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Studies toward the Total Synthesis of Vinigrol. Synthesis of the Octalin Ring

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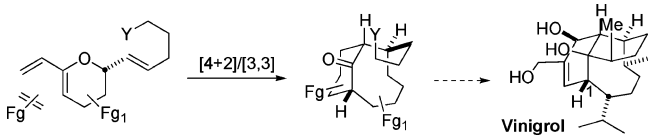
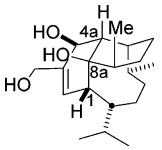


Herein, we disclose our results regarding various strategies toward the assembly of the octanyl ring of vinigrol. Attempts to generate the problematic eight-membered ring through a ring expansion or via unification of the terminal olefins using the ring-closing metathesis were not successful. The cyclooctane ring was created via a sequential hydroxy Diels−Alder/Claisen rearrangement reaction of diene **55** and *N*-benzylmaleimide.

Introduction

Vinigrol (**1**) was isolated in 1987 from a culture of the fungal strain identified as *Virgaria nigra*.[1] This diterpene bears a *cis*-decalin subunit surmounted by an eight-membered ring that constitutes an unprecedented tricyclo[4.4.4.0.^{4a,8a}]tetradecane skeleton. The biological activities of **1** reside in the antihypertensive, platelet aggregation-inhibiting, and tumor necrosis factor (TNF) antagonist properties.[2] Its unusual and complex architecture combined with the promising biological activities have stimulated the creation of several synthetic approaches.[3]

Recently, we reported the synthesis of the *cis*-decalin subunit of vinigrol (**1**) using the tandem oxy-Cope/



Claisen/ene reaction (Scheme 1).[4] Microwave-assisted heating of **2** produces the 10-membered ring **3**, which immediately undergoes a Claisen rearrangement to give enone **4**. The latter is poised to cyclize via a transannular ene reaction to give decalin **5**. However, we observed that large substituents at the terminal allylic position (R ≠ H) are detrimental to the cascade process, thus impeding the installation of the *iso*-propyl group at C9.

In light of these results, we decided to explore new avenues aimed at constructing the tricyclic core of vinigrol (**1**). A cursory inspection of vinigrol (**1**) reveals a compact structure where the formation of the cyclooctane ring overhanging the decalin core represents a major synthetic challenge. We investigated three different synthetic pathways for the formation of this eight-membered ring. The first one involves a ring expansion triggered by a Claisen rearrangement[5] of the corresponding vinyl ether **6** to give the tricycle **7** (eq 1). The second route, illustrated in eq 2, exploits the ring-closing metathesis (RCM) of diene **8** to generate the vinigrol skeleton **9**. Finally, the third approach took advantage of a sequential hydroxy-Diels−Alder/Claisen reaction of diene **10** and *N*-benzylmaleimide to create the corre-

(1) Uchida, I.; Ando, T.; Fukami, N.; Yoshida, K.; Hashimoto, M. *J. Org. Chem.* **1987**, *52*, 5292.

(2) (a) Ando, T.; Tsurumi, Y.; Ohata, N.; Uchida, I.; Yoshida, K.; Okuhara, M. *J. Antibiot.* **1988**, *41*, 25. (b) Ando, T.; Yoshida, K.; Okuhara, M. *J. Antibiot.* **1988**, *41*, 31. (c) Norris, D. B.; Depledge, P.; Jackson, A. P. PCT Int. Appl. W0 91 07 953, 1991; *Chem Abstr.* **1991**, *115*, 64776h.

(3) (a) Paquette, L. A.; Efremov, I.; Liu, Z. *J. Org. Chem.* **2005**, *70*, 505. (b) Paquette, L. A.; Efremov, I. *J. Org. Chem.* **2005**, *70*, 510. (c) Paquette, L. A.; Liu, Z.; Efremov, I. *J. Org. Chem.* **2005**, *70*, 514. (d) Gentric, L.; Hanna, I.; Ricard, L. *Org. Lett.* **2003**, *5*, 1139. (e) Gentric, L.; Hanna, I.; Huboux, A.; Zaghdoudi, R. *Org. Lett.* **2003**, *5*, 3631. (f) Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096. (g) Miyashita, M.; Shirahama, H.; Matsuda, F.; Kito, M.; Sakai, T.; Okada, N. *Tetrahedron* **1999**, *55*, 14369. (h) Devaux, J.-F.; Hanna, I.; Lallemand, J.-Y. *J. Org. Chem.* **1997**, *62*, 5062. (i) Kito, M.; Sakai, T.; Shirahama, H.; Miyashita, M.; Matsuda, F. *Synlett* **1997**, 219. (j) Kito, M.; Sakai, T.; Haruta, N.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 1057. (k) Mehta, G.; Reddy, K. S. *Synlett* **1996**, 625. (l) Devaux, J.-F.; Hanna, I.; Fraisse, P.; Lallemand, J.-Y. *Tetrahedron Lett.* **1995**, *36*, 9471. (m) Devaux, J.-F.; Hanna, I.; Lallemand, J.-Y. *J. Org. Chem.* **1993**, *58*, 2349.

(4) Barriault, L.; Morency, L. *Tetrahedron Lett.* **2004**, *45*, 6105.

(5) Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939.

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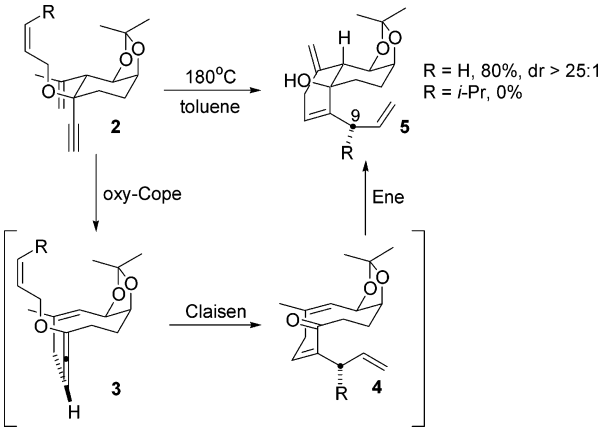
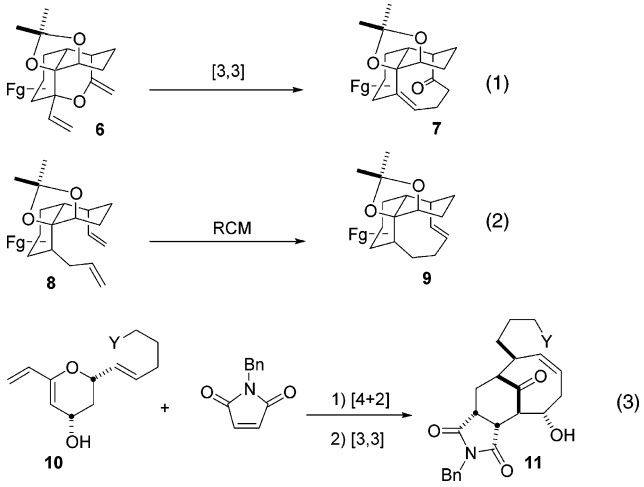
SCHEME 1



sponding bicyclo[5.3.1]undecenone **11** (eq 3). Herein, we report our progress directed toward the synthesis of the cyclooctane belt embedded in vinigrol (**1**).

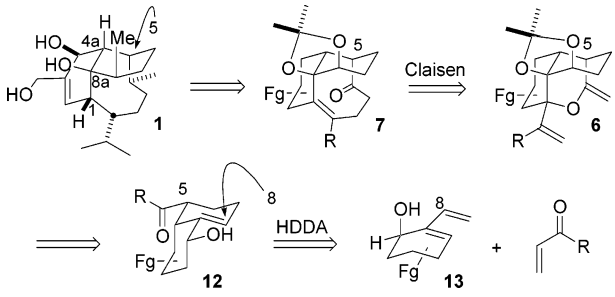


Results and Discussion

Formation of the Cyclooctane Belt through the Claisen Rearrangement. We proposed that the Claisen rearrangement of the vinyl ether **6** could provide the tricyclic core of vinigrol **7** (Scheme 2). The required vinyl ether **6** could be prepared from the cycloadduct **12**. Recently, we reported a highly stereoselective synthesis of bicyclo [4.4.0] decene **12** using the hydroxy-directed Diels–Alder reaction (HDDA) between semicyclic dienes such as **13** and various activated dienophiles (Scheme 3).[6,7] The regio- and stereoselectivity of the reaction was rationalized by the formation of a temporary metal tether intermediate **14**, which underwent an intramolecular Diels–Alder reaction to afford the corresponding cycloadduct **12**, which represents the *cis*-decalin portion of vinigrol.

To probe the feasibility of this approach, a model study was engaged using 2-vinylcyclohexenol **16** as a semicyclic diene (Scheme 4). The synthesis commenced with a 1,2-reduction of enone **15**[6a] with $NaBH_4$ and $CeCl_3 \cdot 7H_2O$ in

SCHEME 2



MeOH to give alcohol **16** in 90% yield. The treatment of **16** with $MgBr_2 \cdot OEt_2/Et_3N$[8] in dichloromethane generated in situ the corresponding magnesium alkoxide which was poised to undergo an HDDA reaction with methyl acrylate to provide the cycloadduct **17**[6a] in 78% yield as a single diastereomer.[9] Reduction of the ester group in **17** with lithium aluminum hydride followed by the protection of the primary alcohol with DPSCl gave silyloxy ether **18** in 78% yield over two steps. The installation of the tertiary alcohol at C8a required the introduction of a benzoate group at C1 (97% yield) followed by a dihydroxylation reaction using OsO_4 and NMO to produce diol **19** in 82% yield.

Treatment of diol **19** with 2-methoxypropene and PTSA in dichloromethane provided the corresponding acetonide **20** in quantitative yield. Removal of the benzoate group with K_2CO_3 in methanol (75% yield) followed by a Dess–Martin periodinane oxidation[10] produced ketone **22** in 100% yield. The addition of vinylmagnesium bromide to ketone **22** was realized in the presence of anhydrous cerium chloride in THF at −78 °C to produce alcohol **23** in 96% yield. Cleavage of the silyl ether group employing TBAF followed by a ruthenium-mediated oxidation[11] of the resulting diol **24** led to the formation in situ of aldehyde **25**, which can exist in equilibrium with lactol **26**. The latter mixture was further oxidized to give lactone **27** in 51% yield. The installation of the enol ether moiety, required for the subsequent Claisen rearrangement, was accomplished by treatment of **27** with the Petasis' reagent[12] in toluene at 65 °C. The desired enol ether **28** was obtained in 85% yield.

At this stage, all the requisite carbons embedded in the vinigrol skeleton were installed. The next objective was the creation of the eight-membered ring. Initial

(6) (a) Barriault, L.; Thomas, J. D. O.; Clément, R. *J. Org. Chem.* **2003**, *68*, 2317. (b) For the first example of Diels–Alder reaction by self-assembly of the components on a Lewis acid, see: Ward, D. E.; Abaee, M. S. *Org. Lett.* **2000**, *2*, 3937. (c) Ward, D. E.; Souweha, M. S. *Org. Lett.* **2005**, *7*, 3533.

(7) (a) For a review on tethers in cycloadditions, see: Shea, K. J.; Zandi, K. S.; Gauthier, D. R. *Tetrahedron* **1998**, *54*, 2289 and references therein. (b) Olsson, R.; Bertozzi, F.; Fredj, T. *Org. Lett.* **2000**, *2*, 1283. (c) Batey, R. A.; Thadani, A. N.; Lough, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 450. (d) Stork, G.; Chan, T. Y. *J. Am. Chem. Soc.* **1995**, *117*, 6595. (e) Nicolaou, K. C.; Ueno, H.; Liu, J.-J.; Nantermet, Z.; Yang, Z.; Renaud, J.; Paulvannan, K.; Chadha, R. *J. Am. Chem. Soc.* **1995**, *117*, 653. (f) Shimada, S.; Osoda, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1254–1257. (g) Stork, G.; Chan, T. Y.; Breault, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7578. (h) Sieburth, S.; Fensterbamk, L. *J. Org. Chem.* **1992**, *57*, 5279. (i) Narasaka, K.; Shimada, K.; Osoda, N.; Iwasawa, N. *Synthesis* **1991**, 1171. (j) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478.

(8) Vedejs, E.; Daugulis, O. *J. Org. Chem.* **1996**, *61*, 5702.

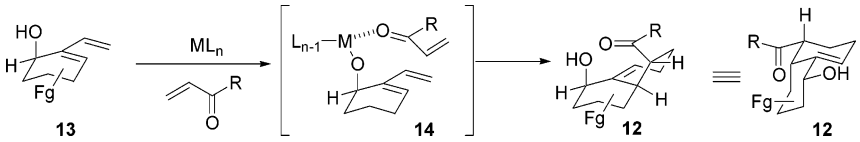
(9) The diastereomeric excess was determined by ^1H NMR 300 and 500 MHz of the crude reaction mixture.

(10) Dess, D. B.; Martin J. C. *J. Am. Chem. Soc.* **1991**, *113*, 2350.

(11) Ley, S. V.; Griffith, W. P. *Aldrichimica Acta* **1990**, *23*, 1.

(12) (a) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392. (b) Petasis, N. A.; Lu, S.-P.; Bzowej, E. I.; Fu, D.-K., Staszewski, J. P.; Akritopoulou-Zanze, I.; Patane, M. A.; Hu, Y.-H. *Pure Appl. Chem.* **1996**, *68*, 667.

