CHEMISTRY
AN ASIAN JOURNAL

DOI: 10.1002/asia.201000556

Synthetic Studies toward Galbulimima Alkaloid (−)-GB 13 and (+)-GB 16 and (−)-Himgaline

Weiwei Zi, Shouyun Yu, and Dawei Ma*[a]

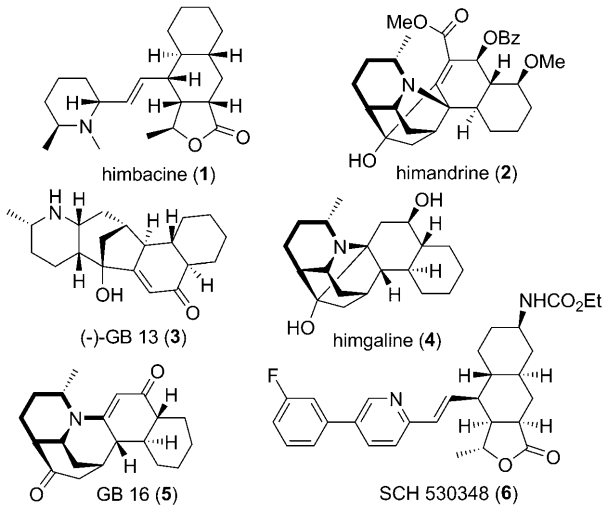
Dedicated to Professor Eiichi Nakamura on the occasion of his 60th birthday

Abstract: Condensation of (*S*)-3-aminobutan-1-ol with 1,3-cyclohexanedione followed by an intramolecular alkylation afforded bicyclic enamine **32**, which was converted into enone **35** through a diastereoselective hydrogenation. Mukaiyama–Michael addition of a bicyclic silyl enol ether to **35** and subsequent stereochemistry inversion by means of an oxidation/reduction strategy provided lactone **41**. After reduction of lactone **41** with LAH, Swern oxidation was carried out to give enone **46** upon a spontaneous intramolecular aldol reaction and cleavage of the ketal protecting group. SmI_2-mediated carbonyl–alkene reductive coupling of **46** proceeded smoothly in refluxing tetrahydrofuran to deliver pentacyclic intermediate **49**, which was oxidized with 2-iodoxybenzoic acid and then treated with trifluoroacetic acid to furnish (−)-GB 13. The overall yield was 6.1% over 19 linear steps. By following the known procedure, our synthetic (−)-GB 13 was converted into himgaline. In addition, by starting from lactone **41**, the first total synthesis of (+)-GB 16, a newly isolated member of the galbulimima alkaloid family, was achieved. This synthesis features an intramolecular condensation between an amine and a 1,3-diketone moiety.

Keywords: alkaloids · condensation · Michael addition · reductive coupling · total synthesis

