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Asymmetric total synthesis of botcinic acid and its derivatives: synthetic revision of the structure of botcinolides

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ABSTRACT

The stereoselective total syntheses of botcinic acid, botcinic acid methyl ester, 3-*O*-acetylbotcinic acid methyl ester, botcineric acid, and botcinin E were achieved. The structures of these compounds have been unequivocally determined through their total synthesis, and they are identified with the revised structures of botcinolide, 4-*O*-methylbotcinolide, 3-*O*-acetyl-5-*O*-methylbotcinolide, homobotcinolide, and 2-epibotcinolide, respectively.

Botcinolide (**1**) was isolated from the culture broth of *Botrytis cinerea* as a significant phytotoxic metabolite in 1993 by Cutler et al.[1a] The relative configuration of **1** was suggested on the basis of the spectroscopic analysis using COSY, TOCSY, HETCORR, HMBC, and NOESY.[1b] In 1996, Collado et al. isolated other metabolites from *B. cinerea* (strain UCA 992) related to **1**, which were called 4-*O*-methylbotcinolide (**2**), 3-*O*-acetyl-5-*O*-methylbotcinolide (**3**), 2-epibotcinolide (**5**), and 3-*O*-acetyl-2-epibotcinolide (**6**).[1c] In the same year, homobotcinolide (**4**) was also isolated from *B. cinerea* by Cutler, and the structure of **4** was assigned by its elemental analysis, IR spectra, and comparison of the ^{13}C NMR and partial ^{1}H NMR spectroscopic data of **4** with those of **1**.[1d] Other botcinolide derivatives were also isolated by Collado's group and similar nine-membered ring structures were proposed as shown in Figure 1.[1e,f]

After one decade, Nakajima et al. obtained metabolites **7**, **11**, and **12** from the culture filtrate of a different strain of *B. cinerea* (strain AEM 211), and some of them showed antifungal activity against *Magnaporthe grisea*, a pathogen of the rice blast disease.[2a] Nakajima first named them botcinic acid (**7**), botcinin E (**11**), and botcinin A (**12**), and later reported that the structure of botcinolide (**1**) should be revised to that of **7**, the structure of 4-*O*-methylbotcinolide (**2**) should be revised to that of botcinic acid methyl ester (**8**), and the structure of 3-*O*-acetyl-2-epibotcinolide (**6**) should be revised to that of **12**.[2b] They also expected that the structures of 3-*O*-acetyl-5-*O*-methylbotcinolide (**3**) and homobotcinolide (**4**) should be revised to those of 3-*O*-acetylbotcinic acid methyl ester (**9**) and botcineric acid (**10**), respectively, based on the studies of the chemical conversion of the botcinic acid derivatives and comparison of their spectroscopic data. Furthermore, they reported that the structure of 2-epibotcinolide (**5**) might be the same as that of **11** because the NMR data of **5** and **11** are almost identical; however, there are four exceptional resonances in the NMR spectra, which should be clarified by advanced investigations in order to determine the exact structure of **5**.

Recently, we have established a method for the synthesis of the proposed structure of 2-epibotcinolide (**5**) by the stereoselective aldol reactions and rapid lactonization using MNBA.[3] We

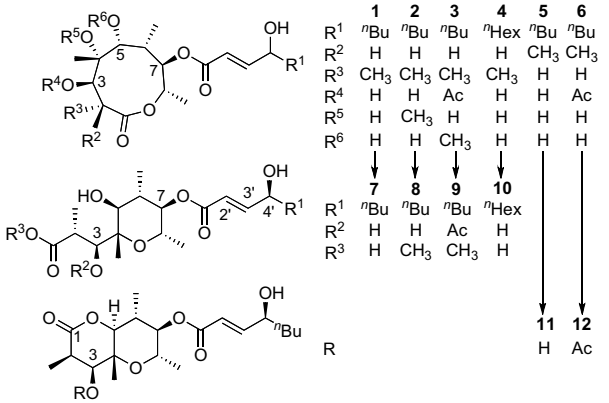

Figure 1. Structure match-up between botcinolides and botcinic acid derivatives.

