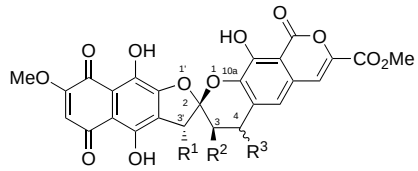
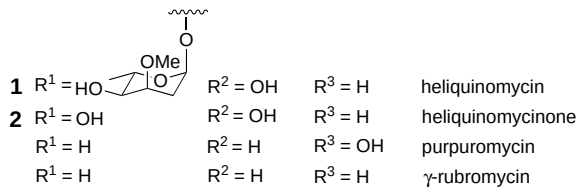
) T. Skrydstrup, *Angew. Chem.* **1997**, *110*, 355 – 357; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 345 – 347.
[15] J. A. Stafford, N. L. Valvano, *J. Org. Chem.* **1994**, *59*, 4346 – 4349. Although one might expect the formation of a seven-membered carbamate upon reaction with 1,1′-carbonyl diimidazole, we hypothesize that in this particular case the formation of five-membered rings is favored exclusively based on considerations of ring strain.
[16] T. Ishiyama, M. Murata, N. Miyaura, *J. Org. Chem.* **1995**, *60*, 7508 – 7510.
[17] A. Padwa, D. Dehm, T. Oine, G. A. Lee, *J. Am. Chem. Soc.* **1975**, *97*, 1837 – 1845.
[18] The addition of HCHO was achieved using the protocol reported by S. Kobayashi, I. Hachiya, *J. Org. Chem.* **1994**, *59*, 3590 – 3596. For a related example, see: P. Bernardelli, O. M. Moradei, D. Friedrich, J. Yang, F. Gallou, B. P. Dyck, R. W. Doskotch, T. Lange, L. A. Paquette, *J. Am. Chem. Soc.* **2001**, *123*, 9021 – 9032.
[19] a) J. L. Namy, P. Girard, H. B. Kagan, *Nouv. J. Chem.* **1977**, *1*, 5 – 7; b) P. Girard, J. L. Namy, H. B. Kagan, *J. Am. Chem. Soc.* **1980**, *102*, 2693 – 2698.
[20] a) G. E. Keck, T. T. Wager, S. F. McHardy, *Tetrahedron* **1999**, *55*, 11755 – 11772; b) J. L. Chiara, C. Destabel, P. Gallego, J. Marco-Contelles, *J. Org. Chem.* **1996**, *61*, 359 – 360; c) G. E. Keck, S. F. McHardy, T. T. Wager, *Tetrahedron Lett.* **1995**, *36*, 7419 – 7422.
[21] J. Marco-Contelles, P. Gallego, M. Rodríguez-Fernández, N. Khiar, C. Destabel, M. Berbabé, A. Martínez-Grau, J. L. Chiara, *J. Org. Chem.* **1997**, *62*, 7397 – 7412. For a preliminary disclosure of the same reductive coupling/N–O cleavage and an example with altered protecting groups, see a) J. L. Chiara, J. Marco-Contelles, N. Khiar, P. Gallego, C. Destabel, M. Bernabé, *J. Org. Chem.* **1995**, *60*, 6010 – 6011; b) S. Bobo, I. Storch de Gracia, J. L. Chiara, *Synlett* **1999**, 1551 – 1554.
[22] The role of H_2O is either as a proton source or, more likely, as a donor ligand which increases the reducing power of SmI_2. For leading references, see: a) S. Hanessian, C. Girard, *Synlett* **1994**, 861 – 862; b) E. Hasegawa, D. P. Curran, *J. Org. Chem.* **1993**, *58*, 5008 – 5010.
[23] Although $POCl_3$/DMF has been reported several times for oxazole formation from ketoamides, use of neat $POCl_3$ is far more rare. For one example, see: R. L. Dow, *J. Org. Chem.* **1990**, *55*, 386 – 388.
[24] In one particularly instructive example, remote substituents played a critical role in the ease of MOM cleavage from an indole substrate: A. I. Meyers, T. K. Highsmith, P. T. Buonara, *J. Org. Chem.* **1991**, *56*, 2960 – 2964.
[25] J. E. Macor, J. T. Forman, R. J. Post, K. Ryan, *Tetrahedron Lett.* **1997**, *38*, 1673 – 1676.
[26] C. T. Brain, J. M. Paul, *Synlett* **1999**, 1642 – 1644.
[27] This protocol represents a new method for MOM cleavage on indoles, particularly for acid-sensitive substrates since typical deprotection procedures utilize HCl at elevated temperatures. Since previous reports have already established the acid-sensitivity of the aryl chlorine atoms on the diazonamide skeleton that bears a free indole (see ref. [2c]), the ability to initially cleave the methyl ether only, followed by basic hydrolysis, is crucial for the survival of the chlorine substituents in **2**.

