Tetrahedron Letters 54 (2013) 2615–2618

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of the naphthoquinone core of divergolides (C–D) and model studies for elaboration of the ansabridge

Sivappa Rasapalli [a,*], Gopalakrishna Jarugumilli [a], Gangadhara Rao Yarrapothu [a], James A. Golen [a], Arnold L. Rheingold [b]

[a] Department of Chemistry and Biochemistry, University of Massachusetts Dartmouth, North Dartmouth, MA 02747, United States
[b] Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA 92093-0358, United States

ARTICLE INFO

Article history:
Received 5 February 2013
Revised 4 March 2013
Accepted 5 March 2013
Available online 14 March 2013

Keywords:
Ansamycins
Divergolides
Hygrocins
Naphthoquinone
3-Methylsalicylic acid

ABSTRACT

Herein, we describe a facile synthesis of the naphthoquinone fragment of the aromatic core of the novel ansamycins such as hygrocins A–B and the divergolides C–D, starting from the inexpensive 2-hydroxy-3-methylbenzoic acid. We demonstrate the utility of naphthalenic synthon for further elaboration of the ansabridge via C5–C6 bond formation by employing a commercially available sterically demanding organomagnesium reagent as a model ansa chain. Facile conversion of the resulting alcohol to the naphthoquinone fragment of the targets in one pot has also been realized. These model studies set the stage for the completion of total synthesis of the biologically important novel ansamycins.

Published by Elsevier Ltd.

Ansamycins, so named because of their 'basket-like structures' consisting of an aromatic chromophore connected by a chain, like the handle of a basket (ansa), at non-adjacent positions are mainly derived from actinomycetes and are proven biologically important macrolides.[1] The structure of the aromatic moiety distinguishes two types of ansamycins: (1) naphthalenic ansamycins (e.g., rifamycins,[2] naphthomycins,[3] streptovaricin,[4] etc.) that exhibit antimicrobial activities (2) benzenic ansamycins (geldanamycin,[5] herbimycin,[6] etc.) that possess anti-cancer activities. Divergolides C–D (**1**–**2**), recently isolated from *Streptomyces* sp. HKI0576—an endophyte of the mangrove tree (*Bruguiera gymnorrhiza*), have been shown to possess antibacterial and anti-cancer activities.[7] They closely resemble hygrocins A–B (**3**–**4**), another family of metabolites isolated from *Streptomyces hygroscopicus*, and differ only in the unusual isobutenyl side chain at C11 instead of the methyl group, and in the oxidation states of the aromatic cores, while the overall topology is conserved.[8] Due to the shortage of the supply of these rare streptomyces metabolites,[7,9] and lack of synthetic routes,[10] the biomedicinal potential of this unique family has not been fully investigated and remain to be explored. Divergolides A–D and hygrocins A–B have attracted the attention of synthetic chemists with their interesting structures and bioactivities.[11] An enantioselective total synthesis amenable to large scale and structural analogue production will not only enable the undertaking SAR studies of these rare metabolites[12] but also the unambiguous stereochemical assignment of the stereocentres (e.g., C8 of hygrocins is unassigned; numbering refers to Hertweck's assignment shown in **1** of Fig. 1).[7,13] We set out to develop a synthetic route to access the analogues of these novel ansamycins as part of our ongoing quest for novel antibacterial leads.[14] We proposed two approaches, namely biomimetic and non-biomimetic. As shown in Scheme 1, our non-biomimetic retrosynthesis of the targets identified two main synthons **13** and **14**, that is, aromatic and chiral fragments, apart from the eastern segment **11**, that is, C1″–C5″ which is thought to be derived from 2-methyl-2-pentenedioicacid chemistry. Depending on the disconnection of either C4–C5 or C5–C6, one could arrive at differently functionalized aromatic and chiral fragments, and shown in Scheme 1 are based on the disconnection of C5–C6.[15]

We initially focused our efforts on construction of the AB rings (i.e., **13** of Scheme 1) of the tricyclic core of the target compounds and planned to rely on the intrinsic biomimetic annulations of *N*-acylated naphthoquinone for the formation of the tricyclic aromatic cores of divergolides C (**1**), D (**2**) and hygrocins B (**4**).[16] 3-Methylsalicylic acid (**15**) with suitable functional groups required for the A-ring was chosen as a starting material. Surprisingly, this readily available and most obvious choice with the suitable substituents at the respective positions has not been employed thus far in the synthesis of aromatic cores of ansa macrolides

* Corresponding author. Tel.: +1 508 999 8276; fax: +1 508 999 9232.
E-mail address: srasapalli@umassd.edu (S. Rasapalli).

