equilibrium had been reached. Reactions were quenched (with 10% HCl, pH ~3-4) immediately after their removal from the constant-temperature bath. In cases where no CTAB or DDAB was present, a simple extraction by CH_2Cl_2 removed both diastereomers without affecting their ratio. However, in order to obtain acceptable analyses with CTAB or DDAB, the following workup procedure was used. After acidification with 10% HCl, the water was removed from the CTAB or DDAB solution by evaporation with benzene used to azeotrope the last traces of water. Diazomethane in ether was added to the residue and the resulting solution chromatographed on silica gel with EtOAc. Control experiments have verified that accurate analyses may be obtained with this procedure.

Acknowledgment. N.A.P. gratefully acknowledges financial support from NIH and NSF.

Supplementary Material Available: Tables of spectroscopic data (^1H and ^{13}C NMR), mass spectral fragmentation data, and combustion analyses for dienones **5a-d** and diacids **1a-d**, atomic positional and thermal parameters, bond lengths and angles, and torsion angles for **1b** and **1c** (22 pages); calculated structure amplitudes (28 pages). Ordering information is given on any current masthead page.

A General Approach to the Stereoselective Synthesis of Spiroketals. A Total Synthesis of the Pheromones of the Olive Fruit Fly and Related Compounds†

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Contribution from the Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742. *Received July 28, 1987*

Abstract: A general, highly stereoselective approach to the synthesis of spiroketal systems of the 1,7-dioxaspiro[5.5]undecane and 1,6-dioxaspiro[4.5]decane families is discussed. The key reaction in the approach features oxidation of a suitably substituted furfurol derivative **1** to afford pyranone **2**, which subsequently undergoes stereoselective intramolecular ketalization under acidic conditions to furnish spiroketal **3**, carrying the 2,6-anti relationship. Analogous methodology is employed to synthesize in a stereoselective fashion model systems for the avermectin spiroketal moieties **9-11** and the pheromones of the olive fruit fly (**39** and **40**).

The spiroketal moiety is found in many natural products, ranging from insect pheromones[1] in which the spiroketal is devoid of substituents about the periphery to structurally and stereochemically complex systems found in monensin,[2] okadaic acid,[3] and the avermectin[4]/milbemycin[5] family of antibiotics. In addition to being a target for natural product synthesis, spiroketals are also excellent systems to study the role of the anomeric effect as a means of controlling the conformational mobility of heterocyclic systems.[6] Recently, several methods for the synthesis of spiroketal systems have been reported.[7] In the majority of these approaches, stereogenic centers on the heterocyclic framework were established prior to formation of the spiroketal center using established methods of acyclic stereocontrol.[8] A few strategies have addressed the problem of establishing the stereochemical relationships about the periphery once the heterocyclic framework has been constructed.[9] The synthetic strategy reported herein relies upon a short, efficient synthesis of highly functionalized spiroketals bearing a minimum of stereochemical information. Subsequent regio- and stereoselective transformations introduce the requisite functional groups. The concept is illustrated in Scheme I.

Previous studies had demonstrated that oxidation of furfurol derivatives such as **1** afforded pyranone **2**. It was anticipated that **2** would undergo highly stereoselective spiroketalization under equilibrating conditions to furnish spiroketals **3** and **4**. Spiroketal **3** should be the predominant product under equilibrating conditions and should exist exclusively as conformation **3A** (Chart I) in which it possesses two equatorial alkyl substituents at carbons 2 and 6 and dual anomeric stabilization at carbon 2.[10] That is, each of the oxygen atoms of the respective pyran systems occupies an axial orientation with respect to the other pyran ring. The alternative conformations of **3** (**3B-D**) are disfavored because they must either sacrifice one of the anomeric effects or the C-6 substituent must adopt an axial orientation (see Scheme I).

Scheme I

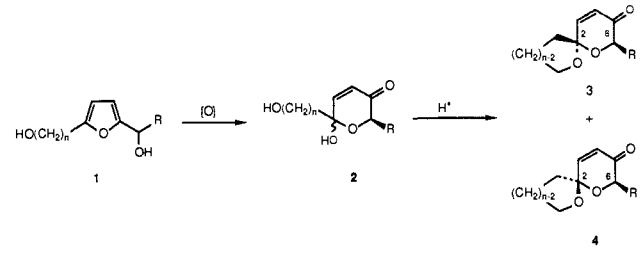
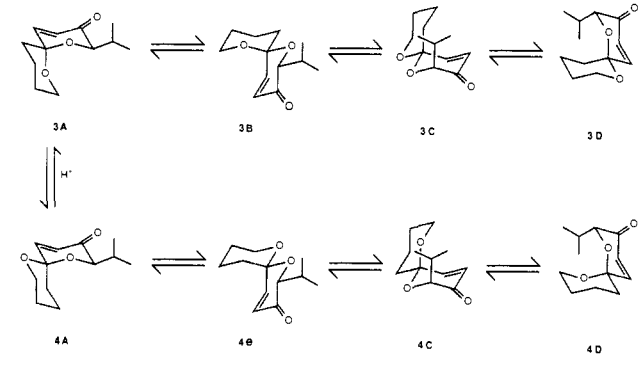


Chart I



† This paper is dedicated to Royston M. Roberts on the occasion of his 70th birthday.

(1) (a) Baker, R.; Herbert, R. H.; Howse, P. E.; Jones, O. T. *J. Chem. Soc., Chem. Commun.* **1980**, 52. (b) Baker, R.; Herbert, R. H.; Parton, A. H. *J. Chem. Soc., Chem. Commun.* **1982**, 601. (c) Francke, W.; Reith, W.; Bergström, G.; Tengö, J. *Naturwissenschaften* **1980**, *67*, 149.

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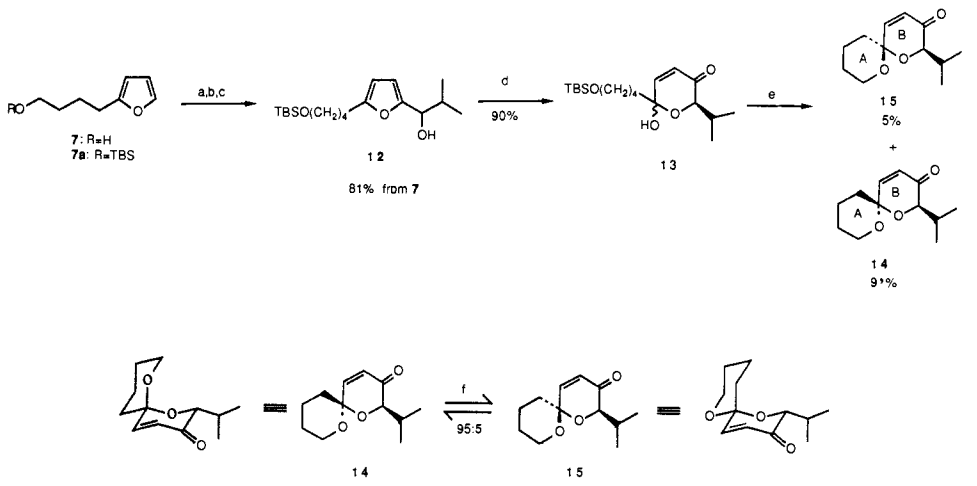
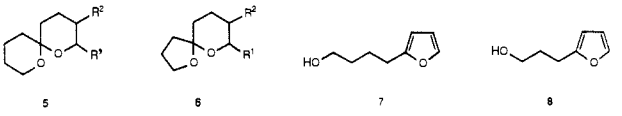
Scheme II[a]



[a] (a) *t*-BuMe$_2$SiCl, imidazole, DMF, 99%; (b) *n*-BuLi, TMEDA, Et$_2$O; (c) Me$_2$CHCHO; (d) *m*-CPBA, CH$_2$Cl$_2$; (e) HF, MeCN; (f) 1:1:1 (w:w:w) HF/H$_2$O/MeCN.

