Tetrahedron Letters 52 (2011) 3397–3400

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Stereo-conserved synthesis of *syn*-diarylheptanoids, active principles of *Zingiber*, starting from D-glucose

Sandeep Bhosale [a], Vinod P. Vyavahare [a], Uppuleti Viplava Prasad [b], Venkata P. Palle [a], Debnath Bhuniya [a,*]

[a] Drug Discovery Facility, Advinus Therapeutics, Quantum Towers, Plot-9, Rajiv Gandhi Infotech Park, Phase-I, Hinjewadi, Pune 411057, India
[b] Department of Organic Chemistry, Andhra University, Visakhapatnam 530003, India

ARTICLE INFO

Article history:
Received 16 February 2011
Revised 22 April 2011
Accepted 23 April 2011
Available online 30 April 2011

Keywords:
Syn-diarylheptanoid
D-Glucose
Wilkinson's catalyst
Wittig reaction

ABSTRACT

A highly efficient and stereo-controlled synthetic strategy has been developed to access *syn*-diarylheptanoids, for example, **2**, **3**, **4**, and **5b** starting from D-glucose as a chiral pool. The 3-(*R*), 5-(*S*)-*syn*-diol stereochemistry present in these heptanoids was obtained after conserving C2 and C4 stereochemistry of D-glucose during the course of synthetic transformation. The key features of this synthetic strategy include: (i) conversion of D-glucose to a known chiral template **6** armored with the required 1,3-*syn*-diol stereochemistry as well as two terminal aldehyde functionalities for building up customized '*diaryl wings*'; (ii) conversion of **6** to **7** via an initial Wittig olefination at the C5-aldehyde; (iii) use of the hemiacetal **7** as a common intermediate to obtain the individual heptanoids via a second Wittig reaction at its anomeric center using appropriately chosen ylides.

Diarylheptanoids (Fig. 1) such as **1** (curcumin), **2**–**5** (octahydrocurcuminoids) are plant metabolites isolated from *Zingiber* (e.g., zingiberaceae; commonly known as ginger family).[1] Rhizomes and fruits of these medicinal plants are especially enriched with diarylheptanoids. There are emerging literature reports indicating potential medicinal applications of these class of compounds[2–6] including **2**–**5**[2e,3a,4a,b,5a] which are of our interest.

In literature, medicinal chemistry around the scaffolds **2**–**4** has been conducted using the compounds either isolated from various plant sources or via rather less controlled semi-synthetic process starting from the commercial curcumin. As shown in Scheme 1a, the compound **2** was obtained in modest yield (15%) along with its partially saturated products by hydrogenation of **1** under 1 atm of H_2 pressure.[5a,6] Higher H_2 pressure (200 psi) and longer reaction time were reported to be the solution to avoid partial hydrogenation.[5a]

A better stereo-controlled synthesis of **5** has been reported by Narasimhulu et al. in 14 steps starting from D-mannitol diacetonide as the chiral pool (Scheme 1b). At the end, **5a** and **b** were separated from a diastereomeric mixture.[2e]

Being interested in this series of biologically active compounds, we came up with a synthetic strategy starting from D-glucose which provided us a completely stereo-conserved synthesis of the *syn*-diarylheptanoids **2**–**5b**. A retro-synthetic map is shown in Scheme 2.[7,8] The acetonide protected aldehyde **6** was conceived for synthetic transformation of its masked C2,C4-1,3-*syn*-diol template into the C3,C5-*syn*-diol stereochemistry present in the heptanoids **2**–**5b**. The required synthetic manipulation was thought to be carried out by involving two Wittig olefination reactions, initially at C5 aldehyde of **6** (to get **7**), followed by another at C1 anomeric position of **7**.