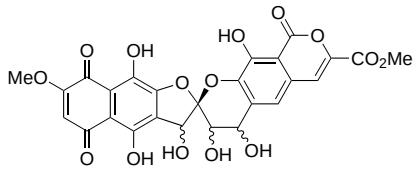
Studies in the Total Synthesis of Heliquinomycinone: Proof of Concept and Assembly of a Fully Mature Spirocyclization Precursor**

Donghui Qin, Rex X. Ren, Tony Siu, Changsheng Zheng, and Samuel J. Danishefsky*

Heliquinomycin (**1**) was isolated by Chino et al. from *Streptomyces sp.* MJ 929-SF2.[1] The structure of its aglycone moiety **2**, which we term heliquinomycinone, is related to structures encountered in the purpuromycin,[2] γ-rubromycin,[3] and griseorhodin antibiotics.[4] Although spiroketal







griseorhodin C

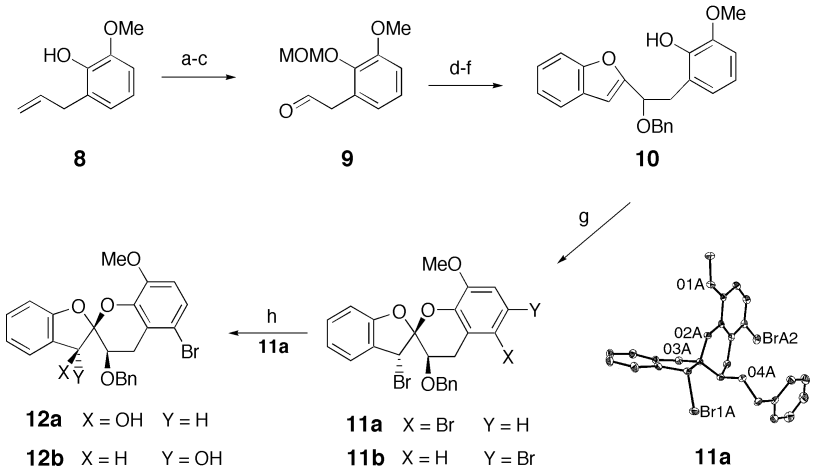
linkages in natural products are well known,[5] it is less common that such a moiety is derived from two phenolic hydroxy groups (C2). An arrangement in which the spiroketal core of the hexacyclic structure is linked to a glycoside, in this case to a 2,6-dideoxyhexose (cymarose) sugar, seems to be unique to **1**.

[*] Prof. S. J. Danishefsky,[+] Dr. D. Qin, Dr. R. X. Ren, T. Siu, Dr. C. Zheng
Department of Chemistry, Columbia University
Havemeyer Hall, New York, NY, 10021 (USA)
E-mail: s-danishefsky@ski.mskcc.org
[+] Laboratory for Bioorganic Chemistry
Sloan – Kettering Institute for Cancer Research
1275 York Ave., New York, NY, 10021 (USA)
Fax: (+1) 212-772-8691

[**] This work was supported by the National Institutes of Health (Grant numbers: AI 16943 and HL25848). A Postdoctoral Fellowship is gratefully acknowledged by R.X.R. (NIH, Grant Number IF32EY06750-0181). The authors thank Dr. Daniel Chen for important initial experiments, Dr. Brian Bridgewater and Prof. Ged Parkin of Columbia University for X-ray crystal structure analysis of **11a**, and Yashuiro Itagaki for high-resolution mass spectral analyses.

