# Intramolecular Oxymercuration of Stereoisomeric Cyclohexyl-Belted Poly(spirotetrahydrofuranyl) Platforms

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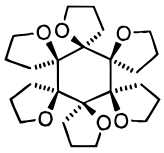
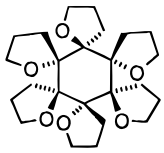
**Abstract:** The four tetraspiro carbinols **28**, **30**, **41**, and **43** and the three trispiro cyclohexenones **25**, **38**, and **53** have been synthesized and individually subjected to intramolecular oxymercuration. The three-dimensional structures of all 10 products have been unequivocally established by X-ray crystallographic analysis. In seven of these structures, the preferred solid-state conformation features an axially disposed C−Hg bond where the mercury atom is internally chelated in a 1,3-diaxial relationship to at least one or, more often, two oxygen centers. An unusually strong preference has been observed for equatorial occupancy on the part of the C−O bonds. This bias can be attributed to the relief of torsional strain effects that arise when gauche $CH_2$- - -$CH_2$ interactions are skirted. An important mechanistic distinction separates the kinetically preferred trans mercuricyclization of the tetraspiro alcohols from the contrasting cis stereochemical ring closure exhibited predominantly by the unsaturated ketones. In the first instance, the approach of $Hg^{2+}$ to the double bond is governed to a large extent by coordination to a proximal axially oriented ether oxygen. Where the ketones are concerned, precoordination to the Lewis basic carbonyl oxygen presumably initiates spirocyclization in a fashion controlled by the conformational preference of the resident tetrahydrofuranyl subunits.

The formulation of polyspirocyclic ionophores[1] such as **1** and **2** (nine stereoisomers including one *d,l* pair are possible[2]) has induced considerable preoccupation with the stereocontrolled introduction of neighboring tetrahydrofuran rings linked in this manner about a cyclohexane core.[2−5] To the present, the major focal points have been concerned with the systematic propagation of spiro rings in cyclohexanone precursors. Thus, the isomeric ketones **3** and **8**, which are conveniently available[1] by



**1**



**2**

2-fold ring expansion of cyclobutanone via oxonium ion-activated pinacol rearrangement,[6] have proven amenable to the stereodefined elaboration of trispiro homologues in two reliable, complementary ways (Scheme 1). The first alternative (route **A**) begins with a Claisen−Schmidt condensation involving an aromatic aldehyde (→ **4**), relies on sterically enforced nucleophilic attack by the Normant reagent[7] from the axial $\pi$-surface and is generally trans-selective in regard to the adjacent C−O bond. The subsequent ring closure (→ **5**) is not disruptive of the original stereoinduction. The second approach (route **B**) proceeds via preliminary α-oxygenation and silylation (→ **6**), takes advantage of the significant steric bulk of the OTBS substituent, and leads ultimately to net cis "capping" of the original carbonyl as in **7**. As exemplified for **8**, it is an equally easy matter to advance to either of the ketones **9** or **10** in preparation for further progression around the ring.

As will be shown herein, both of these protocols are fully iterative and have been effectively utilized for the preparation of the tetraspiro cyclohexanone of choice.

Beyond this point, however, neither option suffices because both methods rely on enolate formation to initiate matters. As reflected in Scheme 2, enolate generation at the tetraspiro level of substitution expectedly results in immediate and irreversible $\beta$-elimination with cleavage of the first tetrahydrofuran subunit originally set in place. Starting from this information base, we viewed the **11** → **12** and related transformations to provide a unique opportunity to examine several unexplored aspects of oxymercuration chemistry.[8]

More specifically, the goal of the present work was to probe those stereochemical factors pertinent to reinstallation of the fractured tetrahydrofuran ring in α,$\beta$-unsaturated ketone **12** and several of its congeners, along with capped analogues of type **14**. These systems offer companion opportunities to clarify relevant mechanistic differences between those processes in-

† To whom inquiries regarding the X-ray crystallographic analyses should be addressed at The University of Alabama.

(1) (a) Negri, J. T.; Rogers, R. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1991**, *113*, 5073. (b) Paquette, L. A.; Negri, J. T.; Rogers, R. D. *J. Org. Chem.* **1992**, *57*, 3947.

(2) (a) Paquette, L. A.; Stepanian, M.; Mallavadhani, U. V.; Curatelli, T. D.; Lowinger, T. B.; Klemeyer, H. J. *J. Org. Chem.* **1996**, *61*, 7492. (b) Bolin, D. G. Ph.D. Thesis, The Ohio State University, 1997.

(3) Paquette, L. A.; Branan, B. M.; Stepanian, M. *Tetrahedron Lett.* **1996**, *37*, 1721.

(4) Paquette, L. A.; Stepanian, M.; Branan, B. M.; Edmondson, S. E.; Bauer, C. B.; Rogers, R. D. *J. Am. Chem. Soc.* **1996**, *118*, 4504.

(5) Stepanian, M.; Trego, W. E.; Bolin, D. G.; Paquette, L. A.; Sareth, S.; Riddell, F. G. *Tetrahedron* **1997**, *53*, 7403.

(6) Review: Paquette, L. A. *Recent Research Developments in Chemical Sciences*; Transworld Research Network: Trivandrum, India, 1997; p 1.

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

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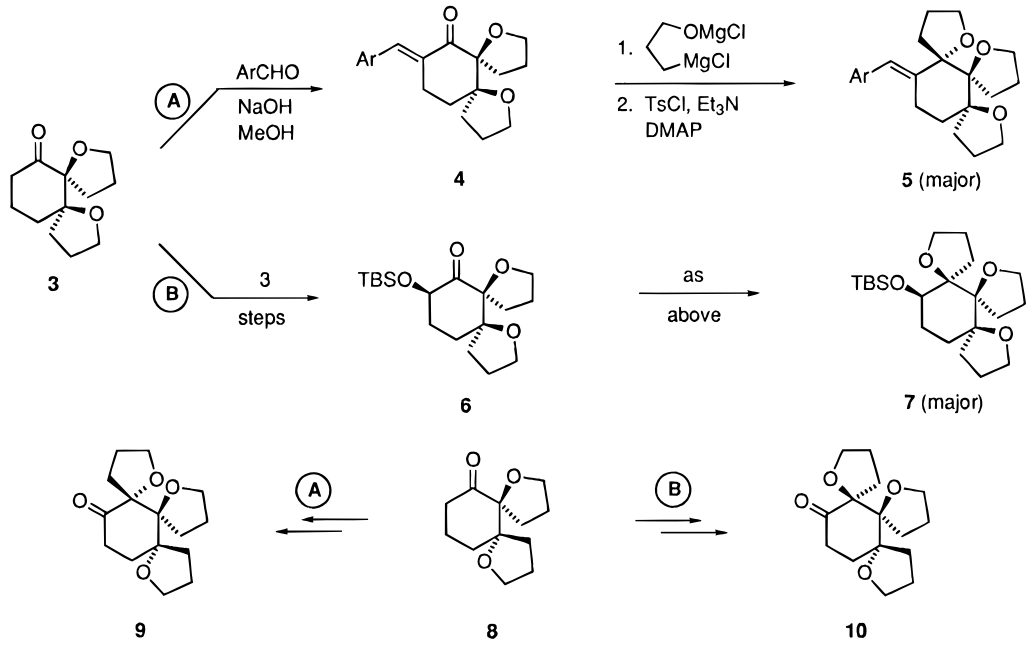
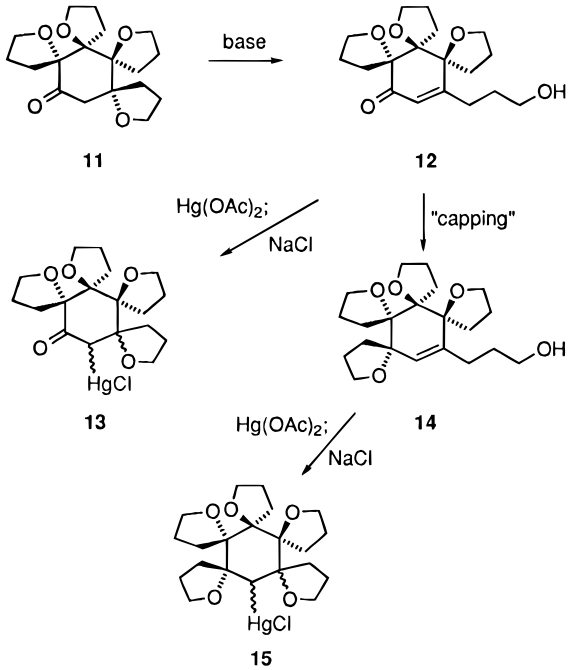
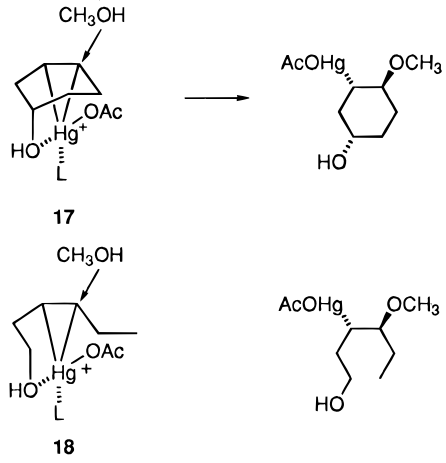
**Scheme 1**




**Scheme 2**




**Scheme 3**

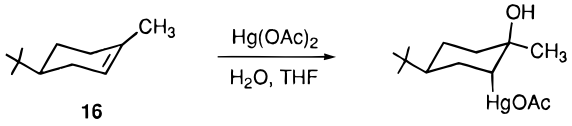



volving the generation of mercuric enolates such as **13** and their pentaspiro counterparts represented by **15**.

## Background

The oxymercuration of cyclohexenes has been extensively studied and is well understood at the mechanistic level. For example, Pasto and Gontarz have shown that reactants such as **16** give rise exclusively to trans-diaxial products as a consequence of kinetically controlled, nucleophile-promoted opening of mercurinium ion intermediates.[9] Previously, Henbest demonstrated that the oxymercuration of cyclohexenes substituted at C-4 with Lewis base groups such as OH, $OCH_3$, OBn, and OAc proved to be exceptionally regio- and stereocontrolled.[10] For example, although four diastereomeric adducts can be anticipated from the methoxymercuration of 3-cyclohexen-1-ol by trans addition of the HgOAc and $OCH_3$ groups, only one product was formed in 95% yield (Scheme 3). The intervention of mercurinium complex **17** was invoked to explain the strong directive effect observed. Acyclic analogues such as (*Z*)-3-hexen-1-ol likewise gave rise to a single methoxymercuration isomer. This phenomenon was similarly rationalized as in **18**.[11] Consequently, a neighboring ether or hydroxy group can be expected to steer the approach of $Hg^{2+}$ to a double bond by coordination and thus exercise a high degree of stereocontrol.

Although spirooxymercuration processes strictly comparable to those explored here do not appear to have been reported,

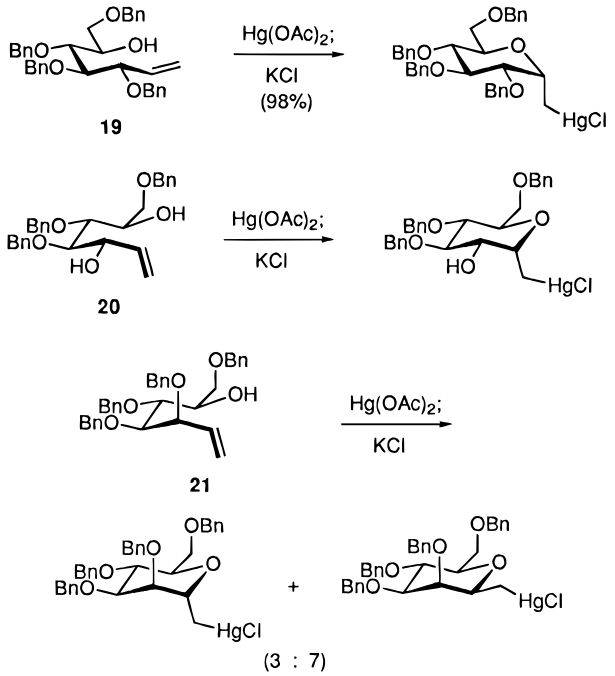



(9) Pasto, D. J.; Gontarz, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 6902.

(10) (a) Henbest, H. B.; Nicholls, B. *J. Chem. Soc.* **1959**, 227. (b) Henbest, H. B.; McElhinney, R. S. *J. Chem. Soc.* **1959**, 1834.

(11) (a) Thaisrivongs, S.; Seebach, D. *J. Am. Chem. Soc.* **1983**, *105*, 7407 and relevant references therein. (b) Chamberlain, P.; Whitham, G. H. *J. Chem. Soc. B* **1970**, 1382. (c) Matsuki, Y.; Kodama, M.; Itô, S. *Tetrahedron Lett.* **1979**, 2901. (d) Giese, B.; Bartmann, D. *Tetrahedron Lett.* **1985**, *26*, 1197.

