Ring-Closing Metathesis in the Synthesis of Large and Medium-Sized Oxacycles. Application to the Synthesis of Polyoxygenated Macrocycles

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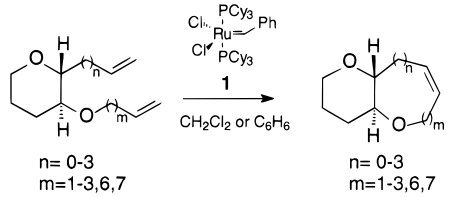
Received January 26, 1999

Ring-closing olefin metathesis (RCM) catalyzed by Grubbs's ruthenium benzylidene complex **1** is applied to the synthesis of unsaturated rings ranging in size from seven to thirteen members in *trans*-fused polyether systems. Reaction occurs with great efficiency in the cyclization of oxepene and oxocene rings, but as ring size increases, yields drop. The influence of the final double bond position is also studied. Better yields and milder reaction conditions are observed when an additional oxygen atom is introduced on the diene. This feature has promoted the application of this reaction to the synthesis of polyoxygenated macrocycles (with sizes ranging from 15 to 21 members), with excellent results.

Introduction

Synthetic organic chemists are continuously searching for new methods and reactions which will allow them to obtain the target molecules in as few steps as possible. In this context, olefin metathesis[1] has emerged as a very powerful tool for carbon−carbon double bond formation. The development of well-defined new catalysts[2] capable of effecting this reaction in a wide range of substrates together with the tolerance shown by ruthenium alkylidene complexes such as **1** toward an ample range of functional groups has allowed its application to several total syntheses and to the preparation of many types of substrates. These features are evident from many examples of the use of these catalysts in the formation of fairly complex five-, six- and seven-membered carbo- and heterocycles by ring-closing metathesis (RCM) of suitable diolefin precursors.[1,3] The formation of medium and large ring systems, however, is yet largely unexplored. Despite the extensive investigation during the past few years on RCM, there are still a few aspects of this reaction which remain unclear and cannot be predicted (e.g. geometry of the resulting double bond, influence of steric environment of reacting olefins, etc.).

Scheme 1



Our interest in developing methodologies for a rapid access to molecules possessing a *trans*-fused polyether structure resembling natural marine toxins such as brevetoxins and ciguatoxins turned our attention toward this reaction as an easy way to prepare these kinds of compounds from appropriate precursors.[4]

Results and Discussion

To assay the scope and limitations of RCM in the cyclization of *trans*-fused polyether systems, a series of simple precursors was prepared and reacted with a catalytic amount of ruthenium complex **1**[5] (Scheme 1). In our models, we considered only terminal olefins on an oxane ring, and we changed chain lengths to explore the influence of ring size and steric environment of reacting olefins.

Precursor Synthesis. The starting material for the preparation of the appropriate precursors was in all cases (2*R*,3*S*)-2-(hydroxymethyl)tetrahydropyran-3-ol **2** avail-

(1) Recent reviews about olefin metathesis and its application to organic synthesis: (a) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, 1997. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (d) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388. (e) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450.

(2) Molybdenum-based catalyst: (a) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886. (b) Bazan, G. C.; Khosravi, E.; Schrock, R. R.; Feast, W. J.; Gibson, V. C.; O'Regan, M. B.; Thomas, J. K.; Davis, W. M. *J. Am. Chem. Soc.* **1990**, *112*, 8378−8387. (c) Bazan, G. C.; Oskam, J. H.; Cho, H.-N.; Park, L.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899−6907. Ruthenium-based catalysts: (d) Nguyen, S. T.; Johnson, L. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 3974−3975. (e) Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9858−9859. (f) Wu, Z.; Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 5503−5511. (g) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039−2041. (h) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100−110.

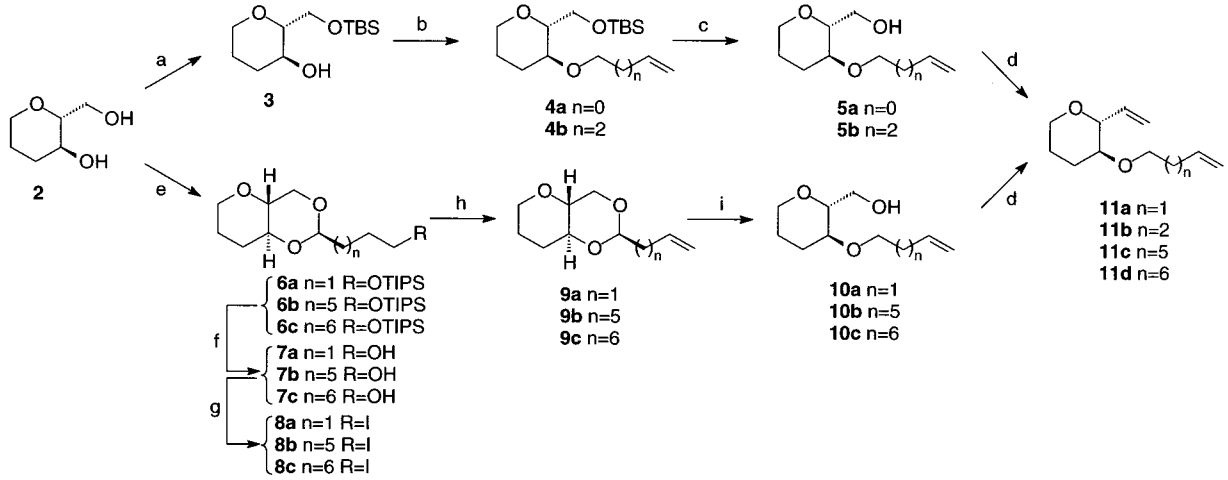
(3) Recent reviews about RCM: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Hashimi, A. S. K. *J. Prakt. Chem.* **1997**, *339*, 195−199.

(4) Examples of the use of RCM in the synthesis of *trans*-fused polyethers: (a) Nicolaou, K. C.; Postema, M. H. D.; Claiborne, C. F. *J. Am. Chem. Soc.* **1996**, *118*, 1565−1566. (b) Nicolaou, K. C.; Postema, M. H. D.; Yue, E. W.; Nadin, A. *J. Am. Chem. Soc.* **1996**, *118*, 10335−10336. (c) Clark, J. S.; Kettle, J. G. *Tetrahedron Lett.* **1997**, *38*, 123−126. (d) Clark, J. S.; Kettle, J. G. *Tetrahedron Lett.* **1997**, *38*, 127−130. (e) Oishi, T.; Nagumo, Y.; Hirama, M. *Synlett* **1997**, 980−982. (f) Oishi, T.; Nagumo, Y.; Hirama, M. *J. Chem. Soc., Chem. Commun.* **1998**, 1041−1042. (g) Rainier, J. D.; Allwein, S. P. *J. Org. Chem.* **1998**, *63*, 5310−5311. (h) Clark, J. S.; Hamelin, O.; Hufton, R. *Tetrahedron Lett.* **1998**, *39*, 8321−8324.

(5) Delgado, M.; Martín, J. D. *Tetrahedron Lett.* **1997**, *38*, 6299−6300.

10.1021/jo9901438 CCC: $18.00
Published on Web 06/06/1999

Scheme 2[a]



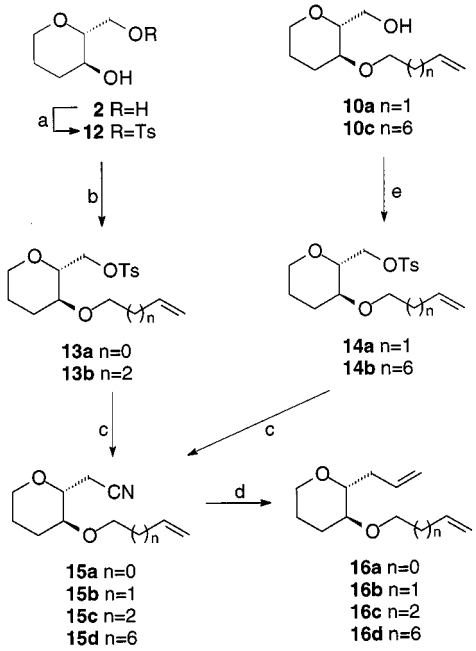
[a] Key: (a) 1.0 equiv of TBDMSCl, 2.5 equiv of imidazole, DMAP catalyst, CH_2Cl_2, 0 °C, 4 h (92%); (b) for **4a** ($n = 0$): 10.0 equiv of allyl bromide, 1.3 equiv of NaH, n-Bu_4NI catalyst, THF, 0−25 °C, 8 h (88%); for **4b** ($n = 2$): 7.0 equiv of 5-bromo-1-pentene, 1.3 equiv of KH, n-Bu_4NI catalyst, THF, 0−25 °C, 8 h (72%); (c) 1.5 equiv of n-Bu_4NF, THF, 25 °C, 2 h (**5a**: 98%, **5b**: 98%); (d) (i) 3.0 equiv of SO_3·pyr, 5.0 equiv of NEt_3, 15.0 equiv of DMSO, CH_2Cl_2, 0 °C, 2 h; (ii) 1.5 equiv of PPh_3CH_3Br, 1.4 equiv of n-BuLi, THF, 0−25 °C, 8 h (**11a**: 38%, **11b**: 62%; **11c**: 81%; **11d**: 83%, two steps); (e) 1.0 equiv of 4-triisopropylsilyloxybutyraldehyde, 8-triisopropylsilyloxyoctanal, or 9-triisopropylsilyloxynonanal, p-TsOH catalyst, 4 Å molecular sieves, CH_2Cl_2, 25 °C, 8 h (**6a**: 95%, **6b**: 87%, **6c**: 84%); (f) 1.5 equiv of n-Bu_4NF, THF, 25 °C, 2 h (**7a**: 99%, **7b**: 99%; **7c**: 99%); (g) 2.0 equiv of I_2, 3.0 equiv of imidazole, 3.0 equiv of PPh_3, C_6H_6, 4 °C, 30 min (**8a**: 85%, **8b**: 86%, **8c**: 86%); (h) 1.5 equiv of KO-t-Bu, THF, 25 °C, 30 min (**9a**: 92%; **9b**: 97%; **9c**: 97%); (i) 1.0 equiv of $NaCNBH_3$, 1.0 equiv of $TiCl_4$, CH_3CN, 0−25 °C, 6 h (**10a**: 82%, **10b**: 88%, **10c**: 85%).

able in three steps and excellent yields from tri-*O*-acetyl-D-glucal.[6] Selective protection of the primary hydroxyl group with TBDMSCl, followed by O-alkylation of the secondary hydroxyl group with either allyl bromide or 5-bromo-1-pentene and desilylation afforded alcohols **5a** and **5b**. Ketalization of the aldehydes derived from 1,4-butanediol, 1,8-octanediol, and 1,9-nonanediol (monoprotected as their TIPS ethers)[7] with **2**, catalyzed by *p*-toluensulfonic acid, produced ketals **6a**−**c** exclusively as their *R* isomers[8] in the newly formed asymmetric center. Desilylation and transformation of the resultant alcohols into their iodo derivatives[9] followed by treatment with ^{t}BuOK afforded compounds **9a**−**c**, which gave regioselectively the primary alcohols **10a**−**c** upon treatment with $TiCl_4$/$NaCNBH_3$.[10] Oxidation of alcohols **5a**,**b** and **10a**−**c** followed by Wittig olefination of the resultant aldehydes yielded dienes **11a**−**d**[11] (Scheme 2).

Another series of dienic precursors **16a**−**d** was prepared starting from tosylates **13a**, **13b**, **14a**, and **14b** (Scheme 3) by transformation into the corresponding nitriles **15a**−**d**, reduction with DIBAL,[12] acid hydrolysis, and Wittig olefination of the resultant aldehydes.

In our effort to explore the influence of steric environment of reacting olefins in RCM, three additional precursors in which double bonds were further away from the oxane ring were synthesized as described in Scheme 4. A derivative of **2** in which the secondary hydroxyl group

Scheme 3[a]



[a] Key: (a) 1.0 equiv of *p*-TsCl, 1.5 equiv of NEt_3, DMAP catalyst, CH_2Cl_2, 0−25 °C, 8 h (77%); (b) for **13a** ($n = 0$): 1.5 equiv of allyl bromide, 1.2 equiv of NaH, n-Bu_4NI catalyst, THF, 0−25 °C, 6 h (93%); for **13b** ($n = 2$): 1.5 equiv of 5-bromo-1-pentene, 1.3 equiv of KH, n-Bu_4NI catalyst, THF, 0−25 °C, 6 h (78%); (c) 3.0 equiv of KCN, DMSO, 50 °C, 6 h (**15a**: 98%, **15b**: 98%, **15c**: 98%, **15d**: 98%); (d) (i) 1.5 equiv of DIBAL, Et_2O, 0 °C, 5 h, (ii) aq HCl (1 N) (iii) 1.5 equiv of PPh_3CH_3Br, 1.4 equiv of n-BuLi, THF, 0−25 °C, 8 h (**16a**: 38%, **16b**: 39%; **16c**: 48%; **16d**: 53%, three steps); (e) 1.1 equiv of *p*-TsCl, 1.5 equiv of NEt_3, DMAP catalyst, CH_2Cl_2, 0−25 °C, 8 h (**14a**: 92%, **14b**: 96%).

is protected as its TBS ether **19** can be easily obtained through a protection−deprotection sequence. Treatment of this alcohol with I_2/PPh_3/Im, nucleophilic substitution with cyanide anion, and reduction of the nitrile afforded

(6) Nicolaou, K. C.; Hwang, C.-K.; Marron, B. E.; DeFrees, S. A.; Couladourus, E. A.; Abe, Y.; Carroll, O. J.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 3040−3054.

(7) For the preparation of these aldehydes, see Supporting Information.

(8) The configuration of the new asymmetric center was unequivocally assigned by NOESY experiments.

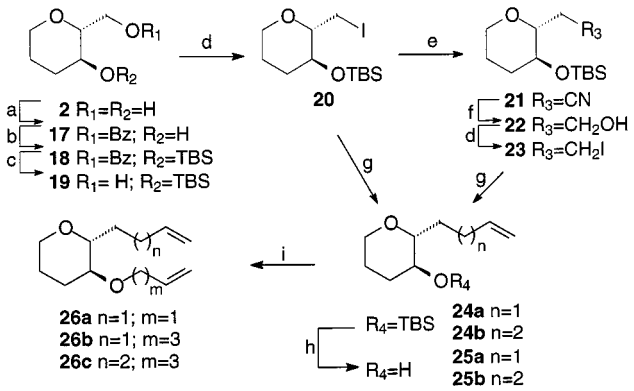
(9) Garegg, P. J.; Samuelson, D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866−2869.

(10) Adam, G.; Seebach, D. *Synthesis* **1988**, 373−375.

(11) Low yields obtained in the case of the smaller dienes are due to the volatility of the products.

(12) Marshall, J. A.; Andersen, N. H.; Schlicher, J. W. *J. Org. Chem.* **1970**, *35*, 858−861.

Scheme 4[a]



[a] Key: (a) 1.1 equiv of BzCl, 3.0 equiv of NEt_3, DMAP catalyst, CH_2Cl_2, 0−25 °C, 4 h (98%); (b) 1.1 equiv of TBDMSCl, 2.5 equiv of imidazole, DMAP catalyst, CH_2Cl_2, 25 °C, 4 h (97%); (c) 0.5 equiv of NaOMe, MeOH, 25 °C, 2 h (99%); (d) 2.0 equiv of I_2, 3.0 equiv of imidazole, 3.0 equiv of PPh_3, C_6H_6, 4 °C, 30 min (95%); (e) 3.0 equiv of KCN, DMSO, 50 °C, 5 h (99%); (f) (i) 1.5 equiv of DIBAL, Et_2O, 0 °C, 5 h, (ii) aq HCl (0.1 N), 4 °C (iii) 2.0 equiv of $NaBH_4$, MeOH, 0 °C, 1 h (42%, three steps); (g) 2.0 equiv of *n*-Bu_3SnCH_2-CH=CH_2, AIBN catalyst, C_6H_6, 80 °C, 6 h (**24a**: 71%, **24b**: 68%); (h) 1.5 equiv of *n*-Bu_4NF, THF, 25 °C, 2 h (**25a**: 98%, **25b**: 98%); (i) for **26a** (m = 1): 1.5 equiv of allyl bromide, 1.2 equiv of NaH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (83%); for **26b** and **26c** (m = 3): 1.5 equiv of 5-bromo-1-pentene, 1.2 equiv of KH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (**26b**: 73%; **26c**: 69%).

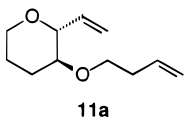
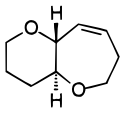
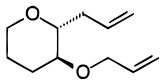
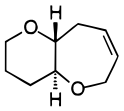
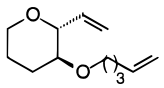
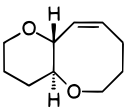
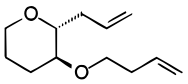
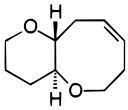
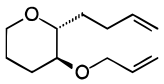
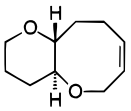
compound **22**, which was transformed into its iodo derivative **23**. Iodo compounds **20** and **23** were subjected to Keck[13] reaction, followed by desilylation and O-alkylation with either allyl bromide or 5-bromo-1-pentene, affording dienes **26a**−**c**.

Metathesis Reactions. Treatment of the acyclic precursors **11a**−**d**, **16a**−**d** and **26a**−**c** with a catalytic amount of **1** (Scheme 1) results in the formation of the unsaturated oxacycles.

Ruthenium-catalyzed RCM is most effective for the cyclization of oxepene and oxocene rings (Table 1), regardless of the position of the reacting olefins. Particularly remarkable are the excellent yields with which oxocene rings are obtained, the formation of eight-membered rings from acyclic precursors being kinetically and thermodynamically disfavored[14] due to conformational and entropic factors and to the development of transannular repulsions during the cyclization. The high yields observed by us are due to the presence of the oxane ring which acts as an element of conformational restriction[15,16] and facilitates the cyclization.

In the case of oxonene to oxotridecene rings (Table 2), yields are substantially lower (below 45%) although the reaction conditions are much stronger (higher catalyst loading, higher temperatures, and longer reaction times).

Table 1. Synthesis of Oxepene and Oxocene Rings by RCM

Entry	Diene	Product[a]	Yield[b] (%)
1	 **11a**	 **27**	>95
2	 **16a**	 **28**	>95
3	 **11b**	 **29**	>95
4	 **16b**	 **30**	>95
5	 **26a**	 **31**	>95

[a] Reaction conditions: 0.2 mmol diene, 10 mol % of **1**, 6×10^{-3} M, CH_2Cl_2, 25 °C, 4 h. [b] Yields were determined by NMR.

As ring size increases, side reactions (such as isomerization and dimerization) more effectively compete with RCM. An extreme case is the oxotridecene ring, which could not be obtained, and treatment of diene **16d** with **1** only gave byproducts. These low yields are attributed to the fact that for larger rings entropic factors do not contribute to the formation of the reaction intermediates[17] to the same extent as in their smaller analogues and therefore side reactions are more favored.

Dependence on final double bond position and steric environment of the reacting olefins is observed in these larger systems. Two 11-membered cycles were prepared between which the only difference was the final double bond position (entry 3 versus entry 4, Table 2). When reacting olefins are further away from the oxane ring, RCM occur under higher dilution and lower temperature conditions, although with no significant improvement in yield. This result can be explained by a decrease in steric congestion around the ruthenium atom in the reaction intermediates in the latter case, which facilitates RCM.

Influence of the Presence of an Additional Heteroatom in the Dienes in RCM. In our effort to improve the yields of RCM in these latter cases, we thought that the introduction of a second heteroatom on the dienic precursors would facilitate the metathesis

(13) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley: M. R. *Tetrahedron* **1985**, *41*, 4079−4094.

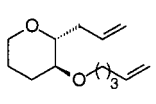
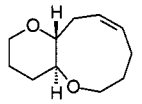
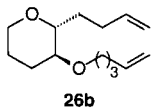
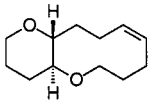
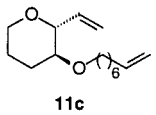
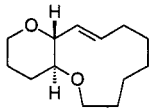
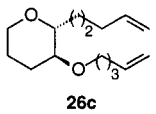
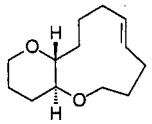
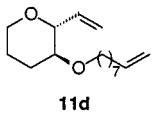
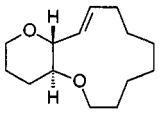
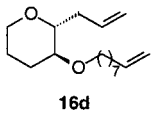
(14) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley and Sons: New York, 1994.

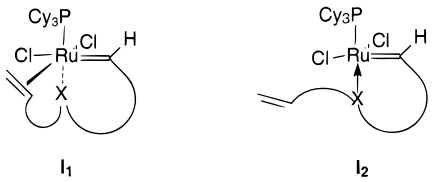
(15) Examples of formation of eight-membered rings by olefin metathesis of acyclic precursors containing some conformational restriction: (a) Linderman, R. J.; Siedlecki, J.; O'Neill, S. A.; Sun, H. *J. Am. Chem. Soc.* **1997**, *119*, 6919−6920. (b) Crimmins, M. T.; Choy, A. L. *J. Org. Chem.* **1997**, *62*, 7548−7549. (c) Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291−4298.

(16) In the precursors of eight-membered rings in which the conformational restriction element is a preexisting cycle, RCM is more effective when the two olefinic chains are in trans disposition on the cycle than when they are *cis*: Miller, S. J.; Kim, S.-H.; Chen, Z.-R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2108−2109.

(17) Detailed studies of RCM mechanism: (a) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897. (b) Aagaard, O. M.; Meier, R. J.; Buda, F. *J. Am. Chem. Soc.* **1998**, *120*, 7174−7182.

Table 2. Preparation of Oxonene−Oxododecene Rings by RCM

Entry	Diene	Product	Geom.	Reaction conditions	Yield (%)
1	 **16c**	 **32**	Z	30 mol % **1**, 0.005 M CH_2Cl_2, 45°C, 2 days 30 mol % **1**, 0.005 M	40 45
2	 **26b**	 **33**	Z	30 mol % **1**, 0.005 M CH_2Cl_2, 45°C, 2 days	42
3	 **11c**	 **34**	E	20 mol % **1**, 0.005 M CH_2Cl_2, 45°C, 2 days	36
4	 **26c**	 **35**	E	10 mol % **1**, 0.005 M CH_2Cl_2, 25°C, 2 days	38
5	 **11d**	 **36**	E	20 mol % **1**, 0.005 M CH_2Cl_2, 45°C, 2 days	20
6	 **16d**	-	-	20 mol % **1**, 0.005 M CH_2Cl_2, 45°C, 2 days	-



I_1 I_2

Figure 1.

through two effects: (i) stabilization of the electron-deficient intermediates through their electron-donating capacity and (ii) bringing together the olefin and the carbene in the appropriate orientation for the formation of the metallacyclobutane intermediate. This would lead to an intermediate I_1 as depicted in Figure 1. If the stabilization became too strong, a chelate[18] as I_2 would be formed, therefore inhibiting the reaction. The formation of either I_1 or I_2 cannot be predicted, and therefore we synthesized a series of appropriate precursors in which an additional oxygen atom was introduced to explore the scope of this approach.

Precursors **37a**, **37b**, and **38a−c** were easily obtained by O-alkylation of **2**, **5a** and **10a** (Scheme 5) with either allyl bromide or 5-bromo-1-pentene. Treatment of **19** with NaH/allyl bromide, followed by deprotection with TBAF and O-alkylation with KH/5-bromo-1-pentene, afforded compound **41**.

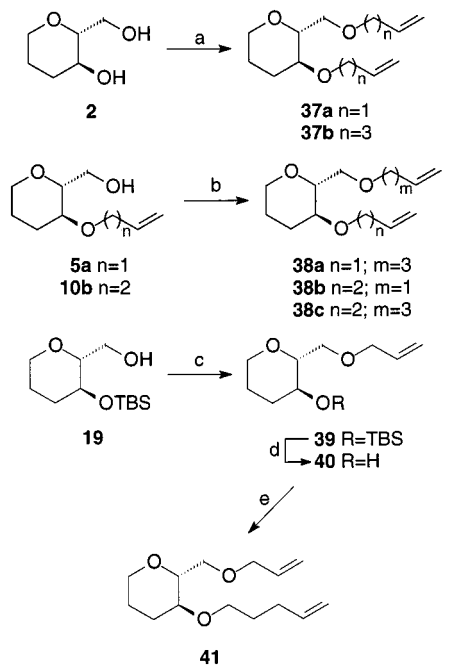
These compounds **37a**, **37b**, **38a−c**, and **41** were reacted with a catalytic amount of ruthenium catalyst (**1**), and results are shown in Table 3.

With the introduction of an additional oxygen atom, the reaction rate appears to be facilitated with improved yields. Entry 1 is an exception: the expected nine-membered ring does not form under these conditions, and this may be due to the formation of a stable chelate such as I_2. On the other hand, the synthesis of a 13-membered ring was achieved with the introduction of this element of restriction.

Mild reaction conditions may be attributed solely to the relief of steric effects around reacting olefins, this reason alone could not justify the improvement of yields seen when comparing the formation of **34** (entry 3, Table 2) and **44** (entry 4, Table 3), between which the only difference is the presence of the additional oxygen atom in the latter case. Only the formation of an intermediate such as I_1 could give a satisfactory explanation for the formation of the latter with better yields.

(18) Examples of formation of chelates in RCM: (a) Kirkland, T. A.; Grubbs, R. H. *J. Org. Chem.* **1997**, *62*, 7310−7318. (b) Ghosh, A. K.; Capiello, J.; Shin, D. *Tetrahedron Lett.* **1998**, *39*, 4651−4654. (c) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 7324−7325. (d) Campagne, J.-M.; Ghosez, L. *Tetrahedron Lett.* **1998**, *39*, 6175−6178. (e) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351. (f) Feldman, J.; Murdzek, J. S.; Davis, W. M.; Schrock, R. R. *Organometallics* **1989**, *8*, 2260−2265. (g) Fürstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130−9136. (h) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J., Jr.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791−799.