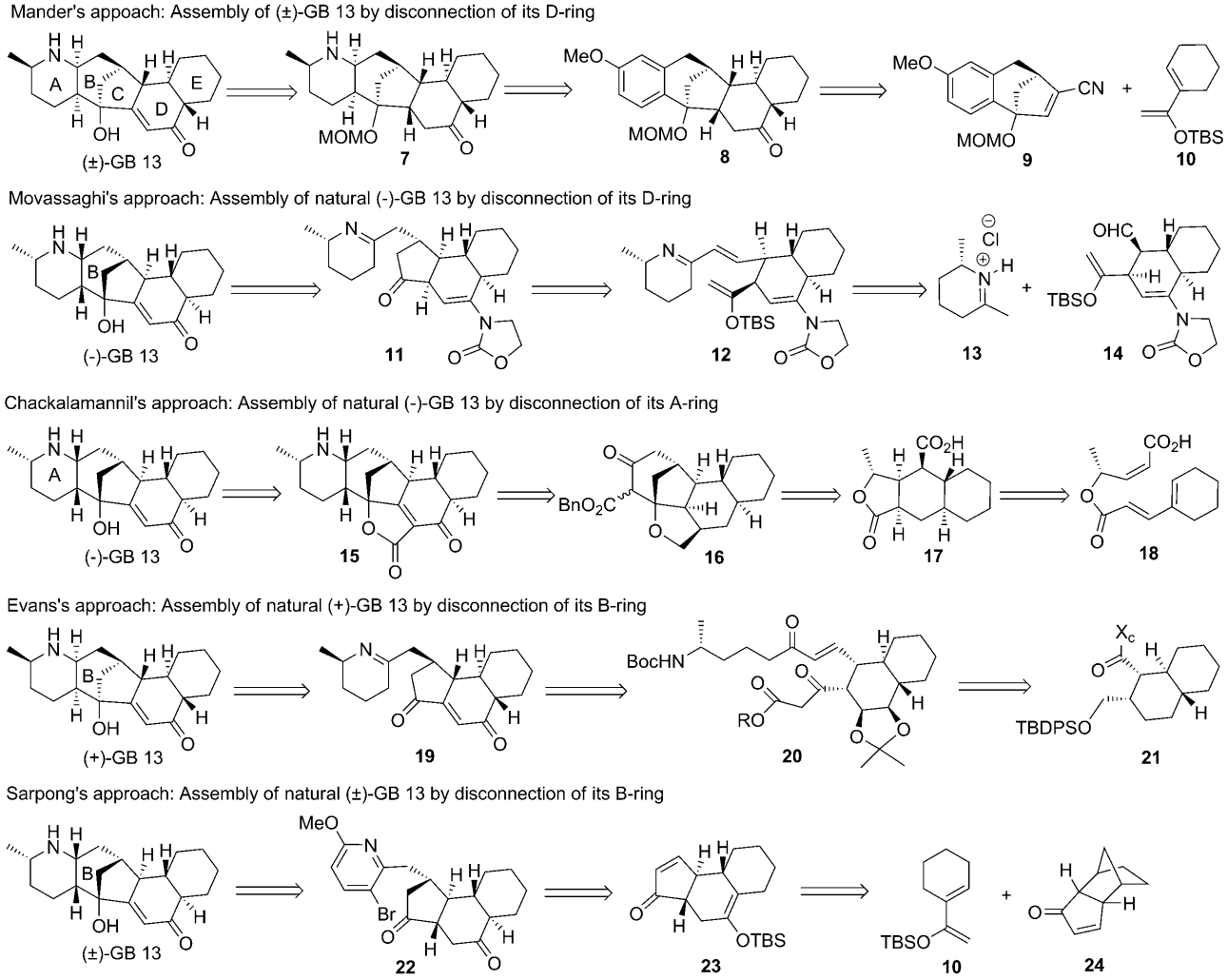
Introduction

Himbacine (**1**),[1] himandrine (**2**),[2] galbulimima alkaloid 13 ((−)-GB 13, **3**),[3] and himgaline (**4**)[4] represent class I–III galbulimima alkaloids that were isolated from the bark of *Galbulimima belgraveana*, a rain forest tree native to Northern Australia and Papua New Guinea. Recently, GB 16 (**5**),[5] a new member of this family, was discovered by Mander and co-workers. These alkaloids have received great attention from the pharmaceutical industry, mainly because the *Galbulimima belgraveana* bark has been used as a medicinal substance and himbacine (**1**) has shown potent muscarinic antagonist activity.[6] On the basis of a series of structure–activity relationship (SAR) studies by using himbacine as a leading compound, a number of thrombin receptor antagonists have been developed. Among them, SCH 530348 (**6**) is now in phase III clinic trials for treatment of acute coronary syndrome.[6a]



During the past decade, the fascinating structure of GB 13 has received considerable attention from synthetic chemists. This campaign has led to a number of total syntheses of

[a] W. Zi, Dr. S. Yu, Prof. Dr. D. Ma
State Key Laboratory of Bioorganic and Natural Products Chemistry
Shanghai Institute of Organic Chemistry
Chinese Academy of Sciences
354 Fenglin Lu, Shanghai 200032 (China)
Fax: (+86) 21-64166128
E-mail: madw@mail.sioc.ac.cn



Scheme 1. Previous studies on the total synthesis of GB 13. MOM = methoxymethyl, TBS = *tert*-butyldimethylsilyl, Bn = benzyl, TBDPS = *tert*-butyldiphenylsilyl.

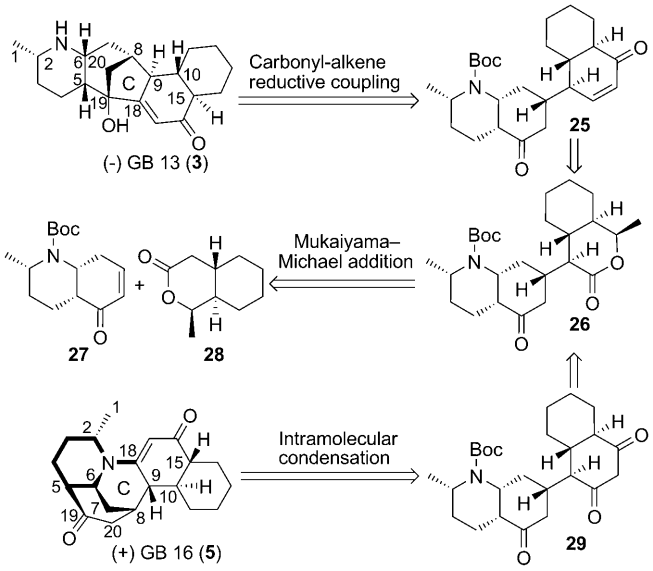
himbacine,[1b–d] five total syntheses of GB 13,[3a–e] two total syntheses of himgaline,[3c,d] and one total synthesis of himandrine.[2d] For the synthesis of (±)-GB 13, Mander and McLachlan used a Diels–Alder reaction of olefin **9** and diene **10** as the key step to set up the D-ring in the intermediate **8**, and then converted the aromatic ring into the required piperidine ring (Scheme 1).[3a] Movassaghi and co-workers achieved the first total synthesis and the assignment of the absolute stereochemistry of natural (−)-GB 13 by forming its B-ring (from **11**) at the final stage by using a biomimetically inspired strategy. The requisite imino ketone **11** was assembled by a vinyl radical cyclization of enol ether **12** that was generated by condensation by iminium chloride **13** and aldehyde **14**.[3b] By constructing the A-ring (from **16** to **15**) at a late stage, Chackalamannil and co-workers accomplished the second total synthesis of (−)-GB 13. Their key intermediate **17** was obtained by an intramolecular Diels–Alder reaction of **18**.[3c] Soon after that, Evans and Adams disclosed their total synthesis towards (+)-GB 13, in which the B-ring was conducted by an intramolecular enamine aldol reaction of **19** at the final stage.[3d] The required enamine ketone **19** was elaborated by an intramolecular Michael addition of enone **20** and subsequent transformations, whereas **20** was synthesized from Diels–Alder adduct **21**. Recently, Larson and Sarpong applied a rhodium(I)-catalyzed ketone hydroarylation of **22** to achieve the total synthesis of (±)-GB 13, in which the key intermediate **22** was generated from the 1,2-addition of the lithioanion of bromomethoxypicoline to enone **23**, a Diels–Alder reaction, and subsequent retro-Diels–Alder reaction product from diene **10** and dienone **24**.[3e]

Abstract in Chinese:

在本文中我们描述了一条合成生物碱(-)-GB 13 及相关天然产物的一条比较会聚的路线。其关键步骤为 Mukaiyama Michael 加成和二碘化钐作用下的羰基-烯烃的还原偶联。

