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Structures of New Alkaloids from Rain Forest Trees *Galbulimima belgraveana* and *Galbulimima baccata* in Papua New Guinea, Indonesia, and Northern Australia

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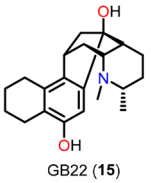
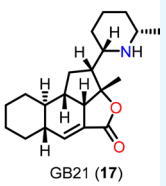
Supporting Information

ABSTRACT: Following on our 60-year research on the chemical constituents of the rain forest trees *Galbulimima belgraveana* and *Galbulimima baccata*, we report the isolation of seven new alkaloids: GB14 (**14**), GB22 (**15**), GB25 (**16**), GB21 (**17**), GB23 (**18**), GB24 (**19**), and GB26 (**20**). Their structures were elucidated by a combination of spectroscopic analyses and single-crystal X-ray crystallography, as well as structure degradation and interconversion. The newly isolated alkaloids are precursors or derivatives of the known family members from our early studies and could be intermediates in the biosynthesis of the *Galbulimima* alkaloids. Therefore, the present study has expanded the range of structures in this family of alkaloids and provided some missing links in the biosynthetic sequences.

Galbulimima baccata



GB22 (**15**)



GB21 (**17**)

INTRODUCTION

Galbulimima belgraveana and *Galbulimima baccata* are large aromatic evergreen trees that grow in thick mountain rainforests in Papua New Guinea, Indonesia, and Northern Australia.[1] These trees are a hallucinogenic plant and have been used by native tribes in religious ceremonies and treated as herbal medicines to induce deep sleep or relieve abdominal pains.[2] The phytochemistry of both *G. belgraveana* and *G. baccata* has been extensively studied and revealed that the bark of both species is a rich source of alkaloids, viz., *Galbulimima* alkaloids.[3] The pioneering research conducted by us led to the isolation of 28 *Galbulimima* alkaloids, 22 of which have been characterized via a combination of spectroscopic analysis, structure degradation, and interconversion, as well as semisynthesis.[4] Following the early studies, we have reported the structures assigned to five of the remaining six alkaloids and two new family members in 2009[5] and 2011,[6] leading to 29 members that have been characterized. Although significant structural diversity exists within this alkaloid family, all the members possess a trans-decalin system and a piperidine ring, and they could be classified into four distinct subgroups (representative structures of four classes are shown in Figure 1). Most of the class I alkaloids (nine members) possess a δ-lactone annulated to a trans-decalin moiety, represented by himbacine (**1**) and himgravine (**2**) from early studies. The newly isolated class I members GB18 (**3**) and GB20 (**4**) slightly differ as the carbon tether connecting the trans-decalin and the piperidine ring is linked with C-7. The class II compounds (15 members) are structurally more complex in terms of their fused ring systems, and the piperidine ring is linked to the decalin moiety via an additional bond. Himandrine (**5**), himandridine (**6**), GB12 (**7**), and GB1 (**8**) are typical class II members, and this subgroup contains approximately one-half of all *Galbulimima* alkaloids isolated and characterized so far. The class III members (three alkaloids) differ from class II ones on the connectivity between the piperidine unit and the trans-decalin system, and this subclass includes GB13 (**9**), himbadine (**10**), and himgaline (**11**). The class IV members (two alkaloids), also known as "Miscellaneous" alkaloids, structurally vary from the other classes and have little resemblance to each other, represented by GB17 (**12**) and GB16 (**13**).[7]

Detailed biological evaluation of *Galbulimima* alkaloids revealed some fascinating properties, for instance, the class I alkaloid himbacine (**1**) was found to be a strong muscarinic receptor antagonist.[8] Because antagonists of the muscarinic receptors elevate the level of acetylcholine, this means that himbacine could act as a potential therapeutics for the treatment of Alzheimer's disease.[9] Moreover, structural modification of himbacine led to the development of vorapaxar (SCH 530348), a thrombin receptor antagonist, which has been approved by the FDA to treat patients with peripheral arterial disease in 2014.[10] Because of their fascinating structural features as well as potential pharmacological applications, the *Galbulimima* alkaloids have attracted considerable attention

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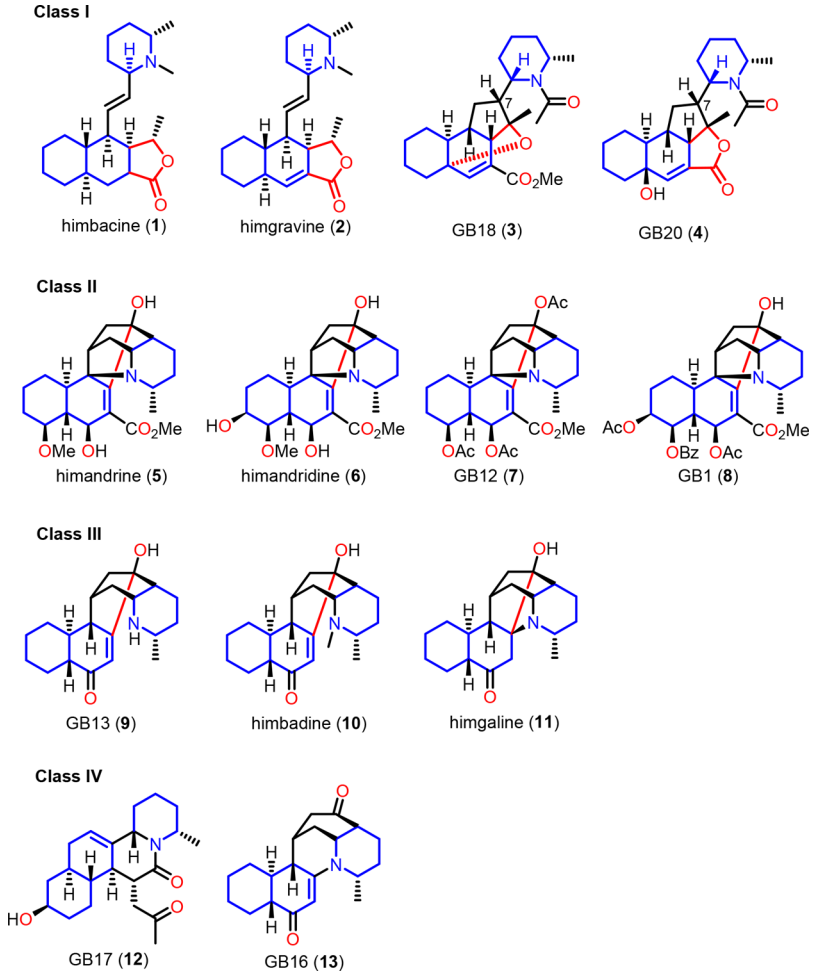

Figure 1. Representative structures of the *Galbulimima* alkaloids.

from the synthetic community. The total syntheses of eight representative members, that is, himbacine,[11] himbeline,[11a] himandravine,[12] himandrine,[13] GB13,[14] himgaline,[14c,d] GB16,[14f] and GB17,[12b,15] have been completed by creative synthetic endeavor.[7,16] Meanwhile, the biogenesis of the *Galbulimima* alkaloids has been discussed extensively within these synthetic works.[17,14b]

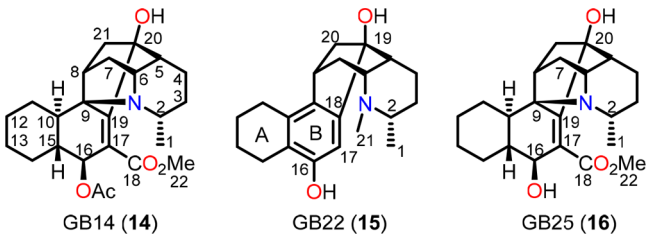

Figure 2. Structures of the new alkaloids isolated from bark extracts.