SCHEME 3



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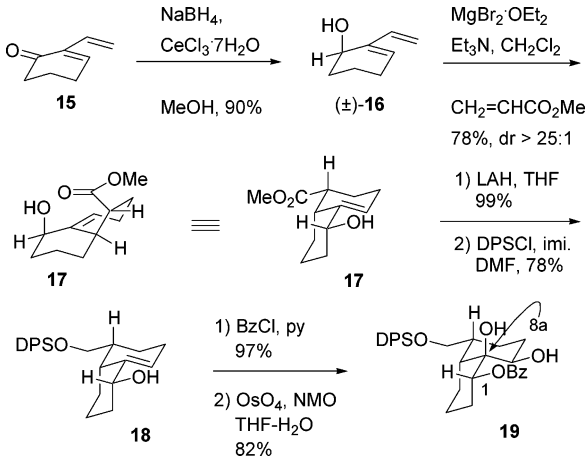

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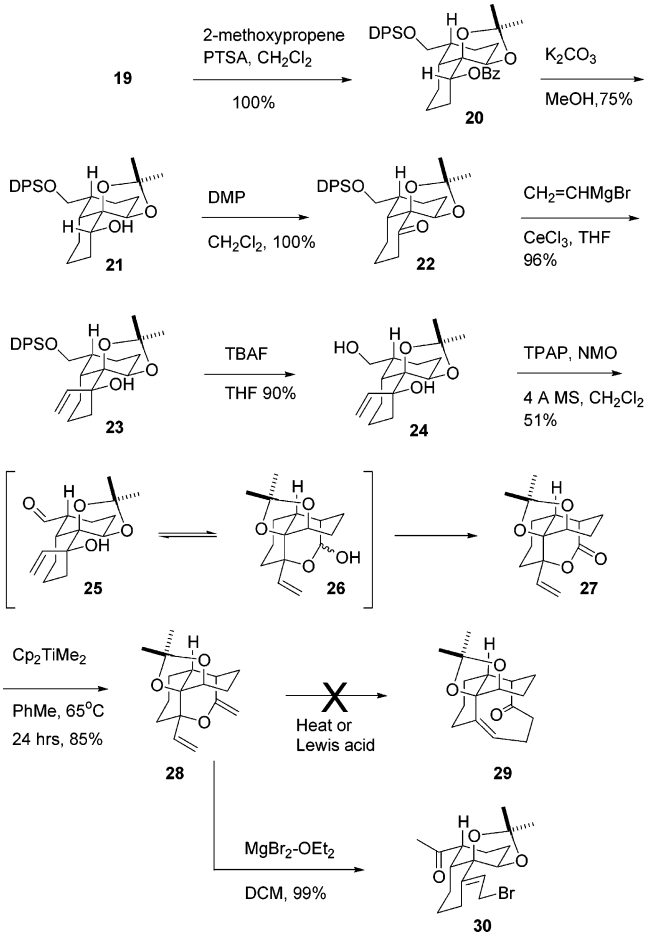
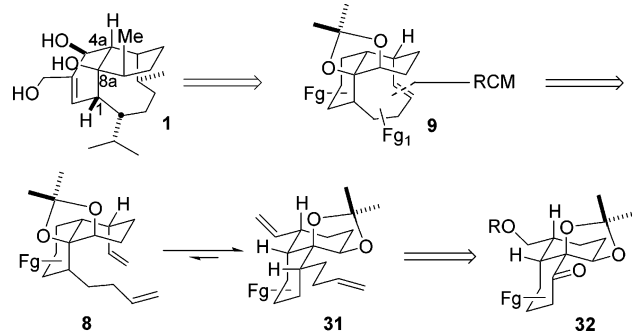


attempts to rearrange vinyl enol ether **28** to ketone **29** under thermal conditions were fruitless. Conventional heating of a solution of **28** (ca. 0.05 M) in toluene at temperatures ranging from 160 to 210 °C in a sealed tube or using microwave irradiation led to recovery of the starting material or the formation of a complex mixture from which no Claisen rearrangement product **29** was isolated. We then turned our attention toward the use of hard and soft Lewis acids to catalyze this rearrangement.[13] Despite considerable experimental efforts, all runs using $Pd(0)L_4$, $Pd(II)L_2$,[14] $AgBF_4$, $AlMe_3$, $AlMe_2Cl$, Dibal-H, *i*-Bu_3Al,[15] bis(4-bromo-di-*tert*-butylphenoxyde (MABr),[16] and $Mg(OTf)_2$ in various solvents and conditions resulted in the degradation of **28** or its partial recovery. Interestingly, enol ether **28** was completely converted into ketone **30** in the presence of $MgBr_2-OEt_2$ in dichloromethane (Scheme 5). It became clear that the formation of the eight-membered ring should be realized by other means.

Formation of the Eight-Membered Ring via Ring-Closing Metathesis. In the second approach, we recognized that the octanyl ring in **9** could be generated from an RCM of diene **8** (Scheme 6).[17] A cursory inspection reveals that conformer **31** should be the favored ground state conformation. The latter compound could be prepared from ketone **32**. Semiempirical calculations (AM1) of conformers **33** and **34** reveal that the heat of formation of **33** is 3.8 kcal/mol higher in energy than that of conformer **34** (Figure 1). On the basis of this and the ease of formation of lactone **27**, we anticipated that the

SCHEME 6



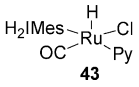
reactive conformer **8** could be trapped in the RCM conditions to give tricycle **9**.

The synthesis began by treatment of ketone **22** with $ClMg(CH_2)_3OMgCl$[18] and $CeCl_3$ in THF to give alcohol **35** in 82% yield (Scheme 7). Protection of the primary alcohol as a TBS ether group (100%) and a subsequent

(13) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205 and references therein.
(14) (a) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579. (b) Baan, J. L.; Bickelhaupt, F. *Tetrahedron Lett.* **1986**, *27*, 6267.
(15) Paquette, L. A.; Friedrich, D.; Rogers, R. D. *J. Org. Chem.* **1991**, *56*, 3841.
(16) Marouka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 7922.
(17) During the course of this research, Paquette and co-workers also explored the formation of the cyclcooctane ring of vinigrol via RCM; see ref 3c

(18) Normant, J. F.; Alexakis, A.; Cahiez, G. *Tetrahedron Lett.* **1978**, *33*, 3013.

TABLE 1. Hydrogenation of 37

Entry	Catalyst	H_2 (psi)	Temp. (°C)	Time	Yield	Ratio **38** : **39**
1	Raney Ni	900	90	24 h	99%	4:1
2	Pd/C 10%	1300	70	40 h	N.D.[a]	1:3[b]
3	 **43**	1300	80	5 days	99%	> 25:1

[a] N.D. = not determined. [b] The TBS group was partially removed during the reduction process.

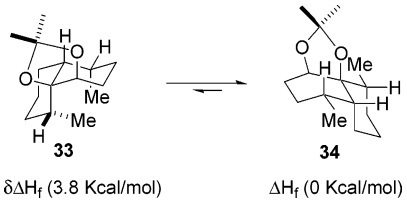
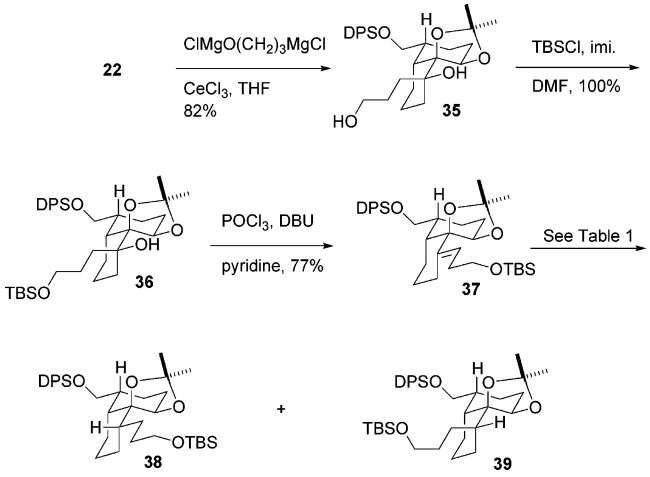


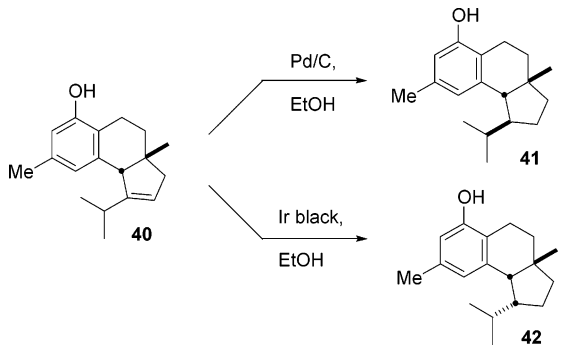
FIGURE 1. Relative heats of formation of **33** and **34**.

SCHEME 7

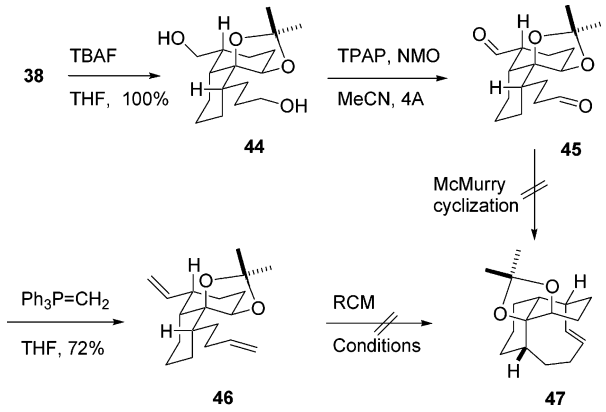


elimination of the tertiary alcohol using $POCl_3$ and DBU in pyridine produced decalin **37** in 77% yield. At this point, a stereoselective reduction of the trisubstituted exocyclic double bond at C1−C2 was investigated. A large number of metal-catalyzed hydrogenation protocols were scanned, though only hydrogenation methods using Pd/C, Raney Ni, and Ru were capable of reducing this olefin to yield decalins **38** and **39** in variable ratios (Table 1). Hydrogenation of **37** with Raney Ni gave a mixture of **38** and **39** in a ratio of 4:1 in 99% yield (entry 1). Surprisingly, the reduction on Pd/C in ethanol afforded **39** as the major product (entry 2). A similar result was recently reported by Trost.[19] They found that high-pressure hydrogenation of **40** with Pd/C afforded exclusively **41** (Scheme 8). They attributed the formation of **41** to "an equilibration in the semihydrogenation step due to a slow final reductive elimination step". They circumvent this problem by hydrogenation of **40** over iridium black, yielding the desired product **42**. In our case, hydrogenation of **37** in the presence of iridium black did not give **38**; rather, starting material was recovered along with several degradation products. Fortunately, hydrogenation of **37** at 1300 psi and in the presence of the ruthenium-based catalyst **43** gave decalin **38** in quantitative yield as the sole detectable isomer.[20,21]

SCHEME 8



SCHEME 9



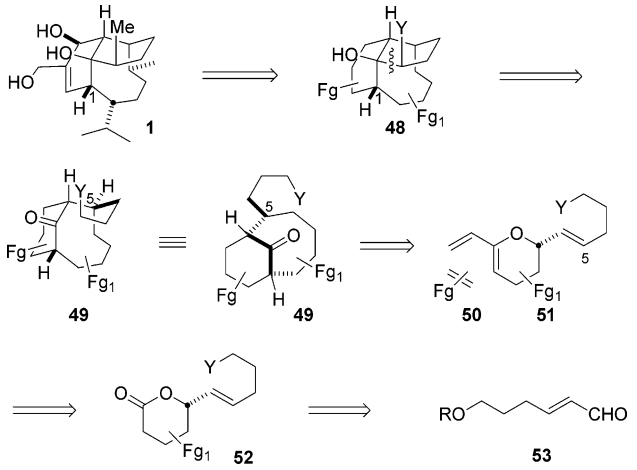
Removal of both silicon protective groups on **38** was realized with TBAF to afford the desired diol **44** in 100% yield (Scheme 9). This diol was subjected to TPAP oxidation,[11] thereby leading to the corresponding dialdehyde **45**. The latter was immediately treated with a slight excess of $Ph_3P{=}CH_2$ to provide diene **46** in 72% yield. We were now in a position to explore the RCM approach aimed at forming the octalin belt. As previously mentioned, our hopes to close the eight-membered ring were based on the ease of the *cis*-decalin framework to adopt the reactive conformation **8** in the RCM reaction conditions.[22] Unfortunately, all attempts to cyclize **46** via RCM

(19) Trost, B. M.; Pissot-Soldermanne, C.; Chen, I.; Schroeder, G. M. *J. Am. Chem. Soc.* **2004**, *126*, 4480.

(20) This catalyst was generated in situ from $H_2Imes(Cl)_2Py_2Ru{=}CHPh$ (6 mol %) in methanol with Et_3N. For procedure, see: (a) Dharmasena, U. L.; Foucault, H. M.; dos Santos, E. N.; Fogg, F. E.; Nolan, S. P. *Organometallics* **2005**, *24*, 1056. (b) Grubbs R. H.; Love, J. A.; Sanford, M. S. *Organometallics* **2001**, *20*, 5314.

(21) The relative stereochemistry of **38** was established by X-ray diffraction. For an ORTEP view of **38** (benzoate derivative), see the Supporting Information.

SCHEME 10

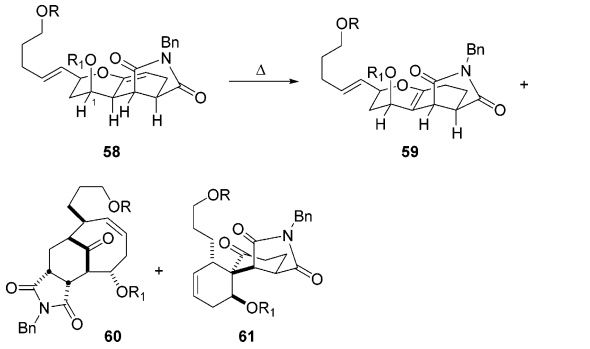


using Grubbs' first- and second-generation catalysts were not productive. We also tried to obtain the tricycle **47** by $TiCl_3$-mediated coupling reaction of the dialdehyde groups in **45**. However, the exposure of dialdehyde **45** to reaction conditions prescribed by McMurry[23] gave only degradation products. In accordance with our results, Paquette and co-workers recently reported unsuccessful approaches to generate the cyclooctane ring by assembling two side chains attached on a *cis*-decalin framework using various ring-closing methods.[3a−c,f]

Sequential HDDA/Claisen Rearrangement. Since our attempts to generate the eight-membered ring in **1** by unifying alkyl chains present on the *cis*-decalin system via a [3,3]-rearrangement or through RCM were not successful, we envisaged the creation vinigrol core **48** via an intramolecular alkylation of **49** (Scheme 10). The bicyclo[5.3.1]undecanone subunit **49** could be prepared from a sequential hydroxy-directed Diels−Alder/Claisen rearrangement[24] between diene **51** and dienophile **50**. Diene **51** could be synthesized from lactone **52** derived from the readily available aldehyde **53**.