0040-4039/$ - see front matter Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.tetlet.2013.03.022

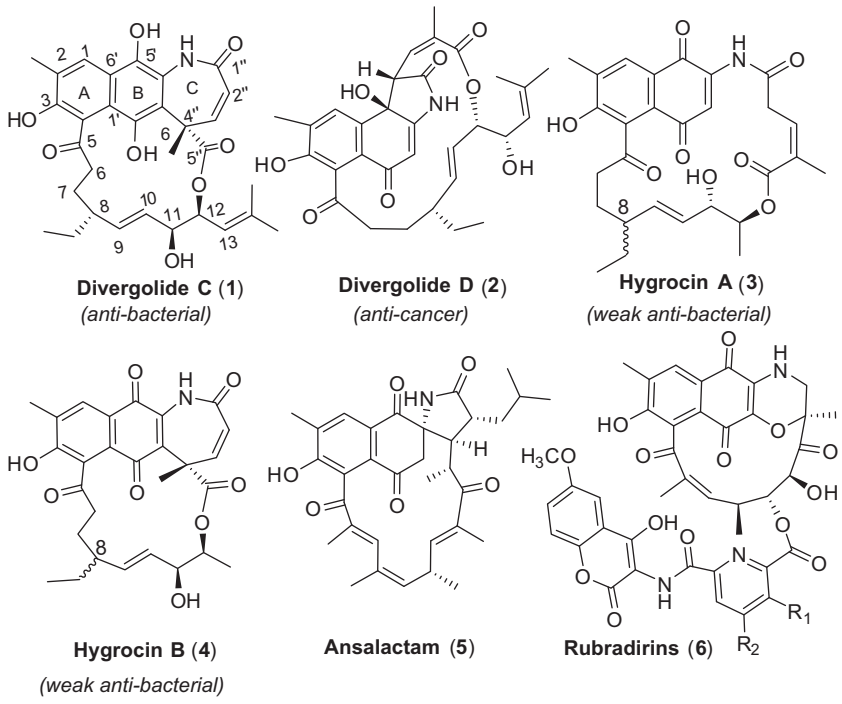
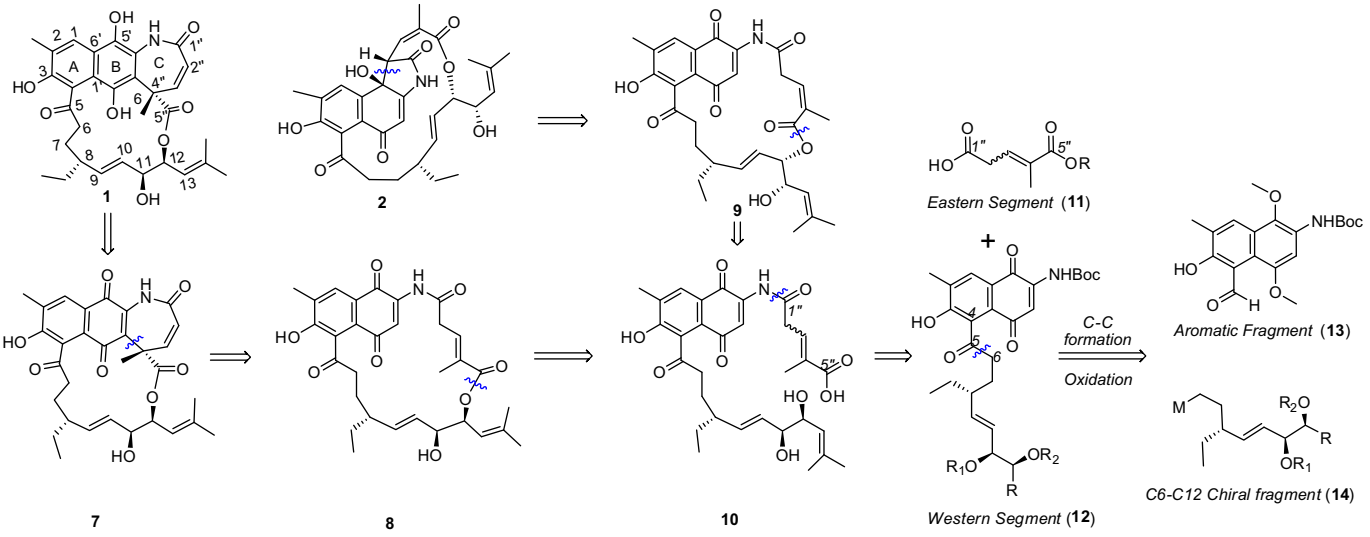