Our continuing efforts to explore the chemical constituents from *G. belgraveana* and *G. baccata* have led to some interesting findings. Herein, we report the isolation and structure elucidation of seven new alkaloids, namely, GB14 (**14**), GB22 (**15**), GB25 (**16**), GB21 (**17**), GB23 (**18**), GB24 (**19**), and GB26 (**20**). Compounds **14**–**16** (Figure 2) were obtained from the extracts of the bark, whereas the remaining four alkaloids **17**–**20** (Figure 3) were isolated from the methanol extracts of fresh leaves of *G. baccata*. GB14 (**14**), GB25 (**16**), and GB24 (**19**) are new class II members, GB22 (**15**) is an oxygenated derivative of class III alkaloid himdabine (**10**), and GB21 (**17**) could be regarded as the precursor of class I alkaloids GB21 (**4**) and GB26 (**20**), whereas GB23 (**18**) is a precursor of known class I member himgravine (**2**).

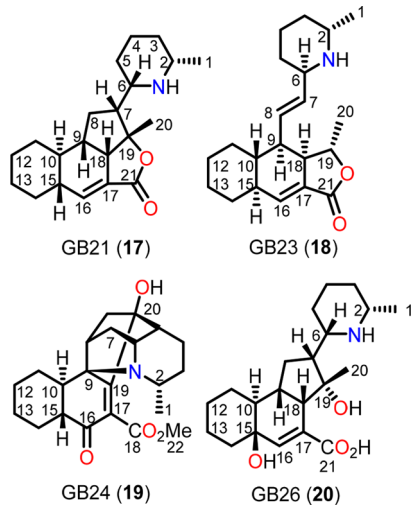

Figure 3. Structures of the new alkaloids isolated from leaf extracts.

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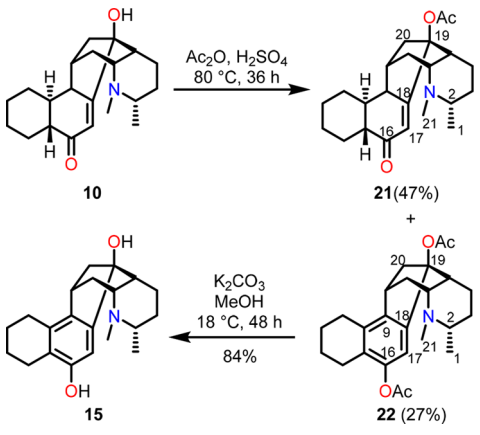
RESULTS AND DISCUSSION

Like all the *Galbulimima* alkaloids identified so far, the new compounds **14**–**16** were isolated from the bark extracts of *G. belgraveana* and *G. baccata*. GB14 (**14**) was obtained as a white amorphous solid, which was recrystallized from methanol to give a white crystalline solid. Its molecular formula was determined as $C_{22}H_{33}NO_5$, according to its electron ionization mass spectrometry (HREIMS) peak at *m*/*z* 416.2438 $[M + H]^+$. The infrared (IR) spectrum showed two absorption bands at 1740 and 1692, corresponding to two ester functions. The ^{13}C NMR spectra showed GB14 to possess two ester functional groups at C-16 and C-17 (δ_c 170.7 and δ_c 169.3) and one tetrasubstituted double bond (δ_c 164.7 and δ_c 116.0). The methyl signals at δ_H 3.74 (H-22), δ_H 2.03 (OAc-16), and δ_H 1.32 (H-1) as well as the absence of the N-methyl group indicated that this compound could be a class II alkaloid with an acetate function. The doublet at δ_H 5.61 (J = 8.5 Hz) suggested that the acetate be located at C-16. After the comparison of the NMR data with class II alkaloid himandrine (**5**), we were then able to arrive at a gross structure **14**. Furthermore, the unequivocal stereochemical assignments (including the absolute configuration) were confirmed via single-crystal X-ray analysis (see the Supporting Information for details).

The NMR spectra of GB22 were puzzling at first because there was one benzene proton at δ_H 6.59 (H-17), yet no ester or double bond signals were observed. *N*-Methyl at the piperidine ring could be found at δ_H 1.96 (H-21); however, the obvious upfield shift of the methyl at C-2 (δ_H 0.78) indicated the presence of a benzenoid B ring. Its molecular formula $C_{21}H_{29}NO_2$ derived from HREIMS was extremely similar to that of class III alkaloid himbadine (**10**) ($C_{21}H_{31}NO_2$). We concluded, therefore, that the new alkaloid was the aromatized derivative of himbadine, and the final structure **15** as well as the absolute configuration was determined by single-crystal X-ray analysis (see the Supporting Information for details). To shed more light on this transformation, various oxidation conditions were applied on himbadine (**10**) with the hope of forming GB22 directly; however, it turned out that this requires an unusual procedure (Scheme 1). Compound **10** was oxidized by H_2SO_4 in acetic anhydride to afford himbadine acetate (**21**) as the major product (47%) and GB22 diacetate (**22**) as the minor one (27%), and the latter compound was then hydrolyzed to give the final target **15** in a good yield (84%).

Scheme 1. Semisynthesis of GB22 (15) from Himbadine (10)



GB25 (**16**) was obtained as a white amorphous solid with a molecular formula $C_{22}H_{31}NO_4$. When its NMR spectra were compared with those of GB14 (**14**), it was apparent that GB25 had almost the same structural features except for the presence of an acetate group. The structure was assigned to compound **16** and again was confirmed by single-crystal X-ray analysis (see the Supporting Information for details).

After three new family members were identified from the bark extracts, we then turned our attention to the alkaloid components from the other parts that remain unexplored, that is, the fresh leaves, to search for new members or metabolites, which resulted in the isolation of four new alkaloids. GB21 (**17**) was the first sample obtained, and it was a white, crystalline solid with a molecular formula $C_{21}H_{31}NO_2$. Structural features from the NMR spectra include a usual piperidine ring system lacking an N-methyl group, a trisubstituted double bond (δ_c 143.4, 131.4; δ_H 6.75, t, J = 3.7 Hz) conjugated to a lactone-type carbonyl group (δ_c 169.5), and a tertiary methyl group (δ_H 1.01) which indicated a class I alkaloid. Fitting these data to a GB20-like[6] skeleton, we arrived at structure **17** which was confirmed by single-crystal X-ray analysis (see the Supporting Information for details). Our sample of GB23 (**18**) had a molecular formula of $C_{21}H_{31}NO_2$, and its NMR spectra were quite similar to that of class I alkaloid (+)-himgravine except for the absence of the N-methyl group. We concluded, therefore, that the new alkaloid was (+)-desmethylhimgravine, whose structure was again confirmed by single-crystal X-ray analysis (see the Supporting Information for details).

