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Total Synthesis of Norsampsones A and B, Garcinielliptones N and O, and Hyperscabrin A

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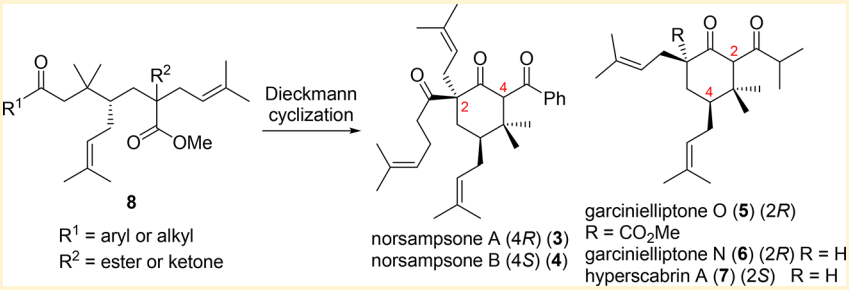
Supporting Information



ABSTRACT: The asymmetric total synthesis of five decarbonyl polycyclic polyprenylated acylphloroglucinols norsampsnes A (**3**) and B (**4**), garcinielliptones O (**5**) and N (**6**), and hyperscabrin A (**7**) is described. The synthesis to construct the core substituted cyclohexanone ring of these natural products was achieved by a key Dieckmann condensation. The chirality of the molecules was introduced by the stereoselective alkylation with Evans' oxazolidinones. The synthesis could be run on grams scale, and the Dieckmann condensation was investigated through the DFT calculations to help improve the yield of garcinielliptone O (**5**). Determination of the absolute configuration of garcinielliptones O (**5**) and N (**6**) was also achieved.

Plants of the genera *Hypericum* and *Garcinia* of the Clusiaceae family have long been used in traditional medicine for the treatment of various diseases, including bacterial and viral infections.[1] The biological activity of these plants is generally attributed to the presence of complex polycyclic polyprenylated acylphloroglucinols (PPAPs), which have recently become popular synthetic targets in pharmaceutical chemistry.[2] The first total syntheses of this kind of natural product, garsubellin A, was conducted by Shibasaki[3] and Danishefsky[4] in 2005. A number of other synthetic efforts toward the PPAPs have been made especially from the groups of Shair,[5] Barriault,[6] Maimone,[7] Plietker,[8] and Porco.[9] Acompanying the isolation of bioactive complex PPAPs, decarbonyl PPAPs such as norsampsones A (**3**) and B (**4**),[10] garcinielliptones N (**5**) and O (**6**),[11] and hyperscabrin A (**7**)[12] sometimes also were found to occur (Scheme 1). The decarbonyl PPAPs are secondary metabolites of complex PPAPs and proposed to be generated by the loss of the C-2/C-3 carbonyl group in a biogenetic pathway through one or two retro-Claisen condensation reactions followed by decarboxylation.[10,13] For example, norsampsones A (**3**) and B (**4**) have been postulated as degradation products from the bioactive nemorosone (**1**), while hyperscabrin A (**7**) and garcinielliptones N (**6**) and O (**5**) originate from the bioactive hyperforin (**2**) or its analogues. On the other hand, decarbonyl PPAPs or related compounds also may be used as building blocks for the synthesis of PPAPs and their derivatives (Scheme 1).[8a] Although great interest is evident in the synthesis of PPAPs, only one achiral synthetic study of the decarbonyl PPAPs toward the norsampsones and their analogues has been reported.[14] On the other hand, for many of these natural products, their absolute configuration is still not determined or has been achieved by the analysis of circular dichroism spectra. It is very desirable to develop asymmetric synthesis procedures to confirm compounds with their absolute configurations.

RESULTS AND DISCUSSION

Retrosynthetic Analysis. Dieckmann condensation and variants thereof are powerful reactions to produce cyclic β-keto esters.[15] The decarbonyl PPAPs that feature at least a dicarbonyl moiety are shown in Scheme 1, which revealed that a Dieckmann condensation with ketone or ester as the nucleophile could be applied. Based on this strategy, a disconnection was performed on either side of the cyclic ketone to afford two possible linear substrates for the synthesis (Scheme 2). Path A provides a conventional diester precursor for the synthesis of garcinielliptone O (**5**). However, a model reaction indicated that a competitive aldol reaction is a challenge for Dieckmann cyclization.[16] In path B, the resulting linear precursor is easy to make, but a ketone has to be used as the nucleophile. As a general asymmetric retrosynthesis procedure for compounds **3**−**7** illustrated in Scheme 2, the decarbonyl PPAPs may be disconnected to the crucial linear intermediates **8** via Dieckmann cyclization. Preparation of **8** is then carried out through an alkylation between **9** and **10**. The

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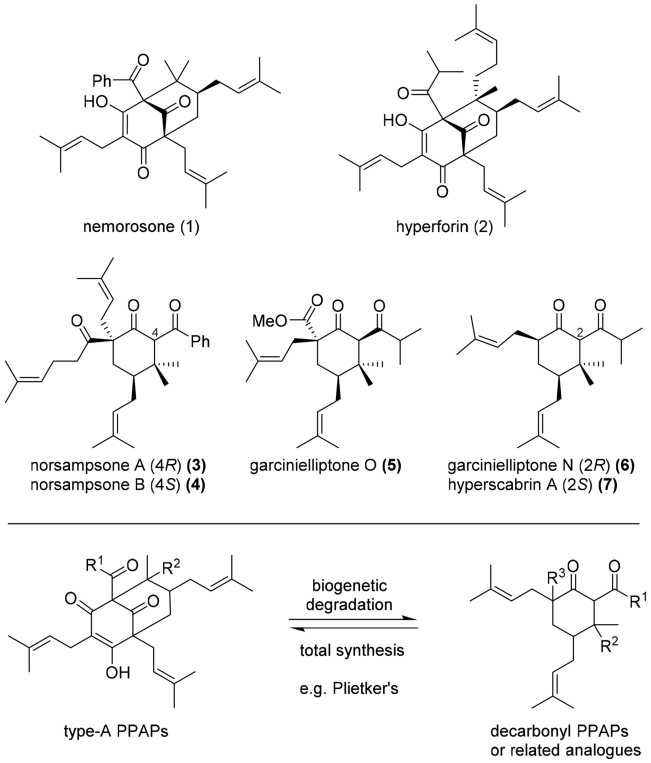
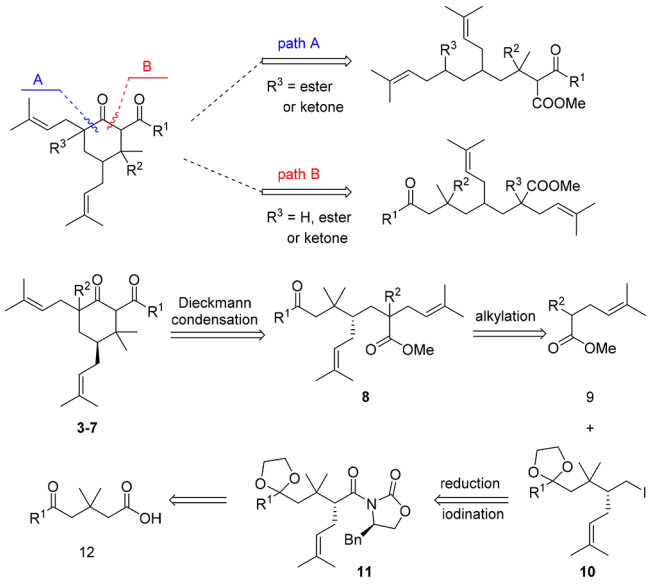
Scheme 1. Examples of Bioactive Complex PPAPs, Decarbonyl PPAPs, and Their Mutual Transformation



Scheme 2. Strategies for the Asymmetric Synthesis of Decarbonyl PPAPs



enantio-enriched compound **10** would be easily synthesized from compound **12** via a four-step reaction with the use of a chiral auxiliary.