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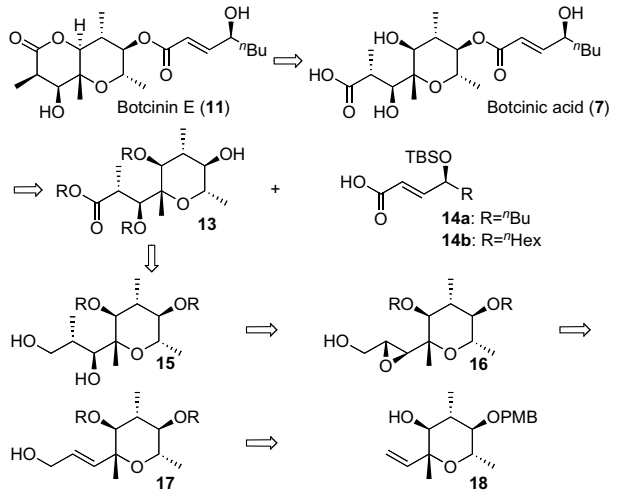
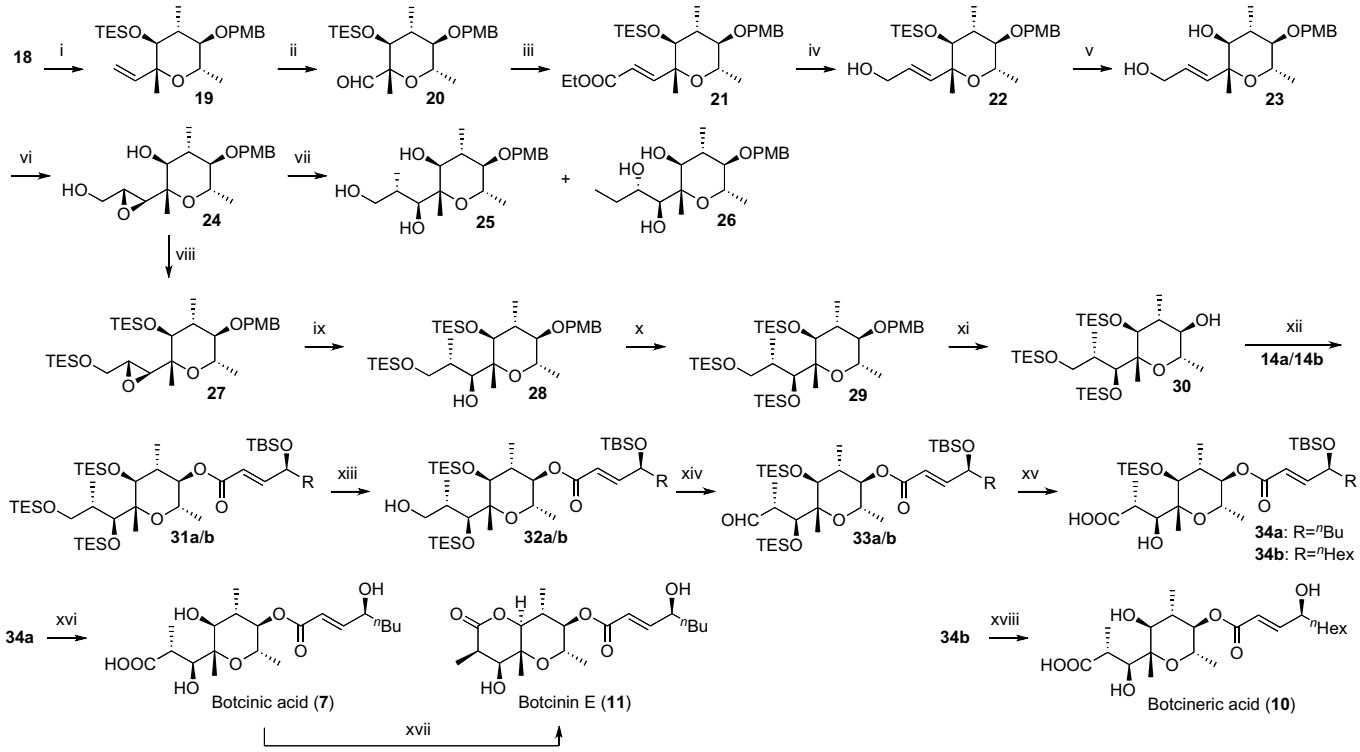
concluded that the reported nine-membered ring structures of 2-epibotcinolide (**5**) and other related compounds are extremely doubtful based on the detailed comparison of the ^{1}H NMR spectrum of the synthetic intermediates with natural products. In this Letter, we report the total synthesis of the botcinic acid analogues (**7**–**10**) and botcinin E (**11**), which have updated the proposed structures of botcinolides in order to show the true forms of these natural products.