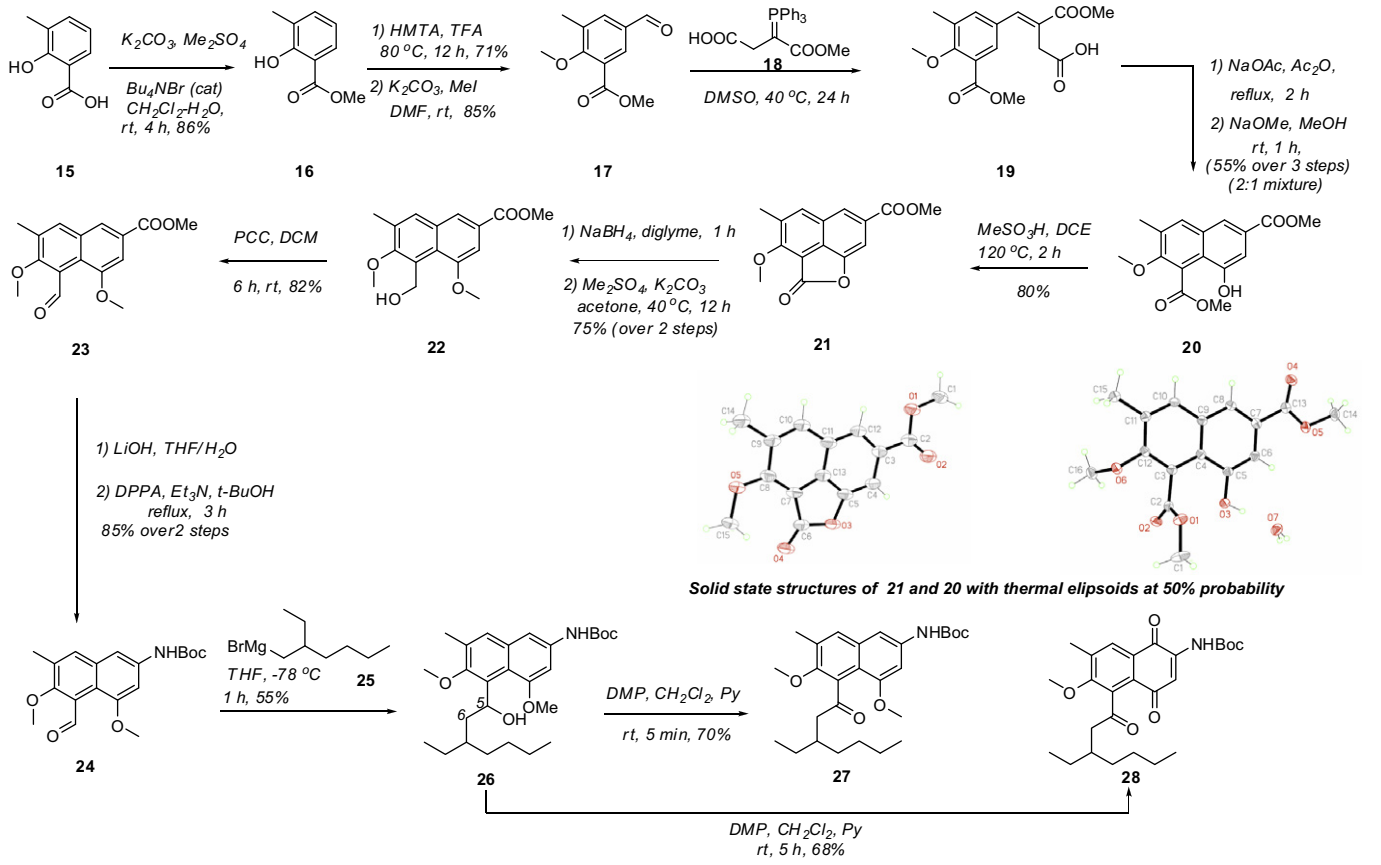
Figure 1. Structures of ansamycins.