Condensation of Weiler's dianion[25] upon aldehydes **53a**[26] and **53b**[27] afforded the corresponding β-ketoesters **54a** and **54b** in 67 and 64% yields, respectively (Scheme 11). The latter was diastereoselectively reduced to the corresponding 1,3-anti diols using Me_4NBH_4 in a mixture of acetic acid/acetonitrile at −25 °C.[28] The resulting diols were treated with trifluoroacetic acid in dichloromethane to give lactones **55a** and **55b** in 40% yield (84% yield based on consumed starting material) and 36% yield (70% yield based on recovered starting material) over two steps as single diastereomers. Protection of the secondary alcohol as triethylsiloxy ether in the presence of TESCl, DMAP, and triethylamine gave **56a** and **56b** in good yields. The completion of dienes **57a** and **57b** required addition of vinylmagnesium bromide in THF at −78 °C to produce the corresponding lactols that upon treatment with $SOCl_2$ and DMAP in methylene chloride and a subsequent exposure to fluorine ion provided semicyclic dienes **57a** and **57b** in 69 and 37% yields, respectively, over three steps.

TABLE 2. Claisen Rearrangement of Cycloadduct 58



entry	starting material	R	R_1	product (yield)
1	**58c**	PMB	MOM	**59c** (25%)[a]
2	**58d**	PMB	TMS	**59d** (35%)[a]
3	**58e**	PMB	Bz	degradation[a]
4	**58f**	DPS	TES	**60f** (40%)[a] and **61f** (15%)[a]
5	**58g**	DPS	TMS	**60g** (42%)[a] and **61g** (30%)[a]
6	**58g**	DPS	TMS	**60g** (65%)[b] and **59g** (14%)[b]

[a] Heating in a sealed tube at 170 °C in toluene and 10 equiv of triethylamine. [b] Irradiation with microwaves at 600 W in acetonitrile at 170 °C for 30 min.

Hydroxy-directed Diels−Alder reaction of **57a**,**b** and *N*-benzylmaleimide provided the desired bicyclo[4.4.0]-decenes **58a** and **58b** in 67 and 64% yield, respectively, as the sole diastereomers. The latter were poised to undergo a thermal Claisen [3,3]-shift. Surprisingly, the thermal rearrangement of **58a** and **58b** in the presence of triethylamine gave only the 1,3-hydrogen shift byproducts **59a** and **59b** in 64 and 28% yields, respectively. The hydroxy moiety in **58a** and **58b** was then protected with various groups, and the resulting cycloadducts **58c**−**g** were heated at 170 °C in toluene (sealed tube) in the presence of triethylamine. The results are summarized in Table 2. Heating of 1,5-dienes **58c**−**e** led to the double bond isomerized products **59c** and **59d** (entries 1 and 2) or a complex mixture from which no desired Claisen product **60** was isolated (entry 3). We were gratified to find that diene **58f** rearranged under the above reaction conditions to produce the expected Claisen product **60f** in 40% yield along with **61f** (15% yield) (entry 4).[29] The latter is the result of a [3,3]-sigmatropic shift of **59f** generated during the course of the reaction. The installation of a TMS protecting group at C1 did not have a significant effect on the chemical yield for the transformation of **58g** to the desired Claisen product **60g** (entry 5). The latter was isolated in 42% yield along with the spiro compound **61g** (30% yield). Fortunately, the exposure of **58g** to microwave radiation[30,31] (170 °C, 600 W)

(22) (a) Scholl, S.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953. (b) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543.

(23) (a) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513. (b) McMurry, J. E. *Acc. Chem. Res.* **1983**, *16,* 405.

(24) Barriault, L.; Ang, P. A. J.; Lavigne, R. M. A. *Org. Lett.* **2004**, *6*, 1317.

(25) Weiler, L.; Huckin, S. N. *J. Am. Chem. Soc.* **1974**, *96*, 1082.

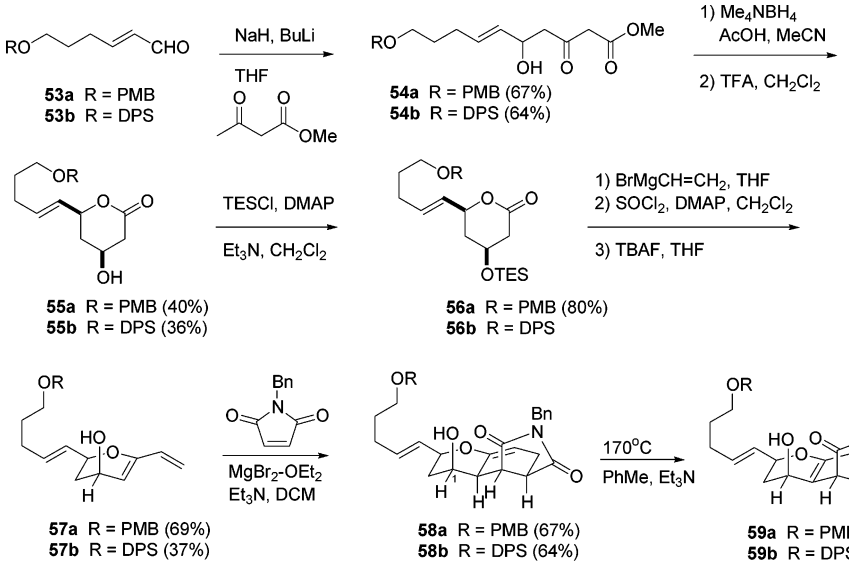
(26) Hayashi, N.; Fujiwara, K.; Murai, A. *Tetrahedron* **1997**, *53*, 12425.

(27) The aldehyde **53b** was made from the corresponding alcohol via a Swern oxidation. See: Brenn, A. P.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *Tetrahedron* **1993**, *49*, 10643.

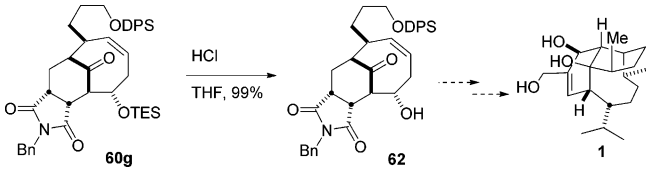
(28) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *10*, 3560.

(29) The structure of **61f** was established by NMR spectroscopy and confirmed by X-ray analysis. For ORTEP view of **61f**, see the Supporting Information.

SCHEME 11



SCHEME 12



for 30 min in acetonitrile furnished **60g** in 65% yield. In this case, we isolated **59g** as a side product in 14% yield. Interestingly, heating of **58g** in acetonitrile in a sealed tube at 170 °C led to a complex mixture from which no desired Claisen products **60g** or **61g** were isolated. It is clear now that the choice of the protecting groups R and R_1 and the heating source are crucial for the Claisen reaction to occur; however, their role in the reaction process remains elusive. Finally, the silicon groups on **60g** were removed with HCl in THF to afford the corresponding monoprotected alcohol **62** in 99% yield (Scheme 12). At this stage, the stereochemistry of the bicyclo[5.3.1]undecenone **62** was established without ambiguity by X-ray diffraction.[32]

In summary, we described three different approaches toward the elaboration of the vinigrol framework. The key feature of the first two synthetic routes was the successful exploitation of the HDDA reaction to construct the vinigrol *cis*-decalin unit **22**. However, this approach was plagued by the inability to form the eight-membered ring of vinigrol via a Claisen rearrangement or by a ring closure metathesis. We thus decided to generate this problematic eight-membered ring earlier in the synthesis employing a sequential HDDA/[3,3] reaction. This approach was rewarded with success, affording the bicyclo-[5.3.1]undecenone subunit embedded in the vinigrol framework. Completion of the tricyclic ring of vinigrol via an intramolecular alkylation upon the bridgehead ketone is currently in progress and will be reported in due course.

General Experimental Section

All reactions were performed under argon in flame-dried glassware equipped with a magnetic stir bar and a rubber septum unless otherwise indicated. Solvents used were freshly distilled prior to use: ether, THF, and 1,2-dimethoxyethane (DME) over sodium and benzophenone; dichloromethane, toluene, and DMF over calcium hydride. All other commercial reagents were used without purification. Microwave reactions were performed using a microwave oven equipped with a pressure-monitoring device and a fiber optic temperature probe. The reaction vessel was a quartz tube, and in each case a carboflon was added to aid in the absorption of microwave radiation. Reactions were monitored by TLC analysis using glass plates precoated (250-μm thickness) with silica gel 60 F_{254}. TLC plates were viewed using UV light, *p*-anisaldehyde staining solution, phosphomolybdic acid staining solution, or potassium permanganate staining solution. Flash chromatography was carried out on 230−400 mesh silica gel 60. ^1H and ^{13}C NMR spectra were recorded on 300 and 500 MHz spectrometer in the specified deuterated solvent. IR spectra were recorded on a FTIR spectrometer. HRMS spectra were obtained using a spectrometer, and melting points were recorded using a melting point apparatus.

5-(*tert*-Butyldiphenylsilanyloxymethyl)-1,2,3,4,4a,5,6,7-octahydronaphthalen-1-ol (18). $LiAlH_4$ (0.075 g, 1.97 mmol) was added to a solution of ester **17**[6a] (0.41 g, 1.97 mmol) in THF (20 mL) at −78 °C. The reaction was stirred for 30 min. A solution of sodium tartrate 1 M (3 mL) was added and stirred for 15 h. The aqueous layer was extracted 3 times with ethyl acetate (3 × 40 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (EtOAc) to afford 360 mg of the primary alcohol (99% yield) as a white solid. The alcohol was dissolved in DMF (10 mL). Imidazole (0.293 g, 4.3 mmol) was added, followed by DPSCl (0.563 mL, 2.2 mmol). The reaction was stirred at room temperature for 1.5 h. The reaction was

(30) For a review on microwaves in organic synthesis, see: (a) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250. (b) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, 1213. (c) Majetich, G.; Hichs, R. J. *Journal of Microwave Power and Electromagnetic Energy* **1995**, *30*, 27. (d) Loupy, A.; Perreux, L. *Tetrahedron* **2001**, *57*, 9199. (e) Lidström, P.; Tierny, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225.

(31) Nonpolar solvents such as toluene do not absorb microwaves, and therefore, a glass-coated Carboflon was placed inside the reaction cell. Carboflon readily absorbs microwave energy and transmits heat to the reaction mixture through conduction. This microwave oven is equipped with a fiber optic probe placed inside the reaction cell to monitor the temperature and pressure of the reaction.

(32) For ORTEP view of **62**, see Supporting Information.

quenched using saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with a mixture of 1:1 hexane/diethyl ether (3 × 30 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10−80% EtOAc/hexanes, gradient elution) to afford 69 mg of starting material and 650 mg of **18** (78% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70−7.62 (m, 4H), 7.43−7.33 (m, 6H), 5.59 (s, 1H), 4.01−3.98 (m, 1H), 3.62−3.50 (m, 2H), 2.12−2.07 (m, 3H), 1.99−1.88 (m, 1H), 1.85−1.72 (m, 1H), 1.65−1.61 (m, 1H), 1.53 (d, J = 1.1 Hz, 1H), 1.52−1.48 (m, 3H), 1.26−1.14 (m, 3H), 1.03 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.4, 135.5 (×4), 134.0 (×2), 129.5 (×2), 127.6 (×4), 114.4, 73.2, 65.9, 39.5, 38.4, 38.2, 27.5, 26.8 (×3), 25.1, 24.4, 21.6, 19.3; IR (neat) 3346, 2929, 2857, 1110 cm^{-1}; EI HRMS calcd for $C_{23}H_{27}O_2Si$ (M^+ − *t*Bu) 363.1870, obsd 363.1874.