Total Synthesis of Norsampsones A (3) and B (4). The total synthesis of norsampsones A (**3**) and B (**4**) was first accomplished. Both of these two molecules feature three chiral centers and one as a quaternary carbon center. The ketone carbonyl group at the C-2 position made a Dieckmann cyclization quite challenging, as a competitive aldol reaction may occur during cyclization. The synthesis was started with **12a** and (*R*)-4-benzyl-2-oxazolidinone to give the enantio-enriched compound **13** in 70% yield. Protection of the ketone carbonyl group with ethylene glycol catalyzed by *p*-toluenesulfonic acid (PTSA) followed by alkylation afforded **11a** diastereoselectively in very high yield. Then, with a sequence of reduction and iodination, the chiral **10a** could be prepared on a gram scale. Coupling of **10a** with **9a** was performed using NaH as the base and with quenching by dilute HCl to afford the linear precursor **8a** in a 60% yield in nearly a 1:1 ratio (Scheme 3). The vital Dieckmann cyclization was then tested with (*S*,*S*)-**8a** in the presence of a variety of bases. The reaction with commonly used MeONa did not proceed. With NaH or lithium bis(trimethylsilyl)amide (LHMDS) as the base, the yield was around 40% and the diastereoselectivity was about 3:1. Improved results were obtained in the presence of *t*-BuOK that gave two diastereomers (6:1 dr) smoothly in a 73% yield. The isomers could be separated by column chromatography and determined to be norsampsones A (**3**) and B (**4**) by comparing their ^{1}H NMR and ^{13}C NMR spectra with reported data.[10] The other precursor, (*R*,*S*)-**8a**, was also processed under the optimized conditions to give two diastereomers (10:1 dr), which, however, could not be separated by column chromatography (Scheme 4).

Total Synthesis of Garcinielliptones N (6) and O (5) and Hyperscabrin A (7). Having completed the total synthesis of norsampsones A (**3**) and B (**4**), the synthesis to the second type of decarbonyl PPAPs illustrated by garcinielliptone O (**5**) was evaluated, which consists of three chiral centers with an ester at the C-6 quaternary carbon center. With a modified synthetic pathway to **8a** employed,[17] the key precursor **8b** was obtained in six steps in a total 13% yield (Scheme 5). The Dieckmann condensation was first carried out with *t*-BuOK as the base, in which two separable diastereoisomers were detected, with the product **21** isolated as the major one along with another isomer, **22**, in a ratio of 1.3:1 (Scheme 6 and Table 1, entry 1). Determination of their structures by NMR analysis revealed compounds **21** and **22** to be epimers of each other, and that was also verified by tautomerization reactions in the presence of *t*-BuOK. However, none of their NMR spectroscopic parameters were identical to those of garcinielliptone O (**5**).

In order to improve the yield of product **5**, a preliminary mechanistic study was performed. In the presence of *t*-BuOK in tetrahydrofuran (THF) at room temperature, compounds **21** and **22** are presumably formed from nonselective protonation from either face of the ketoester enolate product via TS **B**, as TS **C** is highly unfavorable. Density functional theory (DFT) quantum mechanics calculations suggested that the potassium ketoester enolate leading to compounds **21** and **22** is significantly more stable by 2 kcal/mol than the corresponding one that generated compound **5**. The Dieckmann condensation under these conditions is reversible, as the in situ-generated MeOK is likely to attack the ketone carbonyl group to open the cyclohexanone core structure, with product ratios under thermodynamic control. It was reasoned that the difference in activation energy for the formation of the tetrahedral intermediates **A** and **B** should be small. When cyclization is conducted at a temperature higher than the boiling point of the methanol byproduct, the reaction should be rendered irreversible. Based on the above calculations, the reaction was then performed in toluene at reflux with NaH as the base. Although 20% yields of garcinielliptone N (**6**) and hyperscabrin A (**7**) resulted due to decarboxylation, the yield

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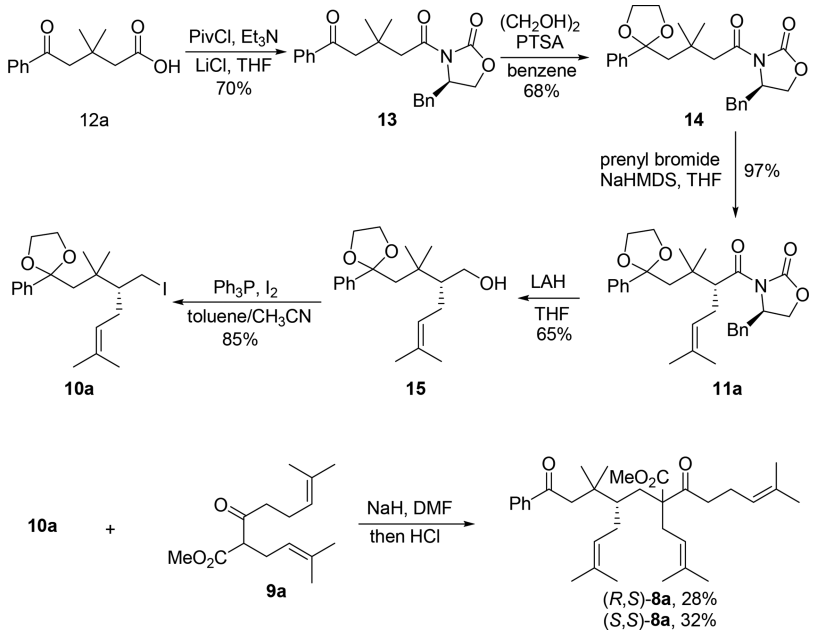
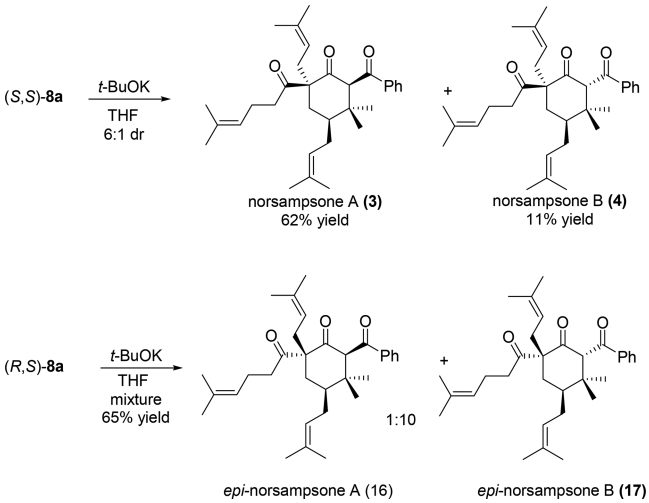
Scheme 3. Synthesis of the Key Linear Precursor 8a



Scheme 4. Synthesis of Norsampsones A (3) and B (4) and Analogues via Dieckmann Condensation



of garcinielliptone O (**5**) was improved to 17% (Table 1, entry 2). Lowering the temperature to 70 °C in order to reduce the decarboxylation led to an incomplete reaction (Table 1, entry 3). Replacement of NaH with LHMDS further increased the yield of garcinielliptone O (**5**) to 21% without decarboxylation products being observed (Table 1, entry 4). The product ratio of 1:2.5 for compound **5** vs **21** and **22** is also consistent with the small difference (<0.2 kcal/mol) for the calculated transition state energy of the two major competing pathways.