Scheme 1. Retrosynthesis of divergolides C (**1**) and D (**2**).

presumably due to the lack of methods/reports for selective ring annulations and further manipulations. We decided to undertake this approach with the hope of developing methods to annulate the B-ring via electrophilic aromatic substitution chemistry. If successful, this work would not only develop the facile chemistry for the large scale access to the aromatic cores of the proposed targets, that is, divergolides C–D (**1**–**2**) and hygrocins A–B (**3**–**4**), but also provides the access to the aromatic cores of other important ansamycins such as ansalactam **5**, rubradirin **6**, salinisporomycins,[3] chaxamycins[17] and rifamycins[2] through slight modifications.

Our synthesis thus commenced from 3-methylsalicylic methyl ester **16**, synthesized from commercially available 3-methylsalicyclic acid **15** using the known literature procedure, as shown in Scheme 2.[18] Formylation of ester **16** under Duff's conditions provided formylated phenol which was converted into its methyl ether **17** before subjecting it to Wittig olefination.[19] The required phosphorane **18** was prepared following the literature protocol.[20] The Wittig olefination of aldehyde **17** was carried out in DMSO at moderate temperatures to obtain acid **19** in good yield after acid–base extraction.[21] The unoptimized intramolecular acylation under $NaOAc/Ac_2O$ refluxing conditions provided the desired naphthalenic compound **20** along with the undesired regioisomer in 2:1 ratio, whose separation was effected quite easily at the phenol stage after the deprotection of the acetate functionality that is formed concomitantly.[22] The connectivity of the required isomer was confirmed through X-ray structure determination. We reasoned that conversion of the bis-ester **20** to a tricyclic naphthalene core with lactone moiety may enable us to differentiate the ester



Scheme 2. Synthesis of naphthoquinone core of divergolides C (**1**) and D (**2**), and model studies of C5–C6 bond formation.

carbonyls for further manipulations. Thus the lactone **21** was prepared in a facile way starting from the ester through the lactonization of naphthol ester **20** with methanesulfonic acid in refluxing dichloroethane conditions, whose structure was confirmed through X-ray crystallography. The lactone **21** was selectively manipulated and converted into *N*-Boc-carbamate derivative **24** through a series of functional group interconversions as shown in Scheme 2. Briefly, the carboxylic acid precursor for Curtius rearrangement was made through the sequence of selective reduction of lactone **21** to alcohol, methylation of the resulting phenol **22**, oxidation of the primary alcohol to aldehyde **23** and hydrolysis of the ester.[23] Facile Curtius rearrangement of the acid under modified conditions[24] in *t*-BuOH allowed the introduction of the carbamate group on to the B-ring. Limited attempts to introduce the missing oxygen on to the B-ring of carbamate **24** at this stage of the synthesis were unproductive.[25] We reasoned that proceeding with monooxygenated B-ring might prove useful for annulation of the C-ring later on in the synthesis efforts *via* aromatic Claisen rearrangement. Hence, we decided to establish the efficacy of the C5–C6 bond formation through the Grignard reaction of the aldehyde **24** as we were aware of the problems due to the steric encumbrance at C5.[26] We were delighted with the clean outcome of the reaction of aldehyde **24** with Grignard reagent **25** to afford the alcohol **26**. Probably, it is the electrophilicity of our aromatic partner that helped us in doing away with the perils associated with this coupling with organomagenisum reagent **24**.[27] It was further gratifying to observe the concomitant oxidation of the alcohol to the naphthoquinone ketone **28** with DMP/pyridine conditions in an opened flask at ambient temperatures.[28] It is pertinent to mention that this transform has not been optimized further and we are currently studying the scope and the limitations of DMP mediated oxidation of such amino compounds to naphthoquinones.