**Scheme 4**

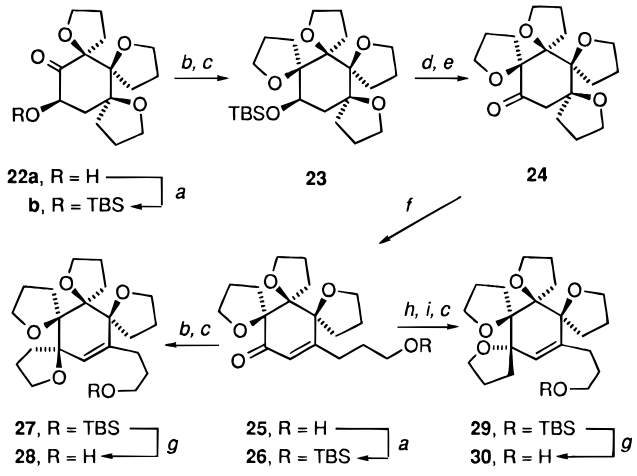



several investigations dealing with carbohydrate substrates are also relevant to the present investigation (Scheme 4). The mercuric acetate-mediated cyclization of **19** proved to be exceptionally stereoselective, an observation that Sinaÿ attributed to coordination by the incoming mercury species to the adjacent benzylic oxygen.[12] Russo and co-workers have examined the consequences of changing the substituent adjacent to the olefin in order to validate the aforementioned hypothesis.[13] When O-2 is free as in **20**, only the α-isomer was obtained. The epimeric benzyl derivative **21** gave rise to a 3:7 ratio of α- and *β*-pyranosyl products. Consequently, it would appear that the oxymercuration reaction may be sensitive to the disposition of the neighboring oxygen substituent.

Indeed, a very recent extended study by Perlmutter et al. of allylic siloxy groups as stereocontrol elements in intramolecular oxymercurations has shown (*Z*)-alkenols to form syn diastereomers predominantly.[14] (*E*)-Alkenols gave very poor diastereoselection under comparable circumstances.

α-Mercurio ketones and esters have been known for some time,[15] but have received very limited attention over the years. Since the C−Hg bonds in these entities are weak, intermediates of this type enter readily into metal-exchange reactions with palladium reagents[16] and undergo halogen replacement,[17] Lewis acid-catalyzed aldol reaction,[18] and atom-transfer chemistry with

**Scheme 5**




[a] TBSCl, imid, DMAP, $CH_2Cl_2$. [b] $ClMg(CH_2)_3OMgCl$, THF. [c] TsCl, $Et_3N$, DMAP, $CH_2Cl_2$. [d] 5% HF, $CH_3CN$. [e] Dess-Martin periodinane, $CH_2Cl_2$. [f] NaOH, MeOH. [g] $Bu_4N^+ F^-$, MeOH. [h] $CH_2=CHCH_2MgBr$, THF. [i] $BH_3$•THF, THF; NaOH, $H_2O_2$.

ease.[19] Curiously, information relating to the oxymercuration stereochemistry of α,*β*-unsaturated acids[20] and ketones is sparse. It might be expected that the direct attachment of an electron-withdrawing substituent to a double bond would lead to relatively late transition states. Other interactions will be shown to be important. The present investigation was initiated in an attempt to define these phenomena in the context of spirocyclization diastereoselectivity.

## Results

**The *cis,cis*-Trispiro Series.** The synthetic plan in this specific instance evolved from the previously described α-ketol **22a** (Scheme 5).[5] Following hydroxyl protection as the *tert*-butyldimethylsilyl derivative, addition of the Normant reagent[7] and exposure of the diol to tosyl chloride resulted in the predominant formation of **23** (68%). Following subsequent conversion to ketone **24**, the stage was set for base-promoted retro-Michael fragmentation to furnish cyclohexenone **25**. The further capping of **25** so as to recover the tetraspiro level of structural complexity necessitated prior formation of **26**. With this intermediate in hand, conversion to the advanced all-cis carbinol **28** was realized by repetition of the Normant capping protocol. The reciprocal stereochemistry required for diastereomer **30** was generated by reaction of **26** with the allyl Grignard reagent. This method utilizes the customary crossover in the preferred direction of attack exhibited by these two nucleophiles.[2] In a typical experiment, hydroboration and cyclization followed immediately to give **29** in 76% yield. The spectroscopic differences between **28** and **30** are detailed in the Experimental Section.

The oxymercuration experiments were performed with mercuric acetate under conditions of perchloric acid catalysis, which allowed for the completion of reaction within a few hours. After treatment with brine, the cyclized chloromercurials could be

(12) Pougny, J.-R.; Nassr, M. A. M.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1981**, 375.

(13) Nicotra, F.; Perego, R.; Ronchetti, F.; Russo, G.; Toma, L. *Gazz. Chim. Ital.* **1984**, *114*, 193.

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(15) For example: (a) Matejka, K. *Chem. Ber.* **1936**, *69*, 274. (b) Prokofjew, M. A.; Botvinnik, M. M. *Dokl. Akac. Nauk SSSR* **1939**, *25*, 488. (c) Nesmejanov, A. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1949**, 601, 602. (d) Whitehead, C. W. *J. Am. Chem.* Soc. **1958**, *80*, 2178, 2182. (e) Patrick, T. B.; Wu, T.-T. *J. Org. Chem.* **1978**, *43*, 1506.

(16) Larock, R. C.; Stinn, D. E. *Tetrahedron Lett.* **1989**, *30*, 2767.

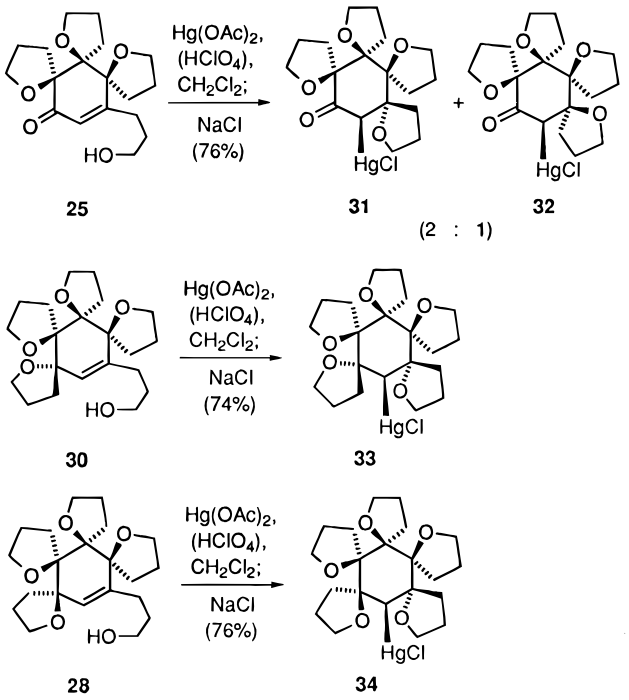
(17) Bloodworth, A. J.; Griffin, I. M. *J. Chem. Soc., Perkin Trans. 1* **1974**, 688.

(18) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1982**, *104*, 2323.

(19) For example: (a) Russell, G. A.; Hershberger, J.; Owens, K. *J. Organomet. Chem.* **1982**, *225*, 43. (b) Giese, B.; Erfort, U. *Chem. Ber.* **1983**, *116*, 1240. (c) Gouzoules, F. H.; Whitney, R. A. *Tetrahedron Lett.* **1985**, *26*, 3441. (d) Gouzoules, F. H.; Whitney, R. A. *J. Org. Chem.* **1986**, *51*, 2024. (e) Russell, G. A.; Kulkarni, S. V.; Khanna, R. K. *J. Org. Chem.* **1990**, *55*, 1080. (f) Russell, G. A.; Kulkarni, S. V. *J. Org. Chem.* **1993**, *58*, 2678.

(20) Park, W. R. R.; Wright, G. F. *J. Org. Chem.* **1954**, *19*, 1325.

**Scheme 6**



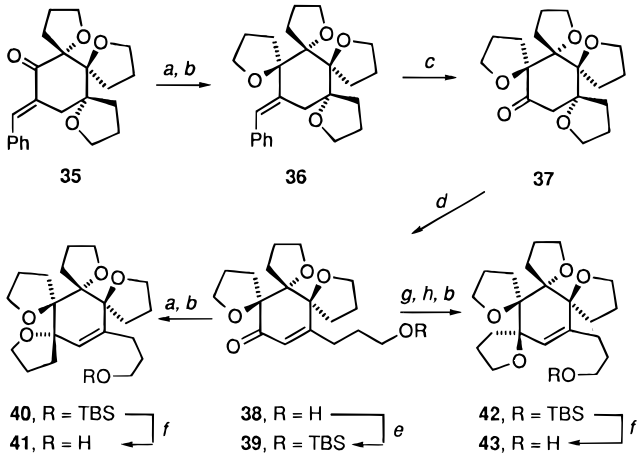

purified chromatographically. Enone **25** gave rise in good yield to a 2:1 mixture of **31** and **32** (Scheme 6). To define the stereochemistry of these products as rigorously as possible, recourse was made to X-ray crystallographic analysis. These studies revealed not only that **31** had materialized by net trans addition but that the carbon−mercury bond had been elaborated syn to the three original tetrahydrofuranyl oxygens. In addition, the conformation adopted in the solid state is that in which the mercury atom is axially disposed and positioned in a 1,3-diaxial relationship to each of two ether oxgens.

Ketone **32** holds special interest because it is the end result of a cis-stereoselective ring closure. Like **31**, the crystals of this product prefer axial orientation of the C−Hg bond in order to permit intramolecular coordination to two proximal axial oxygen centers.

In contrast to the response provided by **25**, the tetraspiro ethers **30** and **28** cyclized to give exclusively **33** and **34**, respectively. On the basis of $^{13}$C NMR, it was possible to recognize the configuration about the newly elaborated C−O centers. Thus, the reduction in the number of observable signals from the 21 exhibited by **34** to only 13 in the case of **33** requires that an internal symmetry plane be resident in the latter product. The relative stereochemistry of the C−Hg bonds could not be similarly deduced, and consequently crystal structure analyses were again undertaken. Once again, the mercury sits on the $\beta$-face of both molecules cis to the oxygens related 1,3 to it. In both examples, net trans addition is the kinetically favored process. Significantly, whereas the solid-state conformation adopted by **34** is quite similar to those earlier observed for **31** and **32**, diastereomer **33** features an equatorial C−Hg bond.

**The Consequences of a *trans,trans* Arrangement.** An assessment of the uniqueness of the stereoselectivity pattern exhibited in the *cis,cis* series requires that the *trans,trans* diastereomers be comparably investigated. A move in this direction was facilitated by the high degree of stereocontrol exhibited by **35**[2] during condensation with the Normant reagent. Application of this two-step capping procedure to **35** furnished **36** in 85% yield (Scheme 7). Arrival at **38** was accomplished

**Scheme 7**




[a] ClMg(CH$_2$)$_3$OMgCl, THF. [b] TsCl, Et$_3$N, DMAP, CH$_2$Cl$_2$. [c] O$_3$, CH$_2$Cl$_2$; Me$_2$S. [d] NaOH, MeOH. [e] TBSCl, Et$_3$N, DMAP, CH$_2$Cl$_2$. [f] Bu$_4$N$^+$ F$^-$, THF. [g] CH$_2$=CHCH$_2$MgBr, THF. [h] BH$_3$•THF; NaOH, H$_2$O$_2$.

by ozonolysis to furnish **37** followed by exposure of this ketone to sodium hydroxide in methanol. Following silylation of the hydroxyl substituent, conversion to **40** and then to **41** was achieved by reiterative submission to the same capping protocol.

The required reversal in stereoinduction at the point of attachment of the fourth spirotetrahydrofuran ring was initially expected to require reaction of **39** with allylmagnesium bromide in the presence of the exceptionally bulky methylaluminum bis-(2,6-di-*tert*-butyl-4-methylphenoxide) reagent.[21] The consequence of coordinating the aluminum reagent to the nodal plane of the C=O $\pi$-cloud[22] in **39** was anticipated to bring about nucleophilic attack preferentially from the $\alpha$-face. However, when experiments involving allylmagnesium bromide alone in THF were found to proceed with a 10:1 preference for carbon−carbon bond formation from the $\alpha$-face, the more elaborate procedure was never pursued. The spectral properties of **42** and **43** ultimately produced by this route were significantly different from those of **40** and **41**.

