Syntheses of manzacidins: a stage for the demonstration of synthetic methodologies

Takuya Hashimoto and Keiji Maruoka*

Received 17th October 2007, Accepted 14th November 2007
First published as an Advance Article on the web 3rd December 2007
DOI: 10.1039/b716062c

Manzacidins, a family of bromopyrrole alkaloids, have attracted much attention from the synthetic community due to their intriguing structures, bearing chiral tertiary and secondary stereocentres in a 1,3-relationship, and biological activities. In this article, we summarise the approaches for the preparation of manzacidins using novel synthetic methodologies. Organocatalysis and Lewis acid catalysis, as well as transition-metal catalysis, offered efficient ways to access these molecules.

1 Introduction

Manzacidins A–C (Fig. 1) were first isolated from the Okinawan sponge *Hymeniacidon* sp. by Kobayashi *et al.* as a small family of the bromopyrrole alkaloids in 1991.[1] Following this discovery, manzacidin D from the coralline demosponge *Astrosclera willeyana*[2] and *N*-methylmanzacidin C from the marine sponge *Axinella brevistyla*[3] were identified as new analogs of the manzacidin family.[4] Despite the interesting pharmacological activities of some bromopyrrole alkaloids, such as α-adrenoceptor blockers, antagonists of the serotonergic receptor and actomyosin ATPase, the scarcity of manzacidins in the marine natural source hampered the evaluation of their biological activities.[5,6] At the same time, from the synthetic point of view, the structural uniqueness of manzacidins, containing a tetrahydropyrimidine core with the asymmetric 1,3-quaternary-tertiary centres, was considered to make them suitable target molecules to demonstrate the power of novel synthetic methodologies.

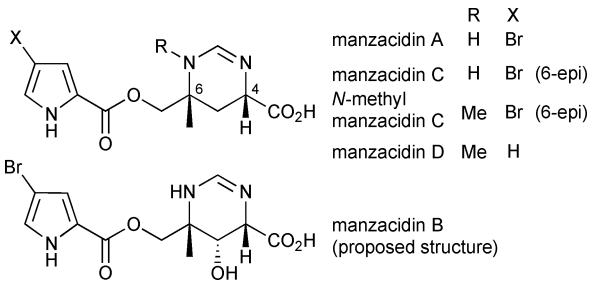


Fig. 1 Structures of manzacidins.

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto, 606-8502, Japan. E-mail: maruoka@kuchem.kyoto-u.ac.jp; Fax: +81 75-753-4041

Takuya Hashimoto was born in Osaka, Japan. He received his Ph.D. degree (2006) from Kyoto University under the direction of Professor Keiji Maruoka. After spending one year as a postdoctoral researcher, he was appointed as an assistant professor at Kyoto University in 2007. His research interests include the design of chiral acid and base catalysts for the development of new synthetic methodologies and the use of diazo compounds in organic synthesis.

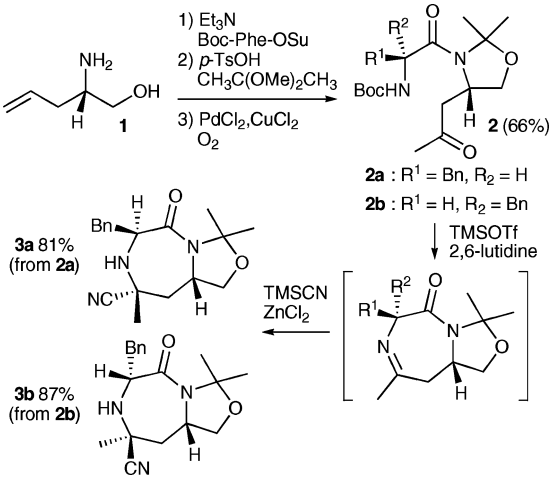
Takuya Hashimoto

Keiji Maruoka

Keiji Maruoka was born in Mie, Japan. He graduated from Kyoto University (1976) and received his Ph.D. (1980) from the University of Hawaii. He became an assistant professor of Nagoya University (1980) and an associate professor (1990) there. He moved to Hokkaido University as a full professor (1995–2001), and has been a professor of chemistry at Kyoto University since 2000. He is a member of the international advisory editorial board of Org. Biomol. Chem.*, and is a fellow of the Royal Society of Chemistry. He has a wide range of research interests in synthetic organic chemistry. His current research interests include bidentate Lewis acids in organic synthesis and practical asymmetric synthesis with designer chiral organocatalysts including chiral C2-symmetric phase-transfer catalysts.*

