Single Stereodifferentiation Associated with Carbon Atom Insertion during the Oxonium Ion-Initiated Pinacol Rearrangement of Dihydrofuranyl and Dihydropyranyl Carbinols

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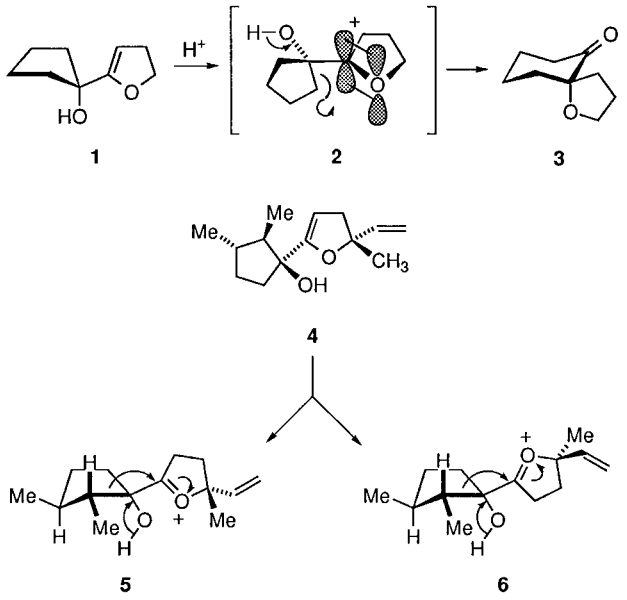
The stereoselectivity of the acid-promoted rearrangement of dihydrofuranyl and dihydropyranyl carbinols to spirocyclic ketones has been examined. These kinetically controlled isomerizations result in the ring expansion of the hydroxyl-substituted ring with generation of a newly stereogenic spirocyclic carbon atom. All of the adducts formed from several 4,5-dihydrofurans and cyclobutanone, cyclopentanone, and 2,2-dimethylcyclopentanone proved to be reactive. Of the 5,6-dihydropyrans examined, only the cyclobutanone adducts were sufficiently reactive to warrant study. The product distributions arising from the furanoid systems were characterized by modest discrimination in most cases. The more stereodifferentiating pyranoid systems show product distributions as high as 30:1. These results are explained in terms of transition state geometries (conformationally more flexible in the five-membered examples) while also taking into account the principle of stereoelectronic control.

The widespread occurrence of substituted tetrahydrofurans and tetrahydropyrans as substructures in an unusually large range of natural products has promoted considerable interest in the development of synthetic routes to these compound classes.[1] This activity has been fueled as well by the awareness that properly designed polyether backbones are eminently capable of binding host ions and enabling their transport across membranes.[2,3] In our own studies, oxonium ions such as **2** are playing an increasingly important role in the development of architecturally unprecedented polyspiro tetrahydrofurans endowed with a highly desirable hydrophilic−lipophilic balance.[4] Generated by the addition of 2-lithio-4,5-dihydrofurans[5] to ketones, carbinols typified by **1** exhibit in acid an overwhelming kinetic preference for protonation of the enol ether double bond and conversion to **2** (Scheme 1). This event is followed by a pinacol-like Wagner−Meerwein shift that leads to ring-expanded spirocyclic products exemplified by **3**.[6]

Scheme 1



As expected, the migratory aptitudes observed during competitive 1,2-translocation to the oxonium ion center correlate well with past experience involving cationic rearrangements[7] in that the group which is more electron-rich migrates more rapidly.[8−11] In the case of **4**, for

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example, the major ring-enlarged spiro ketones are formed as the result of preferred involvement of that adjacent carbon which is the more highly alkyl substituted (see **5** and **6**). The only strict requirement is that the substrate be sufficiently mobile conformationally to allow the migrating C−C bond to become properly stereoaligned with the π-cloud of the electrophilic center as shown in Scheme 1.

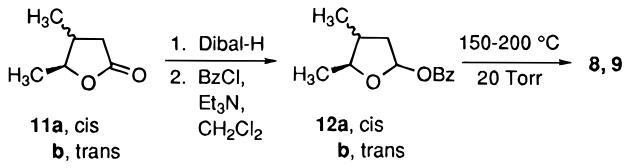
The diastereoselectivity of oxonium ion capture is less well understood. In parallel with the diastereoselective addition of nucleophiles to chiral carbonyl compounds, this phenomenon holds considerable interest. In acyclic examples, stereocontrol is almost always achieved by limiting the degrees of freedom available to the substrate. The facial selectivity of attack with generation of a new stereogenic center is then guided by the preexisting structural staging.

Although chelation control is not at play in cationic intermediates such as **2**, **5**, and **6**, face-selective 1,2-migration will clearly be subject to stereoelectronic influences, remote steric effects, and product stability control. Under normal circumstances, a clear distinction between these several factors could prove quite demanding. In order to circumvent a number of the limitations involved, we have opted to undertake a comparison of the diastereoselectivities exhibited by five- and six-ring oxonium ion acceptors. The more stable conformations adopted by the two differently-sized rings serve to project resident substituents into distinctively different zones around the structural periphery.[12] The change from well defined axial/equatorial status in tetrahydropyrans due to adoption of a chairlike arrangement to a much more flexible envelope arrangement having pseudorotational capability as in tetrahydrofurans is quite dramatic. In the latter situation, the substituents move above and below the average plane of the ring with much greater ease. On this basis, we expected that the diastereoselectivity observed with six-membered oxonium ions could be reasonably interpretable in steric and stereoelectronic terms. The extent to which these effects drop off when five-membered congeners are involved would thus signal how delicately these factors respond to reductions in structural rigidification within the acceptor ring. The present report constitutes a detailed analysis of the stereochemical and regiochemical control realizable during intramolecular migration of a carbon atom to a cyclic oxonium ion.

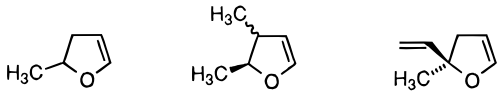
Results

Reactions of the type illustrated by the conversion of **1** to **3** can in principle show two distinct types of stereoselection. Since the carbon atom that is intercalated into the cycloalkanone during the ring expansion becomes stereogenic, it may be formed in one of two relative configurations. If chirality is already present in one of the reaction partners utilized in the preparation of the starting alcohol, the resultant control exercised on the stereochemical outcome falls under the umbrella of simple stereodifferentiation. Both partners in the initial convergent step can, of course, be chiral, and their chemical unison can consequently result in the formation of matched and mismatched diastereomers.[13] In this instance, the impact of the composite stereogenic centers on the outcome of the pinacol-like 1,2-shift is recognized as double stereodifferentiation.[14] While the focus of this investigation has been restricted to the first category, examples of the second type have recently been reported.[10,11]

Scheme 2

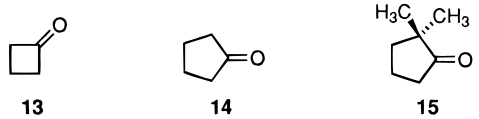


Dihydrofuranoid Systems. Our comprehensive investigation began with the four dihydrofurans **7**−**10**. Monomethyl derivative **7** was to serve as the point of reference for quantification of the level of 1,3-diastereocontrol capable of being exerted by a methyl substituent residing at C-2 in the five-membered heterocycle. In turn, **8** and **9** were selected to allow determination of whether the cis or trans 2,3-dimethyl arrangement is stereoreinforcing. In the case of **10**, the two π-faces differ because of the geminal placement of vinyl and methyl groups at C-2; what would be the consequences of replacing the C-2 hydrogen in **7** by this considerably larger substituent?



Dihydrofuran **10** was prepared from *R*-(−)-linalool as previously reported.[10] Of the two routes to **7** that are known,[15,17] the more efficient process involving reduction of γ-valerolactone to the lactol and pyrolysis of the derived benzoate at 180 °C was utilized. This route was applied as well to the generation of previously unreported **8** and **9** (Scheme 2). Norin's protocol[18] was adopted for the production of lactones **11a** and **11b**. Careful pyrolysis of **12a** and **12b** in a Kugelrohr apparatus furnished **8** and **9**, respectively.

Ketones **13**−**15** were chosen for the purpose of screening the consequences of strain release (in the case of cyclobutanone) and maximum α-substitution (as in **15**) on the rate of the ring expansion and its stereochemical partitioning relative to cyclopentanone.



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(14) For the use of this term in aldol chemistry, see (a) Heathcock, C. H.; Pirrung, M. C.; Buse, C. T.; Hagen, J. P.; Young, S. D.; Sohn, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 7077. (b) Heathcock, C. H.; Pirrung, M. C.; Lampe, J.; Buse, C. T.; Young, S. D. *J. Org. Chem.* **1981**, *46*, 2290.

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(18) Byström, S.; Högberg, H.-E.; Norin, T. *Tetrahedron* **1981**, *37*, 2249.

Dihydrofurans **8** and **9** were deprotonated with *tert*-butyllithium in a 1:1 pentane−THF mixture at −78 °C. Warming of this mixture to 0 °C was found to be paramount to the quantitative deprotonation of these substrates. For **7** and **10**, the deprotonation was effected in THF; when solutions of **10** were warmed in the mixed solvent system, decomposition resulted. In all cases, the resulting lithiated species were treated with neat ketone, and the allylic carbinols so formed were isomerized with a catalytic amount of camphorsulfonic acid in dry CH_2Cl_2. The compositions of the diastereomeric spiro ketone mixtures were determined in advance of chromatographic separation by ^{1}H NMR spectroscopy at 300 MHz. In several cases, the accuracy of these measurements was checked by analytical gas chromatography. The results compiled in Table 1 represent the average of at least duplicate experiments, the precision of which is better than a ±0.3 deviation from a mean.

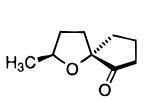
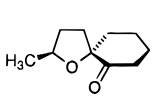
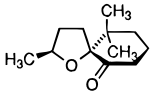
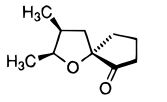
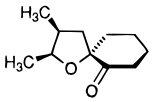
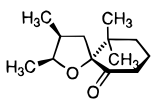
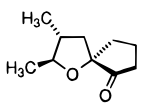
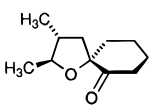
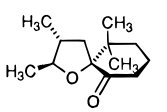
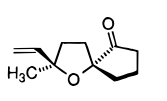
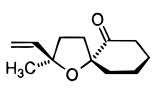
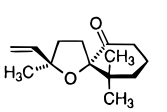
In each series, the cyclobutanol intermediate was the most reactive carbinol. Under the generic conditions utilized in this study, 0.5 h was sufficient time in which to achieve complete consumption of the reactant. The adducts to 2,2-dimethylcyclopentanol were of intermediate reactivity, with 2 h being adequate for total conversion to product. Finally, when cyclopentanone was involved, reaction times up to 5 days proved necessary.