The third new alkaloid obtained was GB24 (**19**), a white amorphous solid, and its molecular formula was determined as $C_{22}H_{29}NO_4$. NMR spectra revealed one ketone (δ_c 196.2) being conjugated to a tetrasubstituted double bond (δ_c 168.4 and δ_c 121.3) and one ester carbonyl group (δ_c 173.4). We assumed the methyl signal (δ_H 3.85) to be a methyl ester that was attached to the double bond. The spectra varied from the class IV member GB16[5] (**13**) to the typical class III member GB13 (**9**) which possessed α,β-unsaturated ketone. Comparisons of both the ^1H and ^{13}C NMR spectra with those of GB25 (**16**) showed the best similarities. However, the structure could not be elucidated because of insufficient functional signals. Fortunately, treatment of the sample with HCl produced a salt that appeared to be a good crystal, and the single-crystal X-ray analysis confirmed the structure to be compound **19** (see the Supporting Information for details). To provide more materials for further biological evaluation, we conducted semisyntheses of GB24 (**19**), GB25 (**16**), and GB14 (**14**), and the three closely related members, from class II alkaloid GB12 (**7**), were obtained by early studies (Scheme 2). Hydrolyzing the triacetate of compound **7** in K_2CO_3 and methanol conditions afforded triol **23** in a good yield, and the allylic hydroxy group was then oxidized selectively by MnO_2 to produce ketone **24** (98%). Removal of the hydroxy group at the C-14 position was investigated by radical deoxygenation; however, the required thiocarbonylimidazolide compound **25** could only be prepared by a solid-state reaction with thiocarbonyldiimidazole (TCDI) in the presence of 3 equiv dimethylaminopyridine (DMAP) at 80 °C.[18] The so-obtained intermediate **25** was then submitted to a radical cleavage with tri-*n*-butyltin hydride (Bu_3SnH) and azabisisobutyronitrile (AIBN) in toluene to give the expected GB24 (**19**) in a 50% yield and a reduced product **24** (20%). GB24 was then reduced by $NaBH_4$ to afford GB25 (**15**) in a 75% yield, and the latter compound was then converted to GB14 (**14**) via the acetylation condition (71%).

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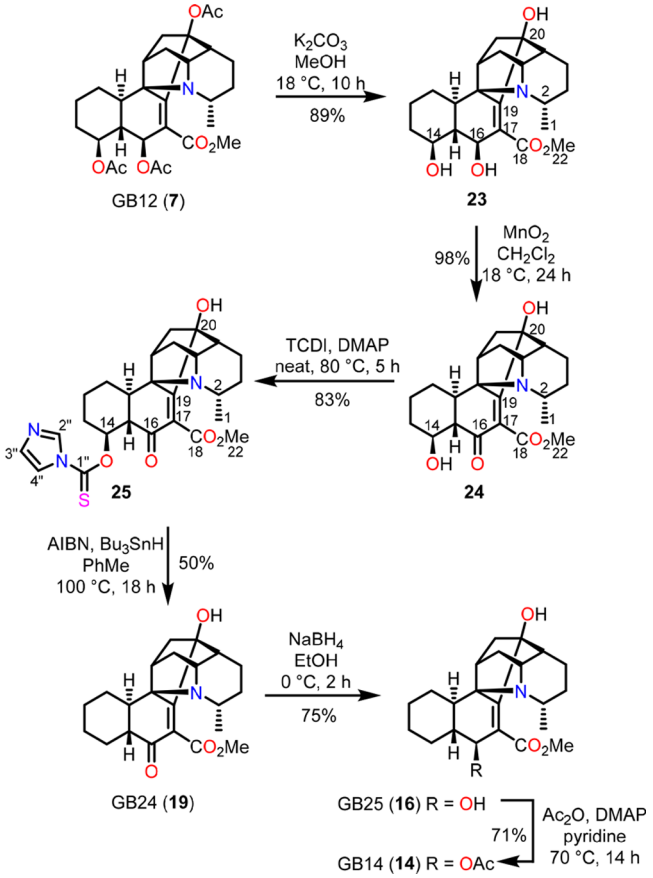
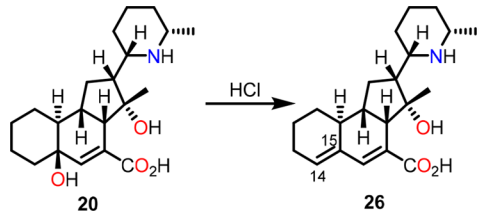
ACS Omega 2018, 3, 1912−1921

Scheme 2. Semisyntheses of GB25 (19), GB24 (16), and GB14 (14) from GB12 (7)



The last alkaloid GB26 had a molecular formula $C_{21}H_{33}NO_4$, and it was the most polar member during column chromatography, assuming it possessed some polar functional groups. It had the same carbon number with GB21 (**17**); furthermore, NMR spectra showed some similarities with those of **17**: a usual piperidine ring system lacking an N-methyl group, a trisubstituted double bond (δ_c 137.3, 136.8; δ_H 6.01, s at C-16 and C-17) conjugated to a carbonyl group (δ_c 173.9, C-21), and a tertiary methyl group (δ_H 1.03). However, ^{13}C NMR indicated that there are four quaternary carbons (δ_c 173.9, 136.8, 81.4, and 67.6), and the proton NMR suggested that there are two tertiary hydroxyl groups at C-15 (δ_H 6.22, δ_c 67.6) and C-19 (δ_H 5.60, δ_c 81.4). After comparing the data with those of GB20[6] (**4**), we then arrived at the structure of GB21 (**17**) possessing an additional hydroxyl at C-15, and the second tertiary hydroxyl at C-19 could be derived from the ring opening of lactone, which also resulted in the release of carboxylic acid at C-17, all of those could attribute to the significant polarity of this compound. With the combined data, we finally came to a unique structure **20**. Initially, we wanted to confirm the proposed structure via single-crystal X-ray analysis; however, evaporation of solutions of this sample in various solvent systems failed to afford a suitable material for single-crystal X-ray analysis. Then, this compound was treated with HCl (4 M solution in dioxane) followed by being dissolved in a CH_2Cl_2/MeOH/EtOAc system. Upon evaporating, a material suitable for single-crystal X-ray analysis (see the Supporting Information for details) was obtained, which was determined to be diene **26**, an eliminated derivative of compound **20** (Scheme 3). Therefore, the final structure as well as the absolute configuration of compound **26** was confirmed. However,

Scheme 3. Derivatization of Compound 20, Leading to Diene 26



because of the very small amounts of the material obtained, no other spectral data could be acquired on this diene.

There has been a great deal of speculation about the biogenesis of the *Galbulimima* alkaloids, and in most of the postulated biosyntheses, the putative polyene **27** (Figure 4) serves as a common precursor and undergoes regiodivergent Diels–Alder cycloaddition to establish the alkaloid skeleton. This hypothesis has been supported by elegant biomimetic syntheses of the class I member himbadine (**1**),[11g] class III alkaloid GB13 (**9**),[14b] and class IV member GB17 (**12**).[12b] We believe that an intramolecular [4 + 2] cycloaddition of polyene **27** following path a (Figure 4) would lead to intermediate **30**, which underwent an imine reduction, and lactone formation process could deliver GB23 (**18**) and then himgravine (**2**). Alternatively, coiling of polyene **27** in the cycloaddition process following path b would afford intermediate **31** with different stereochemistry. A Michael reaction on the latter compound would deliver a new cyclopentanone compound **32**, which could be converted to enone **33** after proton shift and the oxidation process. An enamine-based aldol reaction between the cyclopentanone and the piperidine ring would then result in pentacycle **34**, and in their total syntheses of himandrine (**5**) and GB13 (**9**), Movassaghi[13] and Evans[14d] showed that such a sequence was feasible. This common intermediate **34** en route to class II members passes through GB24 (**19**) and to other ones, that is, GB14 (**14**), GB25 (**19**), himandrine (**5**), himandridine (**6**), GB12 (**7**), and GB1 (**8**) after decarboxylation, oxidation, and other associated processes. Compound **31** could also serve as a precursor to class I alkaloid GB21 (**17**) after a reduction/cyclization sequence, and the latter compound could then be oxidized followed by acetylation to give GB20 (**4**). Hydrolysis on both the lactone ring and the acetamide on GB20 would deliver the new member GB26 (**20**). The biosynthesis of class IV member GB17 (**12**) requires an intramolecular Diels–Alder reaction (IMDA) on the polyene structure such as **35** that could be derived from polyene **27** via path c. In this way, the intermediate **36** from which an azachrysene framework could plausibly be formed, it would serve as a precursor to GB17 (**12**). In a recent biomimetic total synthesis of GB17, Thomson[12b] employed a precursor similar to that of **35**, and the computational investigations indicated that because of the competing orbital interaction and distortion energies, such an IMDA process showed low regioselectivity.