  1433-7851/01/4024-4709 $ 17.50+.50/0

Adding to the interest level in heliquinomycin, is its inhibition of human DNA helicase, an important enzyme that unwinds double-stranded DNA prior to its replication.[6] It seems reasonable that helicase inhibition could be the basis of action for an anticancer drug:[7] selectivity could arise from the increased proclivity for transformed cells to undergo DNA turnover. The chemistry lessons inherent in attempts to build challenging structures such as **1** and **2**, as well as the opportunity to explore a potentially new type of restraint on uncontrolled cell growth, prompted us to undertake a total synthesis program directed toward these agents. Herein and in the following paper, we record a journey, which after serious difficulties led to a total synthesis of heliquinomycinone (**2**), the aglycone of heliquinomycin.[8]

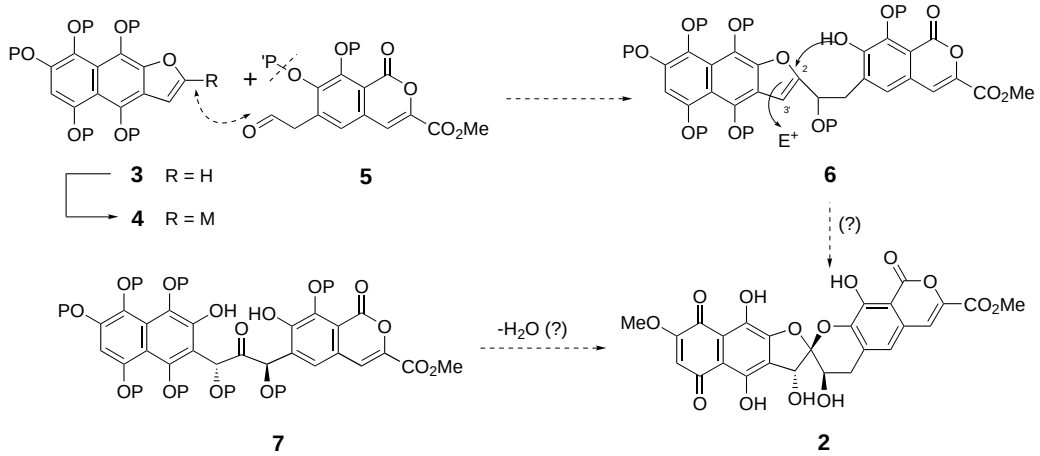


Scheme 2. Reagents and conditions: a) *N*,*N*-diisopropylethylamine, MOMCl, 50 °C, 66 %; b) OsO_4, NMO, acetone/H_2O, 63 %; c) $NaIO_4$, (aq.) $NaHCO_3$, CH_2Cl_2, 99 %, d) 2,3-benzofuran, *n*BuLi, −78 °C, THF; e) KH, BnBr, THF, 70 % (over two steps); f) ethereal HCl (1N), 2-propanol, THF, 93 %; g) NBS, CH_2Cl_2, (**11a**/**11b** 4:5, 85 %); h) AgOTf, wet THF, (**12a**:**12b** 3:1, 81 %). MOM = methoxymethyl; NMO = 4-methylmorpholine *N*-oxide; Bn = benzyl; NBS = *N*-bromosuccinimide.

Our central strategy for the synthesis is shown in Scheme 1: the spiroketal linkage would be fashioned through electrophilic potentiation at C2−C3′ of an appropriate naphthofuran (**6** →**2**). We anticipated that the synthesis of **6** by connecting the required subunits **4** and **5** could well be more straightforward than the assembly of a stereochemically correlated α,α'-difunctionalized ketone **7**, which is a more traditional type of spiroketal precursor. Ring closure of **6** would involve the nucleophilic attack of a proximal suitably differentiated phenolic hydroxy group at C2. It did not escape our attention that if the ring-closing step involved the inversion of the configuration at C2 of the naphthofuranoid system, (in which E^+ is translatable to OH^+), the required anti relationship between the 1,2-spiroketal bond and the putative hydroxy group at C3′ would be assured. Less certain, but still reasonable, was the possibility that the resident hydroxy group at C3 (free or protected), would direct the sense of electrophilic attack of E^+ at the naphthofuran ring. In this way, the nucleophilic cyclization step would also establish the governing configurational relationship between the spiroketal group and the C3 stereogenic center in the pyranoid moiety. In other words, the relative stereochemistry required to reach heliquinomycinone might arise from a structure with only one stereogenic center (C3). Thus if the precursor has the correct absolute configuration at the future C3, the aglycone might be delivered with enantiotopic control.

A model that allowed us to evaluate the concept, albeit at a rather primitive level, was soon assembled (Scheme 2). Various attempts at electrophilic spiroketalization of **10** were initiated. Of these, a favorable result arose only from the bromonium ion induced conversion of **10**.[9] This step was complicated by concurrent and nonspecific bromination of the phenol ring. In spite of this drawback, we took the formation of **11a** (verified by means of X-ray crystal structure analysis) and **11b** to be supportive of the general concept.[10] The benzylic bromine atom was readily replaced through solvolytic displacement by an oxygen-based nucleophile.[9] However, in early studies, compounds **12a** and **12b** were produced in a 3:1 ratio. Clearly, the solvolytic step at C3′ occurred primarily with inversion of configuration.