Scheme 5[a]



[a] Key: (a) for **37a**: 3.0 equiv of allyl bromide, 2.2 equiv of NaH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (73%); for **37b**: 3.0 equiv of 5-bromo-1-pentene, 2.2 equiv of KO-*t*-Bu, THF, 65 °C, 6 h (62%); (b) for **38b** ($m = 1$): 1.5 equiv of allyl bromide, 1.2 equiv of NaH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (99%); for **38a** and **38c** ($m = 3$): 1.5 equiv of 5-bromo-1-pentene, 1.2 equiv of KH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (**38a**: 73%; **38c**: 72%); (c) 3.0 equiv of allyl bromide, 1.2 equiv of NaH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 6 h (92%); (d) 1.5 equiv of *n*-Bu_4NF, THF, 25 °C, 2 h (95%); (e) 2.0 equiv of 5-bromo-1-pentene, 1.2 equiv of KH, *n*-Bu_4NI catalyst, THF, 0−25 °C, 8 h (69%).

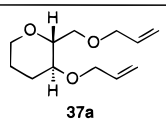
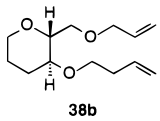
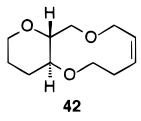
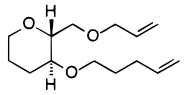
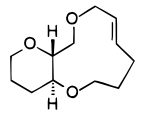
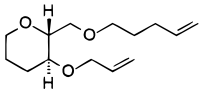
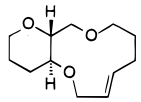
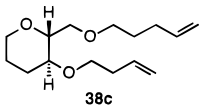
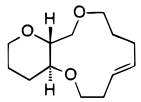
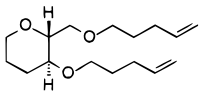
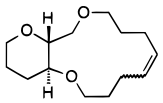
Again the position of the reacting double bonds has a remarkable effect on yields, as can be seen by comparing entries 3 and 4, Table 3: a change in the position of the reacting olefins causes an improvement of approximately 40% in yield.[18h]

A feature of RCM in our systems remains to be analyzed: the geometry of the resultant double bond. For ring size superior to nine, the two possible geometries can occur. In our examples, 9- and 10-membered cycles were obtained exclusively as their *Z*-isomers, while 11- and 12-membered rings were formed as their *E*-isomers. An *E*:*Z* mixture was obtained in the case of the 13-membered ring. With the present level of knowledge it is not possible to account for the results obtained. Double bond geometry seems to depend on subtle stereoelectronic effects which are not perfectly understood.[19]

Application to the Synthesis of Polyoxygenated Macrocyles. Our observation of the improvement of yields in RCM with the presence of oxygen atoms in the diene prompted us to apply this reaction to the synthesis of polyoxygenated macrorings.[20] Several appropriate dienes were prepared to assay the effectiveness of this approach (Scheme 6). Treatment of **2** with ^{t}BuOK[21] and 2 equiv of either allyl toluene *p*-sulfonates[22] **47**, **48a**, or **48b** afforded the corresponding dienes **50**, **51a**, and **51b**. Another series of dienes was prepared starting from **5a** by O-alkylation with the appropriate allyl toluene *p*-sulfonate **48b**−**d** or **49**,[20] affording precursors **52a**−**c** and **53** with good yields.

The expected polyoxygenated macrorings were obtained by treatment of the synthesized precursors with

Table 3. Influence of an Additional Oxygen Atom in RCM

Entry	Diene	Product[a]	Geom.	Yield (%)
1	 **37a**	-	-	-
2	 **38b**	 **42**	*Z*	63
3	 **41**	 **43**	*E*	52
4	 **38a**	 **44**	*E*	90
5	 **38c**	 **45**	*E*	58
6	 **37b**	 **46**	*E*:*Z* 1:2	58

[a] Reaction conditions: 0.2−0.4 mmol diene, 5−10 mol % of **1**, 5 × 10^{-3} M, CH_2Cl_2, 25 °C, 2−4 h.

5 mol % of catalyst **1** in a few hours[23] (Table 4). As we had anticipated, reaction conditions were mild, and

(19) Examples of *Z* geometry in 9-and 10-membered rings obtained by RCM: (a) Barrett, A. G. M.; Baugh, S. P. D.; Gibson, V. C.; Giles, M. R.; Marshall, E. L.; Procopiou, P. A. *Chem. Commun.* **1996**, 2231−2232. (b) Crimmins, M. T.; Choy, A. L. *J. Org. Chem.* **1997**, *62*, 7548−7549. (c) Sukkari, H. E.; Gesson, J.-P.; Renoux, B. *Tetrahedron Lett.* **1998**, *39*, 4043−4046. (d) Oishi, T.; Nagumo, Y.; Hirama. M. *Chem. Commun.* **1998**, 1041−1042. Example of *E* geometry in a 10-membered ring: (e) Fink, B. E.; Kym, P. R.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 4334−4344. (f) Sukkari, H. E.; Gesson, J.-P.; Renoux, B. *Tetrahedron Lett.* **1998**, *39*, 4043−4046 (9-, 11-, and 15-membered rings). (g) Fürstner, A.; Kindler, N. *Tetrahedron Lett.* **1996**, *37*, 7005−7008 (12-membered ring). (h) Borer, B. C.; Deerenberg, S.; Bieräugel, H.; Pandit, U. K. *Tetrahedron Lett.* **1994**, *35*, 3191−3194 (13-membered ring, *Z*). (i) Kim, S. H.; Figueroa, I.; Fuchs, P. L. *Tetrahedron Lett.* **1997**, *38*, 2601−2604 (13-membered ring, *E*). (j) Houri, A. F.; Xu, Z.; Cogan, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 2943−2944 (14-membered ring, *Z*). (k) Fürstner, A.; Langemann, K. *J. Org. Chem.* **1996**, *61*, 3942−3943 (14-, 16-, and 20-membered rings). (l) Ghosh, A. K.; Hussain, K. A. *Tetrahedron Lett.* **1998**, *39*, 1881−1884 (14-membered rings, *Z*, 15-membered rings, *Z* and 16-membered rings, mixtures). (m) Ripka, A. S.; Bohacek, R. S.; Rich, D. H. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 357−360 (15-membered ring, mixtures). (n) Meng, D.; Su, D.-S.; Balog, A.; Bertinato, P.; Sorensen, E. J.; Danishefsky, S. J.; Zheng, Y.-H.; Chou, T.-C.; He, L.; Horwitz, S. *J. Am. Chem. Soc.* **1997**, *119*, 2733−2734.

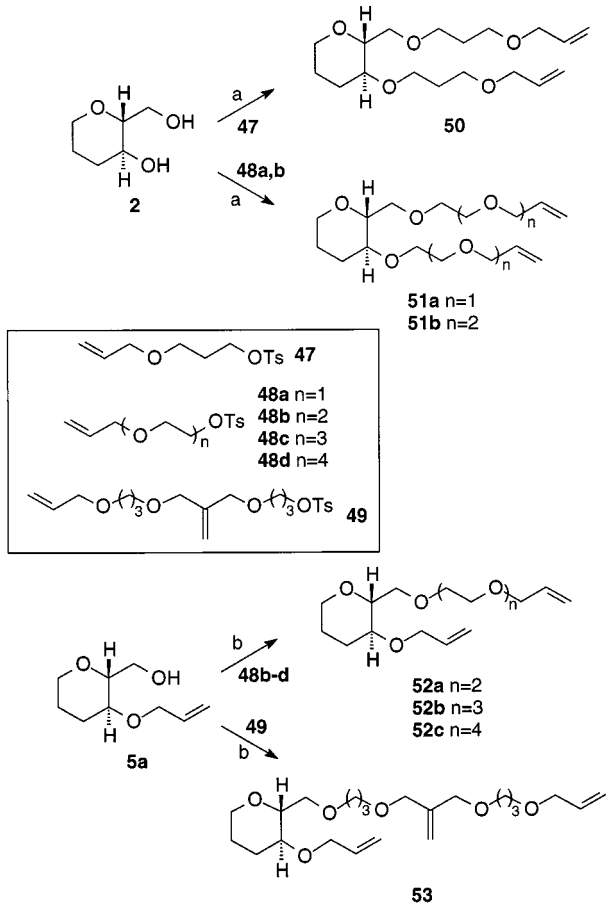
(20) Precedents in the application of RCM to the synthesis of crown ethers: (a) König, B.; Horn, C. *Synlett* **1996**, 1013−1014. (b) Marsella, M. J.; Maynard, H. D.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1101−1103.

(21) Czech, B. P.; Huh, H.; Bartsch, R. A. *J. Org. Chem.* **1992**, *57*, 725−728.

(22) For the preparation of allyl toluene *p*-sulfonates **47**, **48a**−**d**, and **49**, see Supporting Information.

(23) Delgado, M.; Martín, J. D. *Tetrahedron Lett.* **1997**, *38*, 8387−8390.

Scheme 6[a]



[a] Key: (a) 2.2 equiv of KO-*t*-Bu, THF, 25 °C, 1 h; then 2.2 equiv of tosylate, THF, 65 °C, 8 h (**50**: 47%, **51a**: 54%; **51b**: 52%); (b) 1.1 equiv of KO-*t*-Bu, THF, 25 °C, 1 h; then 1.1 equiv of tosylate, THF, 25 °C, 8 h (**52a**: 82%, **52b**: 87%; **52c**: 85%; **53**: 79%).

macrorings (with sizes ranging from 15 to 21 members) were formed in good yields supporting our previous observation of the positive effect of the presence of oxygen atoms on RCM of this type of dienes. When reacting olefins were further away from the oxane rings, yields were lower than when they were closer, due to the greater mobility of the chains (see entries 2 and 3 versus entries 4 and 6, Table 4).

It is also worth noticing the selectivity shown by this catalyst toward the olefin substitution degree in the last entry of Table 4, in which only terminal olefins react, demonstrating that the reaction is tolerant of other olefins in the system, at least disubstituted ones, as in the case of **53**.

Conclusions

RCM has been applied to the synthesis of *trans*-fused bicycles containing oxygens and is found to be very effective for the synthesis of oxepene and oxocene rings. As ring size increases, more difficulties are encountered for the cyclization of the unsaturated rings. The introduction of an additional element of control (an oxygen atom in the diene) is found to have a positive effect on the efficiency of RCM, and, taking advantage of this effect, this reaction is shown to be successful for the synthesis of several *ortho*-condensed oxane-polyoxygenated macrorings. The steric environment of the reacting olefins plays an important role in RCM also.

Experimental Section

General. ^{1}H NMR spectra were recorded on Bruker spectrometers Avance DPX 300 (300 MHz) or Avance DRX 500 (500 MHz). Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, *m* = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were recorded on Bruker spectrometers Avance DPX 300 (75 MHz) or Avance DRX 500 (125 MHz) with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent as the internal reference. Data are reported as follows: chemical shift, number of hydrogen atoms to which that carbon is bonded (q = CH_3, t = CH_2, d = CH and s = C, obtained by DEPT experiments), and assignment. Infrared (IR) spectra were recorded on a Bruker Vector 22 spectrophotometer, ν_{max} in cm^{-1}. High-resolution mass spectra were provided by the Universities of Seville and Cordoba Mass Spectrometry Facilities and were performed on Kratos MS 80 RFA, Finnigan MAT 95 or Micromass AutoSpecQ spectrometers. Microanalyses were performed on Leco CHNS-932 or Fisons EA1108 CHNS-0. Melting points were determined on a Buchi 241 apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 polarimeter, using the sodium D line at 25 °C.

Thin-layer chromatography (TLC) was performed using silica gel 60 F_{254} precoated plates with a fluorescent indicator. Visualization was accomplished with one or more of the following: UV light (254 nm), 10% ethanolic phosphomolybdic acid or H_2O:H_2SO_4:AcOH (1:4:20) solution and heat as a developing agent. Flash column chromatography was carried out with E. Merck silica gel (60, particle size 0.015−0.040 mm) using appropriate mixtures of EtOAc and hexanes as eluents. All chromatographic separations were monitored by TLC analyses.

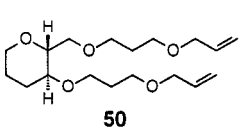
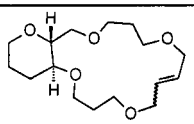
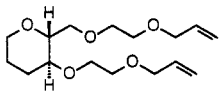
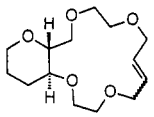
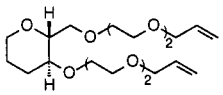
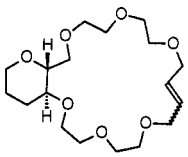
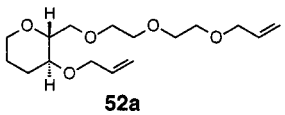
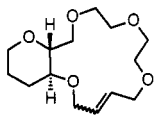
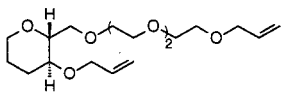
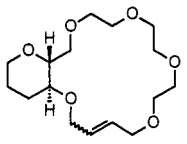
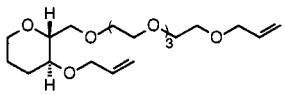
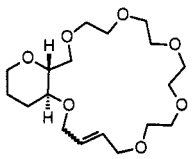
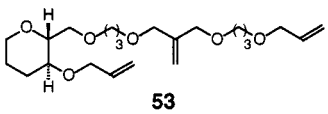
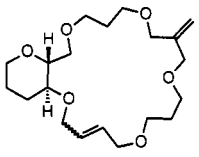
Bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride **1** was purchased from Strem Chemicals, stored in a drybox, and used under argon atmosphere with standard Schlenk techniques. All other reagents were purchased from Aldrich and used without further purification unless otherwise stated.

All reactions were conducted in flame-dried glassware under an inert atmosphere of dry argon. Tetrahydrofuran, diethyl ether, and benzene were distilled from sodium metal/benzophenone ketyl. Methylene chloride, acetonitrile, dimethyl sulfoxide, and triethylamine were dried over CaH_2 and distilled.

General Procedure for Protection of Alcohols as TBDMS Ethers. To a stirring solution of the corresponding alcohol (2.5 mmol) in dry CH_2Cl_2 (12 mL) were added imidazole (425 mg, 6.25 mmol, 2.5 equiv), TBDMSCl (413 mg, 2.75 mmol, 1.1 equiv), and a catalytic amount of DMAP at room temperature. The reaction mixture was stirred until TLC showed no remaining starting material and quenched by addition of NH_4Cl saturated solution (10 mL). The two layers were separated, and the organic layer was washed with brine and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the remaining oil was purified by flash chromatography. For the monoprotection of the primary alcohol in **2**, only 1.0 equiv of TBSCl was used, and the reaction was carried out at 0 °C.

(2*R*,3*S*)-2-(*tert*-Butyldimethylsilyloxymethyl)tetrahydropyran-3-ol (3): colorless oil. R_f = 0.40 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D = -11.8°$ (*c* 0.19, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3481, 2930, 2858, 1464, 1253, 1148, 837 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (m, 2H), 3.73 (br s, 1H, O*H*), 3.66 (dd, *J* = 9.8, 8.5 Hz, 1H), 3.55 (dddd, *J* = 10.3, 9.3, 4.6, 1.3 Hz, 1H), 3.31 (m, 1H), 3.15 (ddd, *J* = 9.3, 8.5, 4.6 Hz, 1H), 2.08 (br dd, *J* = 12.5, 3.2 Hz, 1H), 1.59 (m, 2H), 1.37 (m, 1H), 0.87 (s, 9H, $(CH_3)_3$CSi), 0.07 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3-

Table 4. Application of RCM to Crown Ether Synthesis

Entry	Diene	Crown ether[a]	Yield (*E*:*Z*)
1	 **50**	 **54**	76 (7:1)
2	 **51a**	 **55**	65 (4:1)
3	 **51b**	 **56**	72 (12:1)
4	 **52a**	 **57**	85 (10:3)
5	 **52b**	 **58**	92 (8.5:1)
6	 **52c**	 **59**	88 (13:1)
7	 **53**	 **60**	92 (8:1)

[a] Reaction conditions: 0.2−0.4 mmol of diene, 5 mol % **1**, 5×10^{-3} M, CH_2Cl_2, 25 °C, 2−4 h. [b] *E*:*Z* ratio was determined by NMR and GC.

Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.49 (d), 70.88 (d), 67.57 (t), 66.59 (t), 31.63 (t), 25.81 (q, $(CH_3)_3CSi$), 24.92 (t), 18.16 (s, $(CH_3)_3CSi$), −5.57 (q, CH_3Si), −5.64 (q, CH_3Si). MS *m*/*e* (rel intens) 245 ([M − 1]$^+$, 2), 189 ([M − ^{t}Bu]$^+$, 38), 159 ([M − ^{t}BuMe$_2$]$^+$, 15), 131 ([M − OSi^{t}BuMe$_2$]$^+$, 5). HRMS calcd for $C_{12}H_{26}O_3Si$ (M)$^+$ 246.165123, found 246.163953. Anal. Calcd for $C_{12}H_{26}O_3Si$: C, 58.49; H, 10.63. Found: C, 58.38; H, 10.64.

General Procedure for O-Alkylation. In a typical experimental procedure, the corresponding alcohol (0.3 mmol) was dissolved in dry THF (3 mL), and either allyl bromide or 5-bromo-1-pentene (0.45 mmol, 1.5 equiv) and a catalytic amount of ^{n}Bu$_4$NI were added. The reaction mixture was cooled to 0 °C and either NaH (0.36 mmol, 1.2 equiv, 60% dispersion in mineral oil, in the case of allyl bromide) or KH (0.36 mmol, 1.2 equiv, 35% dispersion in mineral oil, in the case of 5-bromo-1-pentene) were added and left overnight, allowing the temperature to rise. The reaction mixture was cooled again to 0 °C, and water (2 mL) was added. The aqueous layer was extracted with EtOAc (3 × 3 mL), and combined organic layers were washed with brine and dried over $MgSO_4$. Solvent was removed in vacuo, and the residue was purified by flash chromatography. In case of TBDMS-containing compounds, an excess of the bromide was used (10.0 equiv in the case of allyl bromide and 7.0 equiv in the case of 5-bromo-1-pentene) in order to avoid migration of the TBDMS group.

(2′*R*,3′*S*)-(3′-Allyloxytetrahydropyran-2′-ylmethoxy)-*tert*-butyldimethylsilane (4a): colorless oil. $R_f = 0.52$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +55.96°$ (*c* 0.2, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3003, 2929, 2856, 1541, 1377, 1074, 838 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dddd, J = 17.2, 10.4, 5.6,

5.6 Hz, 1H), 5.22 (ddd, J = 17.2, 1.5, 1.5 Hz, 1H), 5.11 (ddd, J = 10.4, 1.5, 1.5 Hz, 1H), 4.07 (dddd, J = 12.6, 5.6, 1.5, 1.5 Hz, 1H), 3.92 (dddd, J = 12.6, 5.6, 1.5, 1.5 Hz, 1H), 3.88 (m, 1H), 3.83 (dd, J = 11.2, 2.0 Hz, 1H), 3.77 (dd, J = 11.2, 4.6 Hz, 1H), 3.28 (m, 2H), 3.12 (ddd, J = 9.1, 4.6, 2.0 Hz, 1H), 2.20 (br dd, J = 12.4, 3.3 Hz, 1H), 1.62 (m, 2H), 1.33 (m, 1H), 0.87 (s, 9 H, $(CH_3)_3CSi$), 0.04 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.25 (d), 116.5 (t), 81.96 (d), 72.86 (d), 69.83 (t), 67.61 (t), 63.32 (t), 29.40 (t), 26.05 (q, $(CH_3)_3CSi$), 25.25 (t), 18.50 (s, $(CH_3)_3CSi$), −5.14 (q, CH_3Si), −5.26 (q, CH_3Si). Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.55. Found: C, 62.68; H, 10.62.

(2′*R*,3′*S*)-*tert*-Butyldimethyl(3′-pent-4″-enyloxytetrahydropyran-2′-ylmethoxy)silane (4b): colorless oil. R_f = 0.69 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +49,39° (*c* 1.10, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3002, 2857, 1640, 1463, 1361 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, J = 17.1, 10.2, 6.5, 6.5 Hz, 1H), 4.99 (d, J = 17.1 Hz, 1H), 4.93 (d, J = 10.2 Hz, 1H), 3.88 (br d, J = 11.2 Hz, 1H), 3.84 (dd, J = 11.2, 1.7 Hz, 1H), 3.74 (dd, J = 11.2, 4.8 Hz, 1H), 3.56 (ddd, J = 9.1, 6.5, 6.5 Hz, 1H), 3.30 (m, 2H), 3.16 (ddd, J = 10.5, 9.1, 4.5 Hz, 1H), 3.09 (ddd, J = 9.1, 4.8, 1.7 Hz, 1H), 2.19 (br d, J = 12.3 Hz, 1H), 2.08 (m, 2H), 1.62 (m, 4H), 1.30 (dddd, J = 12.3, 12.3, 10.5, 5.2 Hz, 1H), 0.88 (s, 9 H, $(CH_3)_3CSi$), 0.05 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.30 (d), 114.71 (t), 82.07 (d), 73.32 (d), 68.05 (t), 67.61 (t), 63.48 (t), 30.34 (t), 29.36 (t), 29.31 (t), 26.06 (q, $(CH_3)_3CSi$), 25.26 (t), 18.51 (s, $(CH_3)_3CSi$), −5.12 (q, CH_3Si), −5.24 (q, CH_3Si). MS *m*/*e* (rel intens) 315 ([M + 1]$^+$, 70). HRMS calcd for $C_{17}H_{35}O_3Si$ (M + H)$^+$ 315.235549, found 315.238184. Anal. Calcd for $C_{17}H_{34}O_3Si$: C, 64.92; H, 10.90. Found: C, 64.64; H, 10.99.

General Procedure for Deprotection of Silyl Ethers. To a solution of the corresponding silyl ether (1.3 mmol) in THF (3 mL) was added ^{n}Bu$_4$NF·10 H$_2$O (510 mg, 1.95 mmol, 1.5 equiv). When TLC showed that the reaction was complete, solvent was removed under reduced pressure, and the residue was purified by flash chromatography.

(2′*R*,3′*S*)-(3′-Allyloxytetrahydropyran-2′-yl)methanol (5a): colorless oil. R_f = 0.36 (silica, 40% EtOAc in hexanes). $[\alpha]^{25}_D$ = +92.58° (*c* 1.30, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3588, 3482, 3013, 2929, 2360, 2341 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (dddd, J = 17.2, 10.4, 5.6, 5.6 Hz, 1H), 5.20 (ddd, J = 17.2, 1.6, 1.3 Hz, 1H), 5.10 (ddd, J = 10.4, 1.3, 1.3 Hz, 1H), 4.05 (ddd, J = 12.6, 5.6, 1.3 Hz, 1H), 3.88 (m, 2H), 3.78 (d, J = 11.1 Hz, 1H), 3.63 (d, J = 11.1 Hz, 1H), 3.32 (ddd, J = 11.6, 11.6, 2.3 Hz, 1H), 3.22 (ddd, J = 10.2, 9.3, 4.5 Hz, 1H), 3.15 (m, 1H), 2.40 (s, 1H, O*H*), 2.19 (br d, J = 12.4 Hz, 1H), 1.59 (m, 2H), 1.32 (dddd, J = 12.4, 12.4, 10.2, 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.95 (d), 116.97 (t), 80.81 (d), 73.90 (d), 69.77 (t), 67.65 (t), 63.01 (t), 29.15 (t), 25.16 (t). MS *m*/*e* (rel intens) 171 ([M − 1]$^+$, 1). HRMS calcd for $C_9H_{16}O_3$ (M)$^+$: 172.109945, found 172.109014. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.62; H, 9.39.

(2′*R*,3′*S*)-(3′-Pent-4″-enyloxytetrahydropyran-2′-yl)methanol (5b): colorless oil. R_f = 0.48 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +34.42° (*c* 1.05, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3589, 3482, 2943, 2872, 1350 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (dddd, J = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 4.99 (d, J = 17.1 Hz, 1H), 4.93 (d, J = 10.2 Hz, 1H), 3.88 (br dd, J = 11.3, 4.6 Hz, 1H), 3.81 (br d, J = 11.5 Hz, 1H), 3.65 (m, 1H), 3.58 (ddd, J = 9.2, 6.4, 6.4 Hz, 1H), 3.33 (m, 2H), 3.15 (m, 2H), 2.23 (m, 2H), 2.07 (m, 2H), 1.61 (m, 4H), 1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.13 (d), 114.88 (t), 80.66 (d), 74.78 (d), 68.03 (t), 67.72 (t), 63.38 (t), 30.25 (t), 29.17 (t), 29.14 (t), 25.21 (t). HRMS calcd for $C_{11}H_{21}O_3$ (M + H)$^+$: 201.149070, found 201.148695. Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.68; H, 10.26.

General Procedure for Ketal Formation. A solution of **2** (2.4 mmol) in dry CH_2Cl_2 (8 mL) was transferred to a flame-dried flask with 4 Å molecular sieves. The corresponding aldehyde (2.4 mmol, 1.0 equiv) dissolved in CH_2Cl_2 (4 mL) was then added, followed by a catalytic amount of *p*-TsOH. The reaction mixture was stirred overnight at room temperature. Neutralization by addition of a few drops of NEt_3, filtration through a Celite pad, and removal of the solvent in vacuo afforded a residue which was purified by flash chromatography (silica, 5% EtOAc in hexanes).