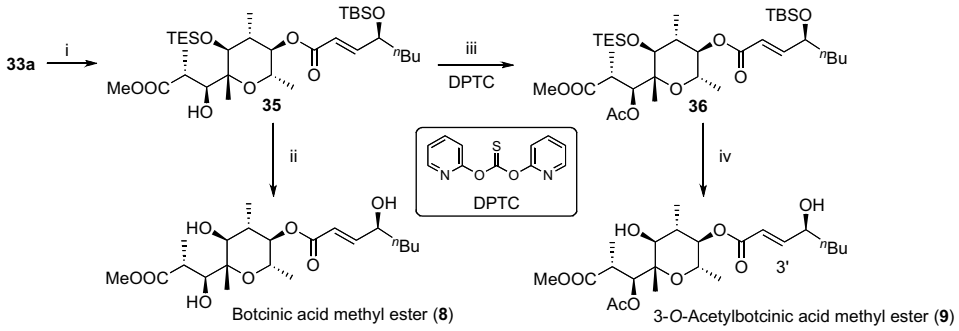
Scheme 1. Retrosynthesis of botcinic acid analogues.

The retrosynthetic analyses of botcinic acid and its derivatives are described as shown in Scheme 1. Botcinin E (**11**) could be prepared from botcinic acid (**7**) via lactonization under acidic conditions.[4] Botcinic acid consists of the highly substituted tetrahydropyran moiety **13** and the side chain parts **14**. The latter moiety **14** has already been synthesized by our group as reported in the previous Letter.[5] The basic skeleton **13** could be synthesized from the 1,3-diol **15**, which might be constructed from the epoxide **16** by regioselective methylation. This epoxide could be prepared from the allylic alcohol **17** by Katsuki-Sharpless asymmetric epoxidation, and **17** might be obtained from the tetrahydropyran derivative **18** by a one-carbon elongation. We have already established an effective method for the synthesis of the key intermediate **18** by utilizing the asymmetric aldol and 6-*endo* ring closure reactions.[5]

The synthetic routes to produce botcinic acid (**7**), botcinin E (**11**), and botcineric acid (**10**) are depicted in Scheme 2. First, the protection of **18**[5] followed by ozonolysis of **19** afforded the corresponding aldehyde **20**. Olefination of the aldehyde **20** and successive reduction of the coupling product **21** yielded the allylic alcohol **22**. After deprotecting the TES group in **22**, the asymmetric epoxidation of **23**[6] was carried out and the desired epoxy alcohol **24** was obtained as a single diastereomer. Chakraborty reported the facile methylation of the epoxy diol **24** to form **25** using lithium dimethylcuprate,[7] however, our attempted epoxy ring-opening reaction of **24** using the cuprate reagent gave not only the desired 1,3-diol **25**, but also the undesired 1,2-diol **26** as a major product via the Payne rearrangement. On the other hand, the methylation of **27**, which was generated from **24** by protection, regioselectively proceeded and the desired compound **28** was exclusively produced. After protection of **28** and removal of the PMB group in **29**, the side chain