As shown in Scheme 3, commercially available D-glucose di-acetonide was converted to 3-deoxy-1,2-*O*-(1-methylethylidene) α-D-*erythro*-pentodialdo-1,4-furanose **6** in four steps using a known procedure amenable for a large scale synthesis.[9] Wittig olefination

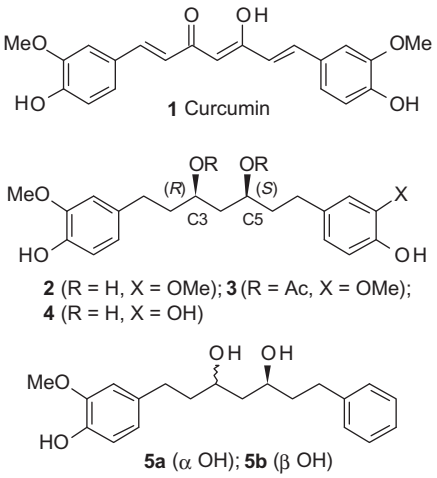
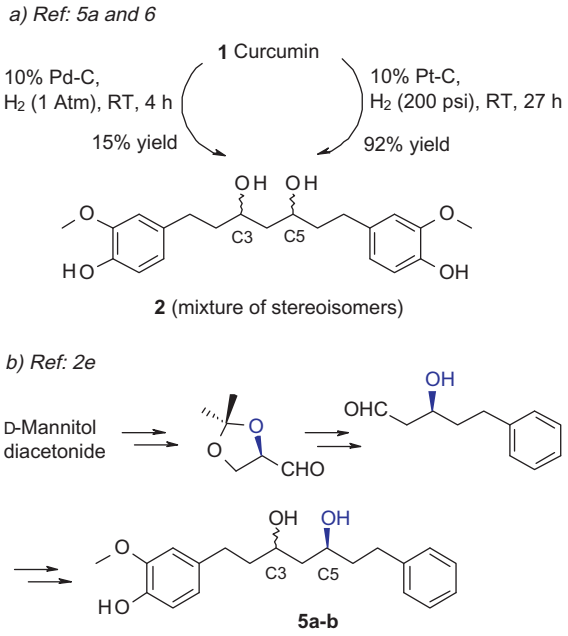


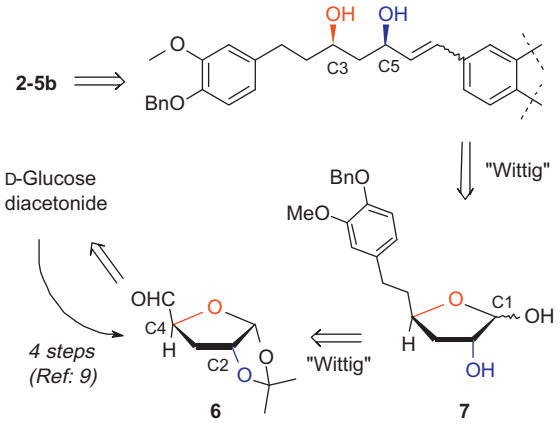
Figure 1. Examples of natural diarylheptanoids.

* Corresponding author. Tel.: +91 20 66539600; fax: +91 20 66539620.
E-mail address: debnath.b@advinus.com (D. Bhuniya).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.04.097