(2′*R*,4′a*R*,8′a*S*)-[2-(Hexahydropyrano[3,2-*d*][1,3]dioxin-2′-yl)-propoxy]triisopropylsilane (6a): colorless oil. R_f = 0.26 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D$ = +2.90° (*c* 1.2, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3008, 2946, 2867, 2338, 1465, 1385, 1341, 1261, 1219, 1148, 1106, 1013, 971, 883 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.58 (dd, J = 5.2, 5.2 Hz, 1H), 4.04 (dd, J = 10.4, 4.9 Hz, 1H), 3.87 (br dd, J = 11.2, 4.5 Hz, 1H), 3.66 (dd, J = 6.2, 6.2 Hz, 2H), 3.42 (m, 2H), 3.27 (ddd, J = 11.2, 8.9, 4.2 Hz, 1H), 3.15 (ddd, J = 10.0, 8.9, 4.9 Hz, 1H), 2.00 (br d, J = 12.1 Hz, 1H), 1.67 (m, 6H), 1.53 (dddd, J = 12.1, 12.1, 11.2, 4.8 Hz, 1H), 1.02 (s, 21 H, 3 × $(CH_3)_2CHSi$, 3 × $(CH_3)_2CHSi$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.56 (d), 77.97 (d), 74.28 (d), 68.95 (t), 68.01 (t), 63.12 (t), 31.04 (t), 28.79 (t), 27.67 (t), 25.53 (t), 18.03 (q, 3 × $(CH_3)_2CHSi$), 11.99 (d, 3 × $(CH_3)_2CHSi$). MS *m*/*e* (rel intens) 357 ([M − 1]$^+$, 1). HRMS calcd for $C_{19}H_{38}O_4Si$ (M)$^+$: 358.25394, found 358.25574. Anal. Calcd for $C_{19}H_{38}O_4Si$: C, 63.64; H, 10.68. Found: C, 63.57; H, 10.92.

(2′*R*,4′a*S*,8′a*S*)-[7-(Hexahydropyrano[3,2-*d*][1,3]dioxin-2′-yl)heptyloxy]triisopropylsilane (6b): colorless oil. R_f = 0.42 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +2.49° (*c* 1.3, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3010, 2943, 2866, 2342, 1465, 1146 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.53 (dd, J = 5.2, 5.2 Hz, 1H), 4.05 (dd, J = 10.4, 4.9 Hz, 1H), 3.88 (br dd, J = 11.5, 4.5 Hz, 1H), 3.66 (dd, J = 6.6, 6.6 Hz, 2H), 3.42 (m, 2H), 3.27 (ddd, J = 11.2, 9.0, 4.2 Hz, 1H), 3.15 (ddd, J = 9.9, 9.0, 4.9 Hz, 1H), 2.01 (br dd, J = 12.0, 3.7 Hz, 1H), 1.74 (m, 2H), 1.57 (m, 3H), 1.50 (m, 2H), 1.34 (m, 2H), 1.27 (m, 6H), 1.03 (s, 21H, 3 × $(CH_3)_2CHSi$, 3 × $(CH_3)_2CHSi$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.65 (d), 77.97 (d), 74.30 (d), 68.97 (t), 68.00 (t), 63.46 (t), 34.49 (t), 33.00 (t), 29.44 (t), 29.31 (t), 28.81 (t), 25.71 (t), 25.54 (t), 24.18 (t), 18.03 (q, 3 × $(CH_3)_2CHSi$), 12.04 (d, 3 × $(CH_3)_2CHSi$). MS *m*/*e* (rel intens) 413 ([M − 1]$^+$, 8). HRMS calcd for $C_{23}H_{46}O_4Si$ (M)$^+$: 414.316539, found: 414.315868. Calcd for $C_{20}H_{39}O_4Si$ (M − C_3H_7)$^+$: 371.261764, found: 371.264656. Anal. Calcd for $C_{23}H_{46}O_4Si$: C, 66.61; H, 11.18. Found: C, 66.66; H, 11.35.

(2′*R*,4′a*S*,8′a*S*)-[8-(Hexahydropyrano[3,2-*d*][1,3]dioxin-2′-yl)octyloxy]triisopropylsilane (6c): colorless oil. R_f = 0.41 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +2.07° (*c* 0.8, $CHCl_3$). IR ($CHCl_3$) ν_{max} 2942, 2866, 2360, 1465, 1238 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.53 (dd, J = 5.2, 5.2 Hz, 1H), 4.06 (dd, J = 10.4, 4.9 Hz, 1H), 3.89 (br dd, J = 11.5, 4.5 Hz, 1H), 3.63 (dd, J = 6.7, 6.7 Hz, 2H), 3.43 (m, 2H), 3.28 (ddd, J = 11.3, 9.0, 4.2 Hz, 1H), 3.16 (ddd, J = 10.0, 9.0, 4.9 Hz, 1H), 2.02 (br dd, J = 12.1, 3.5 Hz, 1H), 1.75 (br s, 2H), 1.54 (br s, 5H), 1.31 (br s, 10H), 1.03 (s, 21H, 3 × $(CH_3)_2CHSi$, 3 × $(CH_3)_2CHSi$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.68 (d), 77.98 (d), 74.30 (d), 68.98 (t), 68.02 (t), 63.50 (t), 34.52 (t), 33.03 (t), 29.50 (t), 29.40 (t), 29.36 (t), 28.81 (t), 25.80 (t), 25.54 (t), 24.23 (t), 18.04 (q, 3 × $(CH_3)_2CHSi$), 12.05 (d, 3 × $(CH_3)_2CHSi$). MS *m*/*e* (rel intens) 427 ([M − 1]$^+$, 7). HRMS calcd for $C_{24}H_{47}O_4Si$ (M − H)$^+$: 427.324364, found: 427.325450. Calcd for $C_{21}H_{41}O_4Si$ (M − C_3H_7)$^+$: 385.277414, found: 385.279723. Anal. Calcd for $C_{24}H_{48}O_4Si$: C, 67.24; H, 11.28. Found: C, 67.20; H, 11.16.

Preparation of (2′*R*,4′a*R*,8′a*S*)-3-(Hexahydropyrano-[3,2-*d*][1,3]dioxin-2′-yl)propan-1-ol (7a). This compound was prepared from **6a** following the procedure described above for deprotection of silyl ethers. Noncrystalline white solid. Mp = 39 °C. R_f = 0.26 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +1.90° (*c* 0.84, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3625, 3471, 3013, 2929, 2858, 1466, 1412, 1293, 1262 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.59 (dd, J = 4.8, 4.6 Hz, 1H), 4.03 (dd, J = 10.4, 4.9 Hz, 1H), 3.86 (br dd, J = 11.5, 4.5 Hz, 1H), 3.58 (dd, J = 6.1, 6.1 Hz, 2H), 3.41 (m, 2H), 3.28 (ddd, J = 11.2, 9.0, 4.2 Hz, 1H), 3.13 (ddd, J = 9.0, 9.0, 4.9, 1H), 2.29 (br s, 1H, O*H*), 1.99 (br dd, J = 12.1, 4.2 Hz, 1H), 1.69 (m, 6H), 1.52 (dddd, J = 12.1, 12.1, 11.2, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.18 (d), 78.01 (d), 74.05 (d), 68.92 (t), 68.03 (t), 62.51 (t), 31.15 (t), 28.71 (t), 27.16 (t), 25.46 (t). MS *m*/*e* (rel intens) 201 ([M − 1]$^+$, 2). HRMS calcd for $C_{10}H_{17}O_4$ (M − H)$^+$: 201.112684, found: 201.113410. Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.23; H, 8.99.

(2′*R*,4′a*R*,8′a*S*)-7-(Hexahydropyrano[3,2-*d*][1,3]dioxin-2′-yl)heptan-1-ol (7b). This compound was prepared from **6b** following the procedure described above for deprotection of silyl ethers. Colorless oil. $R_f = 0.36$ (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D = +3.77°$ (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3626, 3013, 2934, 1466, 1387, 1042 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.52 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.04 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.87 (br dd, $J = 11.5, 4.5$ Hz, 1H), 3.59 (dd, $J = 6.6, 6.6$ Hz, 2H), 3.42 (m, 2H), 3.27 (ddd, $J = 11.2, 9.0, 4.2$ Hz, 1H), 3.15 (ddd, $J = 10.0, 9.0, 4.9$ Hz, 1H), 2.00 (br dd, $J = 12.0, 3.6$ Hz, 1H), 1.73 (m, 2H), 1.54 (m, 5H), 1.33 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.60 (d), 77.96 (d), 74.26 (d), 68.95 (t), 68.00 (t), 62.94 (t), 34.45 (t), 32.74 (t), 29.37 (t), 29.24 (t), 28.78 (t), 25.61 (t), 25.51 (t), 24.11 (t). MS *m/e* (rel intens) 259 ($[M + 1]^+$, 16). HRMS calcd for $C_{14}H_{27}O_4$ $(M + H)^+$: 259.190935, found: 259.189771; calcd for $C_{14}H_{25}O_4$ $(M - H)^+$: 257.175285, found: 257.174785. Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 65.09; H, 10.21.

(2′*R*,4′a*R*,8′a*S*)-8-(Hexahydropyrano[3,2-*d*][1,3]dioxin-2′-yl)octan-1-ol (7c). This compound was prepared from **6c** following the procedure described above for deprotection of silyl ethers. Colorless oil. $R_f = 0.41$ (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D = +3.02°$ (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3619, 3012, 2859, 2361, 1541, 1340, 1091 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.52 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.04 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.87 (br dd, $J = 11.5, 4.6$ Hz, 1H), 3.58 (dd, $J = 6.6, 6.6$ Hz, 2H), 3.41 (m, 2H), 3.27 (ddd, $J = 11.3, 9.0, 4.2$ Hz, 1H), 3.14 (ddd, $J = 9.9, 9.0, 4.9$ Hz, 1H), 2.00 (br dd, $J = 12.0, 3.2$ Hz, 1H), 1.73 (m, 2H), 1.54 (m, 6H), 1.30 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.63 (d), 77.96 (d), 74.27 (d), 68.95 (t), 68.01 (t), 62.96 (t), 34.48 (t), 32.77 (t), 29.42 (t), 29.37 (t), 29.29 (t), 28.79 (t), 25.71 (t), 25.52 (t), 24.17 (t). MS *m/e* (rel intens) 271 ($[M - 1]^+$, 9). HRMS calcd for $C_{15}H_{28}O_4$ $(M)^+$: 272.198760, found: 272.198196; calcd for $C_{15}H_{27}O_4$ $(M - H)^+$: 271.190935, found: 271.191292. Anal. Calcd for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36. Found: C, 66.19; H, 10.43.

General Procedure for Iodination of Alcohols. To a stirring solution of the corresponding alcohol (2.3 mmol) in dry benzene (23 mL) were added imidazole (470 mg, 6.9 mmol, 3.0 equiv), and PPh_3 (1.8 g, 6.9 mmol, 3.0 equiv). The reaction mixture was then cooled to 4 °C, and resublimed iodine (1.2 g, 4.6 mmol, 2.0 equiv) was added. After 30 min, TLC showed no remaining starting material, and the mixture was filtered through a Celite pad. Solvent was removed in vacuo, and the residue was purified by flash chromatography.

(2*R*,4a*R*,8a*S*)-2-(3′-Iodopropyl)hexahydropyrano[3,2-*d*]-[1,3]dioxine (8a): colorless oil. $R_f = 0.28$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +2.65°$ (*c* 0.94, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3011, 2951, 1466, 1441, 1386, 1293 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.58 (dd, $J = 4.9, 4.9$ Hz, 1H), 4.03 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.88 (br dd, $J = 11.2, 4.3$ Hz, 1H), 3.41 (m, 2H), 3.27 (ddd, $J = 11.2, 8.9, 4.3$ Hz, 1H), 3.14 (m, 3H), 2.00 (br dd, $J = 12.1, 4.3$ Hz, 1H), 1.92 (m, 2H), 1.73 (m, 4H), 1.52 (dddd, $J = 12.1, 11.2, 11.2, 5.1$ Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 101.29 (d), 77.99 (d), 74.10 (d), 68.93 (t), 68.02 (t), 35.23 (t), 28.74 (t), 28.26 (t), 25.50 (t), 6.47 (t). MS *m/e* (rel intens) 311 ($[M - 1]^+$, 56), 185 ($[M - I]^+$, 46). HRMS calcd for $C_{10}H_{16}O_3I$ $(M - H)^+$: 311.014422, found: 311.016322; calcd for $C_{10}H_{17}O_3$ $(M - I)^+$: 185.117770, found: 185.119141. Anal. Calcd for $C_{10}H_{17}O_3I$: C, 38.48; H, 5.49. Found: C, 38.50; H, 5.48.

(2*R*,4a*R*,8a*S*)-2-(7′-Iodoheptyl)hexahydropyrano[3,2-*d*]-[1,3]dioxine (8b): colorless oil. $R_f = 0.31$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +2.02°$ (*c* 0.4, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3010, 2933, 2860, 2340, 1558, 1508, 1091, 966 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.54 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.06 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.89 (br dd, $J = 11.5, 4.5$ Hz, 1H), 3.43 (m, 2H), 3.28 (ddd, $J = 11.2, 9.0, 4.2$ Hz, 1H), 3.16 (m, 3H), 2.02 (br dd, $J = 12.1, 3.7$ Hz, 1H), 1.75 (m, 4H), 1.56 (m, 3H), 1.36 (m, 4H), 1.29 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.56 (d), 77.99 (d), 74.28 (d), 68.98 (t), 68.02 (t), 34.44 (t), 33.52 (t), 30.38 (t), 29.21 (t), 28.81 (t), 28.38 (t), 25.54 (t), 24.09 (t), 7.12 (t). MS *m/e* (rel intens) 367 ($[M - 1]^+$, 9), 143 ($[M - C_7H_{14}I]^+$, 92). HRMS calcd for $C_{14}H_{25}O_3I$ $(M)^+$: 368.084847, found: 368.083679; calcd for $C_{14}H_{24}O_3I$ $(M - H)^+$: 367.077022, found: 367.077789. Anal. Calcd for $C_{14}H_{25}O_3I$: C, 45.66; H, 6.84. Found: C, 45.69; H, 6.79.

(2*R*,4a*R*,8a*S*)-2-(8′-Iodooctyl)hexahydropyrano[3,2-*d*]-[1,3]dioxine (8c): colorless oil. $R_f = 0.35$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +2.04°$ (*c* 1.32, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3011, 2859, 1466, 1236, 1091, 1006, 967 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.05 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.88 (br dd, $J = 11.3, 4.5$ Hz, 1H), 3.43 (m, 2H), 3.28 (ddd, $J = 11.3, 9.0, 4.2$ Hz, 1H), 3.15 (m, 3H), 2.01 (br dd, $J = 12.0, 3.4$ Hz, 1H), 1.75 (m, 4H), 1.55 (m, 3H), 1.35 (m, 4H), 1.26 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.59 (d), 77.97 (d), 74.28 (d), 68.98 (t), 68.01 (t), 34.48 (t), 33.53 (t), 30.45 (t), 29.31 (t), 29.23 (t), 28.81 (t), 28.39 (t), 25.54 (t), 24.14 (t), 7.19 (t). MS *m/e* (rel intens) 383 ($[M + 1]^+$, 100), 255 ($[M - HI]^+$, 12). HRMS calcd for $C_{15}H_{28}O_3I$ $(M + H)^+$: 383.108322, found: 383.108533. Anal. Calcd for $C_{15}H_{27}O_3I$: C, 47.13; H, 7.12. Found: C, 47.21; H, 7.37.

General Procedure for Elimination. The corresponding iodo compound (2.1 mmol) was dissolved in dry THF (21 mL) and ^{t}BuOK (353 mg, 3.15 mmol, 1.5 equiv) was added. After stirring for 30 min, TLC showed that the reaction was complete and it was quenched by addition of water (5 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), and combined organic layers were washed with brine and dried over $MgSO_4$. Solvent was removed in vacuo and the residue purified by flash chromatography.

(2*R*,4a*R*,8a*S*)-2-Allylhexahydropyrano[3,2-*d*][1,3]-dioxine (9a): colorless oil. $R_f = 0.39$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +7.45°$ (*c* 1.37, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3082, 2950, 2871, 1644, 1433, 1371 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, $J = 17.2, 10.2, 6.9, 6.9$ Hz, 1H), 5.08 (m, 2H), 4.59 (dd, $J = 5.1, 5.1$ Hz, 1H), 4.06 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.87 (br dd, $J = 11.2, 4.3$ Hz, 1H), 3.42 (m, 2 H), 3.29 (ddd, $J = 11.3, 9.0, 4.3$ Hz, 1H), 3.15 (ddd, $J = 9.9, 9.0, 4.9$ Hz, 1H), 2.37 (dd, $J = 6.9, 5.1$ Hz, 2H), 2.01 (br dd, $J = 12.2, 4.3$ Hz, 1H), 1.73 (m, 2H), 1.54 (dddd, $J = 12.2, 12.2, 11.3, 5.0$ Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.58 (d), 117.67 (t), 101.75 (d), 78.03 (d), 74.11 (d), 69.00 (t), 68.00 (t), 39.07 (t), 28.74 (t), 25.51 (t). MS *m/e* (rel intens) 185 ($[M + 1]^+$, 11). HRMS calcd for $C_{10}H_{17}O_3$ $(M + H)^+$: 185.117769, found: 185.118326. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.14; H, 8.83.

(2*R*,4a*R*,8a*S*)-2-Hept-6′-enylhexahydropyrano[3,2-*d*]-[1,3]dioxine (9b): colorless oil. $R_f = 0.36$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +3.73°$ (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3012, 2861, 2340, 1638, 1466, 1439, 1341, 1264 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.77 (dddd, $J = 17.1, 10.2, 6.7, 6.7$ Hz, 1H), 4.96 (d, $J = 17.1$ Hz, 1H), 4.90 (d, $J = 10.2$ Hz, 1H), 4.54 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.05 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.89 (br dd, $J = 11.3, 4.5$ Hz, 1H), 3.43 (m, 2H), 3.28 (ddd, $J = 11.2, 9.0, 4.2$ Hz, 1H), 3.15 (ddd, $J = 10.0, 9.0, 4.9$ Hz, 1H), 2.01 (m, 3H), 1.75 (m, 2H), 1.56 (m, 3H), 1.37 (m, 4H), 1.27 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.03 (d), 114.21 (t), 102.60 (d), 77.98 (d), 74.29 (d), 68.98 (t), 68.01 (t), 34.45 (t), 33.63 (t), 28.91 (t), 28.81 (t), 28.75 (t), 25.54 (t), 24.05 (t). MS *m/e* (rel intens) 239 ($[M + 1]^+$, 7). HRMS calcd for $C_{14}H_{23}O_3$ $(M - H)^+$: 239.164720, found: 239.164556. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.91; H, 9.83.

(2*R*,4a*R*,8a*S*)-2-Oct-7′-enylhexahydropyrano[3,2-*d*][1,3]-dioxine (9c): colorless oil. $R_f = 0.38$ (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +3.44°$ (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3012, 2932, 2360, 1639, 1236 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.77 (dddd, $J = 17.1, 10.2, 6.7, 6.7$ Hz, 1H), 4.95 (d, $J = 17.1$ Hz, 1H), 4.89 (d, $J = 10.2$ Hz, 1H), 4.53 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.05 (dd, $J = 10.4, 4.9$ Hz, 1H), 3.88 (br dd, $J = 11.4, 4.5$ Hz, 1H), 3.42 (m, 2H), 3.28 (ddd, $J = 11.3, 9.0, 4.2$ Hz, 1H), 3.15 (ddd, $J = 10.0, 9.0, 4.9$ Hz, 1H), 2.00 (m, 3H), 1.74 (m, 2H), 1.55 (m, 3H), 1.35 (m, 4H), 1.28 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.12 (d), 114.16 (t), 102.64 (d), 77.98 (d), 74.29 (d), 68.97 (t), 68.01 (t), 34.49 (t), 33.74 (t), 29.27 (t), 28.95 (t), 28.81 (t), 28.79 (t), 25.54 (t), 24.16 (t). MS *m/e* (rel intens) 253 ($[M - 1]^+$, 8). HRMS calcd for $C_{15}H_{26}O_3$ $(M)^+$: 254.188195, found: 254.186673. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.82; H, 10.39.

General Procedure for the Reductive Opening of Ketals. A solution of the corresponding ketal (1.9 mmol) in dry CH_3CN (3.8 mL) was cooled to 0 °C, and $NaCNBH_3$ (1.9 mL, 1.9 mmol, 1.0 equiv, 1 M solution in THF) was added followed by recently distilled $TiCl_4$ (209 μL, 1.9 mmol, 1.0 equiv). After stirring 6 h at that temperature, the reaction mixture was poured onto a $NaHCO_3$-saturated solution (4 mL) and filtered through a Celite pad, washing thoroughly with CH_2Cl_2. The combined organic layers were washed with brine and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was purified by flash chromatography (silica, 50% EtOAc in hexanes).

(2′*R*,3′*S*)-(3′-But-3″-enyloxytetrahydropyran-2′-yl)methanol (10a): colorless oil. R_f = 0.45 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +84.35° (*c* 1.51, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3590, 3491, 3081, 2945, 1641, 1464, 1438 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.76 (dddd, *J* = 17.2, 10.3, 6.7, 6.7 Hz, 1H), 5.05 (d, *J* = 17.2 Hz, 1H), 5.00 (d, *J* = 10.3 Hz, 1H), 3.87 (br dd, *J* = 11.3, 4.4 Hz, 1H), 3.78 (m, 1H), 3.63 (m, 2H), 3.35 (m, 2H), 3.16 (m, 2H), 2.32 (dd, *J* = 6.2, 6.2 Hz, 1H, O*H*), 2.24 (m, 3H), 1.60 (m, 2H), 1.31 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.16 (d), 116.58 (t), 80.60 (d), 74.96 (d), 68.02 (t), 67.71 (t), 63.38 (t), 34.46 (t), 29.09 (t), 25.18 (t). MS *m*/*e* (rel intens) 186 (M^+, 1). HRMS calcd for $C_{10}H_{18}O_3$ $(M)^+$: 186.12559, found: 186.12654. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.29; H, 9.93.

(2′*R*,3′*S*)-(3′-Oct-7″-enyloxytetrahydropyran-2′-yl)methanol (10b): colorless oil. R_f = 0.56 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +54.76° (*c* 0.8, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3588, 2934, 1638, 1463, 1234 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 17.2, 10.2, 6.7, 6.7 Hz, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 3.89 (br dd, *J* = 11.3, 4.6 Hz, 1H), 3.81 (m, 1H), 3.65 (m, 1H), 3.57 (ddd, *J* = 9.1, 6.5, 6.5 Hz, 1H), 3.33 (m, 2H), 3.16 (m, 2H), 2.22 (br d, *J* = 12.3 Hz, 1H), 2.17 (dd, *J* = 6.2, 6.2 Hz, 1H, O*H*), 2.01 (ddd, *J* = 7.5, 7.5, 6.7 Hz, 2H), 1.66 (m, 2H), 1.52 (m, 2H), 1.33 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.06 (d), 114.23 (t), 80.58 (d), 74.96 (d), 68.88 (t), 67.73 (t), 63.53 (t), 33.70 (t), 30.00 (t), 29.17 (t), 28.90 (t), 28.84 (t), 25.99 (t), 25.23 (t). MS *m*/*e* (rel intens) 242 (M^+, 10). HRMS calcd for $C_{14}H_{26}O_3$ $(M)^+$: 242.188195, found: 242.187541. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.45; H, 10.58.

(2′*R*,3′*S*)-(3′-Non-8″-enyloxytetrahydropyran-2′-yl)methanol (10c): colorless oil. R_f = 0.57 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +55.08° (*c* 1.02, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3596, 3011, 2858, 1639, 1464, 1358 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 17.2, 10.2, 6.7, 6.7 Hz, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 3.89 (br dd, *J* = 11.3, 4.5 Hz, 1H), 3.81 (m, 1H), 3.65 (m, 1H), 3.57 (ddd, *J* = 9.1, 6.5, 6.5 Hz, 1H), 3.33 (m, 2H), 3.16 (m, 2H), 2.23 (br d, *J* = 12.3 Hz, 1H), 2.18 (dd, *J* = 6.5, 6.5 Hz, 1H, O*H*), 2.01 (ddd, *J* = 7.5, 7.5, 6.7 Hz, 2H), 1.61 (m, 2H), 1.50 (m, 2H), 1.31 (m, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.13 (d), 114.16 (t), 80.60 (d), 74.96 (d), 68.91 (t), 67.71 (t), 63.53 (t), 33.75 (t), 30.04 (t), 29.26 (t), 29.17 (t), 29.04 (t), 28.85 (t), 26.07 (t), 25.23 (t). MS *m*/*e* (rel intens) 256 (M^+, 2), 225 ($[M - CH_2OH]^+$, 15). HRMS calcd for $C_{15}H_{28}O_3$ $(M)^+$: 256.203845, found: 256.204205; calcd for $C_{14}H_{25}O_2$ $(M - CH_2OH)^+$: 225.185455, found 225.185322. Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.30; H, 11.15.

General Procedure for Oxidation−Wittig Olefination. To a stirred solution of the alcohol (0.4 mmol) in CH_2Cl_2 (2 mL) were added NEt_3 (280 μL, 2 mmol, 5.0 equiv) and dry DMSO (425 μL, 6 mmol, 15.0 equiv). The reaction mixture was cooled to 0 °C and SO_3·py (191 mg, 1.2 mmol, 3.0 equiv) was added. After 2 h, the reaction was quenched by addition of water, and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL), and the combined organic layers were washed with brine and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was used in the Wittig reaction without further purification.

For the Wittig olefination, a suspension of methyltriphenylphosphonium bromide (214 mg, 0.6 mmol, 1.5 equiv) in THF (1 mL) was treated at 0 °C with ^{n}BuLi (243 μL, 0.56 mmol, 1.4 equiv, 2.3 M in hexanes). After stirring for 1 h at that temperature, the aldehyde (the residue from the previous step) was added *via cannula*, dissolved in dry THF (2 mL). Temperature was allowed to rise overnight. Water was added to quench the reaction. The aqueous layer was extracted with EtOAc (3 × 3 mL), and the combined organic layers were washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography.