It was presumed that an appropriately functionalized naphthofuran moiety (substituted with five methoxy or



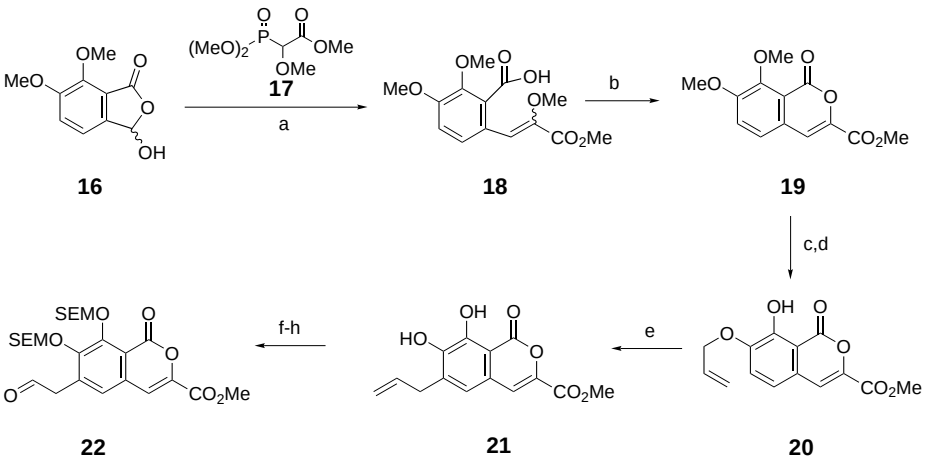
Scheme 1. Strategy for the synthesis of heliquinomycinone (**2**).

  1433-7851/01/4024-4710 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2001**, *40*, No. 24

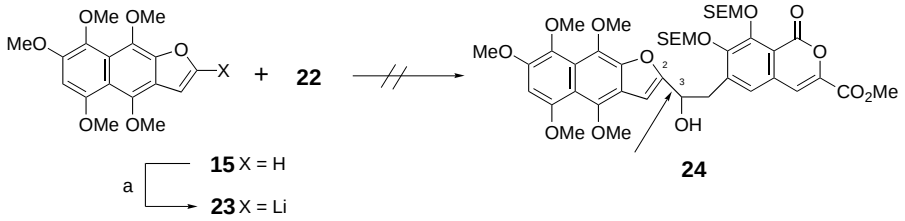
equivalent groups) would be susceptible to a broad range of reagents for realizing the desired integrated oxidative dearomatization and nucleophilic spirocyclization sequence. Accordingly, we set out to assemble functional versions of the two fragments, that is, naphthofuran **3** and aryl acetaldehyde **5**. It was further assumed (naively as it turned out) that a suitable metalo derivative of naphthofuran **4** would couple to **5** to produce a substrate of the type **6**, which we hoped to convert into **2**.

A convergent synthesis of naphthofuran **15** was implemented based on a modified strategy of Perry et al. (Scheme 3).[11] The known nitrile **13**[12] was treated with the dianion of 3-furoic acid to afford furan **14** in 92% yield. Intramolecular Friedel–Crafts acylation, followed by reduction and permethylation[13] provided **15** in moderate yield (44% over two steps).

The synthesis of the aryl acetaldehyde **22**, which includes an isocoumarin moiety, commenced with commercially available opianic acid **16** (Scheme 4). A modified Horner–Emmons reaction of **16** and **17**[14] afforded **18** as a mixture of stereoisomers (98%, 1:1). Cyclization under acidic conditions afforded isocoumarin **19**. Boron tribromide was used for the demethylation of the two aromatic ethers, and selective monoallylation of the resulting compound afforded **20**. Claisen rearrangement of **20** gave rise to product **21** (75% over two steps). The phenol functions were protected as SEM ethers under standard conditions. Cleavage of the double bond in a two-stage dihydroxylation/sodium periodate cleavage[15] provided aldehyde **22**.[16]



Scheme 4. Reagents and conditions: a) NaH, THF, 0° C, 98% (1:1); b) H_2SO_4 (3N), MeOH, reflux, 83%; c) BBr_3, CH_2Cl_2, −78 °C, 98%; d) LiHMDS, DMF, allyl bromide, −40 °C, 84%; e) xylene, 185 °C, 89%; f) SEMCl, DMAP, Et_3N, CH_2Cl_2, 86%; g) OsO_4, NMO, acetone/H_2O, 92%; h) $NaIO_4$, THF/Et_2O, 95%. DMAP = 4-dimethylaminopyridine; SEM = 2-(trimethylsilyl)ethoxymethyl; HMDS = hexamethyldisilazane.