Scheme 2. Reagents and conditions: (i) TESOTf, DMAP, Py, rt, 1 h, quant.; (ii) O_3, CH_2Cl_2/MeOH (10:1), −78 °C, 35 min, then PPh_3, −78 °C for 45 min and 0 °C for 1.5 h, 96%; (iii) Ph_3P=CHCOOEt, toluene, reflux, 20 h, quant.; (iv) DIBAL-H, CH_2Cl_2, 0 °C, 1.5 h, 95%; (v) TBAF, THF, rt, 2 h, 95%; (vi) $Ti(O^iPr)_4$, (−)-DIPT, TBHP, MS 3 Å, CH_2Cl_2, 0 °C, 1.5 h, 93%; (vii) $Me_2CuLi{\cdot}LiI$, Et_2O, −20 °C to rt, 13.5 h, 43% of **25**, 50% of **26**; (viii) TESCl, imidazole, DMF, rt, 12 h, quant.; (ix) $Me_2CuLi{\cdot}LiCN$, Et_2O, −30 °C, 2.5 h, 84%; (x) TESOTf, DMAP, Py, rt, 22 h, quant.; (xi) DDQ, CH_2Cl_2/phosphate buffer (pH 7) (5:1), rt, 1.5 h, 65%; (xii) (a) **14a**, MNBA, Et_3N, DMAP, CH_2Cl_2, rt, 12 h, 91% of **31a**; (b) **14b**, MNBA, Et_3N, DMAP, CH_2Cl_2, rt, 14 h, 93% of **31b**; (xiii) (a) PPTS, CH_2Cl_2/MeOH (1:1), −25 °C, 3 h, 94% of **32a**; (b) PPTS, CH_2Cl_2/MeOH (1:1), −25 °C, 1 h, 90% of **32b**; (xiv) (a) TPAP, NMO, MS 4 Å, CH_2Cl_2, 0 °C, 1 h, 81% of **33a**; (b) TPAP, NMO, MS 4 Å, CH_2Cl_2, 0 °C, 1 h, 88% of **33b**; (xv) (a) **33a**, $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH/H_2O (3.4:1), rt, 22 h; (b) **33b**, $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH/H_2O (3.4:1), rt, 15 h; (xvi) TsOH, THF/H_2O (10:1), rt, 2 days, 56% of **7** and 37% of **11** from **33a** (two steps); (xvii) TsOH, THF, rt, 23 h, 82%; (xviii) TsOH, THF/H_2O (10:1), rt, 24 h, 73% of **10** from **33b** (two steps).



Scheme 3. Reagents and conditions: (i) (a) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, $^tBuOH/H_2O$ (3.4:1), rt, 18.5 h; (b) $TMSCHN_2$, MeOH, rt, 10 min, quant. (two steps); (ii) HF·Py, THF/Py (2:1), rt, 20 min. 74%; (iii) AcOH, DPTC, DMAP, neat, 65 °C, 40 h, 35% of **36** and 57% of the recovered **35**; (iv) HF·Py, THF/Py (2:1), rt, 11 h, 50%.

parts **14a**/**b**[5] were added to the alcohol **30** by the MNBA-promoted coupling reaction.[8] The site-selective deprotection of a TES group in the coupling products **31a**/**b** was realized, and the resulting primary alcohols **32a**/**b** were oxidized to form the corresponding aldehydes **33a**/**b**, which were further converted into carboxylic acids **34a**/**b** under Pinnick's conditions. Finally, deprotection of the TES groups afforded botcinic acid (**7**)[9] and botcinin E (**11**)[10] from **34a**, and also botcineric acid (**10**)[11] from **34b**. It was also confirmed that the acid-catalyzed lactonization of **7** smoothly proceeded to afford **11** at room temperature.

The syntheses of botcinic acid methyl ester (**8**) and 3-*O*-acetylbotcinic acid methyl ester (**9**) are described in Scheme 3. Oxidation of **33a** and successive treatment of the resulting carboxylic acid **34a** with TMS diazomethane afforded the corresponding methyl ester **35**. Deprotection of the TES and TBS groups in **35** gave botcinic acid methyl ester (**8**)[12] in good yield. Preparation of another metabolite **9** was also attempted by acetylation of the 3-hydroxyl group in **35**, but it was revealed that the coupling required very strict conditions. When the acetylation of **35** was performed by conventional methods, such as Ac_2O/DMAP in pyridine or AcCl/Et_3N in dichloromethane, no coupling product was generated at all. We found that only the protocol using *O*,*O*-di(2-pyridyl) thiocarbonate (DPTC)[13] was effective for introducing the acetyl group into **35**, and the desired **36** was successfully obtained in the presence of DPTC/DMAP. Finally, cleavage of the silyl groups in **36** provided 3-*O*-acetylbotcinic acid methyl ester (**9**).[14]

As described above, the asymmetric total syntheses of botcinic acid (**7**), botcinic acid methyl ester (**8**), 3-*O*-acetylbotcinic acid methyl ester (**9**), botcineric acid (**10**), and botcinin E (**11**) were successfully achieved. The ^1H and ^{13}C NMR data of the synthetic **7**, **8**, and **11** are in good agreement with those of the isolated compounds[2] in the same solvent, and the values of the optical rotations of the synthetic **7** and **11** were similar to those of the natural products. These results strongly support the fact that the structures of botcinic acid (**7**), its methyl ester (**8**), and botcinin E (**11**) proposed by Nakajima et al. are absolutely correct.