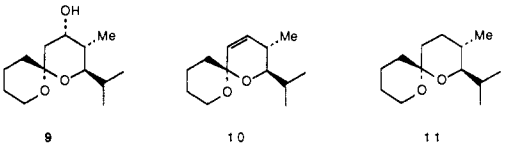
For the other possible diastereomer, spiroketal **4**, the conformation of the spiroketal system which allows dual anomeric stabilization, conformation **4C**, also must place the C-6 substituent into an axial orientation, leading to a severe 1,3-diaxial interaction. Meanwhile, conformations **4A** and **4B**, in which the C-6 substituent is equatorial, have at most a single anomeric effect (Chart I). Thus, it was anticipated that enone **3** would be formed in preference to enone **4** and that the combination of these steric and electronic effects would serve not only to strongly favor spiroketal **3** in the equilibrium with **4**, which establishes the 2,6-anti stereochemistry, but also limits the conformational mobility of the spiroketal system. Having introduced two stereocenters into the spiroketal framework at carbons 2 and 6 and locked the conformation of the spiroketal, we expected that highly regioselective and stereoselective methods for the attachment of functional groups onto the enone moiety of **3** could be developed. The successful implementation of this strategy for spiroketal synthesis is discussed below.

Initial efforts were directed toward the synthesis of functionalized 1,7-dioxaspiro[5.5]undecane (**5**; 6,6-spiroketal) and 1,6-dioxaspiro[4.5]decane (**6**; 6,5-spiroketal) systems as they are the principal structural components found in natural products. These systems were prepared from 4-(2-furyl)butan-1-ol (**7**) and 3-(2-furyl)propan-1-ol (**8**), respectively.



Model Studies for the Avermectins

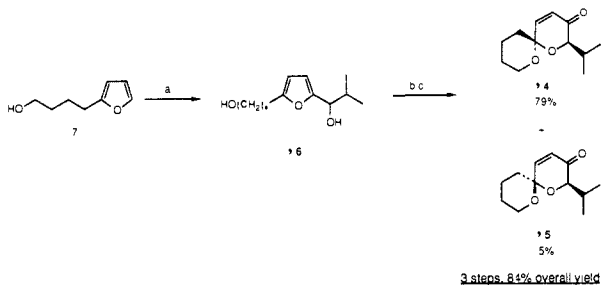
Initial investigations focused on the preparation of spiroketals **9–11**, model systems for the spiroketal moieties found in the avermectin/milbemycin family of antibiotics.



The avermectins and milbemycins are broad-spectrum antiparasitic and insecticidal agents. The isolation and structure of the milbemycins from *Streptomyces hygroscopicus* subsp. *aureolacrimosus* were reported by Mishima et al.[5] The isolation and structure determination of the avermectins from *Streptomyces avermitilis* were reported by Albers-Schönberg in 1981.[4] The avermectins and milbemycins consist of a 16-membered lactone system incorporating a mono or bicyclic "southern" portion and a functionalized 6,6-spiroketal (the "northern" portion). One key structural difference between the milbemycins and avermectins is a disaccharide unit attached at C-13 of the latter class. Degradation studies have demonstrated that the macrolides can be assembled in a convergent fashion from the respective fragments to yield either the natural product or a hybrid molecule.[11] Synthetic efforts have been highlighted by a number of total syntheses of milbemycins[12] and the "northern"[7a,8a-d] and

(2) Chamberlin, J. W.; Agtarap, A.; Steinrauf, L.; Pinkerton, M. *J. Am. Chem. Soc.* **1967**, *89*, 5737.
(3) Tachibana, K.; Scheuer, P. J.; Tsukitani, Y.; Kikuchi, H.; Engen, D. V.; Clardy, J.; Gopichand, Y.; Schmitz, F. *J. Am. Chem. Soc.* **1981**, *103*, 2469.
(4) (a) Albers-Schönberg, G.; Arison, B. H.; Chabala, J. C.; Douglas, A. W.; Eskola, P.; Fisher, M. H.; Lusi, A.; Morzik, H.; Smith, J. L.; Tolman, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 4216. (b) Springer, J. P.; Arison, B. H.; Hirshfield, J. M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1981**, *103*, 4221.
(5) Mishima, H.; Kurabayashi, M.; Tanura, C.; Sato, S.; Kuwano, H.; Saito, A. *Tetrahedron Lett.* **1975**, 711.
(6) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983.
(7) (a) Barrett, A. G. M.; Attwood, S. V.; Florent, J.-C. *J. Chem. Soc., Chem. Commun.* **1981**, 556. (b) Smith. L. R.; Williams, H. J.; Taylor, R. J.; Jacobson, R. *J. Org. Chem.* **1982**, *47*, 3140. (c) Boeckman, R. K., Jr.; Bruza, K. J.; Heinrich, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 7101. (d) Kishi, Y.; Schmid, G.; Wang, C.-L. J.; Karanewsky, D. S.; Akasaka, K.; Fukuyama, T. *J. Am. Chem. Soc.* **1979**, *101*, 262. (e) Danishefsky, S. J.; Pearson, W. H. *J. Org. Chem.* **1983**, *48*, 3865. (f) Ley, S. V.; Lygo, B.; Organ, H. M.; Wonnacott, A. *Tetrahedron* **1985**, *41*, 3825. (g) Kay, I. T.; Williams, E. G. *Tetrahedron Lett.* **1983**, *24*, 5915. (h) Iwata, C.; Hattori, K.; Uchida, S.; Imanishi, T. *Tetrahedron Lett.* **1984**, *25*, 2995. (i) Mori, K.; Watanabe, H.; Yanagi, K.; Minobe, M. *Tetrahedron* **1985**, *41*, 3663. (j) Kocienski, P.; Yeates, C. *Tetrahedron Lett.* **1983**, *24*, 3905. (k) Schreiber, S. L.; Sommer, T. J. *Tetrahedron Lett.* **1983**, *24*, 4781.
(8) (a) Hanessian, S.; Ugolini, A.; Therien, M. *J. Org. Chem.* **1983**, *48*, 4427. (b) Julia, M.; Ardisson, J.; Fĕrĕzou, J. P.; Lenglet, L.; Pancrazi, A. *Tetrahedron Lett.* **1987**, *28*, 1997. (c) Hirama, M.; Nakamine, T.; Ito, S. *Tetrahedron Lett.* **1986**, *27*, 5281. (d) Baker, R.; Head, J. C.; Swain, C. J. *J. Chem. Soc., Chem. Commun.* **1985**, 309. (e) Isobe, M.; Ichikawa, Y.; Bai, D.-L.; Goto, T. *Tetrahedron Lett.* **1985**, *26*, 5203. (f) Grieco, P. A.; Martinez, G. R.; Williams, E.; Kanai, K.-I.; Srinivasan, C. V. *J. Am. Chem. Soc.* **1982**, *104*, 1436. (g) Evans, D. A.; Sacks, C. E.; Kleshick, W. A.; Taber, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789. (h) Crimmins, M. T.; Bankaitis, D. M. *Tetrahedron Lett.* **1983**, *24*, 4551.
(9) (a) Deslongchamps, P.; Ruest, L.; Schwartz, D. A.; Sauvé, G. *Can. J. Chem.* **1984**, *62*, 2929. (b) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1983**, *48*, 1303. (c) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1983**, *48*, 1312. (d) Barrett, A. G. M.; Carr, R. A. E. *J. Org. Chem.* **1986**, *51*, 4254.
(10) Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauvé, T.; Saunders, J. K. *Can. J. Chem.* **1981**, *59*, 1105.
(11) Smith, A. B., III; Thompson, A. S. *Tetrahedron Lett.* **1985**, *26*, 4283.
(12) (a) Smith, A. B., III; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015. (b) Williams, D. R.; Barner, B. A.; Nishitani, K.; Phillips, J. G. *J. Am. Chem. Soc.* **1982**, *104*, 4708. (c) Street, S. D. A.; Yeates, C.; Kocienski, P.; Campbell, S. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1386, 1388. (d) Attwood, S. V.; Barrett, A. G. M.; Carr, R. A. E.; Richardson, G. *J. Chem. Soc., Chem. Commun.* **1986**, 479. (e) Baker, R.; O'Mahony, M. J.; Swain, C. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1326.

Scheme III[a]



[a] (a) 2*n*-BuLi, TMEDA, Et_2O; (b) Me_2CHCHO; (c) *m*-CPBA, CH_2Cl_2; (d) HF, MeCN.