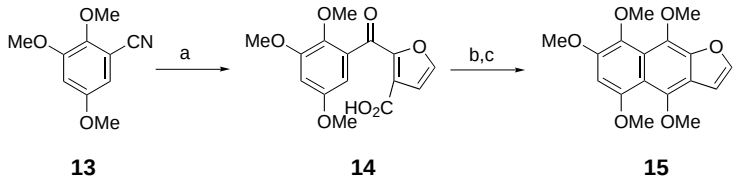


Scheme 5. Reagents and conditions: a) *n*BuLi, THF, −78 °C.

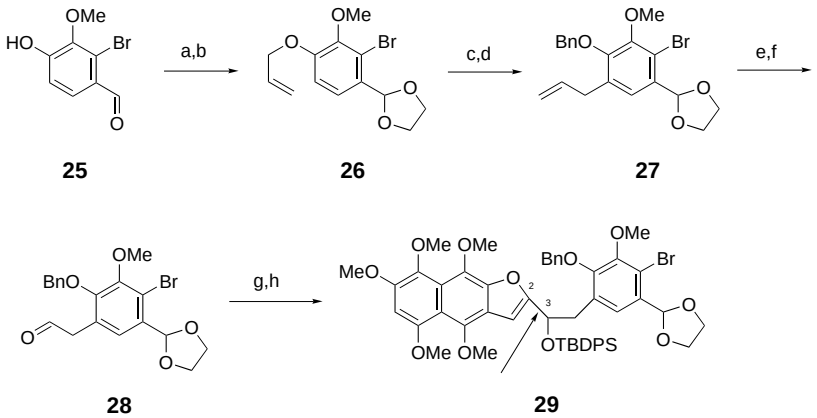
With **22** and **15** in hand, we focused on coupling the two units. Treatment of aldehyde **22** with lithiated naphthofuran **23** did not give any of the desired coupling product **24** (Scheme 5). Instead, naphthofuran **15** and aldehyde **22** were recovered. The formyl group in **22** is not particularly hindered, and thus the failure of the coupling reaction suggested a strong tendency toward proton transfer rather than toward C–C bond formation with the putative nucleophile **23**. Presumably, the ease of deprotonation of the benzylic methylene group of **22** is enhanced by the *para* carbonyl function of the isocoumarin moiety. The effects of cerium[17] and various other metal additives were explored in an attempt to modulate the basicity of the metalated naphthofuran. The inability to form a C–C bond implies that enolization is facile. A striking indication of the difficulty of targeting a carbon nucleophile to the formyl group of **22** is seen in its reaction with *n*-butyllithium. The *n*-butyl group added to the isocoumarin moiety, but left the aldehyde group intact.

Given our interpretation of the role of the C9 isocoumarin carbonyl group in triggering proton transfer between **23** and **22**, and following many failures to accomplish the addition reaction, we reluctantly decided against a fully convergent coupling step. Instead, we would use an aryl acetaldehyde target without a *para* carbonyl group to form the C3–C2 bond. Evidently, it would be necessary to reconstitute the isocoumarin moiety at a later stage in the synthesis. Several suitable aldehydes were examined. Eventually, we decided to couple the *ortho*-bromo dioxolane **28** with the lithio derivative **23**.

Protection of aldehyde **25**[18] and monoalkylation of the phenol afforded **26** in 90% yield (Scheme 6). Claisen rearrangement was induced by heating **26** to 240 °C. The resulting phenol was protected as its benzyl ether to produce **27**. We presumed that the C10a phenol could be exposed at a suitable stage for the oxidative spiroketalization (**6** → **2**). Dihydroxyla-



Scheme 3. Reagents and conditions: a) 3-furoic acid, *n*BuLi (2.2 equiv), THF, −78 °C, then **13**, 92%; b) H_2SO_4, 3 days, 88%; c) $Na_2S_2O_4$, TBABr, KOH, dimethyl sulfate, THF/H_2O, 50%. TBABr = tetrabutylammonium bromide.