The mixture of compounds **21** and **22** was then treated with NaH to give garcinielliptone N (**6**) and hyperscabrin A (**7**) in 43% and 29% yields, respectively (Scheme 7). Under a high temperature with LiCl/DMSO, the compounds decomposed. The NMR and MS data of garcinielliptones N (**6**) and O (**5**) and hyperscabrin A (**7**) were in good agreement with data reported.[11,12]

Determination of the Absolute Configuration and Inhibitory Effect on Cancer Cells. As the absolute configuration of naturally occurring garcinielliptones N (**6**) and O (**5**) was not determined previously, comparison of the specific rotations of the synthetic samples with the reported data[11] revealed the absolute configuration of garcinielliptone N ($[\alpha]^{27}_D$ = −37.6 (*c* 0.40, $CHCl_3$)] [lit. [α] = −42 (*c* 0.38, $CHCl_3$)) and garcinielliptone O ($[\alpha]^{27}_D$ = −258 (*c* 0.35, $CHCl_3$)] [lit. [α] = −277 (*c* 0.16, $CHCl_3$)) to be 2*R*,4*S*,6*R* and 2*R*,4*S*,6*S*, respectively. Furthermore, the absolute configurations of norsampsones A (**3**) and B (**4**) and hyperscabrin A (**7**) were also confirmed by total synthesis in addition to the previous circular dichroism analysis performed.

In view of the biogenetic proposal for the generation of dicarbonyl PPAPs, which are hypothesized as being degraded from complex PPAPs,[10,13] it is reasonable to speculate that all of the diastereoisomers currently prepared via the Dieckmann cyclization should be naturally occurring products, although compounds **16**, **17**, **21**, and **22** have not been reported in the literature so far. The cytotoxicities of compounds norsampsones A (**3**) and B (**4**), garcinielliptones N (**6**) and O (**5**), hyperscabrin A (**7**), **21**, and **22** were evaluated against several cancer cell lines (A549, SNU-1, 786-O, and KMS-11); however, all were deemed inactive (IC_{50} > 10 μM).

EXPERIMENTAL SECTION

General Experiment Procedures. All glassware was dried with a hot air gun, and all reactions were carried out under an atmosphere of dry N_2 unless otherwise stated. All reagents and dry solvents were used as received from the supplier. Melting points were performed using a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were recorded as dilute solutions in the indicated solvent in a 25 mm glass cell using a JASCO P-1010 polarimeter at λ = 589 nm. IR spectra were carried out on either a neat oil or a solid using a PerkinElmer Spectrum 983G instrument. Wavelengths (ν) are reported in cm^{-1}. ^1H and ^{13}C NMR were performed on Bruker AV-400 or Agilent 400 NMR spectrometers in $CDCl_3$ with 0.03% $(CH_3)_4Si$. Chemical shifts (δ) are quoted in ppm; coupling constants (*J*) in Hz. All spectra are referenced to the $CDCl_3$ peaks at 7.26 ppm or $(CH_3)_4Si$ peaks at 0.00 ppm for proton and 77.0 ppm for carbon unless otherwise stated. The following abbreviations apply: (br) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet, and (m)

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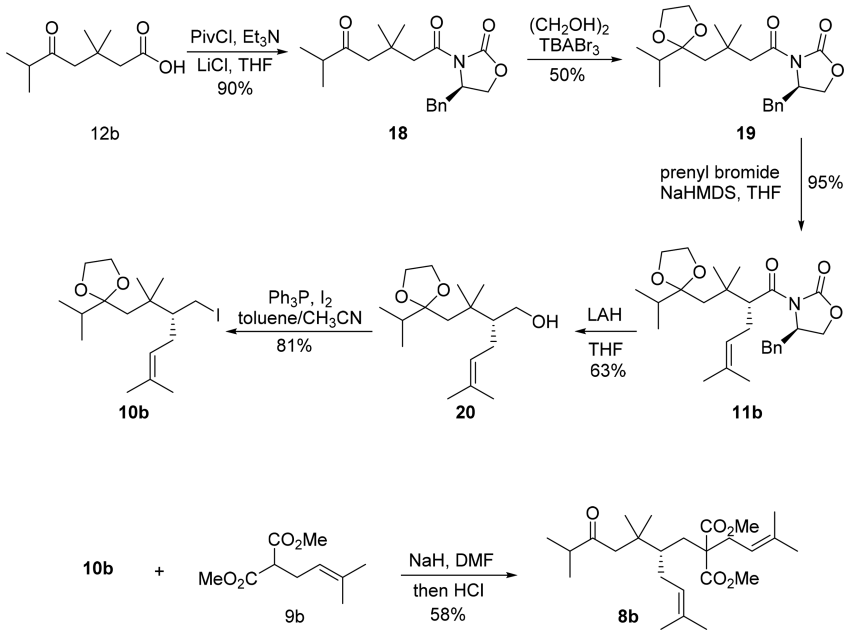
Scheme 5. Synthesis of the Key Linear Precursor 8b



Scheme 6. Synthesis of Garcinielliptones O (5) and Analogues

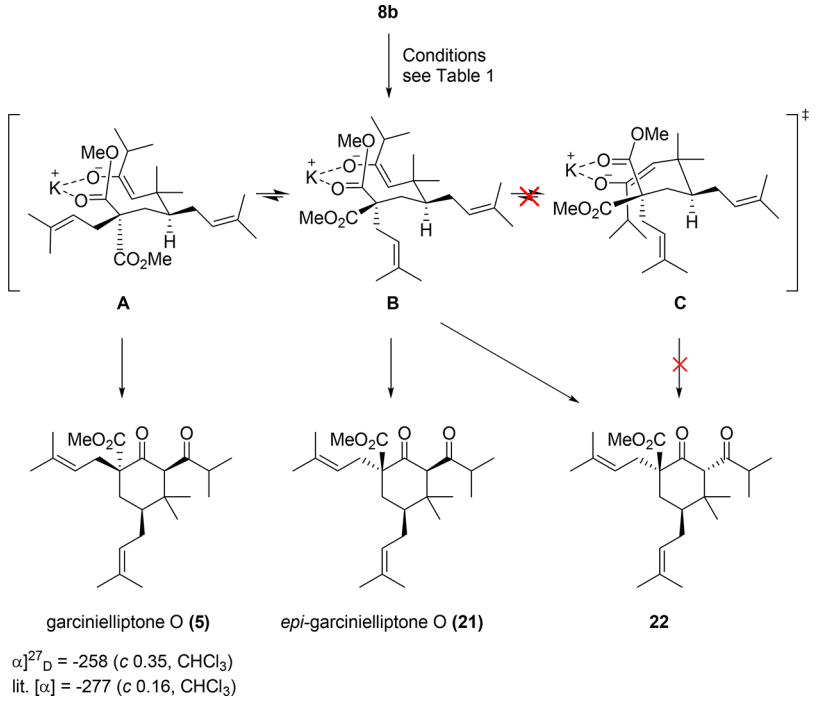


Table 1. Challenges in the Synthesis of Garcinielliptone O (5)[a]

entry	conditions	yield of **5**	yield of **21**	yield of **22**
1	*t*-BuOK, THF, rt	<5%	43%	32%
2[b]	NaH, toluene, reflux	17%	24%	18%
3[c]	NaH, toluene, 70 °C	8%	31%	17%
4	LHMDS, THF, reflux	21%	37%	18%