"southern"[13] subunits of the avermectins.

Silylation of 4-(2-furyl)butan-1-ol (**7**)[14] followed by metalation of the furan and condensation with 2-methylpropanal afforded alcohol **12**. Oxidation of the furan moiety with *m*-CPBA[15] provided pyranone **13** in 90% yield. Analysis of the 200-MHz ^1H NMR spectrum of **13** indicated that the pyranone existed as a single diastereomer; however, the stereochemistry at the anomeric center was not determined.

Treatment of the pyranone with HF in acetonitrile resulted in a spirocyclization and formation of spiroketals **14** and **15** in a combined yield of 96%. The ratio of **14**:**15** was 95:5 (capillary GC). The ratio of spiroketals obtained under these conditions reflected the thermodynamic equilibrium for the system. When either spiroketal **14** or a 1:1 mixture of **14** and **15** was subjected to the HF conditions, the 95:5 mixture of **14**:**15** was established in high yield.

The major diastereomer was assigned as **14** from the precedents established in related systems[6-10] (vide supra). In this instance, the isopropyl group should adopt the equatorial orientation on ring B and effectively eliminate conformational mobility of this ring. Spirocyclization can proceed to afford either **14**, in which the anomeric C–O bond is axial, or **15**, carrying an equatorial C–O bond on ring A. The anomeric effect should favor formation of **14**.[10] The stereochemical assignment was confirmed by subsequent transformations of spiroketal **14**.

The magnitude of the anomeric effect has been estimated to be 1.0–2.0 kcal/mol,[6] and the ratio of **14**:**15** suggested that the maximum stabilization of the anomeric effect was manifested in this system. Alternatively, it may be that two stereoelectronic effects are responsible for the strong preference for the production of **14**. First, there may be an anomeric effect associated with the C–O bond of ring A being axial to ring B. The second factor favoring formation of **14** may be that the enone moiety of ring B is placed equatorial to ring A. Carbonyl groups (and other electron-withdrawing groups) are known to favor equatorial positions at the anomeric center, and this is known as the reverse anomeric effect.[16] In spiroketal system **14**, the anomeric effect and reverse anomeric effect are complementary and should favor the formation of spiroketal **14**.

A more efficient preparation of spiroketals **14** and **15** that avoids the use of protecting groups is outlined in Scheme III. Metalation of alcohol **7** with 2 equiv of *n*-BuLi and treatment with 2-methylpropanal gave diol **16**. Oxidation followed by spirocyclization with HF–CH_3CN afforded enones **14** and **15** in a combined overall 84% yield from **7**. In this manner, enone **14** was prepared in high yield from readily available alcohol **7** without purification of intermediates.

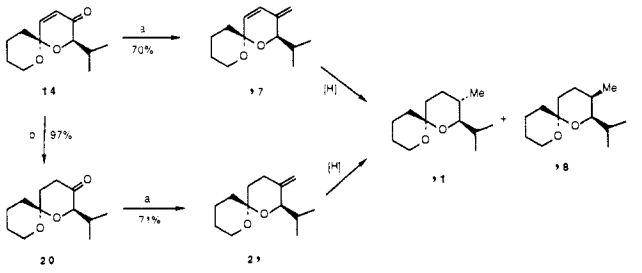
(13) (a) Fraser-Reid, B.; Prashad, M. *J. Org. Chem.* **1985**, *50*, 1564. (b) Crimmins, M. T.; Lever, J. G. *Tetrahedron Lett.* **1986**, *27*, 291. (c) Barrett, A. G. M.; Capps, N. K. *Tetrahedron Lett.* **1986**, *27*, 5571. (d) Hanessian, S.; Beaulieu, P.; Dubé, D. *Tetrahedron Lett.* **1986**, *27*, 5071. (e) Julia, M.; Ardisson, J.; Férézou, J. P.; Pancrazi, A. *Tetrahedron Lett.* **1987**, *28*, 2001. (f) Hanessian, S.; Ugolini, A.; Dubé, D.; Hodges, P. J.; André, C. *J. Am. Chem. Soc.* **1986**, *108*, 2776.

(14) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(15) Williams, P. D.; LeGoff, E. *J. Org. Chem.* **1981**, *46*, 4143.

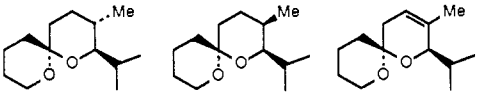
(16) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: New York, 1983.

Scheme IV[a]



[a] (a) $Ph_3P{=}CH_2$, THF; (b) H_2, 1 atm, 5% Pd/C, EtOH.

Table I. Reduction of Diene **17**



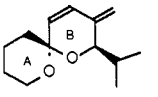
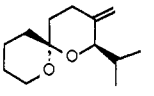
Substrate	Reducing Agent	11 : 18 : 19
	H_2, $(Ph_3P)_3RhCl$	10 : 53 : 0
	H_2, 5% Rh/Alumina	10 : 18 : 11
	H_2, Ra-Ni	10 : 47 : 62
	H_2, 10% Pt/Alumina	10 : 15 : 0
	H_2, 5% Pd/C	10 : 12 : 26
17	HN=NH, THF	20 : 10 : 0

Table II. Reduction of Alkene **21**

Substrate	Reducing Agent	11 : 18
	H_2, $(Ph_3P)_3RhCl$	10 : 23
	H_2, 5% Rh/Alumina	10 : 30
	H_2, Ra-Ni	10 : 66
	H_2, 10% Pt/Alumina	10 : 10
	H_2, 5% Pd/C	10 : 14
	HN=NH, THF	12 : 10
21	HN=NH, Et_2O	16 : 10

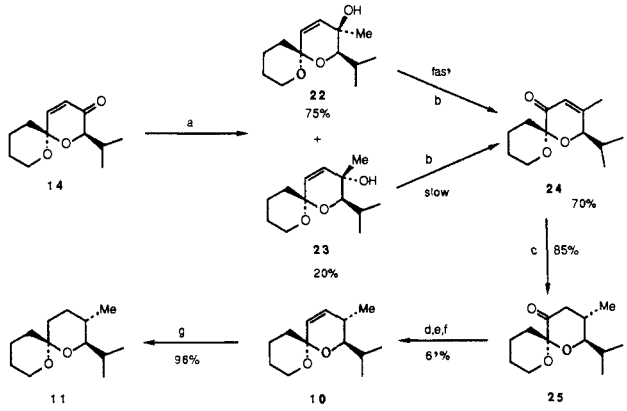
Several strategies for the transformation of enone **14** into spiroketals **9**–**11** were studied. The most direct method for the synthesis of ivermectin model **11** involved Wittig reaction of **14** to provide diene **17** followed by stereoselective catalytic reduction. It was anticipated that reduction of **17** would occur from the least hindered side to produce spiroketal **11**, in preference to diastereomer **18**.

In practice, treatment of enone **14** with methylenetriphenylphopshorane in THF gave diene **17** in 70% yield (Scheme IV). Reduction of diene **17** under a variety of conditions, however, failed to yield the desired spiroketal **11** free of contamination by its diastereomer **18** and, in some instances, 1,4-reduction product alkene **19**. Our results from the reductions are summarized in Table I. The notable feature reflected in the results is that catalytic hydrogenation of diene **17**, irrespective of the catalyst employed, favored formation of spiroketal **18**, instead of **11**. The naive assumption that catalytic reduction would occur from the least hindered side of the diene was not borne out. A possible explanation for the stereoselectivity observed under catalytic reducing conditions is that the anomeric ether oxygen of ring A coordinated with the catalyst surface and directed hydrogen placement onto the undesired face of the diene.[17]

Since catalytic reduction of diene **17** failed to afford avermectin analogue **11**, the stereoselectivity of the reduction of alkene **21** was investigated. Alkene **21** was prepared as outlined in Scheme IV. Catalytic reduction of enone **14** yielded ketone **20**, which reacted with methylenetriphenylphosphorane providing the exo-

(17) Rylander, P. N. *Catalytic Hydrogenation in Organic Syntheses*; Academic: New York, 1979.