CHEMISTRY
AN ASIAN JOURNAL

Upon studying the literature, we were surprised to find that no one has reported a strategy to synthesize GB 13 by introducing its C-ring at a late stage, as this would probably provide a more-convergent approach to GB 13 because we could disconnect it into two equally complex fragments. On the basis of this analysis, we started our retrosynthetic analysis for (−)-GB 13 (**3**). As depicted in Scheme 2, we envisioned that the C-ring of (−)-GB 13 could be constructed by

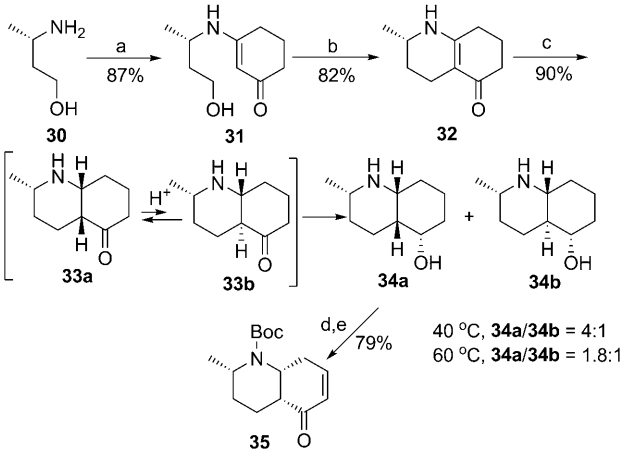


Scheme 2. Retrosynthetic analysis of (−)-GB 13 and (+)-GB 16.

a SmI_2-mediated carbonyl–alkene reductive coupling reaction[7,8] of enone **25**. The enone **25** could be assembled from lactone **26** by ring-opening and a subsequent intramolecular aldol reaction. The bond disconnection of **26** would give two less-complicated bicyclic intermediates **27** and **28**, which could be connected to each other by a Mukaiyama–Michael addition.[9] Apparently, by starting from the lactone **26**, 1,3-diketone **29** could be assembled by ordinary transformations. This intermediate would in turn provide (+)-GB 16 through the intramolecular condensation between its secondary amine moiety and its 1,3-diketone. Herein, we detail our results.[10]

Results and Discussion

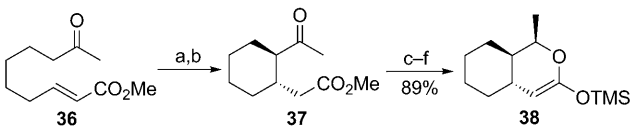
Our synthesis started from the preparation of the two required partners for the Mukaiyama–Michael addition. As shown in Scheme 3, condensation of commercially available (*S*)-3-aminobutan-1-ol (**30**) with 1,3-cyclohexanedione in refluxing tetrahydrofuran gave enamine **31** in 87% yield.[11] Treatment of **31** with CBr_4/Ph_3P followed by Et_3N-mediated substitutive cyclization afforded bicyclic enamine **32**.[12a] The next step was a stereoselective hydrogenation of the C=C double bond of **32**. On the basis of our previous observations,[12] we anticipated that the methyl group would shield



Scheme 3. Reagents and conditions: a) 1,3-cyclohexanedione, 4 Å MS, THF, reflux; b) CBr_4, Ph_3P, CH_3CN, RT; then DIPEA, reflux; c) Pt/C, H_2 (80 atm.), AcOH, 45 °C, *cis*/*trans* 4:1; d) $(Boc)_2O$, NaOH, benzene/THF/H_2O, reflux; e) IBX, DMSO, 65 °C.

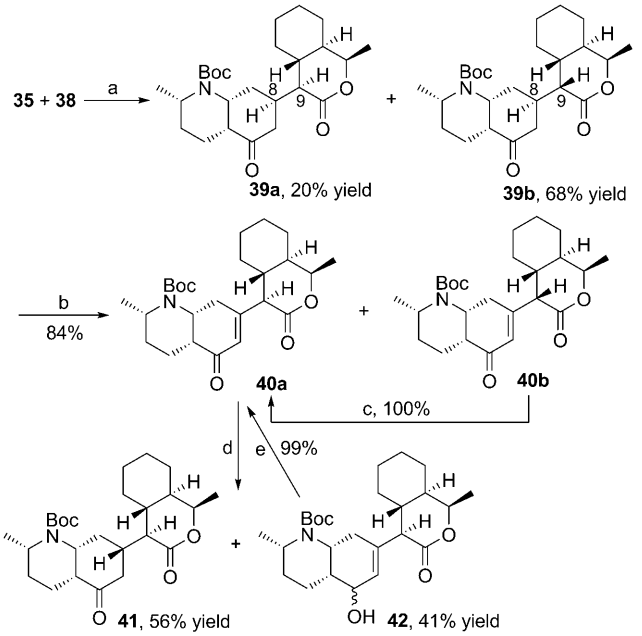
the α face of the enamine **32**, thus directing the hydrogenation to the desired β face to form the reduction product (**34a**). Accordingly, Pt/C-catalyzed hydrogenation of **32** was carried out in acetic acid at 60 °C and 80 atm. After the reaction, the desired **34a** was isolated together with *trans*-isomer **34b** in a ratio of 1.8:1. We reasoned that the formation of **34b** might result from partial epimerization of the hydrogenation intermediate **33a**, and therefore decided to inhibit this side-reaction by reducing the reaction temperature. To our delight, a better ratio (4:1) was observed, when the hydrogenation was conducted at 40 °C. Further reducing of the reaction temperatures inhibited the hydrogenation. The separated **34a** was protected with $(Boc)_2O$ (Boc = *tert*-butoxycarbonyl) and oxidized with 2-iodoxybenzoic acid (IBX)[13] to deliver enone **35**.