2 Diastereoselective Strecker reactions: the first total syntheses of manzacidin A and C by the Ohfune group[7]

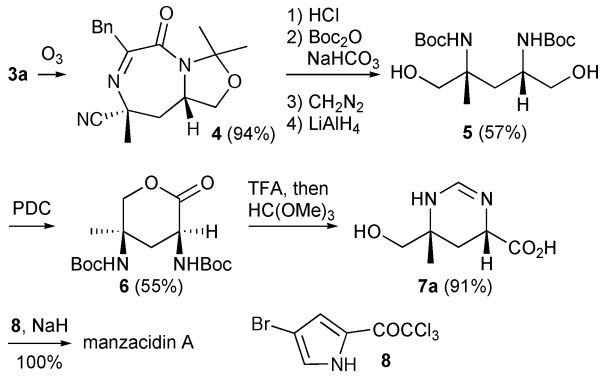
The first total syntheses and the determination of the absolute configurations of manzacidin A and C appeared in 2000 by Ohfune and co-workers.[7] The consideration of the biosynthetic pathway of manzacidins led them to presume the relationship of manzacidin A and C to be C-6 epimers with an identical *S*-configured C-4 stereocentre. According to this assumption, (*S*)-allylglycinol **1**, which has the absolute stereochemistry corresponding to C-4 of manzacidin A and C, was chosen as a starting material (Scheme 1). This material could be readily available from L-allylglycine or *N*-Boc-L-aspartate γ-benzyl ester.[8] At first, amino alcohol **1** was transformed into the key precursor for the diastereoselective Strecker reaction (**2**) incorporating the L- or D-phenylalanine moiety as a chiral auxiliary.[9] The imine formation and Strecker reaction were carried out in one pot by sequential treatment with TMSOTf and 2,6-lutidine,[10] then TMSCN and $ZnCl_2$ to give the corresponding amino nitrile **3** with the requisite quaternary centre as a single diastereomer. The stereochemical outcome could be easily rationalised by the preferential nucleophilic attack of cyanide to the imine from the opposite face of the benzyl group.



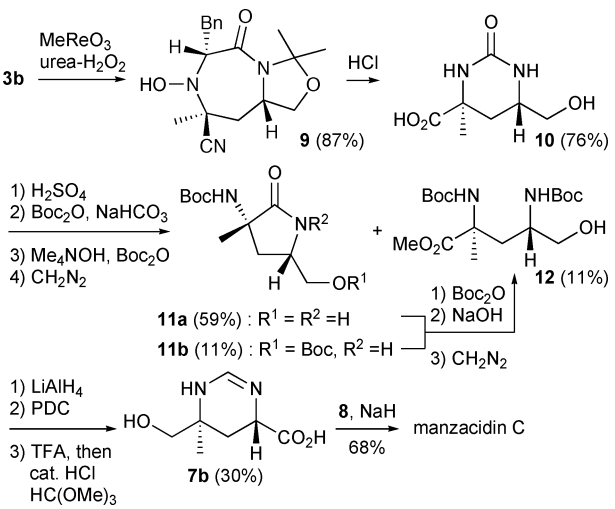
Scheme 1

The stage was now set for the removal of the phenylalanine moiety, which was found to be rather difficult. Consequently, the amino nitrile **3a**, containing the stereochemistries corresponding to manzacidin A, was oxidized with ozone to give the imino ketone **4** (Scheme 2). Acidic treatment of this intermediate provided the fully deprotected and hydrolysed diamino carboxylic acid, which was further converted to Boc-protected amino alcohol **5** in 3 steps. Oxidation of **5** furnished the lactone **6** by the preferential oxidation of the less hindered alcohol, and successive acid-catalyzed Boc removal and tetrahydropyrimidine ring formation with trimethyl orthoformate provided the core unit of manzacidin A (**7a**). The attachment of the bromopyrrole moiety by the treatment of **7a** with NaH followed by **8** in DMF completed the synthesis of manzacidin A. It should be noted that this esterification condition was generally applied to all of the succeeding syntheses of manzacidins.

The synthesis of manzacidin C was then examined using **3b** as a key intermediate (Scheme 3). Since the oxidation of **3b** by ozone was not fruitful, they implemented the rhenium-catalyzed



Scheme 2



Scheme 3

N-oxidation[11] and successive acidic hydrolysis. Treatment of *N*-hydroxy compound **9** with concentrated HCl furnished the unexpected product, cyclic urea **10**, while yielding D-phenylalanine as a side-product. Sequential deprotection–protection of **10** gave the mixture of **11a**, **11b** and a small amount of the desired **12**. Undesired materials **11a** and **11b** were then converged to **12** by an additional 2 steps. The endgame of the synthesis could be easily completed by following the steps delineated in Scheme 3 to give manzacidin C.

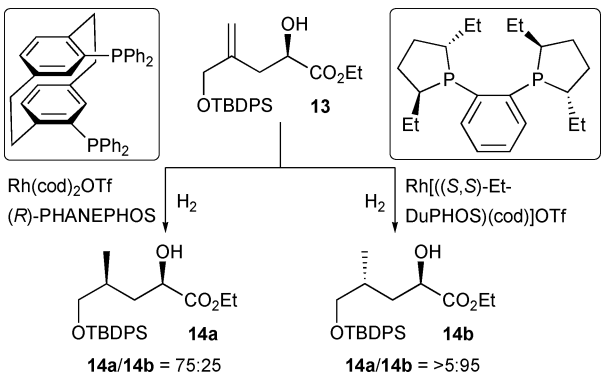
The synthetic compounds were identical in all aspects with natural manzacidins including the sign of $[\alpha]_D$. Thus, the relative and absolute configurations of manzacidin A and C were unambiguously established to be (4*S*,6*R*) and (4*S*,6*S*) respectively.