Scheme V[a]



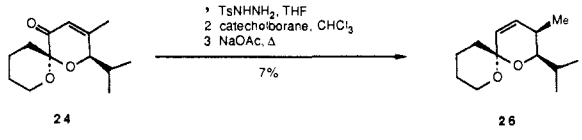
[a](a) MeLi, Et_2O, −55 °C; (b) PCC, CH_2Cl_2; (c) H_2, 1 atm, 5% Pd/C, EtOH; (d) $TsNHNH_2$, THF; (e) 3 equiv at *n*-BuLi; (f) H_2O; (g) H_2, 1 atm, $(Ph_3P)_3RhCl$, C_6H_6.

methylene compound. As observed with diene **17**, catalytic reduction of **21** afforded a mixture of diastereomeric spiroketals **11** and **18** in which **18** predominated (see Table II). Only diimide reduction of **17** or **21** furnished spiroketal **11** stereoselectively, and in these instances the stereoselectivity was modest (1.2–2.0:1).

A stereoselective approach to the elaboration of avermectin analogues **10** and **11** from enone **14** is depicted in Scheme V. Treatment of **14** with methyllithium gave allylic alcohols **22** (75%) and **23** (20%), respectively. The stereochemistry at the allylic alcohol center of the major isomer was assigned as indicated based upon the rates of the subsequent oxidation with PCC. Axial alcohols undergo the allylic rearrangement and oxidation more rapidly than their equatorial counterparts.[18] The major allylic alcohol isomer (**22**) was oxidized by PCC within 8 h, furnishing enone **24**, whereas alcohol **23** was not completely oxidized in 48 h under identical conditions. In practice, oxidation of the mixture **22**/**23** with PCC in methylene chloride afforded rearranged enone **24** in 70% yield.

To our delight, catalytic reduction of enone **24** occurred with total stereoselectivity to provide ketone **25** carrying the equatorial methyl group. Unlike the other systems investigated (vide supra), this reduction had occurred from the least hindered direction. The anti disposition of the vicinal methyl and isopropyl substituents was tentatively assigned based upon the large C-2,C-3 coupling constant ($J_{2,3}$ = 13.6 Hz) observed in the product. Subsequent X-ray analysis of the tosylhydrazone derivative of **25** confirmed the stereochemical assignment. Ketone **25** was subjected to standard Shapiro reaction conditions (tosylhydrazine, *n*-BuLi) to afford alkene **10** (71%).

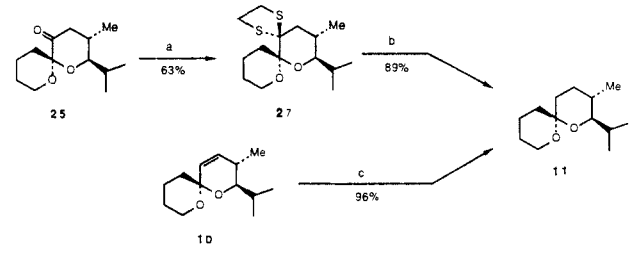
Spiroketal **26**, bearing the β-configuration at C-5, was also prepared in low yield from the tosylhydrazone of enone **24** by reduction with catecholborane in refluxing chloroform.[19] Under these conditions, alkene **26** was the sole reduction product and alkene **10** was not detected (capillary GC) in the reaction mixture.



Ivermectin model system **11** was synthesized from either ketone **25** or alkene **10** as indicated in Scheme VI. Thioketalization of **25** with ethanedithiol–zinc triflate[20] (63%) and Raney nickel desulfurization afforded spiroketal **11** in 60% overall yield.

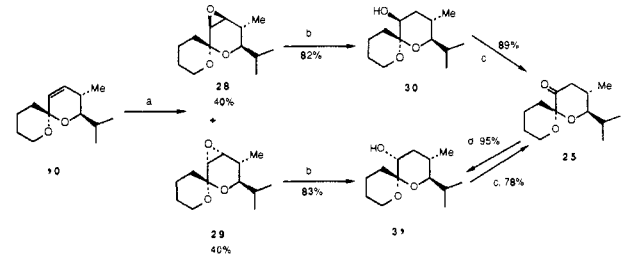
Initially, the preparation of **11** by catalytic reduction of alkene **10** did not appear to be promising because reductive cleavage of the allylic spiroketal function was observed with palladium catalysts. However, the reduction of **10** was accomplished in excellent yield by employing Wilkinson's catalyst in benzene.

Scheme VI[a]



[a](a) $HSCH_2CH_2SH$, ZnOTf, CH_2Cl_2; (b) H_2, 1 atm, room temperature, EtOH; (c) H_2, 1 atm, $(Ph_3P)_3RhCl$, C_6H_6.

Scheme VII[a]



[a](a) *m*-CPBA, Na_2HPO_4, CH_2Cl_2; (b) $LiEt_3BH$, THF; (c) PCC, CH_2Cl_2; (d) $NaBH_4$, MeOH.

Having achieved an efficient synthesis of spiroketals **10** and **11**, we investiated the regio- and stereoselective introduction of the hydroxyl function at C-4. Several strategies were investigated before the goal was achieved. On the basis of the results of catalytic hydrogenation of diene **17** (vide supra, Table I) it was anticipated that the spiroketal oxygen atom of ring A, which is axial to ring B, would coordinate with electrophilic reagents and direct introduction of oxygenation onto the α face of ring B stereoselectively. The results belied this prediction.

Various hydroboration reagents reacted with alkene **10** to furnish products derived solely from reduction of the spiroketal moiety. Apparently, coordination of the spiroketal oxygen to the electrophilic boron reagent rendered the anomeric center susceptible to reductive cleavage, and this strategy was abandoned ultimately.

Epoxidation of alkene **10** with buffered *m*-chloroperbenzoic acid (*m*-CPBA) in methylene chloride afforded a 1:1 mixture of the β-**28** and α-epoxide **29**. In this instance, the axial spiroketal oxygen did not direct epoxidation in Henbest fashion[21] onto the α face of the alkene.

As expected, reduction of β-epoxide **28** occurred in a diaxial manner to provide 3β-alcohol **30**. The regio- and stereochemistry of alcohol **30** were readily assigned by analysis of the ^1H NMR spectrum of **30**. PCC oxidation of **30** afforded ketone **25** and confirmed the regiochemical assignment.

Reduction of α-epoxide **29** with Super-Hydride did not give alcohol **9** as anticipated. Instead, 3α-alcohol **31**, the product of a formal diequatorial opening process, was the only alcohol obtained. The regioselectivity of epoxide opening was demonstrated by oxidation of **31**, which yielded ketone **25**. Analogously, reduction of ketone **25** with $NaBH_4$, a process known to proceed with preferential axial attack, gave exclusively alcohol **31**, which was identical in all respects with the product of epoxide reduction.

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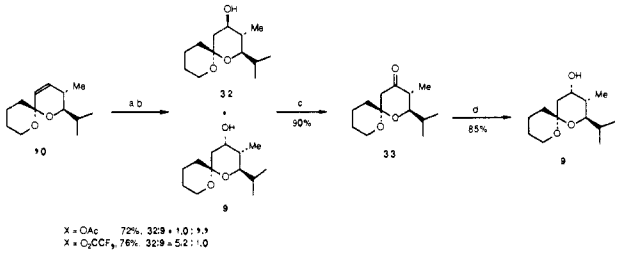
(19) Kabalka, G. W.; Yang, D. T. C.; Baker, J. D., Jr. *J. Org. Chem.* **1976**, *41*, 574.

(20) Corey, E. J.; Shimoji, K. *Tetrahedron Lett.* **1983**, *24*, 169.

(21) Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1957**, 1958.

Scheme VIII[a]



[a] (a) HgX_2, THF, H_2O; (b) $NaBH_4$, NaOH; (c) PCC, CH_2Cl_2; (d) K-Selectride, THF.

Epoxide **29** underwent reduction to afford C-3 alcohol **31** via an S_N1-like process. An S_N2-like, diaxial opening of **29** with the bulky reducing agent was precluded presumably because C-3 is a neopentyl center.