For **7**, the **16**/**17** and **20**/**21** product distributions were seen to be 1:1. Although the first pair of diastereomers were not separable, NMR integration proved particularly conducive to product analysis because the methyl protons in **16** which are positioned syn to the carbonyl group are deshielded (δ 1.26) relative to those in **17** (δ 1.20). The same characteristic trend was quite apparent for the α-oxy proton in **20** (δ 4.04−3.94) and **21** (δ 4.19−4.08). Following their independent isolation in a pure state, structural verification was achieved by their conversion to *cis*- and *trans*-theaspirones, respectively.[17] Like **16** and **17**, the spirocyclohexanones **18** and **19** were also difficult to separate. Reliance was therefore placed on differential integration of the α-oxy signals at δ 3.75−3.65 and δ 3.84−3.77 due to the individual diastereomers.

Identification of **26** and **33** as the major ring expansion products was convincingly made possible by the application of NOE techniques. Particularly telling was the enhancement of one of the *gem*-dimethyl singlets upon irradiation of a specific tetrahydrofuran ring methylene proton (see Experimental Section). The relative stereochemistries of spirocycles **28**, **31**, and **34** were established by single-crystal X-ray diffraction analysis of their 2,4-dinitrophenylhydrazone derivatives. Once these assignments had been firmly established, it proved straightforward to define the structures of the remaining diastereomeric pairs by comparative analysis.

Dihydropyranoid Systems. Although the direct lithiation of dihydropyran is possible,[5] many examples are known where this methodology is not applicable.[19−23] For instance, the presence of MOM, benzyloxy, and

Table 1. Diastereomeric Spiro Ketone Ratios from Rearrangement of Dihydrofuranoid Carbinols

Dihydrofuran	Ketone	Products	Diastereomer ratio
7	**13**	 **16** **17**	1 : 1
	14	 **18** **19**	1.2 : 1
	15	 **20** **21**	1 : 1
8	**13**	 **22** **23**	3.9 : 1
	14	 **24** **25**	4.5 : 1
	15	 **26** **27**	11 : 1
9	**13**	 **28** **29**	1 : 1.5
	14	 **30** **31**	1 : 1.8
	15	 **32** **33**	1 : 1.7
10	**13**	 **34** **35**	1.3 : 1
	14	 **36** **37**	1.1 : 1
	15	 **38** **39**	1.1 : 1

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(20) Hanessian, S.; Martin, M.; Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926.

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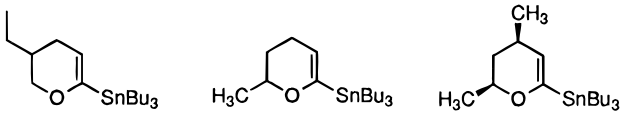
(23) Schmidt, R. R.; Preuss, R.; Betz, R. *Tetrahedron Lett.* **1987**, *28*, 6591.

related substituents effectively redirects the regioselectivity of deprotonation, and silicon protecting groups suffer competing proton abstraction α to the silicon atom.[21b] Often, a significant excess of *tert*-butyllithium is also required.[24] For these reasons, alternative ways to prepare lithiated pyrans have been developed in recent years (Scheme 3). These include the conversion of lactones to enol triflates followed by copper-[25] or palladium-catalyzed[24,26] conversion to the vinylstannane in advance of transmetalation. Alternatively, the lactol can be readily transformed into the anomeric sulfones by reaction with an arylsulfinic acid in the presence of calcium chloride. Deprotonation of these sulfones followed by direct condensation with tributylstannyl chloride and heating in chloroform containing Hunig's base affords the vinylstannane efficiently.[27]

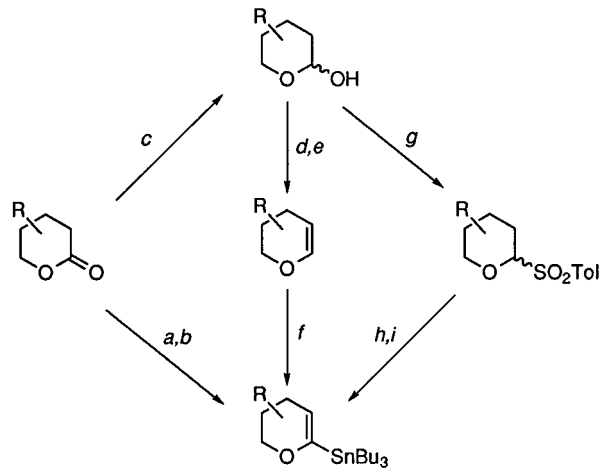
The dihydropyrans **40**−**42** were selected for study. Two factors were considered to be highly desirable: stable, nonvolatile precursors to the 6-lithio derivatives and a means for preparing them free of other potential nucleophiles. Unlike the dihydrofurans **7**−**10**, direct metalation of the dihydropyrans corresponding to **40**−**42**, prepared by benzoate pyrolysis as before, proved not to be suitable. In order to achieve complete deprotonation, approximately 3 equiv of the lithium reagent were required, as were concentrated solutions of the dihydropyran in THF. The excess organometallic then consumed the tin reagent, which was therefore required in excess. Product purification was thereby significantly complicated. Similarly, the approach mediated by the vinyl triflate gave rise to reaction mixtures from which **40**−**42** were difficult to obtain in a pure state because of persistent tin-containing residues.



40 **41** **42**

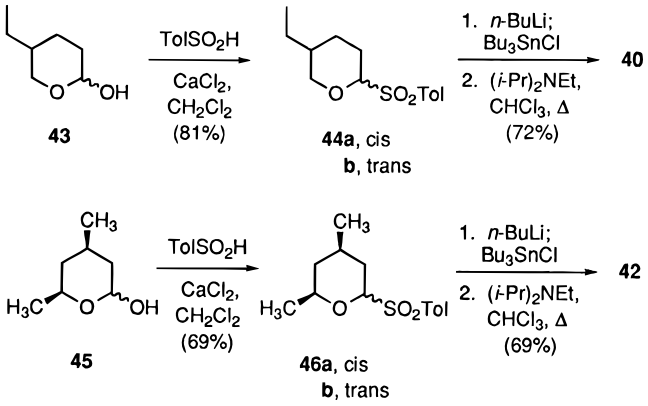
As a consequence, the sulfone route previously developed to prepare **41**[28] was utilized for the synthesis of **40** and **42** (Scheme 4). Lactols **43** and **45** were synthesized conventionally from the lactones.[29] The sulfone diastereomers **44a**,**b** and **46a**,**b** proved to be chromatographically separable, although this proved unnecessary since the cis and trans isomers converged to the same vinylstannane. Transmetalation of **40**−**42**, obtained in a pure state by this means, was readily accomplished at low temperature, and condensation of the resulting anions with **13**−**15** proceeded readily and efficiently. It is also possible to effect the direct condensation of the sulfones

Scheme 3



[a] $LiN(SiMe_3)_2$, THF/HMPA, -78 °C; $PhNTf_2$, -78 °C → rt. [b] Bu_3SnCu, HMPA, rt. [c] $(i\text{-Bu})_2AlH$, CH_2Cl_2, -78 °C. [d] PhCOCl, Et_3N, CH_2Cl_2. [e] 150-200 °C, 30 Torr. [f] *tert*-BuLi, THF, -78 °C →25 °C; Bu_3SnCl. [g] *p*-$CH_3C_6H_4SO_2H$, $CaCl_2$, CH_2Cl_2. [h] *n*-BuLi, THF, -78 °C; Bu_3SnCl, -78 °C → rt. [i] $(i\text{-Pr})_2NEt$, $CHCl_3$, reflux.

Scheme 4



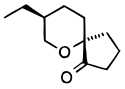
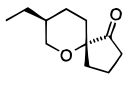
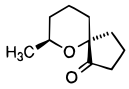
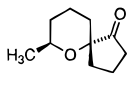
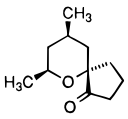
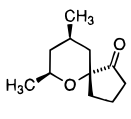
with these ketones as reported by Ley and co-workers[30] and thereby access the desired carbinols rapidly. From a synthetic standpoint, this route and that outlined in Scheme 4 share the attractive advantage of reproducibility.

Under conditions comparable to those utilized earlier, the pyranyl carbinols underwent rearrangement considerably more slowly. For this reason, only the cyclobutanone adducts were studied. Addition of a catalytic quantity of camphorsulfonic acid to the 5-ethyl derivative dissolved in dry CH_2Cl_2 gave the spirocyclic ketones **47** and **48** in a 1:4.2 ratio (Table 2). These isomers could easily be separated chromatographically. That the major diastereomer was indeed **48** required conversion to its highly crystalline 2,4-dinitrophenylhydrazone and confirmatory X-ray crystallographic analysis.

In the other two examples, the product ratios were reversed. The presence of a lone 6-methyl substituent resulted in **49** being formed 11.5 times more than **50**. Matters improved when a second cis-related methyl was present at C-4, in that **51** predominated over **52** by a factor of 30:1. The NOE effects observed for these products (see Experimental Section) were used to assign

(24) Barber, C.; Jarowicki, K.; Kocienski, P. *Synlett* **1991**, 197.
(25) Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K.-S.; Faron, K. L.; Gilbertson, S. R.; Kaesler, R. W.; Yang, D. C.; Murray, C. K. *J. Org. Chem.* **1986**, *51*, 277.
(26) (a) Jarowicki, K.; Kocienski, P.; Marczak, S.; Willson, T. *Tetrahedron Lett.* **1990**, *31*, 3433. (b) Kocienski, P.; Jarowicki, K.; Marczak, S. *Synthesis* **1991**, 1191.
(27) Downham, R.; Edwards, P. J.; Entwistle, D. A.; Hughes, A. B.; Kim, K. S.; Ley, S. V. *Tetrahedron: Asymmetry* **1995**, *6*, 2403.
(28) Genicot, C.; Ley, S. V. *Synthesis* **1994**, 1275.
(29) (a) Smith, N. R.; Wiley, R. H. *Organic Syntheses*; Wiley: New York, 1963; Coll. Vol. IV, p 549. (b) Smith, N. R.; Wiley, R. H. *Organic Syntheses*; Wiley: New York, 1963; Coll. Vol. IV, p 337. (c) McKelvey, R. D.; Kawada, Y.; Sugawara, T.; Iwamura, H. *J. Org. Chem.* **1981**, *46*, 4948. (d) Kocienski, P.; Yeates, C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1879. (e) Rosenberger, M.; Andrews, D.; DiMaria, F.; Duggan, A. J.; Saucy, G. *Helv. Chim. Acta* **1972**, *55*, 249.
(30) Ley, S. V.; Lygo, B.; Sternfeld, F.; Wonnacott, A. *Tetrahedron* **1986**, *42*, 4333.