Benzoic Acid 5-(*tert*-Butyldiphenylsilanyloxymethyl)-8,8a-dihydroxydecahydronaphthalen-1-yl Ester (19). Alcohol **18** (0.729 g, 1.73 mmol) was dissolved in dichloromethane (9 mL). Pyridine (0.42 mL, 5.2 mmol), DMAP (1 crystal), and benzoyl chloride (0.3 mL, 2.6 mmol) were added and stirred for 15 h. HCl 2 N (4 mL) was added, and the aqueous layer was extracted 3 times with dichloromethane (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 84 mg of benzoate (97% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18−8.15 (m, 2H), 7.76−7.71 (m, 4H), 7.59−7.53 (m, 1H), 7.49−7.39 (m, 8H), 5.64 (s, 1H), 5.46 (d, J = 11.0 Hz, 1H), 3.71−3.64 (m, 2H), 2.38−2.35 (m, 1H), 2.27−2.24 (m, 1H), 2.14−2.07 (m, 2H), 1.97−1.93 (m, 1H), 1.86−1.75 (m, 2H), 1.68−1.62 (m, 1H), 1.61−1.59 (m, 1H), 1.57−1.54 (m, 1H), 1.35−1.29 (m, 1H), 1.21−1.15 (m, 1H), 1.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.5, 139.8, 135.5 (×4), 134.0 (×2), 132.7 (×2), 130.7, 129.6 (×2), 129.5 (×2), 128.3 (×2), 127.6 (×2), 127.54, 115.6, 75.2, 65.8, 39.6, 38.4, 34.9, 27.4, 26.9 (×3), 25.0, 24.5, 21.5, 19.2; IR (neat) 3063, 2937, 2854, 1722, 1267, 1102 cm^{-1}; EI HRMS calcd for $C_{30}H_{31}O_3Si$ (M^+ − *t*Bu) 467.2042, obsd 467.1834. The resulting benzoate (84 mg, 0.16 mmol) was dissolved in THF (1.6 mL) and water (0.32 mL). NMO (0.037 g, 0.32 mmol) was added, followed by osmium tetroxide 4% in water (0.050 mL, 0.008 mmol). The reaction was stirred for 6 h at reflux and 18 h at room temperature. The reaction was not finished. NMO (0.02 g, 0.17 mmol) and osmium tetraoxide 4% in water (0.02 mL, 0.003) were added and stirred for 24 h at reflux. After completion, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$. The aqueous layer was extracted 3 times with ethyl acetate (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 73 mg of **19** (82% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96−7.92 (m, 2H), 7.67−7.63 (m, 4H), 7.56 (tt, 1.3, 7.4 Hz, 1H), 7.44−7.34 (m, 8H), 5.12 (dd, J = 4.4, 12.1 Hz, 1H), 4.40−4.35 (m, 1H), 3.55−3.41 (m, 2H), 2.94 (s, 1H), 2.91 (d, J = 2.1 Hz, 1H), 2.46−2.35 (m, 1H), 2.13−2.01 (m, 2H), 1.91−1.80 (m, 2H), 1.75−1.61 (m, 2H), 1.56−1.40 (m, 3H), 1.28−1.13 (m, 2H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 135.6 (×4), 133.7 (×2), 133.3, 129.9, 129.6, 129.5, 129.3 (×2), 128.6 (×2), 127.6 (×4), 83.9, 73.6, 68.4, 65.8, 43.6, 35.8, 29.3, 28.8, 26.8 (×3), 23.6, 21.6, 21.3, 19.2; IR (neat) 3470, 2921, 2854, 1722, 1272, 1106 cm^{-1}; EI HRMS calcd for $C_{30}H_{33}O_5Si$ (M^+ − *t*Bu) 501.2097, obsd 501.1991.

Benzoic Acid 6-(*tert*-Butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-yl Ester (20). Diol **19** (0.693 g, 1.24 mmol) was dissolved in CH_2Cl_2 (12 mL). 2-Methoxypropene (0.356 mL, 3.72 mmol) and TsOH (1 crystal) were added, and then the solution turned dark red. The reaction was done after 10 min. $NaHCO_{3sat}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 × 60 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated by rotary evaporation under vacuum. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 751 mg of **20** (100% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 7.1 Hz, 2H), 7.69−7.66 (m, 4H), 7.58−7.53 (m, 1H), 7.47−7.34 (m, 8H), 5.32 (dd, J = 4.2, 12.0 Hz, 1H), 4.76 (s, 1H), 3.63−3.52 (m, 2H), 2.62−2.57 (m, 1H), 2.17−1.97 (m, 3H), 1.87−1.74 (m, 3H), 1.69−1.55 (m, 1H), 1.50 (s, 3H), 1.47−1.25 (m, 2H), 1.23 (s, 3H), 1.19−1.09 (m, 2H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.4, 135.5 (×4), 133.9, 133.9, 132.9, 130.5, 129.6 (×2), 129.5, 129.5, 128.3 (×2), 127.6 (×4), 107.3, 83.8, 76.8, 72.6, 66.2, 40.8, 32.4, 29.6, 27.5, 26.9, 26.8 (×3), 22.6, 22.5, 19.2, 17.3; IR (neat) 2945, 2856, 1716, 1266, 1101 cm^{-1}; EI HRMS calcd for $C_{37}H_{46}O_5Si$ (M^+) 598.31145, obsd 598.31267.

6-(*tert*-Butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-ol (21). Benzoate **20** (0.818 g, 1.37 mmol) was dissolved in benzene (5 mL) and MeOH (5 mL). K_2CO_3 was added until it did not dissolve and heated to reflux for 6 h, then cooled to room temperature for 72 h, and filtered through a Celite pad with diethyl ether. The solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 510 mg of **21** (75% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.62 (m, 4H), 7.42−7.32 (m, 6H), 4.50 (s, 1H), 3.71−3.68 (m, 1H), 3.56−3.45 (m, 2H), 2.53−2.47 (m, 1H), 2.05−1.94 (m, 2H), 1.86−1.62 (m, 5H), 1.53 (s, 3H), 1.48 (s, 3H), 1.36−1.22 (m, 3H), 1.19−1.07 (m, 2H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.5 (×4), 134.1 (×2), 129.5 (×2), 127.6 (×4), 106.7, 85.9, 75.0, 71.6, 66.3, 40.1, 32.7, 31.1, 27.7, 27.2, 26.8 (×3), 23.6, 23.0, 22.6, 19.3, 17.6; IR (neat) 3456, 2935, 2858, 1103, 1039 cm^{-1}; EI HRMS calcd for $C_{30}H_{42}O_4Si$ (M^+) 494.28524, obsd 494.28459.

6-(*tert*-Butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-one (22). Alcohol **21** (0.004 g, 0.008 mmol) was dissolved in CH_2Cl_2 (10 mL). Dess−Martin periodinane (4 mg, 0.009 mmol) was added, and the reaction was stirred for 3 h at room temperature. A solution of $NaHCO_{3sat}$ was added, followed by $Na_2S_2O_{3sat}$, and stirred for 20 min. The aqueous layer was extracted 3 times with dichloromethane (3 × 20 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 4 mg of **22** (100% yield) as white crystals. mp 76.7−77.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64−7.59 (m, 4H), 7.43−7.32 (m, 6H), 4.12 (t, J = 2.7 Hz, 1H), 3.58−3.45 (m, 2H), 2.58−2.53 (m, 1H), 2.41−2.36 (m, 1H), 2.25−2.15 (m, 2H), 2.10−1.90 (m, 2H), 1.89−1.80 (m, 1H), 1.77−1.60 (m, 2H), 1.54 (s, 3H), 1.52−1.39 (m, 1H), 1.38 (s, 3H), 1.23−1.10 (m, 2H), 1.01 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 209.8, 135.5 (×4), 133.9, 133.8, 129.6 (×2), 127.6 (×4), 109.1, 87.2, 74.3, 65.7, 42.9, 41.1, 32.7, 26.8 (×3), 26.7, 25.3, 25.2, 23,3, 21.3, 19.3, 16.9; IR (neat) 2939, 2861, 1724, 1110 cm^{-1}; EI HRMS calcd for $C_{30}H_{40}O_4Si$ (M^+) 492.26959, obsd 492.27021.

6-(*tert*-Butyldiphenylsilanyloxymethyl)-2,2-dimethyl-10-vinyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-ol (23). A suspension of $CeCl_3$ (0.044 g, 0.18 mmol) in dry THF (0.6 mL) was stirred at 0 °C for 2 h. Ketone **22** (0.03 g, 0.06 mmol) was dissolved in THF (0.2 mL), cannulated into the $CeCl_3$ suspension, and stirred for 15 h at room temperature. The solution was cooled to −78 °C, and vinylmagnesium bromide 0.9 M (0.2 mL, 0.18 mmol) was added dropwise. The reaction was stirred for 30 min at −78 °C. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 × 20 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 30 mg of **23** (96% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.64 (m, 4H), 7.42−7.33 (m, 6H), 6.44 (dd, J = 10.8, 17.3 Hz, 1H), 5.35 (d, J = 17.4 Hz, 1H), 5.21 (d, 10.9 Hz, 1H), 4.56

(s, 1H), 3.79−3.55 (m, 2H), 2.37 (s, 1H), 2.08−2.03 (m, 1H), 1.96−1.89 (m, 1H), 1.81−1.56 (m, 5H), 1.49 (s, 3H), 1.38 (s, 3H), 1.33−1.1 (m, 4H), 1.03 (s, 9H), 0.94−0.84 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.7, 135.6 (×4), 134.1 (×2), 129.5 (×2), 127.6 (×4), 113.1, 107.1, 75.5, 73.6, 65.8, 38.8, 37.4, 27.9, 27.3, 26.9 (×3), 23.3, 23.2, 20.5, 19.3, 18.1; IR (neat) 3464, 2928, 2852, 1109, 1041 cm^{-1}; EI HRMS calcd for $C_{32}H_{44}O_4Si$ (M^+) 520.30089, obsd 520.30007.

6-Hydroxymethyl-2,2-dimethyl-10-vinyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-ol (24). Compound **23** (0.033 g, 0.063 mmol) was dissolved in THF (0.5 mL). TBAF (0.089 mL of a 1 M solution in THF, 0.089 mmol) was added. The reaction was stirred for 15 h, then concentrated in vacuo. The crude product was purified by flash silica column chromatography (80% EtOAc/hexanes) to afford 16 mg of **24** (90% yield) as a white solid. mp 119.9−123.9 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (dd, J = 11.0, 17.3 Hz, 1H), 5.33 (d, J = 17.2 Hz, 1H), 5.20 (d, J = 10.9 Hz, 1H), 4.52 (s, 1H), 3.78−3.54 (m, 2H), 2.18−2.16 (m, 1H), 2.07−1.67 (m, 8H), 1.60−1.53 (m, 1H), 1.46 (s, 3H), 1.36 (s, 3H), 1.32−1.14 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.5, 113.2, 107.2, 75.4, 73.7, 64.9, 38.7, 37.3, 29.7, 28.1, 27.2, 23.6 (×2), 20.0, 18.9; IR (neat) 3427, 2930, 2869, 1250, 1207, 1044, 1011 cm^{-1}; EI HRMS calcd for C15H23O4 (M^+ − Me) 267.15964, obsd 267.1389.

Lactone (27). Molecular sieves 4 Å (0.05 g) were flame-dried under vacuum. Diol **24** (0.01 g, 0.035 mmol) was dissolved in dichloromethane (0.5 mL) and cannulated into the flask containing the sieves. NMO (0.017 g, 0.142 mmol) was added, followed by TPAP (1 grain). The reaction was stirred for 20 min, and the crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 5 mg of **27** (51% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.97 (dd, J = 11.2, 17.5 Hz, 1H), 5.47 (dd, J = 1.4, 7.5 Hz, 1H), 5.21 (dd, J = 1.4, 11.2 Hz, 1H), 4.21 (d, J = 5.1 Hz, 1H), 2.76 (s, 1H), 2.14−2.09 (m, 2H), 2.06−1.87 (m, 4H), 1.83−1.77 (m, 1H), 1.75−1.60 (m, 1H), 1.59−1.50 (m, 3H), 1.46 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 135.8, 114.9, 107.9, 83.3, 77.2, 74.7, 44.6, 37.4, 34.0, 28.6, 28.3, 26.3, 24.7, 23.4, 16.7; IR (neat) 2935, 1741, 1092 cm^{-1}; EI HRMS calcd for $C_{16}H_{22}O_4$ (M+) 278.15181, obsd 278.15268.

Enol Ether (28). A solution of ester **27** (519 mg, 1.8 mmol) in a 0.11 M solution of Petasis' reagent (Cp_2TiMe_2) in toluene (50 mL,5.4 mmol) was heated at 80 °C for 15 h. The solution was concentrated and purified by flash chromatography twice (5% EtOAc/94% hexanes/1% Et_3N) to afford 420 mg of **28** (85% yield) as a yellow oil: ^{1}H NMR (500 MHz, C_6D_6) δ 6.12 (dd, J = 17.4, 11.1 Hz, 1H), 5.63 (dd, J = 17.4, 2.1 Hz, 1H), 5.14 (s, 1H), 4.61 (s, 1H), 4.29−4.28 (m, 1H), 3.95 (s, 1H), 2.45−2.44 (m, 1H), 2.28 (qt, 13.8, 4.7 Hz, 1H), 2.14−1.99 (m, 4H), 1.97 (s, 1H), 1.87−1.79 (m, 2H), 1.55−1.49 (m, 1H), 1.46 (d, J = 0.6 Hz, 3H), 1.45−1.32 (m, 2H), 1.30 (d, J = 0.4 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 163.4, 139.0, 113.5, 107.2, 87.2, 78.4, 78.0, 75.4, 42.7, 37.5, 35.4, 32.6, 28.8, 26.3, 25.5, 23.6, 17.7; IR (neat) 2930, 1245, 1090 cm^{-1}; EI HRMS calcd for $C_{17}H_{24}O_3$ (M^+) 276.17255, obsd 276.17433.

1-[10-(3-Bromopropylidene)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxol-6-yl]-ethanone (30). To a solution of **28** (9 mg, 0.03 mmol) in toluene (1 mL) was added $MgBr_2$, and the mixture was stirred at room temperature for 15 h. The reaction was quenched by adding water. The aqueous layer was extracted 3 times with diethyl ether (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 11 mg of **30** (99% yield) as a colorless oil: ^{1}H NMR (500 MHz, C_6D_6) δ 6.21 (t, J = 8.7 Hz, 1H), 3.77 (t, J = 2.7 Hz, 1H), 3.75−3.67 (m, 2H), 3.18−3.14 (m, 1H), 2.31−2.27 (m, 1H), 2.18 (dt, J = 14.3, 9.9 Hz, 1H), 2.01−1.97 (m, 1H), 1.93−1.88 (m, 1H), 1.74 (s, 3H), 1.73−1.66 (m, 1H), 1.47 (s, 3H), 1.46−1.41 (m, 2H), 1.29 (s, 3H), 1.28−1.23 (m, 1H), 1.16−1.06 (m, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.8, 148.9, 117.4, 107.4, 84.2, 77.0, 45.0, 43.6, 27.4, 27.4, 26.9, 26.3, 26.6, 25.6, 22.3, 13.7, 24.6; IR (neat) 2988, 2934, 1707, 1207, 1056 cm^{-1}; EI HRMS calcd for $C_{17}H_{24}O_3$ (M^+ − HBr) 276.17255, obsd 276.17233.

