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Solvent-Dependent Divergent Functions of $Sc(OTf)_3$ in Stereoselective Epoxide-Opening Spiroketalizations

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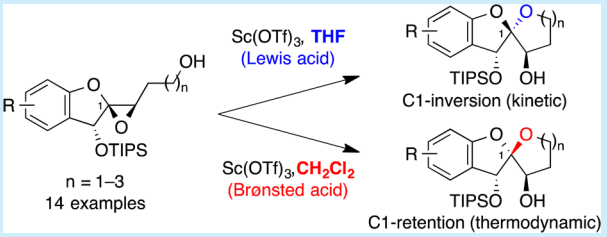
Supporting Information

ABSTRACT: A stereocontrolled synthesis of benzannulated spiroketals has been developed using solvent-dependent Sc-$(OTf)_3$-mediated spirocyclizations of *exo*-glycal epoxides having alcohol side chains. In THF, the reaction proceeds via Lewis acid catalysis under kinetic control with inversion of configuration at the anomeric carbon. In contrast, in CH_2Cl_2, Brønsted acid catalysis under thermodynamic control leads to retention of configuration. The reactions accommodate a variety of aryl substituents and ring sizes and provide stereochemically diverse spiroketals.



Benzannulated spiroketal natural products exhibit a broad array of biological activities.[1] Examples include the matrix metalloproteinase inhibitor berkelic acid,[2] the fungal cell wall glucan synthase inhibitory papulacandins,[3] and the anti-inflammatory aquilarinoside A.[4] Bisbenzannulated spiroketals include the rubromycin family of human telomerase and HIV reverse transcriptase inhibitors,[5] the DNA helicase inhibitor heliquinomycin, and the antibiotic purpuromycin, which inhibits aminoacyl-tRNA synthesis by a novel mechanism involving direct binding to the tRNA substrate.[6] Notably, the benzannulated spiroketal core is essential for telomerase inhibition in the rubromycin family.[7] Numerous approaches to the synthesis of benzannulated spiroketals have been reported.[8,9] Despite these notable advances, most strategies rely upon thermodynamically controlled reactions that often lead to stereoisomeric mixtures at the anomeric carbon.[1]

We have previously developed stereocontrolled approaches to aliphatic spiroketals using stereocomplementary kinetic spirocyclization reactions of *endo*-glycal epoxides that proceed with either inversion or retention of configuration at the anomeric carbon, independent of thermodynamic preferences.[10] We have also extended this approach to benzannulated spiroketals via incorporation of aromatic rings on the cyclizing side chain.[11] Unfortunately, this approach provides low diastereoselectivity in spirocyclization reactions with phenolic nucleophiles (45:55 to 58:42 dr).[11]

To address this problem, we envisioned an alternative entry to phenolic spiroketals involving stereoselective spirocyclizations of benzannulated *exo*-glycal epoxides (dihydrobenzofuran spiroepoxides). Spirocyclizations of exocyclic enol ether epoxides have apparently not been explored previously, although classical acid-catalyzed spiroketalizations of the parent exocyclic enol ethers are well-known,[12] and the corresponding epoxides[13] have been used in intermolecular alcohol additions.[14]

Thus, the requisite benzannulated *exo*-glycal epoxide substrates were synthesized from salicylaldehydes **1** via alkyne additions to form propargyl alcohols **2a–h** (Figure 1).[15] Au(I)-mediated cycloisomerization, previously restricted to aromatic alkynes,[15,16] then afforded *exo*-glycals **5a–h**. Diastereoselective *anti*-epoxidation with dimethyldioxirane (DMDO)[17] provided *exo*-glycal epoxides **6a–h**. Interestingly, these epoxides were