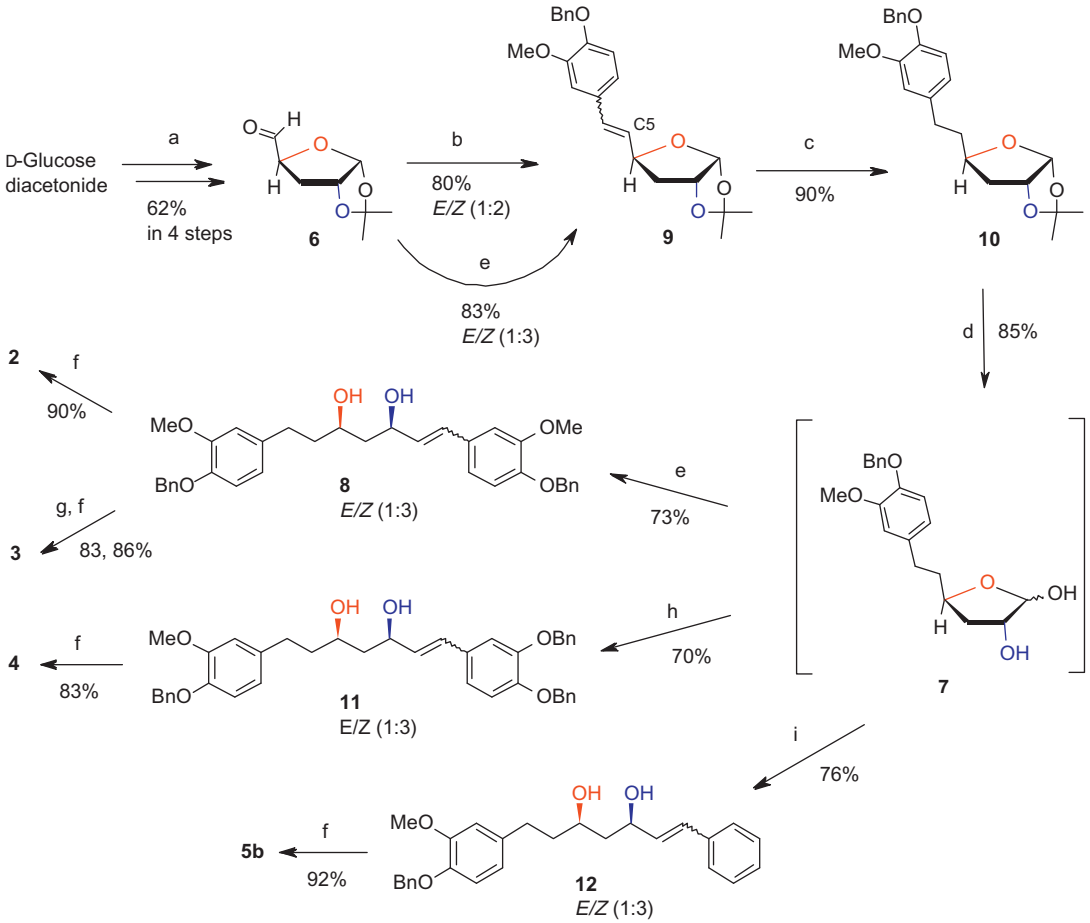


Scheme 1. Synthetic prior-art of diaryheptanoids.



Scheme 2. Retro-synthetic route to **2**–**5b** from D-glucose.

of the aldehyde **6** using ylide generated from 3-methoxy-4-benzyloxybenzyl triphenylphosphonium bromide and *t*-BuOK in THF at 0 °C gave us olefins (*Z*)-**9**[10] and (*E*)-**9**[11] (*E*/*Z* 1:2; separable on column chromatography) in 80% combined isolated yield (condition b).[9b] Based on ^{1}H NMR spectra, C5 olefinic proton signals for (*Z*)-**9** and (*E*)-**9** appearing at δ 5.55 (dd, J_{5-6} = 11.2 Hz, J_{4-5} = 8.8 Hz), and δ 6.02 (dd, J_{5-6} = 15.7 Hz, J_{4-5} = 7.3 Hz) respectively, were assigned for the *cis* and *trans* geometry. Selective reduction of the double bond in **9** was achieved by using 5 mol % Wilkinson's catalyst in *t*-BuOH/THF (1:1) under an atmospheric pressure of H_2