6-(*tert*-Butyldiphenylsilanyloxymethyl)-10-(3-hydroxypropyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]-dioxol-10-ol (35). A suspension of $CeCl_3$ (0.328 g, 1.33 mmol) in dry THF (0.6 mL) was stirred at 0 °C for 2 h. Ketone **22** (0.225 g, 0.44 mmol) was dissolved in THF (8 mL), cannulated into the $CeCl_3$ suspension, and stirred for 15 h at room temperature. The solution was cooled to −78 °C, and $ClMgO(CH_2)_3MgCl$ 0.34 M (8 mL, 2.66 mmol) was added dropwise. Saturated $NH_4Cl_{(aq)}$ and a few drops of glacial acetic acid were added. The aqueous layer was extracted 3 times with diethyl ether (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (80% EtOAc/hexanes) to afford 41 mg of starting material **22** (18%) and 200 mg of **35** (82% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64−7.59 (m, 4H), 7.43−7.31 (m, 6H), 4.69−4.67 (m, 1H), 3.76−3.63 (m, 2H), 3.57−3.46 (m, 2H), 2.49−2.44 (m, 1H), 2.03−1.56 (m, 11H), 1.51 (s, 3H), 1.47 (s, 3H), 1.25−1.10 (m, 6H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.5 (×4), 134.1, 134.0, 129.5 (×2), 127.6 (×4), 107.0, 87.6, 75.0, 73.3, 66.8, 63.5, 38.5, 33.0, 32.9, 30.9, 27.7, 27.4, 26.9, 25.4, 23.4, 22.8, 20.8, 19.3, 17.5; IR (neat) 3399, 2943, 2862, 1099, 1050 cm^{-1}; EI HRMS calcd for $C_{33}H_{48}O_5Si$ (M^+) 552.32710, obsd 552.3249.

10-[3-(*tert*-Butyldimethylsilanyloxy)-propyl]-6-(*tert*-butyldiphenylsilanyloxymethyl)2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxol-10-ol (36). A solution of alcohol **35** (1.03 g, 1.9 mmol), *tert*-butyldimethylsilyl chloride (1.5 g, 10 mmol), and imidazole (1.5 g, 22 mmol) in DMF (25 mL) was stirred at room temperature overnight. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with a mixture of 1:1 diethyl ether/hexanes (3 × 100 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 1.3 g of **36** (100% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 7.1 Hz, 4H), 7.41−7.32 (m, 6H), 4.73 (s, 1H), 3.74−3.59 (m, 2H), 3.56−3.46 (m, 2H), 2.74−2.68 (m, 1H), 2.49−2.42 (m, 1H), 1.97−1.85 (m, 3H), 1.82−1.80 (m, 1H), 1.76−1.65 (m, 4H), 1.62−1.56 (m, 3H), 1.50−1.43 (m, 2H), 1.50 (s, 3H), 1.47 (s, 3H), 1.38−1.17 (m, 6H), 1.01 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.6 (×4), 134.1 (×2), 129.5 (×2), 127.6 (×4), 106.8, 87.5, 74.4, 73.2, 66.8, 63.8, 38.6, 33.3, 30.9, 27.7, 27.4, 26.9 (×3), 26.0 (×3), 25.4, 23.3, 22.8, 20.8, 19.3, 18.3, 17.5, −5.3 (×2); IR (neat) 3417, 2930, 2864, 1257, 1099 cm^{-1}; EI HRMS calcd for $C_{39}H_{62}O_5Si_2$ (M^+) 666.41358, obsd 666.4597.

10-[3-(*tert*-Butyldimethylsilanyloxy)-propylidene]-6-(*tert*-butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxole (37). A solution of the alcohol **36** (20 mg, 0.03 mmol) in DBU (0.1 mL) and pyridine (0.5 mL) was stirred at room temperature. $POCl_3$ (0.1 mL) was added and stirred for 45 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 15 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 15 mg of **37** (77% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65−7.62 (m, 4H), 7.41−7.32 (m, 6H), 5.67 (t, J = 7.4 Hz, 1H), 4.06 (t, J = 2.6 Hz, 1H), 3.58 (t, J = 7.3 Hz, 2H), 3.51 (d, J = 7.4 Hz, 2H), 2.61−2.59 (m, 1H), 2.52−2.45 (m, 1H), 2.25 (q, J = 7.3 Hz, 2H), 2.01−1.98 (m, 1H), 1.89−1.80 (m, 1H), 1.78−1.72 (m, 3H), 1.66−1.57 (m, 1H), 1.54 (s, 3H), 1.36 (s, 3H), 1.33−1.06 (m, 4H), 1.01 (s, 9H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.1, 135.6 (×4), 134.2 (×2), 129.4 (×3), 127.5 (×4), 116.6, 107.1, 84.6, 78.1, 66.7, 63.2, 42.5, 33.4, 31.0, 27.0 (×3), 26.9 (×4), 26.4, 26.0, 24.3, 22.9, 19.3, 18.3,

17.4, −5.2, −5.3; IR (neat) 2931, 2857, 1106 cm^{-1}; EI HRMS calcd for $C_{35}H_{51}O_4Si_2$ ($M^+ - t$Bu) 591.33259, obsd 591.35122.

10-[3-(*tert*-Butyldimethylsilanyloxy)-propyl]-6-(*tert*-butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxole (38). In a glovebox, a solution of $RuCl_2(H_2IMes)(py)_2(CHPh)$ (0.001 g, 0.0014 mmol) in methanol (1 mL) and benzene (1 mL) was added to the olefin **37** (0.014 g, 0.022 mmol). Triethylamine (0.0091 mL) was added, and the solution was pressurized to 1350 psi with H_2. The reaction mixture in the autoclave was stirred and heated for 5 days at 80 °C. The reaction was concentrated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 0.013 g of **38** (93% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.62 (m, 4H), 7.42−7.31 (m, 6H), 4.20−4.19 (m, 1H), 3.61 (d, J = 7 Hz, 2H), 3.50 (d, J = 7 Hz, 2H), 2.69−2.60 (m, 1H), 2.03−1.92 (m, 2H), 1.81−1.58 (m, 8H), 1.56 (s, 3H), 1.50−1.45 (m, 2H), 1.43 (s, 3H), 1.23 (s, 2H), 1.18−1.06 (m, 2H), 1.01 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6 (×2), 134.1 (×2), 129.5 (×2), 127.6 (×4), 106.6, 85.8, 73.5, 66.4, 63.7, 46.4, 41.9, 33.2, 31.7, 28.4, 28.2, 28.0, 26.8 (×3), 26.0 (×3), 25.6, 25.3, 24.4, 22.9, 19.3, 18.3, 17.6, −5.3 (×2); IR (neat) 2929, 2857, 1110 cm^{-1}; EI HRMS calcd for $C_{35}H_{51}O_4Si_2$ (M^+) 650.41866, obsd 650.41375.

10-[3-(*tert*-Butyldimethylsilanyloxy)-propyl]-6-(*tert*-butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydronaphtho[1,8a-*d*][1,3]dioxole (39). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64−7.62 (m, 4H), 7.44−7.32 (m, 6H), 4.08−4.05 (m, 1H), 3.70−3.55 (m, 2H), 3.55−3.50 (m, 2H), 2.30−2.20 (m, 1H), 2.05−1.90 (m, 2H), 1.88−1.60 (m, 10H), 1.55−1.20 (m, 11H), 1.02 (s, 9H).

3-(6-Hydroxymethyl-2,2-dimethyloctahydronaphtho-[1,8a-*d*][1,3]dioxol-10-yl)-propan-1-ol (44). To a solution of protected alcohols **38** (130 mg, 0.2 mmol) in THF (2 mL) was added TBAF (1 mL of a 1 M solution in THF, 0.8 mmol). The reaction was stirred at room temperature for 72 h. The solution was concentrated and purified by flash silica column chromatography (5% MeOH/EtOAc) to afford 60 mg of **44** (100% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21−4.08 (m, 1H), 3.69−3.61 (m, 2H), 3.50 (d, J = 7.5 Hz, 2H), 2.54−2.47 (m, 1H), 2.34−2.21 (m, 1H), 2.05−1.95 (m, 2H), 1.89−1.62 (m, 7H), 1.53 (s, 3H), 1.52−1.43 (m, 3H), 1.43 (s, 3H), 1.30−1.07 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 106.7, 85.8, 73.4, 65.9, 63.1, 46.1, 41.9, 33.5, 31.3, 28.4 (×2), 28.1, 25.4, 25.2, 24.5, 22.9, 17.8; IR (neat) 3377, 2933, 2866, 1033 cm^{-1}; EI HRMS calcd for $C_{17}H_{30}O_4$ (M^+) 298.21441, obsd 298.21567.

10-But-3-enyl-2,2-dimethyl-6-vinyloctahydronaphtho-[1,8a-*d*][1,3]dioxole (46). A catalytic amount of TPAP (1 crystal) and NMO (14 mg, 0.12 mmol) was added to a solution of diol **44** in acetonitrile (1 mL) over 4 Å molecular sieves (50 mg). The reaction was stirred for 20 min. The mixture was filtered through a silica gel pad (5% methanol/95% ethyl acetate). The solvent was evaporated, and the crude dialdehyde **45** was used immediately to avoid decomposition. Methyltriphenylphosphonium iodide (0.057 g, 0.14 mmol) was dissolved in THF (1 mL) and cooled to 0 °C. KHMDS (10.43 M in toluene, 0.325 mL, 0.14 mmol) was added, and the solution turned yellow. Dialdehyde **45** (0.010 g, 0.03 mmol) in THF (1 mL) was cannulated into the ylide solution. The reaction was stirred at 0 °C for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethyl ether (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 7 mg of **46** (72% yield) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88−5.75 (m, 2H), 5.03−4.92 (m, 4H), 4.19 (s, 1H), 3.01−2.99 (m, 1H), 2.25−2.10 (m, 1H), 2.04−1.89 (m, 3H), 1.88−1.65 (m, 6H), 1.53 (s, 3H), 1.42 (s, 3H), 1.37−1.23 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 138.8, 114.4, 113.3, 106.6, 85.9, 73.6, 46.6, 45.5, 35.0, 32.3, 29.7, 28.5, 28.4, 28.2, 28.0, 25.0, 23.2, 19.3; IR (neat) 2930, 2859, 1247, 1036 cm^{-1}; EI HRMS calcd for $C_{19}H_{30}O_2$ (M^+) 290.22458, obsd 290.22256.

6-(4-Methoxybenzyloxy)-hex-2-enal (53a). A solution of oxalyl chloride (0.63 mL, 7.2 mmol) in dichloromethane (50 mL) was cooled to −78 °C. Methylsulfoxide (1.02 mL, 14.4 mmol) was added dropwise, resulting in the formation of a lot of gas. The solution was stirred for 20 min. 6-(4-Methoxybenzyloxy)-*trans*-hex-2-en-1-ol (1.33 g, 5.99 mmol) was dissolved in dichloromethane (10 mL), cannulated into the Swern reagent solution, and stirred for 90 min at −78 °C. Triethylamine (4.2 mL, 30 mmol) was added, and the reaction was warmed to room temperature while being stirred for 20 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 × 100 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 968 mg of **53a** (93% yield) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.46 (d, J = 8 Hz, 1H), 7.23 (d, J = 8 Hz, 2H), 6.86 (d, J = 9 Hz, 2H), 6.80 (t, J = 7 Hz, 1H), 6.08 (ddd, J = 16, 8, 1 Hz, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.46 (t, J = 6 Hz, 2H), 2.42 (q, J = 8 Hz, 2H), 1.78 (quint, J = 6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 159.2, 158.3, 133.1, 130.3, 129.3 (×2), 113.8 (×2), 72.7, 68.7, 55.2, 29.6, 27.9; IR (neat) 2937, 2857, 2838, 2736, 1688, 1612, 1513, 1248, 1100 cm^{-1}; EI HRMS calcd for $C_{14}H_{18}O_3$ (M^+) 234.12560, obsd 234.12515.

5-Hydroxy-10-(4-methoxybenzyloxy)-3-oxo-dec-6-enoic Acid Methyl Ester (54a). Methyl acetoacetate (1.01 mL, 9.36 mmol) was dissolved in THF (40 mL) and cooled to 0 °C. Sodium hydride 60% in mineral oil (0.56 g, 14.04 mmol) was added and stirred for 20 min. *n*-Butyllithium (2.31 M in hexane, 4.5 mL, 10.3 mmol) was added and stirred for 20 min and then cooled to −78 °C. Alcohol **53a** (1.03 g, 4.68 mmol) was dissolved in THF (7 mL) and cannulated into the anion solution, and the resultant mixture was stirred at −78 °C for 20 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethyl ether (3 × 100 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (30% EtOAc/hexanes) to afford 1.09 g of **54a** (67% yield) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J = 8 Hz, 2H), 6.85 (d, J = 8 Hz, 2H), 5.67 (dt, J = 15, 7 Hz, 1H), 5.43 (dd, J = 15, 6 Hz, 1H), 4.54−4.47 (m, 1H), 4.39 (s, 2H), 3.77 (s, 3H), 3.71 (s, 3H), 3.47 (s, 2H), 3.40 (t, J = 2 Hz, 2H), 2.70−2.66 (m, 3H), 2.08 (q, J = 7 Hz, 2H), 1.64 (quint, J = 2 Hz 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 167.3, 159.0, 131.9 (×2), 130.8 (×2), 130.5, 129.2, 113.7, 72.5, 69.1, 68.3, 55.2, 52.4, 51.2, 49.6, 29.0, 28.7; IR (neat) 3408, 2940, 2853, 1745, 1710, 1513, 1247 cm^{-1}; EI HRMS calcd for $C_{19}H_{24}O_5$ ($M^+ - H_2O$) 332.16238, obsd 332.1583.