Once it had been demonstrated that nucleophilic attack at C-3 was disfavored by the quaternary center at C-2, the solution to the problem of introduction of a hydroxyl function at C-4 was obvious. Oxymercuration of the carbon–carbon double bond of alkene **10** proceeded via a mercuronium ion which suffered adduct formation only through oxygen attack at C-4. Mercuration–demercuration of alkene **10** with mercuric acetate provided a 1.0:1.1 mixture of alcohols **32** and **9**, respectively (Scheme VIII). Oxymercuration–demercuration of alkene **10** with mercuric trifluoroacetate displayed high stereoselectivity for production of the undesired equatorial alcohol **32**.

The presence of oxygen at C-4 was confirmed in each case by oxidizing either alcohol **32** or **9** to ketone **33**. The stereochemistry of alcohol **32** was demonstrated by single-crystal X-ray determination.

The failure of the mercuration strategy to furnish alcohol **9** stereoselectively was demonstrated to be of minor significance since reduction of 4-keto spiroketal **33** with K-Selectride afforded only α-alcohol **9**. Therefore, the most efficient protocol for hydroxylation of **10** involved oxymercuration of the alkene, followed by oxidation of the epimeric mixture of C-4 alcohols (**9** and **32**) and reduction to provide stereoselectively alcohol **9** in 60% overall yield.

Scheme IX summarizes the preparation of spiroketals **9–11** from alcohol **7**. Application of this methodology to the total synthesis of the milbemycins and avermectins is under way.

Model Studies: 1,6-Dioxaspiro[4.5]decanes

Once it had been established that oxidation of furfurol derivatives could be exploited for the stereoselective synthesis of functionalized 1,7-dioxaspiro[5.5]undecanes (**9–11**), our attention turned to the preparation of the homologous 1,6-dioxaspiro[4.5]decane system using an analogous approach. Silylation of 3-(2-furyl)propan-1-ol (**8**) with *tert*-butyldimethylsilyl chloride (99%), metalation of the 5-furyl position with *n*-BuLi, and condensation of the lithium reagent with 2-methylpropanal afforded alcohol **35** (Scheme X). Oxidation of **35** with *m*-CPBA furnished pyranone **36** as a single diastereomer. Fluoride-induced removal of the silyl ether and concomitant spirocyclization under the acidic conditions provided spiroketals **37** (84%) and **38** (13%), respectively. The major product was assigned structure **37** based upon results from the related 6,6-spiro system in which the ether oxygen of ring A preferred to be disposed axial to ring B (vide supra).

Equilibration of either pure **37** or a mixture of **37** and **38** with HF/H_2O/MeCN yielded an 87:13 (capillary GC) mixture of enones **37** and **38**, respectively. The homologous 6,6-spiroketal system had furnished a 95:5 mixture of enones under these conditions, and the decrease in the stereoselectivity of the equilibration reaction reflected the decreased anomeric stabilization available to tetrahydrofuran derivatives.[10]

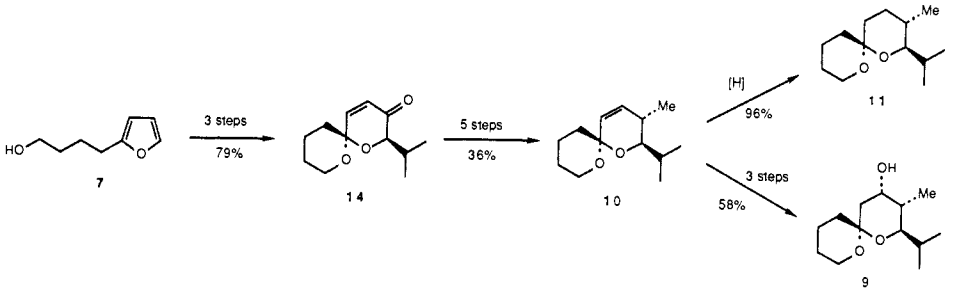
Pheromone Synthesis

To demonstrate the versatility of the furan-based strategy for spiroketal synthesis, spiroketals **39** and **40**, pheromones of the olive fruit fly, were synthesized. Isolation and characterization of **39**

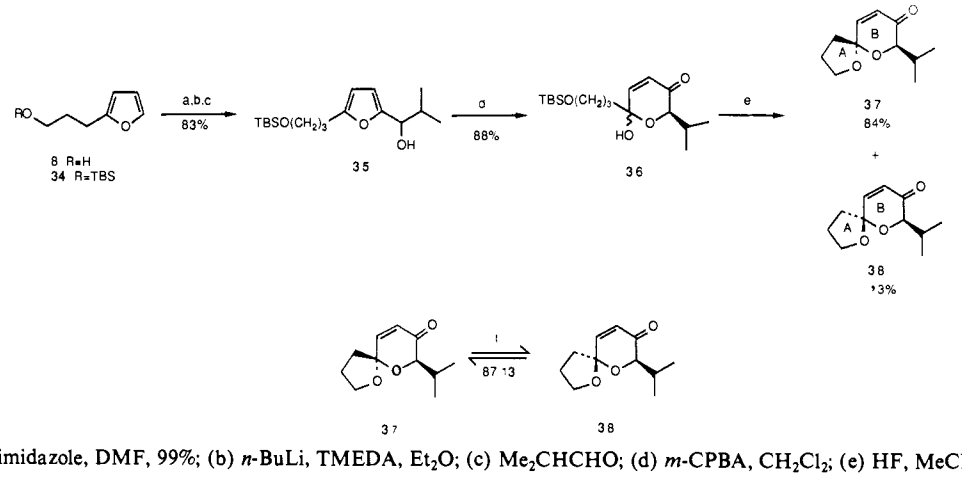
39 **40**

and **40** were reported by Baker in 1980 and 1982,[1a,b] and several total syntheses of both components have been reported.[1a,b,7f,i,j]

Scheme IX

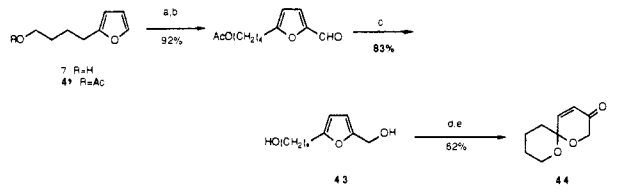


Scheme X[a]



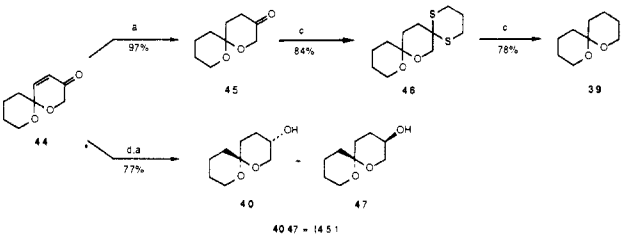
[a] (a) *t*-$BuMe_2SiCl$, imidazole, DMF, 99%; (b) *n*-BuLi, TMEDA, Et_2O; (c) Me_2CHCHO; (d) *m*-CPBA, CH_2Cl_2; (e) HF, MeCN; (f) 1:1:1 (w:w:w) HF/H_2O/MeCN.

Scheme XI[a]



[a] (a) Ac_2O, DMAP, Pyr; (b) $POCl_3$, DMF; (c) $NaBH_4$, NaOH; (d) *m*-CPBA, C_6H_6; (e) CSA, C_6H_6.

Scheme XII[a]



[a] (a) H_2, 1 atm, 5% Pd/C, EtOH; (b) $Zn(OTf)_2$, $HS(CH_2)_3SH$, CH_2Cl_2; (c) H_2, 1 atm, Ra-Ni, EtOH, Δ; (d) $NaBH_4$, $CeCl_3$, MeOH.

The key intermediate in the synthesis of pheromones **39** and **40** was spiroketal **44**, and the synthesis of **44** is outlined in Scheme XI. Acetylation of furan alcohol **7** and Vilsmeier–Haack formylation of the furan nucleus furnished aldehyde **42** in 94% yield. Reduction of the aldehyde with $NaBH_4$ in basic media with concomitant ester hydrolysis gave diol **43**. Oxidation of the furan with *m*-CPBA was followed by spiroketalization with camphorsulfonic acid in benzene to provide enone **44**.