Scheme 3. Synthesis of **2**–**5b**. Reagents and conditions: (a) Following Ref. 9; (b) [(4-benzyloxy-3-methoxybenzyl)P(Ph)$_3$]Br, *t*-BuOK, THF, 0 °C to rt, 3 h; (c) Wilkinson's catalyst, *t*-BuOH/THF (1:1), H_2 balloon pressure, rt, 4–6 h; (d) 4% aq H_2SO_4, THF, 60 °C, 4 h; (e) [(4-benzyloxy-3-methoxybenzyl)P(Ph)$_3$]Br, 18-crown-6, K_2CO_3, dichloromethane, 40 °C, 6 h; (f) 10% Pd/C, H_2 balloon pressure, EtOAc, rt, 5–6 h; (g) Ac_2O, pyridine, cat. 4-(*N*,*N*-dimethylamino)pyridine, dichloromethane, rt, 14 h; (h) [(3,4-dibenzyloxybenzyl)P(Ph)$_3$]Br, 18-crown-6, K_2CO_3, dichloromethane, 40 °C, 6 h; (i) [(benzyl) P(Ph)$_3$]Cl, 18-crown-6, K_2CO_3, dichloromethane, 40 °C, 6 h.

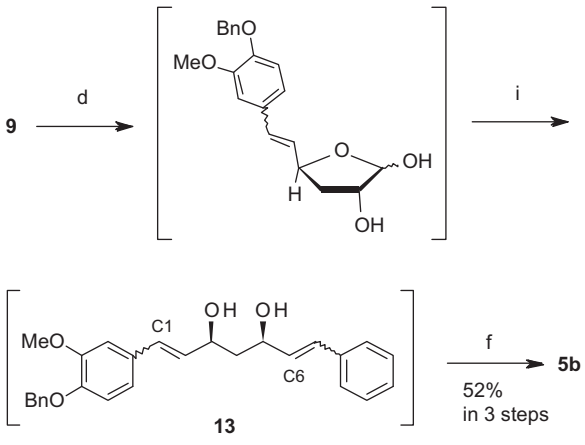
(condition c)[12] to afford **10**[13] in 90% yield. Hydrolysis of 1,2-acetonide functionality in **10** with 4% aq H_2SO_4 in THF at 60 °C (condition d) gave us anomeric mixture of hemiacetals **7**[14] (evident from ^{1}H NMR of crude product) in 85% isolated yield which was deployed as a common intermediate for the synthesis of *syn*-diaryheptanoides **2**–**5b**.

The mixture of hemiacetals **7** was subjected to the intended second Wittig olefination with the ylide generated from 3-methoxy-4-benzyloxybenzyl triphenylphosphonium bromide and potassium carbonate in the presence of 18-crown-6 in dichloromethane at 40 °C (condition e)[15] to obtain the required *syn*-1,3-diol olefin intermediate **8**[16] (*E*/*Z* 1:3) in 73% isolated yield. Subsequently, it was noticed that the above Wittig condition was also very effective for the conversion of **6** to **9** (*E*/*Z* 1:3). On the contrary, use of *t*-BuOK (condition b) was found to be ineffective for the 2nd Wittig reaction (**7** → **8**) presumably because of free C2-OH functionality present in **7**. The present work provides some additional information in conducting the 2nd Wittig reaction without protecting the C2-OH group in light of what was experienced by Pawar and Shinde.[8a]

Reduction of the double bond and simultaneous hydrogenolysis of two benzyloxy protecting groups in **8** (combined regioisomers used) were carried out by global hydrogenation using H_2 (1 atm) in the presence of catalytic amount of 10% Pd/C in EtOAc (condition f) to furnish analytically pure **2**[1b] after column chromatography (80% isolated yield) as a colorless oil. Compound **3**[1b] was obtained (also as colorless oil, 71%, two steps), from the mixture **8**, initially by di-acetylation (condition g), followed by global hydrogenation (condition f).

The diarylheptanoids **4**[1g] and **5b**[1d,2e] were obtained from the hemiacetal intermediate **7** following the same route employed for **2** (**7** → **11** → **4**; **7** → **12**[17] → **5b**) and using appropriately substituted benzyl triphenylphosphonium salt in the Wittig reactions (conditions h and i respectively).