CONCLUSIONS

The work detailed here has expanded the range of structures in the *Galbulimima* alkaloid family, although no new skeleton was found. Most of the new members isolated could be regarded as metabolites or precursors of the known alkaloids. Nevertheless,

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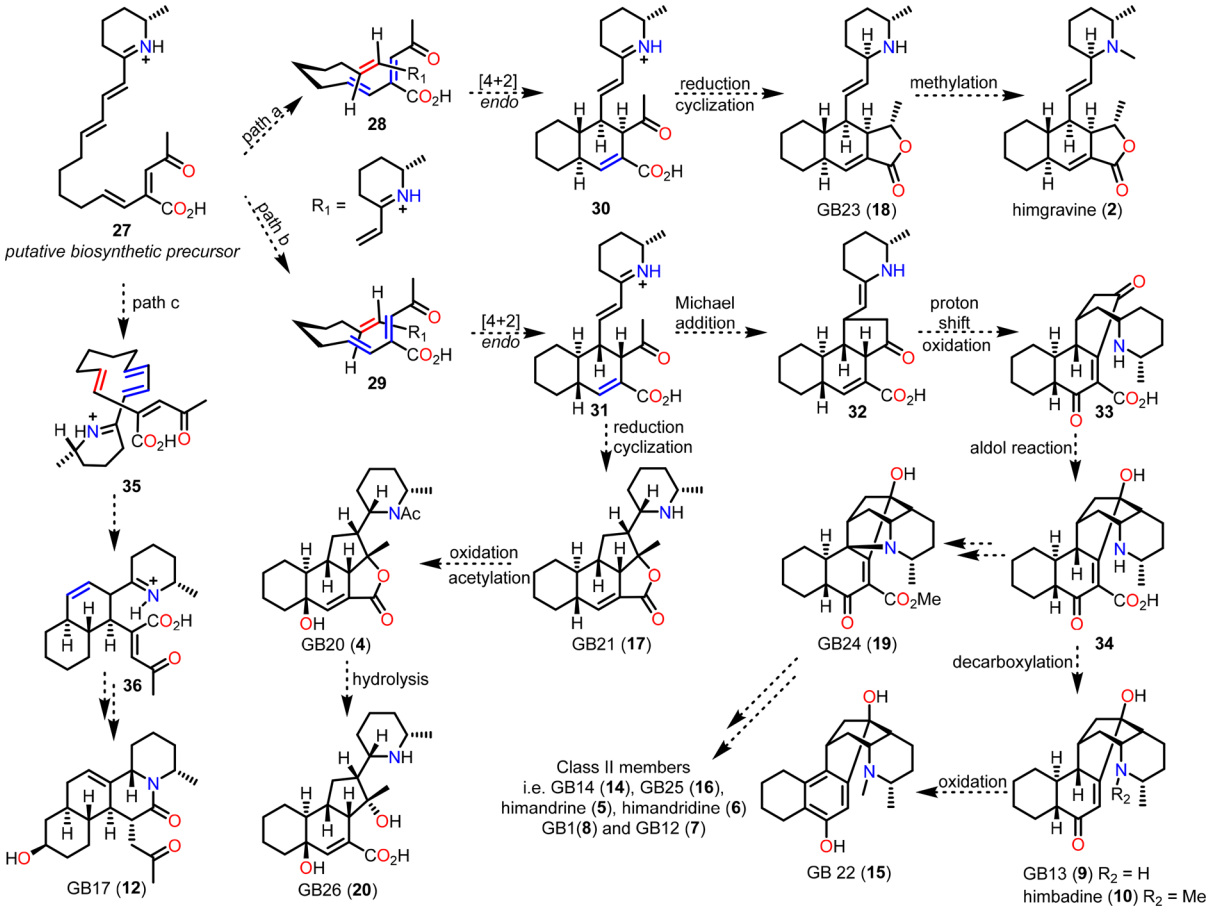

Figure 4. Biosynthetic speculations of *Galbulimima* alkaloids.

the isolation and identification of these new family members have shed more light on the biosynthesis route of the *Galbulimima* alkaloids, which has been proved by the semisynthesis of GB22 (**15**) and the interconversions of GB14 (**14**), GB25 (**16**), and GB24 (**19**). The present work has also found some missing links in the biosynthetic sequences. Our current efforts are focused on undertaking a comprehensive biological evaluation of the new alkaloids we have isolated to date. Results will be reported in due course.

EXPERIMENTAL SECTION

General Experimental Protocols. All reagents and solvents were of commercial grade and purified prior to use when necessary. Thin-layer chromatography was performed on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates as supplied by Merck. Visualization was accomplished with UV light and/or the use of ninhydrin or potassium permanganate solution followed by brief heating with a heat gun. Flash chromatographic separations were carried out with silica gel 60 (40−63 μm) as the stationary phase and using the solvents indicated. IR spectra (ν_{max}) were recorded on a PerkinElmer 1800 Series Fourier transform infrared spectrometer. Samples were applied to KBr plates as $CDCl_3$ solutions followed by generous air drying. Melting points were measured on an Optimelt automated melting point system and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei. Chemical shifts are reported in parts per million relative to residual solvent peaks as an internal standard at the following chemical shifts (^{1}H and ^{13}C, respectively): 7.26 and 77.0 ppm for $CDCl_3$. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, qd = quartet of doublets, br = broad, and m = multiplet), coupling constant (Hz), integration, and assigned position. Low-resolution electrospray ionization (ESI) mass spectra were recorded on a single quadrupole liquid chromatograph−mass spectrometer, and high-resolution measurements were recorded on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic sector machine. Wherever necessary, reactions were performed under a nitrogen atmosphere.

Plant Materials. *G. belgraveana* bark was acquired at Aiyura on the eastern highlands of New Guinea in August 1951. A voucher specimen (sample no. 5091) was housed within the Commonwealth Scientific and Industrial Research Organization (C.S.I.R.O.), Australia. *G. baccata* bark was collected near Boonjie, North Queensland, in August 1947. A voucher specimen (sample no. 4273) was housed within the C.S.I.R.O. The plant materials were identified by Messrs. J. G. Tracey and L. J. Webb at C.S.I.R.O. and Mr. J. S. Womersley, Department of Forests, Lae. *G. baccata* leaf material was obtained from the Royal Botanic Gardens, Sydney, NSW, Australia. The leaves were harvested on May 15, 2012, and a voucher specimen (catalogue number: 05-79352) was deposited at the Royal Botanic Gardens, Sydney, NSW, Australia. The plant materials were identified by Dr. Benjamin Thomas.