The ^1H and ^{13}C NMR data of the synthetic 3-*O*-acetylbotcinic acid methyl ester (**9**) in $CDCl_3$ were almost identical to those of the isolated 3-*O*-acetyl-5-*O*-methylbotcinolide (**3**)[1c] except for one chemical shift in the ^1H NMR spectra. The resonance at δ_H 6.70 ppm (H-3′)[15] in the reported data seems to correspond to the resonance at δ_H 6.99 ppm (H-3′) in our data, however, we have assumed that the chemical shift at δ_H 6.70 ppm in the former paper might be incorrectly typed because the resonances of the protons for H-3′ of the other botcinolides are observed in the range from δ_H 6.97 to 7.04 ppm. Furthermore, Collado reported that 'The ^1H NMR spectrum of **3** was very similar to that of botcinolide (**1**) except for the presence of two new signals at δ_H 3.64 (3H, s) and 2.22 (3H, s)', therefore, it is determined that the structure of the natural product assumed to be 3-*O*-acetyl-5-*O*-methylbotcinolide (**3**) should be revised to that of 3-*O*-acetylbotcinic acid methyl ester (**9**).

The structure of homobotcinolide (**4**) also had to be revised to that of botcineric acid (**10**) because the structure of **4** was conjectured by the homological analysis of the spectroscopic data of botcinolide (**1**), whose structure has been revised to botcinic acid (**7**). Actually, the ^{13}C NMR data of the synthetic botcineric acid (**10**) in CD_3OD were identical to those of the reported homobotcinolide (**4**).[1d]

In summary, we achieved the first asymmetric total syntheses of botcinic acid (**7**), botcinic acid methyl ester (**8**), 3-*O*-acetylbotcinic acid methyl ester (**9**), botcineric acid (**10**), and botcinin E (**11**). The previous synthetic studies[3,5] and the present report on the synthesis of **7**, **8**, and **11** confirmed that the structures of botcinolides (**1**, **2**, and **5**) are incorrect and should be revised to those of **7**, **8**, and **11**. Extensive examinations including a detailed comparison of the spectroscopic data of 3-*O*-acetylbotcinic acid methyl ester (**9**) and botcineric acid (**10**) with those of other reported botcinolides concluded that the true forms of the natural compounds assumed to be 3-*O*-acetyl-5-*O*-methylbotcinolide (**3**) and homobotcinolide (**4**) are unambiguously identified as having the structures of **9** and **10**, respectively.

Acknowledgments

The authors appreciate Prof. Nakajima (Tottori Univ.) to share the spectral data for botcinic acid and botcinin E. The authors thank the Central Glass Co., Ltd (Japan) for kindly providing trifluoromethanesulfonic acid as a bulk sample. This study was partially supported by a Research Grant from the Center for Green Photo-Science and Technology, and Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan.