The preparation of *O*-silylated ketene acetal **38** is depicted in Scheme 4. Intramolecular Michael addition of **36** under the action of (*S*)-1-phenylethylamine proceeded smoothly to deliver γ-keto ester **37**, after KOH-mediated isomerization and subsequent esterification.[14] Diastereoselective reduction of the keto moiety in **37** with $NaBH_4$ at −78 °C followed by cyclization under acidic conditions provided a lactone. Following deprotonation of this lactone with lithium diisopropylamide (LDA), the resultant anion was trapped with trimethylsilyl chloride to deliver an 89% yield over four steps.



Scheme 4. Reagents and conditions: a) (*S*)-1-phenylethylamine, 4 Å MS, $MgSO_4$, THF, RT; b) KOH, MeOH, reflux, acid workup then CH_2N_2, Et_2O; 75% yield for 2 steps; c) $NaBH_4$, MeOH, −78 °C; d) PTSA·H_2O, CH_2Cl_2, reflux; e) LDA, then TMSCl, THF, −78 °C.

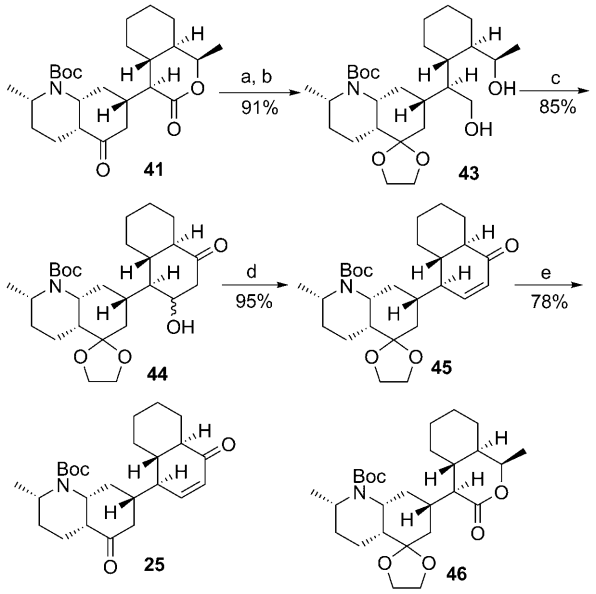
The Michael addition of silyl enol ether **38** onto enone **35** was achieved under $TiCl_4$ catalysis at −78 °C,[9] affording Michael adduct **39** as a diastereomeric mixture in a ratio of about 3.5:1 (Scheme 5). As predicted, the nucleophilic agent **38** favored addition on enone **35** from the *Re* face to give the products with an *R* configuration at the newly generated C8 stereocenter. This result was further confirmed by single-crystal X-ray analysis of **39b**.[15]



Scheme 5. Reagents and conditions: a) $TiCl_4$, CH_2Cl_2, −78 °C; b) IBX, DMSO, 70 °C; c) DBU, CH_2Cl_2, RT; d) Pd/C, H_2, *i*PrOH; e) DMP, $NaHCO_3$, CH_2Cl_2. DMSO = dimethyl sulfoxide.

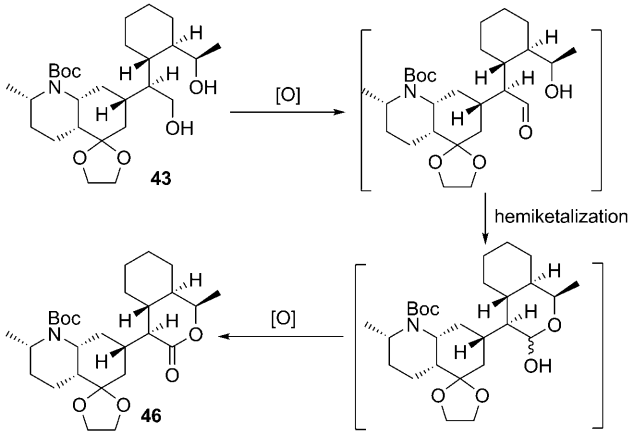
As the stereochemistry at the C8-position in both **39a** and **39b** was not required for synthesizing the target molecule, we decided to invert it by an oxidation/reduction approach. Accordingly, oxidation of the mixture of **39a** and **39b** with IBX produced a mixture of enone **40a** and its C9 epimer **40b**. It was found that, during column chromatography on silica gel, **40b** partially isomerized into **40a**, which indicated that the latter is the thermodynamically more-stable isomer. Complete isomerization was achieved by treatment of the mixture of **40a** and **40b** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), thereby giving **40a** in an 84% yield. Hydrogenation of **40a** afforded the reduced ketone **41** that has the desired stereochemistry at both the C8- and C9-positions. In this case, alcohol **42** was isolated in 41% yield as a side-product. As **42** could be transformed into **40a** by Dess–Martin oxidation,[16] we were able to obtain ketone **42** in 80% combined yield after two cycles.