Table 2. Diastereomeric Spiro Ketone Ratios from Rearrangement of Dihydropyranoid Carbinols

Stannylated dihydropyran	Ketone	Products	Diastereomer ratio
40	**13**	 **47**  **48**	1 : 4.2
41	**13**	 **49**  **50**	11.5 : 1
42	**13**	 **51**  **52**	30 : 1

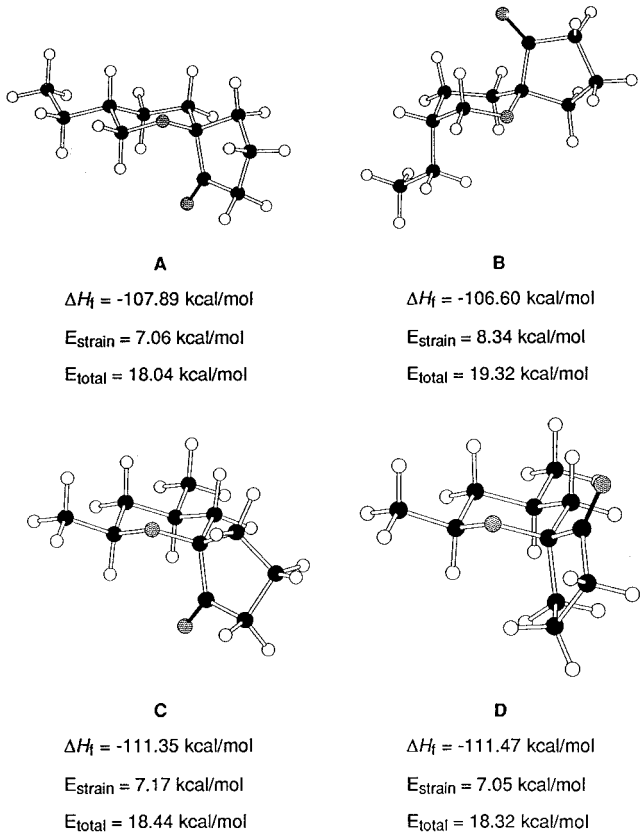
the syn or anti configuration of the spirocyclic ketone ring unambiguously. In all cases, the products were shown to be stable to the reaction conditions. Furthermore, since other acid catalysts (*p*-toluenesulfonic acid, Dowex-50) gave the same product distributions, camphorsulfonic acid was vindicated of its potential for introducing any stereochemical bias.

Molecular Mechanics Evaluation of the Pyranyl Chair Conformations. The relative energies of two or more interconvertible conformational isomers have frequently been calculated by molecular mechanics methods. The soundness of this application by the MM2 force field is based on the remarkably good level to which it reproduces cyclohexane *A*-values. Predicting the preferred ground state of spirocyclic systems without this computational backdrop can be more difficult because less data is available for this class of molecules. For this reason, conformational analysis studies have been performed on **47**, **48**, **51**, and **52** in order to gain insight into which chair arrangement these molecules prefer to adopt.

The performance of MM2 depends on the quality of the parameters, and those adopted for these α-alkoxy ketones appear to be reasonably appropriate. The minimum global energy conformation for **48** (shown as **A** in Chart 1) is expectedly that in which the ethyl functionality and the methylene group of the cyclopentanone ring are simultaneously projected equatorially. This is, of course, not possible in **47**. Under these circumstances, the manner in which the cyclopentanone segment is appended to the pyran chair arises as the controlling influence, causing the ethyl side chain to be positioned axially (see **B**). A modest increase in strain energy and total energy is seen to accompany the epimerization of one center in this series. The solid-state conformation of the 2,4-dinitrophenylhydrazone of **48** is seen to differ from that computed for the parent ketone in the gas phase.

Given the energy ordering reflected above, the situation for **52** should be an overwhelming preference for positioning the two methyl appendages and the methylene group equatorially, such that **C** should be the stable conformer. This is indeed the case. When the configuration of the spiro carbon is reversed in this instance, there could be several consequences. The most unlikely would be to force the pair of methyls into an axial disposition, such that additional 1,3-diaxial interaction

Chart 1. Global Minimal Energy Conformations of 47, 48, 51, and 52 (MM2-based, MODEL KS 2.99)



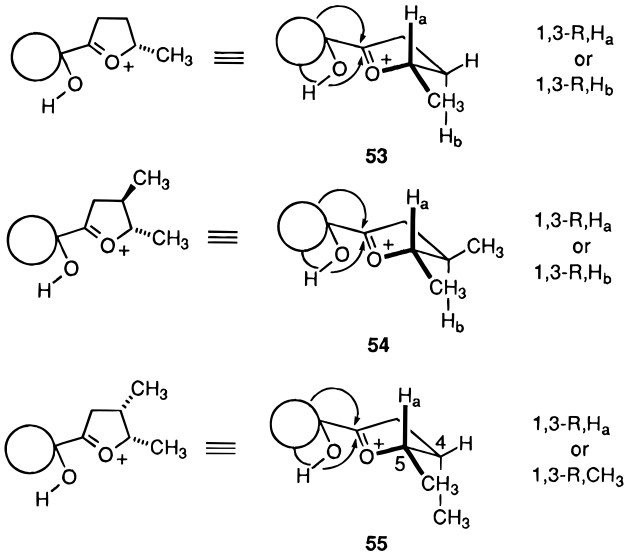
would materialize. Alternatively, a twist-boat geometry could be adopted in order to counterbalance the other energetic demands. The actual scenario is retention of a chair conformation having equatorial methyls, with the methylene group from the five-membered ring axially disposed as in **D**.

Thus, it is seen that the pyranyl spiro ketones generally exhibit a conformational preference for positioning the α-alkoxy carbonyl group axially. The extent of this conformational bias is sufficient to cause a 5-ethyl group to become axially oriented. It is, however, insufficient to overcome the steric demands associated with positioning methyl groups at C-4 and C-6 simultaneously axial.

Purely Steric Origin of the Diastereoselectivity of Dihydrofuranoid Rearrangements. The relative level and direction of stereoselectivity in the dihydrofuran series may be interpreted on purely steric grounds arising from those 1,3-diaxial interactions involving the migrating carbon. In the simplest case (**53**, Scheme 5), relatively low levels of diastereoselection are realized. For this particular oxonium ion, the most stable conformation is assumed to be that in which the 5-methyl substituent is pseudoequatorially disposed as shown. As a consequence, H_a and H_b are projected into pseudoaxial locations and will accordingly present low levels of steric impedance to the migrating carbon. The energy difference between these two sets of interactions is expected to be small based on their identical nature. The stereoselection observed in the several experiments performed herein (1−1.2:1, Table 1) supports this hypothesis.

The modest diastereoselectivity observed in the *trans*-dimethyl series can also be rationalized in terms of similar weak 1,3-diaxial interactions involving H_a and H_b in **54**. Both methyl substituents are expected to reside

Scheme 5

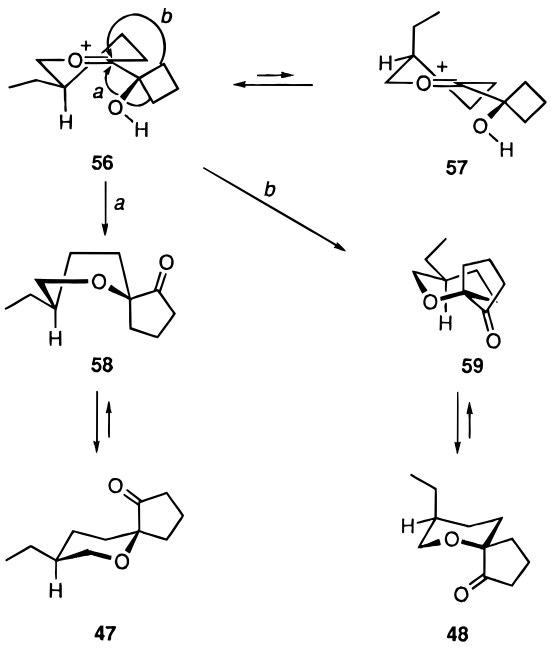


in pseudoequatorial pockets while the associated geminal hydrogens are presented to the developing spiro center in 1,3-fashion. In this light, the relative levels of diastereoselection for **53** and **54** should be quite comparable within experimental error. The somewhat greater imbalances in product distribution recorded for **54** can be attributed to increased conformational rigidity in this oxonium ion relative to **53**. The additional possibility exists that the reduced preference for migration toward H_a in **54** is due to a small decrease in the interconnective C−O bond as a direct consequence of added inductive stabilization of the oxonium ion center.

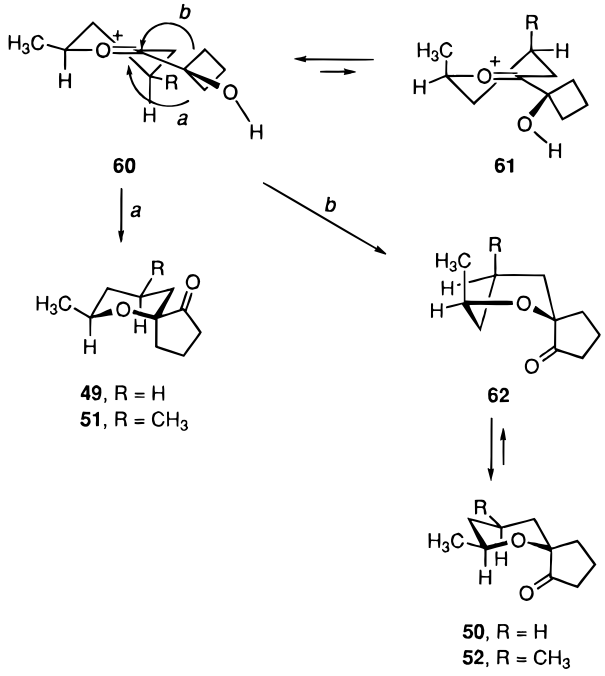
The diastereoselectivity operational in the *cis*-dimethyl series is readily evident upon examination of **55**. Avoidance of 1,3-diaxial interaction involving the 4-methyl group leads to favored formation of **22**, **24**, and **26**. The enhanced level of production of **26** is a reflection of the increased steric bulk of the migrating carbon in that specific example.

Stereoelectronic Control in the Diastereoselective Response of Dihydropyranoid Carbinols. It is reasonable to assume that the processes under consideration in this study occur irreversibly under kinetic control. Given these circumstances, the reaction product ratios bear no direct relationship to the individual thermodynamic stabilities. Rather, product partitioning depends on the relative energies of the transition states involved. In this connection, it is significant that the cyclobutyl carbinols derived from dihydropyrans **40**−**42** undergo rearrangement with much higher diastereoselectivity (up to 30:1, Table 2) than their dihydrofuran analogs (maximum of 3.9:1, Table 1). As presumed earlier, ring expansion is triggered by initial protonation of the enol ether to produce a cyclic oxonium ion. When this functionality resides in a six-membered ring, two rapidly equilibrating conformations such as **56** and **57** result (Scheme 6). The geometry resident in **57** suffers from the obvious thermodynamic disadvantage of axial orientation for its ethyl substituent. Consequently, its role in the isomerization process will be greatly diminished, irrespective of whether an early or late transition state is involved. For this reason, we accord attention only to **56.** Stereoelectronically-controlled pinacolic 1,2-carbon shift in this intermediate along trajectory *a* will necessarily proceed via a sterically disfavored twist-boat

Scheme 6



Scheme 7



arrangement[31] to deliver **58**. Conformational equilibration within **58** would subsequently make **47** available. Alternatively, the utilization of pathway *b* involves uniquely a chairlike process to furnish **59** and ultimately the more thermodynamically favored **48**. Preferred passage of **56** to **59** concisely explains the observed 4.2:1 ratio of **48** to **47**.