(2*R*,3*S*)-3-But-3′-enyloxy-2-vinyltetrahydropyran (11a): colorless liquid. R_f = 0.28 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D$ = +54,82° (*c* 0.23, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3006, 2956, 1642, 1464, 1265 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.98 (ddd, *J* = 17.2, 10.7, 5.5 Hz, 1H), 5.78 (dddd, *J* = 17.2, 10.3, 6.7, 6.7 Hz, 1H), 5.32 (d, *J* = 17.2 Hz, 1H), 5.17 (d, *J* = 10.7 Hz, 1H), 5.05 (d, *J* = 17.2 Hz, 1H), 5.00 (d, *J* = 10.3 Hz, 1H), 3.91 (br dd, *J* = 11.3, 4.1 Hz, 1H), 3.57 (m, 2H), 3.41 (dd, *J* = 16.0, 6.9 Hz, 1H), 3.35 (ddd, *J* = 11.3, 11.3, 3.2 Hz, 1H), 2.97 (ddd, *J* = 10.0, 9.8, 4.3 Hz, 1H), 2.26 (ddd, *J* = 6.9, 6.9, 6.7 Hz, 2H), 2.18 (br dd, *J* = 12.5, 3.5 Hz, 1H), 1.63 (m, 2H), 1.37 (dddd, *J* = 12.5, 12.5, 10.0, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.71 (d), 135.25 (d), 116.32 (t), 116.26 (t), 81.16 (d), 78.16 (d), 68.83 (t), 67.44 (t), 34.51 (t), 29.76 (t), 25.27 (t). MS *m*/*e* (rel intens) 182 (M^+, 1). HRMS calcd for $C_{11}H_{18}O_2$ $(M)^+$: 182.130679, found: 182.131248. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.58; H, 9.47.

(2*R*,3*S*)-3-Pent-4′-enyloxy-2-vinyltetrahydropyran (11b): colorless liquid. R_f = 0.53 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +15.65° (*c* 0.6, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3009, 2927, 1454, 1247 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.96 (ddd, *J* = 17.4, 10.7, 5.5 Hz, 1H), 5.75 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.31 (d, *J* = 17.4 Hz, 1H), 5.15 (d, *J* = 10.7 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.91 (d, *J* = 10.2 Hz, 1H), 3.89 (br dd, *J* = 11.4, 4.5 Hz, 1H), 3.52 (m, 2H), 3.34 (m, 2H), 2.93 (ddd, *J* = 10.6, 9.0, 4.5 Hz, 1H), 2.17 (br dd, *J* = 12.5, 2.9 Hz, 1H), 2.06 (m, 2H), 1.61 (m, 4H), 1.34 (dddd, *J* = 12.5, 12.5, 10.6, 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.25 (d), 136.75 (d), 116.22 (t), 114.73 (t), 81.21 (d), 78.02 (d), 68.57 (t), 67.43 (t), 30.23 (t), 29.74 (t), 29.21 (t), 25.26 (t). MS *m*/*e* (rel intens) 196 (M^+, 1). HRMS calcd for $C_{12}H_{20}O_2$ $(M)^+$: 196.146330, found: 196.146849. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.52; H, 10.44.

(2*R*,3*S*)-3-Oct-7′-enyloxy-2-vinyltetrahydropyran (11c): colorless liquid. R_f = 0.32 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D$ = +48.95° (*c* 1.1, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3079, 3007, 2858, 1640, 1463, 1085 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.97 (ddd, *J* = 17.3, 10.7, 5.5 Hz, 1H), 5.77 (dddd, *J* = 17.0, 10.2, 6.7, 6.7 Hz, 1H), 5.32 (d, *J* = 17.3 Hz, 1H), 5.16 (d, *J* = 10.7 Hz, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 3.90 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.52 (m, 2H), 3.34 (m, 2H), 2.94 (ddd, *J* = 10.5, 9.1, 4.4 Hz, 1H), 2.17 (br dd, *J* = 12.4, 3.0 Hz, 1H), 2.01 (ddd, *J* = 7.2, 7.2, 6.7 Hz, 2H), 1.61 (m, 2H), 1.48 (m, 2H), 1.31 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.05 (d), 136.79 (d), 116.12 (t), 114.18 (t), 81.23 (d), 78.04 (d), 69.44 (t), 67.44 (t), 33.69 (t), 29.99 (t), 29.80 (t), 28.88 (t), 28.86 (t), 25.95 (t), 25.29 (t). MS *m*/*e* (rel intens) 238 (M^+, 1). HRMS calcd for $C_{15}H_{26}O_2$ $(M)^+$: 238.193280, found: 238.193776. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.45; H, 11.19.

(2*R*,3*S*)-3-Non-8′-enyloxy-2-vinyltetrahydropyran (11d): colorless liquid. R_f = 0.36 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D$ = +48.61° (*c* 0.8, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3080, 2857, 1639, 1464 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.97 (ddd, *J* = 17.4, 10.7, 5.5 Hz, 1H), 5.77 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.32 (d, *J* = 17.4 Hz, 1H), 5.16 (d, *J* = 10.7 Hz, 1H), 4.98 (d, *J* = 17.1 Hz, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 3.91 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.52 (m, 2H), 3.34 (m, 2H), 2.94 (ddd, *J* = 10.6, 9.1, 4.5 Hz, 1H), 2.18 (br dd, *J* = 12.5, 3.0 Hz, 1H), 2.01 (ddd, *J* = 7.2, 7.2, 6.7 Hz, 2H), 1.63 (m, 2H), 1.49 (m, 2H), 1.35 (m, 3H), 1.27 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.14 (d), 136.79 (d), 116.17 (t), 114.15 (t), 81.23 (d), 78.03 (d), 69.49 (t), 67.46 (t), 33.77 (t), 30.03 (t), 29.80 (t), 29.26 (t), 29.06 (t), 28.86 (t), 26.04 (t), 25.30 (t). MS *m*/*e* (rel intens) 252 (M^+, 2). HRMS calcd for $C_{16}H_{28}O_2$ $(M)^+$: 252.208930, found: 252.207977. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.22; H, 11.04.

General Procedure for Tosylation. To a stirred solution of **2** (200 mg, 1.5 mmol) in dry CH_2Cl_2 (3 mL) were added NEt_3 (315 μL, 2.25 mmol, 1.5 equiv) and a catalytic amount of DMAP. After cooling to 0 °C, tosyl chloride (286 mg, 1.5 mmol, 1.0 equiv) was added, and the stirring reaction was allowed to reach room-temperature overnight. Reaction was quenched with water (1 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. Solvent was removed in vacuo, and the residue was purified by flash chromatography. For alcohols **10a** and **10c**, the reaction was carried out with 1.2 equiv of tosyl chloride.

Toluene-4-sulfonic acid (2′*R*,3′*S*)-3′-hydroxytetrahydropyran-2′-ylmethyl ester (12): colorless oil. R_f = 0.54 (silica, 60% EtOAc in hexanes). $[\alpha]^{25}_D$ = +8.54° (*c* 2.62, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3616, 3548, 3028, 1599, 1451 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.31 (d, *J* = 8.1 Hz, 2H, Ar*H*), 4.30 (dd, *J* = 11.0, 4.5 Hz, 1H), 4.19 (dd, *J* = 11.0, 1.5 Hz, 1H), 3.85 (br d, *J* = 11.3 Hz, 1H), 3.52 (ddd, *J* = 10.2, 9.2, 5.0 Hz, 1H), 3.27 (ddd, *J* = 11.3, 11.3, 3.7 Hz, 1H), 3.18 (ddd, *J* = 9.2, 4.5, 1.5 Hz, 1H), 2.42 (s, 3H, ArC*H*$_3$), 2.23 (br s, 1H, O*H*), 2.10 (br dd, *J* = 12.3, 3.0 Hz, 1H), 1.66 (m, 2H), 1.39 (dddd, *J* = 12.3, 12.3, 10.2, 5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.94 (s, aromatic C), 132.88 (s, aromatic C), 129.87 (d, 2 aromatic C), 128.00 (d, 2 aromatic C), 80.19 (d), 71.93 (t), 69.81 (t), 65.84 (d), 32.36 (t), 25.41 (t), 21.66 (q, Ar*C*H$_3$). MS *m/e* (rel intens) 269 ([M − OH]$^+$, 1), 114 ([M − TsOH]$^+$, 20). HRMS calcd for $C_{13}H_{18}O_5S$ (M)$^+$: 286.08750, found: 286.08910. Anal. Calcd for $C_{13}H_{18}O_5S$: C, 54.53; H, 6.34; S, 11.20. Found: C, 54.50; H, 6.42; S, 11.43.

Preparation of Toluene-4-sulfonic Acid (2′*R*,3′*S*)-3′-Allyloxytetrahydropyran-2′-ylmethyl Ester (13a). This compound was prepared from **12** as described above (see general procedure for O-alkylation). Colorless oil. R_f = 0.34 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D$ = +39.91° (*c* 2.77, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3029, 2858, 1452, 1189, 1097 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.28 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.76 (dddd, *J* = 17.2, 10.5, 5.6, 5.6 Hz, 1H), 5.15 (d, *J* = 17.2 Hz, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 4.18 (m, 2H), 3.99 (dd, *J* = 12.4, 5.6 Hz, 1H), 3.78 (m, 2H), 3.23 (m, 2H), 3.17 (ddd, *J* = 10.5, 9.9, 4.5 Hz, 1H), 2.39 (s, 3H, ArC*H*$_3$), 2.20 (dddd, *J* = 12.4, 4.5, 3.1, 3.1 Hz, 1H), 1.55 (m, 2H), 1.26 (dddd, *J* = 12.4, 12.4, 10.5, 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.63 (s, aromatic C), 134.70 (d), 133.13 (s, aromatic C), 129.70 (d, 2 aromatic C), 127.95 (d, 2 aromatic C), 116.90 (t), 78.41 (d), 72.51 (d), 69.79 (t), 69.56 (t), 67.73 (t), 29.08 (t), 24.78 (t), 21.60 (q, Ar*C*H$_3$). MS *m/e* (rel intens) 326 (M$^+$, 1). HRMS calcd for $C_{16}H_{22}O_5S$ (M)$^+$: 326.11880, found: 326.11869. Anal. Calcd for $C_{16}H_{22}O_5S$: C, 58.93; H, 6.80; S, 9.83. Found: C, 58.78; H, 6.91; S, 10.12.

Preparation of Toluene-4-sulfonic Acid (2′*R*,3′*S*)-3′-Pent-4″-enyloxytetrahydropyran-2′-ylmethyl Ester (13b). This compound was prepared from **12** as described above (see general procedure for O-alkylation). Colorless oil. R_f = 0.41 (silica, 25% EtOAc in hexanes). $[\alpha]^{25}_D$ = +44.17° (*c* 0.66, $CHCl_3$). IR ($CHCl_3$) ν_{max} 2928, 2360, 1639, 1456 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.30 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.75 (dddd, *J* = 17.2, 10.2, 6.6, 6.6 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 4.21 (dd, *J* = 10.3, 2.1 Hz, 1H), 4.16 (dd, *J* = 10.3, 5.0 Hz, 1H), 3.82 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.51 (ddd, *J* = 9.0, 6.4, 6.4 Hz, 1H), 3.22 (m, 3H), 3.09 (ddd, *J* = 10.0, 9.0, 4.5 Hz, 1H), 2.40 (s, 3H, ArC*H*$_3$), 2.21 (br dd, *J* = 12.5, 3.3 Hz, 1H), 2.00 (dddd, *J* = 7.5, 7.5, 6.6, 1.2 Hz, 2H), 1.56 (m, 4H), 1.24 (dddd, *J* = 12.5, 12.5, 10.0, 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.60 (s, aromatic C), 138.13 (d), 133.14 (s, aromatic C), 129.72 (d, 2 aromatic C), 128.05 (d, 2 aromatic C), 114.83 (t), 78.51 (d), 73.01 (d), 69.87 (t), 67.91 (t), 67.79 (t), 30.22 (t), 29.10 (t), 29.07 (t), 24.81 (t), 21.64 (q, Ar*C*H$_3$). MS *m/e* (rel intens) 355 ([M + 1]$^+$, 13). HRMS calcd for $C_{18}H_{27}O_5S$ (M + H)$^+$: 355.157921, found: 355.156695. Anal. Calcd for $C_{18}H_{26}O_5S$: C, 60.99; H, 7.93; S, 9.05. Found: C, 60.86; H, 8.10; S, 9.23.

Preparation of Toluene-4-sulfonic Acid (2′*R*,3′*S*)-3′-But-3″-enyloxytetrahydropyran-2′-ylmethyl Ester (14a). This compound was prepared from **10a** as described above (see general procedure for tosylation). Colorless oil. R_f = 0.43 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D$ = +44.52° (*c* 0.75, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3031, 2859, 1603, 1443, 1363, 1290 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.30 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.70 (dddd, *J* = 17.0, 10.4, 6.7, 6.7 Hz, 1H), 5.00 (m, 2H), 4.19 (m, 2H), 3.87 (br d, *J* = 11.2 Hz, 1H), 3.56 (ddd, *J* = 8.7, 6.6, 6.6 Hz, 1H), 3.25 (m, 3H), 3.12 (ddd, *J* = 10.3, 9.8, 4.5 Hz, 1H), 2.41 (s, 3H, ArC*H*$_3$), 2.19 (m, 3H), 1.58 (m, 2H), 1.26 (dddd, *J* = 12.1, 12.1, 10.3, 4.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.57 (s, aromatic C), 135.07 (d), 133.21 (s, aromatic C), 129.70 (d, 2 aromatic C), 128.08 (d, 2 aromatic C), 116.45 (t), 78.45 (d), 73.10 (d), 69.84 (t), 67.94 (t), 67.76 (t), 34.40 (t), 29.09 (t), 25.92 (t), 21.65 (q, Ar*C*H$_3$). MS *m/e* (rel intens) 340 (M$^+$, 1). HRMS calcd for $C_{17}H_{24}O_5S$ (M)$^+$: 340.13445, found: 340.13526. Anal. Calcd for $C_{17}H_{24}O_5S$: C, 59.98; H, 7.11; S, 9.42. Found: C, 59.59; H, 6.87; S, 9.04.

Preparation of Toluene-4-sulfonic Acid (2′*R*,3′*S*)-3′-Non-8″-enyloxytetrahydropyran-2′-ylmethyl Ester (14b). This compound was prepared from **10c** as described above (see general procedure for tosylation). Colorless oil. R_f = 0.37 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D$ = +34.30° (*c* 1.8, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3031, 2857, 1454, 1363 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2 H, Ar*H*), 7.30 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.79 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.91 (d, *J* = 10.2 Hz, 1H), 4.19 (m, 2H), 3.82 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.49 (ddd, *J* = 9.0, 6.5, 6.5 Hz, 1H), 3.22 (m, 3H), 3.09 (ddd, *J* = 10.0, 9.0, 4.6 Hz, 1H), 2.41 (s, 3H, ArC*H*$_3$), 2.21 (br dd, *J* = 12.3, 3.2 Hz, 1H), 2.02 (ddd, *J* = 7.5, 6.7, 6.7 Hz, 2H), 1.57 (m, 2H), 1.42 (m, 2H), 1.36 (m, 2H), 1.25 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.50 (s, aromatic C), 139.15 (d, $C_{8''}$), 133.26 (s, aromatic C), 129.66 (d, 2 aromatic C), 128.07 (d, 2 aromatic C), 114.19 (t), 78.55 (d), 73.02 (d), 69.87 (t), 68.85 (t), 67.78 (t), 33.77 (t), 30.00 (t), 29.30 (t), 29.13 (t), 29.05 (t), 28.88 (t), 26.04 (t), 24.84 (t), 21.63 (q, Ar*C*H$_3$). MS *m/e* (rel intens) 410 (M$^+$, 1). HRMS calcd for $C_{22}H_{34}O_5S$ (M)$^+$: 410.212696, found: 410.212832. Anal. Calcd for $C_{22}H_{34}O_5S$: C, 64.36; H, 8.35; S, 7.81. Found: C, 64.42; H, 8.47; S, 7.89.

General Procedure for Nucleophilic Substitution with KCN. To a stirring solution of the corresponding tosylate or iodo compound (0.5 mmol) in dry DMSO (1.7 mL) was added KCN (98 mg, 1.5 mmol, 3.0 equiv), and the reaction mixture was stirred at 50 °C for 6 h. Then it was allowed to cool, and water was added to quench the reaction. The mixture was diluted with EtOAc. The aqueous layer was extracted with EtOAc (3 × 3 mL), and combined organic layers were dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography.

(2′*R*,3′*S*)-(3′-Allyloxytetrahydropyran-2′-yl)acetonitrile (15a): colorless oil. R_f = 0.49 (silica, 25% EtOAc in hexanes). $[\alpha]^{25}_D$ = +89.39° (*c* 1.45, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3020, 2948, 2865, 2254, 1464, 1268, 1212 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (dddd, *J* = 17.1, 10.5, 5.5, 5.5 Hz, 1H), 5.21 (d, *J* = 17.1 Hz, 1H), 5.14 (d, *J* = 10.5 Hz, 1H), 4.07 (dd, *J* = 12.5, 5.5 Hz, 1H), 3.88 (m, 2H), 3.32 (ddd, *J* = 11.9, 11.9, 3.5 Hz, 1H), 3.28 (ddd, *J* = 9.5, 6.1, 3.5 Hz, 1H), 3.14 (ddd, *J* = 10.5, 9.5, 4.5 Hz, 1H), 2.72 (dd, *J* = 16.8, 3.5 Hz, 1H), 2.62 (dd, *J* = 16.8, 6.1 Hz, 1H), 2.24 (br dd, *J* = 12.2, 4.5 Hz, 1H), 1.63 (m, 2H), 1.30 (dddd, *J* = 12.2, 12.2, 10.5, 5.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.70 (d), 117.54 (s, R*C*N), 117.37 (t), 76.16 (d), 75.73 (d), 69.53 (t), 68.03 (t), 28.75 (t), 24.81 (t), 21.46 (t). MS *m/e* (rel intens) 181 (M$^+$, 5). HRMS calcd for $C_{10}H_{15}NO_2$ (M)$^+$: 181.11028, found: 181.10971. Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.38; H, 8.49; N, 7.79.

(2′*R*,3′*S*)-(3′-But-3″-enyloxytetrahydropyran-2′-yl)acetonitrile (15b): colorless oil. R_f = 0.61 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D$ = +79.04° (*c* 0.73, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3020, 2948, 2867, 2254, 1642 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.76 (dddd, *J* = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.07 (d, *J* = 17.0 Hz, 1H), 5.03 (d, *J* = 10.3 Hz, 1H), 3.92 (br d, *J* = 11.0 Hz, 1H), 3.66 (ddd, *J* = 9.1, 6.5, 6.5 Hz, 1H), 3.36 (m, 2H), 3.28 (ddd, *J* = 9.3, 6.0, 3.6 Hz, 1H), 3.10 (ddd, *J* = 10.1, 9.3, 4.4 Hz, 1H), 2.73 (dd, *J* = 16.7, 3.6 Hz, 1H), 2.64 (dd, *J* = 16.7,

6.0 Hz, 1H), 2.27 (m, 3H), 1.68 (m, 2H), 1.30 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.07 (d), 117.65 (s, *R*C*N*), 116.93 (t), 76.39 (d), 76.19 (d), 68.10 (t), 67.90 (t), 34.39 (t), 28.81 (t), 24.87 (t), 21.54 (t). MS *m/e* (rel intens) 195 (M^+, 2). HRMS calcd for $C_{11}H_{17}NO_2$ $(M)^+$: 195.12593, found: 195.12644. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.77; N, 7.17. Found: C, 67.86; H, 9.15; N, 7.27.

(2′*R*,3′*S*)-(3′-Pent-4″-enyloxytetrahydropyran-2′-yl)-acetonitrile (15c): colorless oil. R_f = 0.64 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D$ = +76.36° (*c* 1.1, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3023, 3007, 2928, 2857, 2253, 1640 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (dddd, *J* = 17.1, 10.2, 6.6, 6.6 Hz, 1H), 5.00 (d, *J* = 17.1 Hz, 1H), 4.95 (d, *J* = 10.2 Hz, 1H), 3.92 (br d, *J* = 11.0 Hz, 1H), 3.60 (ddd, *J* = 9.0, 6.3, 6.3 Hz, 1H), 3.32 (m, 3H), 3.09 (ddd, *J* = 10.6, 9.1, 4.4 Hz, 1H), 2.73 (dd, *J* = 16.7, 3.6 Hz, 1H), 2.64 (dd, *J* = 16.7, 6.0 Hz, 1H), 2.27 (br d, *J* = 11.0 Hz, 1 H), 2.08 (ddd, *J* = 6.8, 6.6, 6.6 Hz, 2H), 1.64 (m, 4H), 1.29 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.96 (d), 117.64 (s, *R*C*N*), 115.00 (t), 76.24 (d), 76.20 (d), 68.13 (t), 68.05 (t), 30.32 (t), 29.05 (t), 28.84 (t), 25.16 (t), 21.49 (t). MS *m/e* (rel intens) 210 ($[M + 1]^+$, 93). HRMS calcd for $C_{12}H_{20}NO_2$ $(M + H)^+$: 210.149404, found: 210.149598. Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.52; H, 9.33; N, 6.63.

(2′*R*,3′*S*)-(3′-Non-8″-enyloxytetrahydropyran-2′-yl)-acetonitrile (15d): colorless liquid. R_f = 0.39 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D$ = +60.54° (*c* 1.3, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3022, 2932, 2858, 2254, 1639 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 17.0, 10.2, 6.7, 6.7 Hz, 1H), 4.96 (d, *J* = 17.0 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 3.92 (br dd, *J* = 11.3, 4.2 Hz, 1H), 3.58 (ddd, *J* = 9.1, 6.5, 6.5 Hz, 1H), 3.32 (m, 3H), 3.08 (ddd, *J* = 10.7, 9.2, 4.4 Hz, 1H), 2.73 (dd, *J* = 16.7, 3.6 Hz, 1H), 2.63 (dd, *J* = 16.7, 6.0 Hz, 1H), 2.26 (br dd, *J* = 12.5, 2.8 Hz, 1H), 2.01 (ddd, *J* = 6.8, 6.6, 6.6 Hz, 2H), 1.66 (m, 2H), 1.50 (m, 2H), 1.35 (m, 2H), 1.28 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.10 (d), 117.64 (s, *R*C*N*), 114.20 (t), 76.33 (d), 76.26 (d), 68.78 (t), 68.08 (t), 33.75 (t), 29.95 (t), 29.25 (t), 29.03 (t), 28.84 (t, 2 C), 26.08 (t), 24.91 (t), 21.47 (t). MS *m/e* (rel intens) 265 (M^+, 87). HRMS calcd for $C_{16}H_{27}NO_2$ $(M)^+$: 265.204179, found: 265.202854. Anal. Calcd for $C_{16}H_{27}NO_2$: C, 64.36; H, 10.25; N, 5.28. Found: C, 64.45; H, 10.36; N, 5.23.

General Procedure for Nitrile Reduction−Wittig Olefination. A solution of the corresponding nitrile (0.05 mmol) in dry Et_2O (4 mL) was cooled to 0 °C, and DIBAL (0.75 mL, 0.75 mmol, 1.5 equiv, 1.0 M in hexanes) was added. The reaction mixture was stirred for 5 h, quenched by the addition of 1 N HCl solution (1.5 mL), and filtered through a Celite pad. The precipitate was thoroughly washed with EtOAc. The organic layer was washed with $NaHCO_3$ saturated solution (2 × 4 mL) and dried over $MgSO_4$. Solvent was removed in vacuo, and the residue was used without further purification in the Wittig olefination (procedure described above).

(2*R*,3*S*)-2-Allyl-3-allyloxytetrahydropyran (16a): colorless liquid. R_f = 0.58 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +34.50° (*c* 0.67, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3027, 3011, 2945, 2857, 2360, 1644 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (m, 2H), 5.24 (d, *J* = 17.2 Hz, 1H), 5.14 (d, *J* = 10.4 Hz, 1H), 5.08 (d, *J* = 17.2 Hz, 1H), 5.05 (d, *J* = 10.2 Hz, 1H), 4.09 (dd, *J* = 12.7, 5.6 Hz, 1H), 3.90 (m, 2H), 3.30 (ddd, *J* = 11.6, 11.6, 3.0 Hz, 1H), 3.18 (ddd, *J* = 9.0, 9.0, 3.0 Hz, 1H), 3.04 (ddd, *J* = 10.4, 9.0, 4.5 Hz, 1H), 2.61 (br d, *J* = 14.6 Hz, 1H), 2.21 (m, 2H), 1.61 (m, 2H), 1.32 (dddd, *J* = 12.4, 12.4, 10.4, 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.38 (d), 135.10 (d), 116.86 (t), 116.58 (t), 80.49 (d), 76.71 (d), 69.83 (t), 67.82 (t), 36.66 (t), 29.36 (t), 25.39 (t). MS *m/e* (rel intens) 182 (M^+, 2). HRMS calcd for $C_{11}H_{18}O_2$ $(M)^+$: 182.130679, found: 182.132577. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.57; H, 10.12.

(2*R*,3*S*)-2-Allyl-3-but-3′-enyloxytetrahydropyran (16b): colorless oil. R_f = 0.59 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +45.00° (*c* 0.31, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3007, 2943, 2360, 1642, 1435 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (m, 2H), 5.05 (m, 4H), 3.87 (br dd, *J* = 11.5, 4.2 Hz, 1H), 3.63 (ddd, *J* = 9.0, 6.6, 6.6 Hz, 1H), 3.37 (ddd, *J* = 9.0, 6.9, 6.9 Hz, 1H), 3.30 (ddd, *J* = 11.5, 11.5, 3.1 Hz, 1H), 3.15 (ddd, *J* = 9.3, 8.3, 3.0 Hz, 1H), 2.98 (ddd, *J* = 10.5, 9.3, 4.5 Hz, 1H), 2.59 (br d, *J* = 14.6 Hz, 1H), 2.29 (m, 2H), 2.20 (m, 2H), 1.62 (m, 2H), 1.31 (dddd, *J* = 12.3, 12.3, 10.5, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.44 (d), 135.31 (d), 116.52 (t), 116.35 (t), 80.51 (d), 77.34 (d), 68.27 (t), 67.80 (t), 36.65 (t), 34.57 (t), 29.28 (t), 25.39 (t). MS *m/e* (rel intens) 196 (M^+, 2). HRMS calcd for $C_{12}H_{20}O_2$ $(M)^+$: 196.146330, found: 196.145982. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.62; H, 10.44.