Enone **44** was transformed into pheromones **39** and **40** in a straightforward manner. Catalytic reduction of the enone function of **44**, thioketal formation, and Raney nickel desulfurization afforded spiroketal **39** (Scheme XII).

The synthesis of pheromone **40** from enone **44** proceeded by carbonyl reduction with $NaBH_4/CeCl_3$ to furnish a mixture of allylic alcohols highly enriched in the equatorial alcohol isomer. Catalytic hydrogenation of the mixture of allylic alcohols furnished alcohol **40** contaminated by a trace of epimeric alcohol **47**. This strategy for the synthesis of alcohol **40** was highly stereoselective.

An advantage of this approach to the synthesis of the pheromone alcohol **40** was that acidic reaction conditions are avoided. Several of the previous syntheses of **40** were plagued by the propensity of **40** to undergo acid-catalyzed equilibration, yielding a mixture of 6,6-spiroketal and 6,5-spiroketal products (Scheme XIII).[7i]

Conclusion

It has been demonstrated that the oxidation of appropriately substituted furfurol derivatives afforded functionalized spiroketal systems in a highly stereoselective manner due to the interplay of conformational and electronic effects. The substances prepared in this study have been converted into spiroketals **9–11**, model systems for spiroketal moieties of the avermectin/milbemycin family of antibiotics, and pheromones of the olive fruit fly (**39** and **40**). The application of this methodology for the total synthesis of other natural products will be reported in due course.

Experimental Section

1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-(2-furyl)butane (7a). 4-(2-Furyl)butan-1-ol[22] (7) (3.00 g, 21.4 mmol) in DMF (5 mL) was added slowly to a 0 °C solution of *tert*-butyldimethylsilyl chloride (3.88 g, 25.7 mmol) and imidazole (3.65 g, 53.6 mmol) in DMF (10 mL). The reaction mixture was stirred at room temperature for 2 h. Water (50 mL) was added, the layers were partitioned, and the aqueous layer was extracted with hexane (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 2 in., silica; 1:1 hexane/EtOAc) afforded 5.20 g (99%) of silyl ether **7a** as an oil: IR (neat) 2940 (s), 2920 (s), 2840 (s), 1590 (w), 1230 (s), 1080 (s); ^1H NMR ($CDCl_3$) 0.06 (s, 6), 0.91 (s, 9), 1.64 (m, 4), 2.65 (t, 2, J = 7.2), 3.64 (t, 2, J = 6.1), 5.98 (m, 1), 6.26 (m, 1), 7.29 (m, 1); ^{13}C NMR ($CDCl_3$) -5.3, 18.3, 24.4, 26.0, 27.7, 32.3, 62.8, 104.6, 110.0, 140.7, 156.0; mass spectrum, *m/z* (relative intensity) 197 (M^+ - 57, 100), 179 (5), 169 (9), 155 (38), 105 (15), 81 (20), 75 (77), 73 (20); mass spectrum, *m/z* 197.0992 (M^+ - 57; calcd for $C_{10}H_{17}O_2Si$: 197.0997).

α-(Methylethyl)-5-[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]-2-furanmethanol (12). A solution of *n*-butyllithium (7.50 mL of 1.10 M, 8.25 mmol) was slowly added to a 0 °C solution of silyl ether **7a** (2.00 g, 7.9 mmol) and TMEDA (0.928 g, 8.0 mmol) in ether (50 mL). The reaction mixture was stirred at room temperature for 3 h. The resulting clear, yellow solution was cooled to -78 °C, and freshly distilled isobutyraldehyde (0.80 g, 11.1 mmol) in ether (25 mL) was added dropwise. When the addition was complete, the reaction mixture was allowed to warm to 0 °C and was stirred for 2 h. Saturated aqueous NH_4Cl (30 mL) was added, and the layers were separated. The aqueous layer was extracted with ether (3 × 30 mL), and the combined ether layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 7 in., silica; 10:1 hexane/EtOAc) afforded 2.11 g (82%) of furan alcohol **12** as an oil: IR (neat) 3400 (broad, m), 2940 (s), 2920 (s), 2840 (s), 1560 (m), 1250 (s), 1080 (s); ^1H NMR ($CDCl_3$) 0.06 (s, 6), 0.86 (d, 3, J = 6.8), 0.91 (s, 9), 1.03 (d, 3, J = 6.8), 1.66 (m, 4), 1.87 (broad s, 1), 2.10 (m, 1), 2.63 (t, 2, J = 7.1), 3.64 (t, 2, J = 6.1), 4.31 (d, 1, J = 7.0), 5.92 (d, 1, J = 3.0), 6.11 (d, 1, J = 3.0); mass spectrum, *m/z* (relative intensity) 308 (M^+ - 18, 40), 283 (63), 269 (39), 251 (32), 177 (100), 151 (52), 135 (82), 121 (64), 109 (60), 75 (96); mass spectrum, *m/z* 308.2171 (M^+ - 18; calcd for $C_{18}H_{32}O_2Si$: 308.2171).

***trans*-6-[4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]butyl]-6-hydroxy-2-(1-methylethyl)-2*H*-pyran-3(6*H*)-one (13).** 3-Chloroperbenzoic acid (*m*-CPBA, 80–85%, 1.26 g, ≈5.8 mmol) was added to a 0 °C solution containing furan alcohol **12** (1.76 g, 5.4 mmol) in CH_2Cl_2 (50 mL). After 1 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (25 mL), saturated aqueous $NaHSO_3$ (25 mL), and saturated aqueous $NaHCO_3$ (25 mL). The organic layer was then dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 6 in., silica; 4:1 hexane/EtOAc) gave 1.66 g (90%) of pyranone **13** as an oil: IR (CCl_4) 3580 (w), 3350 (broad, w), 2940 (s), 2840 (s), 1695 (vs), 1230 (s), 1080 (s); ^1H NMR ($CDCl_3$) 0.06 (s, 6), 0.86 (d, 3, J = 6.9), 0.90 (s, 9), 1.04 (d, 3, J = 6.9), 1.16 (s, 1), 1.32 (m, 2), 1.42 (m, 2), 1.60 (m, 2), 1.89 (m, 2), 2.45 (septet of doublets, 1, J = 6.9, 2.7), 3.66 (t, 2, J = 5.7), 4.37 (d, 1, J = 2.7), 6.05 (d, 1, J = 10.1), 6.80 (d, 1, J = 10.1); mass spectrum, *m/z* (relative intensity) 285 (M^+ - 57, 31), 270 (20), 243 (6), 211 (28), 193 (20), 185 (16), 138 (76), 109 (35), 75 (100); mass spectrum, *m/z* 285.1519 (M^+ - 57; calcd for $C_{14}H_{25}O_4Si$: 285.1522).