Our next task was transforming the lactone moiety in **41** into the desired enone part. As outlined in Scheme 6, treatment of the ketone **41** with ethylene glycol followed by lithium aluminum hydride (LAH) reduction afforded diol **43** with 91% yield. At this stage, we planned to synthesize the



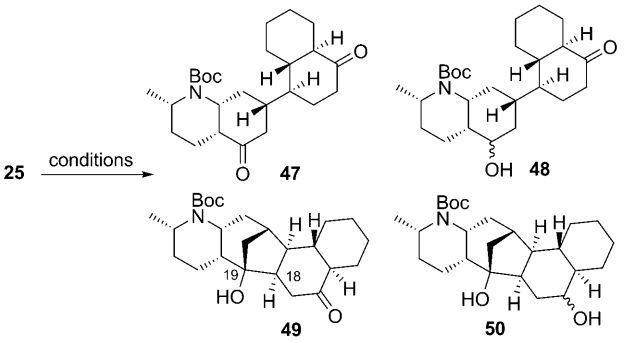
Scheme 6. Reagents and conditions: a) glycol, PTSA·H_2O, toluene, Dean–Stark; b) LAH, THF, 0 °C to RT; c) TFAA/DMSO, DBU, CH_2Cl_2, −78 °C–RT; d) TFAA, Et_3N, CH_2Cl_2, RT; e) PTSA·H_2O, acetone, H_2O, reflux, 4 days.

required β-hydroxy ketone **44** by oxidation of the diol **43** and a subsequent intramolecular aldol reaction. Initially, Dess–Martin periodinane (DMP) was employed as the oxidizing agent. This reaction afforded the desired product **44**, but the yield was not satisfactory owing to formation of lactone **46**. This side-product was probably generated through a cascade oxidation–hemiketalization–oxidation[19] process as indicated in Scheme 7. After the failed attempt of inhibiting the formation of **46** by changing the oxidizing agent to pyridinium chlorochromate (PCC)[17] or tetrapropylammonium perruthenate (TPAP)/*N*-methylmorpholine-*N*-oxide (NMO),[18] we were pleased to find that diol **43** could be converted into **44** with 85% yield under modified Swern oxidation conditions (by using DBU but not triethylamine



Scheme 7. Possible pathway for the conversion of diol **43** into lactone **46**.

Table 1. SmI_2-mediated carbonyl–alkene reductive coupling reaction of the enone **25** under different conditions.

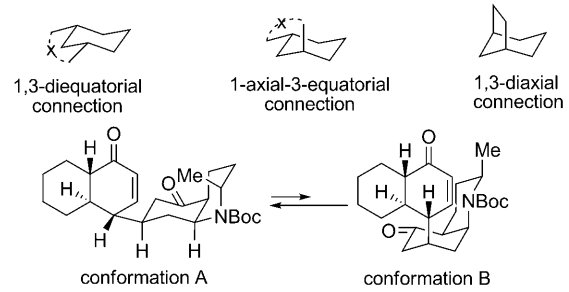


Entry	Conditions	Products (yield [%])	
1	SmI_2/HMPA/*t*BuOH, −78 to 0 °C	**47** (55)	**48** (7)
2	SmI_2/HMPA, RT	**47** (46)	**48** (12)
3	SmI_2/MeOH, RT	**47** (33)	**48** (17)
4	SmI_2, reflux	**49** (45–65)	**50** (12–20)
5	SmI_2, reflux, then Dess–Martin oxidation	**49** (75)	

(TEA) or *N*,*N*-diisopropylethylamine (DIPEA) as a base).[20,21] In this case, no **46** was detected, which indicated that the cascade oxidation–hemiketalization–oxidation process could be blocked by using DBU as a base in the Swern oxidation.[20] Next, treatment of **44** with trifluoroacetic anhydride (TFAA) afforded elimination product **45**. Selective removal of the ketal protecting group in **45** without touching the Boc-protecting group proved to be challenging. After failure to cleave this group under mild conditions, such as pyridinium *para*-toluenesulfonate (PPTS)/acetone/H_2O,[22a] $In(OTf)_3$/acetone,[22b] and $CeCl_3{\cdot}7H_2O$/NaI/CH_3CN,[22c] we were pleased to find that exposure of **45** to *para*-toluenesulfonic acid (PTSA) in wet acetone[22d] under reflux for four days produced the desired enone **25** in 78% yield.

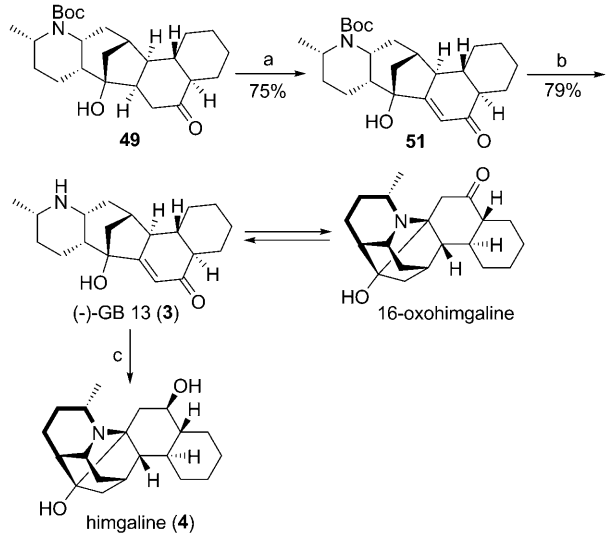
With the enone **25** in hand, SmI_2-mediated carbonyl–alkene reductive coupling was then attempted. Initially, we treated **25** with SmI_2/hexamethylphosphoramide (HMPA)/*tert*-butanol,[23a] SmI_2/HMPA,[23b] or SmI_2/methanol,[23c] at reaction temperatures ranging from −78 to 0 °C and observed that these typical reductive coupling reaction conditions only produced simple reduction products **47** and **48** (Table 1, entries 1–3).[24] After careful screening of the existing reaction conditions, we were pleased to discover that by adding enone **25** slowly to a refluxing solution of SmI_2 in tetrahydrofuran in the absence of any additives,[25] the desired reductive coupling product **49** could be isolated in 45–65% yields, together with the over-reduced product **50** with 12–20% yields (Table 1, entry 4). Further attempts revealed that a satisfactory yield for **49** could be obtained by SmI_2-mediated reductive cyclization and subsequent oxidation of the mixture of the cyclization products with Dess–Martin periodinane (Table 1, entry 5).