[a]The reaction was performed at 0.3 mmol scale, and usually <5% of additional isomers could be detected during the reaction. [b]About 20% yields of garcinielliptone N (**6**) and hyperscabrin A (**7**) were isolated. [c]36% yield of starting material recovered.

multiplet. Mass spectrometry was performed on a SYNAPT G2-Si HDMS (Waters Corp., Manchester, UK). Flash column chromatography was performed using silica gel (300−400 mesh).

Procedures for the Synthesis of 8a. To a solution of 3,3-dimethyl-5-oxo-5-phenylpentanoic acid **12a**[18] (3 g, 13.6 mmol) in THF (56 mL) was added triethylamine (3.6 mL, 27 mmol) and pivaloyl chloride (PivCl) (2 mL, 16.4 mmol) at 0 °C. After stirring for 1 h at 0 °C, LiCl (0.7 g, 6.4 mmol) and (*R*)-4-benzyl-2-oxazolidinone (2.9 g, 16.4 mmol) were added, and the resulting mixture was warmed to rt. After reaction for 20 h at rt, the mixture was concentrated in vacuo, and the residue was dissolved in EtOAc, washed with 1 M HCl, saturated $NaHCO_3$, and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by silica gel with 10% EtOAc/hexanes to yield the title compound, **13**

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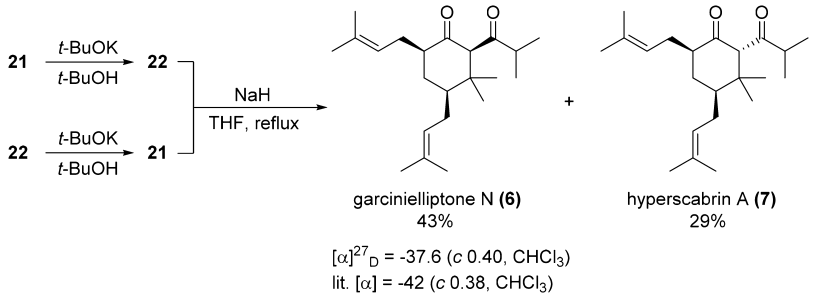
Scheme 7. Synthesis of Garcinielliptone N (6) and Hyperscabrin A (7)



(3.5 g, 70%), as a white powder: $[\alpha]^{27}_{D}$ −33.3 (*c* 0.65, $CHCl_3$); FT-IR ν_{max} 2960, 1783, 1684, 1202, 1137 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, d, *J* = 7.4 Hz), 7.52 (1H, t, *J* = 7.3 Hz), 7.44 (2H, t, *J* = 7.6 Hz), 7.36−7.16 (5H, m), 4.72−4.58 (1H, m), 4.21−4.10 (2H, m), 3.29−3.18 (5H, m), 2.73 (1H, dd, *J* = 12.9, 9.3 Hz), 1.24 (3H, s), 1.22 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0, 171.9, 153.4, 138.2, 135.3, 132.7, 129.3, 128.8, 128.4, 128.0, 127.2, 765.9, 55.1, 46.9, 43.9, 37.9, 33.3, 28.7, 28.6; HRESIMS *m*/*z* 380.1876 $[M + H]^+$ (calcd for $C_{23}H_{26}NO_4$, 380.1861).

To a stirred solution of (*R*)-**13** (3.5 g, 9.6 mmol) and ethylene glycol (2.2 mL, 38.4 mmol) in benzene (20 mL) was added *p*-toluenesulfonic acid monohydrate (83 mg, 0.48 mmol), and the mixture was heated to reflux for 36 h using Dean−Stark conditions. The solvent was removed in vacuo, and purification conducted by flash column chromatography with 10% EtOAc/hexanes to yield compound **14** as a colorless oil (2.8 g, 68% yield): $[\alpha]^{27}_{D}$ −31.8 (*c* 0.3, $CHCl_3$); FT-IR ν_{max} 2955, 1779, 1704, 1198 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* = 7.0 Hz), 7.38−7.20 (8H, m), 4.73−4.59 (1H, m), 4.15−4.09 (2H, m), 4.02−3.91 (2H, m), 3.71−3.60 (2H, m), 3.38 (1H, dd, *J* = 13.3, 3.1 Hz), 3.12 (1H, d, *J* = 17.6 Hz), 2.93 (1H, d, *J* = 17.6 Hz), 2.72 (1H, dd, *J* = 13.2, 10.1 Hz), 2.25 (1H, d, *J* = 15.2 Hz), 2.15 (1H, d, *J* = 15.2 Hz), 1.13 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 153.4, 143.7, 135.6, 129.4, 128.8, 127.9, 127.6, 127.1, 125.6, 110.9, 65.7, 63.6, 63.3, 55.1, 47.6, 44.1, 37.9, 33.1, 30.1, 30.1; HRESIMS *m*/*z* 424.2137 $[M + H]^+$ (calcd for $C_{25}H_{30}NO_5$, 424.2124).

To a solution of **14** (2.0 g, 4.7 mmol) in THF (25 mL) was added sodium bis(trimethylsilyl)amide (NaHMDS) (2.0 M in THF, 3.6 mL, 7.1 mmol) dropwise over 5 min at −78 °C. After the mixture was stirred at −78 °C for 1 h, prenyl bromide (1.1 mL, 9.4 mmol) was added dropwise over 5 min at −78 °C, and the mixture was stirred at −78 °C for 7 h. A saturated NH_4Cl aqueous solution was added to the reaction mixture, and the product was extracted with EtOAc. The combined extracts were dried over Na_2SO_4. The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent hexane/EtOAc, 10:1) to give the desired product **11a** (2.2 g, 97% yield) as a colorless oil: $[\alpha]^{28}_{D}$ −37.9 (*c* 1.40, $CHCl_3$); FT-IR ν_{max} 2963, 1781, 1695, 1381, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 6.9 Hz), 7.40−7.15 (8H, m), 5.20−5.15 (1H, m), 4.76−4.60 (1H, m), 4.47 (1H, dd, *J* = 11.3, 3.5 Hz), 4.16−3.98 (4H, m), 3.73−3.59 (2H, m), 3.19 (1H, dd, *J* = 13.3, 3.1 Hz), 2.63−2.47 (2H, m), 2.33 (1H, d, *J* = 12.9 Hz), 2.08 (1H, d, *J* = 15.4 Hz), 2.01 (1H, d, *J* = 15.4 Hz), 1.67 (3H, s), 1.63 (3H, s), 1.11 (3H, s), 1.04 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 153.2, 144.1, 135.7, 133.1, 129.3, 128.8, 128.0, 127.6, 127.1, 125.6, 122.0, 110.7, 65.1, 63.5, 63.5, 55.6, 48.9, 47.8, 37.6, 36.9, 27.6, 26.7, 25.8, 25.7, 17.7; HRESIMS *m*/*z* 492.2749 $[M + H]^+$ (calcd for $C_{30}H_{38}NO_5$, 492.2750).