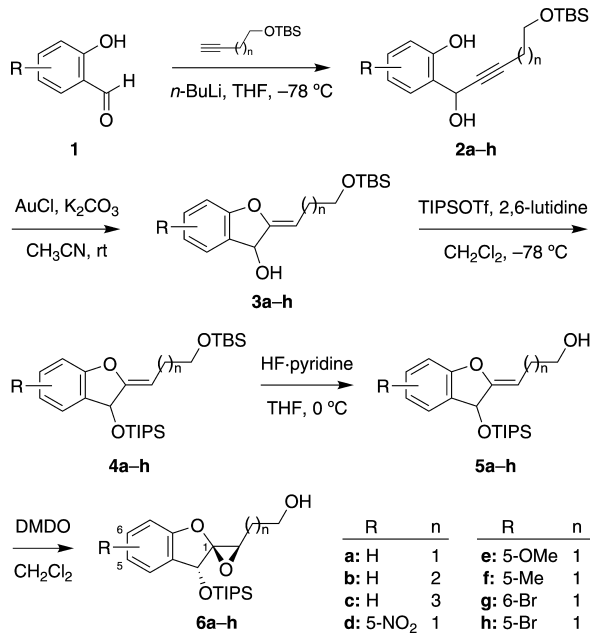


Figure 1. Synthesis of *exo*-glycal epoxide substrates **6a–h**.

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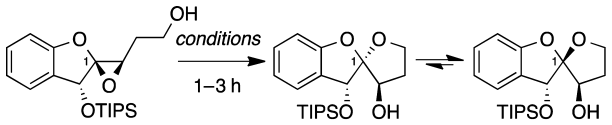
stable upon warming to rt, in stark contrast to the corresponding *endo*-glycal epoxides, which cyclize spontaneously at −35 °C.[18]

We next explored spirocyclization reactions of benzannulated *exo*-glycal epoxide **6a** (Table 1). Notably, **6a** proved unreactive

Table 1. Spirocyclization Reactions of *exo*-Glycal Epoxide 6a[a]



6a **7a** (C1-inversion) **8a** (C1-retention)

entry	reagent (equiv)	solvent, temp (°C)	7a:8a
1	MeOH (excess)	MeOH, rt	NR
2	$Ti(O^iPr)_4$ (2.0)	CH_2Cl_2, rt	NR
3		toluene, 120	NR
4	$Sc(OTf)_3$ (2.0)	CH_2Cl_2, −78 → 0	75:25
5	$Sc(OTf)_3$ (2.0)	THF, −78 → 0	>98:2
6	$Sc(OTf)_3$ (1.0)	THF, −78 → 0	>98:2
7	$Sc(OTf)_3$ (0.1)	THF, −78 → 0	93:7
8	**$Sc(OTf)_3$ (1.0)**	**THF, −20**	**>98:2**
9	$Sc(OTf)_3$ (1.0)	THF, rt	90:10
10	$Sc(OTf)_3$ (1.0)	CH_2Cl_2, 0 → rt	<2:98
11	**$Sc(OTf)_3$ (0.5)**	**CH_2Cl_2, 0 → rt**	**<2:98**
12	$Sc(OTf)_3$ + DTBMP (1.0 + 1.0)	THF, −20	>98:2
13	$ScCl_3$ (1.0)	THF, rt	>98:2
14	TfOH (1.0)	THF, −20	30:70
15	$Sc(OTf)_3$ + DTBMP (0.5 + 0.5)	CH_2Cl_2, 0 → rt	75:25
16	TfOH (0.5)	CH_2Cl_2, 0 → rt	<2:98
17	TfOH + DTBMP (0.5 + 0.5)	CH_2Cl_2, 0 → rt	51:49

[a]Product ratios determined by ^{1}H NMR analysis of crude reaction products. NR = no reaction; DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine. See the Supporting Information for the complete table.

under our previously reported MeOH and $Ti(O\text{-}i\text{-}Pr)_4$ spirocyclization conditions, as well as upon heating to 120 °C in toluene (entries 1−3). After investigating a wide range of Lewis acids,[16] we were encouraged to find that $Sc(OTf)_3$ favored the inversion product **7a** (entry 4), which could be formed exclusively by changing the reaction solvent from CH_2Cl_2 to THF (entry 5). The diastereoselectivity decreased slightly with substoichiometric $Sc(OTf)_3$ (entries 6 and 7). Other Lewis acids gave lower or even reversed diastereoselectivity.[16]

In low-temperature ^{1}H NMR experiments, we found that the $Sc(OTf)_3$-mediated spirocyclization begins to occur at −35 °C.[16] Complete selectivity for spirocyclization with inversion of configuration was maintained when the reaction was run at −20 °C (entry 8), but selectivity decreased at higher temperatures (entry 9), suggesting that the reaction proceeds under kinetic control between −35 and −20 °C.