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Isolation of Compounds 9−15. Compounds **9−11** were isolated from the bark extracts from *G. belgraveana* and *G. baccata* left by our early studies.[4] The crude bark extracts were obtained by using the following procedure: the shade-dried milled bark (10 kg) was exhausted with cold methanol (20 L) three times before being filtered, and the filtrate was concentrated under reduced pressure. The crude bark extracts were suspended in 5% NaOH aqueous solution (3 L) and were extracted with ether (3 × 3 L). The dark aqueous alkaline solution was discarded, and the organic layer was then extracted with 4% HCl (3 × 3 L). The acid extract was washed with ether (3 × 1 L), basified with ammonia to reach a pH value of 10, and then the liberated bases were extracted with chloroform (3 × 3 L). Evaporation of the dried organic layer gave a thick brown oil, which was subjected to gradient chromatography or recrystallization to yield the previously reported *Galbulimima* alkaloids. The unseparated mixtures were then stored under ambient temperature at the Research School of Chemistry and the Australian National University since 1970s. Gradient chromatography (silica, 1:10:0.1 to 5:10:0.1 v/v/v methanol/dichloromethane/NH_3 elution) on these mixtures afforded new compounds **14** (35 mg), **15** (18 mg), and **16** (26 mg). Compounds **17−20** were obtained from the fresh leaf extracts from *G. baccata* using the following procedure: the fresh leaves of *G. baccata* (3 kg) were treated with liquid nitrogen and then crushed in the meantime, and after being warmed to room temperature, the residues were percolated with methanol (10 L) three times at 25 °C. The solution was then filtered, and the filtrates combined were concentrated under reduced pressure. The crude extract (300 g) was suspended in 5% NaOH aqueous solution (1 L) and was extracted with ether (3 × 1 L). The separated organic layer was further extracted with 4% HCl (3 × 1 L). The acid extract was washed with ether (3 × 500 mL), basified with ammonia to reach a pH value of 10, and then extracted with dichloromethane (3 × 500 mL). Evaporation of the dried organic layer gave a thick brown oil (2.7 g), which was subjected to gradient chromatography (silica, 1:10:0.1 to 5:10:0.1 v/v/v methanol/dichloromethane/NH_3 elution) to afford the three major fractions A (450 mg), B (670 mg), and C (810 mg). Further purification on fraction A using 1:10:0.1 v/v/v methanol/dichloromethane/NH_3 elution afforded compound **17** (56 mg) and compound **118** (120 mg); purification on fraction C using 2:10:0.1 v/v/v methanol/dichloromethane/NH_3 elution gave compound **19** (35 mg); the most polar fraction C was purified several times by 3:10:0.1 v/v/v methanol/dichloromethane/NH_3 elution to afford compound **20** (265 mg).

*GB14 (**14**).* A white amorphous solid, and a sample suitable for single-crystal X-ray analysis was recrystallized from methanol, mp 112−114 °C, $[\alpha]_D^{20}$ = −16.3 (*c* 0.22, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.61 (d, *J* = 8.5 Hz, 1H, H-16), 4.59 (s, 1H, OH-20), 3.74 (s, 3H, H-22), 3.45 (m, 1H, H-6), 3.31 (m, 1H, H-2), 2.30 (m, 1H, H-8), 2.21−2.17 (complex m, 1H), 2.13−2.07 (complex m, 2H), 2.03 (s, 3H, OAc-16), 1.98 (m, 1H), 1.89−1.83 (complex m, 2H), 1.83−1.72 (complex m, 4H), 1.69−1.60 (complex m, 3H), 1.55 (complex m, 1H), 1.47−1.42 (complex m, 2H), 1.32 (d, *J* = 7.2 Hz, 3H, H-1), 1.25−1.12 (complex m, 2H), 1.10−0.98 (complex m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7 (OAc-16), 169.3 (C18), 164.7 (C19), 116.0 (C17), 80.9 (C16), 73.9 (C20), 69.3 (C9), 68.0 (C6), 55.6 (C2), 52.0 (C22), 50.3 (C5), 49.0 (C15), 44.7 (C10), 44.6 (C21), 41.0 (C7), 37.3 (C11), 31.7 (C8), 27.6 (C14), 27.4 (C13), 26.4 (C12), 25.9 (C3), 25.5 (C4), 24.1 (OAc-16), 21.1 (C1). IR (KBr) ν_{max}: 3451, 2930, 2855, 1740, 1692, 1436, 1371, 1262, 1233, 1158, 1039, 731 cm^{-1}. MS (ESI, +ve) *m*/*z*: 416 ([M + H]$^+$, 100%), 438 ([M + Na]$^+$, 12). HRMS: [M + H]$^+$ calcd for $C_{24}H_{34}NO_5$, 416.2437; found, 416.2438.

*GB22 (**15**).* A pale-yellow amorphous solid, treatment with HCl in dioxane gave its HCl salt, and a sample suitable for single-crystal X-ray analysis was recrystallized from methanol, mp >250 °C (decomp.), $[\alpha]_D^{20}$ = +84 (*c* 1.3, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59 (s, 1H, H-17), 3.11 (m, 1H, H-6), 2.76 (m, 1H, H-2), 2.68−2.64 (complex m, 1H), 2.61−2.52 (complex m, 3H), 2.22 (complex m, 1H), 2.13 (d, *J* = 9.7 Hz, 1H), 2.08 (m, 1H), 2.02−1.99 (m, 1H), 1.98−1.95 (complex m, 1H), 1.96 (s, 3H, H-21), 1.78−1.71 (complex m, 4H), 1.68−1.63 (complex m, 1H), 1.47−1.37 (complex m, 3H), 1.34−1.31 (complex m, 1H), 0.78 (d, *J* = 6.3 Hz, 3H, H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1 (C16), 144.7 (C18), 137.0 (C9), 131.8 (C10), 121.9 (C15), 106.8 (C17), 82.1 (C19), 60.2 (C6), 55.6 (C2), 50.3 (C5), 43.5 (C20), 38.8 (C7), 34.7 (C11), 30.6 (C8), 29.1 (C14), 25.9 (C13), 23.3 (C12), 22.8 (C3), 22.7 (C4), 21.0 (C21), 20.3 (C1). IR (KBr) ν_{max}: 3280, 2929, 2857, 1683, 1601, 1445, 1294, 1245, 1197, 1104, 1077, 907, 730, 647 cm^{-1}. MS (EI, +70 eV) *m*/*z*: 327 ($M^{+\bullet}$, 43%), 311 (40), 310 (100). HRMS: $M^{+\bullet}$ calcd for $C_{21}H_{29}NO_2$, 327.2198; found, 327.2197.

*GB25 (**16**).* A white amorphous solid, treatment with HCl in dioxane gave its HCl salt, and a sample suitable for single-crystal X-ray analysis was recrystallized from methanol, mp >250 °C (decomp.), $[\alpha]_D^{20}$ = −4.7 (*c* 1.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.83 (s, 1H, OH-20), 4.14 (dd, *J* = 8.3 and 4.6 Hz, 1H, H-16), 3.86 (s, 3H, H-22), 3.43 (m, 1H, H-6), 3.29 (m, 1H, H-2), 2.36 (d, *J* = 4.7 Hz, 1H, H-8), 2.32−2.22 (complex m, 2H), 2.19−2.17 (complex m, 1H), 2.09−1.93 (complex m, 3H), 1.89−1.71 (complex m, 5H), 1.68−1.59 (complex m, 2H), 1.54 (complex m, 1H), 1.45 (td, *J* = 12.6 and 3.5 Hz, 1H), 1.36 (complex m, 1H), 1.32 (d, *J* = 7.2 Hz, 3H, H-1), 1.27−1.20 (complex m, 2H), 1.00−0.90 (complex m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6 (C18), 163.6 (C19), 119.0 (C17), 80.8 (C16), 72.4 (C20), 69.2 (C9), 68.3 (C6), 55.6 (C2), 52.3 (C22), 50.4 (C5), 48.9 (C15), 44.8 (C10), 44.7 (C21), 42.1 (C7), 37.3 (C11), 32.3 (C8), 27.5 (C14), 27.5 (C13), 26.5 (C12), 26.0 (C3), 25.6 (C4), 24.1 (C1). IR (KBr) ν_{max}: 3436, 2931, 2854, 1687, 1456, 1371, 1260, 1229, 1181, 1138, 1078, 1038, 967, 910, 731, 642 cm^{-1}. MS (ESI, +ve) *m*/*z*: 374 ([M + H]$^+$, 100%), 396 ([M + Na]$^+$, 32). HRMS: [M + H]$^+$ calcd for $C_{22}H_{32}NO_4$, 374.2331; found, 374.2331.