(2*R*,3*S*)-2-Allyl-3-pent-4′-enyloxytetrahydropyran (16c): colorless liquid. R_f = 0.55 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +52.11° (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3079, 3004, 2856, 1641, 1464, 1437 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dddd, *J* = 17.3, 10.2, 6.3, 6.3 Hz, 1H), 5.79 (dddd, *J* = 17.1, 10.2, 6.6, 6.6 Hz, 1H), 5.02 (m, 4H), 3.87 (br d, *J* = 11.2 Hz, 1H), 3.58 (ddd, *J* = 9.1, 6.3, 6.3 Hz, 1H), 3.30 (m, 2H), 3.15 (ddd, *J* = 9.0, 8.2, 3.0 Hz, 1H), 2.96 (ddd, *J* = 10.5, 9.0, 4.5 Hz, 1H), 2.60 (br d, *J* = 14.6 Hz, 1H), 2.20 (m, 2H), 2.11 (m, 2H), 1.62 (m, 4H), 1.29 (dddd, *J* = 12.4, 12.4, 10.5, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.27 (d), 135.45 (d), 116.55 (t), 114.81 (t), 80.55 (d), 77.23 (d), 68.09 (t), 67.87 (t), 36.68 (t), 30.34 (t), 29.36 (t), 29.28 (t), 25.41 (t). MS *m/e* (rel intens) 210 (M^+, 11). HRMS calcd for $C_{13}H_{22}O_2$ $(M)^+$: 210.161980, found: 210.162441. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.15; H, 10.63.

(2*R*,3*S*)-2-Allyl-3-non-8′-enyloxytetrahydropyran (16d): liquid. R_f = 0.58 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +40.40° (*c* 1.22, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3078, 3006, 2932, 2857, 1640, 1464, 1437, 1340 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dddd, *J* = 17.3, 10.2, 6.5, 6.5 Hz, 1H), 5.78 (dddd, *J* = 17.1, 10.1, 6.7, 6.7 Hz, 1H), 5.07 (d, *J* = 17.3 Hz, 1H), 5.03 (d, *J* = 10.2 Hz, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 4.90 (d, *J* = 10.1 Hz, 1H), 3.86 (br dd, *J* = 11.2, 4.2 Hz, 1H), 3.55 (ddd, *J* = 9.0, 6.4, 6.4 Hz, 1H), 3.29 (m, 2H), 3.14 (ddd, *J* = 9.1, 8.2, 3.0 Hz, 1H), 2.94 (ddd, *J* = 10.5, 9.1, 4.4 Hz, 1H), 2.59 (br d, *J* = 13.1 Hz, 1H), 2.19 (m, 2H), 2.01 (m, 2H), 1.59 (m, 2H), 1.50 (m, 2H), 1.31 (m, 9H). ^{1}H NMR (500 MHz, C_6D_6) δ 6.25 (dddd, *J* = 17.2, 10.2, 7.0, 7.0 Hz, 1H), 5.85 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.28 (d, *J* = 17.2 Hz, 1H), 5.19 (d, *J* = 10.2 Hz, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 5.05 (d, *J* = 10.2 Hz, 1H), 3.79 (br dd, *J* = 11.2, 4.6 Hz, 1H), 3.49 (ddd, *J* = 8.9, 6.4, 6.4 Hz, 1H), 3.30 (ddd, *J* = 9.0, 8.8, 3.1 Hz, 1H), 3.22 (ddd, *J* = 8.9, 6.5, 6.5 Hz, 1H) 3.13 (ddd, *J* = 12.1, 11.2, 2.2 Hz, 1H), 2.99 (ddd, *J* = 10.5, 9.0, 4.5 Hz, 1H), 2.85 (br d, *J* = 14.3, 1H), 2.53 (ddd, *J* = 14.3, 8.8, 7.0 Hz, 1H), 2.05 (m, 3H), 1.59 (m, 2H), 1.45 to 1.26 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.12 (d), 135.46 (d), 116.46 (t), 114.16 (t), 80.59 (d), 77.21 (d), 68.94 (t), 67.84 (t), 36.66 (t), 33.76 (t), 30.11 (t), 29.39 (t), 29.28 (t), 29.05 (t), 28.86 (t), 26.14 (t), 25.43 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 138.94 (d), 135.94 (d), 116.20 (t), 114.28 (t), 80.92 (d), 77.17 (d), 68.46 (t), 67.43 (t), 36.99 (t), 33.91 (t), 30.38 (t), 29.45 (t, 2 C), 29.21 (t), 29.04 (t), 26.38 (t), 25.58 (t). MS *m/e* (rel intens) 266 (M^+, 3). HRMS calcd for $C_{17}H_{30}O_2$ $(M)^+$: 266.224580, found: 266.224616. Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.81; H, 11.45.

Preparation of Benzoic Acid (2′*R*,3′*S*)-3′-Hydroxytetrahydropyran-2′-ylmethyl Ester (17). A solution of **2** (330 mg, 2.5 mmol) in dry CH_2Cl_2 was cooled to 0 °C, and NEt_3 (1.05 mL, 7.5 mmol, 3.0 equiv), BzCl (319 μL, 2.75 mmol, 1.0 equiv), and a catalytic amount of DMAP were added. The reaction was stirred at room temperature for 4 h and quenched by the addition of 3 mL of NH_4Cl saturated solution. The aqueous layer was extracted with CH_2Cl_2 (2 × 3 mL). Combined organic layers were dried over $MgSO_4$, and solvent was removed under reduced pressure. Purification by flash chromatography (using 40% EtOAc in hexanes as eluent) afforded 578 mg of the benzoate (98%). Noncrystalline white solid. R_f = 0.41 (silica, 40% EtOAc in hexanes). $[\alpha]^{25}_D$ = −9.31° (*c* 0.92, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3618, 3500, 3026, 3014, 2341, 1708, 1603 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (br d, *J* = 8.3 Hz, 2H, Ar*H*), 7.53 (dd, *J* = 7.4, 7.4 Hz, 1H, Ar*H*), 7.41 (dd, *J* = 8.3, 7.4 Hz, 2H, Ar*H*), 4.78 (dd, *J* = 12.2, 4.0 Hz, 1H), 4.41 (dd, *J* = 12.2, 2.2 Hz, 1H), 3.39 (br dd, *J* = 11.5, 4.0 Hz, 1H), 3.42 (m, 1H), 3.35 (m, 1H), 3.30 (ddd, *J* = 9.3, 4.0, 2.2 Hz, 1H), 2.95 (br s, 1H, O*H*), 2.11 (br dd, *J* = 12.5, 4.5 Hz, 1H), 1.64 (m, 2H), 1.45 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ

167.69 (s, Ph*C*OO), 133.26 (d, aromatic C), 129.94 (d, 2 aromatic C), 129.71 (s, aromatic C), 128.39 (d, 2 aromatic C), 81.20 (d), 68.05 (t), 66.17 (d), 64.81 (t), 32.01 (t), 25.38 (t). MS *m/e* (rel intens) 236 (M^+, 1). HRMS calcd for $C_{13}H_{16}O_4$ $(M)^+$: 236.10486, found: 236.10713. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.10; H, 6.80. Found: C, 65.89; H, 7.09.

Preparation of Benzoic Acid (2′*R*,3′*S*)-3′-(*tert*-Butyldimethylsilyloxy)tetrahydropyran-2′-ylmethyl Ester (18). This compound was prepared from **17** according to the procedure described above (see general procedure for protection of alcohol as TBDMS ethers). Yield: 97%. Colorless oil. R_f = 0.41 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D = +46.41°$ (*c* 1.01, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3023, 2954, 2858, 1717, 1603, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (br d, *J* = 8.0 Hz, 2H, Ar*H*), 7.52 (dd, *J* = 7.5, 7.5 Hz, 1H, Ar*H*), 7.41 (dd, *J* = 8.0, 7.5 Hz, 2H, Ar*H*), 4.59 (dd, *J* = 11.7, 2.0 Hz, 1H), 4.36 (dd, *J* = 11.7, 5.5 Hz, 1H), 3.92 (br dd, *J* = 11.7, 4.6 Hz, 1H), 3.63 (ddd, *J* = 10.0, 9.8, 4.7 Hz, 1H), 3.37 (m, 2H), 2.07 (br dd, *J* = 12.5, 4.7 Hz, 1H), 1.67 (m, 2H), 1.48 (dddd, *J* = 12.5, 12.5, 10.0, 4.7 Hz, 1H), 0.84 (s, 9H, $(CH_3)_3CSi$), 0.05 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.58 (s, Ph*C*OO), 132.80 (d, aromatic C), 130.38 (s, aromatic C), 129.70 (d, 2 aromatic C), 128.25 (d, 2 aromatic C), 80.74 (d), 67.90 (t), 67.53 (d), 64.78 (t), 33.53 (t), 25.72 (q, $(CH_3)_3CSi$), 25.41 (t), 17.88 (s, $(CH_3)_3CSi$), −3.99 (q, CH_3Si), −4.95 (q, CH_3Si). MS *m/e* (rel intens) 293 ($[M - {}^tBu]^+$, 14). HRMS calcd for $C_{15}H_{21}O_4Si$ $(M - {}^tBu)^+$: 293.12091, found: 293.12121. Anal. Calcd for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.63. Found: C, 65.36; H, 8.87.

Preparation of (2′*R*,3′*S*)-[3′-(*tert*-Butyldimethylsilyloxy)tetrahydropyran-2′-yl]methanol (19). To a stirring solution of benzoate **18** (832 mg, 2.38 mmol) in MeOH (5 mL) was added MeONa (64 mg, 1.19 mmol, 0.5 equiv) at room temperature. When TLC showed that all starting material has disappeared, solvent was removed in vacuo, and the residue was purified by flash chromatography, using first CH_2Cl_2 as eluent and then 20% EtOAc in hexanes, yielding 580 mg (99%) of **19**. Colorless oil. R_f = 0.60 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D = +50.5°$ (*c* 1.6, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3450, 2952, 2858, 1472, 1253 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.88 (br dd, *J* = 11.1, 3.8 Hz, 1 H, $He_{6'}$), 3.80 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.58 (dd, *J* = 11.4, 5.9 Hz, 1H), 3.46 (ddd, *J* = 10.6, 9.1, 4.7 Hz, 1H), 3.34 (dddd, *J* = 11.1, 11.1, 5.0, 3.7 Hz, 1H), 3.12 (ddd, *J* = 9.1, 5.9, 2.6 Hz, 1H), 1.99 (m, 2H,), 1.63 (m, 2H), 1.23 (dddd, *J* = 12.3, 12.3, 10.6, 5.4 Hz, 1H), 0.85 (s, 9H, $(CH_3)_3CSi$), 0.04 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.37 (d), 67.92 (d), 67.67 (t), 63.17 (t), 33.28 (t), 25.73 (q, $(CH_3)_3CSi$), 25.48 (t), 17.90 (s, $(CH_3)_3CSi$), −4.10 (q, CH_3Si), −4.93 (q, CH_3Si). MS *m/e* (rel intens) 189 ($[M - {}^tBu]^+$, 14). HRMS calcd for $C_{12}H_{27}O_3Si$ $(M + H)^+$: 247.12290, found: 247.12370. Anal. Calcd for $C_{12}H_{26}O_3Si$: C, 58.49; H, 10.63. Found: C, 58.57; H, 10.72.

Preparation of (2*R*,3*S*)-*tert*-Butyl(2-iodomethyltetrahydropyran-3-yloxy)dimethylsilane (20). This compound was synthesized according to the method already described (see procedure for iodination of alcohols). Yield: 95%. Colorless oil. R_f = 0.48 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D = +47.82°$ (*c* 1.38, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3006, 2955, 2858, 1463, 1217, 1111, 838 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.94 (br dd, *J* = 11.3, 4.5 Hz, 1H), 3.48 (dd, *J* = 10.4, 2.7 Hz, 1H, RCH_2I), 3.38 (m, 2H), 3.31 (dd, *J* = 10.4, 5.8 Hz, 1H, RCH_2I), 2.80 (ddd, *J* = 8.5, 5.8, 2.7 Hz, 1H), 2.00 (br dd, *J* = 12.7, 4.7 Hz, 1H), 1.66 (m, 2H), 1.46 (dddd, *J* = 12.7, 12.7, 10.6, 4.5 Hz, 1H), 0.86 (s, 9H, $(CH_3)_3CSi$), 0.09 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 80.81 (d), 71.21 (d), 67.98 (t), 33.15 (t), 25.79 (q, $(CH_3)_3CSi$), 25.49 (t), 17.88 (s, $(CH_3)_3CSi$), 9.33 (t), −3.85 (q, CH_3Si), −4.49 (q, CH_3Si). MS *m/e* (rel intens) 357 ($[M + 1]^+$, 2), 299 ($[M - {}^tBu]^+$, 10). HRMS calcd for $C_8H_{16}IO_2Si$ $(M - {}^tBu)^+$: 298.9964, found: 298.9970. Anal. Calcd for $C_{12}H_{25}IO_2Si$: C, 40.45; H, 7.07. Found: C, 40.62; H, 7.23.

Preparation of (2′*R*,3′*S*)-[3′-(*tert*-Butyldimethylsilyloxy)tetrahydropyran-2′-yl]acetonitrile (21). This compound was prepared according to the procedure for nucleophilic substitution with KCN described above. Yield: 99%. Colorless oil. R_f = 0.38 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D = +50.26°$ (*c* 0.88, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3022, 2954, 2931, 2859, 2360, 2341, 1464, 1362 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.99 (br dd, *J* = 11.5, 4.5 Hz, 1H), 3.40 (ddd, *J* = 10.5, 9.0, 4.6 Hz, 1H), 3.35 (ddd, *J* = 11.5, 11.5, 2.8 Hz, 1H), 3.24 (ddd, *J* = 9.0, 6.2, 3.5 Hz, 1H), 2.70 (dd, *J* = 16.7, 3.5 Hz, 1H), 2.56 (dd, *J* = 16.7, 6.2 Hz, 1H), 2.03 (br d, *J* = 12.8 Hz, 1H), 1.65 (m, 2H), 1.43 (dddd, *J* = 12.8, 12.8, 10.8, 4.6 Hz, 1H), 0.85 (s, 9H, $(CH_3)_3CSi$), 0.08 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 117.59 (s, R*C*N), 77.94 (d), 70.17 (d), 68.04 (t), 33.07 (t), 25.71 (q, $(CH_3)_3CSi$), 25.18 (t), 21.45 (t), 17.84 (s, $(CH_3)_3CSi$), −3.92 (q, CH_3Si), −4.85 (q, CH_3Si). MS *m/e* (rel intens) 256 ($[M + 1]^+$, 100). HRMS calcd for $C_{13}H_{26}NO_2Si$ $(M + H)^+$: 256.173283, found: 256.173538. Anal. Calcd for $C_{13}H_{25}NO_2Si$: C, 61.13; H, 9.87; N, 5.48. Found: C, 61.11; H, 10.00; N: 5.63.

Preparation of (2′*R*,3′*S*)-2-[3′-(*tert*-Butyldimethylsilyloxy)tetrahydropyran-2′-yl]ethanol (22). Nitrile **21** was reduced to the corresponding aldehyde following the procedure described above (see general procedure for nitrile reduction), using for the acid hydrolysis HCl 0.1 N at 4 °C to avoid deprotection of the silyl ether. The resultant aldehyde (without further purification) was dissolved in MeOH, and $NaBH_4$ (2.0 equiv) was added at 0 °C. When TLC showed that the reaction had finished, solvent was removed in vacuo, and the residue was dissolved in EtOAc. Water (3 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 3 mL). Combined organic layers were dried over $MgSO_4$, and solvent was removed under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexanes) affording the expected alcohol (42%). Colorless oil. R_f = 0.26 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D = +50.47°$ (*c* 1.05, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3504, 3009, 2956, 2858, 2360, 1464 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.86 (br dd, *J* = 11.2, 4.1 Hz, 1H), 3.77 (m, 2H), 3.32 (m, 2H), 3.23 (ddd, *J* = 9.0, 9.0, 2.7 Hz, 1H), 2.80 (dd, *J* = 6.5, 4.4 Hz, 1H, O*H*), 2.00 (m, 2H), 1.62 (m, 3H), 1.40 (dddd, *J* = 12.6, 12.6, 10.6, 5.5 Hz, 1H), 0.84 (s, 9H, $(CH_3)_3CSi$), 0.03 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 83.80 (d), 71.00 (d), 67.74 (t), 61.80 (t), 34.08 (t), 33.37 (t), 25.77 (q, $(CH_3)_3CSi$), 25.46 (t), 17.93 (s, $(CH_3)_3CSi$), −4.01 (q, CH_3Si), −4.72 (q, CH_3Si). MS *m/e* (rel intens) 261 ($[M + 1]^+$, 1). HRMS calcd for $C_{13}H_{29}O_3Si$ $(M + H)^+$: 261.188598, found: 261.188033. Anal. Calcd for $C_{13}H_{28}O_3Si$: C, 59.95; H, 10.84. Found: C, 59.95; H, 10.81.

Preparation of (2*R*,3*S*)-*tert*-Butyl-[2-(2′-iodoethyl)tetrahydropyran-3-yloxy]dimethylsilane (23). This compound was prepared according to the procedure described above for the iodination of alcohols. Yield: 87%. Colorless oil. R_f = 0.49 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D = +57.35°$ (*c* 1.12, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3007, 2931, 1464, 1257, 1115 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.84 (br d, *J* = 11.8 Hz, 1H), 3.27 (m, 4H), 3.05 (ddd, *J* = 9.0, 9.0, 2.3 Hz, 1H), 2.33 (m, 1H), 1.97 (br dd, *J* = 12.4, 2.9 Hz, 1H), 1.78 (m, 1H), 1.61 (m, 2H), 1.42 (m, 1H), 0.86 (s, 9H, $(CH_3)_3CSi$), 0.04 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.22 (d), 70.93 (d), 67.77 (t), 36.78 (t), 33.56 (t), 25.79 (q, $(CH_3)_3CSi$), 25.65 (t), 17.94 (s, $(CH_3)_3CSi$), 2.87 (t), −3.94 (q, CH_3Si), −4.74 (q, CH_3Si). MS *m/e* (rel intens) 370 (M^+, 1), 313 ($[M - {}^tBu]^+$, 100). HRMS calcd for $C_{13}H_{27}IO_2Si$ $(M)^+$: 370.082510, found: 370.081932. Anal. Calcd for $C_{13}H_{27}IO_2Si$: C, 42.16; H, 7.35. Found: C, 42.16; H, 7.37.

General Procedure for Keck Reaction. To a stirring solution of the corresponding iodo compound (0.7 mmol) in dry benzene (2 mL) were added allyl tributyl tin (434 μL, 1.4 mmol, 2.0 equiv) and a catalytic amount of AIBN. After stirring at 80 °C overnight, solvent was removed under reduced pressure, and the residue was purified by flash chromatography (silica, 2.5% EtOAc in hexanes).

(2*R*,3*S*)-(2-But-3′-enyltetrahydropyran-3-yloxy)-*tert*-butyldimethylsilane (24a): colorless oil. R_f = 0.49 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D = +38.16°$ (*c* 2.01, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3003, 2930, 1640, 1463, 1362, 1258 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.81 (dddd, *J* = 17.0, 10.2, 6.5, 6.5 Hz, 1H), 4.99 (d, *J* = 17.0 Hz, 1H), 4.91 (d, *J* = 10.2 Hz, 1H), 3.84 (br d, *J* = 11.2 Hz, 1H), 3.26 (m, 2H), 2.98 (ddd, *J* = 8.9, 8.9, 2.1 Hz, 1H), 2.21 (m, 1H), 2.07 (m, 1H), 1.97 (br dd, *J* = 12.4,

3.0 Hz, 1H), 1.88 (m, 1H), 1.60 (m, 2H), 1.39 (m, 2H), 0.86 (s, 9H, (CH_3)$_3$CSi), 0.04 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.88 (d), 114.29 (t), 82.04 (d), 71.37 (d), 67.77 (t), 33.72 (t), 31.48 (t), 29.56 (t), 25.81 (t), 25.77 (q, (CH_3)$_3$CSi), 17.98 (s, (CH$_3$)$_3$$C$Si), −3.94 (q, CH_3Si), −4.71 (q, CH_3Si). MS *m/e* (rel intens) 270 (M^+, 0.2), 213 ([M − ^{t}Bu]$^+$, 16). HRMS calcd for $C_{11}H_{21}O_2Si$ (M − ^{t}Bu)$^+$: 213.1311, found: 213.1311. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.61; H, 11.18. Found: C, 66.61; H, 11.09.

(2*R*,3*S*)-*tert*-Butyldimethyl-(2-pent-4′-enyltetrahydropyran-3-yloxy)silane (24b): colorless oil. R_f = 0.50 (silica, 5% EtOAc in hexanes). $[\alpha]^{25}_D$ = +35.22° (*c* 1.27, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3003, 2858, 1639, 1463, 1362, 1219 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 3.84 (br dd, *J* = 11.5, 4.3 Hz, 1H), 3.26 (m, 2H), 2.96 (ddd, *J* = 8.9, 8.9, 2.4 Hz, 1H), 2.03 (ddd, *J* = 6.9, 6.7, 6.7 Hz, 2H), 1.96 (br dd, *J* = 12.5, 3.2 Hz, 1H), 1.81 (m, 1H), 1.61 (m, 3H), 1.39 (m, 2H), 1.28 (m, 1H), 0.86 (s, 9H, (CH_3)$_3$CSi), 0.03 (s, 6H, 2 × CH_3Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.97 (d), 114.36 (t), 82.61 (d), 71.39 (d), 67.77 (t), 33.88 (t), 33.71 (t), 31.75 (t), 25.81 (q, (CH_3)$_3$CSi), 25.81 (t), 24.76 (t), 17.98 (s, (CH$_3$)$_3$$C$Si), −3.94 (q, CH_3Si), −4.73 (q, CH_3Si). MS *m/e* (rel intens) 284 (M^+, 1), 269 ([M − CH_3]$^+$, 3). HRMS calcd for $C_{16}H_{32}O_2Si$ $(M)^+$: 284.217159, found: 284.215645. Calcd for $C_{15}H_{29}O_2Si$ (M − CH_3)$^+$: 269.193684, found 269.193001. Anal. Calcd for $C_{16}H_{32}O_2$-Si: C, 67.55; H, 11.34. Found: C, 67.42; H, 11.50.

Preparation of (2*R*,3*S*)-2-But-3′-enyltetrahydropyran-3-ol (25a). Alcohol **25a** was prepared from **24a** following the procedure described above for the deprotection of silyl ethers. Yield: 98%. Colorless oil. R_f = 0.57 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +44.42° (*c* 0.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3623, 3079, 3013, 1640, 1235 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.02 (d, *J* = 17.1 Hz, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 3.88 (br d, *J* = 11.3 Hz, 1H), 3.30 (m, 2H), 2.99 (ddd, *J* = 9.0, 9.0, 2.5 Hz, 1H), 2.26 (m, 1H), 2.10 (m, 2H), 1.91 (dddd, *J* = 14.1, 9.5, 6.8, 2.5 Hz, 1H), 1.68 (m, 2H), 1.50 (dddd, *J* = 14.1, 9.5, 9.0, 5.1 Hz, 1H), 1.42 (d, *J* = 5.5 Hz, 1H, O*H*), 1.37 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.68 (d), 114.60 (t), 81.69 (d), 70.52 (d), 67.51 (t), 33.02 (t), 31.33 (t), 29.54 (t), 25.66 (t). MS *m/e* (rel intens) 156 (M^+, 46), 138 ([M − H_2O]$^+$, 7), 120 (7), 114 ([M − C_3H_6]$^+$, 100). HRMS calcd for $C_9H_{16}O_2$ $(M)^+$: 156.115030, found: 156.115170. Calcd for $C_6H_{10}O_2$ (M − C_3H_6)$^+$: 114.068080, found 114.068691. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.23; H, 10.18.

Preparation of (2*R*,3*S*)-2-Pent-4′-enyltetrahydropyran-3-ol (25b). Alcohol **25b** was prepared from **24b** following the procedure described above for the deprotection of silyl ethers. Yield: 98%. Colorless oil. R_f = 0.59 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +39.16° (*c* 0.63, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3620, 3068, 3010, 1640, 1230 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 4.98 (d, *J* = 17.1 Hz, 1H), 4.91 (d, *J* = 10.2 Hz, 1H), 3.86 (br dd, *J* = 11.3, 4.0 Hz, 1H), 3.27 (m, 2H), 2.96 (ddd, *J* = 8.6, 8.6, 2.7 Hz, 1H), 2.06 (m, 3H), 1.82 (m, 1H), 1.63 (m, 3H), 1.55 (d, *J* = 5.0 Hz, 1H, O*H*), 1.40 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.86 (d), 114.48 (t), 82.29 (d), 70.50 (d), 67.53 (t), 33.84 (t), 32.98 (t), 31.52 (t), 25.66 (t), 24.70 (t). MS *m/e* (rel intens) 170 (M^+, 25), 152 ([M − H_2O]$^+$, 9). HRMS calcd for $C_{10}H_{18}O_2$ $(M)^+$: 170.130679, found: 170.130856. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.32; H, 10.81.