Conclusions

In summary, we have developed facile chemistry to convert inexpensive 3-methylsalicylic acid into the naphthoquinone core of ansamycins, specifically suitable for divergolides C–D and hygrocins A–B, and established the efficacy of the difficult C5–C6 bond formation using a model substrate for aliphatic (C6–C12) fragment which is currently being synthesized through the chiron approach in our lab. The inexpensive, readily available starting materials and the sequence of simple operations lend this route amenable to access the naphthalenic intermediates in large scales required for further elaboration to complex ansamycins. The lactone **21** is also poised for coupling studies for C5–C6 bond formation, provided if we can introduce a non-electrophilic group in the place of carbethoxy group and we are currently exploring the Wittig olefination with modified phosphoranes to introduce the nitro or carbamate directly on to the B-ring of **21**. Optimization of the synthesis of **20** using the Knochel's regioselective acylation conditions[29] to improvise the overall synthetic efficiency along with the application of the model studies described herein to complete the total synthesis of the targets is underway in our laboratory and will be reported in near future.

Acknowledgments

This work was supported through the Startup and Healey Foundation funds of UMass Dartmouth, and partly from Microbiotix,

Inc, Worcester. We thank Dr. Venkataraman Dandapani for his help with acquiring some NMR spectra of advanced intermediates in this study.

Supplementary data

Supplementary data (crystallographic data excluding structure factors) for the structures **20** and **21** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication Nos. CCDC 922930 and CCDC 922929, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.03.022.