*GB21 (**17**).* A white crystalline solid, mp 135−138 °C, $[\alpha]_D^{20}$ = −19.0 (*c* 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75 (t, *J* = 3.7 Hz, 1H, H-16), 2.75−2.67 (complex m, 2H, H-6 and H-18), 2.60 (m, 1H, H-2), 2.11 (m, 2H), 2.00−1.92 (complex m, 3H), 1.80−1.70 (complex m, 5H), 1.60 (s, 3H, H-20), 1.59−1.50 (complex m, 1H), 1.42−1.35 (complex m, 1H), 1.34−1.15 (complex m, 6H), 1.13−1.08 (complex m, 1H), 1.01 (d, *J* = 6.1 Hz, 3H, H-1), 0.90−0.75 (complex m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5 (C21), 143.4 (C16), 131.4 (C17), 92.6 (C19), 56.9 (C2), 55.7 (C6), 52.9 (C7), 52.5 (C18), 45.0 (C15), 43.7 (C10), 43.2 (C9), 36.9 (C3), 33.8 (C14), 33.7 (C8), 31.6 (C13), 31.5 (C5), 28.3 (C11), 26.8 (C12), 26.1 (C20), 24.7 (C4), 23.1 (C1). IR (KBr) ν_{max}: 2922, 2853, 1755, 1665, 1445, 1379, 1247, 1171, 1090, 1049, 1019, 924, 722 cm^{-1}. MS (EI, +70 eV) *m*/*z*: 329 ($M^{+\bullet}$, 5%), 98 (100). HRMS: $M^{+\bullet}$ calcd for $C_{21}H_{31}NO_2$, 329.2355; found, 329.2355.

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*GB23 (**18**)*. A white amorphous solid, treatment with HCl in dioxane gave its HCl salt, and a sample suitable for single-crystal X-ray analysis was recrystallized from methanol, mp >250 °C (decomp.), $[\alpha]_D^{20}$ = +6.4 (*c* 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.67 (t, *J* = 3.1 Hz, 1H, H-16), 5.74 (dd, *J* = 15.3 and 6.6 Hz, 1H, H-7), 5.22 (dd, *J* = 15.3 and 10.2 Hz, 1H, H-8), 4.32 (dq, *J* = 9.3 and 6.1 Hz, 1H, H-19), 3.58 (m, 1H, H-6), 3.10 (m, 1H, H-2), 2.69 (m, 1H, H-18), 2.34 (q, *J* = 10.2 Hz, 1H, H-9), 2.05 (m, 1H, H-15), 1.88 (m, 1H), 1.82−1.74 (complex m, 3H), 1.72−1.66 (complex m, 2H), 1.66−1.59 (complex m, 2H), 1.58−1.49 (complex m, 2H), 1.42 (d, *J* = 6.0 Hz, 3H, H-20), 1.30−1.15 (complex m, 4H), 1.11 (d, *J* = 6.4 Hz, 3H, H-1), 0.87 (td, *J* = 12.2 and 3.1 Hz, 1H), 0.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4 (C21), 141.4 (C16), 136.8 (C7), 130.6 (C8), 129.7 (C17), 77.6 (C19), 52.9 (C6), 46.7 (C2), 46.3 (C9), 44.8 (C15), 43.5 (C10), 40.4 (C1), 32.6 (C5), 32.5 (C3), 31.2 (C11), 31.1 (C14), 26.3 (C12), 26.0 (C13), 21.4 (C4), 20.9 (C20), 19.7 (C1). IR (KBr) ν_{max}: 2922, 2851, 1755, 1683, 1445, 1382, 1218, 1047, 1026, 980, 903, 729 cm^{-1}. MS (EI, +70 eV) *m*/*z*: 329 ([M]$^{+\bullet}$, 30%), 314 (80), 218 (22), 164 (30), 111 (45), 98 (100). HRMS: M$^{+\bullet}$ calcd for $C_{21}H_{31}NO_2$, 329.2355; found, 329.2357.

*GB24 (**19**)*. A white amorphous solid, treatment with HCl in dioxane gave its HCl salt, and a sample suitable for single-crystal X-ray analysis was recrystallized from methanol, mp >250 °C (decomp.), $[\alpha]_D^{20}$ = +216.0 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 3H, H-22), 3.46 (m, 1H, H-6), 3.37 (m, 1H, H-2), 2.77 (s, 1H), 2.54 (ddd, *J* = 12.6, 10.8 and 3.4 Hz, 1H), 2.39 (dm, *J* = 13.2 Hz, 1H), 2.30−2.19 (complex m, 2H), 2.12 (m, 1H), 2.01−1.88 (complex m, 3H), 1.86−1.78 (complex m, 3H), 1.76−1.70 (complex m, 2H), 1.66 (d, *J* = 11.2 Hz, 1H), 1.61 (d, *J* = 10.9 Hz, 1H), 1.56−1.43 (complex m, 1H), 1.35−1.30 (complex m, 2H), 1.24 (d, *J* = 7.2 Hz, 3H, H-1), 1.22−1.14 (complex m, 1H), 1.10−1.00 (complex m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2 (C16), 173.4 (C18), 168.3 (C19), 121.3 (C17), 80.3 (C20), 69.0 (C9), 65.5 (C6), 55.2 (C2), 52.5 (C22), 50.4 (C5), 49.4 (C15), 46.8 (C10), 46.4 (C21), 43.7 (C7), 37.1 (C11), 27.6 (C8), 27.5 (C14), 27.1 (C13), 26.2 (C12), 26.1 (C3), 25.3 (C4), 24.2 (C1). IR (KBr) ν_{max}: 3470, 2936, 2858, 1732, 1650, 1448, 1370, 1298, 1273, 1238, 1171, 1134, 1072, 1031, 989, 908, 730, 646 cm^{-1}. MS (ESI, +ve) *m*/*z*: 372 ([M + H]$^+$, 100%), 394 ([M + Na]$^+$, 25). HRMS: [M + H]$^+$ calcd for $C_{22}H_{30}NO_4$, 372.2175; found, 372.2173.

*GB26 (**20**)*. A yellow amorphous solid, $[\alpha]_D^{20}$ = −51 (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.22 (broad s, 1H, OH-15), 6.01 (s, 1H, H-16), 5.60 (broad s, 1H, OH-19), 3.02 (d, *J* = 11.3 Hz, 1H, H-18), 2.74 (dm, *J* = 9.4 Hz, 1H, H-6), 2.65 (m, 1H, H-2), 2.13−2.04 (complex m, 1H), 2.00−1.92 (complex m, 1H), 1.89−1.84 (complex m, 1H), 1.76−1.60 (complex m, 7H), 1.55−1.45 (complex m, 5H), 1.40−1.35 (complex m, 1H), 1.32 (s, 3H, H-20), 1.28−1.06 (complex m, 5H), 1.03 (d, *J* = 6.4 Hz, 3H, H-1), 0.94−0.82 (complex m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9 (C21), 137.3 (C16), 136.8 (C17), 81.4 (C19), 67.6 (C15), 55.8 (C6), 52.3 (C2), 51.2 (C18), 48.7 (C10), 46.1 (C7), 37.5 (C3), 35.3 (C9), 35.2 (C14), 31.9 (C8), 27.7 (C13), 26.2 (C5), 26.1 (C20), 25.3 (C11), 25.1 (C12), 23.0 (C1), 21.4 (C4). IR (KBr) ν_{max}: 3332, 2926, 2856, 1754, 1662, 1638, 1604, 1443, 1378, 1217, 1195, 1128, 1016, 961, 918, 731 cm^{-1}. MS (EI, −70 eV) *m*/*z*: 362 ([M − H]$^+$, 5%), 345 ([M − H_2O]$^+$, 10), 168 (30), 98 (100). HRMS: [M − H]$^+$ calcd for $C_{21}H_{32}NO_4$, 362.2331; found, 362.2339.