Once the complete synthetic route was established, we also examined whether the selective olefinic hydrogenation (**9** → **10**) could be avoided in this general synthetic scheme and instead be carried out as a part of global hydrogenation. As shown in Scheme 4, the idea was applied for the synthesis of **5b**. Initial deprotection of acetonide group in the intermediate **9** (*E*/*Z* mixture), followed by the 2nd Wittig reaction furnished the 1,6-di-olefinic intermediate **13** (as a mixture of four regioisomers). Subsequent global hydrogenation provided us the desired compound **5b** in very good isolated yield (52% overall yield in three steps).



Scheme 4. Reagents and conditions: (d) 4% aq H_2SO_4, THF, 60 °C, 4 h; (i) [(benzyl)P(Ph)$_3$]Cl, 18-crown-6, K_2CO_3, dichloromethane, 40 °C 6 h; (f) 10% Pd/C, H_2 balloon pressure, EtOAc, rt, 5–6 h.

It is rewarding to mention here that partial hydrogenation was not noticed in any of the above hydrogenation reactions, unlike what is known in the case of hydrogenation of curcumin.[5a,6] This is presumably because of the absence of carbonyl groups in the present set of compounds.

In conclusion, we have accomplished synthesis of *syn*-diarylheptanoids **2**, **3**, **4,** and **5b**, which are active principles of *Zingiber* (a genus of ginger family). Starting from a known aldehyde **6**, derived from D-glucose diacetonide in four steps, all the four natural products were obtained via a common intermediate **7**. The present synthesis is very efficient, involves simple reagents and high yielding steps indicating a large scale synthetic feasibility of these biologically promising natural products. For example, **5b** was synthesized in eight steps starting from the commercially available D-glucose diacetonide with 27% overall yield (Schemes 3 and 4). To the best of our knowledge, this is the first completely stereo-controlled synthetic strategy toward accessing diarylheptanoids having 1,3-*syn*-diol moiety where optional '*aryl wings*' can be installed for conducting systematic medicinal chemistry.

Acknowledgments

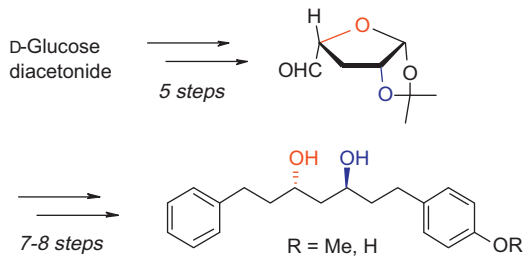
Authors are grateful to Drs. Rashmi Barbhaiya, and Kasim A. Mookhtiar for their support and encouragement. Mahesh Mone (Analytical Dept.) and Ganesh B. Salunke (presently at Nagoya University, Japan) are being acknowledged for their help during this work. Advinus Publication No. ADV-A-009.

Supplementary data

Supplementary data (detailed experimental procedure, spectral characterization of all the compounds and copies of representative ^{1}H and ^{13}C NMR) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.04.097.