Examination of the results realized in the other two examples provides insight into the operation of an *apparent* crossover in product distribution and is supportive of the mechanistic reasoning advanced above. As seen in Scheme 7, protonation of either the 6-methyl or 4,6-dimethyl carbinols will result in the formation of **60**, the diaxial conformation of which (*viz.*, **61**) will be

(31) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, England, 1983; Chapter 2.

strongly destabilized because of the 1,3-diaxial methyl−methyl interactions when R = CH_3. The distinction to be made resides in the differing positioning of the alkyl substituents on the pyranoid ring. While placement at C-5 causes the initial oxonium species to adopt preferably a conformation such as **56**, substitution at C-6 (as well as cis disubstitution at C-4 and C-6) shifts the ground-state conformational bias in the opposite direction (see **60**). The steric factors which control these conformational energetics continue to exert their influence in the ensuing transition states. Since either **56** or **60** has only two stereocontrolled antiperiplanar 1,2-migrations available to it, that proceeding via a twist-boat transition state will normally be too high in energy to be dominant.

It is interesting that the influence of a 6-methyl substituent on product distribution is approximately three times greater than that of a 5-ethyl group. This margin of kinetic control can be understood in terms of the differential strain energy in boat conformers **58** and **62**. When a substituent resides at C-5, its equatorial disposition is maintained when advancing to **58**. This is not the case when **62** is involved. The 6-methyl group now finds itself axial, and this destabilization causes the conversion to **62** to be additionally disfavored kinetically. When R is methyl, **62** experiences additional 1,3-diaxial interaction and is enegetically destabilized to a still greater extent. The high 30:1 ratio of **51** to **52** is construed to be a reflection of this combination of factors.

Conclusion

The above experimental results confirm that oxonium ions present in pyran rings are capable of greater stereodifferentiation during pinacol-like rearrangement with carbon atom intercalation than their furanoid counterparts. Conformational analysis indicates that this enhanced capability is provided by the energetic advantage associated with maintaining existing substituents quasiequatorial in a flattened chair transition state and through subsequent utilization of that antiperiplanar 1,2-shift which skirts twist-boat geometries. In the smaller five-membered oxonium species, conformational preferences are less pronounced and dynamic interconversion between individual conformers proceeds more readily. The product distributions recorded for **54** and **55** are in line with this notion of lower energy barriers.

The five- and six-ring oxonium ions differ in another significant way. The furanoid carbinols undergo rearrangement more rapidly, such that a greater range of product structures lend themselves to preparation in this way. This kinetic enhancement can be interpreted in terms of the increased electrophilicity of those oxonium functionalities resident in five-membered rings because of angle strain. Alternatively and less likely, dispiro ketones typified by **19**, **25**, and **31** could prove to be somewhat less strained than their pyranoid homologues.

Recently completed companion studies have elucidated the stereochemical course of the intramolecular trapping of oxonium ions with allylsilanes[32] as well as the controlling factors involved in the preparation of spirocyclic bis-C,C-glycosides.[33,34]

(32) Paquette, L. A.; Tae, J. *J. Org. Chem.* **1996**, *61*, 7860.

(33) (a) Paquette, L. A.; Kinney, M. J.; Dullweber, U. *J. Org. Chem.* **1997**, *62*, 1713. (b) Paquette, L. A.; Dullweber, U.; Cowgill, L. D. *Tetrahedron Lett.* **1993**, *34*, 8019.

Experimental Section

General Details. All manipulations were performed under a nitrogen atmosphere. Solvents were dried over 4 Å molecular sieves before distillation. Ether, tetrahydrofuran, and toluene were distilled from sodium or sodium/benzophenone ketyl. Dichloromethane, diisopropylamine, dimethyl sulfoxide, dimethylformamide, and triethylamine were each distilled from calcium hydride. Melting points are uncorrected. Exact mass measurements were recorded on Kratos MS-30 or VG-70-2505 mass spectrometers at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark and at Atlantic Microlab, Inc., Norcross, GA. The chromatographic separations were carried out either under flash conditions on Fluka silica gel H or gravimetrically on Woelm silica gel 63−200. The organic extracts were dried over anhydrous magnesium sulfate. All reagents were reagent grade and purified where necessary.

(4*R,5*R**)-Tetrahydro-4,5-dimethyl-2-furanol Benzoate (12a).** A solution of **11a** (1.00 g, 8.76 mmol) in CH_2Cl_2 (7 mL) was cooled to −78 °C and treated dropwise with the diisobutylaluminum hydride (8.93 mL of 1 M in hexanes). The reaction mixture was stirred at −78 °C for 8 h, diluted with saturated Rochelle's salt solution, and extracted 3 h later with ether (3 × 25 mL). The combined organic layers were dried and concentrated to provide the lactol as an epimeric mixture (948 mg, 93%): colorless oil; IR ($CHCl_3$, cm^{-1}) 3600, 1448, 1243, 1224, 1080, 1059, 1024; ^1H NMR (300 MHz, C_6D_6) (major anomer) δ 5.53 (br d, J = 4.5 Hz, 1 H), 4.50 (br s, 1 H), 4.31 (dq, J = 6.4, 6.4 Hz, 1 H), 2.20 (dq, J = 6.8, 6.8 Hz, 1 H), 1.90 (ddd, J = 12.9, 7.3, 2.3 Hz, 1 H), 1.50 (ddd, J = 12.3, 5.8, 5.8 Hz, 1 H), 0.96 (d, J = 6.5 Hz, 3 H), 0.64 (d, J = 7.1 Hz, 3 H); (minor anomer) δ 5.46 (br d, J = 4.2 Hz, 1 H), 4.69 (br s, 1 H), 3.92 (dq, J = 6.4, 6.4 Hz, 1 H), 1.90 (dq, J = 5.7, 5.7 Hz, 1 H), 1.87 (ddd, J = 11.5, 5.7, 5.7 Hz, 1 H), 1.60 (ddd, J = 12.4, 5.9, 3.8 Hz, 1 H), 1.14 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) (major anomer) ppm 97.5, 76.3, 41.9, 34.8, 16.1, 14.4; (minor anomer) ppm 98.8, 78.4, 41.2, 35.9, 17.3, 14.7; MS m/z (M^+) calcd 116.0837, obsd 116.0825.

A cold (0 °C) solution of the above lactol (872 mg, 7.51 mmol) and triethylamine (3.14 mL, 22.5 mmol) in CH_2Cl_2 (10 mL) was treated with benzoyl chloride (0.92 mL, 7.88 mmol) and allowed to warm to rt overnight (12 h). The cloudy mixture was diluted with saturated sodium bicarbonate solution and extracted with ether. Drying and solvent removal in vacuo provided **12a** as a yellowish liquid that was usually pyrolyzed directly. Chromatography of a small sample on silica gel (elution with 20% ether in hexanes) gave the pure major anomer as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1716, 1275, 1204, 1091, 1088; ^1H NMR (300 MHz, C_6D_6) δ 8.16−8.12 (m, 2 H), 7.13−7.01 (m, 3 H), 6.65 (dd, J = 5.2, 1.7 Hz, 1 H), 4.22 (dq, J = 6.5, 6.5 Hz, 1 H), 2.12 (dq, J = 7.1, 7.1 Hz, 1 H), 1.96 (ddd, J = 13.5, 7.3, 1.5 Hz, 1 H), 1.53 (ddd, J = 13.0, 7.3, 5.3 Hz,1 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.60 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 165.6, 132.8, 131.4, 129.9, 128.5, 99.1, 78.3, 40.5, 34.1, 15.9, 14.1; MS m/z (M^+) calcd 220.1099, obsd 220.1102. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.19; H, 7.42.

***cis*-2,3-Dihydro-2,3-dimethylfuran (8).** The unpurified benzoate from the preceding experiment was heated to 150−200 °C in a Kugelrohr apparatus under reduced pressure (30 Torr). The distillate collected in a dry ice-isopropyl alcohol trap consisted of **8**, a colorless liquid (615 mg, 83%): ^1H NMR (300 MHz, C_6D_6) δ 6.21 (dd, J = 2.1, 2.1 Hz, 1 H), 4.72 (dd, J = 2.6, 2.6 Hz, 1 H), 4.41 (dq, J = 9.1, 6.6 Hz, 1 H), 2.60−2.49

(34) Crystallographic experimental details, bond lengths, bond lengths involving the hydrogen atoms, bond angles, positional parameters and B(eq) values, anisotropic displacement parameters, and positional parameters for the hydrogen atoms for **28**-2,4-DNP, **31**-2,4-DNP, **34**-2,4-DNP, and **48**-2,4-DNP have been deposited with the Cambridge Crystallographic Data Centre. These data can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(m, 1 H), 1.11 (d, J = 6.6 Hz, 3 H), 0.72 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 145.3, 106.8, 80.4, 39.9, 15.1, 15.0.

***trans*-2,3-Dihydro-2,3-dimethylfuran (9).** A 3.79 g (33.2 mmol) sample of **11b** dissolved in CH_2Cl_2 (50 mL) was reduced with diisobutylaluminum hydride (36.5 mL of 1 M in hexanes) in the predescribed manner to furnish 3.85 g (100%) of the lactol as a colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 5.50−5.46 (m, 1 H), 5.41−5.39 (m, 1 H), 4.11−4.07 (m, 2 H), 3.78 (dq, J = 6.1, 6.1 Hz, 1 H), 3.41 (dq, J = 6.1, 6.1 Hz, 1 H), 2.16−2.05 (m, 1 H), 2.04−1.94 (m, 2 H), 1.56−1.29 (m, 3 H), 1.25 (d, J = 6.1 Hz, 3 H), 1.11 (d, J = 6.0 Hz, 3 H), 0.78 (d, J = 6.4 Hz, 3 H), 0.69 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 98.03, 97.96, 83.0, 80.0, 42.86, 42.83, 41.1, 38.7, 21.0, 18.8, 16.3, 16.1; MS m/z (M^+) calcd 116.0837, obsd 116.0864.

A cold (0 °C) solution of this lactol (2.52 g, 21.7 mmol) was benzoylated as before, and the unpurified oil was heated at 150−180 °C and 15 Torr in a Kugelrohr apparatus. Condensation of the distillate at −78 °C furnished 1.18 g (56% for two steps) of **9** as a colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 6.17 (dd, J = 2.6, 2.6 Hz, 1 H), 4.65 (dd, J = 2.5, 2.5 Hz, 1 H), 3.97 (pent, J = 6.5 Hz, 1 H), 2.36−2.29 (m, 1 H), 1.13 (d, J = 6.2 Hz, 3 H), 0.84 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 145.0, 105.4, 85.1, 44.3, 20.8, 20.5.