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9. *Compound* **7**: $[\alpha]_D^{21}$ −17.9 (*c* 0.42, EtOH) [lit[2b] $[\alpha]_D^{25}$ −14 (*c* 0.35, EtOH)]; IR (neat): 3411, 2931, 1706, 1655 cm^{-1}; ^1H NMR (CD_3OD): δ 6.98 (dd, *J* = 15.5, 5.0 Hz, 1H), 6.02 (dd, *J* = 15.5, 1.8 Hz, 1H), 4.33 (dd, *J* = 10.5, 10.0 Hz, 1H), 4.26–4.22 (m, 1H), 3.77 (d, *J* = 11.1 Hz, 1H), 3.60 (dq, *J* = 10.0, 6.3 Hz, 1H), 3.56 (br s, 1H), 2.75–2.71 (m, 1H), 1.91–1.83 (m, 1H), 1.61–1.53 (m, 2H), 1.49–1.28 (m, 4H), 1.32 (d, *J* = 7.0 Hz, 3H), 1.22 (s, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD): δ 180.3, 167.7, 153.6, 120.2, 80.0, 78.5, 77.7, 72.4, 71.6, 69.3, 39.7, 39.3, 37.3, 28.7, 23.6, 18.1, 17.5, 14.9, 14.7, 14.3; HR MS: calcd for $C_{20}H_{34}O_8Na$ (M + Na^+) 425.2146, found 425.2147.
10. *Compound* **11**: $[\alpha]_D^{30}$ −88.9 (*c* 0.38, EtOH), [lit[2b] $[\alpha]_D^{25}$ −69 (*c* 0.23, EtOH)]; IR (neat): 3445, 2934, 2874, 1730 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.02 (dd, *J* = 15.5, 4.5 Hz, 1H), 6.07 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.53 (dd, *J* = 11.0, 9.5 Hz, 1H), 4.37–4.32 (m, 1H), 4.15 (dd, *J* = 9.2, 3.8 Hz, 1H), 3.73 (dq, *J* = 9.5, 6.0 Hz, 1H), 3.70 (d, *J* = 10.8 Hz, 1H), 3.06 (dq, *J* = 9.2, 7.0 Hz, 1H), 2.18 (ddq, *J* = 11.0, 10.8, 6.0 Hz, 1H), 1.98 (d, *J* = 3.8 Hz, 1H), 1.68 (d, *J* = 4.0 Hz, 1H), 1.63–1.55 (m, 2H), 1.48–1.33 (m, 4H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.28 (s, 3H), 1.12 (d, *J* = 6.0 Hz, 3H), 1.06 (d, *J* = 6.0 Hz, 3H), 0.92 (t, *J* = 6.0 Hz, 3H); ^1H NMR (CD_3OD): δ 7.02 (dd, *J* = 15.5, 5.0 Hz, 1H), 6.05 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.50 (dd, *J* = 11.0, 9.5 Hz, 1H), 4.26–4.22 (m, 1H), 4.08 (d, *J* = 9.3 Hz, 1H), 3.94 (d, *J* = 11.0 Hz, 1H), 3.78 (dq, *J* = 9.5, 6.0 Hz, 1H), 3.20 (dq, *J* = 9.3, 7.0 Hz, 1H), 2.25–2.17 (m, 1H), 1.62–1.49 (m, 2H), 1.40–1.26 (m, 4H), 1.17 (s, 3H), 1.14 (d, *J* = 7.0 Hz, 1H), 1.07 (d, *J* = 6.0 Hz, 1H), 0.97 (d, *J* = 6.0 Hz, 3H), 0.92 (t, *J* = 6.0 Hz, 3H);^{13}C NMR ($CDCl_3$): δ 174.0, 165.8, 151.8, 119.1, 78.4, 77.2, 76.2, 74.0, 71.1, 68.4, 38.3, 36.4, 35.6, 27.4, 22.5, 18.2, 13.9, 13.7, 11.0, 10.3; ^{13}C NMR (CD_3OD): δ 177.4, 167.6, 154.1, 119.8, 79.6, 78.1, 77.9, 75.0, 71.5, 69.5, 39.5, 37.2, 36.8, 28.7, 23.6, 18.6, 14.3, 14.0, 11.6, 10.5; HR MS: calcd for $C_{20}H_{32}O_7Na$ (M+Na^+) 407.2040, found 407.2034.
11. *Compound* **10**: $[\alpha]_D^{30}$ −7.9 (*c* 0.90, EtOH); IR (neat): 3418, 2929, 1716, 1462, 1273, 1166, 1107 cm^{-1}; ^1H NMR (CD_3OD): δ 6.97 (dd, *J* = 15.6, 4.9 Hz, 1H), 6.02 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.33 (dd, *J* = 10.4, 10.1 Hz, 1H), 4.25–4.22 (m, 1 H), 3.76 (d, *J* = 10.4 Hz, 1H), 3.63–3.57 (m, 1H), 3.53 (br s, 1H), 2.76–2.67 (m, 1H), 1.91–1.83 (m, 1H), 1.60–1.49 (m, 2H), 1.40–1.28 (m, 8H), 1.32 (d, *J* = 6.6 Hz, 3H), 1.23 (s, 3H), 0.99 (d, *J* = 6.1 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD): δ 180.8,* 167.7, 153.6, 120.2, 80.0, 78.5, 78.0, 72.5, 71.6, 69.3, 39.9, 39.3, 37.5, 32.9, 30.3, 26.4, 23.6, 18.3, 17.8, 15.0, 14.7, 14.4; HR MS: calcd for $C_{22}H_{38}O_8Na$ (M+Na^+) 458.2459, found 458.2448. * This resonance was observed as a cross peak in HMBC spectrum.