References and notes

1. (a) Uehara, S.-I.; Yasuda, I.; Akiyama, K.; Morita, H.; Takeya, K.; Itokawa, H. *Chem. Pharm. Bull.* **1987**, *35*, 3298–3304; (b) Kikuzaki, H.; Usuguchi, J.; Nakatani, N. *Chem. Pharm. Bull.* **1991**, *39*, 120–122; (c) Ali, M. S.; Tezuka, Y.; Awale, S.; Banskota, A. H.; Kadota, S. *J. Nat. Prod.* **2001**, *64*, 289–293; (d) Shin, D.; Kinoshita, K.; Koyama, K.; Takahashi, K. *J. Nat. Prod.* **2002**, *65*, 1315–1318; (e) Ma, J.; Jin, X.; Yang, L.; Liu, Z.-L. *Phytochemistry* **2004**, *65*, 1137–1143; (f) Chattopadhyay, I.; Biswas, K.; Bandyopadhyay, U.; Banerjee, R. K. *Curr. Sci.* **2004**, *87*, 44–53; (g) Akiyama, K.; Kikuzaki, H.; Aoki, T.; Okuda, A.; Lajis, N.; Nakatani, N. *J. Nat. Prod.* **2006**, *69*, 1637–1640.
2. (a) Ref. 1c; (b) Ishida, J.; Ohtsu, H.; Tachibana, Y.; Nakanishi, Y.; Bastow, K.; Nagai, M.; Wang, H.-K.; Itokawa, H.; Lee, K.-H. *Bioorg. Med. Chem.* **2002**, *10*, 3481–3487; (c) Yokosuka, A.; Mimaki, Y.; Sakagami, H.; Sashida, Y. *J. Nat. Prod.* **2002**, *65*, 283–289; (d) Tian, Z.; An, N.; Zhou, B.; Xiao, P.; Kohane, I.; Wu, E. *Cancer Chemother. Pharmacol.* **2009**, *63*, 1131–1139; (e) Narasimhulu, M.; Reddy, T. S.; Mahesh, K. C.; Krishna, A. S.; Rao, J. V.; Venkateswarlu, Y. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3125–3127.
3. (a) Ref. 1d; (b) Yang, Y.; Kinoshita, K.; Koyama, K.; Takahashi, K.; Kondo, S.; Watanabe, K. *Phytomedicine* **2002**, *9*, 146–152.
4. For antioxidant effect, see: (a) Feng, J.-Y.; Liu, Z.-Q. J. *Agric. Food Chem.* **2009**, *57*, 11041–11046; (b) Ref. 1g; (c) Yang, M. H.; Yoon, K. D.; Chin, Y.-W.; Park, J. H.; Kim, J. *Bioorg. Med. Chem.* **2009**, *17*, 2689–2694.
5. For antiinflammatory effects, see: (a) Lee, S.-L.; Huang, W.-J.; Lin, W.-W.; Lee, S.-S.; Chen, C.-H. *Bioorg. Med. Chem.* **2005**, *13*, 6175–6181; (b) Lee, H.-J.; Kim, J.-S.; Ryu, J.-H. *Planta Med.* **2006**, *72*, 68–71.
6. For antiprotozoan effect, see: Changtam, C.; de Koning, H. P.; Ibrahim, H.; Sajid, M. S.; Gould, M. K.; Suksamrarn, A. *Eur. J. Med. Chem.* **2010**, *45*, 941–956.
7. Initial findings were presented in 13th CRSI meeting, 4–6th Feb. 2011, Poster No. 183 (http://www.crsi.org.in).
8. While this manuscript was under preparation, we noticed a simultaneous report along the line of similar synthetic strategy where *anti*-diaryheptanoids (structures shown below) were synthesized from D-glucose diacetonide in 12–13 steps. Please see: (a) Pawar, V. U.; Shinde, V. S. *Tetrahedron: Asymmetry* **2011**, *22*, 8–11; (b) Pawar, V. U.; Ghosh, S.; Chopade, B. A.; Shinde, V. S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 7243–7245



.