$LiAlH_4$ (LAH) powder (190 mg, 5 mmol) was dispersed in dry THF (5 mL) portionwise at 0 °C carefully. At this temperature, a solution of **11a** (1.0 g, 2 mmol) in THF (5 mL) was added dropwise into the mixture very slowly. After addition, the mixture was warmed to rt and stirred for 0.5 h. The reaction was diluted with ether and quenched by the addition of 0.19 mL of H_2O, 0.19 mL of 15% aqueous NaOH, and 0.57 mL of H_2O at 0 °C very slowly and carefully. The mixture was then warmed to rt and stirred for 30 min until a white solid precipitated. Then $MgSO_4$ powder was added to dry the mixture for 15 min, and the mixture was filtered through Celite. The filtrate was concentrated to run the column with 10% EtOAc/hexane on silica gel to afford the product **15** as an oil (413 mg, 65% yield): $[\alpha]^{25}_{D}$ −28.8 (*c* 0.45, $CHCl_3$); FT-IR ν_{max} 3460, 2964, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 8.4 Hz), 7.37−7.23 (3H, m), 5.22−5.18 (1H, m), 4.06−3.94 (2H, m), 3.77−3.64 (3H, m), 3.58 (1H, dd, *J* = 11.2, 5.1 Hz), 2.21−2.02 (3H, m), 2.00−1.83 (2H, m), 1.71 (3H, s), 1.71−1.64 (1H, m), 1.64 (3H, s), 0.94 (3H, s), 0.93 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 132.3, 128.1, 127.7, 125.7, 124.7, 111.2, 64.1, 63.6, 63.4, 49.7, 48.9, 36.0, 30.9, 27.2, 26.8, 26.4, 25.9, 17.8; HRESIMS *m*/*z* 319.2272 $[M + H]^+$ (calcd for $C_{20}H_{31}O_3$, 319.2273).

A solution of **15** (1.1 g, 3.5 mmol) in toluene (20 mL) was stirred vigorously. Then PPh_3 (5.3 mmol, 1.4 g), imidazole (0.72 g, 10.6 mmol), and I_2 (1.3 g, 4.9 mmol) were added into the solution sequentially at rt. The mixture was stirred vigorously for 5 min at rt, and 1.5 mL of CH_3CN was added dropwise to convert the sticky brown solid on the bottom to a white precipitate. The reaction was monitored by TLC and quenched by aqueous $Na_2S_2O_3$. Water and EtOAc were added, and the mixture was extracted with hexane. The extracts were dried over Na_2SO_4 and concentrated to a small volume, from which PPh_3=O precipitated. Hexanes were added, and the mixture was filtered to remove the PPh_3=O. The filtrate was concentrated and purified by column chromatography with 1% EtOAc/hexane on silica gel (treated with 5% Et_3N/hexanes) to give **10a** as an oil (1.3 g, 85% yield): $[\alpha]^{27}_{D}$ −45.3 (*c* 0.55, $CHCl_3$); FT-IR ν_{max} 2963, 2888, 1390, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* = 6.9 Hz), 7.40−7.15 (3H, m), 5.09 (1H, t, *J* = 7.0 Hz), 4.00 (2H, t, *J* = 4.3 Hz), 3.76−3.63 (2H, m), 3.50 (1H, dd, *J* = 9.8, 3.1 Hz), 3.12 (1H, dd, *J* = 9.8, 7.2 Hz), 2.33−2.15 (1H, m), 2.12−2.03 (1H, m), 2.01 (1H, d, *J* = 15.3 Hz), 1.94 (1H, d, *J* = 15.3 Hz), 1.86−1.78 (1H, m), 1.69 (3H, s), 1.66 (3H, s), 0.96 (3H, s), 0.95 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 131.8, 128.1, 127.7, 125.7, 123.8, 110.8, 63.7, 63.5, 49.0, 48.4, 37.8, 29.1, 26.6, 26.0, 25.9, 18.2, 10.8; HRESIMS *m*/*z* 429.1298 $[M + H]^+$ (calcd for $C_{20}H_{30}IO_2$, 429.1291).

At 0 °C, to a solution of **9a** (883 mg, 3.5 mmol) in DMF (10 mL) was added NaH (140 mg, 60% in mineral oil, 3.5 mmol) slowly, and the mixture was warmed to rt and stirred for 30 min. Next, the mixture was cooled to 0 °C again and **10a** (750 mg, 1.75 mmol) was added dropwise. The mixture was stirred at rt for 48 h, quenched by 5% dilute HCl solution (5 mL), and stirred for an additional 2 h. The mixture was then extracted by hexanes, with the organic layer dried over Na_2SO_4 and the solvent removed under a vacuum. The residue was purification by flash chromatography with 5% EtOAc/hexane on silica gel to give (*R*,*S*)-**8a** (248 mg, 28% yield) and (*S*,*S*)-**8a** (284 mg, 32% yield) as oils.

*(S,S)-**8a**:* $[\alpha]^{27}_{D}$ −78.3 (*c* 1.00, $CHCl_3$); FT-IR ν_{max} 2966, 1743, 1712, 1693, 1448, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (2H, d, *J* = 7.3 Hz), 7.51 (1H, t, *J* = 7.3 Hz), 7.42 (2H, t, *J* = 7.6 Hz), 5.05−5.00 (2H, m), 4.79 (1H, t, *J* = 6.5 Hz), 3.65 (3H, s), 3.02 (1H, d, *J* = 15.9 Hz), 2.72 (1H, d, *J* = 15.9 Hz), 2.67 (2H, d, *J* = 6.5 Hz), 2.46−2.32 (2H, q, *J* = 6.9 Hz), 2.22 (2H, q, *J* = 7.2 Hz), 2.12−1.94 (2H, m), 1.89 (1H, dd, *J* = 14.6, 10.4 Hz), 1.83−1.69 (2H, m), 1.65 (3H, s), 1.62 (3H, s), 1.60 (3H, s), 1.59 (3H, s), 1.50 (3H, s), 1.46

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(3H, s), 1.01 (3H, s), 0.96 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1, 199.8, 173.6, 138.5, 135.3, 132.5, 129.8, 128.4, 127.9, 125.3, 122.85, 117.59, 62.18, 52.02, 46.67, 41.08, 39.36, 37.62, 32.31, 30.14, 29.13, 25.87, 25.85, 25.67, 25.6, 25.0, 22.6, 18.2, 17.9, 17.6; HRESIMS m/z 509.3630 $[M + H]^+$ (calcd for $C_{33}H_{49}O_4$, 509.3631).