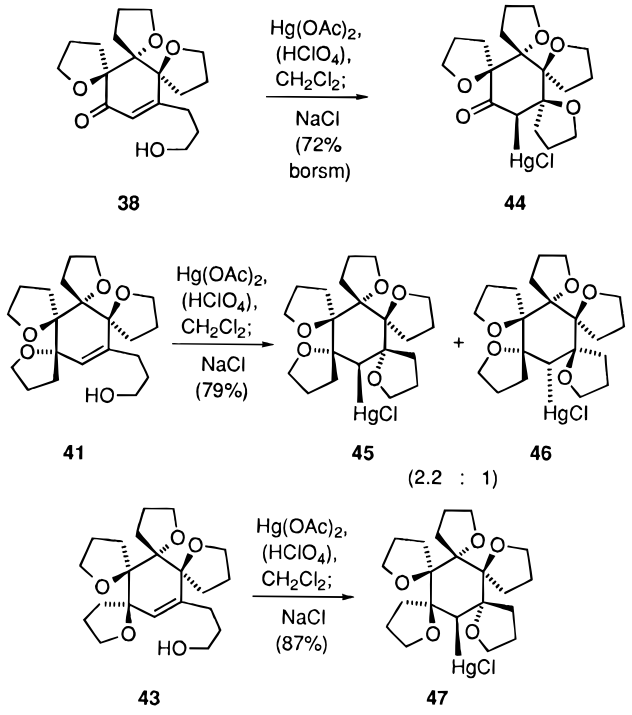
The oxymercuration chemistry of enone **38** as well as of the tetraspiro ethers **41** and **43** is summarized in Scheme 8. The situation for **38** is one in which the highly crystalline **44** is formed as the very predominant cyclization product, provided that reaction time is relatively short (5 h). Extended reaction times (viz., 48 h) led to increased consumption of **38** while simultaneously giving rise to a new product. The latter proved to be very labile on chromatography and was not characterized.

The cyclizations of **41** and **43** under identical conditions were complete within 45 min and 2 h, respectively. In the first instance, two pentaspiro ethers were produced in a ratio of 2.2:1.[4] Since no firm basis for configurational assignment to **45** and **46** emerged from close scrutiny of their $^1$H and $^{13}$C NMR spectra, a cocrystal of these two mercuric chlorides was subjected to X-ray structural analysis. These measurements were decisive in establishing that trans addition had materialized along both reaction pathways. In addition, it was made clear that intramolecular capture of that mercurinium ion resulting from approach to the $\beta$-face was favored by a factor of

(21) (a) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573. (b) Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588.

(22) (a) Power, M. B.; Bott, S. G.; Atwood, J. L.; Barron, A. R. *J. Am. Chem. Soc.* **1990**, *112*, 3446. (b) Healy, M. D.; Ziller, J. W.; Barron, A. R. *J. Am. Chem. Soc.* **1990**, *112*, 2949.

**Scheme 8**

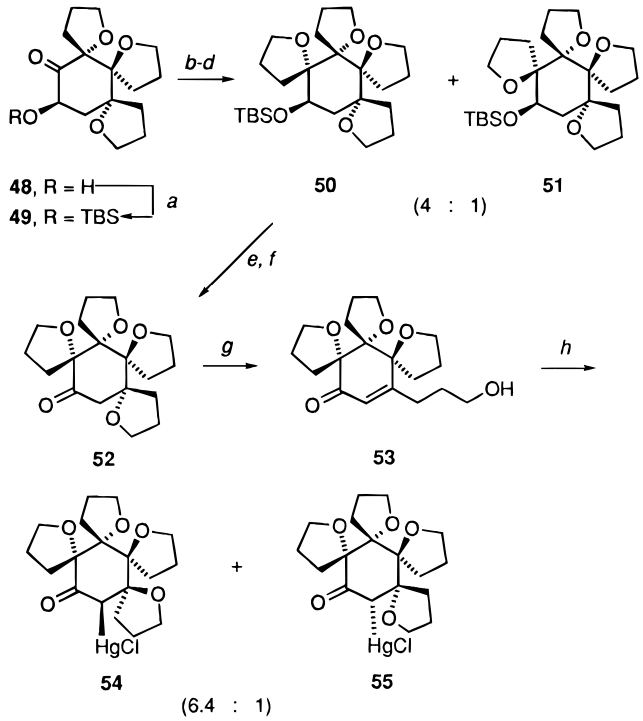



approximately 2. By comparison, **43** underwent conversion to **47** exclusively along this particular pathway. Product **47** proved to be conformationally dynamic in solution at room temperature, exhibiting two sets of signals of comparable magnitude in its $^1$H and $^{13}$C spectra. Although the thermal sensitivity of this substance precluded the implementation of useful variable temperature studies, it was possible to establish that **47** adopted a single conformation in the solid state by application of crystallographic and CPMAS techniques.[23] Notably, the high-resolution $^{13}$C NMR spectrum of this solid exhibits three sets of signals at 96.8−89.8 (5 C), 70.2−67.5 (6 C), and 39.1−28.6 (10 C) ppm.

**Spirocyclization of the *cis,trans* Enone.** To complete our systematic investigation of the degree and direction of stereoselectivity capable of being exerted by three contiguous spirotetrahydrofuran rings, the need existed to prepare **53**. The construction of this substrate began by silylation of the known α-hydroxy ketone **48**[5] (Scheme 9). The requirement to cap **49** in a manner that would lead predominantly to **50** was best met by reaction with allylmagnesium bromide and methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide).[21] Earlier precedent was adapted for the three-step conversion of **50** into **53**. Subsequent oxymercuration of **53** gave rise to a 6.4:1 mixture of the stable mercuric chlorides **54** and **55**. The relative stereochemistry associated with the newly introduced stereogenic centers in these two products was again firmly established by X-ray crystallography. The predominant formation of **54** via cis ring closure warrants comparison with the other members of this class. Indeed, both **25** and **38** give evidence of proceeding preferentially along a comparable mechanistic route, although to different degrees. This relationship does not persist when the carbonyl group is replaced by a spirotetrahydrofuran ring. Thus, **28**, **30**, and **43** give rise exclusively to a single trans oxymercuration product. Isomer **41** affords trans products **45** and **46**, demonstrating a lower degree of selectivity.

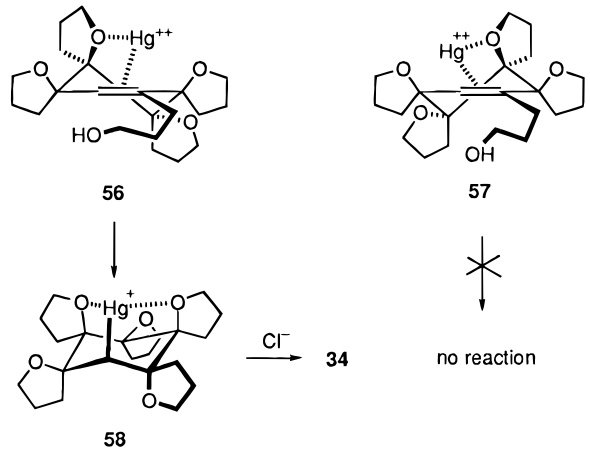
(23) Pihlaja, K.; Kleinpeter, E. *Carbon-13 NMR Chemical Shifts in Structural and Stereochemical Analysis*; VCH Publishers: New York; 1994; pp 273−280.

**Scheme 9**



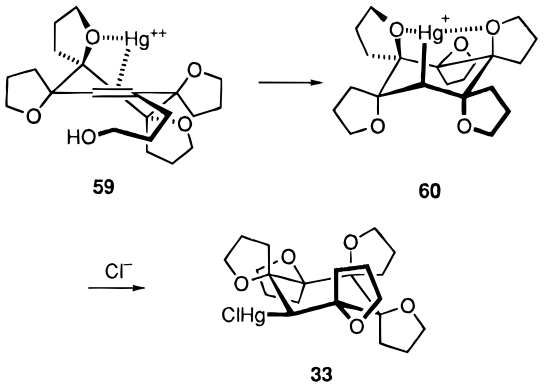

[a] TBSCl, imid, DMAP, $CH_2Cl_2$. [b] $CH_2$=$CHCH_2MgBr$, MeAl (*O*-2,6-di-*tert*-butyl-4-methylphenoxide), toluene, -78 ° → 20 °C. [c] $BH_3$•THF, THF; NaOH, $H_2O_2$. [d] TsCl, $Et_3N$, DMAP, $CH_2Cl_2$. [e] 5% HF, $CH_3CN$. [f] PDC, 3Å MS, $CH_2Cl_2$. [g] NaOH, MeOH. [h] $Hg(OAc)_2$, ($HClO_4$), $CH_2Cl_2$; NaCl.

**Scheme 10**

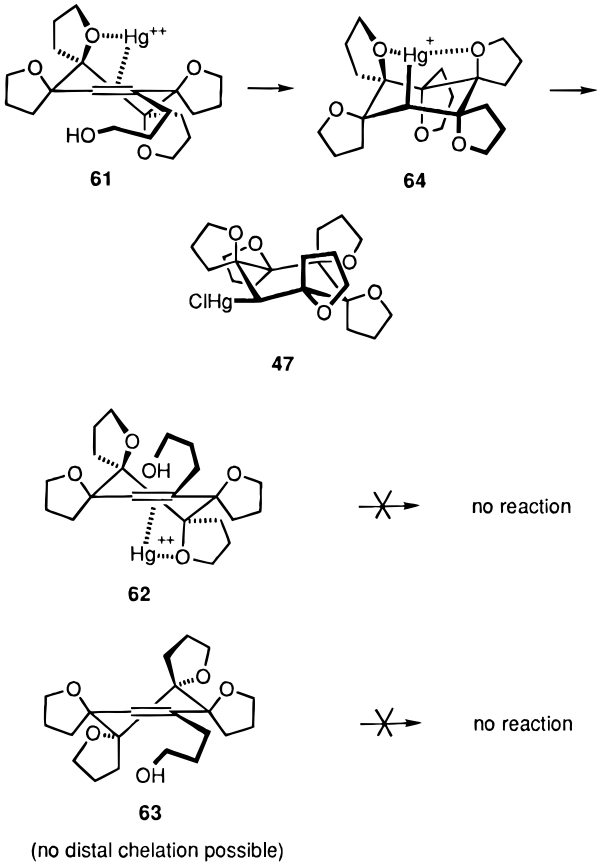



**Mechanistic Considerations.** The mercuricyclizations of tetraspiro alcohols **28**, **30**, **41**, and **43** exhibit a pattern of selectivity that gives evidence of being similarly governed. For example, **28** can be expected to undergo conversion to **56** and **57** without any obvious bias (Scheme 10). Although both structures enjoy the capacity for chelation-controlled approach of $Hg^{2+}$ to the top side of the double bond, only in the case of **56** will a chairlike arrangement develop as the system progresses to formation of the mercurinium species and beyond. If the involvement of **57** is suppressed because of the need to advance to a distorted boatlike six-membered ring, then bottom side attack by the hydroxyl group with opening of the mercurinium ion derived from **56** should be kinetically advantaged and give rise to **58**. Subsequent addition of chloride ion delivers **34**, which is seen to retain the original trans diaxial arrangement

**Scheme 11**




**Scheme 12**

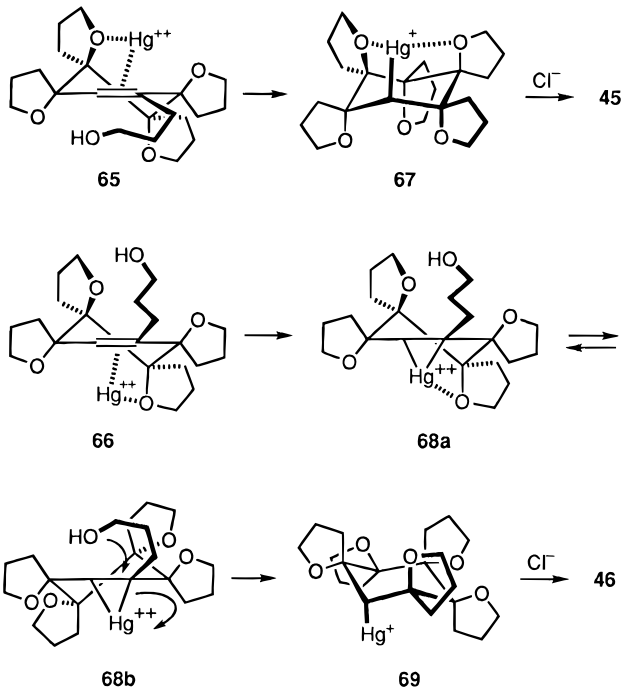



of the C−Hg and C−O bonds just formed (X-ray). The pair of diaxial 1,3 Hg/O interactions resident in **34** is believed to contribute in part to the maintenance of this geometry.

An entirely similar fate should accompany the oxymercuration of **30** since the only configurational change is at a noncritical position of the cyclohexene core (see **59**, Scheme 11). The evolution of a mercurinium ion from **59** serves to generate **60** and ultimately **33**. In contrast to **58** where three C−O bonds are projected axially, **60** has four spatial projections of this type. Evidently, the accompanying gauche $CH_2$- - -$CH_2$ interactions involving neighboring tetrahydrofuran rings are sufficiently elevated to promote adoption of the alternative chair conformation as observed for mercuric chloride **33** (X-ray).