***trans*-2-(1-Methylethyl)-1,7-dioxaspiro[5.5]undec-4-en-3-one (14) and *cis*-2-(1-Methylethyl)-1,7-dioxaspiro[5.5]undec-4-en-3-one (15). Method A.** In a polyethylene flask, pyranone **13** (0.643 g, 1.88 mmol) was stirred with 20:1 (w/w) acetonitrile/HF (10 mL). The reaction was monitored by neutralizing aliquots of the reaction mixture with aqueous K_2CO_3. After 1 h, the reaction was quenched by careful addition of aqueous K_2CO_3. Ether (50 mL) was added and the layers were partitioned. The aqueous layer was extracted with ether (3 × 30 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (15-mm diameter, 4 in., silica; CH_2Cl_2) afforded 0.380 g (96%) of a 95:5 (150 °C, R_f = 6.56, 7.09) mixture of the spiroketals **14** and **15** as oils. Separation was effected by radial chromatography (2 mm, 1 L of hexane, 1 L of 100:1 hexane/EtOAc). **Spiroketal 14**: oil; IR (CCl_4) 2940 (s), 2860 (s), 1695 (s), 1460 (s), 1000 (s); ^1H NMR ($CDCl_3$) 0.87 (d, 3, J = 6.9), 1.11 (d, 3, J = 6.9), 1.70 (m, 4), 1.89 (m, 2), 2.47 (septet of doublets, 1, J = 6.9, 2.9), 3.78 (m, 2), 4.16 (d, 1, J = 2.9), 6.00 (d, 1, J = 10.1), 6.67 (d, 1, J = 10.1); ^{13}C NMR ($CDCl_3$) 15.9, 18.0, 19.3, 24.7, 28.4, 34.3, 62.5, 77.5, 92.7, 127.6, 148.1, 197.2; mass spectrum, *m/z* (relative intensity) 210 (M^+, 0.42), 167 (2), 138 (100), 109 (13), 95 (7), 82 (21), 55 (42); mass spectrum, *m/z* 210.1260 (M^+; calcd for $C_{12}H_{18}O_3$: 210.1256). **Spiroketal 15**: oil; IR (CCl_4) 2940 (s), 2870 (m), 1695 (vs), 1195 (s), 1015 (s); ^1H NMR ($CDCl_3$) 0.96 (d, 3, J = 6.9), 1.08 (d, 3, J = 6.9), 1.67 (m, 5), 1.98 (m, 1), 2.44 (septet of doublets, 1, J = 6.9, 3.6), 3.77 (m, 1), 3.89 (d, 1, J = 3.6), 4.12 (m, 1), 6.01 (d, 1, J = 10.3), 6.73 (d, 1, J = 10.3); ^{13}C NMR ($CDCl_3$) 16.7, 18.6, 19.3, 24.5, 29.6, 29.8, 61.8, 81.1, 94.7, 127.3, 150.2, 196.7; mass spectrum, *m/z* (relative intensity) 210 (M^+, 8), 167 (7), 154 (6), 138 (100), 127 (11), 109 (13), 99 (19), 82 (30), 55 (29).

Method B. A solution of *n*-butyllithium (61.1 mL of 2.47 M, 150.8 mmol) was added slowly to a 0 °C solution of 4-(2-furyl)butan-1-ol (7) (10.05 g, 71.8 mmol) and TMEDA (17.5 g, 150.8 mmol) in ether (400 mL). The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was cooled to -78 °C, and freshly distilled isobutyraldehyde (11.2 g, 155 mmol) in ether (10 mL) was added dropwise. When the addition was complete, the reaction mixture was allowed to

(22) Hands, A. R.; Mercer, A. J. H. *J. Chem. Soc. C* **1968**, 2448.

warm to 0 °C and was stirred for 2 h. Saturated aqueous NH_4Cl (100 mL) was added and the layers were separated. The aqueous layer was extracted with ether (3 × 100 mL), and the combined ether layers were dried ($MgSO_4$) and concentrated in vacuo. The crude furfurol derivative **16** was dissolved in CH_2Cl_2 (400 mL), the solution was cooled to 0 °C, and *m*-CPBA (80–85%, 23.3 g, ≈108 mmol) was added in five portions over 1 h. The reaction mixture was stirred for 24 h at room temperature and was then concentrated in vacuo. The crude white solid was dissolved in acetonitrile (100 mL) and transferred to a polyethylene flask where 12.0 mL of aqueous HF (53%) was added. The reaction mixture was stirred for 16 h. The reaction was quenched by the careful addition of aqueous K_2CO_3. Ether (100 mL) was added and the layers were partitioned, the aqueous layer was extracted with Et_2O (3 × 100 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (60-mm diameter, 7 in., silica; 2 L of hexane, 2 L of 15:1 hexane/EtOAc) afforded 12.72 g (84%) of a 95:5 (150 °C, R_t = 6.56, 7.09) mixture of the spiroketals **14** and **15** as oils.

Equilibration of Spiroketals 14 and 15. In a polyethylene flask, 15 mg of a 47:53 mixture of spiroketals **14** and **15** was stirred in 5 mL of 25:1 (w/w) acetonitrile/HF (5 mL) at room temperature for 2 h. The reaction mixture was quenched by careful addition of saturated aqueous K_2CO_3. The aqueous layer was extracted with ether (3 × 15 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Gas chromatographic analysis of the residue (14 mg, 94% recovery) indicated a 95:5 mixture of spiroketals **14** and **15**.

***trans*-3-Methylene-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-4-ene (17).** Spiroketal **14** (0.319 g, 1.5 mmol) in THF (10 mL) was added slowly to a solution of methyltriphenylphosphorane prepared from methyltriphenylphosphonium iodide (0.675 g, 1.67 mmol) and 2.00 mL of 0.84 M (1.68 mmol) *n*-butyllithium in THF (20 mL). The reaction mixture was stirred at room temperature for 10 h and then was concentrated in vacuo. Hexane/ether (10:1, 100 mL) was added and triphenylphosphine oxide was removed by vacuum filtration. The filtrate was concentrated in vacuo and the resulting oil was purified by flash chromatography (20-mm diameter, 6 in., silica; CH_2Cl_2), affording 220 mg (70%) of spiroketal **17** as an oil: IR (CCl_4) 3080 (w), 3040 (w), 2950 (s), 2940 (s), 2860 (m), 1600 (w); ^1H NMR ($CDCl_3$) 0.95 (d, 3, J = 6.8), 1.18 (d, 3, J = 6.8), 1.61 (m, 4), 1.89 (m, 2), 2.26 (septet of doublets, 1, J = 6.8, 2.5), 3.65 (m, 1), 3.87 (dt, 1, J = 7.0, 3.4), 4.33 (m, 1), 4.94 (s, 1), 5.00 (s, 1), 5.65 (d, 1, J = 9.8), 6.21 (d, 1, J = 9.8); mass spectrum, *m/z* (relative intensity) 208 (M^+, 27), 165 (100), 150 (12), 107 (32), 77 (7), 55 (11); mass spectrum, *m/z* 208.1451 (M^+; calcd for $C_{13}H_{20}O_2$: 208.1463).

***trans*-2-(1-Methylethyl)-1,7-dioxaspiro[5.5]undecan-3-one (20).** A solution of spiroketal **14** (500 mg, 2.38 mmol) and 5% Pd/C (75 mg) in ethanol (20 mL) was stirred under a hydrogen atmosphere for 4 h. Vacuum filtration through Celite, concentration in vacuo, and purification by flash chromatography (10-mm diameter, 1 in., silica; Et_2O) afforded 493 mg (97%) of spiroketal **20** as an oil: IR (CCl_4) 2940 (s), 2860 (s), 1720 (s), 990 (s); ^1H NMR ($CDCl_3$) 0.86 (d, 3, J = 6.9), 1.02 (d, 3, J = 6.9), 1.60 (m, 4), 1.80 (m, 2), 1.90 (m, 2), 2.30 (m, 3), 3.66 (m, 2), 3.80 (d, 1, J = 3.6); ^{13}C NMR ($CDCl_3$) 16.4, 18.9, 19.4, 25.1, 28.9, 34.7, 34.9, 61.7, 76.4, 78.7, 95.5, 211.1; mass spectrum, *m/z* (relative intensity) 212 (M^+, 4), 140 (16), 112 (100), 98 (17), 83 (13), 56 (26).

Dinitrophenylhydrazone of Spiroketal 20. 2,4-Dinitrophenylhydrazine (49 mg, 0.25 mmol) was added at room temperature to a solution of spiroketal **20** in ethanol (5 mL) and glacial acetic acid (0.3 mL). The reaction was stirred for 2 h at room temperature and then filtered to yield the crude product. Recrystallization from ethanol/water yielded 78 mg (80%) of the hydrazone as needles: mp 143–144 °C; IR (CCl_4) 3310 (s), 3095 (m), 2940 (s), 2860 (s), 1440 (s), 990 (s); ^1H NMR ($CDCl_3$) 1.02 (d, 3, J = 6.7), 1.16 (d, 3, J = 6.7), 1.60 (m, 5), 1.93 (m, 4), 2.57 (m, 3), 3.71 (m, 2), 4.19 (d, 1, J = 3.7), 7.92 (d, 1, J = 9.6), 8.32 (dd, 1, J = 9.6, 2.5); mass spectrum, *m/z* (relative intensity) 392 (M^+, 3.6), 349 (100), 331 (24), 321 (15), 166 (20), 151 (37), 138 (23), 111 (32), 82 (44), 55 (47). Anal. Calcd for $C_{18}H_{24}N_4O_6$: C, 55.09; H, 6.16. Found: C, 54.87; H, 6.22.