Scheme 6. Reagents and conditions: a) ethylene glycol, benzene, reflux, 95%; b) K_2CO_3, allyl bromide, acetone, reflux, 95%; c) decalin, 240°C; d) K_2CO_3, BnBr, acetone, reflux, 57% (over two steps); e) OsO_4, NMO, acetone/H_2O, 97%; f) $NaIO_4$, acetone/H_2O, 88%; g) **23**, THF, −78°C; h) TBDPSCl, imidazole, CH_2Cl_2, 64% (over two steps). TBDPS = *tert*-butyldiphenylsilyl.

tion of the terminal vinyl function of **27** was followed by oxidative cleavage, thus giving the desired aldehyde precursor **28**.

The coupling reaction of **23** with **28** proceeded moderately well. The resulting secondary alcohol (C3) was protected as a silyl ether (**29**, 64% over two steps). We next addressed the formation the isocoumarin from **29** (Scheme 7). For this purpose, the lithio derivative of **29** was carboxylated and the resulting acid was methylated to afford ester **30**. The cyclic ketal was cleaved and the resulting aldehyde was condensed with **31**[14] to form **32**. The TBS silyl ether protecting group in **32** was cleaved with tetrabutylammonium fluoride. The product, which was not completely characterized, was treated with potassium carbonate in methanol to afford **33**. The benzyl group of **33** was cleaved to give phenol **34**, and the stage was set for the spirocyclization step.

Finally, a suitable precursor for **2** was in hand. In the following communication,[19] we show that it was indeed possible to reach heliquinomycinone via **33**, but only after overcoming some unforeseen and serious difficulties.

Received: September 5, 2001 [Z17859]

[1] a) M. Chino, K. Nishikawa, M. Umekia, C. Hayashi, T. Yamazaki, T. Tsuchida, T. Sawa, M. Hamada, T. Takeuchi, *J. Antibiot.* **1996**, *49*, 752; b) M. Chino, K. Nishikawa, T. Tsuchida, R. Sawa, H. Nakamura, K. T. Nakamura, Y. Muraoka, D. Ikeda, H. Naganawa, T. Sawa, T. Takeuchi, *J. Antibiot.* **1997**, *50*, 143.

[2] M. R. Bardone, E. Martinelli, L. F. Zerilli, C. Coronelli, *Tetrahedron* **1974**, *30*, 2747.

[3] H. Brockmann, A. Zeeck, *Chem. Ber.* **1970**, *103*, 1709.

[4] R. M. Stroshane, J. A. Chen, E. A. Rubalcuba, A. L.Garietson, A. A. Aszalos, P. P. Roller, *J.Antibiot.* **1979**, *32*, 197.

[5] F. Perron, K. F. Albizati, *Chem. Rev.* **1989**, *89*, 1617.

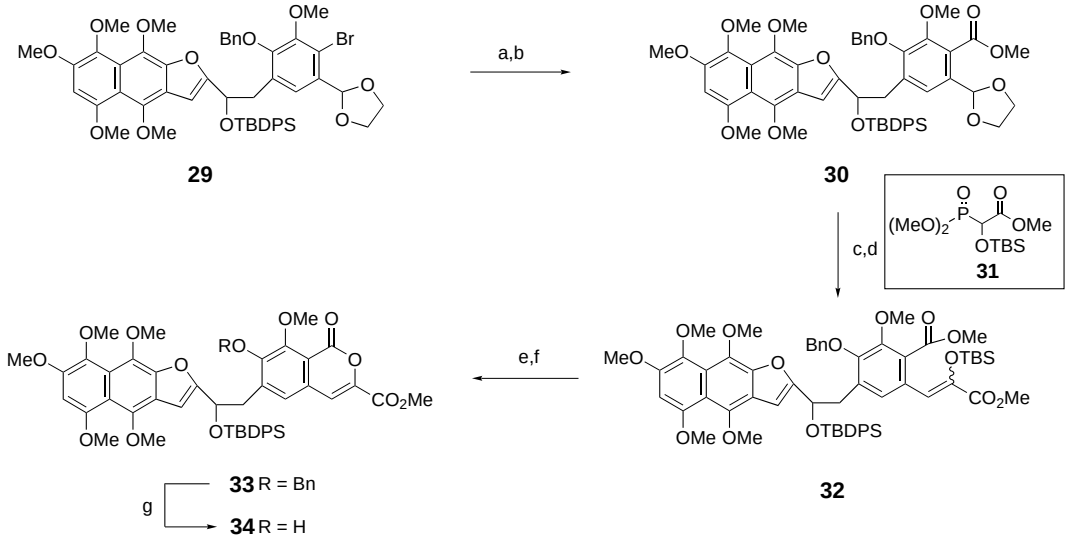
[6] S. W. Matson, K. A. Kaiser-Rogers, *Annu. Rev. Biochem.* **1990**, *59*, 289.