(2*R,5*R**)- and (2*R**,5*S**)-2-Methyl-1-oxaspiro[4.4]nonan-6-one (16 and 17).** A solution of **7** (1.412 g, 16.8 mmol) in anhydrous THF (20 mL) was cooled to −78 °C under argon and treated with a solution of *tert*-butyllithium in hexanes (9.80 mL, 16.7 mmol). After 2 h of stirring, cyclobutanone (1.20 mL, 16.1 mmol) was introduced, and the reaction mixture was stirred overnight with gradual warming to rt, recooled to −78 °C, and quenched with saturated $NaHCO_3$ solution (10 mL). The separated aqueous layer was extracted with ether, and the combined organic phases were washed with brine, dried, and concentrated in vacuo. The resultant carbinol (1.412 g, 91%) was suitable for direct isomerization.

A 793 mg (5.14 mmol) sample of the alcohol was dissolved in CH_2Cl_2 (60 mL), treated with camphorsulfonic acid (20 mg), stirred for 30 min, and concentrated. The residue was triturated with ether−hexanes (1:3), filtered to remove the catalyst, and chromatographed on silica gel. Elution with ether−pentane (3:22) afforded 668 mg (84%) of an inseparable 1:1 mixture of **16** and **17** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1745, 1446, 1422, 1265, 1111, 1070; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24−4.14 (m, 1 H), 2.32−1.62 (series of m, 10 H), 1.26 (d, J = 6 Hz, 1.5 H), 1.20 (d, J = 6 Hz, 1.5 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 219.0, 218.4, 87.2, 86.5, 76.9, 76.4, 36.6, 36.2, 35.2, 35.0, 34.0, 33.3, 33.1, 32.5, 21.0, 20.8, 18.0, 17.8; MS m/z (M^+) calcd 154.0994, obsd 154.0993.

For the 2,4-DNP derivative of **16**/**17**: yellow solid, mp 90−91 °C. Anal. Calcd for $C_{15}H_{18}N_4O_5$: C, 53.89; H, 5.43. Found: C, 53.48; H, 5.37.

(2*R,5*R**)- and (2*R**,5*S**)-2-Methyl-1-oxaspiro[4.5]decan-6-one (18 and 19).** Metalation of **7** (247 mg, 2.94 mmol) with *tert*-butyllithium (1.40 mL in hexanes, 2.38 mmol) as above for 2 h, followed by the addition of cyclopentanone (0.20 mL, 2.26 mmol) afforded an alcohol which was dissolved in CH_2Cl_2 (10 mL), treated with camphorsulfonic acid (10 mg), stirred for 2 h, and concentrated. The predescribed workup afforded 236 mg (62% overall) of a 1.6:1 mixture of **18** and **19** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1745, 1446, 1422, 1265, 1111, 1070; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.19−4.08 (m, 0.5 H), 4.04−3.94 (m, 0.5 H), 2.77−1.06 (series of m, 11 H), 1.21 (d, J = 6 Hz, 1.5 H), 1.18 (d, J = 6 Hz, 1.5 H), 0.86−0.79 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 211.2, 210.8, 87.7, 76.1, 75.6, 40.1, 39.8, 39.2, 33.3, 33.2, 32.7, 32.2, 27.3, 27.1, 22.8, 22.5, 21.1; MS m/z (M^+) calcd 168.1150, obsd 168.1150. For the 2,4-DNP derivative of **18**/**19**: Anal. Calcd for $C_{16}H_{20}N_4O_5$: C, 55.17; H, 5.79. Found: C, 55.36; H, 5.62.

(2*R,3*R**,5*R**)- and (2*R**,3*R**,5*S**)-2,3-Dimethyl-1-oxaspiro[4.4]nonan-6-one (22 and 23).** A cold (−78 °C) solution of **8** (161 mg, 1.64 mmol) in 1:1 THF−pentane (4 mL) was treated with *tert*-butyllithium (0.96 mL of 1.7 M in pentane), warmed to 0 °C for 15 min, recooled to −78 °C prior to the introduction of cyclobutanone (77 mg, 1.09 mmol), and stirred for 45 min with slow warming to −20 °C. The reaction mixture was quenched at that temperature with water (2 mL), extracted with ethyl acetate (3 × 5 mL), dried, and concentrated. The unpurified alcohol was taken up in CH_2Cl_2 (16 mL), stirred with camphorsulfonic acid (0.5 mg) for 2 h, adsorbed onto silica gel, and chromatographed (elution with 40% ether in hexanes) to give a total of 165 mg (89%) of the separable spiro ketones **22** and **23** in a 3.9:1 ratio.

For **22**: colorless oil; IR (neat, cm^{-1}) 1750, 1464, 1380, 1111, 1090, 1055, 1038; ^{1}H NMR (300 MHz, C_6D_6) δ 3.98 (dq, J = 6.5, 6.5 Hz, 1 H), 2.17−1.98 (m, 2 H), 1.88−1.70 (m, 2 H), 1.68−1.54 (m, 2 H), 1.48−1.32 (m, 2 H), 1.30−1.21 (m, 1 H), 1.05 (d, J = 6.5 Hz, 3 H), 0.79 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.1, 85.8, 79.0, 39.8, 37.5, 37.4, 35.3, 18.2, 16.6, 13.8; MS m/z (M^+) calcd 168.1150, obsd 168.1185. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.11; H, 9.52.

For **23**: colorless oil; ^{1}H NMR (300 MHz, C_6D_6) δ 4.24 (dq, J = 6.6, 6.6 Hz, 1 H), 2.24−2.13 (m, 2 H), 2.08−1.96 (m, 1 H), 1.92−1.84 (m, 1 H), 1.77−1.63 (m, 2 H), 1.45−1.35 (m, 1 H), 1.32−1.22 (m, 1 H), 1.08−1.00 (m, 1 H), 0.96 (d, J = 6.4 Hz, 3 H), 0.70 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.2, 84.6, 77.7, 39.4, 37.4, 36.6, 34.8, 18.6, 16.1, 14.9; MS m/z (M^+) calcd 168.1150, obsd 168.1185.

(2*R,3*R**,5*R**)- and (2*R**,3*R**,5*S**)-2,3-Dimethyl-1-oxaspiro[4.5]decan-6-one (24 and 25).** Metalation of **8** (80 mg, 0.82 mmol) in 1:1 THF−pentane (2 mL) with *tert*-butyllithium (0.48 mL of 1.7 M in pentane) as delineated above followed by the addition of cyclopentanone (46 mg, 0.54 mmol) gave a carbinol which was stirred with camphorsulfonic acid (0.5 mg) in dry CH_2Cl_2 (12 mL) for 4 days. Flash chromatography of the crude product on silica gel (elution with 20% ether in hexanes) provided a total of 58 mg (73%) of the separable spiro ketones **24** and **25** in a 4.5:1 ratio.

For **24**: colorless oil; IR (neat, cm^{-1}) 1722; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.17 (dq, J = 6.4, 6.4 Hz, 1 H), 2.72 (ddd, J = 13.6, 8.9, 5.4 Hz, 1 H), 2.50 (dd, J = 12.7, 7.6 Hz, 1 H), 2.36−2.26 (m, 2 H), 2.09 (dd, J = 12.7, 7.9 Hz, 1 H), 1.78 (dd, J = 12.7, 7.5 Hz, 1 H), 1.96−1.54 (series of m, 5 H), 1.01 (d, J = 6.5 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.9, 86.8, 78.2, 40.5, 39.8, 38.8, 36.3, 27.5, 22.4, 16.1, 13.9; MS m/z (M^+) calcd 182.1307, obsd 182.1305. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.49; H, 9.92.

For **25**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.05 (dq, J = 6.5, 6.5 Hz, 1 H), 2.67 (ddd, J = 13.8, 7.9, 5.8 Hz, 1 H), 2.36−2.26 (m, 1 H), 2.25−2.18 (m, 1 H), 1.96−1.54 (series of m, 7 H), 1.30 (dd, J = 12.7, 6.9 Hz, 1 H), 1.09 (d, J = 6.5 Hz, 3 H), 0.91 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.3, 86.6, 77.4, 41.0, 40.2, 39.0, 35.8, 27.2, 22.9, 16.6, 14.9; MS m/z (M^+) calcd 182.1307, obsd 182.1305.

(2*R,3*R**,5*S**)-2,3,10,10-Tetramethyl-1-oxaspiro[4.5]-decan-6-one (26).** Metalation of **8** (194 mg, 1.98 mmol) with *tert*-butyllithium (1.19 mL of 1.7 M in pentane) in 1:1 THF−pentane (4 mL) as described above followed by the addition of 2,2-dimethylcyclopentanone (44 mg, 0.40 mmol) gave a carbinol which was immediately taken up in dry CH_2Cl_2 (6 mL) and stirred vigorously in the presence of camphorsulfonic acid (0.5 mg) for 2 h. The usual workup and chromatography on silica gel furnished a total of 75 mg (91%) of the separable spiro ketones **26** and **27** in an 11:1 ratio.

For **26**: colorless oil; IR (neat, cm^{-1}) 1715, 1462, 1380, 1087, 1039; ^{1}H NMR (300 MHz, C_6D_6) δ 3.93 (dq, J = 6.4, 6.4 Hz, 1 H), 2.97 (ddd, J = 12.0, 12.0, 8.3 Hz, 1 H), 2.37 (dd, J = 13.0, 6.7 Hz, 1 H), 2.15 (ddd, J = 12.0, 3.4, 3.4 Hz, 1 H), 2.06−1.88 (m, 2 H), 1.59 (dd, J = 13.0, 8.1 Hz, 1 H), 1.54−1.45 (m, 2 H), 1.05−0.91 (m, 1 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.85 (s, 3 H), 0.70 (d, J = 7.0 Hz, 3 H), 0.62 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.9, 92.4, 79.5, 42.0, 37.7, 37.6, 35.6, 32.1, 24.1, 22.8, 21.6, 16.2, 14.2; MS m/z (M^+) calcd 210.1620, obsd 210.1620. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.12; H, 10.55.

(2*R,3*S**,5*R**)- and (2*R**,3*S**,5*S**)-2,3-Dimethyl-1-oxaspiro[4.4]nonan-6-one (28 and 29).** The condensation of **9** with **13** and the subsequent isomerization was performed in a manner identical to that utilized for the cis isomer. There was produced a 1:1.5 mixture of **28** and **29** in 89% yield.

For **28**: colorless oil; IR (neat, cm^{-1}) 1749; ^1H NMR (300 MHz, C_6D_6) δ 3.47 (dq, J = 8.8, 6.0 Hz, 1 H), 2.13−1.27 (series of m, 8 H), 1.23 (d, J = 5.9 Hz, 3 H), 1.07 (dd, J = 12.4, 7.1 Hz, 1 H), 0.72 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.1, 85.8, 82.9, 42.1, 41.1, 36.8, 34.9, 19.5, 18.3, 15.9; MS m/z (M^+) calcd 168.1150, obsd 168.1157.