*(R,S)-**8a**:* $[\alpha]^{27}_D$ +46.5 (c 1.50, $CHCl_3$); FT-IR ν_{max} 2966, 1742, 1712, 1694, 1448, 1209 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (2H, d, J = 7.2 Hz), 7.57−7.47 (1H, m), 7.47−7.37 (2H, m), 5.05−5.00 (2H, m), 4.85 (1H, t, J = 6.2 Hz), 3.68 (3H, s), 3.01 (1H, d, J = 15.8 Hz), 2.74 (1H, d, J = 15.8 Hz), 2.68−2.59 (2H, m), 2.49−2.28 (2H, m), 2.26−2.04 (4H, m), 1.80−1.69 (2H, m), 1.65 (3H, s), 1.64 (3H, s), 1.62−1.59 (1H, m), 1.59 (6H, s), 1.50 (3H, s), 1.45 (3H, s), 1.01 (3H, s), 0.95 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.4, 199.9, 173.3, 138.6, 135.2, 132.5, 132.5, 130.0, 128.4, 127.9, 125.8, 122.8, 117.8, 63.5, 52.1, 46.6, 42.1, 39.6, 37.8, 33.2, 30.5, 30.4, 25.9, 25.7, 25.5, 25.5, 24.7, 22.5, 18.1, 17.9, 17.5; HRESIMS m/z 509.3622 $[M + H]^+$ (calcd for $C_{33}H_{49}O_4$, 509.3631).

Procedures for the Synthesis of Norsampsone A (3) and Norsampsone B (4). To a solution of (*S,S*)-**8a** (50 mg, 0.1 mmol) in THF (10 mL) at 0 °C was added *t*-BuOK (33 mg, 0.3 mmol) in one portion. The mixture turned yellow immediately. After stirring at 0 °C for 5 min, the reaction was quenched by saturated NH_4Cl solution and extracted by EtOAc three times, and the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, with the crude product purified using silica gel with 5% EtOAc/hexanes to yield the natural products norsampsones A (28 mg, 62%) and B (5 mg, 11%) as colorless oils. A similar procedure was used for the cyclization of (*R,S*)-**8a**, and a mixture of the two products **16** and **17** with total 65% yield (1:10 dr) was obtained (the two compounds could not be separated).

*Norsampsone A (**3**):* $[\alpha]^{27}_D$ +31.7 (c 0.50, $CHCl_3$); FT-IR ν_{max} 2968, 2925, 1734, 1717, 1699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (2H, d, J = 7.2 Hz), 7.51 (1H, t, J = 7.2 Hz), 7.40 (2H, t, J = 7.2 Hz), 5.05 (1H, 5, J = 7.2 Hz), 5.03 (1H, t, J = 7.2 Hz), 4.82 (1H, t, J = 6.8 Hz), 4.49 (1H, s), 2.84−2.71 (2H, m), 2.55−2.41 (2H, m), 2.32−2.20 (3H, m), 1.95 (1H, dd, J = 14.4, 12.7 Hz), 1.88−1.76 (3H, m), 1.71 (3H, s), 1.70 (3H, s), 1.63 (6H, s), 1.59 (3H, s), 1.56 (3H, s), 1.23 (3H, s), 1.10 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 197.4, 139.2, 135.4, 133.6, 133.1, 132.7, 128.8, 127.9, 123.3, 122.8, 118.7, 66.3, 64.7, 44.9, 44.0, 40.4, 34.1, 32.7, 27.6, 27.4, 26.1, 25.9, 23.0, 18.5, 18.1, 17.8, 16.9; HRESIMS m/z 477.3365 $[M + H]^+$ (calcd for $C_{32}H_{45}O_3$, 477.3369).

*Norsampsone B (**4**):* $[\alpha]^{27}_D$ −33.8 (c 0.50, $CHCl_3$); FT-IR ν_{max} 3967, 2925, 1698, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (2H, d, J = 7.4 Hz), 7.52 (1H, t, J = 7.3 Hz), 7.43 (2H, t, J = 7.3 Hz), 5.11 (1H, t, J = 6.7 Hz), 5.01 (1H, t, J = 7.2 Hz), 4.73 (1H, t, J = 6.8 Hz), 4.48 (1H, s), 2.59 (1H, dd, J = 15.0, 7.6 Hz), 2.53−2.39 (3H, m), 2.35−2.12 (5H, m), 1.91−1.74 (2H, m), 1.70 (3H, s), 1.63 (3H, s), 1.60 (3H, s), 1.58 (6H, s), 1.50 (3H, s), 1.14 (3H, s), 1.01 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.9, 207.1, 196.0, 138.6, 135.6, 133.3, 133.2, 132.9, 128.9, 128.7, 123.4, 123.1, 118.8, 67.4, 66.8, 41.5, 41.2, 39.4, 32.3, 32.2, 27.5, 26.1, 25.9, 25.9, 25.9, 24.5, 22.9, 18.2, 18.2, 17.8; HRESIMS m/z 477.3366 $[M + H]^+$ (calcd for $C_{32}H_{45}O_3$, 477.3369).

*epi-Norasmpsone B (**17**) (with the minor product epi-norasmpsone A as mixture):* FT-IR ν_{max} 2925, 1716, 1699, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, d), 7.58−7.50 (1H, m), 7.49−7.41 (2H, m), 5.20 (1H, d, J = 8.0 Hz), 4.99 (2H, dd, J = 13.9, 6.8 Hz), 4.42 (1H, s), 2.55−2.38 (3H, m), 2.39−2.27 (3H, m), 2.28−2.17 (2H, m), 1.79−1.70 (4H, m), 1.67 (3H, s), 1.66 (4H, s), 1.63 (3H, s), 1.62 (3H, s), 1.59 (4H, s), 1.13 (3H, s), 1.04 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 205.4, 197.5, 139.0, 134.9, 133.4, 133.1, 132.8, 128.6, 128.0, 122.7, 122.5, 118.4, 67.8, 66.7, 46.1, 43.9, 37.8, 35.8, 33.0, 27.4, 26.8, 25.9, 25.8, 25.7, 22.2, 18.0, 17.9, 17.7, 16.5; HRESIMS m/z 477.3365 $[M + H]^+$ (calcd for $C_{32}H_{45}O_3$, 477.3369).

Procedures for the Synthesis of 8b. *Compound **18**.* A similar procedure to that used for **13** afforded **18** (1.8 g, 90%) as a colorless oil: $[\alpha]^{27}_D$ −31.4 (c 0.45, $CHCl_3$); FT-IR ν_{max} 2968, 2873, 1778, 1711, 1693, 1359, 1102 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.17 (5H, m), 4.74−4.60 (1H, m), 4.22−4.02 (2H, m), 3.29 (1H, dd, J = 13.4, 3.2 Hz), 3.20 (1H, d, J = 16.8 Hz), 3.14 (1H, d, J = 16.8 Hz), 2.76 (1H, d, J = 13.0 Hz), 2.73 (1H, d, J = 13.0 Hz), 2.58 (1H, p, J = 6.9 Hz), 1.15 (3H, s), 1.14 (3H, s), 1.08 (3H, s), 1.06 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.5, 172.0, 153.4, 135.4, 129.4, 128.9, 127.2, 65.8, 55.1, 49.5, 43.6, 41.9, 37.9, 32.9, 28.5, 28.3, 18.08, 18.05; HRESIMS m/z 344.1856 $[M - H]^+$ (calcd for $C_{20}H_{26}NO_4$, 344.1862).