12. *Compound* **8**: $[\alpha]_D^{21}$ −22.9 (*c* 0.70, EtOH); IR (neat): 3437, 2932, 2874, 1715, 1653 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.99 (dd, *J* = 15.5, 4.5 Hz, 1H), 6.05 (dd, *J* = 15.5, 2.0 Hz, 1H), 4.40 (dd, *J* = 10.7, 9.8 Hz, 1H), 4.35–4.31 (m, 1H), 3.90 (dd, *J* = 11.0, 5.6 Hz, 1H), 3.71 (d, *J* = 11.1 Hz, 1H), 3.65 (s, 3H), 3.59–3.53 (m, 2H), 2.78 (dq, *J* = 2.1, 7.2 Hz, 1H), 2.15 (d, *J* = 5.6 Hz, 1H), 1.88 (ddq, *J* = 11.0, 10.7, 6.4 Hz, 1H), 1.64 (d, *J* = 4.5 Hz, 1H), 1.64–1.57 (m, 2H), 1.46-1.32 (m, 4H), 1.36 (d, *J* = 7.2 Hz, 3H), 1.24 (s, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.0 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H);^1H NMR (C_6D_6): δ 7.11 (dd, *J* = 16.1, 4.3 Hz, 1H), 6.24 (dd, *J* = 16.1, 1.2 Hz, 1H), 4.78 (dd, *J* = 10.4, 9.7 Hz, 1H), 4.05–4.01 (m, 1H), 3.94 (d, *J* = 10.4 Hz, 1H), 3.87–3.81 (m, 1H), 3.61 (dq, *J* = 9.7, 6.3 Hz, 1H), 3.56 (d, *J* = 11,3 Hz, 1H), 3.34 (s, 3H), 2.74 (q, *J* = 6.8 Hz, 1H), 1.99–1.93 (m, 1H), 1.84 (br s, 1H), 1.36 (d, *J* = 6.8 Hz, 1H), 1.28–1.20 (m, 2H), 1.24 (d, *J* = 4.3 Hz, 1H), 1.16–1.12 (m, 4H), 1.16 (s, 3H), 1.14 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.83 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 176.7, 165.9, 151.1, 119.5, 78.6, 77.0, 76.7, 71.8, 71.2, 68.0, 51.4, 38.0, 37.8, 36.4, 27.4, 22.5, 18.1, 17.0, 14.4, 14.0, 13.9; ^{13}C NMR (C_6D_6): δ 176.6, 165.9, 151.9, 119.6, 79.1, 77.3, 77.0, 71.6, 70.9, 68.4, 51.0, 38.4, 38.2, 36.5, 27.6, 22.8, 18.4, 17.2, 14.4, 14.3, 14.1; HR MS: calcd for $C_{21}H_{36}O_8Na$ (M+Na^+) 439.2308, found 439.2307.
13. Saitoh, K.; Shiina, I.; Mukaiyama, T. *Chem. Lett* **1998**, 679–680.
14. *Compound* **9**: $[\alpha]_D^{22}$ −14.7 (*c* 1.20, EtOH); IR (neat): 3477, 2935, 1723, 1254, 1167 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.99 (dd, *J* = 15.5, 4.5 Hz, 1H), 6.05 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.98 (d, *J* = 3.8 Hz, 1H), 4.40 (dd, *J* = 10.5, 9.8 Hz, 1H), 4.35–4.30 (m, 1H), 3.66 (s, 3H), 3.57 (dq, *J* = 9.8, 6.0 Hz, 1H), 3.10 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.01 (dd, *J* = 3.8, 6.8 Hz, 1H), 2.99 (d, *J* = 4.5 Hz, 1H), 2.23 (s, 3H), 1.91 (ddq, *J* = 10.5, 10.5, 6.3 Hz, 1H), 1.64–1.54 (m, 2H), 1.40–1.31 (m, 4H), 1.34 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.0 Hz, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 174.0, 172.9, 165.9, 151.0, 119.5, 78.3, 77.9, 76.6, 72.1, 71.2, 68.1, 51.5, 38.8, 37.0, 36.4, 27.4, 22.5, 20.9, 18.0, 16.1, 14.9, 14.3, 13.9; HR MS: calcd for $C_{23}H_{38}O_9Na$ (M+Na^+) 481.2408, found 481.2379.
15. The proton positions in parentheses are numbered according to the botcinin skeleton nomenclature by Nakajima.