3 Rhodium-catalyzed stereospecific C–H amination: syntheses of manzacidin A and C by the Du Bois group[13]

The Du Bois group has been extensively working on the oxidative C–H amination by the use of rhodium catalysis.[12] They set out the syntheses of manzacidin A and C to highlight the distinctive power of their stereospecific C–H amination strategy.[13]

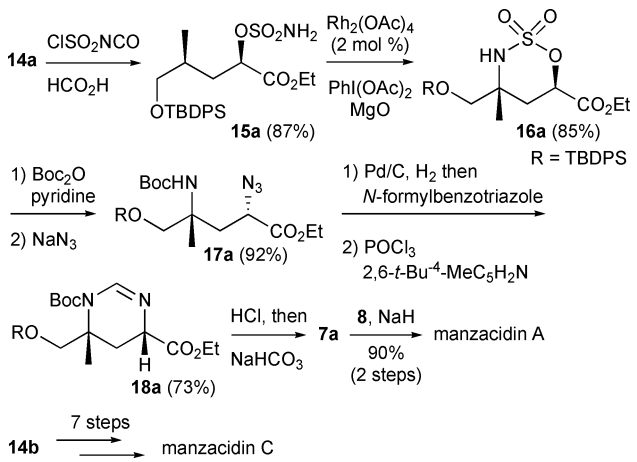
Their syntheses began with the chiral α-hydroxy ester **13**, which could be obtained in >90% ee by the use of Evans and co-workers' asymmetric ene reaction of ethyl glyoxylate.[14]

Diastereoselective hydrogenation of this material catalyzed by cationic Rh(I) species was then examined to prepare appropriate substrates for the successive C–H amination reaction (Scheme 4). Use of (*R*)-PHANEPHOS as a chiral ligand favorably furnished the hydrogenated compound **14a** as a precursor for the synthesis of manzacidin A, whereas the Rh(I)-(*S*,*S*)-Et-DuPHOS catalyzed reaction yielded **14b** exclusively.



Scheme 4

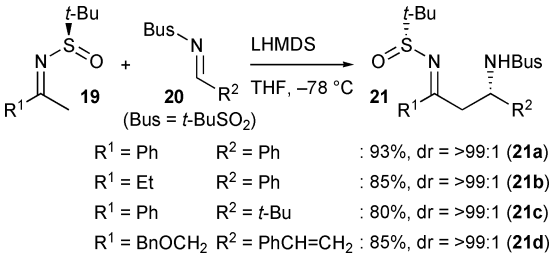
After sulfamoylation of **14a** and separation of the minor isomer derived from the concomitant **14b**, the key stereospecific rhodium-catalyzed C–H amination of **15a** was carried out to give the oxathiazinane **16a** in 85% yield as a single isomer (Scheme 5). Following *N*-Boc protection of **16a**, the azide group was introduced by the inversion of the configuration to give **17a**. Hydrogenation of the azide, formylation of the so-obtained amine and dehydration by $POCl_3$ afforded the Boc-protected core unit **18a**. Removal of protecting groups and attachment of the bromopyrrole moiety completed the synthesis of manzacidin A. Manzacidin C could also be successfully synthesised from **14b** by following the same procedure.



Scheme 5

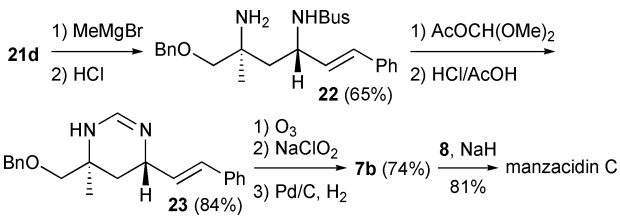
4 Asymmetric aza-Mannich reactions: synthesis of manzacidin C at Johnson & Johnson[15]

Lanter and co-workers at Johnson & Johnson developed the intermolecular asymmetric aza-Mannich reactions and applied this method to the synthesis of manzacidin C.[15] By the use of the sulfinimine strategy developed by Davis's and Ellman's groups,[16] they achieved the highly diastereoselective addition of chiral *N*-*tert*-butylsulfinimines of methyl ketones (**19**) to (*E*)-*N*-*tert*-butylsulfonyl (Bus) imines **20** to give β-sulfonamido sulfinylimines **21** (Scheme 6).



Scheme 6

To demonstrate the synthetic utility of this aza-Mannich approach, the synthesis of manzacidin C was implemented starting from **21d** (Scheme 7). Addition of methyl Grignard to the imine proceeded in a highly diastereoselective manner, and the following removal of the *N*-sulfinyl group by treatment with HCl furnished the diamine **22**. Incorporation of the formate equivalent and acidic removal of the *N*-sulfonyl group provided **23** without epimerization. The olefin part of **23** was then converted to the carboxylic acid by sequential ozonolysis and oxidation. Deprotection of the benzyl group and esterification of so-obtained **7b** by the procedure of Ohfune *et al.* completed the synthesis of manzacidin C.



Scheme 7

5 Lewis acid-catalyzed enantioselective 1,3-dipolar cycloadditions of diazoacetates and α,β-unsaturated carbonyls: synthesis of manzacidin A by the Maruoka and Sibi groups[17,18]

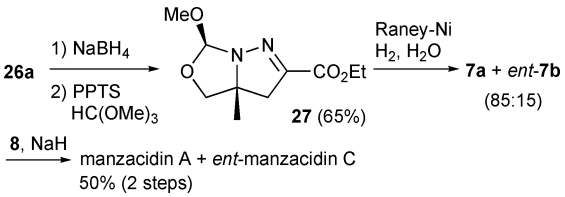
In 2006, we reported the chiral titanium Lewis acid-catalyzed asymmetric 1,3-dipolar cycloadditions of α-substituted acroleins **24** and alkyl diazoacetates **25** as a means of producing 2-pyrazolines containing a chiral quaternary stereocentre (Scheme 8).[17] The use of titanium BINOLate, composed of (*S*)-BINOL and $Ti(O^iPr)_4$ or $\{(^iPrO)_3Ti\}_2O$,[19] provided the cycloadducts **26** in moderate yields with the enantiomeric excesses ranging from 80 to 94%.