A solution of **28** (1 equiv) dissolved in a minimal amount of ethanol was added in dropwise fashion to a 0.1 M solution of 2,4-dinitrophenylhydrazine (1.05 equiv) in H_3PO_4/ethanol. The derivative was isolated by extraction with $CHCl_3$ and recrystallization from ethanol: yellow crystals, mp 170−171 °C.

For **29**: colorless oil; IR (neat, cm^{-1}) 1749, 1455, 1381, 1158, 1094, 1072; ^1H NMR (300 MHz, C_6D_6) δ 3.65 (dq, J = 8.5, 6.0 Hz, 1 H), 2.08−1.96 (m, 1 H), 1.88−1.74 (m, 2 H), 1.72−1.60 (m, 2 H), 1.55−1.21 (m, 4 H), 1.06 (d, J = 6.0 Hz, 3 H), 0.79 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.4, 84.6, 81.9, 41.8, 40.4, 37.2, 35.1, 18.7, 18.4, 15.5; MS m/z (M^+) calcd 168.1150, obsd 168.1157. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.11; H, 9.64.

(2*R,3*S**,5*R**)- and (2*R**,3*S**,5*S**)-2,3-Dimethyl-1-oxaspiro[4.5]decan-6-one (30 and 31).** Reaction of **9** with **14** in a manner identical to that employed for the cis isomer afforded a 1:1.8 mixture of **30** and **31** in 71% yield after chromatographic separation.

For **30**: colorless oil; IR (neat, cm^{-1}) 1720; ^1H NMR (300 MHz, C_6D_6) δ 3.39 (dq, J = 9.3, 6.0 Hz, 1 H), 2.83 (dd, J = 12.9, 5.7 Hz, 1 H), 2.75 (dd, J = 12.1, 7.2 Hz, 1 H), 2.18 (dddd, J = 13.0, 4.1, 4.1, 1.3 Hz, 1 H), 1.91−1.74 (m, 2 H), 1.73−1.61 (m, 1 H), 1.59−1.50 (m, 1 H), 1.37−1.18 (m, 3 H), 1.10 (d, J = 6.0 Hz, 3 H), 0.86 (dd, J = 11.8, 11.8 Hz, 1 H), 0.69 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 208.5, 86.4, 82.2, 41.7, 41.4, 40.1, 38.9, 27.5, 22.4, 19.4, 15.8; MS m/z (M^+) calcd 182.1307, obsd 182.1301.

For **31**: colorless oil; IR (neat, cm^{-1}) 1720; ^1H NMR (300 MHz, C_6D_6) δ 3.30 (dq, J = 9.0, 5.0 Hz, 1 H), 2.70 (ddd, J = 13.3, 11.1, 5.8 Hz, 1 H), 2.19 (dd, J = 11.1, 8.4 Hz, 1 H), 2.15 (dddd, J = 13.3, 4.6, 4.6, 1.0 Hz, 1 H), 1.84−1.70 (m, 2 H), 1.56−1.14 (series of m, 6 H), 1.10 (d, J = 6.0 Hz, 3 H), 0.75 (d, J = 6.3 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 208.6, 85.7, 81.6, 41.1, 40.6, 39.6, 39.1, 27.2, 22.2, 18.9, 15.7; MS m/z (M^+) calcd 182.1307, obsd 182.1301. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.68; H, 9.90.

The 2,4-dinitrophenylhydrazone of **31** was obtained as yellow crystals, mp 179.5−180 °C (from ethanol).

(2*R,3*S**,5*S**)- and (2*R**,3*S**,5*R**)-2,3,10,10-Tetramethyl-1-oxaspiro[4.5]decan-6-one (32 and 33).** Reaction of **9** with **15** in a manner identical to that employed for the cis isomer afforded a 1:1.7 mixture of **32** and **33** in 61% yield after chromatographic separation.

For **32**: colorless oil; IR (neat, cm^{-1}) 1716; ^1H NMR (300 MHz, C_6D_6) δ 3.32 (dq, J = 9.7, 6.0 Hz, 1 H), 2.96 (m, 1 H), 2.63 (dd, J = 12.1, 6.6 Hz, 1 H), 2.13 (dddd, J = 12.3, 4.0, 4.0, 1.5 Hz, 1 H), 2.01 (ddd, J = 13.1, 13.1, 8.6 Hz, 1 H), 1.69−1.56 (m, 1 H), 1.53−1.38 (m, 2 H), 1.16 (dd, J = 11.9, 11.9 Hz, 1 H), 1.04 (d, J = 6.0 Hz, 3H), 0.98 (dddd, J = 13.3, 3.4, 3.4, 1.3 Hz, 1 H), 0.90 (s, 3 H), 0.71 (d, J = 6.5 Hz, 3 H), 0.61 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 209.8, 91.8, 83.7, 41.5, 41.1, 37.1, 35.9, 34.7, 24.1, 22.4, 21.5, 19.5, 15.5; MS m/z (M^+) calcd 210.1620, obsd 210.1613.

For **33**: colorless oil; IR (neat, cm^{-1}) 1716; ^1H NMR (300 MHz, C_6D_6) δ 3.14 (dq, J = 9.3, 3.8 Hz, 1 H), 2.82−2.72 (m, 1 H), 2.15−2.04 (m, 2 H), 1.91−1.81 (m, 1 H), 1.62 (dd, J = 13.0, 9.1 Hz, 1 H), 1.56−1.43 (m, 2 H), 1.42−1.29 (m, 1 H), 1.06 (d, J = 5.9 Hz, 3 H), 1.04−0.95 (m, 1 H), 0.88 (s, 3 H), 0.74 (d, J = 6.5 Hz, 3 H), 0.65 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.0, 91.3, 80.9, 42.0, 40.5, 37.2, 35.4, 34.1, 23.6, 22.23, 22.17, 18.3, 15.9; MS m/z (M^+) calcd 210.1620, obsd 210.1613. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.34; H, 10.52.

(2*R*,5*R*)- and (2*R*,5*S*)-2-Methyl-2-vinyl-1-oxaspiro[4.4]nonan-6-one (34 and 35). A cold (−78 °C), magnetically stirred solution of **10** (174 mg, 1.58 mmol) in THF (4 mL) was treated with *tert*-butyllithium (0.93 mL of 1.7 M in pentane), stirred at this temperature for 1.5 h prior to the addition of cyclobutanone (74 mg, 1.1 mmol), and allowed to warm to −20 °C during 20 min. The reaction mixture was quenched with saturated $NaHCO_3$ solution (2 mL), and the product was extracted into ether (3 × 10 mL), dried, and concentrated. The resulting oil was dissolved in CH_2Cl_2 (20 mL), treated with camphorsulfonic acid (0.5 mg), and stirred at rt for 30 min prior to the addition of K_2CO_3 (1 mg). Chromatography on silica gel (elution with 30% ether in hexanes) furnished a total of 127 mg (67%) of a 1.3:1 separable mixture of **34** and **35**.

For **34**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1746; ^1H NMR (300 MHz, $CDCl_3$) δ 5.91 (dd, J = 17, 11 Hz, 1 H), 5.22 (dd, J = 17, 2 Hz, 1 H), 5.00 (dd, J = 11, 2 Hz, 1 H), 2.27 (dd, J = 9, 7 Hz, 2 H), 2.19−1.62 (series of m, 8 H), 1.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 218.4, 144.1, 111.7, 87.9, 85.0, 37.1, 36.6, 34.9, 33.1, 26.6, 17.8; MS m/z (M^+) calcd 180.1150, obsd 180.1159; $[\alpha]^{22}_D$ +14.4 (*c* 0.43, $CHCl_3$). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.96; H, 9.09.

The 2,4-dinitrophenylhydrazone of **34** was isolated as yellow crystals, mp 139−140 °C (from ethanol).

For **35**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1746; ^1H NMR (300 MHz, $CDCl_3$) δ 6.11 (dd, J = 17.3, 10.8 Hz, 1 H), 5.45 (dd, J = 17.3, 1.5 Hz, 1 H), 5.02 (dd, J = 10.7, 1.5 Hz, 1 H), 1.80−1.64 (m, 6 H), 1.61−1.45 (m, 2 H), 1.43−1.30 (m, 2 H), 1.23 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 215.8, 144.4, 112.2, 87.3, 84.5, 38.2, 37.2, 35.1, 32.6, 27.0, 18.2; MS m/z (M^+) calcd 180.1150, obsd 180.1159; $[\alpha]^{20}_D$ −43.1 (*c* 0.54, $CHCl_3$).

(2*R*,5*R*)- and (2*R*,5*S*)-2-Methyl-2-vinyl-1-oxaspiro[4.5]decan-6-one (36 and 37). Metalation of **10** (174 mg, 1.58 mmol) with *tert*-butyllithium (0.93 mL of 1.7 M in pentane) in THF (4 mL), followed by reaction with cyclopentanone (44 mg, 0.53 mmol) and acid-catalyzed rearrangement as before (5 days), provided 68 mg (63%) of a 1.1:1 mixture of **36** and **37**.

For **36**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1717; ^1H NMR (300 MHz, C_6D_6) δ 5.80 (dd, J = 17.3, 10.7 Hz, 1 H), 5.24 (dd, J = 17.2, 1.9 Hz, 1 H), 4.90 (dd, J = 10.4, 1.9 Hz, 1 H), 2.82 (dd, J = 12.2, 6.0 Hz, 1 H), 2.61−2.50 (m, 1 H), 2.17 (ddd, J = 9.4, 4.3, 1.2 Hz, 1 H), 1.91−1.43 (series of m, 5 H), 1.41−1.21 (m, 4 H), 1.20 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 208.6, 144.4, 111.2, 88.1, 84.3, 40.2, 39.3, 37.4, 31.6, 27.6, 27.5, 22.4; MS m/z (M^+) calcd 194.1307, obsd 194.1306. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.38; H, 9.47.

For **37**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1717; ^1H NMR (300 MHz, C_6D_6) δ 5.75 (dd, J = 17.1, 10.6 Hz, 1 H), 5.13 (dd, J = 17.3, 1.5 Hz, 1 H), 4.86 (dd, J = 10.6, 1.4 Hz, 1 H), 2.76 (dd, J = 11.9, 5.9 Hz, 1 H), 2.53−2.46 (m, 1 H), 2.13 (ddd, J = 8.5, 4.4, 1.1 Hz, 1 H), 1.91−1.43 (series of m, 5 H), 1.41−1.21 (m, 4 H), 1.18 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 209.0, 145.2, 111.7, 88.0, 84.4, 41.1, 38.9, 37.6, 31.2, 27.7, 27.2, 22.2; MS m/z (M^+) calcd 194.1307, obsd 194.1306.