During the course of the SmI_2-mediated reductive cyclization, a [3.2.1] bicyclic core structure was created. Among the three possibilities to form a [3.2.1] bicyclic core, as shown in Scheme 8, only a 1,3-diaxial connection is favored. Obviously, only conformation B is suitable for this transformation, and therefore, heating the reaction mixture was required to get the thermodynamically less-stable conformation B. As such, only the conditions indicated in Table 1, entry 5 successfully produced the desired cyclization products.



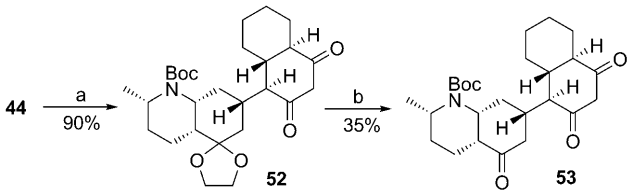
Scheme 8. Favored conformation for carbonyl–alkene reductive coupling of **46**.

The completion of the synthesis of (−)-GB 13 and its transformation into (−)-himgaline are outlined in Scheme 9. Dehydrogenation of the ketone **49** with IBX[3b,13] afforded *N*-Boc-protected GB 13 **51** with 75% yield. Removal of the Boc group of **51** with TFA followed by an aqueous workup provided target molecule **3** in 79% yield. Owing to the known balance between GB 13 and 16-oxahimgaline, our synthetic (−)-GB 13 contained about 25% 16-oxohimgaline in C_6D_6, which is consistent with the observation of Evans and Adams[3d] (containing 10% 16-oxohimgaline) and Larson and Sarpong[3e] (containing 30% 16-oxohimgaline). To further confirm our synthetic result, conversion of this mixture into (−)-himgaline (**4**) was conducted through HOAc treatment and subsequent reduction with $NaBH(OAc)_3$. The analytical data for synthetic **4** were in agreement with those of natural himgaline.



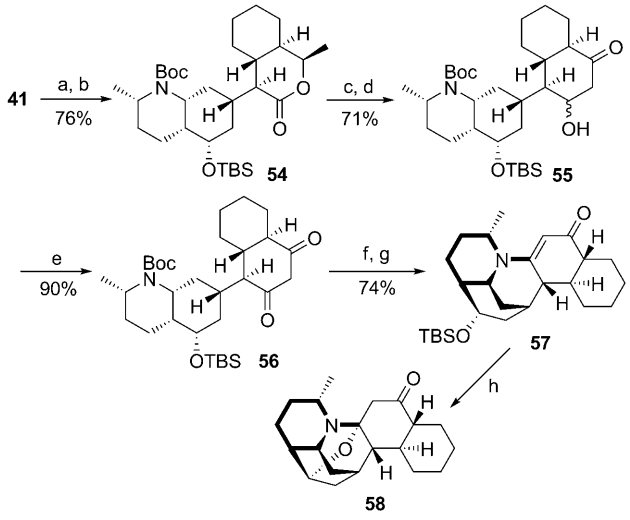
Scheme 9. Reagents and conditions: a) IBX, DMSO, 70 °C; b) TFA, CH_2Cl_2, and then NaOH; c) HOAc, CH_3CN; then $NaBH(OAc)_3$.

We next moved our attention to the synthesis of (+)-GB 16. Initially, β-hydroxy ketone **44** was chosen as an advanced intermediate. However, after its oxidation to 1,3-diketone **52**,[26] cleavage of the ketal protecting group gave ketone **53** in only 35% yield owing to the formation of some unidentified side products (Scheme 10). This result



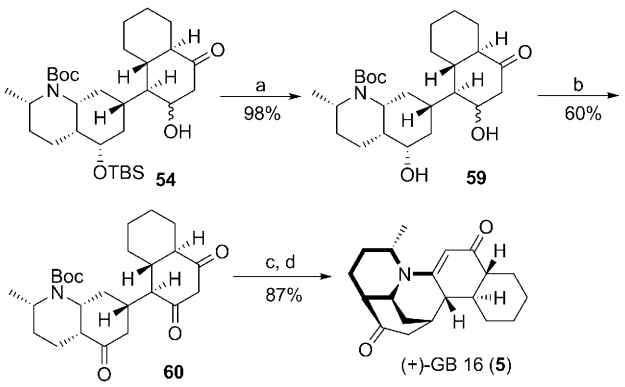
Scheme 10. Reagents and conditions: a) PCC, CH_2Cl_2, RT; b) PTSA/acetone/H_2O, reflux.

made us want to continue our synthesis by using lactone **41**. At this stage, we decided to reduce the ketone group of **41** and then protect the resulting hydroxyl group with an easily removable silyl ether. Consequently, reduction of **41** with $NaBH_4$ at −78 °C followed by treatment with TBSCl in *N*,*N*-dimethylformamide provided **54** in 76% yield (Scheme 11). LAH reduction of the lactone **54** to the corresponding diol, which was subjected to Swern oxidation and subsequent intramolecular aldol reaction provided β-hydroxy ketone **55** in 71% yield. PCC oxidation of **55** produced 1,3-diketone **56**, which was treated with TFA to remove the Boc group. The liberated amine was heated in toluene to furnish condensation product **57**. Unfortunately, desilylation of **57** under various conditions (HF/CH_3CN,[27a] HF/pyridine,[27b] PTSA/MeOH,[27c] and tetrabutylammonium fluoride (TBAF)/THF[27d]) did not provide the free alcohol, but gave the intramolecular Michael addition product **58**, presumably because the free hydroxyl group is close to the enone moiety.