Specific Chemical Transformations. *Compounds **21** and **22***. A magnetically stirred mixture of himbadine (**10**) (1.5 g, 4.55 mmol) in acetic anhydride (50 mL) was treated with 98% sulfuric acid (0.5 mL). The solution was heated at 80 °C for 36 h under nitrogen atmosphere. Acetic anhydride was distilled off under reduced pressure, and the residue was then dissolved in dichloromethane (100 mL) and basified by NaOH (50 mL of a 10% aqueous solution). The organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting brown residue was subjected to chromatography (silica, 20:1 v/v CH_2Cl_2/MeOH elution) to afford two fractions. Concentration of fraction A (R_f = 0.9) gave himbadine acetate **21** (0.8 g, 47%) as a yellow oil, $[\alpha]_D^{20}$ = −4.6 (*c* 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.00 (d, *J* = 2.2 Hz, 1H, H-17), 3.21 (dt, *J* = 11.4 and 2.4 Hz, 1H, H-2), 3.06 (m, 1H), 2.54−2.51 (m, 2H), 2.36−2.31 (m, 1H), 2.28−2.21 (complex m, 2H), 2.17 (s, 3H, H-21), 2.08 (s, 3H, H-19), 1.93−1.88 (complex m, 1H), 1.86−1.82 (complex m, 5H), 1.73−1.71 (complex m, 1H), 1.59−1.54 (complex m, 1H), 1.50−1.43 (complex m, 1H), 1.39−1.28 (complex m, 3H), 1.26−1.20 (complex m, 2H), 1.12−1.09 (complex m, 1H), 1.07−1.00 (complex m, 1H), 0.93 (d, *J* = 6.0 Hz, 3H, H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.3 (C16), 176.1 (OAc-19), 169.3 (C18), 119.2 (C17), 87.3 (C19), 62.6 (C2), 58.8 (C6), 52.6, 47.8, 46.9, 43.4, 43.2, 39.4, 33.9, 33.6, 31.6, 30.0, 26.0, 25.9, 25.1, 24.6, 22.2, 21.7 (C1). IR (KBr) ν_{max}: 2928, 2855, 2775, 1739, 1664, 1447, 1367, 1235, 1184, 1092, 1069, 978, 868, 734, 594 cm^{-1}. MS (EI, +70 eV) *m*/*z*: 371 (M$^{+\bullet}$, 25%), 313 (32), 312 (100). HRMS: M$^{+\bullet}$ calcd for $C_{23}H_{33}NO_3$, 371.2460; found, 371.2464.

Concentration of fraction B (R_f = 0.4) gave GB22 diacetate **22** (0.5 g, 27%) as a yellow oil, $[\alpha]_D^{20}$ = +102.5 (*c* 1.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.72 (s, 1H, H-17), 3.19 (m, 1H, H-6), 2.96 (m, 1H, H-2), 2.78 (d, *J* = 9.8 Hz, 1H), 2.69 (m, 1H), 2.64−2.57 (m, 2H), 2.54−2.48 (m, 2H), 2.44−2.40 (complex m, 1H), 2.28 (s, 3H, OAc-19), 2.09 (s, 3H, OAc-16), 2.05 (m, 1H), 1.89−1.81 (complex m, 2H), 1.79 (s, 3H, H-21), 1.77−1.72 (complex m, 4H), 1.64−1.61 (complex m, 1H), 1.39−1.25 (complex m, 3H), 0.74 (d, *J* = 6.1 Hz, 3H, H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2 (OAc-19), 169.4 (OAC-16), 147.4 (C16), 143.5 (C18), 140.5 (C9), 131.9 (C10), 127.5 (C15), 113.6 (C17), 89.5 (C19), 61.3 (C6), 57.5 (C2), 51.4, 40.7, 38.5, 36.8, 29.8, 29.2, 25.9, 23.5, 22.5(3), 22.5(0), 22.4, 21.9, 21.1, 20.9. IR (KBr) ν_{max}: 2930, 2855, 2763, 1759, 1736, 1444, 1366, 1249, 1230, 1215, 1197, 1066, 1018, 910, 732, 646 cm^{-1}. MS (ESI, +ve) *m*/*z*: 412 ([M + H]$^+$, 100%), 434 (5). HRMS: [M + H]$^+$ calcd for $C_{25}H_{34}NO_4$, 412.2488; found, 412.2482.

*GB22 (**15**)*. A magnetically stirred mixture of compound **22** (0.3 g, 0.73 mmol) in MeOH (10 mL) was added to potassium carbonate (0.6 g, 4.38 mmol). The reaction mixture was stirred at 18 °C for 48 h before being concentrated under reduced pressure. The resulting residue was subjected to chromatography (silica, 9:1 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.4), GB22 (**15**) (0.2 g, 84%) as a pale-yellow amorphous solid. The structural data were, in all respects, similar to those of an authentic sample from isolation work.

*Compound **23***. A magnetically stirred mixture of GB12 (**7**) (400 mg, 0.78 mmol) in MeOH (10 mL) was added to potassium carbonate (540 mg, 3.88 mmol). The reaction mixture was stirred at 18 °C for 10 h before being concentrated under reduced pressure. The resulting white solid was subjected

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ACS Omega 2018, 3, 1912−1921

to chromatography (silica, 10:1 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.4), triol **23** (270 mg, 89%) as a white amorphous solid, $[\alpha]_D^{20}$ = +36.6 (*c* 2.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.60 (d, *J* = 7.9 Hz, 1H, H-16), 4.57 (broad s, 1H, OH), 3.85 (s, 3H, H-22), 3.63 (broad s, 1H, OH), 3.50 (td, *J* = 10.0 and 4.3 Hz, 1H, H-14), 3.45 (s, 1H, H-6), 3.43−3.36 (complex m, 1H, H-2), 3.29 (broad s, 1H, OH), 2.28 (ddd, *J* = 14.0, 6.2 and 2.6 Hz, 1H), 2.18−2.10 (complex m, 2H), 2.09−2.01 (complex m, 1H), 2.00−1.96 (complex m, 2H), 1.88−1.78 (complex m, 2H), 1.78−1.70 (complex m, 2H), 1.64−1.56 (complex m, 2H), 1.53 (d, *J* = 10.8 Hz, 1H), 1.48−1.37 (complex m, 2H), 1.34 (d, *J* = 7.1 Hz, 3H, H-1), 1.36−1.33 (complex m, 1H), 1.30−1.20 (complex m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5 (C18), 161.6 (C19), 118.0 (C17), 80.7 (C20), 77.6 (C16), 72.5 (C9), 69.2 (C14), 67.7 (C6), 55.5, 52.4, 50.0, 49.0, 48.1, 44.7, 42.4, 37.2, 35.6, 27.2, 26.6, 25.4, 24.1, 23.9. IR (KBr) ν_{max}: 3435, 2936, 2862, 1687, 1448, 1436, 1281, 1261, 1231, 1182, 1140, 1114, 1078, 1048, 1030, 974, 910, 878, 729, 643 cm^{-1}. MS (ESI, +ve) *m*/*z*: 390 ([M + H]$^+$, 100%). HRMS: [M + H]$^+$ calcd for $C_{22}H_{32}NO_5$, 390.2280; found, 390.2283.