Where **43** is concerned, the choices are between **61**, **62**, and **63** (Scheme 12). Ring closure from the mercurinium ion that would develop from **62** would require the generation of a boatlike cyclohexane and is therefore kinetically disadvantaged.

**Scheme 13**

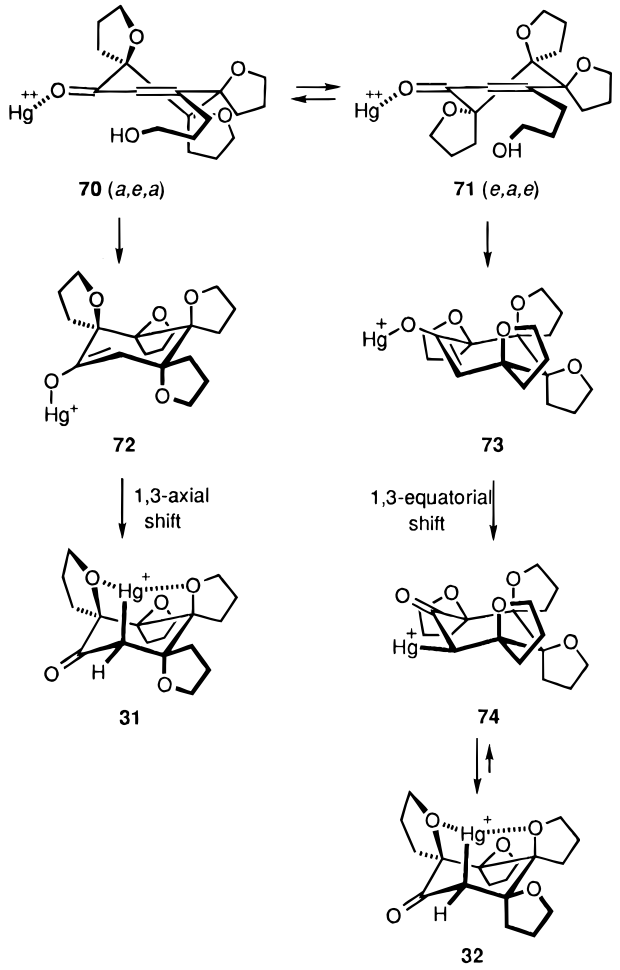



The third option has no opportunity for coordination of the incoming mercuric ion to an ether oxygen on either surface of the $\pi$-bond and is therefore unimportant to the ensuing chemistry. Therefore, **61** is preferentially transformed via **64** into **47**. The relative configurations of the oxygen substituents in **64** (four axial, one equatorial) are again such that conformational inversion of the cyclohexane core is expected. The crystal structure of **47** provides experimental support for this conclusion.

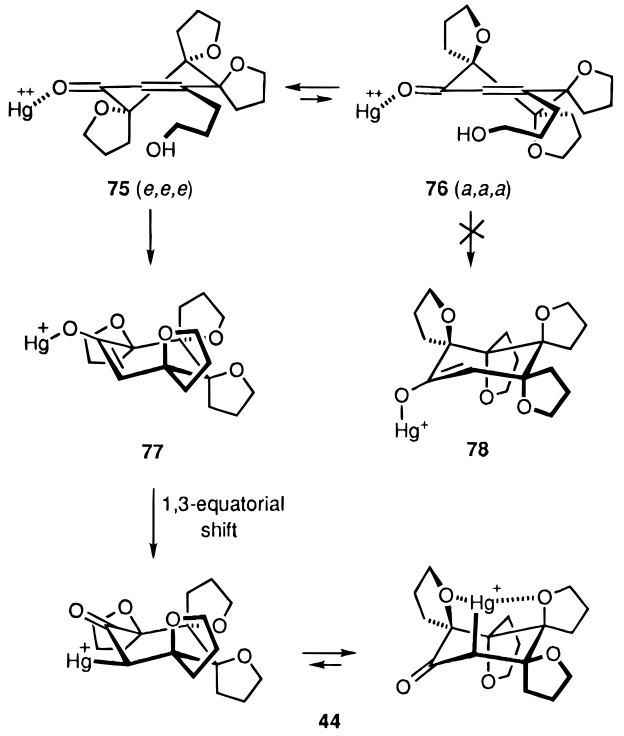
The cyclization of **41** constitutes a particularly informative example (Scheme 13). Precoordination of an ether oxygen to $Hg^{2+}$ can arise only in **65** and **66**. As progress is made along the reaction coordinate involving **65**, the flexible 3-hydroxypropyl side chain must move into the requisite axial position to serve as the anion source and complete the process. The occurrence of this intramolecular cyclization necessarily orients all six C−O bonds axially as in **67**. This feature so disfavors the **65** → **67** ring closure that the involvement of the alternative complex **66** now has an opportunity to compete. As is illustrated, the conversion of **66** into **68a** is met with the same level of $CH_2$ interaction and is therefore not impeded. Should this mercurinium ion be capable of equilibration with **68b**, a reaction channel for accessing **69** and subsequently **46** would become available. It is noteworthy however that the mercurinium ion and transition state that are precursors to **67** will maintain mercury−axial oxygen interactions, while the transformation from **68a** to **68b** as well as the transition state leading to **69** requires breaking the Hg−O interaction present in **68a**.

It will be recalled that a 2.2:1 ratio is observed for the conversion to **45** and **46**. Accordingly, despite the need to overcome a loss in intramolecular chelation to mercury, the **66** → **69** option remains reasonably competitive. In line with preceding considerations, the more stable conformation of **45** must be that in which all six C−O bonds are equatorial, and the solid-state structural analysis confirms this fact. On the other hand, the prevailing disposition of the oxygen atoms in **69** warrants that they not be altered. The informative crystal structure of **46** reveals the pattern adopted by **46** indeed to be that defined by **69**.

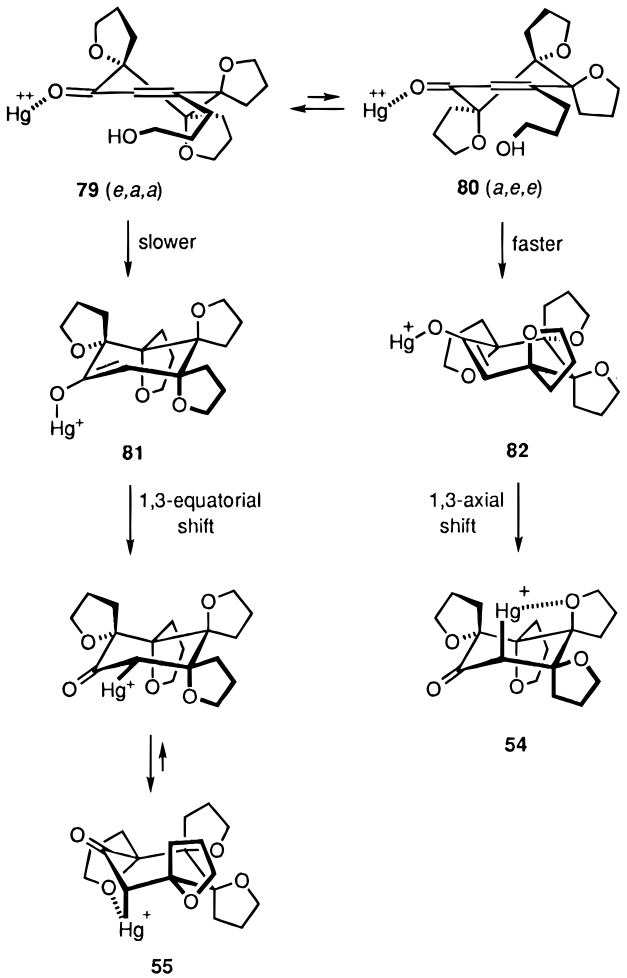
**Scheme 14**




**Scheme 15**




**Scheme 16**




The stereoselectivities observed for the α,β-unsaturated ketones **25**, **38**, and **53** suggest that a different mechanism is operative in these examples. All three reactants deliver a significant amount of cis cyclization product. In fact, for **38** and **53** the product configurations are exclusively cis! The only way that these results can be reconciled with the intervention of mercurinium ion intermediates is if the product mercuric enolates were subject to epimerization at the carbon substituted by mercury. We have not found evidence for this phenomenon with our systems, nor has evidence to this effect been uncovered in the limited literature on mercuric enolates. For these reasons, the plausible schemes presented below are offered as a tentative rationalization of these findings.

The unique stereochemical pattern exhibited by the three enones can be explained on the basis of precoordination of the mercuric ion to the Lewis base carbonyl oxygen. The polarization of the neighboring double bond brought on by this event initiates cyclization. Schemes 14−16 show the pathway analysis for the three ketones. Some noteworthy patterns emerge. The complex arising from stereoisomer **25** can be defined in terms of the pair of conformations **70** and **71**. Neither structure is unduly crowded since the triad of spirotetrahydrofuran rings in **70** is arranged with the C−O bonds oriented either in axial−equatorial−axial (a,e,a) fashion or in the complementary e,a,e mode. For the usual stereoelectronic reasons, **70** and **71** will be converted into **72** and **73**, respectively. After these allowed steps have taken place, the final 1,3-migration of the mercury atom from O to C will occur. As will be seen, the end result is often translocation of the Hg atom to the equatorial site. One exception to the contrary is **72**, which gives rise to **31**. The relative ease of this isomerization may be associated with the 2-fold coordination available to the axially oriented metal as

illustrated. No equivalent high-level 1,3-diaxial Hg- - -O interaction is available to **73** or **77**.

Comparable evaluation of **38** reveals a complication not previously encountered. While conformer **75** is clearly devoid of any gauche $CH_2$- - -$CH_2$ interactions as a consequence of its e,e,e character, the overall a,a,a arrangement in **76** is maximally destabilized. As a result, **75** should heavily dominate this equilibrium. Assuming that the rates of cyclization of **75** and **76** are not greatly imbalanced, we would expect the production of **77** to outweigh that of **78** by a substantial margin. The experimental facts support this analysis. Once the 1,3-equatorial shift of mercury occurs, ring inversion to permit intramolecular chelation in **44** completes the process.

The same mechanistic dissection has been applied to **53** in Scheme 16. In this particular example, it is important to recognize that the e,a,a relationship resident in conformer **79** is more sterically demanding than the a,e,e arrangement present in **80**. Consequently, the equilibrium should be skewed toward **79**. Beyond this, cyclization to form **81** results in formation of three adjacent equatorial $CH_2$ groups, while cyclization to form **82** results in no adjacent equatorial $CH_2$ groups. Therefore, preferential cyclization to **54** is predicted, and the preferred (6.4:1) formation of **54** is very reasonable. Note that arrival at **55** can be construed as before to be the end result of a 1,3-equatorial shift of mercury from oxygen to carbon with ultimate ring inversion to achieve chelation. In contrast, **82** parallels **72** in its kinetically preferred 1,3-axial shift of the mercury atom so as to achieve internal chelation directly.

**Overview.** The results indicate that tetraspiro carbinols such as **28**, **30**, **41**, and **43** undergo mercuric acetate-promoted spirocyclization by a different mechanism than the structurally related trispirocyclohexenones **25**, **38**, and **53**. In the first instance, the approach of $Hg^{2+}$ to a specific surface of the cyclohexene double bond is likely directed by precoordination to an axially disposed ether oxygen positioned $\gamma$ to the reaction site. As reaction progresses to the mercurinium ion stage and into ring closure, the systems are recognized to be sensitive to the customary stereoelectronic effects, viz., the development of chairlike characteristics. An added energetic factor is associated with the preferred equatorial projection of the C−O bonds that form part of the several existing spirotetrahydrofuran rings. The associated gauche O- - -O interactions obviously bring about less steric congestion than those of the $CH_2$- - -$CH_2$ type, which arise when the C−C bonds of these pendant rings are oriented equatorially. The latter scenario is skirted if it is possible to do so.

The electrophilic mercuric salt appears to coordinate alternatively in Lewis acidic fashion to the carbonyl oxygen of enones **25**, **38**, and **53**. The resulting activation of the conjugated double bond leads again to intramolecular attack by the OH of the hydroxypropyl side chain. Unlike the concerted back side opening of a mercurinium ion which leads directly to trans products, the second option delivers a mercuric enolate. The stereodefining step may occur in a subsequent 1,3 O → C shift by the metal atom. In the majority of the examples studied here, the migration culminates in formation of an equatorial C−Hg bond and delivery of cis products. The low-energy conformations ultimately adopted by these mercuric ketones can be understood by considering the opportunities available for 1,3-diaxial Hg- - -O chelation and the minimization of buttressing contributions from neighboring equatorial $CH_2$ segments of the multiple spirotetrahydrofuran rings.

The picture that emerges from the present investigation is both interesting and provocative. Despite high degrees of substitution, general patterns of reactivity and conformational free energy preferences have emerged. Chelation of oxygen to $Hg^{2+}$ gives evidence of playing a strikingly powerful role in directing the stereochemical course of spirocyclization as well as the overall ground-state topography of the product. The torsional energies of existing bonds give evidence of displaying additivity. While the estimation of torsional energies for developing bonds is very difficult, their impending thermodynamic contributions are subject to qualitative evaluation, probably because the cyclizations in question occur via relatively late transition states.