The highly functionalised nature of the cycloadduct containing ester, aldehyde, imine and amine moieties was envisaged to be a suitable precursor for the preparation of manzacidins. The synthesis was initiated with the reduction of the aldehyde moiety

R^1 = Me R^2 = Et : 52%, 95% ee (**26a**)
R^1 = Me R^2 = *t*-Bu : 43%, 94% ee (**26b**)
R^1 = Et R^2 = *t*-Bu : 48%, 84% ee (**26c**)
R^1 = Cy R^2 = *t*-Bu : 77%, 94% ee (**26d**)
R^1 = $BnOCH_2CH_2$ R^2 = *t*-Bu : 81%, 80% ee (**26e**)

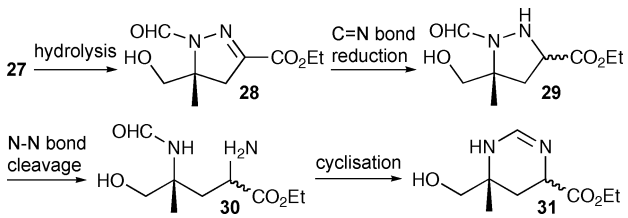
Scheme 8

by $NaBH_4$ (Scheme 9). Methyl orthoformate was then introduced to give the bicyclic compound **27** as a bench stable compound.



Scheme 9

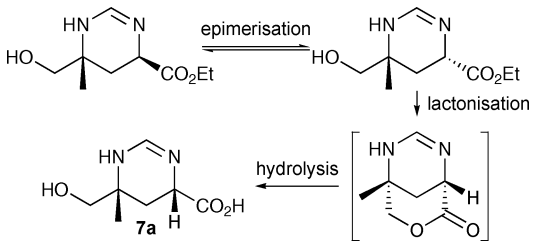
With this key intermediate in hand, we devised the one-pot sequential transformations of **27** under hydrogenation conditions, expecting the tandem hydrolytic release of the *N*-formyl group, imine hydrogenation, reductive N–N bond cleavage and tetrahydropyrimidine formation as shown in Scheme 10.



Scheme 10

Several experiments unraveled the usefulness of the Raney nickel-catalyzed hydrogenation in an ^iPrOH–H_2O co-solvent system, giving the mixture of **7a** and *ent*-**7b**. Involvement of the hydrolysis of **27** to **28** at the first stage was experimentally confirmed by the fact that the tandem reaction of **27** conducted in the presence of only small amounts of water was found to be very sluggish, while the reaction of the separately synthesized compound **28** proceeded smoothly. The intermediacy of the imine reduction product **29** could be ascertained by the LC-MS analysis of the reaction showing the gradual accumulation of the peak at *m*/*z* 239.2 (**29** + Na^+). Cyclisation of diamine **30** to **31** seems to be fast, since no peak corresponding to **30** was observed by LC-MS.

What we did not anticipate in this tandem reaction was the rather good diastereoselectivity for the imine hydrogenation (dr = 85 : 15) and the ester hydrolysis *in situ*, giving the free carboxylic acid **7a** as a major product. As the Merck Frosst group's research on manzacidin D (*vide infra*) revealed the facile epimerisation of the ester similar to **31** under basic conditions, we speculated that the epimerisation of **31** might be rather feasible. In this scenario, the tetrahydropyrimidine moiety of **31** might be acting as a base (Scheme 11). The lactonisation could be facilitated when

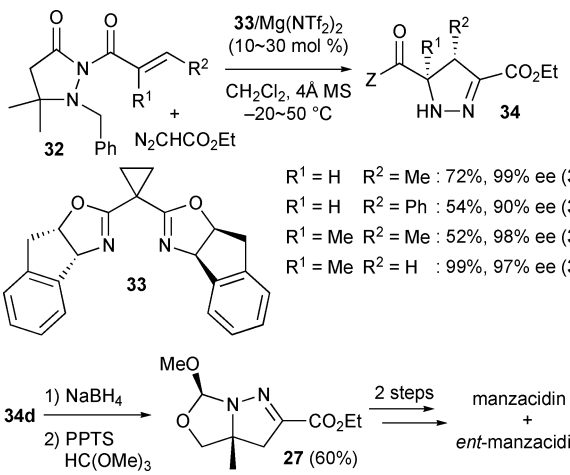


Scheme 11

the alcohol and ethyl ester moieties came to the *cis*-orientation. The successive hydrolytic opening of the lactone would lead to the preferential formation of **7a**. The direct hydrolysis of the ester by water or the partial epimerisation of **7a** could be the pathway for the formation of *ent*-**7b**.

Attachment of the bromopyrrole moiety to the mixture of **7a** and *ent*-**7b**, and separation of the diastereomers by preparative HPLC provided the analytically pure manzacidin A in 50% from **27**, concomitant with a small amount of *ent*-manzacidin C (Scheme 9). The distinctive feature of our method is the avoidance of any protection–deprotection steps, which enabled the expeditious synthesis of manzacidin A (only 5 steps starting from the commercial sources).