Preparation of (2*R*,3*S*)-3-Allyloxy-2-but-3″-enyltetrahydropyran (26a). This compound was prepared from **25a** following the procedure described above for O-alkylation. Yield: 83%. Colorless oil. R_f = 0.53 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +54.47° (*c* 0.44, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3080, 3008, 2928, 2360, 1640, 1454, 1262, cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (dddd, *J* = 17.2, 10.4, 5.6, 5.6 Hz, 1H), 5.82 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.23 (d, *J* = 17.2 Hz, 1H), 5.13 (d, *J* = 10.4 Hz, 1H), 5.00 (d, *J* = 17.1 Hz, 1H), 4.91 (d, *J* = 10.2 Hz, 1H), 4.07 (dd, *J* = 12.6, 5.6 Hz, 1H), 3.90 (dd, *J* = 12.6, 5.6 Hz, 1H), 3.85 (br dd, *J* = 11.5, 4.5 Hz, 1H), 3.28 (ddd, *J* = 11.5, 11.5, 2.8 Hz, 1H), 3.07 (ddd, *J* = 8.9, 8.9, 2.5 Hz, 1H), 2.99 (ddd, *J* = 10.5, 8.9, 4.4 Hz, 1H), 2.22 (m, 2H), 2.07 (m, 1H), 1.94 (dddd, *J* = 14.0, 9.3, 6.6, 2.5 Hz, 1H), 1.60 (m, 2H), 1.43 (dddd, *J* = 14.0, 9.5, 9.3, 5.0 Hz, 1H), 1.31 (dddd, *J* = 12.6, 12.6, 10.5, 4.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.87 (d), 135.15 (d), 116.80 (t), 114.36 (t), 80.38 (d), 77.34 (d), 69.87 (t), 67.62 (t), 31.59 (t), 29.72 (t), 29.43 (t), 25.49 (t). MS *m/e* (rel intens) 196 (M^+, 11). HRMS calcd for $C_{12}H_{20}O_2$ $(M)^+$: 196.146330, found: 196.146954. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.48; H, 10.36.

Preparation of (2*R*,3*S*)-2-But-3″-enyl-3-pent-4′-enyloxytetrahydropyran (26b). This compound was prepared from **25a** following the procedure described above for O-alkylation. Yield: 73%. Colorless oil. R_f = 0.55 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +25.45° (*c* 0.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3008, 2927, 2360, 2338, 1640 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (m, 2H), 5.01 (m, 2H), 4.93 (m, 2H), 3.86 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.58 (ddd, *J* = 9.2, 6.3, 6.3 Hz, 1H), 3.33 (m, 2H), 3.05 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H), 2.91 (ddd, *J* = 10.6, 9.0, 4.4 Hz, 1H), 2.22 (m, 2H), 2.08 (m, 3H), 1.93 (m, 1H), 1.63 (m, 4H), 1.44 (m, 1H), 1.28 (dddd, *J* = 12.5, 12.5, 10.6, 4.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.92 (d), 138.27 (d), 114.79 (t), 114.33 (t), 80.48 (d), 77.95 (d), 68.18 (t), 67.68 (t), 31.64 (t), 30.32 (t), 29.71 (t), 29.47 (t), 29.27 (t), 25.53 (t). MS *m/e* (rel intens) 224 (M^+, 61), 182 ([M − C_3H_6]$^+$, 11). HRMS calcd for $C_{14}H_{24}O_2$ $(M)^+$: 224.177630, found: 224.177639. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.02; H, 10.86.

Preparation of (2*R*,3*S*)-2-Pent-4″-enyl-3-pent-4′-enyloxytetrahydropyran (26c). This compound was prepared from **25b** following the procedure described above for O-alkylation. Yield: 73%. Colorless oil. R_f = 0.58 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +41.26° (*c* 0.99, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3079, 3004, 2942, 2857, 2360, 1639, 1439 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (m, 2H), 4.96 (m, 4H), 3.85 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.57 (ddd, *J* = 9.2, 6.3, 6.3 Hz, 1H), 3.29 (m, 2H), 3.03 (ddd, *J* = 8.9, 8.9, 2.7 Hz, 1H), 2.89 (ddd, *J* = 10.6, 8.9, 4.4 Hz, 1H), 2.17 (br dd, *J* = 12.3, 3.1 Hz, 1H), 2.06 (m, 4H), 1.83 (m, 1H), 1.61 (m, 5H), 1.40 (m, 2H), 1.29 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.01 (d), 138.28 (d), 114.76 (t), 114.30 (t), 81.01 (d), 77.92 (d), 68.15 (t), 67.69 (t), 33.93 (t), 31.82 (t), 30.32 (t), 29.47 (t), 29.28 (t), 25.52 (t), 24.83 (t). MS *m/e* (rel intens) 238 (M^+, 17). HRMS calcd for $C_{15}H_{26}O_2$ $(M)^+$: 238.193280, found: 238.193325. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.72; H, 11.22.

General Procedure for Olefin Metathesis. The amount of catalyst necessary in each case was weighed and dissolved in dry CH_2Cl_2 or benzene (see tables) in a flame-dried vessel. A solution of the corresponding diene in CH_2Cl_2 or benzene was then added dropwise *via cannula* to the above solution under an atmosphere of dry argon (final concentration of diene was 5 × 10^{-3} M). When addition finished, the vessel was sealed, and the reaction mixture was stirred at room temperature or at the temperature shown on the tables. Progress of reaction was tested by TLC and NMR. When reaction finished or when no further progress was observed, solvent was removed in vacuo, and the residue was purified by flash chromatography, affording the expected unsaturated cycle.

(*Z*)-(4a*S*,9a*R*)-3,4,4a,6,7,9a-Hexahydro-2*H*-1,5-dioxabenzocycloheptene (27): colorless liquid. R_f = 0.49 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = −9.58° (*c* 0.18, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3008, 2928, 2856, 1452 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (dddd, *J* = 12.1, 8.5, 3.5, 3.5 Hz, 1H, C*H*═CH), 5.58 (ddd, *J* = 12.1, 2.3, 2.3 Hz, 1H, CH═C*H*), 4.00 (ddd, *J* = 11.8, 3.5, 3.5 Hz, 1H), 3.86 (br dd, *J* = 11.3, 3.9 Hz, 1H), 3.73 (br dd, *J* = 8.9, 2.3 Hz, 1H), 3.46 (ddd, *J* = 11.8, 11.8, 1.7 Hz, 1H), 3.27 (m, 1H), 3.03 (ddd, *J* = 11.0, 8.9, 4.6 Hz, 1H), 2.41 (dddd, *J* = 13.5, 11.8, 3.5, 3.5 Hz, 1H), 2.06 (m, 2H), 1.64 (m, 2H), 1.42 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.24 (d, *C*H═CH), 127.54 (d, CH═*C*H), 82.39 (d), 78.80 (d), 71.03 (t), 67.39 (t), 31.85 (t), 31.10 (t), 25.40 (t). HRMS calcd for $C_9H_{15}O_2$ $(M+H)^+$: 155.10720, found: 155.10891. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 9.42.

(*Z*)-(4a*S*,9a*R*)-3,4,4a,6,9,9a-Hexahydro-2*H*-1,5-dioxabenzocycloheptene (28): colorless liquid. R_f = 0.49 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = −4.96° (*c* 0.4, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3035, 3008, 2928, 2360, 1463 cm^{-1}. ^{1}H NMR (500 MHz,

$CDCl_3$) δ 5.91 (m, 1H, C*H*=CH), 5.85 (dddd, J = 11.1, 11.1, 2.7, 2.7 Hz, 1H, CH=C*H*), 4.19 (dd, J = 14.9, 6.2 Hz, 1H), 3.99 (br dd, J = 14.9, 3.8 Hz, 1H), 3.85 (br dd, J = 11.1, 4,2 Hz, 1H), 3.30 (ddd, J = 11.1, 11.1, 3.5 Hz, 1H), 3.21 (ddd, J = 11.0, 8.8, 4.7 Hz, 1H), 3.02 (ddd, J = 10.4, 8.8, 3.6 Hz, 1H), 2.49 (ddd, J = 11.1, 8.1, 3.6 Hz, 1H), 2.35 (m, 1H), 2.06 (br dd, J = 12.5, 3.1 Hz, 1H), 1.69 (m, 2H), 1.46 (dddd, J = 12.5, 12.5, 11.0, 5.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.94 (d, *C*H=CH), 128.70 (d, CH=*C*H), 83.30 (d), 78.51 (d), 67.55 (t), 67.49 (t), 35.11 (t), 31.32 (t), 25.83 (t). HRMS calcd for $C_9H_{14}O_2$ $(M)^+$: 154.099379, found: 154.099948. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.32; H, 9.34.

(*Z*)-(4a*S*,10a*R*)-2,3,4,4a,6,7,8,10a-Octahydro-1,5-dioxabenzocyclooctene (29): colorless liquid. R_f = 0.50 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +14.69° (*c* 0.82, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3026, 3009, 2946, 1464, 1354 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.54 (m, 2H, 2 × C*H*=CH), 3.93 (dd, J = 12.1, 5.6 Hz, 1H), 3.84 (m, 2H), 3.47 (ddd, J = 12.1, 12.1, 3.8 Hz, 1H), 3.26 (m, 1H), 2.99 (ddd, J = 10.7, 9.2, 4.6 Hz, 1H), 2.39 (dddd, J = 13.2, 10.0, 10.0, 5.5 Hz, 1H), 2.07 (br dd, J = 12.6, 2.9 Hz, 1H), 2.00 (m, 1H), 1.90 (m, 1H), 1.64 (m, 2H), 1.42 (m, 1H), 1.29 (dddd, J = 13.5, 13.2, 4.6, 4.6 Hz, 1H). ^{1}H NMR (500 MHz, C_6D_6) δ 5.97 (dd, J = 11.0, 5.2 Hz, 1H, C*H*=CH), 5.44 (dddd, J = 11.0, 10.5, 10.5, 1.9 Hz, 1H, CH=C*H*), 3.92 (m, 2H), 3.77 (br d, J = 11.3 Hz, 1H), 3.39 (ddd, J = 12.0, 12.0, 3.8 Hz, 1H), 3.07 (ddd, J = 11.7, 11.7, 2.2 Hz, 1H), 3.00 (ddd, J = 10.3, 9.1, 4.7 Hz, 1H), 2.54 (dddd, J = 13.0, 10.5, 10.5, 5.5 Hz, 1H), 2.06 (m, 1H), 1.85 (m, 2H), 1.48 (m, 2H), 1.26 (br d, J = 10.7 Hz, 1H), 1.06 (dddd, J = 13.5, 13.0, 4.4, 3.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.60 (d, *C*H=CH), 127.40 (d, CH=*C*H), 80.07 (d), 79.73 (d), 68.11 (t), 67.24 (t), 31.32 (t), 29.10 (t), 25.58 (t), 23.40 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 134.66 (d, *C*H=CH), 126.61 (d, CH=*C*H), 80.45 (d), 80.05 (d), 67.84 (t), 66.92 (t), 31.68 (t), 29.34 (t), 25.74 (t), 23.51 (t). MS *m/e* (rel intens) 168 (M^+, 18). HRMS calcd for $C_{10}H_{16}O_2$ $(M)^+$: 168.115029, found: 168.116284. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.55; H, 9.88.

(*Z*)-(4a*S*,10a*R*)-2,3,4,4a,6,7,10,10a-Octahydro-1,5-dioxabenzocyclooctene (30): colorless liquid. R_f = 0.50 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +51.13° (*c* 1.01, $CHCl_3$). IR ($CHCl_3$) ν_{max} 2950, 2850, 1650, 1600, 1460, 1440 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (m, 2H, 2 × C*H*=CH), 3.83 (br dd, J = 11.4, 4.5 Hz, 1H), 3.72 (ddd, J = 11.6, 5.6, 5.6 Hz, 1H), 3.52 (ddd, J = 11.6, 5.6, 5.6 Hz, 1H), 3.28 (ddd, J = 11.4, 11.4, 3.5 Hz, 1H), 3.14 (m, 2H), 2.58 (ddd, J = 11.2, 8.0, 2.6 Hz, 1H), 2.26 (m, 3H), 1.98 (br d, J = 12.2 Hz, 1H), 1.62 (m, 2H), 1.40 (m, 1H). ^{1}H NMR (500 MHz, C_6D_6) δ 5.95 (ddd, J = 10.2, 9.2, 6.8 Hz, 1H, C*H*=CH), 5.70 (ddd, J = 10.2, 9.5, 8.0 Hz, 1H, CH=C*H*), 3.71 (br dd, J = 11.3, 2.9 Hz, 1H), 3.62 (ddd, J = 10.7, 6.9, 3.6 Hz, 1H), 3.21 (m, 2H), 3.10 (ddd, J = 9.4, 9.0, 4.5 Hz, 1H), 3.05 (m, 1H), 2.75 (ddd, J = 13.3, 9.2, 3.8 Hz, 1H), 2.42 (ddd, J = 13.3, 6.8, 6.5 Hz, 1H), 2.09 (m, 1H), 1.90 (m, 2H), 1.38 (m, 2H), 1.23 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.25 (d, *C*H=CH), 128.72 (d, CH=*C*H), 82.22 (d), 77.97 (d), 69.26 (t), 68.05 (t), 31.66 (t), 31.63 (t), 28.93 (t), 26.15 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 129.25 (d, *C*H=CH), 129.12 (d, CH=*C*H), 82.69 (d), 77.93 (d), 69.10 (t), 67.67 (t), 31.82 (t, 2C), 29.27 (t), 26.38 (t). MS *m/e* (rel intens) 168 (M^+, 25). HRMS calcd for $C_{10}H_{16}O_2$ $(M)^+$: 168.11503, found: 168.11487. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.32; H, 9.63.

(*Z*)-(4a*S*,10a*R*)-2,3,4,4a,6,9,10,10a-Octahydro-1,5-dioxabenzocyclooctene (31): colorless liquid. R_f = 0.50 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +34.17° (*c* 0.4, $CHCl_3$). IR ($CHCl_3$) ν_{max} 2949, 2847, 1651, 1600, 1459, 1443 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (ddd, J = 11.5, 9.0, 8.6 Hz, 1H, C*H*=CH), 5.25 (br d, J = 11.5 Hz, 1H, CH=C*H*), 4.44 (d, J = 17.2 Hz, 1H), 4.06 (br dd, J = 17.2, 3.7 Hz, 1H), 3.82 (br dd, J = 11.2, 4.4 Hz, 1H), 3.24 (m, 3H), 2.61 (m, 1H), 2.07 (m, 3H), 1.59 (m, 2H), 1.42 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.06 (d, *C*H=CH), 126.91 (d, CH=*C*H), 79.78 (d), 77.97 (d), 69.32 (t), 67.42 (t), 34.09 (t), 30.64 (t), 25.66 (t), 22.56 (t). HRMS calcd for $C_{10}H_{16}O_2$ $(M)^+$: 168.115029, found: 168.115942. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.62; H, 9.64.

(*Z*)-(4a*S*,11a*R*)-3,4,4a,6,7,8,11,11a-Octahydro-2*H*-1,5-dioxabenzocyclononene (32): colorless liquid. R_f = 0.55 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +26.78° (*c* 0.42, $CHCl_3$). IR ($CHCl_3$) ν_{max} 2949, 2853, 1648, 1600, 1443, 1328 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.63 (m, 2H, 2 × C*H*=CH), 3.93 (ddd, J = 11.0, 5.5, 5.5 Hz, 1H), 3.85 (br dd, J = 11.2, 4.2 Hz, 1H), 3.45 (m, 1H), 3.30 (ddd, J = 11.2, 11.2, 3.7 Hz, 1H), 3.16 (ddd, J = 9.1, 8.8, 3.9 Hz, 1H), 3.09 (ddd, J = 10.9, 9.1, 4.1 Hz, 1H), 2.73 (ddd, J = 12.8, 9.1, 4.1 Hz, 1H), 2.38 (dddd, J = 12.5, 9.0, 8.5, 3.6 Hz, 1H), 2.26 (m, 1H), 2.07 (m, 2H), 1.72 (m, 1H), 1.60 (m, 3H), 1.37 (m, 1H). ^{1}H NMR (500 MHz, C_6D_6) δ 5.90 (ddd, J = 10.5, 10.5, 7.1 Hz, 1H, C*H*=CH), 5.65 (ddd, J = 10.5, 10.5, 7.1 Hz, 1H, CH=C*H*), 3.79 (m, 2H), 3.27 (m, 2H), 3.13 (m, 2H), 3.04 (ddd, J = 13.5, 10.5, 3.5 Hz, 1H), 2.48 (m, 2H), 1.95 (m, 2H), 1.44 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.42 (d, *C*H=CH), 126.04 (d, CH=*C*H), 80.26 (d, 2C), 68.33 (t), 65.81 (t), 30.69 (t), 30.42 (t), 27.51 (t), 26.03 (t), 22.67 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 132.07 (d), 126.54 (d), 80.47 (d), 78.80 (d), 69.05 (t), 67.93 (t), 30.63 (t), 30.38 (t), 27.65 (t), 26.25 (t), 22.37 (t). HRMS calcd for $C_{11}H_{18}O_2$ $(M)^+$: 182.130679, found: 182.131598. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.56; H, 10.09.

(*Z*)-(4a*S*,12a*R*)-2,3,4,4a,6,7,8,11,12,12a-Decahydro-1,5-dioxabenzocyclodecene (33): colorless oil. R_f = 0.55 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +31.18° (*c* 0.24, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3025, 3008, 2944, 2872, 1463 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 (ddd, J = 10.5, 8.4, 8.0 Hz, 1H, C*H*=CH), 5.27 (ddd, J = 10.5, 9.6, 8.0 Hz, 1H, CH=C*H*), 3.80 (br dd, J = 11.2, 4.1 Hz, 1H), 3.60 (ddd, J = 8.2, 4.7, 4.7 Hz, 1H), 3.24 (m, 3H), 3.01 (ddd, J = 10.6, 9.2, 4.9 Hz, 1H), 2.34 (m, 3H), 2.04 (m, 3H), 1.69 (m, 1H), 1.60 (m, 2H), 1.48 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.01 (d, *C*H=CH), 125.80 (d, CH=*C*H), 80.36 (d), 78.50 (d), 67.48 (t), 65.04 (t), 35.30 (t), 29.42 (t), 26.80 (t), 25.55 (t), 22.90 (t), 22.34 (t). HRMS calcd for $C_{12}H_{20}O_2$ $(M)^+$: 196.146330, found: 196.146987. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.29; H, 10.39.

(*E*)-(4a*S*,13a*R*)-3,4,4a,6,7,8,9,10,11,13a-Decahydro-2*H*-1,5-dioxabenzocycloundecene (34): colorless oil. R_f = 0.56 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +22.09° (*c* 0.53, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3028, 3008, 2945, 2870, 1462, 1354 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddd, J = 15.1, 11.0, 4.1 Hz, 1H, C*H*=CH), 5.37 (ddd, J = 15.1, 9.0, 1.0 Hz, 1H, CH=C*H*), 3.86 (br d, J = 11.4 Hz, 1H), 3.67 (ddd, J = 9.2, 3.6, 3.6 Hz, 1H), 3.48 (m, 2H), 3.32 (m, 1H), 2.92 (ddd, J = 11.3, 9.2, 4.6 Hz, 1H), 2.31 (ddddd, J = 13.1, 9.4, 4.1, 4.1, 1.0 Hz, 1H), 2.11 (br dd, J = 12.4, 3.1 Hz, 1H), 1.95 (dddd, J = 13.1, 12.4, 11.0, 4.5 Hz, 1H), 1.64 (m, 4H), 1.44 (m, 2H), 1.21 (m, 4H), 1.04 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.25 (d, *C*H=CH), 128.56 (d, CH=*C*H), 84.43 (d), 78.57 (d), 68.46 (t), 67.40 (t), 34.39 (t), 30.94 (t), 29.12 (t), 25.99 (t), 25.96 (t), 24.91 (t), 23.87 (t). MS *m/e* (rel intens) 210 (M^+, 21), 153 ($[M - C_4H_9]^+$, 8). HRMS calcd for $C_{13}H_{22}O_2$ $(M)^+$: 210.161980, found: 210.162152; calcd for $C_9H_{13}O_2$ $(M - C_4H_9)^+$: 153.091555, found: 153.090822. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.55; H, 10.72.

(*E*)-(4a*S*,13a*R*)-3,4,4a,6,7,8,11,12,13,13a-Decahydro-2*H*-1,5-dioxabenzocycloundecene (35): colorless oil. R_f = 0.56 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = +23.89° (*c* 0.35, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3030, 3007, 2946, 2868, 1465, 1352 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (ddd, J = 15.1, 10.5, 4.6 Hz, 1H, C*H*=CH), 5.32 (dddd, J = 15.1, 10.8, 5.1, 1.2 Hz, 1H, CH=C*H*), 3.92 (br dd, J = 9.5, 4.8 Hz, 1H), 3.82 (br dd, J = 11.5, 4.4 Hz, 1H), 3.29 (ddd, J = 11.5, 11.5, 3.0 Hz, 1H), 3.11 (m, 1H), 2.99 (m, 2H), 2.31 (br d, J = 13.3 Hz, 1H), 2.19 (br dd, J = 12.2, 3.1 Hz, 1H), 2.13 (m, 1H), 1.87 (m, 1H), 1.77 (m, 1H), 1.59 (m, 6H), 1.24 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.96 (d, *C*H=CH), 128.12 (d, CH=*C*H), 80.73 (d), 73.76 (d), 69.69 (t), 67.94 (t), 33.98 (t), 32.47 (t), 29.13 (t), 28.93 (t), 26.29 (t), 25.29 (t), 20.53 (t). HRMS calcd for $C_{13}H_{22}O_2$ $(M)^+$: 210.161980, found: 210.162008. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.48; H, 10.82.

(*E*)-(4a*S*,14a*R*)-2,3,4,4a,6,7,8,9,10,11,12,14a-Dodecahydro-1,5-dioxabenzocyclododecene (36): colorless oil. R_f = 0.57 (silica, 10% EtOAc in hexanes). $[\alpha]^{25}_D$ = −2.53° (*c* 0.48, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3009, 2946, 2872, 1463, 1355 cm^{-1}. ^{1}H NMR

(500 MHz, $CDCl_3$) δ 5.73 (ddd, J = 15.1, 10.8, 4.0 Hz, 1H, C*H*═CH), 5.35 (ddd, J = 15.1, 8.8, 1.5 Hz, 1H, CH═C*H*), 3.87 (br dd, J = 11.1, 4.1 Hz, 1H), 3.76 (ddd, J = 9.1, 4.1, 4.1 Hz, 1H), 3.49 (dd, J = 9.1, 8.8 Hz, 1H), 3.33 (m, 1H), 3.20 (ddd, J = 9.1, 9.1, 2.5 Hz, 1H), 2.87 (ddd, J = 10.9, 9.1, 4.5 Hz, 1H), 2.31 (m, 1H), 2.20 (br dd, J = 12.5, 3.1 Hz, 1H), 1.91 (m, 1H), 1.65 to 0.85 (13H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.64 (d, *C*H═CH), 128.07 (d, CH═*C*H), 83.36 (d), 78.29 (d), 68.65 (t), 67.51 (t), 32.32 (t), 29.78 (t), 28.54 (t), 28.33 (t), 25.54 (t), 24.63 (t), 24.45 (t), 23.65 (t). HRMS calcd for $C_{14}H_{24}O_2$ $(M)^+$: 224.177630, found: 224.178159. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.04; H, 10.88.

Preparation of (2*R*,3*S*)-3-Allyloxy-2-allyloxymethyltetrahydropyran (37a). This compound was prepared from **2** according to the procedure described above (see general procedure for O-alkylation), using 3.0 equiv of allyl bromide and 2.2 equiv of NaH. Yield: 73%. Colorless oil. R_f = 0.31 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +57.28° (*c* 0.6, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3009, 2944, 2860, 1647, 1458 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (m, 2H), 5.23 (m, 2H), 5.13 (m, 2H), 4.02 (m, 3H), 3.91 (m, 2H), 3.66 (br d, J = 10.3 Hz, 1H), 3.57 (dd, J = 10.3, 4.5 Hz, 1H), 3.33 (m, 1H), 3.26 (m, 2H), 2.20 (br d, J = 12.4 Hz, 1H), 1.65 (m, 2H), 1.33 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.09 (d), 134.92 (d), 117.08 (t), 116.69 (t), 80.46 (d), 73.31 (d), 72.52 (t), 69.90 (t), 69.85 (t), 67.87 (t), 29.48 (t), 25.19 (t). MS *m*/*e* (rel intens) 211 ($[M - 1]^+$, 9). HRMS calcd for $C_{12}H_{19}O_3$ $(M - H)^+$: 211.133419, found: 211.133021. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.85; H, 9.53.

Preparation of (2*R*,3*S*)-3-Pent-4′-enyloxy-2-pent-4‴-enyloxymethyltetrahydropyran (37b). This compound was prepared from **2** according to the procedure described above (see general procedure for O-alkylation), using 3.0 equiv of 5-bromo-1-pentene and 2.2 equiv of KO-*t*-Bu, and heating overnight at 65 °C. Yield: 62%. Colorless oil. R_f = 0.40 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +46.89° (*c* 0.72, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3080, 3009, 2941, 2855, 1641, 1465 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (m, 2H), 4.97 (m, 4H), 3.92 (br d, J = 12.1 Hz, 1H), 3.65 (dd, J = 10.4, 1.9 Hz, 1H), 3.57 (m, 2H), 3.49 (ddd, J = 9.5, 6.7, 6.7 Hz, 1H), 3.42 (ddd, J = 9.5, 6.8, 6.8 Hz, 1H), 3.33 (m, 2H), 3.23 (ddd, J = 9.3, 5.2, 1.9 Hz, 1H), 3.18 (ddd, J = 10.4, 9.3, 4.5 Hz, 1H), 2.21 (br dd, J = 12.4, 2.9 Hz, 1H), 2.09 (m, 4H), 1.65 (m, 6H), 1.31 (dddd, J = 12.4, 10.4, 10.4, 5.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.41 (d), 138.25 (d), 114.80 (t), 114.59 (t), 80.50 (d), 73.77 (d), 71.07 (t), 70.67 (t), 68.20 (t), 67.92 (t), 30.34 (t), 30.30 (t), 29.45 (t), 29.27 (t), 28.72 (t), 25.21 (t). MS *m*/*e* (rel intens) 268 (M^+, 10). HRMS calcd for $C_{16}H_{28}O_3$ $(M)^+$: 268.203845, found: 268.204862. Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 71.54; H, 10.68.