## Experimental Section

Melting points are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded at the indicated field strengths. High-resolution mass spectra were measured at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark, or at Atlantic Microlab, Inc., Norcross, GA. All reactions were carried out under a nitrogen atmosphere, and the ensuing separations were effected either with Merck Lobar columns (Lichroprep Si-60) fitted to a Fluid Metering INC pump (MPLC) or on Merck silica gel $HF_{254}$ (flash chromatography). The organic extracts were dried over anhydrous magnesium sulfate or sodium sulfate. Solvents were reagent grade and in many cases dried prior to use.

**(5*R**,6*R**,11*R**,17*S**)-17-(*tert*-Butyldimethylsiloxy)-1,7,12-trioxatrispiro[4.0.4.0.4.3]octadecan-16-one (22b).** To a magnetically stirred solution of **22a**[5] (1.25 g, 4.4 mmol), imidazole (0.90 g, 13.2 mmol), and DMAP (100 mg) in $CH_2Cl_2$ (125 mL) was added *tert*-butyldimethylsilyl chloride (1.33 g, 8.8 mmol). The reaction mixture was stirred for 48 h, and saturated $NaHCO_3$ solution (80 mL) was added. The aqueous layer was extracted with $CH_2Cl_2$ (4 × 75 mL), and the combined organic phases were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 5% methanol in dichloromethane) gave **22b** (1.79 g, 100%) with mp 125−127 °C: IR (KBr, cm$^{-1}$) 1736, 1472, 1256, 1162; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.34 (dd, $J$ = 6.9, 13.0 Hz, 1 H), 4.12 (ddd, $J$ = 3.2, 8.1, 8.1 Hz, 1 H), 4.02−3.87 (m, 3 H), 3.82−3.65 (m, 2 H), 2.37 (t, $J$ = 12.5 Hz, 1 H), 2.27−1.57 (m, 13 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.03 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) ppm 207.4, 94.1, 92.2, 85.3, 71.6, 70.4, 67.9, 67.2, 41.7, 33.6, 33.0, 27.3, 26.7, 26.4, 25.8 (3 C), 25.3, 18.5, −4.2, −5.1; MS *m*/*z* ($M^+$) calcd 396.2332, obsd 396.2341.

Anal. Calcd for $C_{21}H_{36}O_5Si$: C, 63.60; H, 9.15. Found: C, 63.28; H, 9.12.

***tert*-Butyldimethyl[[(5*R**,6*R**,11*S**,16*S**,21*S**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-yl]oxy]silane (23).** A cold (0 °C), magnetically stirred solution of **22b** (0.74 g, 1.9 mmol) in THF (60 mL) was treated with the Normant reagent[7] (10.8 mL of 0.26 M, 2.8 mmol) and processed in the usual way.[2,5] The residue was purified by chromatography on silica gel (elution with 5% methanol in dichloromethane) to give 0.64 g (74%) of diol. This diol was cyclized in the presence of *p*-toluenesulfonyl chloride (0.64 g, 3.4 mmol) as previously detailed.[2,5] Chromatography of the resulting material on silica gel (elution with 5% methanol in dichloromethane with 1% triethylamine as additive) afforded 0.57 g (68%) of **23** as a white solid, mp 95−100 °C: IR ($CHCl_3$, cm$^{-1}$) 1074; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.10−3.82 (m, 4 H), 3.91−3.82 (m, 3 H), 3.63 (q, $J$ = 8.2 Hz, 1 H), 3.48 (dd, $J$ = 12.2, 3.8 Hz, 1 H), 2.43 (t, $J$ = 12.2 Hz, 1 H), 2.09−1.62 (m, 16 H), 1.44 (dd, $J$ = 12.3, 3.8 Hz, 1 H), 0.84 (s, 9 H), 0.25 (s, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) ppm 92.9, 91.0, 90.8, 86.7, 74.8, 70.9, 70.3, 69.6, 66.4, 37.8, 33.8, 33.6, 30.5, 28.7, 27.0, 26.6, 26.4, 25.7 (3 C), 25.4, 17.9, −4.2, −4.8; MS *m*/*z* ($M^+$) calcd 438.2802, obsd 438.2803.

Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.71; H, 9.65. Found: C, 65.63; H, 9.56.

**(5*R**,6*R**,11*R**,16*R**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]-docosan-21-one (24).** Silyl ether **23** (220 mg, 0.50 mmol) was deprotected with 5% hydrofluoric acid in acetonitrile as previously described.[2,5] The residue was purified by chromatography on silica

gel (elution with 5% methanol in dichloromethane) to give 150 mg (92%) of the alcohol as a white solid, mp 154−155 °C. This alcohol (150 mg, 0.46 mmol) was dissolved in $CH_2Cl_2$ (20 mL), and Dess−Martin periodinane[24] (336 mg, 0.92) was added. The reaction mixture was stirred at room temperature for 90 min and washed twice with a saturated $Na_2S_2O_3$ solution (10 mL) and once with a saturated $NaHCO_3$ solution (10 mL). The combined aqueous layers were extracted with $CH_2Cl_2$ (3 × 30 mL). The combined organics were dried, filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 5% methanol in dichloromethane) and triturated with hot pentane to give 146 mg (99%) of **24** as a white solid, mp 146−148 °C: IR ($CHCl_3$, $cm^{-1}$) 1712, 1063; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 4.31−4.14 (m, 2 H), 3.84−3.57 (m, 5 H), 3.38−3.36 (br s, 1 H), 2.41 (br s, 1 H), 2.25 (d, $J$ = 12.2 Hz, 1 H), 1.80−1.31 (m, 16 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 93.7, 87.8, 70.7, 70.3, 69.3, 67.1, 46.1, 33.1, 27.1, 27.0, 25.8, 25.2 (6 C signals not resolved); MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1788.

Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.92; H, 8.17.

**(5*R**,6*R**,11*R**)-18-[3-(*tert*)-Butyldimethylsiloxy)propyl]-1,7,12-trioxatrispiro[4.0.4.0.4.3]octadec-17-en-16-one (26).** Ketone **24** (75 mg, 0.23 mmol) was dissolved in MeOH (10 mL) and treated with NaOH (25 mg, 0.46 mmol). The reaction mixture was stirred at room temperature for 2.5 h, quenched with cold HCl/$H_2O$ (1.5 mL), and diluted with $CH_2Cl_2$ (30 mL). The separated aqueous layer was extracted with $CH_2Cl_2$ (4 × 30 mL), and the combined organics were dried, filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 5% methanol in dichloromethane) to give 63 mg (85%) of **25**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.78 (s, 1 H), 4.30 (dt, $J$ = 7.8, 2.8 Hz, 1 H), 4.22−4.15 (m, 1 H), 3.99−3.78 (m, 4 H), 3.66−3.59 (m, 2 H), 2.48−2.34 (m, 2 H), 2.27−2.10 (m, 3 H), 2.03−1.71 (series of m, 12 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 199.5, 167.4, 122.3, 94.8, 91.0, 90.4, 70.4, 70.2, 69.4, 61.4, 36.3, 33.9, 30.9, 27.5 (2 C), 27.3, 27.0, 25.0; MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1772.

To a magnetically stirred solution of **25** (262 mg, 0.81 mmol), imidazole (165 mg, 2.4 mmol), and DMAP (50 mg) in $CH_2Cl_2$ (20 mL) was added *tert*-butyldimethylsilyl chloride (244 mg, 1.6 mmol). The reaction mixture was stirred for 12 h, and a saturated $NaHCO_3$ solution (15 mL) was added. The aqueous layer was extracted with $CH_2Cl_2$ (4 × 50 mL), and the combined organic phases were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 50% ethyl acetate in petroleum ether) gave 332 mg (94%) of **26** as a white solid, mp 91−92 °C: IR (KBr, $cm^{-1}$) 1684, 1630, 1472, 1420; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.77 (s, 1 H), 4.33 (dt, $J$ = 7.9, 2.7 Hz, 1 H), 4.16 (dt, $J$ = 7.9, 4.6 Hz, 1 H), 4.03−3.80 (m, 4 H), 3.73−3.57 (m, 2 H), 2.47−2.36 (m, 1 H), 2.31−2.12 (m, 4 H), 2.06−1.61 (m, 11 H), 0.88 (s, 9 H), 0.34 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 199.7, 167.4, 121.5, 94.6, 91.2, 90.2, 70.4, 70.3, 69.4, 62.5, 36.2, 34.0, 30.2, 27.8, 27.6, 27.4, 27.1, 25.9 (3 C), 25.0, 18.3, −5.3, −5.4; MS $m/z$ ($M^+$) calcd 436.2645, obsd 436.2637.

Anal. Calcd for $C_{24}H_{40}O_5Si$: C, 66.02; H, 9.23. Found: C, 66.15; H, 9.19.

***tert*-Butyldimethyl[3-[(5*R**,6*R**,11*S**,16*R**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-en-21-yl]propoxy]silane (27).** A cold (0 °C), magnetically stirred solution of **26** (38 mg, 0.09 mmol) in THF (5 mL) was treated with the Normant reagent[7] (0.52 mL of 0.25 M, 0.13 mmol) and processed in the usual way.[2,5] The residue was purified by chromatography on silica gel (elution with 5% methanol in dichloromethane) to give a quantitative amount of diol. This diol was subjected to the standard cyclization conditions as previously detailed. Chromatography of the resulting material on silica gel (elution with 5% methanol in dichloromethane with 1% triethylamine additive) afforded **27** as an unstable brown oil (77% for two steps), which was utilized without delay: IR ($CHCl_3$, $cm^{-1}$) 1470, 1257, 1063; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.31 (s, 1 H), 4.40−3.88 (m, 5 H), 3.82−3.70 (m, 3 H), 3.68−3.54 (m, 2 H), 2.21−1.92 (m, 2 H), 1.92−1.01 (m, 18 H), 0.99 (s, 9 H), 0.07 (s, 6 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 128.2, 127.2, 92.9, 90.7, 89.5, 85.3, 69.5, 69.3, 69.1, 67.9, 62.9, 35.8, 35.4, 32.2, 31.8, 30.3, 28.0, 27.8, 27.0 (2 C), 26.2, 25.9 (3 C), 18.2, −5.4 (2 C); MS $m/z$ ($M^+$) calcd 478.3115, obsd 478.3117.

***tert*-Butyldimethyl[3-[(5*R**,6*R**,11*S**,16*R**)-1,7,12,17-tetraoxotetraspiro[4.0.4.0.4.0.4.2]docos-21-en-21-yl]propoxy]silane (29).** To a cooled (0 °C) solution of **26** (99 mg, 0.23 mmol) in THF (2 mL) was added a solution of allylmagnesium bromide in ether (0.46 mL, 0.46 mmol). After 5 min, the reaction mixture was allowed to warm slowly to 20 °C, stirred overnight, and quenched with a saturated $NH_4Cl$ solution (12 mL). The layers were separated, and the aqueous phase was extracted with $CH_2Cl_2$ (4 × 20 mL). The combined organic solutions were dried, filtered, and concentrated. The crude product was chromatographed on silica gel (elution with 5% methanol in dichloromethane containing 1% $Et_3N$) to give 62 mg (57%) of the syn alcohol and 34 mg (31%) of the anti isomer.

To a cooled (0 °C) solution of the anti alcohol (135 mg, 0.28 mmol) in THF (10 mL) was added borane−THF complex (0.42 mL of 1 N in THF, 0.42 mmol). The reaction mixture was stirred at 0 °C for 1 h, treated with sodium hydroxide (3 N, 0.4 mL) and $H_2O_2$ (30%, 0.4 mL), allowed to warm slowly to room temperature with stirring for 2 h, and partitioned between brine (10 mL) and $CH_2Cl_2$ (20 mL). The separated aqueous layer was extracted with $CH_2Cl_2$ (4 × 20 mL). The combined organics were dried, filtered, and concentrated. The crude product was chromatographed on silica gel (elution with 5% methanol in dichloromethane) to give 120 mg (86%) of the diol which was used directly in the next step.

This diol was cyclized in the presence of *p*-toluenesulfonyl chloride (55 mg, 0.29 mmol) for 3 d under previously described conditions. Chromatography of the resulting material on silica gel (elution with 5% methanol in dichloromethane with 1% triethylamine additive) afforded 102 mg (76%) of **29** as a brown oil: IR ($CHCl_3$, $cm^{-1}$) 1470, 1256, 1059; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.08 (s, 1 H), 3.98−3.65 (m, 5 H), 3.64−3.44 (m, 5 H), 2.63−2.53 (m, 1 H), 2.07−1.48 (series of m, 19 H), 0.77 (s, 9 H), 0.08 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 140.3, 127.2, 94.1, 90.9, 90.2, 87.8, 69.8, 69.7, 69.1, 67.4, 63.3, 36.0, 35.0, 33.0, 31.1, 28.4, 28.2, 27.4, 27.0, 26.9, 26.2, 26.0 (3 C), 18.3, −5.3 (2 C); MS $m/z$ ($M^+$) calcd 478.3115, obsd 478.3101.