[7] M. Chino, K. Nishikawa, A. Yamada, M. Ohsono, T. Sawa, F. Hanaoka, M. Ishizaka, T. Takeuchi, *J. Antibiot.* **1998**, *51*, 480.

[8] For model studies toward the spiroketal core of heliquinomycin and related structures, see: a) T. Capecchi, C. B. de Koning, J. P. Michael, *Tetrahedron Lett.* **1998**, *39*, 5429; b) T. Capecchi, C. B. de Koning, J. P. Michael, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2681; for syntheses of the isocoumarin subunit, see: c) T. P. Thrash, T. D. Welton, V. Behar, *Tetrahedron Lett.* **2000**, *41*, 29; d) S. P. Waters, M. C. Kozlowski, *Tetrahedron Lett.* **2001**, *42*, 3567; for a synthesis of the naphthalene subunit of heliquinomycin and related structures, see: e) X. Xie, M. C. Kozlowski, *Org. Lett.* **2001**, *3*, 2661.

[9] NBS was previously used for the activation of a benzofuran: G. F. Miknis, R. M. Williams, *J. Am. Chem. Soc.* **1993**, *115*, 536.

[10] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-169848 (**11a**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).



Scheme 7. Reagents and conditions: a) *n*BuLi (3.0 equiv), CO_2 (g), −78°C, THF; b) $TMSCHN_2$, MeOH/benzene, 81% (over two steps); c) HCl (3N), acetone/THF, 95%; d) LiHMDS, **31**, THF, −78→25°C, then aldehyde, 96%; e) TBAF (1.0 equiv), THF, 0°C; f) K_2CO_3, MeOH, 72% (over two steps); g) H_2, Pd/C (5%), EtOAc, 92%. TBAF = tetrabutylammonium fluoride; TBS = *tert*-butyldimethylsilyl.

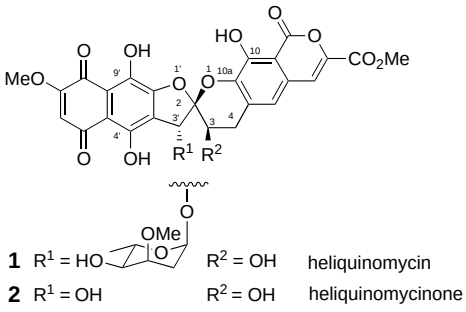
  1433-7851/01/4024-4712 $ 17.50+.50/0

[11] a) P. J. Perry, V. H. Pavalidis, J. H. Hadfield, I. G. C. Coutts, *J. Chem. Soc. Perkin Trans. 1* **1995**, 1085; b) P. J. Perry, V. H. Pavalidis, J. H. Hadfield, *Tetrahedron* **1997**, *53*, 3195.
[12] M. A. Rizzacasa, M. V. Sargent, *J. Chem. Soc. Perkin Trans. 1* **1988**, 2425.
[13] G. A. Kraus, T. O. Man, *Syn. Commun.* **1986**, *16*, 1037.
[14] a) E. Nakamura, *Tetrahedron Lett.* **1981**, *22*, 663; b) D. Horne, J. Gaudino, W. J. Thompson, *Tetrahedron Lett.* **1984**, *25*, 3529.
[15] The Lemieux Johnson protocol was not applicable because under those conditions the only product observed was the benzaldehyde: R. Pappo, D. S. Allen Jr., R. U. Lemieux, W. S. Johnson, *J. Org. Chem.* **1956**, *21*, 478.
[16] Behar and co-workers independently described the synthesis of a related compound by an analogous route; see ref. [8c].
[17] T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, Y. Kamiya, *J. Am. Chem. Soc.* **1989**, *111*, 4392.
[18] R. A. Hill, G. W. Kirby, G. J. O'Loughlin, D. J. Robins, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1967.
[19] T. Siu, D. Qin, S. J. Danishefsky, *Angew. Chem.* **2001**, *113*, 4849; *Angew. Chem. Int. Ed.* **2001**, *40*, 4713.

