, 133.2, 133.6, 138.1, 138.3, 156.2, 162.4, 177.9. IR (v_{max} , cm⁻¹): 3059, 3027, 2919, 2896, 2880, 1648, 1631, 1612, 1467, 1396, 1104,762, 696.

Anal. Calcd for C₄₄H₄₀O₆: C, 79.50; H, 6.06. Found: C, 79.55; H, 6.09.

3-((E)-3-((2S,4S,5R)-4-(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-2-phenyl-4H-chromen-4-one (6b)

Condition A: 29 mg (21%), colorless oil.

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 1.61-1.68 (m, 1H), 2.06 (dd, J = 13.1 Hz, J = 4.9 Hz, 1H), 2.31-2.52 (m, 2H), 3.41-3.55 (m, 2H), 3.99-4.01 (m, 1H), 4.08-4.10 (m, 1H), 4.16-4.19 (m, 1H), 4.49 (s, 2H), 4.54 (s, 2H), 6.16 (d, J = 15.8 Hz, 1H), 6.79-6.84 (m, 1H), 7.29 (m, 8H), 7.38 (m, 5H), 7.47 (m, 2H), 7.56 (m, 3H), 8.26 (d, J = 8.1 Hz, 1H).

 13 C NMR (90 MHz, CDCl₃): δ (ppm) = 37.5, 39.9, 70.9, 71.0, 73.3, 78.2, 81.2, 83.4, 117.7, 117.9, 123.1, 123.5, 124.9, 126.2, 126.3, 127.6, 128.3, 129.0, 129.7, 130.4, 133.2, 133.3, 138.2, 155.5, 162.0, 177.5.

IR (v_{max}, cm⁻¹): 2954, 2923, 2853, 1637, 1465, 1315, 1097, 758, 696;

Anal. Calcd for $C_{37}H_{34}O_5$: C, 79.55; H, 6.13; H, 6.06. Found: C, 79.58; H, 6.15.

General procedure for the synthesis of chromone-ribose derivatives by Mizoroki-Heck reaction

Condition A (Jeffery's condition): A stirred, preheated mixture of bromochromone (1a,b) (56 mg, 0.249 mmol), 3-(2,3,5-tribenzyloxy-β-D-ribofuranozyl)-prop-1-ene (2a) (0.249 mmol, 1.0 equiv) or 3-(3,5-dibenzyloxy-β-D-ribofuranozyl)-prop-1-ene (2b) (0.249 mmol, 1.0 equiv), potassium carbonate (52 mg, 0.375 mmol, 1.5 equiv), potassium chloride (19 mg, 0.250 mmol, 1.0 equiv), tetrabutylammonium bromide (162 mg, 0.500 mmol, 2.0 equiv) and palladium acetate (4 mg, 0.015 mmol, 6 mol%) in dry DMF (5 mL) was heated at 110 °C for 2 hours under nitrogen atmosphere. The mixture was cooled then silica gel was added to the mixture and the solvent was

evaporated under reduced pressure. Then it was purified by column chromatography to obtain the pure product.

7-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-4H-chromen-4-one (9a)

Condition A: 115 mg (79%), colorless oil.

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 2.43-2.57 (m, 2H), 3.50 (m, 2H), 3.61-3.66 (m, 1H), 3.90 (m, 1H), 4.19 (m, 2H), 4.44-4.62 (m, 6H), 6.24 (d, J = 5.9 Hz, 1H), 6.38 (m, 2H), 7.27 (m, 17H), 7.72 (d, J = 5.9 Hz, 1H), 8.05 (d, J = 8.2 Hz,1H). ¹³C NMR (90 MHz, CDCl₃): δ (ppm) = 36.5, 70.1, 71.5, 71.7, 73.2, 76.8, 79.7, 79.9, 81.4, 112.7, 114.8, 122.8, 123.2, 125.5, 127.3, 127.4, 127.5, 127.6, 127.8, 127.9, 128.1, 130.4, 137.5, 137.6, 137.8, 137.9, 143.0, 155.0, 156.6, 177.0. IR (v_{max} , cm⁻¹): 3063, 3029, 2901, 2865, 1654, 1621, 1430, 1127, 1027, 736, 698; Anal. Calcd for C₃₈H₃₆O₆: C, 77.53; H, 6.16;. Found: C, 77.58; H, 6.19.