**(5*R**,6*S**,11*R**,16*R**,22*S**)-22-(Chloromercurio)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docosan-21-one (31) and (5*R**,6*S**,11*R**,16*R**,22*R**)-22-(Chloromercurio)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docosan-21-one (32).** Enone **25** (63 mg, 0.20 mmol) was dissolved in $CH_2Cl_2$, and $Hg(OAc)_2$ (77 mg, 0.25 mmol) was added followed by a drop of $HClO_4$. The reaction mixture was stirred at room temperature for 5 h, diluted with EtOAc (20 mL) and brine (10 mL), and stirred at room temperature for 5 min. The separated organic layer was washed with brine (2 × 10 mL), and the combined organic layers were dried, filtered, and concentrated. The residue was purified by chromatography (elution with 5% methanol in dichloromethane with 1% triethylamine additive) to give 58 mg (51%) of **31** and 27 mg (25%) of **32**.

For **31:** mp 105−117 °C; IR ($CHCl_3$, $cm^{-1}$) 1693, 1062, 1050; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.30−4.23 (m, 1 H), 4.17−4.05 (m, 2 H), 4.03−3.93 (m 2 H), 3.90−3.86 (m, 2 H), 3.70−3.63 (m,1 H), 3.07 (s, 1 H), 2.49−2.42 (m, 1 H), 2.28−1.55 (series of m, 15 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 206.7, 91.9, 91.8, 90.4, 89.9, 71.2, 70.9, 69.0, 68.4, 37.4, 34.1, 34.0, 29.2, 26.9, 26.6, 26.2, 25.8, 24.3; MS $m/z$ ($M^+$) calcd 558.1097, obsd 558.1050.

For X-ray crystallographic analysis, see the Supporting Information.

For **32:** mp 190−195 °C; IR (film, $cm^{-1}$) 1682, 1446, 1085; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 4.29−4.23 (m, 1 H), 4.17−4.05 (m, 1 H), 4.04−3.88 (m, 4 H), 3.70−3.55 (m, 2 H), 3.03 (s, 1 H), 2.37−2.30 (m, 1 H), 2.13−1.55 (series of m, 15 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 207.6, 91.8, 91.3, 89.4, 88.6, 70.8, 70.6, 68.5, 67.2, 60.1, 35.4, 33.2, 28.6, 26.8, 26.7, 25.9, 25.8, 23.9; MS $m/z$ ($M^+$) calcd 558.1097, obsd 558.1091.

Anal. Calcd for $C_{18}H_{25}O_5HgCl$: C, 38.78; H, 4.52. Found: C, 38.86; H, 4.56.

For X-ray crystallographic analysis, see the Supporting Information.

**(5α,6*β*,11*β*,16*β*,21α,26*β*)-26-(Chloromercurio)-1,7,12,17,22-pentaoxapentaspiro[4.0.4.0.4.0.4.0.4.1]hexacosane (33).** To a solution of **29** (258 mg, 0.54 mmol) in THF (15 mL) was added TBAF (1.0

(24) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

M/THF, 1.0 mL). The reaction mixture was stirred at room temperature for 2 h, the solvent was removed in vacuo, and the residue was absorbed onto silica gel. The product was purified by chromatography on silica gel (5% methanol in dichloromethane) to give a quantitative amount of **30** which was used directly.

To a solution of **30** (197 mg, 0.54 mmol) in $CH_2Cl_2$ (20 mL) was added $Hg(OAc)_2$ (430 mg, 1.4 mmol), followed by a drop of $HClO_4$. The reaction mixture was stirred at room temperature for 8 h, diluted with EtOAc (20 mL) and brine (10 mL), and stirred for an additional 5 min. The separated aqueous layer was extracted with EtOAc (4 × 40 mL), and the combined organic layers were dried, filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 25% ethyl acetate in petroleum ether containing 1% triethylamine) to afford 240 mg (74%) of **33** as a white solid: mp 212−215 °C; IR ($CHCl_3$, $cm^{-1}$) 1060; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 3.94 (t, $J$ = 6.4 Hz, 2 H), 3.66−3.60 (m, 2 H), 3.50−3.31 (m, 6 H), 3.14−3.07 (m, 2 H), 2.88 (s, 1 H), 2.00−1.28 (series of m, 17 H), 0.91−0.89 (m, 1 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 95.4, 94.4 (2 C), 91.0 (2 C), 70.7, 69.2 (2 C), 67.5 (2 C), 36.2 (2 C), 33.1 (2 C), 30.6, 30.4, 28.8 (2 C), 28.4 (2 C), 27.0; MS $m/z$ ($M^+$) calcd 600.1566, obsd 600.1564.

Anal. Calcd for $C_{21}H_{31}O_5HgCl$: C, 42.07; H, 5.21. Found: C, 42.18; H, 5.23.

For X-ray crystallographic analysis, see the Supporting Information.

**(5α,6α,11α,16α,21*β*,26α)-26-(Chloromercurio)-1,7,12,17,22-pentaoxapentaspiro[4.0.4.0.4.0.4.0.4.1]hexacosane (34).** To a solution of **27** (78 mg, 0.16 mmol) in THF (3 mL) was added TBAF (1.0 M/THF, 0.5 mL). The reaction mixture was stirred at room temperature for 2 h. The solvent was removed in vacuo, and the residue was absorbed on silica. The product was purified by chromatography on silica gel (elution with 7.5% methanol in dichloromethane) to give 62 mg (100%) of **28**, which was used directly.

To a solution of **28** (62 mg, 0.17 mmol) in $CH_2Cl_2$ (10 mL) was added $Hg(OAc)_2$ (135 mg, 0.43 mmol), followed by a drop of $HClO_4$. The reaction mixture was stirred at room temperature for 8 h, diluted with EtOAc (20 mL) and brine (10 mL), and stirred for an additional 5 min. The separated aqueous layer was extracted with EtOAc (4 × 20 mL), and the combined organic layers were dried, filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 30% ethyl acetate in petroleum ether containing 1% triethylamine) to give 80 mg (76%) of **34** as white crystals: mp 195−198 °C; IR ($CHCl_3$, $cm^{-1}$) 1220, 1049; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 4.23−4.13 (m, 2H), 4.02−3.96 (m, 1 H), 3.82−3.76 (m, 1 H), 3.65−3.50 (m, 4 H), 3.38−3.25 (m, 2 H), 2.51−2.44 (m, 1 H), 2.22 (s, 1 H), 1.79−1.07 (series of m, 19 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 93.7, 92.1, 90.3, 90.2, 89.9, 71.0, 70.2, 69.0, 67.5, 65.6, 57.6, 39.0, 34.2, 32.5, 29.3, 29.0, 27.7, 27.0 (2 C), 26.6, 25.6; MS $m/z$ ($M^+$) calcd 600.1566, obsd 600.1560.

Anal. Calcd for $C_{21}H_{31}O_5HgCl$: C, 42.07; H, 5.21. Found: C, 41.86; H, 5.14.

For X-ray crystallographic analysis, see the Supporting Information.

**(5*R**,6*S**,11*S**,16*R**)-21-[(*E*)-Benzylidene]-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docosane (36).** The Normant reagent[7] (81.3 mL of a 0.3 M solution in THF, 24.6 mmol) was added via syringe to a stirred solution of **35**[2] (8.77 g, 24.6 mmol) in dry THF (400 mL) under $N_2$ at −78 °C. The reaction mixture was allowed to warm to room temperature over 5 h, diluted with a saturated $NH_4Cl$ solution, and extracted with ether. The extracts were dried, concentrated, and submitted directly to cyclization conditions.

The above diol (10.72 g, 25.9 mmol) in $CH_2Cl_2$ (300 mL) was treated with triethylamine (8.8 mL, 62.5 mmol), *p*-toluenesulfonyl chloride (6.17 g, 32.6 mmol), and DMAP (250 mg). The reaction mixture was stirred at room temperature for 24 h, at which time TLC indicated that starting material remained. Additional *p*-toluenesulfonyl chloride (3.57 g, 18.7 mmol) and triethylamine (2.6 mL, 18.7 mmol) were added, and the mixture was stirred for an additional 12 h, diluted with 1 N HCl, and extracted with ether. The extracts were dried and concentrated, and the residue was chromatographed on silica gel (elution with 7.5% ethyl acetate in hexanes) to give after recrystallization ($CH_2Cl_2$, MeOH) 8.29 g (85%) of **36** as a white solid: mp 149 °C; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.33−7.25 (m, 2 H), 7.22−7.16 (m, 3 H), 6.70 (s, 1 H), 3.98−3.86 (m, 2 H), 3.84−3.79 (m, 1 H), 3.78−3.51 (m, 4 H), 3.51−3.43 (m, 1 H), 2.76 (d, $J$ = 13.8 Hz, 1 H), 2.51−2.26 (m, 2 H), 2.23−1.66 (series of m, 13 H), 1.49−1.32 (m 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 140.4, 138.0, 128.8, 126.2, 125.5, 101.2, 91.1, 91.0, 90.9, 87.7, 69.2, 68.7, 67.7, 67.6, 36.3, 31.7, 29.9, 29.7, 29.6, 28.2 (2 C), 26.4, 25.9; MS $m/z$ ($M^+$) calcd 396.2301, obsd 396.2293.

Anal. Calcd for $C_{25}H_{32}O_4$: C, 75.72; H, 8.13. Found: C, 75.54; H, 8.09.

**(5*R**,6*S**,11*R**,16*S**)-1,7,12,17-Tetraoxatetraspiro[4.0.4.0.4.0.4.2]docosan-21-one (37).** Ozone was bubbled through a solution of **36** (2.85 g, 7.18 mmol) in $CH_2Cl_2$ (340 mL) containing a saturated ethereal solution of Sudan Red 7B (23 mL) at −78 °C for 10 min. Dimethyl sulfide (24 mL) was added, and the mixture was stirred overnight. The solvent was evaporated, and the residue was dissolved in $CH_2Cl_2$ and washed with water. The organic phase was dried and concentrated. Product purification by chromatography on silica gel (gradient elution with hexanes to 40% ethyl acetate in hexanes) afforded 2.13 g (92%) of **37** as a colorless oil that slowly solidified: IR ($CHCl_3$, $cm^{-1}$) 1720; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 4.04−3.97 (m, 1 H), 3.86−3.78 (m, 2 H), 3.75−3.64 (m, 2 H), 3.62−3.53 (m, 2 H), 3.41−3.33 (m, 1 H), 2.65 (d, $J$ = 13.7 Hz, 1 H), 2.54 (ddd, $J$ = 11.1, 8.6, 8.6 Hz, 1 H), 2.44−2.06 (series of m, 6 H), 2.02−1.94 (m, 1 H), 1.91−1.81 (m, 1 H), 1.78−1.68 (m, 1 H), 1.56−1.27 (series of m, 7 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 206.6, 94.6, 91.1, 89.5, 86.0, 69.4, 69.3, 67.6, 67.5, 48.8, 31.5, 30.8, 30.7, 30.6, 28.6 (2 C), 26.5, 25.6; MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1795.

Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.05; H, 8.12. Found: C, 67.25; H, 8.21.

**(5*R**,6*S**,11*R**)-18-(3-Hydroxypropyl)-1,7,12-trioxatrispiro[4.0.4.0.4.3]octadec-17-en-16-one (38).** A solution of **37** (0.79 g, 2.5 mmol) in methanol (39.5 mL) was treated with sodium hydroxide (0.29 g, 7.3 mmol), stirred, and heated to 70 °C for 90 min. The cooled reaction mixture was acidified with 6 N HCl and extracted with ethyl acetate. The combined extracts were dried and concentrated to leave **38** as a clear oil (0.79 g, 100%): IR (neat, $cm^{-1}$) 3600−3100, 1738; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.76 (t, $J$ = 1.1 Hz, 1 H), 4.19−4.13 (m, 1 H), 4.01 (ddd, $J$ = 4.0, 7.7, 7.7 Hz, 1 H), 3.88−3.70 (m, 4 H), 3.63 (t, $J$ = 6.1 Hz, 2 H), 2.73 (ddd, $J$ = 12.8, 8.5, 8.5 Hz, 1 H), 2.40−1.61 (series of m, 16 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 200.7, 169.0, 123.1, 91.8, 90.7, 89.8, 70.4, 70.1, 68.9, 61.6, 34.1, 32.2, 31.2, 31.1, 28.0, 27.3, 27.2, 25.9; MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1783.

Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.74; H, 8.21.