Recently, Sibi and co-workers have developed the enantioselective 1,3-dipolar cycloadditions of diazoacetates and α,β-unsaturated pyrazolidinone imides **32** using $Mg(NTf_2)_2$–**33** as a chiral Lewis acid catalyst (Scheme 12).[18] The notable advantage of this protocol was the applicability to various α- and/or β-substituted unsaturated carbonyls providing the cycloadducts in good yields with an excellent level of enantiocontrol. The cycloadduct **34d** was successfully converted to manzacidin A, following the procedure developed by us.[17a]



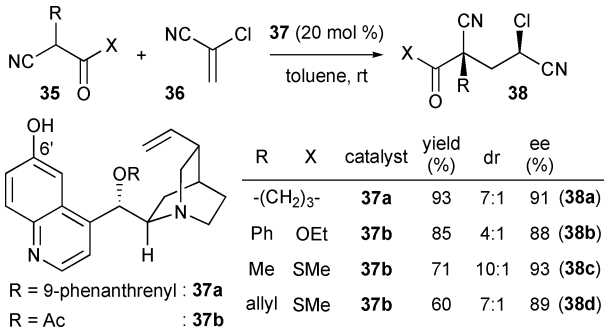
R^1 = H R^2 = Me : 72%, 99% ee (**34a**)
R^1 = H R^2 = Ph : 54%, 90% ee (**34b**)
R^1 = Me R^2 = Me : 52%, 98% ee (**34c**)
R^1 = Me R^2 = H : 99%, 97% ee (**34d**)

Scheme 12

6 Organocatalyzed asymmetric tandem conjugate addition–protonation: formal syntheses of manzacidin A and C by the Deng group[20]

Deng *et al.* have been working on the development of organocatalysis, focusing on the use of cinchona alkaloids and their derivatives as catalysts.[21] Along this line, asymmetric Michael addition of

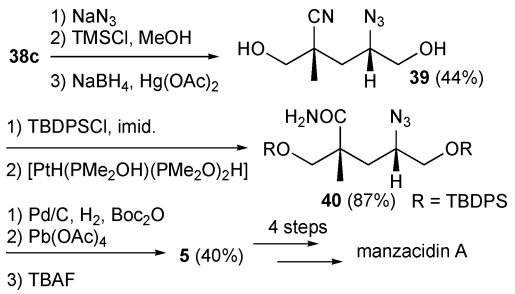
α-substituted cyanoacetates and ketones **35** to 2-chloroacrylonitrile **36** was investigated using quinine- and quinidine-derived catalysts with a C6′-OH group as dual-function catalysts (Scheme 13).[20a] The uniqueness of this catalytic system is the two sequential stereo-induction steps comprised of asymmetric conjugate addition and protonation, which enabled the formation of 1,3-tertiary-quaternary centres with high stereoselectivities.



R	X	catalyst	yield (%)	dr	ee (%)
-$(CH_2)_3$-		**37a**	93	7:1	91 (**38a**)
Ph	OEt	**37b**	85	4:1	88 (**38b**)
Me	SMe	**37b**	71	10:1	93 (**38c**)
allyl	SMe	**37b**	60	7:1	89 (**38d**)

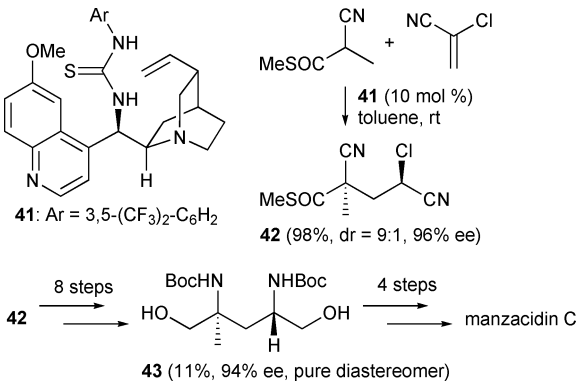
Scheme 13

As 1,3-tertiary-quaternary centres were considered to be the fundamental structure of manzacidins, they set out the formal synthesis of manzacidin A starting from **38c** obtained by the reaction of **35** (R = Me, X = SMe) and **36** catalyzed by **37b** (Scheme 14). To introduce the nitrogen moiety to the carbon skeleton, nucleophilic substitution of chloride to azide was first accomplished. Diol **39** could be obtained through the methanolysis of the less-hindered cyanide group and the reduction of the thus-formed ester and thioester. Silylation of the diol and hydrolysis of the remaining cyanide by Ghaffar and Parkins' procedure[22] provided the amide **40**. After the hydrogenation and Boc-protection of **40**, the additional amine moiety could then be introduced by Hoffman rearrangement.[23] Desilylation of this compound led to **5**, the common intermediate developed by Ohfune *et al.*, thus completing the formal synthesis of manzacidin A.



Scheme 14

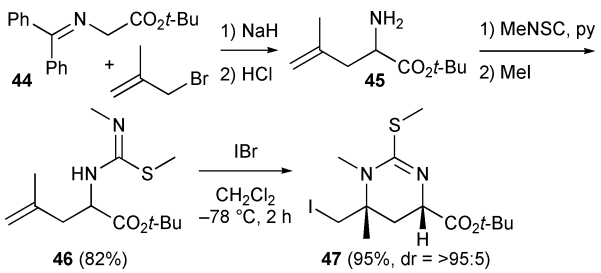
Shortly after this discovery, Deng *et al.* also reported a method which bestows the complementary sense of diastereoselectivity in this asymmetric tandem asymmetric conjugate addition–protonation process by using the quinine- or quinidine-derived catalyst bearing a thiourea moiety such as **41** (Scheme 15).[20b] By the use of this method, Michael adduct **42**, the diastereomer of **38c**, with the (*R*)-configuration at the quaternary centre could be obtained in 98% yield with 96% ee. Following the synthetic plan described above, **42** was transformed into Boc-protected diamine **43** to complete the formal synthesis of manzacidin C.