Preparation of (2*R*,3*S*)-3-Allyloxy-2-pent-4‴-enyloxymethyltetrahydropyran (38a). This compound was prepared from **5a** according to the procedure described above (see general procedure for O-alkylation). Yield: 73%. Colorless oil. R_f = 0.51 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D$ = +54.98° (*c* 0.74, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3081, 3009, 2941, 2857, 1640, 1464, 1329 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dddd, J = 17.2, 10.5, 5.6, 5.6 Hz, 1H), 5.78 (dddd, J = 17.1, 10.2, 6.6, 6.6 Hz, 1H), 5.23 (d, J = 17.2 Hz, 1H), 5.13 (d, J = 10.5 Hz, 1H), 4.99 (d, J = 17.1 Hz, 1H), 4.92 (d, J = 10.2 Hz, 1H), 4.07 (dd, J = 12.6, 5.6 Hz, 1H), 3.91 (m, 2H), 3.65 (br d, J = 10.4 Hz, 1H), 3.56 (dd, J = 10.4, 4.8 Hz, 1H), 3.50 (ddd, J = 9.5, 6.7, 6.7 Hz, 1H), 3.41 (ddd, J = 9.5, 6.8, 6.8 Hz, 1H), 3.32 (m, 1H), 3.27 (m, 2H), 2.21 (br d, J = 12.3 Hz, 1H), 2.10 (m, 2H), 1.66 (m, 4H), 1.34 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.39 (d), 135.10 (d), 116.72 (t), 114.59 (t), 80.49 (d), 73.34 (d), 71.04 (t), 70.59 (t), 69.93 (t), 67.89 (t), 30.38 (t), 29.49 (t), 28.72 (t), 25.20 (t). MS *m*/*e* (rel intens) 240 (M^+, 8). HRMS calcd for $C_{14}H_{24}O_3$ $(M)^+$: 240.172545, found: 240.171764. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.99; H, 9.75.

Preparation of (2*R*,3*S*)-2-Allyloxymethyl-3-but-3′-enyloxytetrahydropyran (38b). This compound was prepared from **10b** according to the procedure described above (see general procedure for O-alkylation). Yield: 99%. Colorless liquid. R_f = 0.33 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +56.74° (*c* 1.6, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3082, 3009, 2944, 2861, 1642, 1464 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (dddd, J = 17.2, 10.3, 5.8, 5.8 Hz, 1H), 5.77 (dddd, J = 17.2, 10.3, 6.7, 6.7 Hz, 1H), 5.24 (d, J = 17.2 Hz, 1H), 5.14 (d, J = 10.3 Hz, 1H), 5.05 (d, J = 17.2 Hz, 1H), 4.99 (d, J = 10.3 Hz, 1H), 4.00 (m, 2H), 3.91 (br d, J = 11.8 Hz, 1H), 3.63 (m, 2H), 3.55 (dd, J = 10.3, 5.1 Hz, 1H), 3.34 (m, 2H), 3.21 (m, 2H), 2.26 (m, 2H), 2.21 (br d, J = 12.1 Hz, 1H), 1.63 (m, 2H), 1.31 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.33 (d), 134.94 (d), 117.12 (t), 116.32 (t), 80.42 (d), 73.84 (d), 72.53 (t), 69.88 (t), 68.29 (t), 67.88 (t), 34.51 (t), 29.40 (t), 25.19 (t). MS *m*/*e* (rel intens) 227 ($[M+1]^+$, 50), 226 (M^+, 81). HRMS calcd for $C_{13}H_{22}O_3$ $(M)^+$: 226.156895, found: 226.157829. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.98; H, 9.86.

Preparation of (2*R*,3*S*)-3-But-3′-enyloxy-2-pent-4‴-enyloxymethyltetrahydropyran (38c). This compound was prepared from **10b** according to the procedure described above (see general procedure for O-alkylation). Yield: 72%. Colorless liquid. R_f = 0.36 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +50.90° (*c* 1.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3080, 3007, 2944, 2866, 1640, 1440 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (m, 2H), 4.99 (m, 4H), 3.91 (br d, J = 11.5 Hz, 1H), 3.62 (m, 2H), 3.54 (dd, J = 10.4, 4.9 Hz, 1H), 3.48 (ddd, J = 9.5, 6.7, 6.7 Hz, 1H), 3.36 (m, 3H), 3.20 (m, 2H), 2.26 (m, 2H), 2.21 (br d, J = 12.3 Hz, 1H), 2.07 (m, 2H), 1.68 (m, 2H), 1.61 (m, 2H), 1.31 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.39 (d), 135.31 (d), 116.33 (t), 114.56 (t), 80.49 (d), 73.85 (d), 71.02 (t), 70.61 (t), 68.33 (t), 67.87 (t), 34.54 (t), 38.28 (t), 29.42 (t), 28.72 (t), 25.20 (t). MS *m*/*e* (rel intens) 254 (M^+, 11), 213 ($[M - C_3H_5]^+$, 10). HRMS calcd for $C_{15}H_{26}O_3$ $(M)^+$: 254.188195, found: 254.187764; calcd for $C_{12}H_{21}O_3$ $(M - C_3H_5)^+$: 213.149070, found: 213.149290. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.84; H, 9.92.

Preparation of (2*R*,3*S*)-(2-Allyloxymethyltetrahydropyran-3-yloxy)-*tert*-butyldimethylsilane (39). This compound was prepared from **19** according to the procedure described above (see general procedure for O-alkylation). Yield: 92%. Colorless oil. R_f = 0.50 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +45.86° (*c* 1.3, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3008, 2952, 2931, 2858, 2360, 1472, 1463 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (dddd, J = 17.2, 10.4, 5.8, 5.8 Hz, 1H), 5.23 (d, J = 17.2 Hz, 1H), 5.13 (d, J = 10.4 Hz, 1H), 3.98 (m, 2H), 3.90 (br dd, J = 11.5, 4.5 Hz, 1H), 3.64 (dd, J = 10.2, 1.8 Hz, 1H), 3.49 (m, 2H), 3.31 (ddd, J = 11.5, 11.5, 2.4 Hz, 1H), 3.18 (ddd, J = 8.5, 8.0, 1.8 Hz, 1H), 1.98 (br d, J = 12.3 Hz, 1H), 1.63 (m, 2H), 1.39 (m, 1H), 0.84 (s, 9H, $(CH_3)_3$CSi), 0.02 (s, 3H, C*H*$_3$-Si), 0.01 (s, 3H, C*H*$_3$Si). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.89 (d), 117.21 (t), 81.98 (d), 72.56 (t), 69.96 (t), 67.89 (t), 67.32 (d), 33.53 (t), 25.76 (q, $(CH_3)_3$CSi), 25.40 (t), 17.90 (s, $(CH_3)_3$*C*Si), −4.05 (q, *C*H$_3$Si), −4.95 (q, *C*H$_3$Si). MS *m*/*e* (rel intens) 285 ($[M - 1]^+$, 4). HRMS calcd for $C_{15}H_{31}O_3Si$ $(M + H)^+$: 287.204249, found: 287.203597. Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.55. Found: C, 62.91; H, 10.38.

Preparation of (2*R*,3*S*)-2-Allyloxymethyltetrahydropyran-3-ol (40). This compound was prepared from **39** according to the procedure described above (see general procedure for deprotection of silyl ethers). Yield: 95%. Colorless liquid. R_f = 0.23 (silica, 40% EtOAc in hexanes). $[\alpha]^{25}_D$ = −2.97° (*c* 1.1, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3614, 3496, 3012, 2946, 2861 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (dddd, J = 17.2, 10.5, 5.7, 5.7 Hz, 1H), 5.24 (d, J = 17.2 Hz, 1H), 5.17 (d, J = 10.5 Hz, 1H), 4.01 (br d, J = 5.7 Hz, 2H), 3.88 (br dd, J = 11.4, 4.4 Hz, 1H), 3.66 (dd, J = 9.8, 5.0 Hz, 1H), 3.59 (dd, J = 9.8, 5.7 Hz, 1H), 3.52 (m, 1H), 3.31 (ddd, J = 11.4, 11.4, 3.5 Hz, 1H), 3.22 (ddd, J = 9.0, 5.7, 5.0 Hz, 1H), 2.74 (d, J = 2.9 Hz, 1H, O*H*), 2.09 (br d, J = 12.5 Hz, 1H), 1.65 (m, 2H), 1.39 (dddd, J = 12.5, 12.5, 11.0, 5.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.20 (d), 117.63 (t), 79.60 (d), 72.67 (t), 71.98 (t), 69.34 (d), 67.72 (t), 32.09 (t), 25.13 (t). MS *m*/*e* (rel intens) 171 ($[M - 1]^+$, 32). HRMS calcd for $C_9H_{15}O_3$ $(M - H)^+$: 171.102118, found: 171.101957. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.75; H, 9.63.

Preparation of (2*R*,3*S*)-2-Allyloxymethyl-3-pent-4′-enyloxytetrahydropyran (41). This compound was prepared

from **40** according to the procedure described above (see general procedure for O-alkylation). Yield: 69%. Colorless liquid. R_f = 0.47 (silica, 20% EtOAc in hexanes). $[\alpha]^{25}_D$ = +49.47° (*c* 0.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3081, 3009, 2865, 1640 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.91 (dddd, *J* = 17.3, 10.4, 5.8, 5.8 Hz, 1H), 5.78 (dddd, *J* = 17.1, 10.2, 6.7, 6.7 Hz, 1H), 5.25 (d, *J* = 17.3 Hz, 1H), 5.15 (d, *J* = 10.4 Hz, 1H), 5.00 (d, *J* = 17.1 Hz, 1H), 4.94 (d, *J* = 10.2 Hz, 1H), 4.01 (m, 2H), 3.92 (br d, *J* = 11.8 Hz, 1H), 3.67 (dd, *J* = 10.3, 1.8 Hz, 1H), 3.57 (m, 2H), 3.33 (m, 2H), 3.25 (ddd, *J* = 9.3, 5.4, 1.8 Hz, 1H), 3.18 (ddd, *J* = 10.0, 9.3, 4.5 Hz, 1H), 2.21 (br d, *J* = 12.3 Hz, 1H), 2.09 (m, 2H), 1.62 (m, 4H), 1.31 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.26 (d), 134.94 (d), 117.16 (t), 114.78 (t), 80.47 (d), 73.77 (d), 72.56 (t), 69.94 (t), 68.14 (t), 67.91 (t), 30.31 (t), 29.44 (t), 29.25 (t), 25.20 (t). MS *m*/*e* (rel intens) 240 (M^+, 10), 198 ($[M - C_3H_6]^+$, 10). HRMS calcd for $C_{14}H_{24}O_3$ $(M)^+$: 240.172545, found: 240.172242; calcd for $C_{11}H_{18}O_3$ $(M - C_3H_6)^+$: 198.125595, found: 198.125529. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.82; H, 10.46.

Preparation of (*Z*)-(4a*S*,12a*R*)-2,3,4,4a,7,10,12,12a-Octahydro-6*H*-1,5,11-trioxabenzocyclodecene (42). See general procedure for metathesis. Colorless oil. R_f = 0.19 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +114.07° (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3011, 2942, 2865, 1602, 1460 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.78 (dddd, *J* = 11.1, 11.1, 5.0, 2.5 Hz, 1H, C*H*═CH), 5.66 (dddd, *J* = 11.1, 6.0, 2.3, 1.6 Hz, 1H, CH═C*H*), 4.50 (dddd, *J* = 14.3, 3.3, 2.5, 2.3 Hz, 1H), 4.07 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.95 (br dd, *J* = 11.3, 4.4 Hz, 1H), 3.83 (dd, *J* = 14.3, 6.0 Hz, 1H), 3.72 (m, 2H), 3.64 (ddd, *J* = 11.2, 9.2, 4.2 Hz, 1H), 3.46 (d, *J* = 10.2 Hz, 1H), 3.34 (m, 2H), 3.13 (br dd, *J* = 9.2, 2.7 Hz, 1H), 2.16 (br dd, *J* = 12.1, 3.3 Hz, 1H), 1.74 (m, 3H), 1.34 (dddd, *J* = 12.1, 11.2, 10.7, 5.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.46 (d, *C*H═CH), 127.82 (d, CH═*C*H), 81.06 (d), 70.04 (d), 68.43 (t), 67.06 (t), 66.03 (t), 65.48 (t), 29.25 (t), 28.64 (t), 25.89 (t). MS *m*/*e* (rel intens) 198 (M^+, 17), 155 ($[M - C_2H_3O]^+$, 8). HRMS calcd for $C_{11}H_{18}O_3$ $(M)^+$: 198.125595, found: 198.126341; calcd for $C_6H_{10}O_2$ $(M - C_5H_8O)^+$: 114.068080, found: 114.068200. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.72; H, 9.23.

Preparation of (*E*)-(4a*S*,13a*R*)-2,3,4,4a,6,7,8,11,13,13a-Decahydro-1,5,12-trioxabenzocycloundecene (43). See general procedure for metathesis. Colorless oil. R_f = 0.21 (silica, 25% EtOAc in hexanes). $[\alpha]^{25}_D$ = −36.90° (*c* 0.7, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3007, 2945, 2866, 1458 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.74 (ddd, *J* = 15.2, 10.7, 4.6 Hz, 1H, C*H*═CH), 5.57 (dddd, *J* = 15.2, 10.2, 5.0, 0.9 Hz, 1H, CH═C*H*), 4.14 (dd, *J* = 11.8, 5.0 Hz, 1H), 3.96 (br dd, *J* = 10.0, 4.5 Hz, 1H), 3.91 (br dd, *J* = 11.2, 4.5 Hz, 1H), 3.73 (dd, *J* = 11.5, 2.2 Hz, 1H), 3.68 (dd, *J* = 11.5, 1.2 Hz, 1H), 3.45 (dd, *J* = 11.8, 10.2 Hz, 1H), 3.28 (m, 2H), 2.99 (ddd, *J* = 10.0, 10.0, 2.0 Hz, 1H), 2.90 (br d, *J* = 9.2 Hz, 1H), 2.35 (dd, *J* = 12.8, 4.6 Hz, 1H), 2.22 (br dd, *J* = 12.0, 3.3 Hz, 1H), 1.92 (dddd, *J* = 12.8, 10.7, 10.7, 4.0 Hz, 1H), 1.67 (m, 2H), 1.60 (m, 2H), 1.23 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.00 (d, *C*H═CH), 124.60 (d, CH═*C*H), 80.68 (d), 72.09 (d), 71.15 (t), 67.40 (t), 68.42 (t), 65.21 (t), 33.58 (t), 29.02 (t), 28.77 (t), 24.90 (t). MS *m*/*e* (rel intens) 212 (M^+, 74). HRMS calcd for $C_{12}H_{20}O_3$ $(M)^+$: 212.141245, found: 212.141701; calcd for $C_6H_{10}O_2$ $(M - C_5H_8O)^+$: 114.068080, found: 114.068200. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.83; H, 9.59.

Preparation of (*E*)-(4a*S*,13a*R*)-2,3,4,4a,6,9,10,11,13,13a-Decahydro-1,5,12-trioxabenzocycloundecene (44). See general procedure for metathesis. Colorless oil. R_f = 0.28 (silica, 25% EtOAc in hexanes). $[\alpha]^{25}_D$ = +28.43° (*c* 1.5, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3007, 2944, 2865, 1457, 1363 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 15.2, 10.5, 4.5 Hz, 1H, C*H*═CH), 5.54 (dddd, *J* = 15.2, 10.3, 4.9, 1.0 Hz, 1H, CH═C*H*), 4.06 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.94 (br dd, *J* = 10.0, 4.1 Hz, 1H), 3.90 (br dd, *J* = 11.2, 4.4 Hz, 1H), 3.51 (m, 4H), 3.26 (ddd, *J* = 11.2, 11.2, 3.0 Hz, 1H), 2.97 (m, 2H), 2.31 (br dd, *J* = 12.5, 4.5 Hz, 1H), 2.11 (br dd, *J* = 12.6, 3.2 Hz, 1H), 1.92 (dddd, *J* = 12.5, 10.6, 10.5, 3.6 Hz, 1H), 1.81 (m, 1H), 1.63 (m, 3H), 1.32 (dddd, *J* = 12.6, 12.6, 11.4, 4.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.77 (d, *C*H═CH), 123.93 (d, CH═*C*H), 80.11 (d), 72.55 (t), 70.15 (d), 70.04 (t), 68.15 (t), 68.10 (t), 33.43 (t), 30.13 (t), 29.15 (t), 25.58 (t). MS *m*/*e* (rel intens) 212 (M^+, 30). HRMS calcd for $C_{12}H_{20}O_3$ $(M)^+$: 212.141245, found: 212.140259; calcd for $C_6H_{10}O_2$ $(M - C_5H_8O)^+$: 114.068080, found: 114.068200. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.97; H, 9.62.

Preparation of (*E*)-(4a*S*,14a*R*)-2,3,4,4a,7,10,11,12,14,14a-Decahydro-6*H*-1,5,13-trioxabenzocyclododecene (45). See general procedure for metathesis. Colorless oil. R_f = 0.22 (silica, 15% EtOAc in hexanes). $[\alpha]^{25}_D$ = +41.90° (*c* 1.12, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3009, 2944, 2865, 1602, 1332 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.61 (ddd, *J* = 14.5, 9.4, 5.0 Hz, 1H, C*H*═CH), 5.28 (ddd, *J* = 14.5, 6.4, 6.4 Hz, 1H, CH═C*H*), 3.94 (br dd, *J* = 11.2, 4.5 Hz, 1H), 3.84 (ddd, *J* = 9.9, 5.1, 4.4 Hz, 1H), 3.69 (m, 2H), 3.60 (m, 2H), 3.32 (m, 2H), 3.20 (ddd, *J* = 9.9, 5.2, 5.2 Hz, 1H), 3.05 (br d, *J* = 9.1 Hz, 1H), 2.35 (m, 1H), 2.24 (m, 2H), 2.04 (m, 2H), 1.67 (m, 4H), 1.19 (dddd, *J* = 12.6, 12.6, 11.4, 4.6 Hz, 1H). ^1H NMR (500 MHz, C_6D_6) δ 5.74 (ddd, *J* = 14.5, 9.1, 5.4 Hz, 1H, C*H*═CH), 5.35 (ddd, *J* = 14.5, 6.5, 6.5 Hz, 1H, CH═C*H*), 3.88 (dd, *J* = 9.2, 2.2 Hz, 1H), 3.84 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.77 (ddd, *J* = 11.0, 9.0, 4.5 Hz, 1H), 3.67 (m, 2H), 3.51 (dd, *J* = 9.2, 1.7 Hz, 1H), 3.42 (ddd, *J* = 10.5, 6.2, 3.5 Hz, 1H), 3.20 (br d, *J* = 9.0 Hz, 1H), 3.15 (m, 2H), 2.29 (m, 1H), 2.23 (m, 1H), 2.04 (m, 3H), 1.55 (m, 3H), 1.28 (br d, *J* = 11.8 Hz, 1H), 1.13 (dddd, *J* = 12.2, 11.8, 11.0, 4.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.25 (d, *C*H═CH), 124.14 (d, CH═*C*H), 80.30 (d), 72.76 (t), 68.60 (d), 68.48 (t), 68.46 (t), 63.85 (t), 33.13 (t), 31.67 (t), 28.24 (t), 28.15 (t), 25.01 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 134.12 (d, *C*H═CH), 124.46 (d, CH═*C*H), 80.78 (d), 72.16 (t), 69.60 (d), 69.40 (t), 67.94 (t), 63.96 (t), 33.45 (t), 32.01 (t), 28.47 (t), 28.42 (t), 25.29 (t). MS *m*/*e* (rel intens) 226 (M^+, 7). HRMS calcd for $C_{13}H_{22}O_3$ $(M)^+$: 226.156895, found: 226.156994; calcd for $C_6H_{10}O_2$ $(M - C_5H_8O)^+$: 114.068080, found: 114.068200. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.09; H, 9.97.

Preparation of (4a*S*,15a*R*)-2,3,4,4a,6,7,8,11,12,13,15,15a-dodecahydro-1,5,14-trioxabenzocyclotridecene (46): See general procedure for metathesis. Colorless oil. *Z*-isomer (major): R_f = 0.55 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D$ = +68.08° (*c* 0.84, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3007, 2943, 2867, 1602, 1464, 1371 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.37 (m, 2H, C*H*═C*H*), 3.92 (br dd, *J* = 11.4, 4.4 Hz, 1H), 3.72 (dd, *J* = 9.9, 2.5 Hz, 1H), 3.63 (ddd, *J* = 10.4, 4.4, 4.4 Hz, 1H), 3.53 (m, 2H), 3.36 (m, 4H), 3.14 (ddd, *J* = 9.3, 2.5, 2.5 Hz, 1H), 2.22 (m, 5H), 1.66 (m, 6H), 1.28 (dddd, *J* = 12.4, 12.4, 11.2, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.45 (d, *C*H═CH), 129.96 (d, CH═*C*H), 80.77 (d), 73.69 (d), 70.49 (t), 68.57 (t), 68.31 (t), 66.82 (t), 30.18 (t), 29.84 (t), 28.84 (t), 25.33 (t), 23.52 (t), 23.32 (t). MS *m*/*e* (rel intens) 240 (M^+, 47), 181 ($[M - C_3H_7O]^+$, 18). HRMS calcd for $C_{14}H_{24}O_3$ $(M)^+$: 240.172545, found: 240.173652. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.87; H, 10.13. *E*-isomer (minor, selected data): R_f = 0.54 (silica, 30% EtOAc in hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 5.46 (ddd, *J* = 14.9, 7.1, 6.7 Hz, 1H, C*H*═CH), 3.08 (ddd, *J* = 9.3, 2.3, 2.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.81 (d, *C*H═CH), 128.74 (d, CH═*C*H), 81.27 (d), 73.15 (d), 71.44 (t), 70.24 (t), 68.20 (t), 67.82 (t), 31.39 (t), 30.14 (t), 28.91 (t), 28.52 (t), 28.08 (t), 25.52 (t).

Preparation of (2*R*,3*S*)-3-(3′-allyloxypropoxy)-2-(3^{iv}-allyloxypropoxymethyl)tetrahydropyran (50). General Procedure for Di-O-alkylation with Tosylates. To a stirring solution of **2** (0.4 mmol) in dry THF (2 mL) was added ^{t}BuOK (99 mg, 0.88 mmol, 2.2 equiv). After 1 h at room temperature, the corresponding tosylate (0.88 mmol, 2.2 equiv) was added *via cannula*, dissolved in dry THF (2 mL), and the reaction was heated overnight at 65 °C. Reaction mixture was allowed to cool to room temperature, and water was added (2 mL). Aqueous layer was extracted with EtOAc (3 × 2 mL), combined organic layers were dried over $MgSO_4$, and solvent was removed under reduced pressure. The residue was purified by flash chromatography. Colorless oil. R_f = 0.49 (silica, 30% EtOAc in hexanes). $[\alpha]^{25}_D$ = +49.32° (*c* 1.35, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3083, 3008, 2866, 1454, 1422 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.86 (m, 2H), 5.22 (m, 2H), 5.12 (m, 2H), 3.92 (m, 5H), 3.70 (m, 2H), 3.53 (m, 2H), 3.47 (m, 5H), 3.39 (ddd, *J* = 9.2, 6.3, 6.3 Hz, 1H), 3.30 (m, 1H), 3.21 (ddd, *J* = 9.3, 5.5,

1.9 Hz, 1H), 3.14 (ddd, J = 10.5, 9.3, 4.5 Hz, 1H), 2.20 (br dd, J = 12.4, 3.0 Hz, 1H), 1.85 (ddddd, J = 6.5, 6.5, 6.5, 6.5, 1.6 Hz, 2H), 1.78 (dddd, J = 6.3, 6.3, 6.3, 6.3 Hz, 2H), 1.59 (m, 2H), 1.30 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.00 (d), 134.93 (d), 116.75 (t), 116.63 (t), 80.47 (d), 73.86 (d), 71.89 (t), 71.81 (t), 70.82 (t), 68.66 (t), 67.84 (t), 67.42 (t), 67.18 (t), 65.75 (t), 30.45 (t), 29.96 (t), 29.37 (t), 25.16 (t). HRMS (FAB) calcd for $C_{18}H_{32}O_5Na$ $(M + Na)^+$: 351.214744, found: 351.214036. Anal. Calcd for $C_{18}H_{32}O_5$: C, 65.82; H, 9.82. Found: C, 65.77; H, 9.98.

(2*R*,3*S*)-3-(2′-Allyloxyethoxy)-2-(2^{iv}-allyloxyethoxymethyl)tetrahydropyran (51a): colorless oil. R_f = 0.45 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +34.75° (*c* 0.51, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3010, 2868, 2360, 1245, 1216 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (m, 2H), 5.23 (m, 2H), 5.13 (m, 2H), 3.97 (m, 4H), 3.88 (br d, J = 11.1 Hz, 1H), 3.72 (m, 2H), 3.65 (m, 3H), 3.57 (m, 2H), 3.51 (m, 3H), 3.26 (m, 3H), 2.19 (br dd, J = 12.6, 2.8 Hz, 1H), 1.59 (m, 2H), 1.34 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.88 (d), 134.79 (d), 116.91 (t), 116.84 (t), 80.41 (d), 74.34 (d), 72.15 (t), 72.13 (t), 71.22 (t), 70.82 (t), 69.72 (t), 69.40 (t), 68.50 (t), 67.80 (t), 29.43 (t), 25.22 (t). MS *m*/*e* (rel intens) 301 ($[M + 1]^+$, 6). HRMS calcd for $C_{16}H_{29}O_5$ $(M + H)^+$: 301.201499, found: 301.201031. Anal. Calcd for $C_{16}H_{28}O_5$: C, 63.97; H, 9.40. Found: C, 63.58; H, 9.82.

(2*R*,3*S*)-3-[2′-(2″-Allyloxyethoxy)ethoxy]-2-[2^{v}-(2^{vi}-allyloxyethoxy)ethoxymethyl]tetrahydropyran (51b): colorless oil. R_f = 0.46 (silica, EtOAc). $[\alpha]^{25}_D$ = +35.38° (*c* 0.85, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3084, 3010, 1463, 1244 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (dddd, J = 17.2, 10.4, 5.6, 5.6 Hz, 2H), 5.22 (d, J = 17.2 Hz, 2H), 5.13 (d, J = 10.4 Hz, 2H), 3.97 (br d, J = 5.6 Hz, 4H), 3.87 (br d, J = 11.8 Hz, 1H), 3.72 (m, 2 H), 3.58 (m, 16H), 3.24 (m, 3H), 2.19 (br dd, J = 12.3, 2.8 Hz, 1H), 1.58 (m, 2H), 1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.84 (d), 134.80 (d), 117.04 (t), 117.03 (t), 74.35 (d), 72.25 (d), 71.24 (t, 2C), 70.89 (t), 70.84 (t), 70.65 (t), 70.60 (t), 70.49 (t), 69.49 (t), 69.47 (t), 68.45 (t), 67.78 (t), 65.84 (t), 29.43 (t), 25.22 (t). HRMS (FAB) calcd for $C_{18}H_{32}O_7Na$ $(M - C_2H_4+Na)^+$: 383.204573, found: 383.203854. Anal. Calcd for $C_{20}H_{36}O_7$: C, 61.83; H, 9.34. Found: C, 61.94; H, 9.32.