10-(*tert*-Butyldiphenylsilanyloxy)-5-hydroxy-3-oxo-dec-6-enoic Acid Methyl Ester (54b). Methyl acetoacetate (14.5 mL, 136.5 mmol) was dissolved in THF (200 mL) and cooled to 0 °C. Sodium hydride 60% in mineral oil (8.2 g, 204.6 mmol) was added and stirred for 20 min. *n*-Butyllithium (2.5 M, 60 mL, 150 mmol) was added and stirred for 20 min and then cooled to −78 °C. 6-(*tert*-Butyldiphenylsilanyloxy)-hex-2-enal (24 g, 68.2 mmol) was dissolved in THF (30 mL) and cannulated into the anion solution. The resulting mixture was stirred at −78 °C for 20 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethyl ether (3 × 200 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 20.7 g of **54b** (64% yield) as a light yellow oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.70 (dd, J = 8, 2 Hz, 4H), 7.48−7.42 (m, 6H), 5.70 (dt, J = 15, 7 Hz, 1H), 5.53 (dd, J = 15, 6 Hz, 1H), 4.52−4.50 (m, 1H), 3.95 (d, J = 4 Hz, 1H), 3.72 (t, J = 6 Hz, 2H), 3.66 (s, 3H), 3.58 (s, 2H), 2.84−2.65 (m, 2H), 2.15 (q, J = 7 Hz, 2H), 1.67 (quint,

J = 7 Hz, 2H), 1.06 (s, 9H); ^{13}C NMR (125 MHz, acetone-d_6) δ 202.5, 168.4, 136.3 (×4), 134.8 (×2), 133.9, 130.8, 130.6 (×2), 128.7 (×4), 69.1, 63.9, 52.2, 51.2, 50.3, 32.9, 29.1, 27.3 (×3), 19.8; IR (neat) 3448, 2932, 2857, 1748, 1716, 1428, 1111 cm^{-1}; EI HRMS calcd for $C_{23}H_{27}O_5Si$ ($M^+ - t$Bu) 411.16278, obsd 411.16135.

5-Hydroxy-10-(4-methoxybenzyloxy)-3-oxo-dec-6-enoic Acid Methyl Ester (55a). Acetonitrile (13 mL) and acetic acid (13 mL) were mixed at 0 °C. Tetramethylammonium borohydride (1.1 g, 12.5 mmol) was added and stirred for 20 min. The mixture was frozen in a bath at −78 °C, and a solution of ketone **54a** (1.09 g, 3.1 mmol) in acetonitrile (5 mL) was cannulated into the flask. The reaction was kept in the freezer for 15 h at −25 °C. The reaction was quenched by adding sodium potassium tartrate 0.5 M (40 mL) and warming to room temperature. The organic layer was washed with $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 60 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was dissolved in dichloromethane (26 mL) and treated directly with trifluoroacitic acid (0.047 mL, 0.63 mmol). The reaction was stirred for 15 h at room temperature. The reaction was stopped by adding Na_2CO_3 until a neutral pH was obtained. The reaction was filtered and concentrated. The crude product was purified by flash silica column chromatography (70% EtOAc) to afford 442 mg (40%) of starting material and 407 mg of **55a** (40% yield) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.22 (m, 2H), 6.85 (d, J = 9 Hz, 2H), 5.75 (dt, J = 15, 7 Hz, 1H), 5.46 (dd, J = 15, 7 Hz, 1H), 4.61−4.54 (m, 1H), 4.40 (s, 2H), 4.25−4.20 (m, 1H), 3.78 (s, 3H), 3.41 (t, J = 6 Hz, 2H), 2.87 (ddd, J = 17, 6, 1 Hz, 1H), 2.42 (dd, J = 17, 8 Hz, 1H), 2.27−2.09 (m, 4H), 1.71−1.55 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 159.1, 134.5, 130.5, 129.3 (×2), 127.6, 113.8 (×2), 77.6, 72.5, 69.0, 63.8, 55.3, 39.4, 38.3, 28.7 (×2); IR (neat) 3427, 2933, 2860, 1732, 1512, 1245 cm^{-1}; EI HRMS calcd for $C_{14}H_{24}O_5$ (M^+) 320.16238, obsd 320.16072.

6-[5-(*tert*-Butyldiphenylsilanyloxy)-pent-1-enyl]-4-hydroxytetrahydropyran-2-one (55b). Acetonitrile (17 mL) and acetic acid (17 mL) were mixed at 0 °C. Tetramethylammonium borohydride (1.7 g, 19.3 mmol) was added and stirred for 20 min. The mixture was frozen in a bath at −78 °C, and a solution of ketone **54b** (2.26 g, 4.82 mmol) in acetonitrile (5 mL) was cannulated into the flask. The reaction was kept in the freezer for 15 h at −25 °C. The reaction was quenched by adding sodium potassium tartrate 0.5 M (60 mL) and warmed to room temperature. The organic layer was washed with $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 100 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was dissolved in dichloromethane (26 mL) and treated directly with trifluoroacetic acid (0.065 mL, 0.84 mmol). The reaction was stirred for 15 h at room temperature. The reaction was stopped by adding Na_2CO_3 until a neutral pH was obtained. The reaction was filtered and concentrated. The crude product was purified by flash silica column chromatography (25% EtOAc/hexanes to 35% EtOAc/hexanes) to afford 767 mg (34%) of starting material and 759 mg of **55b** (36% yield) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66−7.64 (m, 4H), 7.40−7.34 (m, 6H), 5.75 (dt, J = 15, 6 Hz, 1H), 5.47 (dd, J = 15, 7 Hz, 1H), 4.58−4.54 (m, 1H), 4.19 (br s, 1H), 3.84 (s, 1H), 3.65 (t, J = 6 Hz, 2H), 2.84 (dd, J = 17, 5 Hz, 1H), 2.43 (dd, J = 17, 8 Hz, 1H), 2.22−2.13 (m, 3H), 1.63−1.59 (m, 3H), 1.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 135.4 (×4), 134.6, 133.7 (×2), 129.5, 127.6 (×4), 127.4, 77.9, 63.3, 62.9, 39.3, 38.0, 31.5, 28.3, 26.8 (×3), 19.1; IR (neat) 3420, 3071, 2931, 2858, 1733, 1428, 1242, 969 cm^{-1}; EI HRMS calcd for $C_{10}H_{14}O_3$ ($M^+ - t$BDPSOH) 182.0943, obsd 182.0506.

6-[5-(4-Methoxybenzyloxy)-pent-1-enyl]-4-triethylsilanyloxytetrahydropyran-2-one (56a). Alcohol **55a** (0.407 g, 1.27 mmol) was dissolved in THF (13 mL). Triethylamine (1.1 mL, 7.63 mmol) and (dimethylamino)pyridine (0.014 g, 0.11 mmol) were added, followed by triethylsilyl chloride (0.064 mL, 3.81 mmol). The reaction was stirred for 30 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethyl ether (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (15% EtOAc/hexanes) to afford 442 mg of **56a** (80% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.21 (m, 2H), 6.88−6.83 (m, 2H), 5.75 (dt, J = 15, 6 Hz, 1H), 5.52−5.44 (m, 1H), 4.60−4.53 (m, 1H), 4.40 (s, 2H), 4.16−4.07 (m, 1H), 3.78 (s, 3H), 3.42 (t, J = 6 Hz, 2H), 2.80 (ddd, J = 17, 6, 2 Hz, 1H), 2.40 (dd, J = 17, 8 Hz, 1H), 2.16−2.07 (m, 3H), 1.71−1.62 (m, 3H), 0.93 (t, J = 8 Hz, 9H), 0.50 (q, J = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 159.1, 134.4, 130.5, 129.2 (×2), 127.8, 113.7 (×2), 77.7, 72.5, 69.1, 64.3, 55.3, 40.3, 39.1, 28.8, 28.7, 6.7 (×3), 4.7 (×3); IR (neat) 2954, 2876, 1741, 1513, 1247, 1096 cm^{-1}; EI HRMS calcd for $C_{22}H_{33}O_5Si$ (M^+ − Et) 405.20973, obsd 405.20812.

2-[5-(4-Methoxybenzyloxy)-pent-1-enyl]-6-vinyl-3,4-dihydro-2*H*-pyran-4-ol (57a). The lactone **56a** (0.745 g, 1.72 mmol) was dissolved in THF (17 mL) and cooled to −78 °C. Vinylmagnesium bromide, 0.9 M in THF, (5.72 mL, 5.15 mmol) was added, and the reaction was stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethyl ether (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was used directly to avoid decomposition. The lactol intermediate was dissolved in dichloromethane (17 mL) and cooled to 0 °C. 2,6-(Dimethylamino)pyridine (0.63 g, 5.16 mmol) was added, followed by thionyl chloride (0.125 mL, 1.72 mmol), and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was used directly to avoid decomposition. The diene was dissolved in THF (17 mL), and tetrabutylammonium fluoride 1 M in THF (1.9 mL, 1.89 mmol) was added. The reaction turned dark brown, and the solvent was evaporated after 30 min. The crude product was purified by flash silica column chromatography (50% EtOAc/hexanes) to afford 392 mg of **57a** (69% yield) as a colorless oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.26 (d, J = 9 Hz, 2H), 6.89 (d, J = 9 Hz, 2H), 6.08 (dd, J = 17, 11 Hz, 1H), 5.84−5.78 (m, 1H), 5.61 (ddt, J = 15, 6, 1 Hz, 1H), 5.46 (dd, J = 17, 2 Hz, 1H), 5.03 (dd, J = 11, 2 Hz, 1H), 4.84 (s, 1H), 4.48 (m, 1H), 4.41−4.38 (m, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.45 (t, J = 6 Hz, 2H), 2.12−2.10 (m, 2H), 2.11 (quint, J = 4 Hz, 2H), 1.67 (quint, J = 6 Hz, 2H), 1.61−1.53 (m, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 160.6, 152.0, 134.0, 133.2 (×2), 132.5, 131.5, 130.4 (×2), 114.9, 114.3, 109.4, 76.7, 73.4, 70.2, 64.2, 56.0, 39.6, 30.5, 30.1; IR (neat) 3420, 2941, 2857, 1614, 1599, 1515 cm^{-1}; EI HRMS indeterminable.

2-[5-(*tert*-Butyldiphenylsilanyloxy)-pent-1-enyl]-6-vinyl-3,4-dihydro-2*H*-pyran-4-ol (57b). The lactone **55b** (2.04 g, 4.65 mmol) was dissolved in dichloromethane (47 mL). Triethylamine (3.9 mL, 27.9 mmol) and (dimethylamino)pyridine (0.051 g, 0.42 mmol) were added, followed by triethylsilyl chloride (2.3 mL, 14 mmol). The reaction was stirred for 30 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford a colorless oil that dissolved in THF (41 mL) and cooled to −78 °C. Vinylmagnesium bromide, 0.9 M in THF (13.6 mL, 12.2 mmol), was added, and the reaction was stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethyl ether (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was

evaporated. The crude product was used directly to avoid decomposition. The lactol intermediate was dissolved in dichloromethane (41 mL) and cooled to 0 °C. (Dimethylamino)-pyridine (1.5 g, 12.3 mmol) was added, followed by thionyl chloride (0.3 mL, 4.1 mmol), and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 50 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was used directly to avoid decomposition. The diene was dissolved in THF (40 mL) and cooled to −78 °C, and tetrabutylammonium fluoride, 1 M in THF (4 mL, 4 mmol), was added. The reaction turned dark brown, and the solvent was evaporated after 30 min. The crude product was purified by flash silica column chromatography (30% EtOAc/hexanes) to afford 777 mg of **57b** (37% yield) as a colorless oil: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.80−7.69 (m, 4H), 7.49−7.34 (m, 6H), 6.09 (dd, J = 17, 11 Hz, 1H), 5.85−5.76 (m, 1H), 5.63 (ddd, J = 15, 6, 1 Hz, 1H), 5.47 (dd, J = 17, 2 Hz, 1H), 5.03 (dd, J = 11, 2 Hz, 1H), 4.84 (s, 1H), 4.52−4.42 (m, 1H), 4.38 (dd, J = 6, 5 Hz, 1H), 3.87 (d, J = 6 Hz, 1H), 3.74 (t, J = 6 Hz, 2H), 2.22 (q, J = 7 Hz, 1H), 2.11 (ddt, J = 13, 6, 2 Hz, 1H), 2.06−2.04 (m, 1H), 1.70 (quint, J = 6 Hz, 2H), 1.63−1.52 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 152.0, 136.8 (×4), 135.1 (×2), 133.9, 133.1, 131.4, 131.1 (×2), 129.1 (×4), 114.3, 109.4, 76.6, 64.3, 64.2, 39.6, 33.1, 29.6, 27.7 (×3), 20.2; IR (neat) 3345, 2955, 2930, 2857, 1111 cm^{-1}; EI HRMS calcd for $C_{28}H_{34}O_2$ ($M^+ - H_2O$) 430.23281, obsd 430.23637.