Scheme 15

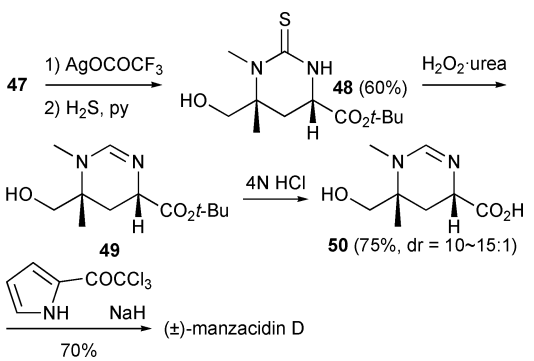
7 Diastereoselective isothiourea iodocyclization: synthesis of (±)-manzacidin D at Merck Frosst[24]

A group at Merck Frosst planned to synthesize manzacidins by the isothiourea cyclisation to give the heterocyclic core.[24] The requisite substrate for the key cyclisation was easily prepared in 4 steps starting from benzophenone imine glycine *tert*-butyl ester **44** (Scheme 16). Namely, the alkylation of **44** with methallyl bromide, followed by acid hydrolysis of benzophenone imine gave amino acid ester **45**, which in turn was sequentially treated with methyl isothiocyanate and methyl iodide to give the isothiourea **46**. By conducting the reaction of **46** and IBr at low temperature, the heterocycle **47** could be obtained in nearly quantitative yield with exclusive stereoselectivity.



Scheme 16

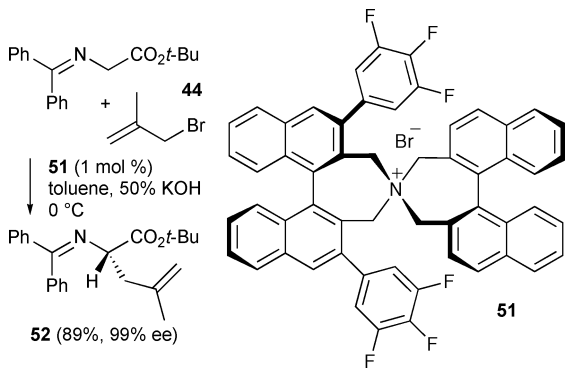
The remaining challenge to accomplish the synthesis was the effective conversion of cyclic thiourea **48**, which could be obtained by the hydrolysis and demethylation of **47**, to the tetrahydropyrimidine (Scheme 17). After some unfruitful experiments using



Scheme 17

metal-promoted processes, the focus was then moved to the desulfurisation under oxidative conditions.[25] Consequently, the clean conversion of **48** to **49** was finally realised by treatment with urea hydrogen peroxide. As the isolation of **49** by silica gel column chromatography was problematic due to the epimerisation of the α-carbon of the ester, the crude material was directly hydrolysed to give **50** with minimal epimerisation. By the use of similar strategy to Ohfune *et al.*, the pyrrole moiety could be introduced to give manzacidin D.

The additional notion of this synthesis is the potential utility of phase-transfer catalyzed asymmetric alkylation of **44** using **51** as catalyst, which is known to give the optically enriched intermediate **52** with 99% ee, as a means to provide optically pure manzacidin D (Scheme 18).[26]