Strikingly, when the room-temperature reaction was carried out in CH_2Cl_2 instead of THF, thermodynamic equilibration of an initially formed diastereomeric mixture afforded the retention product **8a** with complete stereoselectivity (entries 10, 11).[19] A structural rationale for the observed thermodynamic preference is nonobvious, due to the conformational flexibility of 5-membered rings,[20] and remains a subject for further investigation. However, on the basis of these results, it is apparent that $Sc(OTf)_3$ plays divergent roles in the spirocyclization reactions depending upon solvent selection (THF vs CH_2Cl_2, entry 9 vs 10).

It is known that metal triflates can serve as a mild source of triflic acid.[21] Thus, we carried out mechanistic studies to differentiate between the Lewis and Brønsted acid activities of $Sc(OTf)_3$. Inclusion of the noncoordinating Brønsted base, 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP),[21a] in the reaction in THF did not affect diastereoselectivity (entry 8 vs 12). Treatment with $ScCl_3$ at rt also led to complete stereoselectivity for the contrathermodynamic spiroketal **7a** (entry 13). In contrast, spirocyclization with TfOH afforded a diastereomeric mixture favoring the retention product **8a** (entry 14). Taken together, these results suggest that $Sc(OTf)_3$ acts as a Lewis acid in THF at reduced temperatures, catalyzing formation of the contrathermodynamic spiroketal **7a** under kinetic control.

We next carried out the analogous experiments in CH_2Cl_2 where, upon warming to rt, $Sc(OTf)_3$ favors the retention product **8a** (entry 11). In contrast, inclusion of DTBMP resulted in a diastereomeric mixture favoring the inversion product **7a** (entry 15). However, spirocyclization with TfOH provided the retention product **8a** exclusively (entry 16). Treatment with both TfOH and DTBMP afforded a diastereomeric mixture of spiroketals, similar to the result observed with $Sc(OTf)_3$ and DTBMP (entry 17 vs 15). Collectively, these results suggest that $Sc(OTf)_3$ acts as a mild source of Brønsted acid in CH_2Cl_2 at rt, catalyzing formation of the thermodynamically favored spiroketal **8a** under equilibrium control.

We then investigated the scope of these stereocomplementary $Sc(OTf)_3$-catalyzed spirocyclization reactions. Substrates with longer side chains (**6b**, **6c**) and various aryl substituents (**6d**−**h**) were synthesized from the corresponding alkyne and salicylaldehyde precursors (Figure 1). The bromide intermediate **4h** was also used to introduce other substituents (aryl, alkyne, azide, aldehyde, ester, imide) in **4i**−**n** to examine the functional group tolerance of the spirocyclization reactions (Figure S2, Supporting Information).[16] The *exo*-glycals **4i**−**n** were then converted to the corresponding epoxide substrates **6i**−**n** (Figure S2, Supporting Information).[16]

In the spirocyclization reactions, both diastereomers of the larger 6- and 7-membered ring spiroketals (**7b**,**c** and **8b**,**c**) could be obtained with complete diastereoselectivity based on solvent selection (Figure 2). For **8b**, equilibration with $Sc(OTf)_3$ in CH_2Cl_2 required elevated temperature (60 °C). The 7-membered ring spiroketal **7c** was obtained in somewhat lower yield due to an unexpected anti-Markovnikov 6-*exo* epoxide opening side reaction leading to a benzofuran product.[16]

Next, we investigated the electronic effects of various aryl substituents. A wide range of electron-withdrawing and -donating groups were tolerated (**7d**−**n**, **8d**−**n**), and high diastereoselectivities were maintained. Notably, the nitro-substituted substrate **6d** was less reactive and required more forcing conditions (**7d**: rt; **8d**: 6 h). Conversely, the methoxy-substituted substrate **6e** was highly reactive, providing slightly decreased diastereoselectivity in the THF reaction (**7e**: 93:7 dr) and rapid equilibration in the CH_2Cl_2 reaction (**8e**: 1 h). These results are consistent with the expected electronic influence of these *para* substituents upon the reactive anomeric spiro-epoxide center.[18]