2-Benzyl-9-hydroxy-7-[5-(4-methoxybenzyloxy)-pent-1-enyl]-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (58a). To a suspension of $MgBr_2{\cdot}Et_2O$ (0.568 g, 1.1 mmol) in dichloromethane (4 mL) was added triethylamine (0.46 mL, 3.3 mmol), and the mixture was stirred for 20 min at room temperature. The alcohol **57a** (0.361 g, 1.1 mmol) and benzylmaleimide (2.1 g, 11 mmol) in dichloromethane (4 mL) were cannulated into the magnesium solution and stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 30 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 383 mg of **58a** (67% yield) as a yellow oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.36−7.23 (m, 7H), 6.90 (d, J = 6 Hz, 2H), 5.70 (dt, J = 15, 7 Hz, 1H), 5.37 (dd, J = 15, 6 Hz, 1H), 4.88−4.85 (m, 1H), 4.67 (d, J_{AB} = 15 Hz, 1H), 4.63 (d, J_{AB} = 15 Hz, 1H), 4.42 (s, 2H), 4.36−4.29 (m, 1H), 4.25−4.20 (m, 1H), 3.79 (s, 3H), 3.75 (dd, J = 9, 6 Hz, 1H), 3.45 (t, J = 6 Hz, 2H), 3.31−3.27 (m, 1H), 3.12−3.09 (m, 1H), 2.61 (ddd, J = 15, 8, 2 Hz, 1H), 2.21−2.16 (m, 2H), 2.12 (q, J = 7 Hz, 2H), 1.94−1.88 (m, 1H), 1.66 (quint, J = 7 Hz, 2H), 1.63−1.57 (m, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 181.7, 180.1, 160.0, 154.2, 136.7, 132.4, 131.9, 131.0 (×2), 129.8 (×2), 129.2 (×2), 128.0 (×3), 114.3, 97.0, 76.4, 72.7, 69.6, 66.1, 66.0, 55.4, 42.7, 42.5, 42.3, 39.2, 38.6, 29.4, 23.9; IR (neat) 3665, 2924, 2853, 1688 cm^{-1}; EI HRMS calcd for $C_{31}H_{33}NO_5$ ($M^+ - H_2O$) 499.23587, obsd 499.23767.

2-Benzyl-7-[5-(*tert*-butyldiphenylsilanyloxy)-pent-1-enyl]-9-hydroxy-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (58b). To a suspension of $MgBr_2{\cdot}Et_2O$ (0.041 g, 0.16 mmol) in dichloromethane (1 mL) was added triethylamine (0.033 mL, 0.23 mmol), and the mixture was stirred for 20 min at room temperature. The alcohol **57b** (0.035 g, 0.08 mmol) and benzylmaleimide (0.150 g, 0.8 mmol) in dichloromethane (1 mL) were cannulated into the magnesium solution and stirred for 30 min. The reaction was done, so quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 33 mg of **58b** (64% yield) as a yellow oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.70 (dd, J = 8, 2 Hz, 4H), 7.47−7.42 (m, 6H), 7.29−7.22 (m, 5H), 5.68 (dtd, 15, 7, 1 Hz, 1H), 5.36 (ddq, 16, 7, 1 Hz, 1H), 4.88−4.85 (m, 1H), 4.66 (d, J_{AB} = 15 Hz, 1H), 4.62 (d, J_{AB} = 15 Hz, 1H), 4.35−4.28 (m, 1H), 4.21 (dd, J = 11, 7 Hz, 1H), 4.19 (d, J = 11 Hz, 1H), 3.76−3.73 (m, 1H), 3.73 (t, J = 6 Hz, 2H), 3.30−3.27 (m, 1H), 3.10 (tq, 7, 2 Hz, 1H), 2.61 (ddd, J = 15, 8, 2 Hz, 1H), 2.17 (q, J = 7 Hz, 2H), 1.86 (ddd, J = 13, 5, 2 Hz, 1H), 1.68 (quint, J = 7 Hz, 2H), 1.61 (q, J = 12 Hz, 2H), 1.06 (s, 9H); ^{13}C NMR (125 MHz, acetone-d_6) δ 181.2, 179.5, 153.7, 136.2, 135.6 (×4), 134.0 (×2), 131.9, 130.4, 129.9 (×2), 128.6 (×2), 128.0 (×4), 127.5, 127.4 (×2), 96.4, 75.9, 65.6, 63.2, 42.2, 42.0, 41.8, 38.7, 38.1, 32.0, 28.4, 26.6 (×3), 23.3, 19.1; IR (neat) 3426, 2936, 2859, 1689, 1436, 1347, 1103 cm^{-1}; EI HRMS calcd for $C_{39}H_{43}NO_4Si$ ($M^+ - H_2O$) 617.29614, obsd 617.29546.

2-Benzyl-7-[5-(4-methoxybenzyloxy)-pent-1-enyl]-9-methoxymethoxy-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano[3,2-e]-isoindole-1,3-dione (58c). Alcohol **58a** (0.02 g, 0.03 mmol) was dissolved in dichloromethane (2 mL). Diisopropylethylamine (0.052 mL, 0.3 mmol) was added, followed by MOMCl (0.005 mL, 0.06 mmol). The reaction was heated to reflux for 5 h. The reaction was cooled to room temperature and quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 15 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 12 mg of **58c** (71% yield) as a colorless oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.30−7.22 (m, 7H), 6.90 (d, J = 9 Hz, 2H), 5.71 (td, 15, 7 Hz, 1H), 5.46 (dd, J = 15, 7 Hz, 1H), 4.84−4.82 (m, 1H), 4.66 (d, J = 7 Hz, 1H), 4.60−4.59 (m, 3H), 4.41 (s, 2H), 4.33−4.28 (m, 2H), 3.78 (s, 3H), 3.68 (dd, J = 9, 6 Hz, 1H), 3.44 (t, J = 6 Hz, 2H), 3.33 (s, 3H), 3.18 (dt, J = 8, 2 Hz, 1H), 3.04−3.01 (m, 1H), 2.52 (ddd, J = 9, 7, 2 Hz, 1H), 2.31−2.23 (m, 2H), 2.12 (q, J = 7 Hz, 2H), 2.04−2.00 (m, 1H), 1.65 (quint, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 179.2, 177.4, 159.3, 153.2, 136.7, 131.7, 131.4, 130.5 (×2), 129.1 (×2), 128.4 (×2), 127.5 (×2), 127.2, 113.6, 96.2, 95.8, 75.7, 72.1, 71.8, 68.0, 54.9, 54.7, 41.7, 41.2, 41.1. 36.2, 35.1, 29.1, 28.7, 23.4; IR (neat) 2938, 2852, 1699, 1506 cm^{-1}.

2-Benzyl-7-[5-(4-methoxybenzyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano-[3,2-e]isoindole-1,3-dione (58d). Alcohol **58a** (0.02 g, 0.04 mmol) was dissolved in dichloromethane (1 mL) and then cooled to 0 °C. Lutidine (0.045 mL, 0.39 mmol) was added, followed by trimethylsilyltriflate (0.014 mL, 0.77 mmol), and the reaction was stirred for 30 min. The reaction was quenched by adding $NHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 24 mg of **58d** (quant yield) as a colorless oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.29−7.21 (m, 7H), 6.89 (d, J = 9 Hz, 2H), 5.71 (dt, J = 15, 8 Hz, 1H), 5.43 (dd, J = 15, 7 Hz, 1H), 4.78−4.76 (m, 1H), 4.61−4.55 (m, 3H), 4.40 (s, 2H), 4.32−4.29 (m, 1H), 3.78 (s, 3H), 3.69 (dd, J = 9, 5 Hz, 1H), 3.44 (t, J = 6 Hz, 2H), 3.16 (td, 9, 2 Hz, 1H), 2.90−2.87 (m, 1H), 2.48 (ddd, J = 15, 7, 2 Hz, 1H), 2.36 (q, J = 13 Hz, 1H), 2.26−2.22 (m, 1H), 2.11 (q, J = 8 Hz, 2H), 1.85−1.81 (m, 1H), 1.65 (quint, J = 7 Hz, 2H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, acetone-d_6) δ 180.1, 178.1, 160.2, 155.0, 137.5, 132.5, 132.0, 131.3, 130.0 (×2), 129.2 (×2), 128.3 (×2), 128.1, 114.5(×2), 96.3, 76.9, 72.9, 69.9, 67.5, 55.6, 42.5, 42.4, 42.2, 39.1, 38.5, 30.0, 25.1, 0.4 (×3); IR (neat) 2946, 2855, 1704, 1250, 1097 cm^{-1}; EI HRMS calcd for $C_{34}H_{43}NO_6Si$ (M^+) 589.28597, obsd 589.28510.

2-Benzyl-7-[5-(*tert*-butyldiphenylsilanyloxy)-pent-1-enyl]-9-triethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (58f). Alcohol **58b** (0.033 g, 0.05 mmol) was dissolved in THF (1 mL). Triethylamine (0.042 mL, 0.3 mmol) and (dimethylamino)pyridine (0.001 g, 0.0045 mmol) were added, followed by triethylsilyl chloride (0.026 mL, 0.155 mmol). The reaction was stirred for 30 min.

Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethyl ether (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 24 mg of **58f** (64% yield) as a colorless oil: ^{1}H NMR (500 MHz, acetone-d_6) δ 7.71 (dd, J = 7, 2 Hz, 4H), 7.48−7.42 (m, 6H), 7.27−7.18 (m, 5H), 5.71 (dt, J = 14, 6 Hz, 1H), 5.42 (dd, J = 15, 6 Hz, 1H), 4.76−4.73 (m, 1H), 4.61−4.53 (m, 3H), 4.28 (dd, J = 11, 6 Hz, 1H), 3.76−3.75 (m, 1H), 3.72 (t, J = 6 Hz, 2H), 3.20−3.16 (m, 1H), 2.91−2.80 (m, 1H), 2.51 (ddd, J = 15, 8, 1 Hz, 1H), 2.44 (q, J = 12 Hz, 1H), 1.81−1.77 (m, 1H), 1.68 (quint, J = 6 Hz, 2H), 1.05−1.00 (m, 3H), 1.05 (s, 9H), 1.00 (t, J = 8 Hz, 9H), 0.68 (q, J = 8 Hz, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 180.6, 178.4, 155.7, 138.0, 136.8 (×4), 135.2 (×2), 133.0, 131.8, 131.1, 129.7 (×2), 129.2 (×2), 128.7 (×4), 128.5 (×2), 96.2, 77.4, 68.0, 64.4, 43.2, 43.0, 42.9, 39.8, 38.9, 33.2, 29.6, 27.8 (×3), 25.8, 20.3, 7.8 (×3), 6.1 (×3); IR (neat) 2954, 2874, 1705, 1112 cm^{-1}.

2-Benzyl-7-[5-(*tert*-butyldiphenylsilanyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (58g). Alcohol **58b** (0.015 g, 0.03 mmol) was dissolved in dichloromethane (1 mL) and then cooled at 0 °C. Lutidine (0.036 mL, 0.3 mmol) was added, followed by trimethylsilyltriflate (0.011 mL, 0.06 mmol), and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash column chromatography (15% EtOAc/hexanes) to afford 15 mg of **58g** (71% yield) as a colorless oil: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.72−7.69 (m, 4H), 7.46−7.41 (m, 6H), 7.29−7.20 (m, 5H), 5.70 (dt, J = 15, 7 Hz, 1H), 5.44 (dd, J = 15, 7 Hz, 1H), 4.79−4.76 (m, 1H), 4.63−4.52 (m, 3H), 4.30 (dd, J = 9, 7 Hz, 1H), 3.72 (t, J = 6 Hz, 2H), 3.69−3.67 (m, 1H), 3.24−3.13 (m, 1H), 2.91−2.90 (m, 1H), 2.49 (ddd, J = 15, 7, 2 Hz, 1H), 2.37 (q, J = 11 Hz, 1H), 2.28−2.14 (m, 4H), 1.81 (ddd, J = 13, 5, 2 Hz, 1H), 1.68 (quint, J = 7 Hz, 1H), 1.05 (s, 9H), 0.16 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 180.1, 178.5, 155.4, 137.9, 136.8 (×4), 135.1 (×2), 132.9, 131.8, 131.0 (×2), 129.6 (×2), 129.1 (×4), 128.7 (×2), 128.4, 96.7, 77.3, 67.9, 64.3, 42.9, 42.8, 42.6, 39.5, 38.9, 33.1, 29.6, 27.7 (×3), 25.5, 20.2, 0.8 (×3); IR (neat) 2936, 2857, 1704, 1397, 1111 cm^{-1}.

2-Benzyl-9-hydroxy-7-[5-(4-methoxybenzyloxy)-pent-1-enyl]-3a,5,7,8,9,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (59a). A solution of alcohol **58a** (0.014 g, 0.03 mmol) and triethylamine (0.01 mL) in toluene (3 mL) was degassed with argon. The mixture was heated to 160 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (60% EtOAc/hexanes) to afford 9 g of **59a** (64% yield) as a colorless oil: ^{1}H NMR (500 MHz, C_6D_6) δ 7.46 (d, J = 7 Hz, 2H), 7.32 (d, J = 9 Hz, 2H), 7.16 (t, J = 7 Hz, 2H), 7.09 (d, J = 7 Hz, 1H), 6.90 (d, J = 9 Hz, 2H), 6.01 (dd, J = 15, 7 Hz, 1H), 5.62 (dd, J = 15, 7 Hz, 1H), 5.39 (d, J = 4 Hz, 1H), 4.50−4.43 (m, 3H), 4.41 (s, 2H), 4.28−4.27 (m, 1H), 3.40 (s, 3H), 3.38 (t, J = 6 Hz, 2H), 2.82 (d, J = 9 Hz, 1H), 2.29−2.26 (m, 1H), 2.17−2.11 (m, 3H), 1.83−1.66 (m, 6H), 1.36−1.31 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 180.5, 178.1, 159.6, 152.2, 136.3, 132.12, 131.5, 129.9 (×2), 129.3 (×2), 129.1 (×2), 128.9 (×2), 114.0, 101.1, 75.7, 72.7, 69.3, 64.4, 29.1, 25.5, 23.9; IR (neat) 3418, 2932, 2854, 1690 cm^{-1}; EI HRMS calcd for $C_{31}H_{33}NO_5$ ($M^+ - H_2O$) 499.23587, obsd 499.2335.