(2*R*,5*S*)- and (2*R*,5*R*)-2,10,10-Trimethyl-2-vinyl-1-oxaspiro[4.5]decan-6-one (38 and 39). Metalation of **10** (227 mg, 2.06 mmol) in dry THF (4 mL) with *tert*-butyllithium (1.21 mL of 1.7 M in pentane) at −78 °C for 1 h was followed by transfer via cannula into an equally cold slurry of anhydrous cerium trichloride (2.27 mmol) in dry THF. The mixture was stirred at −78 °C for 1 h, treated with 2,2-dimethylcyclopentanone (0.13 mL, 1.03 mmol), and allowed to warm to rt overnight. The usual workup and acid-catalyzed rearrangement (2 h) provided 203 mg (89%) of a 1.1:1 mixture of **38** and **39**.

For **38**: colorless oil; IR (neat, cm^{-1}) 1717; ^1H NMR (300 MHz, C_6D_6) δ 5.79 (dd, J = 17.4, 10.8 Hz, 1 H), 5.04 (dd, J = 17.4, 1.3 Hz, 1 H), 4.83 (dd, J = 10.6, 1.3 Hz, 1 H), 3.02−2.87 (m, 1 H), 2.57−2.43 (m, 1 H), 2.16−2.10 (m, 1 H), 2.01−1.89 (m, 1 H), 1.64 (dd, J = 7.8, 6.3 Hz, 1 H), 1.53−1.37 (m, 5 H), 1.16 (s, 3 H), 0.89 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 210.5, 144.6, 111.5, 93.6, 84.2, 41.0, 37.7, 37.6, 35.7, 26.6, 25.1, 24.1, 22.6, 22.0; MS m/z (M^+) calcd 222.1620, obsd 222.1605. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.68; H, 9.90.

For **39**: colorless oil; IR (neat, cm^{-1}) 1717; ^1H NMR (300 MHz, C_6D_6) δ 5.86 (dd, J = 17.4, 10.8 Hz, 1 H), 5.11 (dd, J = 17.4, 1.4 Hz, 1 H), 4.87 (dd, J = 10.4, 1.4 Hz, 1 H), 3.02−2.87 (m, 1 H), 2.57−2.43 (m, 1 H), 2.16−2.10 (m, 1 H), 2.01−1.89 (m, 1 H), 1.85−1.79 (m, 1 H), 1.64 (dd, J = 7.8, 6.3 Hz, 1 H), 1.53−1.37 (m, 4 H), 1.11 (s, 3 H), 0.63 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 211.5, 144.5, 110.9, 93.3, 84.0, 40.8, 37.9, 37.4,

35.7, 26.4, 25.2, 24.2, 22.6, 22.0; MS *m/z* (M^+) calcd 222.1620, obsd 222.1605.

***cis*- and *trans*-5-Ethyltetrahydro-2-(*p*-tolylsulfonyl)-2*H*-pyran (44a and 44b).** Lactol **43**[29d] (739 mg, 5.68 mmol) dissolved in CH_2Cl_2 (10 mL) was treated with anhydrous calcium chloride (2.77 g, 25.1 mmol) and freshly prepared *p*-toluenesulfinic acid (1.26 g, 7.07 mmol), stirred overnight under N_2, and partitioned between CH_2Cl_2 (10 mL) and saturated $NaHCO_3$ solution (10 mL). The mixture was filtered through a pad of Celite, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic solutions were dried and concentrated. The residue was purified by flash chromatography on silica gel (elution with 17% ether in petroleum ether) to give 1.23 g (81%) of a mixture of sulfone diastereomers. Rechromatography (elution with 12% ether in petroleum ether) resulting in separation of **44a** from **44b**, with **44b** eluting first.

For **44a**: colorless crystals, mp 58−59 °C; IR ($CHCl_3$, cm^{-1}) 1598, 1464, 1316, 1151, 1081; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 8 Hz, 2 H), 6.79 (d, J = 8 Hz, 2 H), 4.33 (t, J = 5 Hz, 1 H), 3.99 (dd, J = 11, 7 Hz, 1 H), 3.34 (dd, J = 11, 8 Hz, 1 H), 2.41−2.35 (m, 1 H), 1.85 (s, 3 H), 1.69−1.59 (m, 2 H), 1.25−0.86 (m, 4 H), 0.62 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.0, 136.0, 129.5, 129.4, 89.8, 69.5, 36.0, 25.0, 24.3, 21.5, 21.1, 11.3; MS *m/z* (M^+) calcd 113.0966, obsd 113.0968. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51. Found: C, 62.52; H, 7.47.

For **44b**: colorless solid, mp 23−25 °C; IR ($CHCl_3$, cm^{-1}) 1596, 1461, 1302, 1237, 1143, 1085; ^1H NMR (300 MHz, C_6D_6) δ 7.97 (d, J = 8 Hz, 2 H), 6.81 (d, J = 8 Hz, 2 H), 4.06 (dd, J = 11.4, 2.4 Hz, 1 H), 3.70−3.64 (m, 1 H), 2.47 (t, J = 11 Hz, 1 H), 2.13−2.05 (m, 1 H), 1.85 (s, 3 H), 1.68 (dq, J = 12.9, 4.2 Hz, 1 H), 1.48−1.42 (m, 1 H), 1.05−0.91 (m, 1 H), 0.68−0.45 (m, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.2, 135.0, 130.2, 129.4, 91.9, 73.5, 36.3, 28.3, 24.6, 24.2, 21.1, 10.9; MS *m/z* (M^+ − $TolSO_2$) calcd 113.0966, obsd 113.0959. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51. Found: C, 62.37; H, 7.56.

Tributyl(3-ethyl-3,4-dihydro-2*H*-pyran-6-yl)stannane (40). The **44a**/**44b** mixture (1.01 g, 3.78 mmol) was dissolved in dry THF (12 mL), cooled to −78 °C under argon, and treated via syringe with *n*-butyllithium (1.50 mL, 4.00 mmol). The yellow solution was stirred at −78 °C for 1.5 h prior to the introduction of tributylstannyl chloride (1.05 mL, 3.87 mmol), at which point gradual warming to rt was allowed to occur during 5 h. The solvent was removed in vacuo, and the residue was taken up in $CHCl_3$ (20 mL), treated with diisopropylethylamine (2.00 mL, 11.5 mmol), and heated at 80 °C for 3 h. The reaction mixture was diluted with $CHCl_3$ (30 mL) and filtered through a pad of Celite prior to concentration in vacuo. The residue was partitioned between hexane (20 mL) and acetonitrile (15 mL), and the separated acetonitrile phase was extracted with hexane (10 mL). The combined hexane layers were concentrated to provide **40** as a colorless liquid (1.10 g, 72%) that was pure by ^1H NMR spectroscopy: ^1H NMR (300 MHz, C_6D_6) δ 4.92−4.90 (m, 1 H), 3.95−3.90 (m, 1 H), 3.44 (t, J = 10 Hz, 1 H), 2.04−1.97 (m, 1 H), 1.81−0.70 (series of m, 34 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 162.4, 111.7, 70.2, 34.7, 29.5, 28.0, 27.7, 25.5, 14.0, 11.3, 9.9; MS *m/z* (M^+) calcd 402.1936, obsd 402.1940. Anal. Calcd for $C_{19}H_{38}OSn$: C, 56.88; H, 9.55. Found: C, 57.11; H, 9.82.

(2*R,4*S**,6*S**)- and (2*R**,4*S**,6*R**)-Tetrahydro-2,4-dimethyl-6-(*p*-tolylsulfonyl)-2*H*-pyran (46a and 46b).** Reaction of **45**[29c] (4.35 g, 33.4 mmol) with calcium chloride (16.51 g, 148.8 mmol) and freshly prepared *p*-toluenesulfinic acid (5.24 g, 33.5 mmol) in CH_2Cl_2 (200 mL) in the manner described earlier provided 6.15 g (69%) of a mixture of **46a** and **46b**. Rechromatography on silica gel (elution with 8% ether in hexane) afforded pure samples of these diastereomers, with **46b** eluting first.

For **46a**: colorless solid, mp 23−25 °C; IR ($CHCl_3$, cm^{-1}) 1598, 1457, 1311, 1214, 1149, 1084; ^1H NMR (300 MHz, C_6D_6) δ 7.98 (d, J = 8 Hz, 2 H), 6.79 (d, J = 8 Hz, 2H), 4.17 (dd, J = 11.5, 2.2 Hz, 1 H), 2.91−2.81 (m, 1 H), 2.13−2.07 (m, 1 H), 1.23 (q, J = 11.9 Hz, 1 H), 0.91 (d, J = 6 Hz, 3 H), 1.10−0.84 (m, 2 H), 0.57 (d, J = 6.4 Hz, 2 H), 0.57 (d, J = 6.4 Hz, 3 H), 0.49−0.37 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.3, 134.9, 130.1, 129.4, 92.0, 75.1, 40.8, 31.9, 29.5, 21.7, 21.4, 21.2; MS *m/z* (M^+ − $TolSO_2$) calcd 113.0966, obsd 113.0948. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51. Found: C, 62.49; H, 7.64.

For **46b**: colorless crystals, mp 90−91 °C; IR ($CHCl_3$, cm^{-1}) 1596, 1468, 1372, 1308, 1220, 1138, 1084; ^1H NMR (300 MHz, C_6D_6) δ 7.81 (d, J = 8 Hz, 2 H), 6.80 (d, J = 8 Hz, 2 H), 4.72−4.61 (m, 1 H), 4.56 (d, J = 7 Hz, 1 H), 2.68−2.61 (m, 1 H), 2.49−2.34 (m, 1 H), 1.88 (s, 3 H), 1.32−1.25 (m, 1 H), 1.10−1.01 (m, 1 H), 0.97 (d, J = 6 Hz, 3 H), 0.65 (d, J = 6.5 Hz, 3 H), 0.61−0.52 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 143.7, 136.1, 129.3, 128.9, 90.0, 69.2, 40.7, 29.8, 24.9, 22.0, 21.8, 20.9; MS *m/z* (M^+ − $TolSO_2$) calcd 113.0966, obsd 113.0974. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51. Found: C, 62.81; H, 7.57.

Tributyl(3,4-dihydro-2-methyl-2*H*-pyran-6-yl)stannane (41). The lactol[29e] (7.58 g, 65.3 mmol) dissolved in CH_2Cl_2 (200 mL) was treated with anhydrous calcium chloride (32.29 g, 290.9 mmol) and freshly prepared *p*-toluenesulfinic acid (10.28 g, 65.8 mmol), stirred under N_2 overnight, and diluted with CH_2Cl_2 (200 mL) and saturated $NaHCO_3$ solution (100 mL). This mixture was filtered through a small pad of Celite, and the separated aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic fractions were dried and concentrated, and the residue was purified by flash column chromatography (silica gel, petroleum ether:ether, 3:1) to yield a colorless oily mixture of diastereomers (12.25 g, 74%). Separation was achieved by flash column chromatography using petroleum ether:ether (22:3) as eluent.