To a stirred solution of (*R*)-1-(4-benzyl-2-oxooxazolidin-3-yl)-3,3,6-trimethylheptane-1,5-dione (**18**) (13.7 g, 43 mmol) in ethylene glycol (9.6 mL, 170 mmol) were added trimethoxymethane (7.1 mL, 64.5 mmol) and tetrabutylammonium tribromide ($TBABr_3$) (1.03 g, 2.15 mmol), and the mixture was stirred at room temperature for 2 days. The reaction was quenched with water and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was evaporated to afford a crude oil, which was purified by flash chromatography on silica gel with 10% EtOAc/hexanes to give **19** (8.3 g, 50% yield) as a colorless oil: $[\alpha]^{27}_D$ −29.4 (c 1.35, $CHCl_3$); FT-IR ν_{max} 2960, 1779, 1705, 1360, 1212 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.21 (5H, m), 4.75−4.61 (1H, m), 4.18−4.07 (2H, m), 4.02−3.82 (4H, m), 3.34 (1H, dd, J = 13.3, 3.1 Hz), 3.12 (1H, d, J = 17.3 Hz), 2.93 (1H, d, J = 17.3 Hz), 2.71 (1H, dd, J = 13.3, 9.9 Hz), 1.97 (1H, d, J = 15.2 Hz), 1.89−1.78 (2H, m), 1.17 (6H, s), 0.91 (6H, d, J = 8.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 153.5, 135.6, 129.4, 128.8, 127.1, 114.8, 65.8, 63.7, 63.6, 55.1, 44.3, 38.5, 37.9, 34.9, 32.5, 30.1, 30.1, 17.4, 17.3; HRESIMS m/z 390.2280 $[M + H]^+$ (calcd for $C_{22}H_{32}NO_5$, 390.2280).

*Compound **11b**.* A similar procedure to that used for **14** afforded **11b** (0.56 g, 95% yield) as a colorless oil: $[\alpha]^{27}_D$ −69.4 (c 1.15, $CHCl_3$); FT-IR ν_{max} 3028, 2962, 1781, 1732, 1693, 1208 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.20 (5H, m), 5.24−5.12 (1H, m), 4.72−4.59 (1H, m), 4.34 (1H, dd, J = 11.4, 3.6 Hz), 4.13−4.01 (4H, m), 3.95−3.84 (2H, m), 3.20 (1H, dd, J = 13.2, 3.1 Hz), 2.61−2.48 (2H, m), 2.28 (1H, d, J = 13.9 Hz), 1.94−1.80 (1H, m), 1.75 (2H, s), 1.66 (3H, s), 1.62 (3H, s), 1.13 (3H, s), 1.10 (3H, s), 0.92 (3H, d, J = 6.1 Hz), 0.89 (3H, d, J = 6.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.4, 153.2, 135.8, 133.1, 129.4, 128.8, 127.1, 122.0, 114.3, 65.1, 63.8, 63.6, 55.6, 49.1, 38.6, 37.6, 36.1, 35.0, 27.6, 26.4, 25.8, 17.7, 17.4, 17.3; HRESIMS m/z 458.2903 $[M + H]^+$ (calcd for $C_{27}H_{40}NO_5$, 458.2906).

*Compound **20**.* A similar procedure to that used for **15** afforded **20** as an oil (358 mg, 63% yield): $[\alpha]^{27}_D$ −18.4 (c 0.70, $CHCl_3$); FT-IR ν_{max} 3428, 2969, 2882, 1469, 1024 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.21 (1H, t, J = 7.2 Hz), 4.06−3.86 (4H, m), 3.76−3.64 (1H, m), 3.64−3.51 (1H, m), 2.27−2.08 (2H, m), 1.94−1.79 (3H, m), 1.69 (3H, s), 1.65−1.61 (2H, m), 1.63 (3H, s), 1.02 (3H, s), 0.98 (3H, s), 0.91 (3H, s), 0.90 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.3, 124.8, 115.1, 64.1, 63.8, 63.7, 49.7, 39.7, 35.5, 35.2, 27.3, 26.8, 26.4, 25.9, 17.8, 17.44, 17.39; HRESIMS m/z 307.2253 $[M + Na]^+$ (calcd for $C_{17}H_{32}O_3Na$, 307.2249).

*Compound **10b**.* A similar procedure to that used for **10a** afforded **10b** as an oil (1.1 g, 81% yield): $[\alpha]^{27}_D$ −9.8 (c 1.0, $CHCl_3$); FT-IR ν_{max} 2961, 2886, 1470, 1099 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (1H, t, J = 7.4 Hz), 4.06−3.84 (4H, m), 3.49 (1H, dd, J = 9.8, 3.2 Hz), 3.13 (1H, dd, J = 9.8, 7.0 Hz), 2.33−2.21 (1H, m), 2.06 (1H, dt, J = 15.2, 7.7 Hz), 1.85 (1H, p, J = 6.5 Hz), 1.79−1.73 (1H, m), 1.69−1.67 (7H, m), 1.59 (1H, d, J = 15.4 Hz), 1.03 (3H, s), 1.01 (3H, s), 0.91 (3H, d, J = 6.9 Hz), 0.90 (3H, d, J = 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.8, 123.9, 114.6, 63.8, 49.1, 39.1, 37.1, 35.3, 29.1, 26.6, 26.0, 25.9, 18.2, 17.4, 17.3, 11.2; HRESIMS m/z 417.1271 $[M + Na]^+$ (calcd for $C_{17}H_{31}IO_2Na$, 417.1266).

*Compound **8b**.* A similar procedure to that used for **8a** afforded **8b** (205 mg, 58% yield) as an oil: $[\alpha]^{27}_D$ −96.8 (c 1.0, $CHCl_3$); FT-IR ν_{max} 2965, 2929, 2875, 1732, 1699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (1H, t, J = 6.5 Hz), 4.90 (1H, t, J = 6.6 Hz), 3.65 (3H, s), 3.62 (3H, s), 2.60 (2H, d, J = 6.8 Hz), 2.52−2.37 (2H, m), 2.26 (1H, d, J = 16.1 Hz), 2.12−1.95 (2H, m), 1.79−1.73 (2H, m), 1.63 (3H, s), 1.60 (3H, s), 1.56 (4H, s), 1.52 (3H, s), 1.00 (3H, d, J = 3.9 Hz), 0.99 (3H, d, J = 3.6 Hz), 0.92 (3H, s), 0.88 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.4, 172.4, 172.3, 135.3, 129.6, 125.4, 117.8,

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57.4, 52.2, 52.1, 48.9, 42.1, 41.9, 37.4, 33.4, 31.2, 29.5, 25.9, 25.6, 25.0, 24.4, 18.2, 18.0, 17.9; HRESIMS m/z 423.3109 $[M + H]^+$ (calcd for $C_{25}H_{43}O_5$, 423.3110).

Procedures for the Synthesis of Garcinielliptone O (5), Garcinielliptone N (6), and Hyperscabrin A (7). To a solution of **8b** (130 mg, 0.3 mmol) in THF (18 mL) at rt was added LHMDS (0.6 mL, 0.6 mmol, 1.0 mol/L in THF) dropwise. The mixture was then heated to reflux for 1 h. The reaction was cooled and quenched with saturated NH_4Cl solution and extracted by EtOAc three times, and the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by passage over silica gel with 5% EtOAc/hexanes to yield garcinielliptone O (**5**) (24 mg, 21% yield) and compounds **21** (43 mg, 37% yield) and **22** (21 mg, 18% yield) as colorless oils.