Compound ***24***. A magnetically stirred mixture of triol **23** (400 mg, 1.03 mmol) in CH_2Cl_2 (30 mL) was treated with MnO_2 (887 mg, 10.2 mmol). The reaction mixture was stirred at 18 °C for 24 h before being filtered through a pad of Celite, the filter cake was washed with CH_2Cl_2 (100 mL), and the combined filtrate was concentrated under reduced pressure. The resulting colorless oil was subjected to chromatography (silica, 10:1 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.5), ketone **24** (390 mg, 98%) as a white amorphous solid, $[\alpha]_D^{20}$ = +235.8 (*c* 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.03 (s, 1H, OH), 3.86 (s, 3H, H-22), 3.82−3.73 (complex m, 1H, H-14), 3.52−3.47 (complex m, 1H, H-6), 3.37 (m, 1H, H-2), 2.70 (s, 1H), 2.65 (dd, *J* = 13.1 and 8.6 Hz, 1H), 2.32−2.19 (complex m, 2H), 2.17−2.14 (complex m, 1H), 2.07−2.01 (complex m, 1H), 2.00−1.90 (complex m, 2H), 1.88−1.81 (complex m, 2H), 1.79−1.71 (complex m, 2H), 1.70−1.64 (complex m, 2H), 1.64−1.61 (complex m, 1H), 1.56−1.45 (complex m, 1H), 1.37−1.30 (complex m, 2H), 1.28 (d, *J* = 7.3 Hz, 3H, H-1), 1.23 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.8 (C16), 175.5 (C18), 167.6 (C19), 121.2 (C17), 80.3 (C20), 71.8 (C9), 69.1 (C14), 65.1 (C6), 55.2, 52.6, 52.2, 50.7, 49.8, 44.0, 43.5, 37.0, 34.1, 27.3, 26.9, 25.3, 24.4, 23.7. IR (KBr) ν_{max}: 3466, 2942, 2865, 1732, 1634, 1448, 1434, 1299, 1269, 1240, 1169, 1136, 1103, 1071, 1035, 1017, 989, 915, 877, 729, 646 cm^{-1}. MS (ESI, +ve) *m*/*z*: 388 ([M + H]$^+$, 100%), 410 ([M + Na]$^+$, 18). HRMS: [M + H]$^+$ calcd for $C_{22}H_{30}NO_5$, 388.2124; found, 388.2123.

Compound ***25***. Following a reported protocol,[18] a magnetically stirred mixture of ketone **24** (380 mg, 0.98 mmol) in Et_2O (5 mL) was treated with TCDI (530 mg, 3.0 mmol) and DMAP (370 mg, 3.0 mmol). The solvent was evaporated, and the resulting oil was heated at 80 °C for 5 h. The black residue was subjected to chromatography (silica, 50:1 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.7), thionoester **25** (400 mg, 83%) as a yellow amorphous solid, $[\alpha]_D^{20}$ = +215.5 (*c* 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H, H-2″), 7.59 (s, 1H, H-4″), 6.99 (m, 1H, H-3″), 5.71 (m, 1H, H-14), 3.80 (s, 3H, H-22), 3.55 (m, 1H, H-6), 3.41 (m, 1H, H-2), 3.26 (dd, *J* = 13.5 and 9.6 Hz, 1H, H-15), 2.88 (s, 1H), 2.46−2.40 (complex m, 1H), 2.32−2.26 (complex m, 2H), 2.14 (m, 1H), 2.04−1.86 (complex m, 5H), 1.83−1.71 (complex m, 2H), 1.70−1.61 (complex m, 4H), 1.46−1.42 (complex m, 1H), 1.40 (d, *J* = 7.2 Hz, 3H), 1.37−1.35 (complex m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3 (C16), 183.5 (C1″), 173.0 (C18), 167.5 (C19), 136.9 (C2″), 130.4 (C3″), 121.4 (C4″), 118.3 (C17), 81.0 (C14), 80.2 (C20), 69.3 (C9), 65.2 (C6), 55.4 (C2), 52.7, 50.1, 49.8, 49.5, 45.0, 43.8, 37.1, 30.8, 27.3, 26.5, 25.4, 24.9, 23.0 (C1). IR (KBr) ν_{max}: 2946, 2864, 1734, 1648, 1464, 1384, 1333, 1285, 1235, 1166, 1095, 1043, 1027, 988, 907, 728, 653 cm^{-1}. MS (ESI, +ve) *m*/*z*: 498 ([M + H]$^+$, 100%), 520 ([M + Na]$^+$, 5). HRMS: [M + H]$^+$ calcd for $C_{26}H_{32}N_3O_5S$, 498.2063; found, 498.2063.

*GB24 (****19****)*. A magnetically stirred mixture of thionoester **25** (320 mg, 0.64 mmol) in dry toluene (20 mL) at 100 °C was treated with AIBN (5.25 mg, 0.0032 mmol) and Bu_3SnH (0.21 mL, 0.77 mmol). After stirring under the same temperature for 16 h, further portions of AIBN (10.5 mg, 0.0064 mmol) and Bu_3SnH (0.21 mL, 0.77 mmol) were added. The reaction mixture was stirred for another 2 h before being concentrated under reduced pressure. The resulting yellow residue was subjected to chromatography (silica, 50:1 v/v CH_2Cl_2/MeOH elution) to afford two fractions. Concentration of fraction A (R_f = 0.55) gave GB24 (120 mg, 50%) as a white amorphous solid. The structural data were, in all respects, similar to those of an authentic sample from isolation work. Concentration of fraction B (R_f = 0.50) gave a white amorphous solid tentatively identified as ketone **24** (50 mg, 20%).

*GB25 (****16****)*. A magnetically stirred mixture of compound **19** (100 mg, 0.27 mmol) in EtOH (6 mL) at 0 °C was treated with $NaBH_4$ (102 mg, 2.70 mmol). The mixture was stirred at the same temperature for 2 h before being quenched by Na_2CO_3 (10 mL of a 1 M aqueous solution), and the solution was then extracted by CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The colouless oil was subjected to chromatography (silica, 50:2 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.4), GB25 (75 mg, 75%) as a white amorphous solid. The structural data were, in all respects, similar to those of an authentic sample from isolation work.

*GB14 (****14****)*. A magnetically stirred mixture of compound **16** (50 mg, 0.13 mmol) in pyridine (6 mL) was treated with Ac_2O (122 μL, 1.30 mmol) and DMAP (1.6 mg, 0.013 mmol). The mixture was stirred and heated at 70 °C for 14 h before being concentrated under high vacuum. The yellow oil so-formed was subjected to chromatography (silica, 50:2 v/v CH_2Cl_2/MeOH elution) to afford, after concentration of the relevant fractions (R_f = 0.6), GB14 (40 mg, 71%) as a white amorphous solid. The structural data were, in all respects, similar to those of an authentic sample from isolation work.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.7b02065.

^{1}H and ^{13}C NMR spectra of compounds **14**−**25** (PDF)

X-ray data for compounds **14** (CIF), **15** (CIF), **16** (CIF), **17** (CIF), **18** (CIF), **19** (CIF), and **26** (CIF) (ZIP)

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Notes

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