3-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-enyl)-4H-chromen-4-one (12a)

Condition A: 73 mg (50%), colorless oil.

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 2.16-2.56 (m, 2H), 3.53 (m, 2H), 3.68 (t, J = 5.6 Hz, 1H), 3.89 (t, J = 4.9 Hz, 1H), 4.16 (m, 2H), 4.48-4.61 (m, 6H), 6.32 (d, J = 15.8 Hz, 1H), 6.47 (m, 1H), 7.28 (m, 15H), 7.40 (m, 2H), 7.64 (t, J = 7.2 Hz, 1H), 7.76 (s, 1H), 8.24 (d, J = 7.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) = 37.4, 70.3, 71.7, 72.0, 73.3, 77.1, 79.3, 80.5, 81.2, 117.9, 121.9, 122.4, 124.0, 124.9, 126.1, 127.5, 127.6, 127.8, 128.0, 128.3, 128.4, 128.9, 133.3, 137.8, 138.1, 151.9, 155.8, 176.4. IR (v_{max} , cm⁻¹): 3063, 3029, 2901, 2865, 1654, 1621, 1430, 1127, 1027, 736, 698; Anal. Calcd for C₃₈H₃₆O₆: C, 77.53; H, 6.16. Found: C, 77.58; H, 6.18.

3-((E)-3-((2S,3S,4R,5R)-3,4-bis(benzyloxy)-5-(benzyloxymethyl)tetrahydrofuran-2-yl)allyl)-4H-chromen-4-one (13a)

Condition A: 26 mg (18%), colorless oil.

¹H NMR (360 MHz, CDCl₃): δ (ppm) = 3.22 (m, 2H), 3.51 (d, 2H), 3.66 (t, J = 6.1 Hz, 1H), 3.91 (t, J = 4.9 Hz, 1H), 4.00-4.21 (m, 2H), 4.44-4.61 (m, 6H), 5.56 (dd, J = 15.3 Hz, J = 7.3 Hz, 1H), 5.94 (dt, J = 15.3 Hz, J = 6.8 Hz, 1H), 7.28 (m, 15H), 7.35 (m, 2H), 7.65 (m, 2H), 8.22 (d, J = 7.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) = 29.8, 70.4, 72.0, 72.2, 73.5, 77.5, 81.4, 81.5, 81.6, 118.1, 123.0, 123.8, 125.0, 126.0, 127.7, 127.8, 127.8, 128.0, 128.1, 128.3, 128.4, 130.2, 131.5, 133.5, 138.0, 137.9, 152.8, 156.5, 177.5. IR (v_{max} , cm⁻¹): 2924, 2856, 1718, 1646, 1609, 1464, 1126, 1100, 751, 698. Anal. Calcd for C₃₈H₃₆O₆: C, 77.53; H, 6.16. Found: C, 77.55; H, 6.19.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Short title:

Synthesis of Flavone/Chromone- β -D-Ribofuranose Derivatives

Graphical abstract:

$$R^{1} = Ph, H$$

$$R^{2} = Ph, H$$

$$R^{2} = H, OBn$$

$$R^{2} = H, OBn$$

$$R^{2} = H, OBn$$

$$R^{2} = H + OBn$$

$$R^{3} = H + OBn$$

$$R^{4} = H + OBn$$

$$R^{2} = H + OBn$$

$$R^{2} = H + OBn$$

$$R^{3} = H + OBn$$

$$R^{4} = H + OBn$$

$$R^{2} = H + OBn$$