9. (a) Kucera, D.; Haley, G. J.; Rueden, E. J.; Wang, T. in PCT Publication No. WO2008/140549 A1.; (b) Suresh, V.; Selvam, J. J. P.; Rajesh, K.; Venkateswarlu, Y. *Tetrahedron: Asymmetry* **2008**, *19*, 1509–1513.
10. (*Z*)-**9**: R_f-value: 0.6 (30% ethyl acetate in hexanes). Mp: 117–119 °C. $[\alpha]_D^{25}$+67.9 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.32 (s, 3H), 1.44 (s, 3H), 1.71 (ddd, *J* = 15.6, 11, 4.6 Hz, 1H), 2.21 (dd, *J* = 13.4, 4.1 Hz, 1H); 3.93 (s, 3H), 4.78 (t, *J* = 4.1 Hz, 1H), 5.06 (dt, *J* = 10.7, 3.9 Hz, 1H), 5.17 (s, 2H), 5.55 (dd, *J* = 11.2, 8.8 Hz, 1H), 5.89 (d, *J* = 3.9 Hz, 1H), 6.63 (d, *J* = 11.5 Hz, 1H), 6.79 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 7.07 (d, *J* = 1.2 Hz, 1H), 7.27–7.31 (aromatics, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.4 Hz, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ 26.36, 26.89, 40.41, 56.16, 71.13, 73.96, 80.97, 105.55, 111.03, 112.53, 113.70, 121.84, 127.47(2C), 127.63, 128.07, 128.79 (2C), 129.89, 134.74, 137.25, 147.87, 149.51. HPLC-MS (*m*/*z*): 400.3 [M+18] base peak, HPLC purity: 99.0%, rt: 15.6 min.
11. (*E*)-**9**. R_f-value: 0.65 (30% ethyl acetate in hexanes). Mp: 121–123 °C. $[\alpha]_D^{25}$ −15.5 (*c* 0.2, $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.35 (s, 3H), 1.56 (s, 3H), 1.71 (ddd, *J* = 13.7, 10.8, 4.9 Hz, 1H), 2.23 (dd, *J* = 13.7, 4.4 Hz, 1H); 3.89 (s, 3H), 4.76–4.82 (m, 2H), 5.16 (s, 2H), 5.89 (d, *J* = 3.9 Hz, 1H), 6.02 (dd, *J* = 15.7, 7.3 Hz, 1H), 6.60 (d, *J* = 16 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.84 (dd, *J* = 8.3, 2 Hz, 1H), 6.96 (d, *J* = 2 Hz, 1H), 7.28–7.31 (aromatics, 1H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ 26.18, 26.76, 39.87, 55.98, 70.99, 78.70, 80.67, 105.43, 109.37, 111.09, 113.76, 119.90, 125.54, 127.29 (2C), 127.93, 128.63(2C), 129.96, 132.54, 137.06, 148.22, 149.68. HPLC-MS (*m*/*z*): 383.2 [M+1], 400.2 [M+18] base peak, purity: 99.44%, rt: 17 min.
12. Jourdant, A.; González-Zamora, E.; Zhu, J. *J. Org. Chem.* **2002**, *67*, 3163–3164.
13. **10**: R_f-value: 0.6 (30% ethyl acetate in hexanes). Mp: 61–63 °C. $[\alpha]_D^{25}$ −5.6 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.32 (s, 3H), 1.43–1.51 (m, 1H), 1.48 (s, 3H), 1.79–1.84 (m, 1H), 1.85–1.95 (m, 1H), 2.08 (dd, *J* = 13.2, 4.1 Hz, 1H), 2.57–2.65 (m, 1H), 2.68–2.76 (m, 1H), 3.88 (s, 3H), 4.16–4.24 (m, 1H), 4.72 (t, *J* = 4.2 Hz, 1H), 5.12 (s, 2H), 5.83 (d, *J* = 3.7 Hz, 1H), 6.66 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.76 (d, *J* = 1.0 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 7.27–7.30 (aromatics, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ 26.44, 26.92, 32.30, 36.43, 39.26, 56.24, 71.57, 77.36, 80.86, 105.55, 111.06, 112.76, 114.74, 120.50, 127.55(2C), 127.99, 128.74 (2C), 135.39, 137.74, 146.71, 149.93. HPLC-MS (*m*/*z*): 402.3 [M+18] base peak, HPLC purity: 97%, rt: 15.66 min.