The reactions also tolerated other reactive functionalities including alkyne (**7j**, **8j**), azide (**7k**, **8k**), aldehyde (**7l**, **8l**), ester (**7m**, **8m**), and phthalimide (**7n**, **8n**) groups. In the case of

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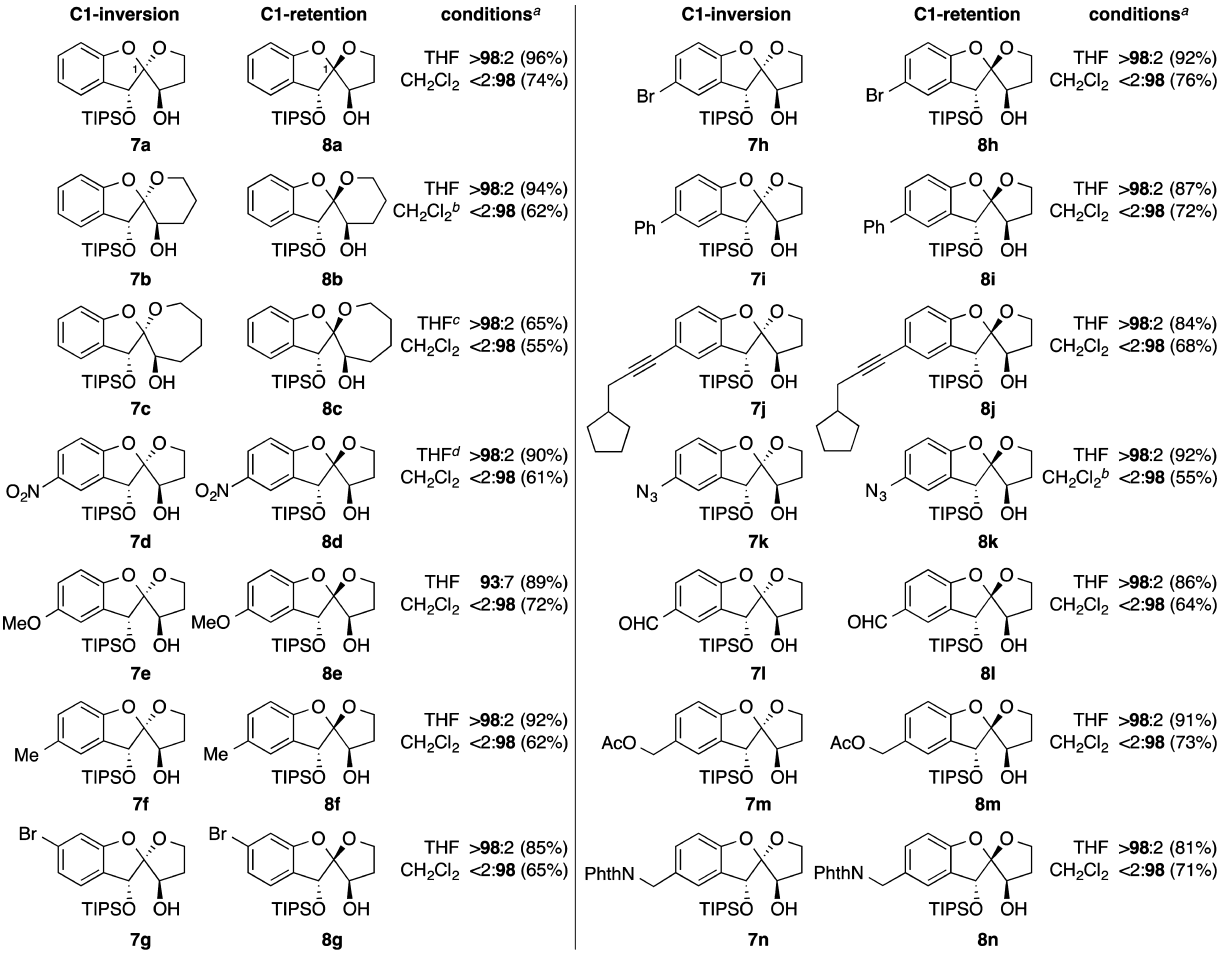