References and notes

1. For recent reviews on ansamycin natural products, see: (a) Wrona, I. E.; Agouridas, V.; Panek, J. S. C. R. *Acad. Sci. (Paris)* **2008**, *11*, 1483; (b) Floss, H. G.; Yu, T. W. *Chem. Rev.* **2005**, *105*, 621; (c) Kang, Q.; Shen, Y.; Bai, L. *Nat. Prod. Rep.* **2012**, *29*, 243; (d) Funayama, S.; Cordell, G. A. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier Science: Amsterdam, 2000; Vol. 23, p 51.; (e) Bryskier, A. In Antimicrobial Agents; Bryskier, A., Ed.; ASM Press: Washington, DC, 2005; p 906.
2. (a) Calvori, C.; Frontali, L.; Leoni, L.; Tecce, G. *Nature* **1965**, *207*, 417–418; (b) Sensi, P.; Margalith, P.; Timbal, M. *Farmaco Ed. Sci.* **1959**, *14*, 146; (c) Xu, W.; Neckers, L. *Clin. Cancer Res.* **2007**, *13*, 1625; (d) Miyata, Y. *Curr. Pharm. Des.* **2005**, *11*, 1131.
3. (a) Bhuyan, B. K.; Owen, S. P.; Dietz, A. *Antimicrob. Agents Chemother.* **1965**, *10*, 91; (b) Williams, T. H. *J. Antibiot.* **1975**, *28*, 85; (c) Lu, C. H.; Shen, Y. M. *J. Antibiot.* **2007**, *60*, 649; (d) Meyer, M.; Keller-Schierlein, W.; Megahed, S.; Zahner, H.; Segre, A. *Helv. Chim. Acta* **1986**, *69*, 1356; (e) Mukhopadhyay, T.; Franco, C. M.; Reddy, G. C.; Ganguli, B. N.; Fehlhaber, H. W. *J. Antibiot.* **1985**, *38*, 948; (f) Yang, Y. H.; Fu, X. L.; Li, L. Q.; Zeng, Y.; Li, C. Y.; He, Y. N.; Zhao, P. J. *J. Nat. Prod.* **2012**, *75*, 1409; (g) Chen, M.; Roush, W. R. *J. Org. Chem.* **2013**, *78*, 3.
4. (a) Rinehart, K. L.; Shield, L. S. *Prog. Chem. Org. Nat. Prod.* **1976**, *33*, 231; (b) Rinehart, K. L., Jr.; Antosz, F. J.; Deshmukh, P. V.; Kakinuma, K.; Martin, P. K.; Milavetz, B. I.; Sasaki, K.; Witty, T. R.; Li, L. H.; Ruesser, F. *J. Antibiot.* **1976**, *29*, 201; (c) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348; (d) Roush, W. R.; Coffey, D. S.; Madar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 11331.
5. (a) Fukuyo, Y.; Hunt, C. R.; Horikoshi, N. *Cancer Lett.* **2010**, *290*, 24; (b) DeBoer, C.; Meulman, P. A.; Wnuk, R. J.; Peterson, D. H. *J. Antibiot. (Tokyo)* **1970**, *23*, 442; (c) Sasaki, K.; Rinehart, K. L., Jr.; Slomp, G.; Grostic, M. F.; Olson, E. C. *J. Am. Chem. Soc.* **1970**, *92*, 7591; (d) Johnson, R. D.; Haber, A.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 3316; (e) BeBoer, C.; Dietz, A. *J. Antibiot.* **1976**, *29*, 1182; (f) Porter, J. R.; Ge, J.; Lee, J.; Normant, E.; West, K. *Curr. Top. Med. Chem.* **2009**, *9*, 1386; Li, T.; Ni, S.; Jia, C.; Wang, H.; Sun, G.; Wu, L.; Gan, M.; Shan, G.; He, W.; Lin, L.; Zhou, H.; Wang, Y. *J. Nat. Prod.* **2012**, *75*, 1480.
6. (a) Rascher, A.; Hu, Z.; Buchanan, G. O.; Reid, R.; Hutchinson, C. R. *Appl. Environ. Microbiol.* **2005**, *71*, 4862–4871; (b) Omura, S. Y.; Iwai, Y.; Takahashi, N.; Sadakane, A.; Nakagawa, H.; Oiwa, Y.; Hasegawa; Ikai, T. *J. Antibiot.* **1979**, *32*, 255; (c) Canova, S.; Bellosta, V.; Bigot, A.; Mailliet, P.; Mignani, S.; Cossy, J. *Org. Lett.* **2007**, *9*, 145; (d) Omura, S.; Iwai, Y.; Sakadane, N.; Nakagawa, A.; Oiwa, H.; Hasegawa, Y.; Ikai, T. *J. Antibiot.* **1979**, *32*, 255; (e) Omura, S.; Nakagawa, A.; Sadakane, N. *Tetrahedron Lett.* **1979**, *44*, 4323; (f) Furusaki, A.; Matsumoto, T.; Nakagawa, A.; Omura, S. *J. Antibiot.* **1980**, *33*, 781; (g) Shibata, K.; Satsumabayashi, S.; Sano, H.; Komiyama, K.; Nakagawa, A.; Omura, S. *J. Antibiot.