For the trans sulfone: colorless oil; IR ($CHCl_3$, cm^{-1}) 1597, 1444, 1385, 1318, 1208, 1150, 1122, 1086, 1049; ^1H NMR (300 MHz, C_6D_6) δ 7.80 (d, J = 8 Hz, 2 H), 6.81 (d, J = 8 Hz, 2 H), 4.63−4.53 (m, 1 H), 4.47 (dd, J = 6.7, 1.6 Hz, 1 H), 2.54−2.45 (m, 1 H), 2.23−2.07 (m, 1 H), 1.87 (s, 3 H), 1.51−1.38 (m, 1 H), 1.34−1.24 (m, 2 H), 0.98−0.83 (m, 1 H), 0.97 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.0, 136.2, 129.6, 129.2, 89.5, 69.2, 32.0, 21.9, 21.8, 21.2, 18.8; MS *m/z* (M^+) calcd 254.0977, obsd 254.0983. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 61.39; H, 7.13. Found: C, 61.12; H, 7.06.

For the cis sulfone: colorless oil; IR (C_6D_6, cm^{-1}) 1598, 1443, 1384, 1324, 1151, 1081, 1046; ^1H NMR (300 MHz, C_6D_6) δ 7.96 (d, J = 8 Hz, 2 H), 6.79 (d, J = 8 Hz, 2 H), 4.16 (dd, J = 11.6, 2.3 Hz, 1 H), 2.90−2.79 (m, 1 H), 2.08−2.00 (m, 1 H), 1.84 (s, 3H), 1.53 (qd, J = 12.4, 4.1 Hz, 1 H), 1.40−1.31 (m, 1 H), 0.99−0.66 (m, 3 H), 0.88 (d, J = 6.4 Hz, 2 H), 0.57 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.2, 134.9, 130.2, 129.3, 92.3, 75.4, 32.1, 23.8, 22.4, 21.6, 21.1; MS *m/z* (M^+) calcd 254.0977, obsd 254.0991. Anal. Calcd for $C_{14}H_{20}O_3S$: C, 61.39; H, 7.13. Found: C, 61.24; H, 7.08.

The sulfone isomers (6.12 g, 24.1 mmol) were dissolved in THF (25 mL), cooled to −78 °C under argon, and treated with *n*-butyllithium (16.0 mL, 25.6 mmol) via syringe. The resulting red solution was stirred at −78 °C for 1.5 h, when tributylstannyl chloride (6.50 mL, 24.0 mmol) was introduced neat via syringe over 10 min. The reaction mixture was stirred 4 h while being allowed to warm gradually to rt. The solvent was removed *in vacuo*, and the residue was dissolved in $CHCl_3$ (200 mL), treated with Hünig's base (14.8 mL, 85.0 mmol), and stirred at ambient temperature for 15 h and at 80 °C for 2 h before cooling to rt for 1 h. The mixture was concentrated *in vacuo*, and the residue was partitioned between hexane (160 mL) and acetonitrile (110 mL). The separated acetonitrile layer was washed with hexane (100 mL), and the hexane solutions were combined and concentrated to produce a colorless liquid. This liquid was chromatographed on deactivated silica gel (1% ether, 1% triethylamine, 98% petroleum ether) to afford **41** as a colorless oil (5.93 g, 64%), the spectral features of which were identical to those reported in the literature.[28]

Tributyl(*cis*-3,4-dihydro-2,4-dimethyl-2*H*-pyran-6-yl)stannane (42). Reaction of **46a**/**46b** (4.07 g, 15.2 mmol) with *n*-butyllithium (10.5 mL, 16.8 mmol) and tributylstannyl chloride (4.10 mL, 15.1 mmol) followed by heating with Hünig's base in the manner described for **40** produced a colorless liquid, chromatography of which on silica gel (elution with 1% ether and 1% triethylamine in petroleum ether) afforded 4.17 g (69%) of pure **42** as a colorless oil: ^1H NMR (300 MHz, C_6D_6) δ 4.76

(t, J = 1.8 Hz, 1 H), 3.86−3.76 (m, 1 H), 2.33−2.23 (m, 1 H), 1.80−1.32 (series of m, 14 H), 1.21−1.01 (m, 10 H), 0.94 (t, J = 7 Hz, 9 H), 1.00−0.82 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 161.3, 118.9, 72.1, 40.1, 29.5, 28.6, 27.6, 22.0, 21.9, 14.0, 9.9; MS m/z (M^+) calcd 402.1936, obsd 402.1964.

(5*R,8*R**)- and (5*R**,8*S**)-8-Ethyl-6-oxaspiro[4.5]decan-1-one (47 and 48).** A cold (−78 °C), magnetically stirred solution of **40** (932 mg, 2.32 mmol) in dry THF (10 mL) under argon was treated with *n*-butyllithium (1.30 mL, 2.08 mmol) in hexanes. After 1 h of stirring, cyclobutanone (150 μL, 2.0 mmol) was introduced, and the reaction mixture was allowed to warm to rt during 16 h, recooled to −78 °C, and quenched with saturated $NaHCO_3$ solution (4 mL). The aqueous phase was extracted with ether, and the combined organic layers were washed with brine, dried, and concentrated. The carbinol was purified by column chromatography (silica gel, elution with 20% ether in petroleum ether) to furnish a clear oil (257 mg, 70%).

A 94 mg (0.52 mmol) sample of this alcohol was dissolved in CH_2Cl_2 (25 mL), treated with camphorsulfonic acid (15 mg), stirred for 24 h, and concentrated. Flash chromatography of the residue on silica gel yielded the pure spiro ketones **47** (16.8 mg, 18%) and **48** (71.1 mg, 76%).

For **47**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1735, 1466, 1404, 1064; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (m, 1 H), 3.19−3.12 (t, J = 11 Hz, 1 H), 2.43−2.32 (m, 1 H), 2.23−1.89 (m, 3 H), 1.84−1.38 (series of m, 7 H), 1.29−1.12 (m, 2 H), 0.85−0.80 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.0, 99.9, 68.5, 38.1, 37.2, 36.5, 29.0, 24.9, 24.8 17.5, 11.2; MS m/z (M^+) calcd 182.1307, obsd 182.1306. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.48; H, 9.91.

For **48**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1746, 1467, 1404, 1076; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87−3.81 (m, 1 H), 3.20−3.12 (t, J = 10.5 Hz, 1 H), 2.32−2.14 (m, 3 H), 2.07−1.85 (m, 3 H), 1.78−1.66 (m, 1 H), 1.61−1.45 (m, 3 H), 1.30−1.02 (m, 3 H), 0.90−0.85 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.0, 80.5, 68.5, 36.6, 35.4, 31.7, 28.1, 25.5, 25.0, 17.5, 11.1; MS m/z (M^+) calcd 182.1307, obsd 182.1307. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.28; H, 9.91.

The 2,4-dinitrophenylhydrazone of **48** was isolated as yellow crystals, mp 155−156 °C. Anal. Calcd for $C_{16}H_{20}N_4O_5$: C, 55.17; H, 5.79. Found: C, 55.07; H, 5.77.

(5*R,7*S**)- and (5*R**,7*R**)-7-Methyl-6-oxaspiro[4.5]decan-1-one (49 and 50).** Metalation of **41** (274 mg, 1.08 mmol) with *n*-butyllithium in hexanes (0.70 mL, 1.12 mmol) followed by condensation with cyclobutanone (85 μL, 1.14 mmol) gave a mixture of diastereomeric carbinols (144 mg, 98%) which was rearranged as before in the presence of camphorsulfonic acid. Chromatography of the residue on silica gel (elution with 25% ether in petroleum ether) gave 280 mg (69%) of **49** and 22 mg (6%) of **50**.

For **49**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1746, 1447, 1052; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.61−3.50 (m, 1 H), 2.31−2.19 (m, 3 H), 2.05−1.90 (m, 2 H), 1.82−1.18 (series of m, 7 H), 1.14 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.7, 81.4, 68.9, 35.4, 32.6, 31.6, 27.9, 22.2, 19.7, 17.6; MS m/z (M^+) calcd 168.1150, obsd 168.1150. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.47; H, 9.75.

For **50**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1735, 1456, 1404, 1214, 1077, 1036; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02−3.91 (m, 1 H), 2.44−2.32 (m, 1 H), 2.22−1.92 (m, 4 H), 1.80−1.41 (series of m, 6 H), 1.21−1.12 (m, 1 H), 1.09 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 215.6, 77.7, 68.7, 39.3, 36.7, 33.5, 29.3, 22.5, 19.5, 17.7; MS m/z (M^+) calcd 168.1150, obsd 168.1149. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.44; H, 9.83.

(5*R,7*R**,9*S**)- and (5*R**,7*S**,9*R**)-7,9-Dimethyl-6-oxaspiro[4.5]decan-1-one (51 and 52).** Sequential exposure of **42** (1.37 g, 3.41 mmol) to *n*-butyllithium in hexanes (2.00 mL, 3.20 mmol) and cyclobutanone (230 μL, 3.08 mmol) as detailed above afforded 382 mg (68%) of chromatographically purified carbinol, which was directly rearranged in the presence of camphorsulfonic acid (10 mg). Flash chromatographic purification (silica gel, elution with 25% ether in petroleum ether) delivered 339 mg (89%) of **57** and 11 mg (3%) of **52**.

For **51**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1744, 1456, 1372, 1213, 1152, 1064; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62−3.51 (m, 1 H), 2.33−2.15 (m, 3 H), 2.06−1.90 (m, 2 H), 1.83−1.64 (m, 2 H), 1.61−1.54 (m, 1 H), 1.43−1.37 (m, 1 H), 1.15 (d, J = 6 Hz, 3 H), 0.92 (d, J = 6.5 Hz, 3 H), 1.14−0.89 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.8, 81.5, 68.9, 41.4, 36.3, 35.4, 32.2, 26.4, 22.2, 22.0, 17.7; MS m/z (M^+) calcd 182.1307, obsd 182.1307. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.51; H, 10.02.

For **52**: colorless oil; IR ($CHCl_3$, cm^{-1}) 1736, 1457, 1374, 1220, 1008; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00−3.89 (m, 1 H), 2.45−2.34 (m, 1 H), 2.27−1.94 (m, 4 H), 1.84−1.55 (m, 3 H), 1.35−1.18 (m, 1 H), 1.10 (d, J = 6 Hz, 3 H), 0.87 (d, J = 6.5 Hz, 3 H), 1.08−0.72 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.6, 78.4, 68.6, 41.8, 39.1, 37.6, 36.7, 27.4, 22.4, 22.1, 17.5; MS m/z (M^+) calcd 182.1307, obsd 182.1307. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.35; H, 9.94.

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Supporting Information Available: NOE and long-range DEPT data for **26**, **32**, **33**, and **52**, as well as ORTEP drawings for **28**-2,4-DNP, **31**-2,4-DNP, **34**-2,4-DNP, and **48**-2,4-DNP (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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