Scheme 11. Reagents and conditions: a) $NaBH_4$, MeOH/THF, −78 °C; b) TBSCl, imidazole, cat. DMAP, DMF, RT; c) LAH, THF, RT; d) TFAA/DMSO, DBU, CH_2Cl_2, −78 °C to RT; e) PCC, CH_2Cl_2, RT; f) TFA, CH_2Cl_2, RT; g) toluene, NaOAc, Dean–Stark; h) HF, CH_3CN, 75% yield; or TBAF, THF, 82% yield. DMAP = 4-dimethylaminopyridine.

To solve the intramolecular Michael addition problem, it seemed reasonable to remove the TBS group before the formation of the enone part. Thus, treatment **37** with aqueous HF in acetonitrile afforded diol **59**, which was then oxidized with PCC to provide ketone **60** (Scheme 12). Deprotection of the Boc group with TFA followed by heating the free amine in toluene delivered (+)-GB 16 (**6**) in 87% yield. The analytical data of synthetic **5** are identical with those reported for natural (+)-GB 16. Its structure was further confirmed by X-ray crystal structure analysis,[15] as indicated in Scheme 12.



Scheme 12. Reagents and conditions: a) HF, CH_3CN, −20 °C; b) PCC, CH_2Cl_2, RT; c) TFA, CH_2Cl_2, RT; d) toluene, NaOAc, Dean–Stark.

CHEMISTRY
AN ASIAN JOURNAL

Conclusions

We have developed a novel and convergent route for the asymmetric syntheses of alkaloids (−)-GB 13, (+)-GB-16, and himgaline. The key transformations in our synthesis include: 1) the connection of two bicyclic parts by means of a Mukaiyama–Michael addition, 2) the formation of the C-ring by a SmI_2-mediated carbonyl–alkene reductive coupling (for alkaloid (−)-GB 13), and 3) the intramolecular condensation between an amine and a 1,3-diketone moiety (for alkaloid (+)-GB 16). Our new strategy offers a more-convergent approach for assembling these natural products and their analogues, which will prompt the syntheses of other galbulimima alkaloids and their SAR studies.

Acknowledgements

The authors are grateful to the National Basic Research Program of China (973 Program, grant no.2010CB833200), the Chinese Academy of Sciences, and the National Natural Science Foundation of China (grant nos. 20632050 and 20921091) for their financial support.

[1] For isolation, see: a) R. F. C. Brown, R. Drummond, A. C. Fogerty, G. K. Hughes, J. T. Pinhey, E. Ritchie, W. C. Taylor, *Aust. J. Chem.* **1956**, *9*, 283; synthesis see: b) D. J. Hart, W.-L. Wu, A. P. Kozikowski, *J. Am. Chem. Soc.* **1995**, *117*, 9369; c) S. Chackalamannil, R. J. Davies, T. Asberom, D. Doller, D. Leone, *J. Am. Chem. Soc.* **1996**, *118*, 9812; d) M. Takadoi, T. Katoh, A. Ishiwata, S. Terashima, *Tetrahedron Lett.* **1999**, *40*, 3399; e) K. Tchabanenko, R. M. Adlington, A. R. Cowley, J. E. Baldwin, *Org. Lett.* **2005**, *7*, 585; f) K. Tchabanenko, R. J. S. Chesworth, Parker, N. K. Anand, A. T. Russell, R. M. Adlington, J. E. Baldwin, *Tetrahedron* **2005**, *61*, 11649.

[2] For isolation, see: a) S. V. Binns, P. J. Dunstan, G. B. Guise, G. M. Holder, A. F. Hollis, R. S. McCredie, J. T. Pinhey, R. H. Prager, M. Rasmussen, E. Ritchie, W. C. Taylor, *Aust. J. Chem.* **1965**, *18*, 569; b) L. N. Mander, R. H. Prager, M. Rasmussen, E. Ritchie, W. C. Taylor, *Aust. J. Chem.* **1967**, *20*, 1473; c) L. N. Mander, R. H. Prager, M. Rasmussen, E. Ritchie, W. C. Taylor, *Aust. J. Chem.* **1967**, *20*, 1705. Synthesis: see d) M. Movassaghi, M. Tjandra, J. Qi, *J. Am. Chem. Soc.* **2009**, *131*, 9648.

[3] For isolation, see references [2a–c]; for syntheses, see: a) L. N. Mander, M. M. McLachlan, *J. Am. Chem. Soc.* **2003**, *125*, 2400; b) M. Movassaghi, D. K. Hunt, M. Tjandra, *J. Am. Chem. Soc.* **2006**, *128*, 8126; c) U. Shah, S. Chackalamannil, A. K. Ganguly, M. Chelliah, S. Kolotuchin, A. Buevich, A. McPhail, *J. Am. Chem. Soc.* **2006**, *128*, 12654; d) D. A. Evans, D. J. Adams, *J. Am. Chem. Soc.* **2007**, *129*, 1048; e) K. K. Larson, R. Sarpong, *J. Am. Chem. Soc.* **2009**, *131*, 13244.

[4] For isolation, see references [2a–c]; for syntheses, see references [3c] and [3d].

[5] L. N. Mander, A. C. Willis, A. J. Herlt, W. C. Taylor, *Tetrahedron Lett.* **2009**, *50*, 7089.

[6] a) S. Chackalamannil, Y. Wang, W. J. Greenlee, Z. Hu, Y. Xia, H.-S. Ahn, G. Boykow, Y. Hsieh, J. Palamanda, J. Agans-Fantuzzi, J. Agans-Fantuzzi, S. Kurowski, M. Graziano, M. Chintala, *J. Med. Chem.* **2008**, *51*, 3061; b) M. J. Malaska, A. H. Fauq, A. P. Kozikowski, P. J. Aagaard, M. McKinney, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 61.