Figure 2. Scope of $Sc(OTf)_3$-mediated spirocyclization reactions. (a) THF: 1.0 equiv $Sc(OTf)_3$, THF, −20 °C, 2−3 h; CH_2Cl_2: 0.5 equiv $Sc(OTf)_3$, CH_2Cl_2, 0 °C to rt, 1−12 h; diastereomeric ratios determined by ^1H NMR analysis of crude reaction mixtures; stereochemistry assigned based on NOESY analysis except **8b**, which was determined by X-ray crystallography;[16] isolated yields after column chromatography shown in parentheses. (b) 60 °C. (c) 30% anti-Markovnikov 6-*exo*-cyclization side product also recovered.[16] (d) rt.

azide **8k**, $Sc(OTf)_3$ equilibration in CH_2Cl_2 required elevated temperature (60 °C).

In conclusion, we have developed novel, solvent-dependent $Sc(OTf)_3$-mediated spirocyclizations of *exo*-glycal epoxides for the stereocontrolled synthesis of benzannulated spiroketals. This *exo*-glycal-based approach overcomes a key limitation of our previous *endo*-glycal-based approach and tolerates a wide range of functionalities. Applications to the diversity-oriented synthesis of stereochemically diverse spiroketal libraries are ongoing and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Reviewed in: (a) Sperry, J.; Wilson, Z. E.; Rathwell, D. C. K.; Brimble, M. A. *Nat. Prod. Rep.* **2010**, *27*, 1117−1137. For general reviews on spiroketals, see: (b) Aho, J. E.; Pihko, P. M.; Rissa, T. K. *Chem. Rev.* **2005**, *105*, 4406−4440. (c) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617−1661.

(2) (a) Stierle, A. A.; Stierle, D. B.; Kelly, K. *J. Org. Chem.* **2006**, *71*, 5357−5360. (b) Buchgraber, P.; Snaddon, T. N.; Wirtz, C.; Mynott, R.; Goddard, R.; Fürstner, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 8450−8454.

(3) (a) Traxler, P.; Fritz, H.; Fuhrer, H.; Richter, W. J. *J. Antibiot.* **1980**, *33*, 967−978. (b) Barrett, A. G. M.; Peña, M.; Willardsen, J. A. *J. Org. Chem.* **1996**, *61*, 1082−1100. (c) Varona, R.; Perez, P.; Duran, A. *FEMS Microbiol. Lett.* **1983**, *20*, 243−247.

(4) Qi, J.; Lu, J.-J.; Liu, J.-H.; Yu, B.-Y. *Chem. Pharm. Bull.* **2009**, *57*, 134−137.