**(5*R**,6*S**,11*R**)-18-[3-(*tert*-Butyldimethylsiloxy)propyl]-1,7,12-trioxatrispiro[4.0.4.0.4.3]octadec-17-en-16-one (39).** To a magnetically stirred solution of **38** (2.03 g, 6.3 mmol) in $CH_2Cl_2$ (150 mL) were added triethylamine (3.94 mL, 25 mmol), DMAP (500 mg), and *tert*-butyldimethylsilyl (2.56 g 17.0 mmol). After being stirred for 36 h, the reaction mixture was diluted with a saturated $NH_4Cl$ solution and extracted with $CH_2Cl_2$. The combined extracts were dried and concentrated to provide a residue that was chromatographed on silica gel (elution with 50% ether in hexanes containing 1% triethylamine). There was isolated 2.68 g (97%) of **39** as a colorless oil: IR ($CDCl_3$, $cm^{-1}$) 1670; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.70 (s, 1 H), 4.21−4.15 (m, 1 H), 4.03−3.90 (m, 1 H), 3.89−3.70 (m, 4 H), 3.68−3.58 (m, 2 H), 2.79−2.69 (m, 1 H), 2.41−2.31 (m, 2 H), 2.27−1.58 (series of m, 13 H), 0.89 (s, 9 H), 0.04 (s, 6 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 200.9, 169.8, 122.6, 91.8, 90.7, 89.7, 70.5, 69.9, 68.9, 62.4, 34.2, 32.2, 31.3, 31.0, 28.1, 28.0, 27.3, 25.9 (3 C), 18.3, −5.3 (2 C) (1 C not observed); MS $m/z$ ($M^+$) calcd 436.2645, obsd 436.2657.

Anal. Calcd for $C_{24}H_{40}O_5Si$: C, 66.01; H, 9.23. Found: C, 65.96; H, 9.26.

***tert*-Butyldimethyl[3-[(5*R**,6*S**,11*S**,16*R**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-en-21-yl]propoxy]silane (40).** A solution of **39** (412 mg, 0.94 mmol) in THF (5 mL) was cooled to 0 °C and treated via syringe with the Normant reagent[7] (3 mL of 0.38 M in THF, 1.13 mmol). The ice bath was removed, and the reaction mixture was stirred at room temperature for 15 min before being diluted with a saturated $NH_4Cl$ solution and extracted with ether and with $CH_2Cl_2$. The combined organic phases were dried and evaporated to leave

the diol which was immediately taken up in $CH_2Cl_2$ (15 mL), treated with triethylamine (0.26 mL, 1.9 mmol), DMAP (50 mg), and *p*-toluenesulfonyl chloride (360 mg, 1.9 mmol), and stirred at 25 °C for 6 h. Additional quantities (80% of the above values) of these reagents were introduced at this point, and again 12 h later. When TLC analysis showed that no starting material remained, a saturated $NH_4Cl$ solution was added and the product was extracted into ether and $CH_2Cl_2$. The combined organic phases were dried and concentrated to leave a residue which was purified chromatographically on silica gel (elution with 20% ethyl acetate in hexanes containing 1% triethylamine). There was isolated 450 mg (100%) of **40** as a colorless oil: $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.32 (s, 1 H), 3.88−3.49 (series of m, 10 H), 2.81 (ddd, $J$ = 12.6, 8.3, 8.3 Hz, 1 H), 2.71 (ddd, $J$ = 12.1, 8.6, 8.6 Hz, 1 H), 2.52−2.38 (m, 2 H), 2.27−1.98 (m, 6 H), 1.88−1.62 (m, 8 H), 1.57−1.45 (m, 2 H), 0.97 (s, 9 H), 0.06 (s, 6 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 141.0, 128.3, 91.6, 90.6, 90.4, 87.6, 69.5, 69.2, 68.6, 67.4, 63.2, 34.9, 33.7, 32.9, 31.9, 31.5, 28.8, 28.7, 28.6, 27.6, 27.3, 26.2, 18.5, −5.2; MS *m*/*z* ($M^+$) calcd 478.3115, obsd 478.3114.

**(5*R**,6*S**,11*S**,16*R**)-1,7,12,17-Tetraoxatetraspiro[4.0.4.0.4.0.4.2]-docos-21-ene-21-propanol (41).** A magnetically stirred solution of **40** (25.5 mg, 0.053 mmol) in dry THF (2 mL) was treated with tetra-*n*-butylammonium fluoride (0.16 mL of 1 M in THF, 0.16 mmol), stirred overnight, diluted with a saturated $NaHCO_3$ solution, and extracted with ether. The combined extracts were dried and concentrated, and the resulting residue was purified chromatographically (silica gel, elution with 50% ethyl acetate in hexanes containing 1% triethylamine) to give 18.7 mg (96%) of **41** as a colorless oil: IR (neat, $cm^{-1}$) 3700−3100; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.36 (s, 1 H), 3.94−3.85 (m, 2 H), 3.80−3.69 (m, 4 H), 3.66−3.54 (m, 4 H), 2.87−2.69 (m, 2 H), 2.57−2.44 (m, 2 H), 2.31−1.96 (m, 6 H), 1.89−1.65 (m, 9 H), 1.56−1.48 (m, 2 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 140.1, 128.9, 91.3, 90.5, 90.3, 87.2, 69.3, 68.8, 68.4, 67.2, 61.4, 34.5, 33.3, 32.7, 31.7, 31.2, 28.4, 28.3, 28.2, 27.3, 25.9; MS *m*/*z* ($M^+$) calcd 364.2250, obsd 364.2249.

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.43; H, 8.93.

***tert*-Butyldimethyl[3-[(5*R**,6*R**,11*R**,16*S**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-en-21-yl]propoxy]silane(42).** To a cold (0 °C) solution of **39** (277 mg, 0.634 mmol) in dry THF (5 mL) was added a solution of allylmagnesium bromide in ether (3.0 mL of 1 N, 3.0 mmol). The reaction mixture was allowed to warm to 20 °C overnight and quenched with a saturated $NH_4Cl$ solution (10 mL). The separated aqueous layer was extracted with $CH_2Cl_2$ (2 × 20 mL), and the combined organic layers were dried, filtered, and concentrated. The residue was purified by chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to afford 260 mg (86%) of the product as a white solid.

The alcohols (260 mg, 0.540 mmol) were dissolved in THF (10 mL), cooled to 0 °C, and treated with a borane−THF complex (1.1 mL of 1 N, 1.1 mmol). After 1 h at 0 °C, 3 N NaOH (1.1 mL) and 30% $H_2O_2$ (1.1 mL) were introduced, and the reaction mixture was warmed to room temperature for 2 h and quenched with brine (10 mL) and $CH_2Cl_2$ (20 mL). The predescribed workup gave the diol mixture, which was dissolved in $CH_2Cl_2$ (50 mL) and cyclized in the presence of *p*-toluenesulfonyl chloride (617 mg, 3.24 mmol), triethylamine (0.56 mL, 4.05 mmol), and DMAP (10 mg) at 20 °C overnight. The reaction mixture was washed with brine (20 mL), dried, and concentrated. The residue was subjected to chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to afford 180 mg (69%) of **42** and 19 mg (7%) of **40**.

For **42**: white solid, mp 81−83 °C; IR ($CHCl_3$, $cm^{-1}$) 1462, 1255, 1086, 1058; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.16 (s, 1 H), 3.90−3.50 (series of m, 10 H), 3.16 (m, 1 H), 2.77 (m, 1 H), 2.50 (m, 2 H), 2.25−1.50 (series of m, 13 H), 1.50−1.25 (m, 3 H), 0.95 (s, 9 H), 0.04 (s, 6 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 144.6, 127.3, 92.6, 90.6, 89.9, 85.7, 69.4, 68.8 (2 C), 68.7, 63.1, 34.3, 34.1, 32.7, 32.3, 31.6, 29.0, 28.7, 28.3, 27.6, 26.7, 26.2 (3 C), 18.5, −5.2 (2 C); MS *m*/*z* ($M^+$) calcd 478.3115, obsd 478.3114.

Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68. Found: C, 67.70; H, 9.74.

**Spirooxymercuration of 38.** Enone **38** (50 mg, 0.15 mmol) and mercuric acetate (61 mg, 0.19 mmol) were dissolved in dry $CH_2Cl_2$ (1 mL) and treated with 1 $\mu$L of 70% perchloric acid via syringe. The reaction mixture was stirred for 5 h, diluted with ethyl acetate (10 mL), and washed with brine (3 × 10 mL). The organic phase was dried and freed of solvent to leave a residue which was chromatographed on silica gel (elution with 20% ethyl acetate in hexanes) and recrystallized from hexanes−$CH_2Cl_2$ to give **44** as colorles crystals: mp 212−213 °C (62 mg, 72%); IR ($CHCl_3$, $cm^{-1}$) 1651, 1056; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.18−4.11 (m, 2 H), 4.09−3.83 (m, 4 H), 3.70−3.60 (m, 2 H), 3.09 (s, 1 H), 2.53−2.44 (m, 1 H), 2.14−1.73 (series of m, 14 H), 1.54−1.47 (m, 1 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 206.6, 91.6, 89.9, 87.2, 77.4, 71.1, 70.6, 69.2, 67.6, 60.0, 35.1, 29.7, 28.8, 27.0, 26.9, 26.4, 26.0, 25.2; MS *m*/*z* ($M^+$) the molecular ion was too fleeting for accurate mass measurement.

Anal. Calcd For $C_{18}H_{25}HgClO_5$: C, 38.78; H, 4.52. Found: C, 38.72; H, 4.64.

For X-ray crystallographic analysis, see the Supporting Information.

**Spirooxymercuration of 41.** A stirred suspension of **41** (2.17 g, 5.95 mmol) in $CH_2Cl_2$ (70 mL) was treated with mercuric acetate (4.80 g, 15.1 mmol) and 70% perchloric acid (1 drop). After 4 h, brine (50 mL) and ethyl acetate (15 mL) were added, and the mixture was stirred for 45 min prior to dilution with $CH_2Cl_2$ (100 mL). The aqueous phase was extracted wtih $CH_2Cl_2$ (3 × 100 mL), and the combined organic layers were dried, filtered, and evaporated. Chromatography of the residue on silica gel (gradient elution with 10−20% ether in petroleum ether containing 1% triethylamine) afforded 760 mg of **45**, 1.65 g of a mixture of **45** and **46**, and 370 mg of **46** (combined yield of 79%).

For **45**: white solid, mp 200 °C (dec); IR ($CHCl_3$, $cm^{-1}$) 1215, 1055, 930; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 3.63−3.53 (m, 4 H), 3.52−3.44 (m, 4 H), 3.37−3.29 (m, 2 H), 2.89 (s, 1 H), 2.53−2.36 (m, 4 H), 2.21−2.16 (m, 2 H), 2.03−1.96 (m, 2 H), 1.92−1.62 (series of m, 10 H), 1.27−1.18 (m, 2 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 94.3, 91.8, 88.7, 74.2, 68.7, 67.5, 67.2, 34.4, 30.64, 30.58, 29.2, 28.7, 28.4; MS *m*/*z* ($M^+$) calcd 598.1543, obsd 598.1496.

Anal. Calcd for $C_{21}H_{31}ClHgO_5$: C, 42.07; H, 5.21. Found: C, 41.59; H, 5.25.

For X-ray crystallographic analysis carried out on a **45**/**46** cocrystal, see the Supporting Information.

For **46**: colorless solid, mp 181 °C; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 3.62−3.40 (m, 10 H), 3.30−3.21 (m, 1 H), 2.95−2.91 (m, 1 H), 2.65−2.53 (m, 2 H), 2.50−2.41 (m, 2 H), 2.33−2.25 (m, 1 H), 1.93−1.24 (series of m, 13 H), 0.80−0.71 (m, 1 H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 93.1, 91.4, 90.04, 89.99, 69.4, 69.3, 68.9, 68.1, 68.0, 66.8, 38.2, 32.6, 30.9, 29.2, 28.9, 28.6, 27.6, 25.8; MS *m*/*z* ($M^+$ − HgCl) calcd 363.2163, obsd 363.2174.

For X-ray crystallographic analysis carried out on a **45**/**46** cocrystal, see the Supporting Information.

**Preparation and Spirooxymercuration of 43.** A solution of **42** (88 mg, 0.184 mmol) in THF (3 mL) was treated with tetra-*n*-butylammonium fluoride (0.5 mL of 1 M in THF, 0.5 mmol), stirred at 20 °C for 2 h, and freed of solvent in vacuo. The residue was purified by chromatography on silica gel (elution with 25% ethyl acetate in hexanes) to give 60 mg (90%) of **43**. The latter was dissolved in $CH_2Cl_2$ (10 mL), treated with mercuric acetate (79 mg, 0.25 mmol) followed by a drop of 70% perchloric acid, stirred for 4 h at 20 °C, and diluted with brine (10 mL) and $CH_2Cl_2$ (10 mL). After 10 min, the separated aqueous layer was extracted with $CH_2Cl_2$ (2 × 20 mL) and the combined organic phases were dried and concentrated. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in hexanes) afforded 87 mg (87%) of **47** as a white solid: mp 214−216 °C (dec); IR ($CHCl_3$, $cm^{-1}$) 1453, 1304, 1265, 1193, 1056; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.20−3.45 (series of m, 10 H), 3.06 (s, 0.5 H), 2.70 (s, 0.5 H), 2.80−1.70 (series of m, 19 H), 1.65−1.51 (m, 0.5 H), 1.51−1.38 (m, 0.5 H); $^{13}$C NMR (75 MHz, $CDCl_3$) ppm 94.00, 93.96, 93.7, 92.6, 90.7, 90.6, 90.1, 90.0, 89.8, 89.6, 72.2, 71.1, 70.2, 69.8, 69.4, 68.1, 67.8, 67.3, 65.8, 57.4, 39.6, 37.0, 33.9, 33.4, 31.7, 31.5, 31.2, 30.4, 29.2, 29.0, 28.8, 28.6, 28.2, 28.1, 27.6, 26.7, 26.4, 25.7, 24.5; MS *m*/*z* ($M^+$ − HgCl) calcd 363.2163, obsd 363.2191.