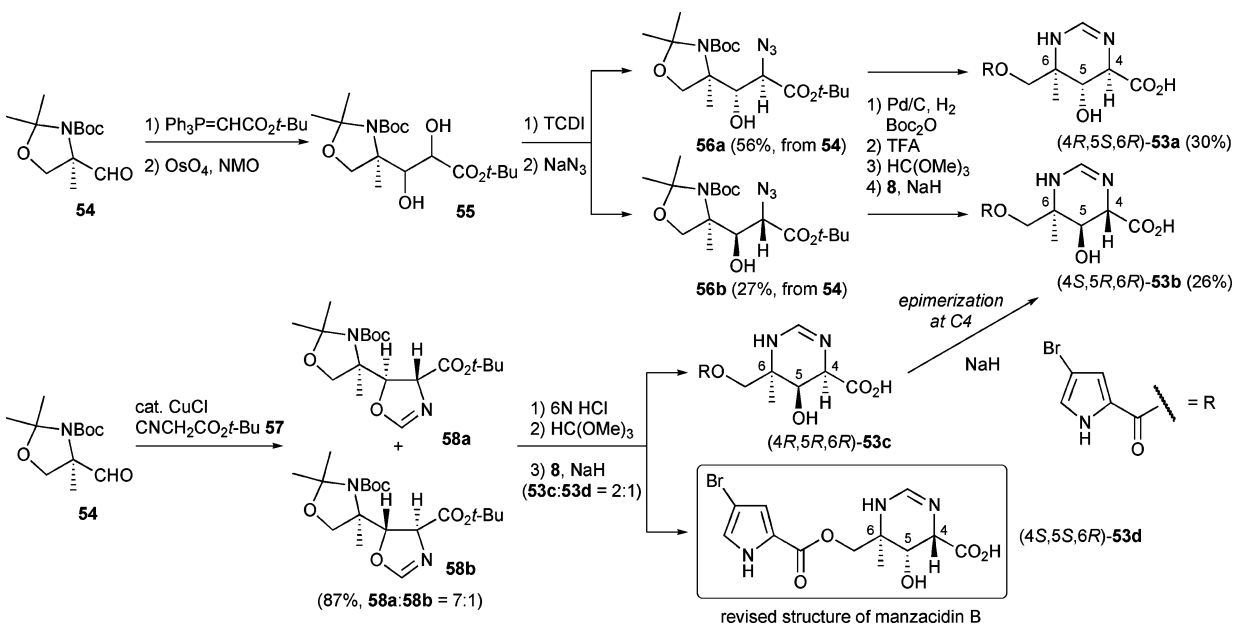


Scheme 18

8 Structural revision of manzacidin B by the syntheses of four possible isomers[27]

Compared to the growing number of methods available for the syntheses of manzacidin A, C and D as described above, the synthesis of manzacidin B bearing one additional chiral centre has remained elusive. In 2007, Ohfune, Shinada and co-workers, who took a leading role in the syntheses of manzacidin A and C, succeeded in confirming the relative and absolute structure of manzacidin B by synthesizing all of its 4 possible diastereomers (**53a–d**) with the fixed (6*R*)-configuration (Scheme 19).[27] The optically active (*R*)-α-methyl Garner aldehyde **54**, which could be easily prepared by their own protocol in multigram quantities,[9a] was employed as a starting material for all syntheses. Thus, the stereochemistries required for the syntheses of (4*R*,5*S*,6*R*)-**53a** and (4*S*,5*R*,6*R*)-**53b** could be introduced by the Wittig olefination of **54** and the osmium-catalyzed dihydroxylation of the thus-formed (*E*)-olefin. The diol **55**, isolated as a mixture of two diastereomers, was converted to **56a** and **56b** by the sequential treatment with 1,1′-thiocarbodiimidazole (TCDI) and sodium azide.[28] After the separation of the two isomers, each isomer was then transformed into the desired possible isomers of manzacidin B by hydrogenation of the azide, global deprotection, tetrahydropyrimidine formation and bromopyrrole attachment. However, the spectra of **53a** and **53b** were not identical to natural manzacidin B.

To access two other possible isomers, copper-catalyzed aldol reaction of isonitrile **57** with aldehyde **54** was implemented with consideration of the dominant formation of *trans*-oxazolines by this method.[29] As anticipated, *trans*-oxazolines **58a** and **58b** could be obtained in the ratio of 7 : 1 as an inseparable mixture. Acidic removal of the protecting groups furnished the diamine without changing the diastereomeric ratio. However, after the final amidination and esterification, the products were obtained as a 2 : 1 mixture of **53c** and **53d** along with the unexpected **53b**. This observation indicated the possibility of the epimerization of **53c** under the reaction conditions. This assumption was then confirmed by the re-subjection of the isolated **53c** to sodium hydride in DMF, which actually led to the complete conversion of **53c** to **53b**. On the other hand, the other isomer **53d** remained



Scheme 19

intact under these basic conditions. Since the spectra of **53d** was identical to natural manzacidin B in all aspects, the relative and absolute structure of manzacidin B was finally revised and established as (4*S*,5*S*,6*R*).

Conclusions

Based on the leading works of Ohfune *et al.*, syntheses of manzacidins became the appropriate scaffold to highlight the utility of new synthetic methodologies. A few hundred milligrams of manzacidins can be now available, thus enabling the evaluation of their biological activities in depth. At the same time, this research would allow facile access to the derivatives of manzacidins for biological and medical studies.

However, the synthetic approaches reported to date seem to be inapplicable to manzacidin B, a simple analogue which contains a chiral secondary alcohol moiety in the tetrahydropyrimidine core. The challenge still remains in the development of methods which realise the concise and scalable total synthesis of manzacidin B.