14. **7**: R_f-value: 0.3 (60% ethyl acetate in hexanes). Mp: 74–76 °C. $[\alpha]_D^{25}$+11.66 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.70–1.90 (m, 3H, $-CH_2-$, –OH), 1.90–2.10 (m, 2H), 2.54–2.74 (m, 2H+0.66H, $-CH_2-$ and –OH), 3.02 (s, 0.33H, –OH), 3.87 (s, 3H), 4.24–4.36 (m, 2H), 5.12 (s, 2H), 5.26 (s, 0.33H, anomeric-H), 5.38 (d, *J* = 3.4 Hz, 0.66H, anomeric-H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.74 (s, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 7.27–7.31 (aromatics, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.43 (d, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ [31.92, 32.21, 37.71, 38.06, 38.53, 39.52 account for 3C)], 56.21, 71.40, 71.82 (0.7C), 76.48 (0.7C), 76.80 (0.3C), 79.42 (0.3C), 96.97 (0.7C), 102.81 (0.3C), 112.60, 114.46, 120.45, 127.55 (2C), 128.00, 128.71 (2C), 135.18, 137.50, 146.55, 149.71. HPLC-MS (*m*/*z*): 362.2 [M+18] base peak, HPLC purity: 94.0%, rt: 11.68 min.
15. Motoshima, K.; Noguchi-Yachide, T.; Sugita, K.; Hashimoto, Y.; Ishikawa, M. *Bioorg. Med. Chem.* **2009**, *17*, 5001–5014.
16. (*Z*)-**8**. R_f-value: 0.6 (60% ethyl acetate in hexanes). Mp: 64–65 °C. $[\alpha]_D^{25}$+20.36 (*c* 0.5 in $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.67–1.82 (m, 4H), 2.56–2.72 (m, 2H), 2.76 (br s, 1H, –OH), 2.99 (br s, 1H, –OH), 3.85–3.94 (m, 1H), 3.86 (s, 6H, –OMe), 4.85 (t, *J* = 8.3 Hz, 1H), 5.12 (s, 2H), 5.16 (s, 2H), 5.59 (dd, *J* = 11.2, 9.3 Hz, 1H), 6.45 (d, *J* = 11.7 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.74 (s, 1H), 6.76–6.82 (aromatics, 2H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.88 (s, 1H), 7.30 (app. t, *J* = 6.8 Hz, 2H), 7.30–7.40 (aromatics, 4H), 7.43 (d, *J* = 7.4 Hz, 4H). ^{13}C NMR (100 MHz; $CDCl_3$): δ 31.65, 40.17, 43.76, 56.33(2C), 69.38, 71.34, 71.59, 72.01, 112.71, 113.05, 114.06, 114.70, 120.53, 121.70, 127.58 (2C), 127.62 (2C), 128.09, 128.22, 128.83 (2C), 128.91 (2C), 130.14, 131.18, 132.84, 135.47, 137.36, 137.73, 146.78, 148.02, 149.72, 150.01. HPLC-MS (*m*/*z*): 572.4 [M+18] base peak, HPLC purity: 99%, rt: 16.12 min. IR (neat): 3401, 2936, 1602, 1514 cm^{-1}.
17. (*Z*)-**12**. R_f-value: 0.6 (40% ethyl acetate in hexanes). Mp: 66–69 °C. $[\alpha]_D^{25}$+34.0 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz; $CDCl_3$): δ 1.66–1.84 (m, 4H and –OH), 2.58–2.73 (m, 2H and -OH), 3.86 (s, 3H), 3.88–3.95 (m, 1H), 4.84 (dt, *J* = 9.3, 2.9 Hz, 1H), 5.12 (s, 2H), 5.68 (dd, *J* = 11.7, 9.3 Hz, 1H), 6.54 (d, *J* = 11.7 Hz, 1H), 6.65 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 7.27–7.34 (aromatics, 6H), 7.36 (app. t, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 7.4 Hz, 2H). ^{13}C NMR (100 MHz; $CDCl_3$): δ 31.38, 39.83, 43.17, 56.03, 69.03, 71.24, 71.71, 112.32, 114.27, 120.26, 127.35 (2C), 127.47, 127.84, 128.48 (2C), 128.60 (2C), 128.83 (2C), 130.84, 133.88, 135.22, 136.49, 137.45, 146.40, 149.63. HPLC-MS (*m*/*z*): 436.2 [M+18] base peak, HPLC purity: 98.52%, rt: 16.27 min.