2-Benzyl-7-[5-(*tert*-butyldiphenylsilanyloxy)-pent-1-enyl]-9-hydroxy-3a,5,7,8,9,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (59b). A solution of alcohol **58b** (0.033 g, 0.05 mmol) and triethylamine (0.01 mL) in toluene (3 mL) was degassed with argon. The mixture was heated to 160 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes to 30% EtOAc/hexanes) to afford 7 mg of starting material (21%) and 9 g of **59b** (28% yield) as a colorless oil: ^{1}H NMR (500 MHz, C_6D_6) δ 7.88−7.86 (m, 4H), 7.48 (d, J = 7 Hz, 2H), 7.34 (s, 6H), 7.17 (t, J = 7 Hz, 2H), 7.10 (t, J = 7 Hz, 1H), 6.01 (dd, J = 15, 7 Hz, 1H), 5.61 (dt, J = 15, 8 Hz, 1H), 5.42 (d, J = 4 Hz, 1H), 4.50 (d, J_{AB} = 14 Hz, 1H), 4.45 (d, J_{AB} = 14 Hz, 1H), 4.30 (d, J = 4 Hz, 1H), 3.70 (t, J = 6 Hz, 2H), 2.85 (d, J = 8 Hz, 1H), 2.30−2.27 (m, 1H), 2.17−2.13 (m, 4H), 1.84−1.63 (m, 5H), 1.39−1.35 (m, 2H), 1.27 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 180.2, 177.8, 151.9, 136.0, 135.7 (×4), 134.0 (×2), 132.0, 129.6 (×2), 129.5, 128.8 (×2), 128.6 (×4), 127.9, 127.7, 98.9, 75.5, 64.2, 63.1, 43.3, 42.3, 39.7, 37.1, 32.0, 28.4, 26.8 (×3), 25.2, 23.7, 19.1; IR (neat) 3420, 2931, 2857, 1691, 1428, 1399, 1110 cm^{-1}; EI HRMS calcd for $C_{39}H_{43}NO_4Si$ ($M^+ - H_2O$) 617.29614, obsd 617.29653.

Procedure for the [3 + 3] Rearrangement of 58g with Microwave Irradiation. A solution of alcohol **58g** (0.033 g, 0.05 mmol) and triethylamine (0.05 mL) in toluene (14 mL) was degassed with argon. The mixture was heated gradually to 170 °C for 5 min and maintained at 170 °C for 30 min. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 21 mg of **60g** (65%) as a light yellow oil and 5 g of **59g** (14% yield) as a colorless oil.

2-Benzyl-7-[5-(*tert*-butyldiphenylsilanyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,5,7,8,9,9b-hexahydro-4*H*-pyrano[3,2-e]isoindole-1,3-dione (59g). ^{1}H NMR (500 MHz, C_6D_6) δ 7.83−7.79 (m, 4H), 7.44 (d, J = 7 Hz, 2H), 7.28−7.26 (m, 6H), 7.13 (t, J = 7 Hz, 2H), 7.03 (t, J = 7 Hz, 1H), 6.14 (dd, J = 15,9 Hz, 1H), 5.47 (dt, J = 14,6 Hz, 1H), 4.55 (d, J_{AB} = 14 Hz, 1H), 4.49 (d, J_{AB} = 14 Hz, 1H), 4.48−4.47 (m, 1H), 4.14 (t, J = 3 Hz, 1H), 3.65 (t, J = 6 Hz, 2H), 2.81 (d, J = 8 Hz, 1H), 2.31−2.27 (m, 1H), 2.09 (q, J = 7 Hz, 2H), 2.02−1.95 (m, 1H), 1.82−1.75 (m, 4H), 1.68−1.61 (m, 3H), 1.20 (s, 9H), 0.35 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 177.2, 175.5, 151.5, 136.7, 135.6 (×4), 134.0 (×2), 131.3, 130.1, 129.6 (×2), 128.4 (×2), 128.3 (×2), 128.2, 127.9 (×4), 101.3, 75.0, 64.5, 64.1, 44.6, 41.7, 40.4, 36.9, 32.1, 28.5, 26.7 (×3), 24.9, 21.3, 19.1, 0.4 (×3); IR (neat) 2931, 2857, 1709, 1110 cm^{-1}; EI HRMS calcd for $C_{38}H_{44}NO_5Si$ ($M^+ - t$Bu) 650.27580, obsd 650.27368.

4-Benzyl-9-[3-(*tert*-butyldiphenylsilanyloxy)-propyl]-13-trimethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (60g). ^{1}H NMR (500 MHz, C_6D_6) δ 7.88−7.86 (m, 4H), 7.58 (d, J = 7 Hz, 2H), 7.37−7.36 (m, 6H), 7.23 (t, J = 8 Hz, 2H), 7.15 (t, J = 7 Hz, 1H), 5.37−5.33 (m, 1H), 5.30−5.26 (m, 1H), 4.72 (d, J = 4 Hz, 1H), 4.68 (d, J = 4 Hz, 1H), 4.51−4.49 (m, 1H), 3.73−3.69 (m, 2H), 2.87−2.84 (m, 2H), 2.61−2.54 (m, 2H), 2.30−2.16 (m, 3H), 2.07 (dd, 18, 5 Hz, 1H), 1.69−1.53 (m, 3H), 1.41−1.31 (m, 1H), 1.26 (s, 9H), 1.01 (dt, J = 33, 7 Hz, 1H), 0.12 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 212.3, 178.2, 176.4, 137.1, 136.3 (×4), 134.7 (×2), 134.6, 130.3 (×2), 129.9 (×2), 129.2 (×2), 128.7, 128.4 (×4), 126.5, 67.0, 64.5, 54.1, 51.4, 43.0, 42.5, 42.1, 37.0, 35.1, 31.9, 31.8, 31.1, 27.5 (×3), 19.8, 0.5 (×3); IR (neat) 3070, 2933, 2858, 1706, 1395, 1110 cm^{-1}.

Procedure for the [3 + 3] Rearrangement of 58f in a Sealed Tube. A solution of alcohol **58f** (0.06 g, 0.08 mmol) and triethylamine (0.03 mL) in toluene (14 mL) was degassed with argon. The mixture was heated at 170 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (15% EtOAc/hexanes) to afford 24 mg of **60f** (40%) as a colorless oil and 9 mg of **61f** (15%) as white crystals. mp 158.5−158.9 °C.

4-Benzyl-9-[3-(*tert*-butyldiphenylsilanyloxy)-propyl]-13-triethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (60f). ^{1}H NMR (500 MHz, C_6D_6) δ 7.82−7.79 (m, 4H), 7.52 (d, J = 7 Hz, 2H), 7.32−7.23 (m, 6H), 7.10 (t, J = 8 Hz, 2H), 7.02 (t, J = 7 Hz, 1H), 5.30−5.25 (m, 1H), 5.23−5.19 (m, 1H), 4.60 (s, 2H), 4.38−4.36 (m, 1H), 3.64 (t, J = 6 Hz, 2H), 2.88 (dd, J = 11, 5 Hz, 1H), 2.67−2.61 (m, 1H), 2.58−2.52 (m, 1H), 2.51 (t, J = 10 Hz, 1H), 2.33 (dt, J = 17, 7 Hz, 1H), 2.10 (q, J = 7 Hz, 1H), 2.02 (q, J = 160−150 Hz, 3H),

1.60−1.50 (m, 1H), 1.40−1.35 (m, 1H), 1.23−1.15 (m, 2H), 1.21 (s, 9H), 1.02 (t, J = 8 Hz, 9H), 0.65−0.62 (m, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 211.1, 178.2, 175.8, 136.9, 136.4 (×4), 135.6, 134.8 (×2), 130.3 (×2), 130.2, 129.2 (×2), 128.7 (×2), 128.5 (×4), 127.1, 69.1, 64.7, 54.6, 53.0, 43.1, 41.6, 40.0, 36.0, 35.6, 31.4, 31.1, 29.1, 27.5 (×3), 19.9, 7.7 (×3), 5.6 (×3); IR (neat) 2953, 2876, 1706, 1110, 1089 cm^{-1}.

Spiro 61f ^{1}H NMR (500 MHz, C_6D_6): δ 7.80 (t, J = 8 Hz, 4H), 7.54 (d, J = 7 Hz, 2H), 7.34 (t, J = 7 Hz, 2H), 7.32−7.27 (m, 4H), 7.11 (t, J = 7 Hz, 2H), 7.04 (t, J = 8 Hz, 1H), 5.36−5.34 (m, 1H), 4.92−4.90 (m, 1H), 4.87 (dd, J = 10, 8 Hz, 1H), 4.58 (d, J_{AB} = 13 Hz, 1H), 4.50 (d, J_{AB} = 13 Hz, 1H), 3.56−3.49 (m, 2H), 3.44 (d, J = 9 Hz, 1H), 2.93 (dd, J = 16, 10 Hz, 1H), 2.33−2.24 (m, 3H), 2.15 (dt, J = 17, 4 Hz, 1H), 1.96−1.85 (m, 2H), 1.9 (s, 9H), 1.82−1.75 (m, 1H), 1.53−1.45 (m, 1H), 1.44−1.37 (m, 1H), 1.26−1.13 (m, 2H), 1.08 (t, J = 8 Hz, 9H), 0.71 (sept, J = 8 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.1, 178.4, 176.6, 137.3, 136.4 (×4), 134.6 (×2), 130.3 (×2), 130.2 (×2), 129.1 (×2), 128.7 (×4), 128.4, 126.7, 126.6, 67.5, 63.9, 58.2, 42.9, 41.9, 40.6, 39.3, 38.4, 33.2, 30.9, 30.7,27.5 (×3), 19.9, 19.8, 7.7 (×3), 5.8 (×3); IR (neat) 2954, 1707, 1095 cm^{-1}; MS ESI calcd for $C_{45}H_{59}NNaO_5Si_2$ (M^+ Na) 772.4, found 772.1.

Procedure for the [3 + 3] Rearrangement of 58g in a Sealed Tube. A solution of alcohol **58g** (0.03 g, 0.04 mmol) and triethylamine (0.03 mL) in toluene (20 mL) was degassed with argon. The mixture was heated to 170 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (25% EtOAc/hexanes) to afford 50 mg of **60g** (42% yield) as a light yellow oil and 13 mg of **61g** (30%) as a yellow oil.

Spiro (61g). ^{1}H NMR (300 MHz, C_6D_6) δ 7.82−7.74 (m, 4H), 7.53 (d, J = 7 Hz, 2H), 7.36−7.26 (m, 6H), 7.13−7.01 (m, 3H), 5.36−5.32 (m, 1H), 4.98−4.93 (m, 1H), 4.82 (dd, J = 10, 7 Hz, 1H), 4.58 (d, J = 14 Hz, 1H), 4.50 (d, J = 14 Hz, 1H), 3.57−3.47 (m, 2H), 3.38 (d, J = 9 Hz, 1H), 2.87−2.78 (m, 1H), 2.42−2.21 (m, 3H), 2.16−2.03 (m, 2H), 2.02−1.84 (m, 2H), 1.81−1.67 (m, 1H), 1.62−1.34 (m, 3H), 1.19 (s, 9H), 0.21 (s, 9H); ^{13}C NMR (75 MHz,C_6D_6) δ 208.3, 178.5, 176.7, 137.3, 136.4 (×4), 134.6 (×2), 130.3 (×4), 130.1 (×2), 129.2, 129.1 (×4), 126.9, 126.4, 67.9, 64.0, 58.0, 42.9, 42.0, 40.6, 40.6, 39.2, 38.4, 33.2, 30.8, 30.7, 27.5 (×3), 20.3, 19.8, 0.9 (×3); IR (neat) 2959, 2858, 1703, 1110 cm^{-1}; MS EI calcd for $C_{38}H_{44}NO_5Si_2$ (M^+ − *t*Bu) 650.27580, found 650.27348.

4-Benzyl-9-[3-(*tert*-butyldiphenylsilanyloxy)-propyl]-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,-14-trione (62). Compound **60g** (0.039 g, 0.06 mmol) was dissolved in THF (1 mL). HCl (2 N, 0.1 mL) was added and stirred for 30 min at room temperature. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with diethyl ether (3 × 15 mL). The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 15 mg of (99% yield) as white crystals. mp 133.3−134.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66−7.62 (m, 4H), 7.42−7.35 (m, 8H), 7.26−7.22 (m, 3H), 5.49 (q, J = 9 Hz, 1H), 5.44 (t, J = 13 Hz, 1H), 5.16 (t, J = 9 Hz, 1H), 4.69 (d, J = 14 Hz, 1H), 4.60 (d, J = 14 Hz, 1H), 3.87−3.81 (m, 1H), 3.74 (dd, J = 12, 11 Hz, 1H), 3.56−3.51 (m, 3H), 3.05 (t, J = 10 Hz, 1H), 2.80 (d, J = 14 Hz, 1H), 2.20−2.18 (m, 1H), 2.15−1.95 (m, 3H), 1.52−1.48 (m, 1H), 1.27−1.16 (m, 2H), 1.12−1.08 (m, 1H), 1.04 (s, 9H), 0.94−0.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 181.0, 178.5, 136.6, 135.4 (×4), 134.2, 133.8 (×2), 129.5 (×2), 129.4 (×2), 128.7 (×2), 128.4, 127.5 (×4), 126.7, 73.7, 63.5, 54.6, 54.0, 43.4, 39.5, 35.7, 34.3, 33.4, 29.4, 27.6, 26.7 (×3), 23.9, 19.0; IR (neat) 3430, 2920, 2857, 1685, 1428, 1402, 1110 cm^{-1}; EI HRMS calcd for $C_{35}H_{36}NO_5Si$ (M^+ − *t*Bu) 578.23628, obsd 578.23824.

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Supporting Information Available: High-field ^{1}H and ^{13}C NMR spectra for compounds **18**−**24**, **27**, **28**, **30**, **35**−**38**, **44**−**46**, **53**−**62**, and ORTEP views of **38** (benzoate derivative) and **62**. This material is available free of charge via the Internet at http://pubs.acs.org.

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