Anal. Calcd for $C_{21}H_{31}ClO_5$: C, 42.07; H, 5.21. Found: C, 41.80; H, 5.20.

**(5*R**,6*S**,11*R**17*R**)-17-[(*tert*-Butyldimethylsiloxy)-1,7,12-trioxatrispiro[4.0.4.0.4.3]octadecan-16-one (49).** A solution of **48** (430 g, 1.52 mmol), imidazole (210 mg, 3.1 mmol), and DMAP (100 mg, 0.82 mmol) in $CH_2Cl_2$ (50 mL) was treated with *tert*-butyldimethylsilyl chloride (350 mg, 2.3 mmol), stirred for 16 h, and quenched with a saturated $NaHCO_3$ solution (50 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the combined organic solutions were dried and concentrated. Chromatography of the residue on silica gel (elution with 50% ether in petroleum ether) furnished 450 mg (75%) of **49** as a colorless oil: IR (neat, $cm^{-1}$) 1740, 1465, 1255, 1175, 1080; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.87 (dd, $J$ = 10.1, 6.0 Hz, 1 H), 4.00−3.87 (m, 5 H), 3.77−3.70 (m, 1 H), 2.66−2.59 (m, 1 H), 2.09−1.62 (series of m, 13 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.03 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 207.4, 92.8, 92.5, 87.1, 70.9, 70.4, 69.4, 68.6, 42.3, 33.5, 28.3, 27.8, 27.2, 25.8 (3 C), 25.1 (2 C), 18.4, −4.8, −5.4; MS $m/z$ ($M^+$) calcd 396.2332 obsd 396.2336.

Anal. Calcd for $C_{21}H_{36}O_5Si$: C, 63.59; H, 9.16. Found: C, 63.25; H, 8.88.

***tert*-Butyldimethyl[[(5*R**,6*S**,11*S**,16*S**,21*R**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-yl]oxy]silane (50) and *tert*-Butyldimethyl[[(5*R**,6*S**,11*S**,16*R**,21*R**)-1,7,12,17-tetraoxatetraspiro[4.0.4.0.4.0.4.2]docos-21-yl]oxy]silane (51).** To a magnetically stirred solution of 2,6-di-*tert*-butyl-4-methylphenol (1.41 g, 6.39 mmol) in toluene (68 mL) was added trimethylaluminum (1.6 mL of 2.0 M in hexanes, 3.2 mmol). After 1 h, the mixture was cooled to −78 °C and ketone **49** (960 mg, 2.42 mmol) dissolved in toluene (16 mL) was introduced followed by allylmagnesium bromide (4.5 mL of 1.0 M in ether, 4.5 mmol). The mixture was slowly warmed to room temperature overnight and partitioned between a saturated $NH_4Cl$ solution (60 mL) and ether (60 mL). The aqueous phase was extracted with ether (3 × 60 mL), and the combined organic layers were dried and concentrated. Chromatography of the residue on silica gel (gradient elution with 0−5% ether in petroleum ether) gave a mixture of allylic alcohol stereoisomers (890 mg, 84%) as an oil that solidified on standing. This solid proved to be the $\beta$-allylated carbinol: IR ($CHCl_3$, $cm^{-1}$) 3567, 1637, 1073; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 6.06−5.97 (m, 1 H), 5.13−5.06 (m, 2 H), 3.88 (br s, 1 H), 3.82−3.59 (m, 5 H), 3.55−3.46 (dd, $J$ = 15.4, 7.8 Hz, 1 H), 2.59−2.41 (m, 6 H), 2.36−2.09 (m, 4 H), 2.07 (s, 1 H), 1.89−1.67 (m, 6 H), 0.94 (s, 9 H), 0.03 (s, 3 H), 0.01 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 135.5, 117.2, 92.6, 91.9, 87.8, 78.9, 73.7, 68.5, 68.3, 66.6, 38.8, 38.4, 32.0, 31.4, 29.4, 28.6, 28.4, 27.2, 26.3 (3 C), 18.3, −3.2, −5.2; MS $m/z$ ($M^+$) calcd 438.2871, obsd 438.2801.

Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.71; H, 9.65. Found: C, 65.63; H, 9.54.

A stirred solution of the alcohols (940 mg, 2.14 mmol) in THF (20 mL) was treated with borane−THF (7.0 mL of 1.0 N, 7.00 mmol). After 6 h, 30% hydrogen peroxide (10 mL) and NaOH (10 mL of 3 M in $H_2O$) were added, and the mixture was stirred overnight and diluted with ether. The aqueous layer was extracted with ether (3 × 50 mL), and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel (elution with ether) gave the diol as a white foam (860 mg, 88%), which was directly cyclized with *p*-toluenesulfonyl chloride, triethylamine, and DMAP in the usual way. After workup and chromatography on silica gel (gradient elution with 20−40% ether in petroleum ether), there were obtained 360 mg of **50** and 90 mg of **51** (55% combined yield).

For **50**: white solid, mp 96 °C; IR ($CHCl_3$, $cm^{-1}$) 1220; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.20−3.60 (series of m, 9 H), 2.55−1.30 (series of m, 18 H), 0.86 (s, 9 H), 0.30 (s, 3 H), 0.02 (s, 3 H) (all other peaks are broadened); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 92.5, 90.0 (several broad peaks), 87.4 (br), 72.5 (br), 69.0 (br), 68.7 (br), 66.5 (br), 38.0 (br), 31.0 (br), 30.2 (br), 28.8 (br), 28.0 (br), 27.0 (br), 25.9, 17.9, −0.0 (br), −0.6 (br); MS $m/z$ ($M^+$) calcd 438.2781, obsd 438.2803.

Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.71; H, 9.65. Found: C, 65.67; H, 9.59.

For **51**: white solid, mp 94 °C; IR ($CHCl_3$, $cm^{-1}$) 1470, 1385, 1260, 1050, 900; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.79−3.48 (m, 9 H), 2.54−2.00 (series of m, 6 H), 1.97−1.33 (series of m, 12 H), 0.87 (s, 9 H), 0.05 (s, 3 H), −0.01 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 91.6, 90.7, 88.4, 87.2, 74.4, 68.8, 68.3, 67.9, 66.7, 39.7, 32.0, 30.5, 30.1, 28.5, 28.2, 27.4, 26.8, 25.9 (3 C), 18.2, −4.9, −5.8 (one C not observed); MS $m/z$ ($M^+$) calcd 438.2781, obsd 438.2794.

Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.71; H, 9.65. Found: C, 65.78; H, 9.59.

**(5*R**,6*S**,11*R**,16*R**)-1,7,12,17-Tetraoxatetraspiro[4.0.4.0.4.0.4.2]-docosan-21-one (52).** To a 920 mg (2.1 mmol) sample of **50** was added a solution of 5% HF in acetonitrile (20 mL). After 2 h, the mixture was quenched with a saturated $NaHCO_3$ solution and diluted with $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL), and the combined organic layers were dried and concentrated to give 810 mg (100%) of the alcohol. This material was taken up in $CH_2Cl_2$ (125 mL), treated with pyridinium dichromate (8.0 g, 0.021 mmol) and powdered 3 Å molecular sieves (16 g), stirred for 24 h, diluted with ether, and filtered through a pad of silica gel. Concentration of the filtrate gave ketone **52** (540 mg, 67%) as white crystals: mp 85.0−85.4 °C; IR (film, $cm^{-1}$) 1725, 1440, 1185, 1057; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.99 (ddd, $J$ = 7.8, 7.8, 2.8 Hz, 1 H), 3.93−3.53 (m, 7 H), 3.32 (d, $J$ = 12.1 Hz, 1 H), 2.84−2.74 (m, 1 H), 2.50−1.25 (series of m, 16 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 207.9, 93.5, 91.7, 88.9, 86.4, 69.9, 68.8, 68.7, 67.6, 47.7, 30.9, 30.8, 30.3, 28.3, 27.6, 26.6, 24.8 (1 C not observed); MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1782.

Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 67.17; H, 8.17.

**(5*R**,6*S**,11*S**)-18-[3-Hydroxypropyl)-1,7,12-trioxatrispiro-[4.0.4.0.4.3]octadec-17-en-16-one (53).** To a stirred solution of **52** (0.23 g, 0.71 mmol) in $CH_3OH$ (10 mL) was added NaOH (0.1 g, 2.5 mmol). After 6 h, the mixture was neutralized with HCl (6 M) and diluted with $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 25 mL). The combined organic layers were dried, filtered, and concentrated to give **53** (0.23 g, 100%) as a clear pale yellow oil: IR (film, $cm^{-1}$) 3443 (br), 1660, 1050; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.85 (s, 1 H), 4.06−3.83 (m, 4 H), 3.75−3.55 (m, 3 H), 3.05 (ddd, $J$ = 7.5, 7.5, 7.5 Hz, 1 H), 2.48−1.68 (series of m, 16 H), 1.55−1.41 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 195.7, 169.2, 123.7, 90.9, 90.23, 90.15, 71.1, 69.9, 69.1, 61.7, 35.1, 32.9, 31.3, 27.8, 26.9, 26.6, 25.9, 25.5; MS $m/z$ ($M^+$) calcd 322.1780, obsd 322.1783.

**Spirooxymercuration of 53.** A solution of **53** (58 mg, 0.18 mmol) in $CH_2Cl_2$ (8 mL) was treated with $Hg(OAc)_2$ (235 mg, 0.24 mmol) followed by 1 drop of 70% perchloric acid, stirred at room temperature for 17 h, treated again with an identical quantity of both reagents, and agitated for another day. The usual workup and flash chromatography on silica gel (gradient elution with 16−60% ethyl acetate in petroleum ether containing 1−3% methanol) gave 10.3 mg (13%) of **55**, 66.4 mg (85%) of **54**, and 13.1 mg of recovered **53**.

For **54**: colorless crystals, mp 178.1−179.3 °C; IR ($CHCl_3$, $cm^{-1}$) 1686, 1216, 1063; $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$ 4.01−3.59 (m, 8 H), 3.31 (s, 1 H), 2.38−2.17 (m, 2 H), 2.11−1.59 (series of m, 14 H); $^{13}C$ NMR (75 MHz, DMSO-$d_6$) ppm 207.1, 91.7, 90.9, 90.8, 90.0, 69.7, 69.1, 67.5, 66.5, 63.8, 35.9, 28.2, 27.7, 26.4, 26.2, 25.5, 25.2, 25.0; MS $m/z$ ($M^+ - HgCl_2$) calcd 321.1717, obsd 321.1716.

Anal. Calcd for $C_{18}H_{25}ClHgO_5$: C, 38.78; H, 4.52. Found: C, 38.87; H, 4.60.

For **55**: colorless crystals, mp 179.5−180.2 °C; IR ($CHCl_3$, $cm^{-1}$) 1732, 1216, 1048; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 3.70−3.35 (m, 8 H), 3.25−3.05 (m, 2 H), 2.89 (s, 1 H), 2.85−2.70 (m, 1 H), 2.45−2.30 (m, 2 H), 2.23−2.08 (m, 1 H), 1.89−1.68 (m, 2 H), 1.68−1.35 (m, 6 H), 1.25−1.15 (m, 1 H), 1.15−1.00 (m, 1 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) ppm 204.9, 92.3, 91.3, 89.3, 88.6, 70.0, 69.8, 68.4, 67.3, 65.1, 34.5, 33.0, 30.3, 28.9, 27.8, 26.8, 25.9, 25.7; MS $m/z$ ($M^+ - HgCl$) calcd 321.1766, obsd 321.1746.

Anal. Calcd for $C_{18}H_{25}ClHgO_5$: C, 38.78; H, 4.52. Found: C, 38.86; H, 4.48.

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**Supporting Information Available:** Discussion of the molecular structure and conformation of all the organomercurials, together with a comparison of coordination parameters, absolute values of the ether O−C−C−O torsion angles, computer-generated perspective drawings, tables of X-ray crystal data, bond distances and angles, final atomic coordinates, and anisotropic/isotropic displacement parameters for **31, 32, 33, 34, 44, 45, 46, 47, 54**, and **55** (92 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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