(5) Reviewed in: Brasholz, M.; Soergel, S.; Azap, C.; Reissig, H.-U. *Eur. J. Org. Chem.* **2007**, 3801−3814.
(6) (a) Bardone, M. R.; Martinelli, E.; Zerilli, L. F.; Coronelli, C. *Tetrahedron* **1974**, *30*, 2747−2751. (b) Kirillov, S.; Vitali, L. A.; Goldstein, B. P.; Monti, F.; Semenkov, Y.; Makhno, V.; Ripa, S.; Pon, C. L.; Gualerzi, C. O. *RNA* **1997**, *3*, 905−913.
(7) Ueno, T.; Takahashi, H.; Oda, M.; Mizunuma, M.; Yokoyama, A.; Goto, Y.; Mizushina, Y.; Sakaguchi, K.; Hayashi, H. *Biochemistry* **2000**, *39*, 5995−6002.
(8) For examples from benzannulated spiroketal natural product total synthesis, see the following. Berkelic acid: (a) Wu, X.; Zhou, J.; Snider, B. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 1283−1286. (b) Bender, C. F.; Yoshimoto, F. K.; Paradise, C. L.; De Brabander, J. K. *J. Am. Chem. Soc.* **2009**, *131*, 11350−11352. (c) Snaddon, T. N.; Buchgraber, P.; Schulthoff, S.; Wirtz, C.; Mynott, R.; Fürstner, A. *Chem.—Eur. J.* **2010**, *16*, 12133−12140. (d) McLeod, M. C.; Wilson, Z. E.; Brimble, M. A. *Org. Lett.* **2011**, *13*, 5382−5385. (e) Wenderski, T. A.; Marsini, M. A.; Pettus, T. R. R. *Org. Lett.* **2011**, *13*, 118−121. (f) Fañanás, F. J.; Mendoza, A.; Arto, T.; Temelli, B.; Rodriguez, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 4930−4933. Papulacandins: (g) Barrett, A. G. M.; Peña, M.; Willardsen, J. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1147−1148. (h) Denmark, S. E.; Regens, C. S.; Kobayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 2774−2776. Heliquinomycinone: (i) Qin, D.; Ren, R. X.; Siu, T.; Zheng, C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4709−4713. (j) Siu, T.; Qin, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4713−4716. Rubromycins: (k) Reviewed in refs 1 and 5. (l) Akai, S.; Kakiguchi, K.; Nakamura, Y.; Kuriwaki, I.; Dohi, T.; Harada, S.; Kubo, O.; Morita, N.; Kita, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 7458−7461. (m) Rathwell, D. C. K.; Yang, S.-H.; Tsang, K. Y.; Brimble, M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 7996−8000. (n) Wu, K.-L.; Mercado, E. V.; Pettus, T. R. R. *J. Am. Chem. Soc.* **2011**, *133*, 6114−6117. (o) Wei, L.; Xue, J.; Liu, H.; Wang, W.; Li, Y. *Org. Lett.* **2012**, *14*, 5302−5305. (p) Wang, W.; Xue, J.; Tian, T.; Zhang, J.; Wei, L.; Shao, J.; Xie, Z.; Li, Y. *Org. Lett.* **2013**, *15*, 2402−2405.
(9) For other selected approaches to benzannulated spiroketals, see the following. (a) Acid-catalyzed *endo*-glycal spirocyclization: Knabe, J.; Schaller, K. *Arch. Pharm.* **1968**, *301*, 457−464. (b) Chromone intramolecular Michael addition and chromone epoxide spirocyclization: Cremins, P. J.; Wallace, T. W. *J. Chem. Soc., Chem. Commun.* **1986**, 1602−1603. (c) Dihydroxy ketone bicyclization: Tanaka, T.; Miyaguchi, M.; Mochisuki, R. K.; Tanaka, S.; Okamoto, M.; Kitajima, Y.; Miyazaki, T. *Heterocycles* **1987**, *25*, 463−484. (d) *endo*-Glycal epoxide spirocyclization: Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 5808−5810. (e) *endo*-Glycal intramolecular alkoxyselenation: Elsley, D. A.; MacLeod, D.; Miller, J. A.; Quayle, P.; Davies, G. M. *Tetrahedron Lett.* **1992**, *33*, 409−412. (f) Glycoside dehydrative spirocyclization: Barrett, A. G. M.; Peña, M.; Willardsen, J. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1147−1148. (g) Alkyne cyclotrimerization: McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605−6606. (h) *C*-Aryl glycoside ring rearrangement: Kumazawa, T.; Asahi; Matsuba, S.; Sato, S.; Furuhata, K.; Onodera, J.