* **1986**, *39*, 415; (h) Lin, L.-Z.; Blasko, G.; Cordell, G. A. *J. Nat. Prod.* **1988**, *51*, 1161; (i) Yamaki, H.; Iguchi-Ariga, S. M. M.; Ariga, H. *J. Antibiot.* **1989**, *42*, 604; (j) Yamashita, T.; Sakai, M.; Kawai, Y.; Aono, M.; Takahashi, K. *J. Antibiot.* **1989**, *42*, 1015; (k) Suzukake-Tsuchiya, K.; Moriya, Y.; Hori, M.; Uehara, Y.; Takeuchi, T. *J. Antibiot.* **1989**, *42*, 1831; (l) Nagaishi, K.; Adachi, R.; Matsui, S.; Yamaguchi, T.; Kasahara, T.; Suzuki, K. J. *J. Cell. Phys.* **1999**, *180*, 345; (m) Sakagami, M.; Morrison, P.; Welch, W. J. *Cell Stress Chaperones* **1999**, *4*, 19; (n) Janin, Y. L. *J. Med. Chem.* **2005**, *48*, 7503.
7. Ding, L.; Maier, A.; Fiebig, H.-H.; Goerls, H.; Lin, W.-H.; Peschel, G.; Hertweck, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1630.
8. Cai, P.; Kong, F. M.; Ruppen, M. E.; Glasier, G.; Carter, G. T. *J. Nat. Prod.* **2005**, *68*, 1736.
9. (a) Keller-Schierlein, W.; Meyer, M.; Cellai, L.; Cerrini, S.; Lamba, D.; Segre, A.; Fedeli, W.; Brufani, M. J. *J. Antibiot.* **1984**, *37*, 1357; (b) Lu, C.; Shen, Y. *J. Antibiot.* **2007**, *60*, 649; (c) Wilson, M. C.; Nam, S.-J.; Gulder, T. A. M.; Kauffman, C. A.; Jensen, P. R.; Fenical, W.; Moore, B. S. *J. Am. Chem. Soc.* **2011**, *133*, 1971; (d) Whitfield, G. B.; Olson, E. C.; Herr, R. R.; Fox, J. A.; Bergy, M. E.; Boyack, G. A. *Am. Rev. Tuberc. Pulm. Dis.* **1957**, *75*, 584; (e) DeBoer, C.; Meulman, P. A.; Wnuk, R. J.; Peterson, D. H. *J. Antibiot.* **1970**, *23*, 442; (f) Sasaki, K.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 7591; (g) Omura, S.; Iwai, Y.; Takahashi, Y.; Sadakane, N.; Nakagawa, A. *J. Antibiot.* **1979**, *32*, 255; (h) Omura, S.; Nakagawa, A.; Sadakane, N. *Tetrahedron Lett.* **1979**, *20*, 4323.
10. Yun, H.; Chou, T.; Dong, H.; Tian, Y.; Li, Y.; Danishefsky, S. J. *J. Org. Chem.* **2005**, *70*, 10375.
11. (a) Kuttruff, C. A.; Geiger, S.; Cakmak, M.; Mayer, P.; Trauner, D. *Org. Lett.* **2012**, *14*, 1070; (b) Zhao, G.; Wu, J.; Dai, W.-M. *Synlett* **2012**, 2845; (c) Pennington, L. L.; Moody, C. J. *Abstracts of Papers*, 238th ACS National Meeting, Washington, DC, United States, 2009
12. (a) Fenical, W.; Jensen, P. R. *Nat. Chem. Biol.* **2006**, *2*, 666; (b) Koehn, F. E.; Carter, G. T. *Nat. Rev. Drug Disc.* **2005**, *4*, 206.
13. Stereochemistry of the C8 (as per the numbering of the divergolides of Hertweck) has not been assigned unequivocally: Cai, P.; Kong, F. M.; Ruppen, M. E.; Glasier, G.; Carter, G. T. *J. Nat. Prod.* **2005**, *68*, 1736.
14. (a) Shah, A.; Sivappa, R.; Mello, C.; Singh, B. R.; Cai, S. *J. Med. Plants Res.* **2012**, *6*, 234–242; (b) Rasapalli, S.; Saibu, A. A. 38th ACS Northeast Regional Meeting, Rochester, NY, USA, Sept 30–Oct 3, 2012.; (c) Rasapalli, S.; Dhawane, A. 242nd ACS National Meeting, Philadelphia, USA, Aug 19–23, 2012
15. The alternative disconnection has also been under communication.
16. (a) Ding, L.; Maier, A.; Fiebig, H.-H.; Goerls, H.; Lin, W.-H.; Peschel, G.; Hertweck, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1630; (b) Cai, P.; Kong, F. M.; Ruppen, M. E.; Glasier, G.; Carter, G. T. *J. Nat. Prod.* **2005**, *68*, 1736.
17. Rateb, M. E.; Houssen, W. E.; Arnold, M.; Abdelrahman, M. H.; Deng, H.; Harrison, W. T. A.; Okoro, C. K.; Asenjo, J. A.; Andrews, B. A.; Ferguson, G.; Bull, A. T.; Goodfellow, M.; Ebel, R.; Jaspars, M. *J. Nat. Prod.* **2011**, *74*, 1491–1499.