The Total Synthesis of Heliquinomycinone**

Tony Siu, Donghui Qin, and Samuel J. Danishefsky*

In the preceding communication,[1] we described the assembly of intermediate **3**, which was envisioned as a substrate for an oxidative dearomatization-spiroketalization sequence (**3** → **4**, Scheme 1), en route to heliquinomycinone (**2**), the aglycone of the naturally occurring helicase inhibitor



1 R^1 = HO R^2 = OH heliquinomycin
2 R^1 = OH R^2 = OH heliquinomycinone

heliquinomycin (**1**). A large number of reagent combinations were used in attempts to bring about the conversion of **3** into a product of the type **4** (Scheme 1). In particular, we were seeking electrophiles that could be introduced concomitantly with nucleophilic spirocyclization. Unfortunately, even after screening a large number of possibilities, this strategy was not successful. When projected electrophilic cyclizations were attempted by using halonium equivalents such as NBS, NIS, NCS, or iodine in the presence of sodium bicarbonate, oxidative demethylation and quinone formation occurred. Similar results were observed when various epoxidations of the furanoid ring were attempted.[2] An important constraining factor was the electron richness of the pentamethoxynaphthalene moiety present in **3**. This pattern lent itself to ready pairwise oxidative demethylations to produce ring A or ring B quinones, with subsequent deactivation of the furan double bond. Furthermore, no reaction occurred when metal-based reagents such as $Pd(OAc)_2$, $Ti(OAc)_3$, Re_2O_7,[3] and Hg^{II} salts were explored to activate the furan double bond for nucleophilic attack. Even after extensive experimentation, we were unable to carry out the transformation **3** → **4**. In substance, we were unable to overcome the combination of nonreactivity of the furanoid moiety to some reagent combinations, and the high vulnerability of the pentamethoxynaphthalene structure to others.

The one successful oxidation which targeted the furan ring and did not compromise the integrity of the pentamethoxynaphthalene moiety, arose from the action of osmium tetroxide on **5**,[4] which gave a diastereomeric mixture of **6** (Scheme 2, 50–60%). The product was difficult to separate and could not be satisfactorily characterized by means of ^{1}H NMR spectroscopy. Our decision to go forward with this material was based largely on a supportive mass spectrum. Deprotection of the benzyl ether exposed the C10a phenolic function, again as a poorly characterized mixture of diastereomers **7**.

With triol **7** in hand, all that remained to reach hydroquinonoid versions of **2** was acid-induced spiroketalization (Scheme 3). Remarkably, this seemingly attainable goal could not be accomplished. The hydroxy group at the pre-C3′ benzylic position was unexpectedly vulnerable.[5] An attempt at a spirocyclization under Mitsunobu-type conditions was unsuccessful and instead led to the transformation of diastereomers **7** into **9**.[6]

In retrospect, this result reflects the ease of formation of a quinone-methide-like heterolysis product, presumably mediated by the strong electron-donating nature of the five methoxy groups on the naphthalene system. Various protections of C3 and C3′ in the hope of favoring the desired spirocyclization were not productive.

A chance observation proved to be critical in solving the problem. Exposure of diastereomers **6** to air, in the presence of triethylamine/methanol led to oxidation at C3′, thus forming the α-hydroxyketone (Scheme 4).[7] Subsequent debenzylation gave **10** as a 1:1 mixture of anomers. It was hoped that the presence of the ketone would prevent bond formation between the "C10a" phenol and "C3′" (except for that arising from a presumably reversible hemicacetal link). However, the feasibility of spirocyclization in **10**, adjacent to a ketone linkage, was by no means certain.

Under Mitsunobu conditions,[6] the desired cyclization was achieved and mixture **10** afforded compounds **11** and **12** in a 1:1 ratio after removal of the silyl ethers. These products were

[*] Prof. S. J. Danishefsky,[+] T. Siu, Dr. D. Qin
Department of Chemistry, Columbia University
Havemeyer Hall, New York, NY, 10021 (USA)
E-mail: s-danishefsky@ski.mskcc.org
[+] Laboratory for Bioorganic Chemistry
Sloan–Kettering Institute for Cancer Research
1275 York Ave., New York, NY, 10021 (USA)
Fax: (+1) 212-772-8691

[**] This work was supported by the National Institutes of Health (Grant numbers: AI 16943 and HL25848). The authors thank Dr. Makoto Chino of Nippon Kayaku Co., Ltd. for kindly providing a sample of heliquinomycin, and Yashuiro Itagaki of Columbia University for high-resolution mass spectral analyses.