[7] For reviews, see: a) D. J. Edmonds, D. Johnston, D. Procter, *J. Chem. Rev.* **2004**, *104*, 3371; b) K. C. Nicolaou, S. P. Ellery, J. S. Chen, *Angew. Chem.* **2009**, *121*, 7276; *Angew. Chem. Int. Ed.* **2009**, *48*, 7140.

[8] For some applications in the natural product synthesis of this method, see: a) H. Takakura, K. Noguchi, M. Sasaki, K. Tachibana, *Angew. Chem.* **2001**, *113*, 1124; *Angew. Chem. Int. Ed.* **2001**, *40*, 1090; b) N. Hori, H. Matsukura, T. Nakata, *Org. Lett.* **1999**, *1*, 1099; c) K. Suzuki, T. Nakata, *Org. Lett.* **2002**, *4*, 3943; d) T. M. Nguyen, D. Lee, *Tetrahedron Lett.* **2002**, *43*, 4033.

[9] K. Narasaka, K. Soai, T. Mukaiyama, *Chem. Lett.* **1974**, 1223.

[10] Part of this work has been disclosed in a previous communication, see: W. Zi, S. Yu, D. Ma, *Angew. Chem.* **2010**, *122*, 6023; *Angew. Chem. Int. Ed.* **2010**, *49*, 5887.

[11] Y. Aoyagi, T. Mizusaki, M. Shishikura, T. Komine, T. Yoshinaga, H. Inaba, A. Ohta, K. Takeya, *Tetrahedron* **2006**, *62*, 8533.

[12] a) X. Pu, D. Ma, *Angew. Chem.* **2004**, *116*, 4318; *Angew. Chem. Int. Ed.* **2004**, *43*, 4222; b) X. Pu, D. Ma, *J. Org. Chem.* **2006**, *71*, 6562; c) X. Pu, D. Ma, *J. Org. Chem.* **2003**, *68*, 4400.

[13] K. C. Nicolaou, T. Montagnon, P. S. Baran. Y.-L. Zhong, *J. Am. Chem. Soc.* **2002**, *124*, 2245.

[14] a) J. d'Angelo, F. Dumas, *Tetrahedron: Asymmetry* **1990**, *1*, 167; b) Y. Hirai, T. Terada, T. Momose, *J. Chem. Soc. Perkin Trans. 1* **1992**, 509; c) Y. Fujiwara, M. Okamoto, *Chem. Pharm. Bull.* **1989**, *37*, 1458.

[15] CCDC 770766 (**39b**) and CCDC 770765 ((+)-GB 16) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif..

[16] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155.

[17] E. J. Corey, J. W. Suggs, *Tetrahedron Lett.* **1975**, *16*, 2647.

[18] S. V. Ley, J. Norman, W. P. Griffith, S. P. Marsden, *Synthesis* **1994**, 639.

[19] a) R. Carter, K. Hodgetts, J. McKenna, P. Magnus, S. Wren, *Tetrahedron* **2000**, *56*, 4367; b) J. Młynarski, A. Banaszek, *Tetrahedron: Asymmetry* **2000**, *11*, 3737.

[20] a) D. L. Boger, O. Hueter, M. Zhang, *J. Am. Chem. Soc.* **1995**, *117*, 11839; b) D. L. Boger, L. C. Jacobson, *J. Org. Chem.* **1990**, *55*, 1919.

[21] K. Omura, A. K. Sharma, D. Swern, *J. Org. Chem.* **1976**, *41*, 957.

[22] a) R. Sterzycki, *Synthesis* **1979**, 724; b) B. T. Gregg, K. C. Golden, J. F. Quinn, *J. Org. Chem.* **2007**, *72*, 5890; c) E. Marcantoni, F. Nobili, G. Brtoli, M. Bosco, L. Sambri, *J. Org. Chem.* **1997**, *62*, 4183; d) S. Borrelly, L. A. Paquette, *J. Am. Chem. Soc.* **1996**, *118*, 727.

[23] a) H. Sakai, H. Hagiwara, Y. Ito, T. Hoshi, T. Suzuki, M. Ando, *Tetrahedron Lett.* **1999**, *40*, 2965; b) T. Kan, S. Hosokawa, M. Oikawa, S. Ito, F. Matsuda, H. Shirahama, *J. Org. Chem.* **1994**, *59*, 5532; c) M. Kito, T. Sakai, N. Haruta. H. Shirahama, F. Matsuda, *Synlett* **1996**, 1057.

[24] a) G. A. Molander, C. Kenny, *J. Am. Chem. Soc.* **1989**, *111*, 8236; b) J. H. Rigby, A. Cacezza, M. J. Heeg, *J. Am. Chem. Soc.* **1998**, *120*, 3664.

[25] a) K. Takatori, Y. Takeuchi, Y. Shinohara, K. Yamaguchi, M. Nakamura, T. Hirosawa, T. Shimizu, M. Saito, S. Aizawa, O. Sugiyama, Y. Ohtsuka, M. Kajiwara, *Synlett* **1999**, 975; b) H. M. R. Hoffmann. I. Münnich. O. Nowitzki, H. Stucke, D. J. Williams, *Tetrahedron* **1996**, *52*, 11783; c) O. Nowitzki, I. Münnich, H. Stucke, H. M. R. Hoffmann, *Tetrahedron* **1996**, *52*, 11799.

[26] K. P. Cole, R. R. Hsung, *Org. Lett.* **2003**, *5*, 4843.

[27] a) R. F. Newton, D. P. Reynolds, M. A. W. Finch, D. P. Kelly, S. M. Roberts, *Tetrahedron Lett.* **1979**, *20*, 3981; b) K. C. Nicolaou, S. E. Webber, *Synthesis* **1986**, 453; c) H. Wetter, K. Oertle, *Tetrahedron Lett.* **1985**, *26*, 5515; d) E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190.

Received: August 11, 2010
Published online: December 14, 2010