18. Deng, B. L.; Hartman, T. L.; Buckheit, R. W., Jr.; Pannecouque, C.; De Clercq, E.; Fanwick, P. E.; Cushman, M. *J. Med. Chem.* **2005**, *48*, 6140.
19. Caulfield, T. J.; J. Clemens, R. S.; Francis, B. S.; Freed, S.; John, T.-B.; Le, B.; Pedgrift, A. D.; Ramos, G.; Rosse, M.; Smrcina, D. S.; Thorpe, W.; Wire, J. Z. PCT Int. Appl. WO 2008151211, 2008.; (b) Duff, J. C. *J. Chem. Soc.* **1947**, 547.
20. (a) Hoveyda, H.; Brantis, C. E.; Dutheuil, G.; Zoute, L.; Schils, D.; Fraser, G. PCT Int. Appl. WO 2011076732, 2011.; (b) Caulfield, T. J.; J. Clemens, R. S.; Francis, B. S.; Freed, S.; John, T.-B.; Le, B.; Pedgrift, A. D.; Ramos, G.; Rosse, M.; Smrcina, D. S.; Thorpe, W.; Wire, J. Zhao. PCT Int. Appl. WO 2008151211, 2008.; (c) McKenna, J.; Papa, P. W.; Sakata, S. T.; Erdman, P. E.; Packard, G. K. PCT Int. Appl. 2007084560.; (d) Hoveyda, H.; Brantis, C. E.; Dutheuil, G.; Zoute, L.; Schils, D.; Bernard, J. PCT Int. Appl. 2010066682.
21. (a) Nishiyama, T.; Miyazawa, M. *J. Oleo Sci.* **2003**, *52*, 331.
22. (a) Rizzacasa, M. A.; Sargent, M. V. *Aust. J. Chem.* **1987**, *40*, 1737; (b) Borsche, W. *Justus Liebigs Ann. Chem.* **1936**, *526*, 1; (c) Tietze, L. F.; Liu, D. *ARKIVOC* **2008**, *8*, 193; (d) Nishiyama, T.; Miyazawa, M. *J. Oleo Sci.* **2003**, *52*, 331; (e) Vela, M. A.; Fronczek, F. R.; Horn, G. W.; McLaughlin, M. L. *J. Org. Chem.* **1990**, *55*, 2913; (f) Boger, D. L.; Turnbull, P. *J. Org. Chem.* **1998**, *63*, 8004; (g) Comber, M. F.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2783; (h) Hughes, A. B.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1989**, 449; (i) Cason, J. *J. Am. Chem. Soc.* **1941**, *63*, 828; (j) El-Abbady, A. M.; Doss, S. H.; Moussa, H. H.; Nosseir, M. *J. Org. Chem.* **1961**, *26*, 4871; (k) House, H. O.; Larson, J. K. *J. Org. Chem.* **1968**, *33*, 448.
23. (a) Packer, R. J.; Smith, D. C. C. *J. Chem. Soc.* **1967**, 2194; (b) Cammidge, A. N.; Ozturk, O. *J. Org. Chem.* **2002**, *67*, 7457.
24. (a) Shioiri, T.; Ninomiya, K.; Yamada, S. *J. Am. Chem. Soc.* **1972**, *94*, 6203; (b) Lebel, H.; Leogane, O. *Org. Lett.* **2006**, *8*, 5717; (c) Ninomiya, K.; Shioiri, T.; Yamada, S. *Tetrahedron* **1974**, *30*, 2151; (d) Murato, K.; Shioiri, T.; Yamada, S. *Chem. Pharm. Bull.* **1975**, *23*, 1738; (e) Capson, T. L.; Poulter, C. D. *Tetrahedron Lett.* **1984**, *25*, 3515; (f) Wolff, O.; Waldvogel, S. R. *Synthesis* **2004**, 1303; (g) Sawada, D.; Sasayama, S.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **2006**, *47*, 7219.
25. (a) Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411; (b) Ueda, S.; Nagasawa, H. *J. Org. Chem.* **2009**, *74*, 4272.
26. Kuttruff, C. A.; Geiger, S.; Cakmak, M.; Mayer, P.; Trauner, D. *Org. Lett.* **2012**, *14*, 1070.
27. We are currently evalauting the addition of long chain *RLis* which is not as straightforward.
28. (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155; (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277; (c) Luo, H. B.; Xie, Y. Y. *Chin. Chem. Lett.* **2003**, *14*, 555; (d) Magdziak, D.; Rodriguez, A. A.; Van De Water, R. W.; Pettus, T. R. R. *Org. Lett.* **2002**, *4*, 285. and references there in.
29. (a) Wunderlich, S. H.; Bresser, T.; Dunst, C.; Monzon, G.; Knochel, P. *Synthesis* **2010**, *15*, 2670; (b) Wunderlich, S. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7685.