References

1 J. Kobayashi, F. Kanda, M. Ishibashi and H. Shigemori, *J. Org. Chem.*, 1991, **56**, 4574.
2 T. Jahn, G. M. König, A. D. Wright, G. Wörheide and J. Reitner, *Tetrahedron Lett.*, 1997, **38**, 3883.
3 S. Tsukamoto, K. Tane, T. Ohta, S. Matsunaga, N. Fusetani and R. W. M. van Soest, *J. Nat. Prod.*, 2001, **64**, 1576.
4 Manzacidins A and C, as well as *N*-methylmanzacidin C, were also isolated from the Mediterranean sponge *Axinella verrucosa*: A. Aiello, M. D'Esposito, E. Fattorusso, M. Menna, W. E. G. Müller, S. Perović-Ottstadt and H. C. Schröder, *Bioorg. Med. Chem.*, 2006, **14**, 17.
5 D. J. Faulkner, *Nat. Prod. Rep.*, 1998, **15**, 113.
6 G. M. König, A. D. Wright and S. G. Franzblau, *Planta Med.*, 2000, **66**, 337.
7 K. Namba, T. Shinada, T. Teramoto and Y. Ohfune, *J. Am. Chem. Soc.*, 2000, **122**, 10708.
8 O. Ouerfelli, M. Ishida, H. Shinozaki, K. Nakanishi and Y. Ohfune, *Synlett*, 1993, 409.
9 (*a*) S.-H. Moon and Y. Ohfune, *J. Am. Chem. Soc.*, 1994, **116**, 7405; (*b*) Y. Ohfune, S.-H. Moon and M. Horikawa, *Pure Appl. Chem.*, 1996, **68**, 645; (*c*) M. Horikawa, T. Nakajima and Y. Ohfune, *Synlett*, 1997, 253; (*d*) Y. Ohfune, K. Nanba, I. Takada, T. Kan, M. Horikawa and T. Nakajima, *Chirality*, 1997, **9**, 459; (*e*) Y. Ohfune and M. Horikawa, *J. Synth. Org. Chem. Jpn.*, 1997, **55**, 982.
10 (*a*) M. Sakaitani and Y. Ohfune, *J. Org. Chem.*, 1990, **55**, 870; (*b*) K. Shimamoto and Y. Ohfune, *J. Med. Chem.*, 1996, **39**, 407.
11 A. Goti and L. Nannelli, *Tetrahedron Lett.*, 1996, **37**, 6025.
12 (*a*) C. G. Espino, P. M. Wehn, J. Chow and J. Du Bois, *J. Am. Chem. Soc.*, 2001, **123**, 6935; (*b*) C. G. Espino and J. Du Bois, *Angew. Chem., Int. Ed.*, 2001, **40**, 598; (*c*) P. M. Wehn, J. Lee and J. Du Bois, *Org. Lett.*, 2003, **5**, 4823; (*d*) C. G. Espino, K. W. Fiori, M. Kim and J. Du Bois, *J. Am. Chem. Soc.*, 2004, **126**, 15378; (*e*) M. Kim, J. V. Mulcahy, C. G. Espino and J. Du Bois, *Org. Lett.*, 2006, **8**, 1073; (*f*) K. W. Fiori and J. Du Bois, *J. Am. Chem. Soc.*, 2007, **129**, 562.
13 P. W. Wehn and J. Du Bois, *J. Am. Chem. Soc.*, 2002, **124**, 12950.
14 D. A. Evans, S. W. Tregay, C. S. Burgey, N. A. Paras and T. Vojkovsky, *J. Am. Chem. Soc.*, 2000, **122**, 7936.
15 J. C. Lanter, H. Chen, X. Zhang and Z. Sui, *Org. Lett.*, 2005, **7**, 5905.
16 For reviews, see: (*a*) F. A. Davis and B.-C. Chen, *Chem. Soc. Rev.*, 1998, **27**, 13; (*b*) J. A. Ellman, T. D. Owens and T. P. Tang, *Acc. Chem. Res.*, 2002, **35**, 984.
17 (*a*) T. Kano, T. Hashimoto and K. Maruoka, *J. Am. Chem. Soc.*, 2006, **128**, 2174; (*b*) T. Hashimoto, *Ph.D. Dissertation*, Kyoto University, 2006.
18 M. P. Sibi, L. M. Stanley and T. Soeta, *Org. Lett.*, 2007, **9**, 1553.
19 (*a*) H. Hanawa, T. Hashimoto and K. Maruoka, *J. Am. Chem. Soc.*, 2003, **125**, 1708; (*b*) H. Hanawa, D. Uraguchi, S. Konishi, T. Hashimoto and K. Maruoka, *Chem.–Eur. J.*, 2003, **9**, 4405; (*c*) T. Kano, T. Hashimoto and K. Maruoka, *J. Am. Chem. Soc.*, 2005, **127**, 11926.
20 (*a*) Y. Wang, X. Liu and L. Deng, *J. Am. Chem. Soc.*, 2006, **128**, 3928; (*b*) B. Wang, F. Wu, Y. Wang, X. Liu and L. Deng, *J. Am. Chem. Soc.*, 2007, **129**, 768.
21 For a review, see: S.-K. Tian, Y. Chen, J. Hang, L. Tang, P. McDaid and L. Deng, *Acc. Chem. Res.*, 2004, **37**, 621.
22 T. Ghaffar and A. W. Parkins, *J. Mol. Catal. A: Chem.*, 2000, **160**, 249.
23 K. Burgess and C.-Y. Ke, *Synthesis*, 1996, 1463.
24 (*a*) J. C. S. Woo and D. B. MacKay, *Tetrahedron Lett.*, 2003, **44**, 2881; (*b*) C. Drouin, J. C. S. Woo, D. B. MacKay and R. M. A. Lavigne, *Tetrahedron Lett.*, 2004, **45**, 7197.
25 (*a*) W. Walter and K.-P. Rueß, *Chem. Ber.*, 1969, **102**, 2640; (*b*) J. J. Havel and R. Q. Kluttz, *Synth. Commun.*, 1974, **4**, 389; (*c*) G. Frachey, C. Crestini, R. Bernini, R. Saladino and E. Mincione, *Heterocycles*, 1994, **38**, 2621.
26 (*a*) T. Ooi, M. Kameda and K. Maruoka, *J. Am. Chem. Soc.*, 1999, **121**, 6519; (*b*) T. Ooi, M. Kameda and K. Maruoka, *J. Am. Chem. Soc.*, 2003, **125**, 5139.
27 T. Shinada, E. Ikebe, K. Oe, K. Namba, M. Kawasaki and Y. Ohfune, *Org. Lett.*, 2007, **9**, 1765.
28 S. Y. Ko, *J. Org. Chem.*, 1995, **60**, 6250.
29 (*a*) Y. Itoh, M. Sawamura and T. Hayashi, *J. Am. Chem. Soc.*, 1986, **108**, 6405; (*b*) A. Togni and S. D. Pastor, *Helv. Chim. Acta*, 1989, **72**, 1038.