-I. *Carbohydr. Res.* **1998**, *308*, 213−216. (i) Arylfuran Achmatowicz reaction: Balachari, D.; O'Doherty, G. A. *Org. Lett.* **2000**, *2*, 4033−4036. (j) *C*-Vinyl *O*-arylglycoside Claisen rearrangement−spirocyclization: Van Hooft, P. A. V.; Van Swieten, P. F.; Van der Marel, G. A.; Van Boeckel, C. A. A.; Van Boom, J. H. *Synlett* **2001**, 269−271. (k) *o*-Quinone methide−*exo*-glycal hetero-Diels−Alder: Zhou, G.; Zheng, D.; Da, S.; Xie, Z.; Li, Y. *Tetrahedron Lett.* **2006**, *47*, 3349−3352. (l) *β*-Diketone−*exo*-glycal 1,3-dipolar cycloaddition: Lindsey, C. C.; Wu, K. L.; Pettus, T. R. R. *Org. Lett.* **2006**, *8*, 2365−2367. (m) Alkyne diol hydroalkoxylation: Messerle, B. A.; Vuong, K. Q. *Organometallics* **2007**, *26*, 3031−3040. (n) Oxidative radical spirocyclization: Liu, Y.-C.; Sperry, J.; Rathwell, D. C. K.; Brimble, M. A. *Synlett* **2009**, 793−797. (o) Intramolecular Ullmann ether coupling: Yoshioka, K.; Takaishi, I.; Shiozawa, K.; Fukushi, Y.; Tahara, S. *Biosci., Biotechnol., Biochem.* **2008**, *72*, 2632−2639. (p) Multicomponent cascade reaction: Barluenga, J.; Mendoza, A.; Rodriguez, F.; Fananas, F. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 1644−1647. (q) Enantioselective *endo*-glycal spirocyclization: Sun, Z.; Winschel, G. A.; Borovika, A.; Nagorny, P. *J. Am. Chem. Soc.* **2012**, *134*, 8074−8077.
(10) (a) Potuzak, J. S.; Moilanen, S. B.; Tan, D. S. *J. Am. Chem. Soc.* **2005**, *127*, 13796−13797. (b) Moilanen, S. B.; Potuzak, J. S.; Tan, D. S. *J. Am. Chem. Soc.* **2006**, *128*, 1792−1793.
(11) Liu, G.; Wurst, J. M.; Tan, D. S. *Org. Lett.* **2009**, *11*, 3670−3673.
(12) (a) Fittig, R.; Strom, K. T. *Justus Liebigs Ann. Chem.* **1892**, *267*, 191−203. (b) Dedek, V.; Trska, P. *Collect. Czech. Chem. Commun.* **1970**, *35*, 651−660. (c) Ley, S. V.; Lygo, B.; Organ, H. M.; Wonnacott, A. *Tetrahedron* **1985**, *41*, 3825−3836.
(13) (a) Ahmad, M. S.; Baddeley, G. *J. Chem. Soc.* **1961**, 4303−4306. (b) Ernest, I.; Fritz, H.; Rihs, G. *Helv. Chim. Acta* **1987**, *70*, 203−209. (c) Adam, W.; Hadjiarapoglou, L.; Jaeger, V.; Seidel, B. *Tetrahedron Lett.* **1989**, *30*, 4223−4226. (d) Adam, W.; Hadjiarapoglou, L.; Wang, X. *Tetrahedron Lett.* **1989**, *30*, 6497−6500.
(14) (a) Brady, B. A.; Geoghegan, M.; O'Sullivan, W. I. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1557−1562. (b) Nicotra, F.; Panza, L.; Russo, G. *Tetrahedron Lett.* **1991**, *32*, 4035−4038.
(15) Harkat, H.; Blanc, A.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2008**, *73*, 1620−1623.
(16) See the Supporting Information for full details.
(17) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661−6666.
(18) Wurst, J. M.; Liu, G.; Tan, D. S. *J. Am. Chem. Soc.* **2011**, *133*, 7916−7925.
(19) A benzylidenedihydrofuranone, presumed to arise from opening of the benzannulated ring followed by elimination of the C2-OTIPS group, was also recovered as a minor byproduct (Figure S1, Supporting Information).[16]
(20) Tlais, S. F.; Dudley, G. B. *Org. Lett.* **2010**, *12*, 4698−4701.
(21) (a) Wabnitz, T. C.; Yu, J.-Q.; Spencer, J. B. *Chem.—Eur. J.* **2004**, *10*, 484−493. (b) Rosenfeld, D. C.; Shekhar, S.; Takemiya, A.; Utsunomiya, M.; Hartwig, J. F. *Org. Lett.* **2006**, *8*, 4179−4182. (c) Dang, T. T.; Boeck, F.; Hintermann, L. *J. Org. Chem.* **2011**, *76*, 9353−9361.