Garcinielliptone O (5): $[\alpha]^{27}_D$ −258 (*c* 0.35, $CHCl_3$); FT-IR ν_{max} 2968, 2928, 2874, 1730, 1688, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.13 (1H, t, J = 7.3 Hz), 5.04 (1H, t, J = 7.5 Hz), 3.75 (3H, s), 3.71 (1H, s), 2.53−2.43 (3H, m), 2.28 (1H, dd, J = 14.6, 7.6 Hz), 2.18 (1H, dd, J = 14.2, 6.2 Hz), 1.73 (3H, s), 1.67 (1H, m), 1.67 (3H, s), 1.59 (3H, s), 1.57 (1H, m), 1.56 (3H, s), 1.28 (1H, dd, J = 14.2, 12.4 Hz), 1.06 (3H, d, J = 6.7 Hz), 1.02 (3H, s), 1.00 (3H, d, J = 6.7 Hz), 0.99 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 203.9, 172.2, 135.3, 132.9, 122.8, 118.1, 69.4, 61.4, 52.4, 52.4, 45.7, 43.4, 42.5, 36.8, 33.2, 27.4, 26.5, 25.9, 25.8, 18.1, 17.9, 17.8, 17.1, 15.6; HRESIMS m/z 391.2850 $[M + H]^+$ (calcd for $C_{24}H_{39}O_4$, 391.2848).

Compound 21: $[\alpha]^{27}_D$ +39.8 (*c* 0.8, $CHCl_3$); FT-IR ν_{max} 2964, 2926, 2873, 1747, 1731, 1688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.14−4.99 (2H, m), 3.74 (3H, s), 3.68 (1H, s), 2.78−2.51 (2H, m), 2.46−2.30 (1H, m), 2.29−2.18 (1H, m), 2.15−2.04 (1H, m), 1.95 (1H, dd, J = 14.4, 3.8 Hz), 1.80−1.61 (11H, m), 1.60 (3H, s), 1.14 (3H, s), 1.06 (3H, s), 1.03 (3H, d, J = 6.7 Hz), 1.00 (3H, d, J = 7.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.5, 207.0, 172.2, 135.4, 133.2, 122.7, 118.9, 67.3, 62.0, 52.4, 44.5, 42.9, 42.8, 34.6, 32.6, 27.2, 26.6, 25.9, 25.8, 18.2, 18.1, 17.9, 17.0, 15.9; HRESIMS m/z 391.2844 $[M + H]^+$ (calcd for $C_{24}H_{39}O_4$, 391.2848).

Compound 22. $[\alpha]^{27}_D$ −47.8 (*c* 0.50, $CHCl_3$); FT-IR ν_{max} 2964, 2926, 1729, 1688, 1461 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.14 (1H, t, J = 7.0 Hz), 5.02 (1H, t, J = 7.2 Hz), 3.86 (1H, s), 3.73 (3H, s), 2.79−2.60 (1H, m), 2.50 (1H, dd, J = 14.3, 8.2 Hz), 2.39−2.23 (2H, m), 2.22−2.09 (1H, m), 2.04−1.91 (2H, m), 1.72 (4H, s), 1.67 (3H, s), 1.62 (3H, s), 1.61 (3H, s), 1.08 (3H, s), 1.06 (3H, d, J = 7.1 Hz), 1.04 (3H, d, J = 6.7 Hz), 0.98 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.0, 205.1, 173.3, 135.7, 132.8, 123.0, 118.8, 69.4, 60.8, 52.4, 42.1, 41.2, 40.7, 33.1, 32.8, 26.9, 25.9, 25.9, 25.1, 24.2, 18.4, 18.1, 17.9, 17.1; HRESIMS m/z 391.2845 $[M + H]^+$ (calcd for $C_{24}H_{39}O_4$, 391.2848).

To a mixture of **21** and **22** (50 mg, 0.13 mmol) in THF (2.0 mL) at rt was added NaH (26 mg, 0.64 mmol, 60% dispersion in mineral oil) in one portion. The mixture was then heated to reflux for 6 h. The reaction was cooled, quenched with saturated NH_4Cl solution, and extracted by EtOAc three times, with the organic layer dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by silica gel with 5% EtOAc/hexanes to yield garcinielliptone N (**6**) (18 mg, 43% yield) and hyperscabrin A (**7**) (12 mg, 29% yield) as a colorless oil.

Garcinielliptone N (6): $[\alpha]^{27}_D$ −37.6 (*c* 0.40, $CHCl_3$); FT-IR ν_{max} 2965, 2926, 1728, 1700, 1456 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.10 (1H, t, J = 8.0 Hz), 5.05 (1H, t, J = 8.0 Hz), 3.60 (1H, s), 2.44−2.27 (3H, m), 2.18 (1H, dd, J = 13.8, 5.8 Hz), 2.09 (1H, dd, J = 6.4, 3.6 Hz), 2.00−1.89 (1H, m), 1.70 (3H, s), 1.67 (1H, m), 1.66 (3H, s), 1.57 (6H, s), 1.54 (1H, m), 1.16 (1H, d, J = 6.4 Hz), 1.03 (3H, s), 1.03 (3H, d, J = 6.4 Hz), 1.00 (3H, s), 0.99 (3H, d, J = 6.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.8, 208.7, 133.1, 132.8, 123.2, 121.4, 70.6, 51.0, 48.2, 43.4, 42.9, 34.8, 27.5, 27.4, 26.6, 25.8, 25.7, 18.0, 17.8, 17.2, 15.8; HRESIMS m/z 333.2792 $[M + H]^+$ (calcd for $C_{22}H_{37}O_2$, 333.2794).

Hyperscabrin A (7): $[\alpha]^{27}_D$ −67.8 (*c* 0.50, $CHCl_3$); FT-IR ν_{max} 2968, 2928, 2874, 1695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.09 (1H, t, J = 7.2 Hz), 4.97 (1H, t, J = 7.3 Hz), 3.52 (1H, s), 2.69−2.56 (2H, m), 2.35 (1H, tt, J = 11.5, 3.6 Hz), 2.25 (1H, dt, J = 15.0, 5.5 Hz), 2.06−2.00 (2H, m), 1.85 (1H, dt, J = 14.8, 8.3 Hz), 1.65 (3H, s), 1.60 (3H, s), 1.57−1.53 (1H, m), 1.51 (6H, s), 0.99 (1H, m), 0.98 (3H, d, J = 6.8 Hz), 0.96 (3H, d, J = 6.5 Hz), 0.93 (3H, s), 0.74 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.4, 208.0, 132.9, 132.4, 123.6, 121.8, 47.5, 43.9, 42.9, 40.0, 34.4, 28.0, 27.5, 26.0, 25.8, 25.77, 21.9, 17.9, 17.8, 17.3; HRESIMS m/z 333.2799 $[M + H]^+$ (calcd for $C_{22}H_{37}O_2$, 333.2794).

Cytotoxicity Testing. Cytotoxic activities against the human-derived cell lines A 549 (lung carcinoma), SNU-1 (gastric carcinoma), 786-O (renal cell adenocarcinoma), and KMS-11 (multiple myeloma) were determined as previously reported.[19] Staurosporine was included as a positive control.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jnatprod.8b00763.

Data comparison of the synthetic and natural products, computational details, and ^1H and ^{13}C NMR spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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