Preparation of (2*R*,3*S*)-3-Allyloxy-2-[2‴-(2^{iv}-allyloxyethoxy)ethoxymethyl]tetrahydropyran (52a). General Procedure for O-Alkylation with Tosylates. To a stirring solution of **5a** (0.3 mmol) in dry THF (2 mL) was added ^{t}BuOK (37 mg, 0.33 mmol, 1.1 equiv). After 1 h at room temperature, the corresponding tosylate (0.36 mmol, 1.2 equiv) was added *via cannula*, dissolved in dry THF (2 mL), and the reaction was stirred overnight at room temperature. The reaction mixture was filtered through a Celite pad, and solvent was removed under reduced pressure. The residue was purified by flash chromatography. Colorless oil. R_f = 0.35 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +39.33° (*c* 0.68, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3084, 3009, 2868, 1463 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (m, 2H), 5.22 (m, 2H), 5.11 (m, 2H), 4.05 (br dd, J = 12.7, 5.7 Hz, 1H), 3.97 (br d, J = 5.7 Hz, 2H), 3.90 (m, 2H), 3.71 (dd, J = 10.6, 1.2 Hz, 1H), 3.62 (m, 7H), 3.54 (m, 2H), 3.30 (m, 1H), 3.23 (m, 2H), 2.16 (br d, J = 12.4 Hz, 1H), 1.59 (m, 2H), 1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.12 (d), 134.79 (d), 117.05 (t), 116.71 (t), 80.47 (d), 73.25 (d), 72.24 (t), 71.18 (t), 70.82 (t), 70.59 (t), 70.50 (t), 69.96 (t), 69.43 (t), 67.81 (t), 29.49 (t), 25.19 (t). HRMS (FAB) calcd for $C_{16}H_{28}O_5Na$ $(M + Na)^+$: 323.183444, found: 323.182996. Anal. Calcd for $C_{16}H_{28}O_5$: C, 63.97; H, 9.40. Found: C, 63.70; H, 9.73.

(2*R*,3*S*)-3-Allyloxy-2-{2‴-[2^{iv}-(2^{v}-allyloxyethoxy)ethoxy]ethoxymethyl}tetrahydropyran (52b): colorless oil. R_f = 0.53 (silica, EtOAc). $[\alpha]^{25}_D$ = +40.86° (*c* 1.53, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3084, 3010, 2868, 1463, 1265 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (m, 2H), 5.22 (m, 2H), 5.12 (m, 2H), 4.05 (br dd, J = 12.7, 5.7 Hz, 1H), 3.98 (br d, J = 5.7 Hz, 2H), 3.90 (m, 2H), 3.71 (dd, J = 10.5, 1.4 Hz, 1H), 3.62 (m, 11H), 3.56 (m, 2H), 3.30 (m, 1H), 3.23 (m, 2H), 2.18 (br dd, J = 12.4, 2.5 Hz, 1H), 1.59 (m, 2H), 1.33 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.12 (d), 134.78 (d), 117.07 (t), 116.73 (t), 80.47 (d), 73.26 (d), 72.23 (t), 71.18 (t), 70.81 (t), 70.64 (t, 2C), 70.58 (t), 70.46 (t), 69.95 (t), 69.43 (t), 67.81 (t), 29.49 (t), 25.19 (t). MS *m*/*e* (rel intens) 345 ($[M + 1]^+$, 6). HRMS calcd for $C_{18}H_{33}O_6$ $(M + H)^+$: 345.227714, found: 345.225694. Anal. Calcd for $C_{18}H_{32}O_6$: C, 62.77; H, 9.36. Found: C, 62.59; H, 9.51.

(2*R*,3*S*)-3-Allyloxy-2-(2‴-{2^{iv}-[2^{v}-(2^{vi}-allyloxyethoxy)ethoxy]ethoxy}ethoxymethyl)tetrahydropyran (52c): colorless oil. R_f = 0.42 (silica, EtOAc). $[\alpha]^{25}_D$ = +37.85° (*c* 1.22, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3010, 2869, 1463, 1350 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (m, 2H), 5.20 (m, 2H), 5.10 (m, 2H), 4.03 (br dd, J = 12.6, 5.6 Hz, 1H), 3.96 (br d, J = 5.7 Hz, 2H), 3.88 (m, 2H), 3.69 (dd, J = 10.6, 1.2 Hz, 1H), 3.61 (m, 15H), 3.54 (m, 2H), 3.28 (m, 1H), 3.20 (m, 2H), 2.17 (br d, J = 12.5 Hz, 1H), 1.57 (m, 2H), 1.30 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.11 (d), 134.77 (d), 117.04 (t), 116.70 (t), 73.24 (d), 72.21 (d), 71.17 (t), 70.80 (t), 70.61 (t), 70.59 (t), 70.55 (t), 70.44 (t), 69.93 (t), 69.41 (t), 67.79 (t), 29.48 (t), 25.18 (t). HRMS (FAB) calcd for $C_{18}H_{33}O_6Na$ $(M + Na)^+$: 411.2358738, found: 411.236023. Anal. Calcd for $C_{20}H_{36}O_7$: C, 61.83; H, 9.34. Found: C, 61.79; H, 9.50.

(2*R*,3*S*)-3-Allyloxy-2-{3‴-[2^{iv}-(3^{vi}-allyloxypropoxymethyl)allyloxy]propoxymethyl}tetrahydropyran (53): colorless oil. R_f = 0.50 (silica, 50% EtOAc in hexanes). $[\alpha]^{25}_D$ = +41.97° (*c* 1.35, $CHCl_3$). IR ($CHCl_3$) ν_{max} 3009, 2945, 2865, 1647, 1455 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (m, 2H), 5.24 (m, 2H), 5.14 (m, 4H), 4.06 (br dd, J = 12.6, 5.6 Hz, 1H), 3.92 (m, 8H), 3.66 (d, J = 10.4 Hz, 1H), 3.57 (m, 2H), 3.49 (m, 7H), 3.33 (m, 1H), 3.24 (m, 2H), 2.21 (br d, J = 12.8 Hz, 1H), 1.85 (m, 4H), 1.62 (m, 2H), 1.35 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.09 (s), 135.09 (d), 134.97 (d), 116.78 (t, 2C), 113.43 (t), 80.46 (d), 73.36 (d), 71.88 (t), 71.57 (t), 71.52 (t), 70.74 (t), 69.95 (t), 68.70 (t), 67.87 (t), 67.50 (t), 67.31 (t, 2C), 30.14 (t), 29.94 (t), 29.48 (t), 25.20 (t). MS *m*/*e* (rel intens) 398 (M^+, 1), 357 ($[M - C_3H_5]^+$, 2), 339 ($[M - C_3H_7O]^+$, 7). HRMS calcd for $C_{22}H_{38}O_6$ $(M)^+$: 398.266839, found: 398.267199; calcd for $C_{19}H_{31}O_5$ $(M - C_3H_7O)^+$: 339.217149, found: 339.217046. Anal. Calcd for $C_{22}H_{38}O_6$: C, 66.30; H, 9.61. Found: C, 66.28; H, 9.73.

Preparation of (4a*S*,19a*R*)-2,3,4,4a,7,8,10,13,16,17,19,19a-dodecahydro-6*H*,15*H*-1,5,9,14,18-pentaoxabenzocycloheptadecene (54): *E*:*Z* 7:1. See general procedure for metathesis. Colorless oil. IR ($CHCl_3$) ν_{max} 3018, 2945, 2872, 2361, 1603 cm^{-1}. HRMS (FAB) calcd for $C_{16}H_{28}O_5Na$ $(M + Na)^+$: 323.183444, found: 323.183291. Anal. Calcd for $C_{16}H_{28}O_5$: C, 63.97; H, 9.40. Found: C, 63.99; H, 9.08. *E*-isomer (major): R_f = 0.16 (silica, 30% EtOAc in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (m, 2H, C*H*=C*H*), 3.98 (m, 5H), 3.58 (m, 8H), 3.36 (m, 3H), 3.20 (ddd, J = 9.3, 5.2, 1.8 Hz, 1H), 3.13 (ddd, J = 10.5, 9.3, 4.5 Hz, 1H), 2.20 (br dd, J = 12.3, 3.0 Hz, 1H), 1.77 (m, 4H), 1.60 (m, 2H), 1.28 (m, 1H). ^{1}H NMR (500 MHz, C_6D_6) δ: 5.77 (ddd, J = 15.5, 5.1, 5.1 Hz, 1H, C*H*=CH), 5.69 (ddd, J = 15.5, 5.3, 5.3 Hz, 1H, CH=C*H*), 4.06 (dd, J = 13.1, 5.1 Hz, 1H), 3.93 (dd, J = 13.6, 5.1 Hz, 1H), 3.86 (m, 2H), 3.79 (m, 3H), 3.72 (m, 1H), 3.60 (m, 5H), 3.44 (m, 2H), 3.34 (ddd, J = 9.2, 4.5, 1.8 Hz, 1H), 3.28 (ddd, J = 10.3, 9.2, 4.5 Hz, 1H), 3.12 (ddd, J = 12.1, 12.1, 2.2 Hz, 1H), 2.04 (br d, J = 10.6 Hz, 1H), 1.87 (m, 4H), 1.46 (m, 1H), 1.24 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.60 (d, *C*H=CH), 129.48 (d, CH=*C*H), 80.50 (d), 73.61 (d), 71.67 (t), 70.60 (t), 70.38 (t), 68.29 (t), 67.90 (t), 66.67 (t), 66.24 (t), 65.65 (t), 30.49 (t), 30.37 (t), 29.30 (t), 25.11 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 130.51 (d, *C*H=CH), 129.71 (d, CH=*C*H), 81.41 (d), 73.71 (d), 71.73 (t), 70.58 (t), 70.09 (t), 68.17 (t), 67.40 (t), 66.37 (t), 66.07(t), 65.57 (t), 30.95 (t), 30.79 (t), 29.58 (t), 25.38 (t). *Z*-isomer (minor, selected data): 0.15 (silica, 30% EtOAc in hexanes). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.27 (d, *C*H=CH), 129.57 (d, CH=*C*H), 73.17 (d), 68.14 (t), 68.01 (t), 67.12 (t), 66.98 (t), 66.35 (t), 30.62 (t), 30.17 (t), 29.64 (t), 25.22 (t).

Preparation of (4a*S*,17a*R*)-2,3,4,4a,6,7,9,12,14,15,17,17a-dodecahydro-1,5,8,13,16-pentaoxabenzocyclopentadecene (55): *E*:*Z* 4:1. See general procedure for metathesis. Colorless oil. IR ($CHCl_3$) ν_{max} 3015, 2945, 2872, 2360, 1603, 1456, 1351 cm^{-1}. HRMS (FAB) calcd for $C_{14}H_{24}O_5Na$ $(M + Na)^+$: 295.152144, found: 295.153863. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.91; H, 8.61. *E*-isomer (major): R_f = 0.35 (silica, EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (m, J = 15.7 Hz, 2H, C*H*=C*H*), 4.06 (m, 2H), 3.97 (m, 3H), 3.91 (br d, J = 11.5 Hz, 1H), 3.66 (m, 8H), 3.34 (m, 3H), 3.21 (ddd, J = 10.4, 9.3, 4.5 Hz, 1H), 2.22 (br dd, J = 12.3, 3.2 Hz, 1H), 1.61 (m, 2H), 1.32 (m, 1H). ^{13}C NMR (125 MHz,

$CDCl_3$) δ 129.73 (d, 2C, *C*H=*C*H), 80.28 (d), 74.14 (d), 70.93 (t), 70.84 (t), 70.37 (t), 70.24 (t), 69.70 (t), 69.42 (t), 67.83 (t), 67.78 (t), 28.99 (t), 25.00 (t). *Z*-isomer (minor, selected data): 0.34 (silica, EtOAc). ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.72 (m, J = 11.3 Hz, 2H, C*H*=C*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.68 (d, *C*H=CH), 128.91 (d, CH=*C*H), 80.40 (d), 73.35 (d), 71.00 (t), 70.34 (t), 70.34 (t), 69.13 (t), 68.12 (t), 68.00 (t), 66.69 (t), 66.64 (t), 29.11 (t), 25.12 (t).

Preparation of (4a*S*,23a*R*)-2,3,4,4a,6,7,9,10,12,15,17,18,20,21,23,23a-hexadecahydro-1,5,8,11,16,19,22-heptaoxabenzocycloheneicosene (56): *E*:*Z* 12:1. See general procedure for metathesis. Colorless oil. R_f = 0.20 (silica, EtOAc). IR ($CHCl_3$) ν_{max} 2945, 2872, 2358, 1600, 1454, 1351 cm^{-1}. HRMS (FAB) calcd for $C_{18}H_{32}O_7Na$ $(M + Na)^+$: 383.204573, found: 383.203250. Anal. Calcd for $C_{18}H_{32}O_7$: C, 59.98; H, 8.95. Found: C, 59.95; H, 8.83. *E*-isomer (major): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (m, J = 15.4 Hz, 2H, C*H*=C*H*), 4.01 (m, 4H), 3.90 (br d, J = 11.9 Hz, 1H), 3.63 (m, 18H), 3.29 (m, 1H), 3.23 (m, 2H), 2.19 (br d, J = 12.1 Hz, 1H), 1.61 (m, 2H), 1.34 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.42 (d, *C*H=CH), 129.30 (d, CH=*C*H), 80.54 (d), 74.11 (d), 71.30 (t), 71.14 (t), 70.83 (t), 70.78 (t), 70.77 (t), 70.69 (t, 2C), 70.65 (t), 69.38 (t), 69.31 (t) 68.76 (t), 67.89 (t), 29.51 (t), 25.27 (t). *Z*-isomer (minor, selected data): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (m, 2H, C*H*=CH), 4.14 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.92 (d, *C*H=CH), 129.72 (d, CH=*C*H), 71.21 (t), 70.52 (t), 70.51 (t), 69.51 (t), 69.22 (t), 68.81 (t), 67.95 (t), 66.74 (t), 66.68 (t), 29.58 (t).

Preparation of (4a*S*,17a*R*)-2,3,4,4a,6,9,11,12,14,15,17,17a-dodecahydro-1,5,10,13,16-pentaoxabenzocyclopentadecene (57): *E*:*Z* 10:3. See general procedure for metathesis. Colorless oil. R_f = 0.34 (silica, EtOAc). IR ($CHCl_3$) ν_{max} 3015, 2944, 2360, 1603, cm^{-1}. HRMS (FAB) calcd for $C_{14}H_{24}O_5Na$ $(M + Na)^+$: 295.152144, found: 295.151159. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.74; H, 8.80. *E*-isomer (major): ^{1}H NMR (500 MHz, C_6D_6) δ 6.22 (m, J = 15.7 Hz, 1H, C*H*=CH), 5.69 (ddd, J = 15.7, 4.4, 4.4 Hz, 1H, CH=C*H*), 4.24 (br d, J = 10.2 Hz, 1H), 4.09 (dd, J = 10.2, 2.8 Hz, 1H), 3.99 (m, 2H), 3.89 (ddd, J = 10.3, 9.5, 4.5 Hz, 1H), 3.82 (br dd, J = 11.3, 4.4 Hz, 1H), 3.66 (dd, J = 10.1, 1.6 Hz, 1H), 3.54 (m, 7H), 3.40 (m, 2H), 3.28 (br d, J = 9.5 Hz, 1H), 3.15 (ddd, J = 11.3, 11.3, 2.0 Hz, 1H), 2.11 (br dd, J = 12.1, 3.4 Hz, 1H), 1.47 (m, 1H), 1.32 (m, 2H). ^{13}C NMR (125 MHz, C_6D_6) δ 129.73 (d, *C*H=CH), 129.06 (d, CH=*C*H), 81.10 (d), 71.27 (t), 71.25 (t), 71.16 (t), 70.54 (t), 70.39 (t), 70.16 (t), 69.57 (d), 67.71 (t), 66.97 (t), 28.74 (t), 25.32 (t). *Z*-isomer (minor, selected data): ^{1}H NMR (500 MHz, C_6D_6) 5.85 (m, J = 11.2 Hz, 2H, C*H*=C*H*), 4.48 (ddd, J = 11.8, 6.0, 6.0 Hz, 2H), 4.32 (dd, J = 12.5, 3.8 Hz, 1H), 3.74 (ddd, J = 10.7, 9.9, 4.5 Hz, 1H), 3.21 (br d, J = 9.2 Hz, 1H). ^{13}C NMR (125 MHz, C_6D_6) δ 131.25 (d, *C*H=CH), 129.39 (d, CH=*C*H), 81.90 (d), 72.47 (t), 72.19 (d), 70.77 (t), 70.49 (t), 70.45 (t), 68.46 (t), 67.69 (t), 67.04 (t), 66.24 (t), 31.63 (t), 25.83 (t).

Preparation of (4a*S*,20a*R*)-2,3,4,4a,6,9,11,12,14,15,17,18,20,20a-tetradecahydro-1,5,10,13,16,19-hexaoxabenzocyclooctadecene (58): *E*:*Z* 8.5:1. See general procedure for metathesis. Colorless oil. R_f = 0.24 (silica, EtOAc). IR ($CHCl_3$) ν_{max} 3016, 2945, 2361, 1603, 1456 cm^{-1}. HRMS (FAB) calcd for $C_{16}H_{28}O_6Na$ $(M + Na)^+$: 339.178359, found: 339.176358. Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.74; H, 9.23. *E*-isomer (major): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (ddd, J = 15.6, 5.8, 5.8 Hz, 1H, C*H*=CH), 5.77 (ddd, J = 15.6, 5.0, 5.0 Hz, 1H, CH=C*H*), 4.14 (ddd, J = 12.8, 5.8, 1.1 Hz, 1H), 4.08 (ddd, J = 13.7, 5.0, 1.1 Hz, 1H), 4.01 (ddd, J = 13.7, 5.0, 1.1 Hz, 1H), 3.91 (m, 2H), 3.72 (m), 3.62 (m) (14H), 3.38 (ddd, J = 10.7, 9.3, 4.5 Hz, 1H), 3.32 (m, 1H), 3.20 (m, 1H), 2.19 (br dd, J = 12.2, 3.0 Hz, 1H), 1.62 (m, 2H), 1.29 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.72 (d, *C*H=CH), 129.10 (d, CH=*C*H), 80.50 (d), 71.89 (d), 71.29 (t), 71.04 (t), 70.92 (t), 70.82 (t), 70.67 (t), 70.55 (t), 70.32 (t), 69.03 (t), 68.19 (t), 68.01 (t), 29.11 (t), 25.17 (t). *Z*-isomer (minor, selected data): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.70 (ddd, J = 11.1, 6.1, 6.1 Hz, 1H, C*H*=CH), 5.64 (ddd, J = 11.1, 6.3, 6.3 Hz, 1H, CH=*C*H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.33 (d, *C*H=CH), 128.35 (d, CH=*C*H), 80.80 (d), 73.31 (d), 71.66 (t), 71.49 (t), 70.77 (t), 70.73 (t), 68.91 (t), 68.14 (t), 66.75 (t), 66.39 (t), 30.43 (t), 25.47 (t).

Preparation of (4a*S*,23a*R*)-2,3,4,4a,6,9,11,12,14,15,17,18,20,21,23,23a-hexadecahydro-1,5,10,13,16,19,22-heptaoxabenzocycloheneicosene (59): *E*:*Z* 13:1. See general procedure for metathesis. Colorless oil. R_f = 0.20 (silica, EtOAc). IR ($CHCl_3$) ν_{max} 3014, 2944, 2870, 2360, 1603, 1452 cm^{-1}. HRMS (FAB) calcd for $C_{18}H_{32}O_7Na$ $(M + Na)^+$: 383.204573, found: 383.202856. Anal. Calcd for $C_{18}H_{32}O_7$: C, 59.98; H, 8.95. Found: C, 59.99; H, 8.90. *E*-isomer (major): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (m, 2H, C*H*=C*H*), 4.14 (dd, J = 12.5, 3.6 Hz, 1H), 4.04 (d, J = 3.5 Hz, 2H), 3.93 (m, 2H), 3.70 (m, 18H), 3.33 (m, 2H), 3.20 (m, 1H), 2.19 (m, 1H), 1.65 (m, 2H), 1.29 (m, 1H). ^{1}H NMR (500 MHz, C_6D_6) δ 6.01 (ddd, J = 15.6, 5.5, 5.5 Hz, 1H, C*H*=CH), 5.93 (ddd, J = 15.6, 5.1, 5.1 Hz, 1H, CH=C*H*), 4.20 (ddd, J = 12.8, 5.5, 1.0 Hz, 1H), 4.04 (d, J = 5.1 Hz, 2H), 3.98 (m, 2H), 3.80 (m, 2H), 3.57 (m, 17H), 3.31 (ddd, J = 9.2, 3.8, 1.8 Hz, 1H), 3.12 (ddd, J = 12.6, 12.6, 2.2 Hz, 1H), 2.05 (m, 1H), 1.46 (m, 1H), 1.27 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.43 (d, *C*H=CH), 129.23 (d, CH=*C*H), 80.60 (d), 72.57 (d), 71.04 (t), 70.96 (t), 70.93 (t), 70.74 (t, 6C), 69.42 (t), 68.74 (t), 67.99 (t), 29.49 (t), 25.24 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 129.57 (d, *C*H=CH), 129.46 (d, CH=*C*H), 81.51 (d), 72.23 (d), 71.28 (t, 2C), 71.19 (t), 71.06 (t), 71.04 (t), 70.98 (t), 70.92 (t), 70.87 (t), 70.85 (t), 69.67 (t), 68.63 (t), 67.55 (t), 29.82 (t), 25.49 (t). *Z*-isomer (minor, selected data): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (m, 2H, C*H*=C*H*). ^{1}H NMR (500 MHz, C_6D_6) δ 5.86 (ddd, J = 11.3, 6.0, 6.0 Hz, 1H, C*H*=CH), 5.79 (ddd, J = 11.3, 6.2, 6.2 Hz, 1H, CH=C*H*), 4.30 (m), 3.25 (ddd, J = 9.2, 3.3, 1.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.30 (d, *C*H=CH), 128.87 (d, CH=*C*H), 80.69 (d), 73.03 (d), 71.33 (t), 70.58 (t), 69.51 (t), 66.72 (t), 65.23 (t), 29.65 (t), 25.31 (t). ^{13}C NMR (125 MHz, C_6D_6) δ 130.64 (d, *C*H=CH), 128.77 (d, CH=*C*H), 81.67 (d), 73.04 (d), 71.65 (t), 71.40 (t), 71.14 (t), 70.65 (t), 69.81 (t), 67.12 (t), 65.66 (t), 30.23 (t), 25.57 (t).

Preparation of (4a*S*,23a*R*)-16-methylene-2,3,4,4a,6,9,12,13,16,17,20,21,23,23a-tetradecahydro-11*H*,15*H*,19*H*-1,5,10,14,18,22-hexaoxabenzocycloheneicosene (60): *E*:*Z* 8:1. See general procedure for metathesis. Colorless oil. R_f = 0.27 (silica, 50% EtOAc in hexanes). IR ($CHCl_3$) ν_{max} 2958, 2928, 2363, 1463, 1262 cm^{-1}. HRMS (FAB) calcd for $C_{20}H_{34}O_6Na$ $(M + Na)^+$: 393.225309, found: 393.225578. Anal. Calcd for $C_{20}H_{34}O_6$: C, 64.84; H, 9.25. Found: C, 64.93; H, 9.37. *E*-isomer (major): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (m, J = 15.8 Hz, 2H, C*H*=C*H*), 5.13 (s, 1H, C=CH_2), 5.12 (s, 1H, C=CH_2), 4.14 (br d, J = 11.2 Hz, 1H), 3.94 (m, 8H), 3.62 (m, 2H), 3.51 (m, 8H), 3.33 (m, 2H), 3.21 (ddd, J = 9.3, 3.0, 3.0 Hz, 1H), 2.20 (br dd, J = 12.3, 3.0 Hz, 1H), 1.89 (m, 2H), 1.80 (m, 2H), 1.65 (m, 2H), 1.33 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.41 (s, *C*=CH$_2$), 129.55 (d, *C*H=CH), 129.25 (d, CH=*C*H), 113.72 (t, C=*C*H$_2$), 80.50 (d), 72.99 (d), 71.86 (t), 71.34 (t), 70.73 (t), 70.50 (t), 68.91 (t), 68.58 (t), 68.06 (t), 66.93 (t), 66.84 (t), 66.34 (t), 30.15 (t), 29.98 (t), 29.52 (t), 25.25 (t). *Z*-isomer (minor, selected data): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (m, 2H, C*H*=C*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.87 (d, *C*H=CH), 129.39 (d, CH=*C*H), 114.35 (t), 80.59 (d), 72.99 (t), 71.93 (t), 68.64 (t), 67.84 (t), 67.36 (t), 65.07 (t), 30.14 (t), 29.94 (t), 29.88 (t), 25.34 (t).

Acknowledgment. MEC (Spain, PB97-1123) and the Ramón Areces Foundation are gratefully acknowledged for funding this work. We should like to thank Prof. Ernesto Carmona's group for helpful advice and Dr. P. Nieto for some special NMR experiments.

Supporting Information Available: Experimental procedures and characterization data for 4-triisopropylsilyloxybutyraldehyde, 8-triisopropylsilyloxyoctanal, 9-triisopropylsilyloxynonanal, and compounds **47**, **48a**−**d**, and **49**; ^{1}H NMR and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9901438