***trans*-3-Methylene-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecane (21).** Spiroketal **20** (500 mg, 2.4 mmol) in THF (10 mL) was added slowly to a solution of methyltriphenylphosphorane prepared from methyltriphenylphosphonium iodide (1.06 g, 2.6 mmol) and 3.30 mL of 0.803 M (2.6 mmol) *n*-butyllithium in THF (20 mL). The reaction mixture was stirred at room temperature for 8 h and then was concentrated in vacuo. Hexane/ether (10:1, 100 mL) was added and the resulting triphenylphosphine oxide was removed by vacuum filtration through celite. The filtrate was concentrated in vacuo, and the resulting oil was purified by flash chromatography (20-mm diameter, 7 in., silica; CH_2Cl_2), affording 354 mg (71%) of spiroketal **21** as an oil: IR (CCl_4) 3080 (s), 2930 (s), 2855 (s), 1645 (m), 1000 (s); ^1H NMR ($CDCl_3$) 1.01 (d, 3, J = 6.7), 1.05 (d, 3, J = 6.7), 1.65 (m, 8), 2.10 (m, 2), 2.50 (m, 1), 3.75 (m, 3), 4.75 (d, 1, J = 1.3), 4.86 (d, 1, J = 1.3); mass spectrum, *m/z* (relative intensity) 210 (M^+, 5), 182 (4), 167 (100), 149 (9), 139 (11), 109 (20), 98 (29), 83 (23), 55 (44).

(2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecane (18). Spiroketal **17** (118 mg, 0.57 mmol) and tris(triphenylphosphine)rhodium(I) chloride (10 mg) in benzene (3 mL) were stirred under a hydrogen atmosphere for 36 h. Concentration in vacuo and flash chromatography (10-mm diameter, 7 in., silica; CH_2Cl_2) afforded 104 mg (87%) of a 5.3:1 (150 °C, R_t = 4.71, 5.40) mixture of the spiroketals **18** and **11** as oils. **Spiroketal 18**: IR (CCl_4) 2940 (s), 2860 (s); ^1H NMR ($CDCl_3$) 0.83 (d, 3, J = 6.8), 0.89 (d, 3, J = 6.8), 1.05 (d, 3, J = 6.4), 1.55 (m, 9), 1.90 (m, 3), 3.22 (dd, 1, J = 10.1, 2.3), 3.63 (m, 2); ^{13}C NMR ($CDCl_3$) 10.6, 18.3, 18.8, 20.4, 25.5, 26.4, 27.5, 29.9, 30.2, 35.9, 60.2, 76.4, 95.4; mass spectrum, *m/z* (relative intensity) 212 (M^+, 2), 169 (5), 140 (30), 111 (10), 98 (100), 83 (13), 69 (6), 55 (17); mass spectrum, *m/z* 212.1793 (M^+; calcd for $C_{13}H_{24}O_2$: 212.1776).

***trans*-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-3-ene (19).** Spiroketal **17** (133 mg, 0.66 mmol) and 5% Pd/$BaSO_4$ (30 mg) in ethanol (3 mL) were stirred under a hydrogen atmosphere at −6 °C for 2 h. The reaction mixture was filtered through quantitative filter paper, washed with Et_2O (50 mL), and concentrated in vacuo. Column chromatography (10-mm diameter, 6 in., neutral alumina; 100 mL of hexane, 100 mL of 1:1 hexane/Et_2O) afforded 75 mg (53%) of spiroketal **19** as an oil: IR (CCl_4) 2930 (s), 2840 (s), 2800 (s); ^1H NMR ($CDCl_3$) 0.77 (d, 3, J = 6.8), 1.09 (d, 3, J = 6.8), 1.56 (m, 5), 1.61 (m, 3), 2.01 (m, 4), 3.68 (m, 2), 3.89 (m, 1), 5.40 (m, 1); mass spectrum, *m/z* (relative intensity) 210 (M^+, 14), 167 (100), 111 (30), 95 (38), 85 (40).

(2α,3α,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-4-en-3-ol (22) and (2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-4-en-3-ol (23). A solution of methyllithium (0.80 mL of 1.19 M, 0.95 mmol) was added slowly to a −55 °C solution of spiroketal **14** (194 mg, 0.92 mmol) in ether (20 mL). The reaction mixture was allowed to slowly warm to room temperature over 2 h, and saturated aqueous NH_4Cl was added until neutral pH was attained. The layers were separated and the aqueous layer was extracted with ether (3 × 15 mL). The combined ether layers were dried ($MgSO_4$) and concentrated in vacuo. Purification and separation of the resultin, 3.7:1 mixture of spiroketals **22** and **23** (150 °C, R_t = 7.25, 8.09) by flash chromatography (20-mm diameter, 7 in., silica; 4:1 hexane/EtOAc) afforded 198 mg (95%) of the spiroketals **22** and **23** as solids. **Spiroketal 22**: needles, recrystallized from MeOH/H_2O; mp 79–80 °C; IR (CCl_4) 3580 (m), 2925 (s), 2860 (s), 1050 (s), 970 (s); ^1H NMR ($CDCl_3$) 1.12 (d, 3, J = 6.8), 1.13 (d, 3, J = 6.8), 1.24 (s, 3), 1.65 (m, 5), 1.74 (s, 1), 1.96 (m, 1), 2.17 (septet of doublets, 1, J = 6.8, 3.8), 3.56 (d, 1, J = 3.8), 3.60 (m, 1), 3.90 (m, 1), 5.58 (d, 1, J = 9.9), 5.76 (d, 1, J = 9.9); ^{13}C NMR ($CDCl_3$) 17.9, 18.5, 23.3, 23.9, 25.1, 27.8, 35.3, 61.5, 67.7, 78.2, 93.7, 130.4, 136.1; mass spectrum, *m/z* (relative intensity) 226 (M^+, 0.16), 165 (8), 154 (100), 127 (16), 111 (53), 96 (22). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.78; H, 9.85. **Spiroketal 23**: needles, recrystallized from MeOH/H_2O; mp 79–80 °C; IR (CCl_4) 3590 (m), 3430 (broad, m), 2940 (s), 2845 (s), 1095 (s), 970 (s); ^1H NMR ($CDCl_3$) 1.10 (d, 3, J = 6.7), 1.11 (d, 3, J = 6.7), 1.19 (s, 3), 1.60 (m, 5), 1.93 (m, 2), 2.10 (s, 1), 3.30 (d, 1, J = 8.4), 3.60 (m, 1), 3.88 (m, 1), 5.47 (d, 1, J = 9.9), 5.67 (d, 1, J = 9.9); ^{13}C NMR ($CDCl_3$) 18.3, 20.5, 21.0, 25.1, 28.9, 35.2, 61.5, 70.0, 79.1, 93.7, 128.6, 138.1; mass spectrum, *m/z* (relative intensity) 226 (M^+, 1), 165 (7), 154 (100), 127 (8), 111 (49), 97 (18), 77 (30); mass spectrum, *m/z* 226.1573 (M^+; calcd for $C_{13}H_{22}O_3$: 226.1569).

***trans*-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-3-en-5-one (24).** PCC (187 mg, 0.87 mmol) was added at room temperature to a mixture of spiroketals **22** and **23** (**22**:**23**, 3.7:1, 49 mg, 0.22 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was stirred at room temperature for 12 h and Et_2O (125 mL) was added. The reaction mixture was vacuum filtered through Florosil and washed with Et_2O (125 mL). Concentration in vacuo followed by flash chromatography of the residue (20-mm diameter, 5 in., silica; 4:1 hexane/EtOAc) afforded 34 mg (70%) of spiroketal **24** as an oil: IR (CCl_4) 2950 (s), 2930 (s), 2860 (s), 1690 (s), 1630 (w), 1140 (s), 1010 (s); ^1H NMR ($CDCl_3$) 0.82 (d, 3, J = 6.8), 1.18 (d, 3, J = 6.8), 1.67 (m, 5), 1.91 (t, 3, J = 1.0), 2.18 (m, 2), 3.72 (m, 2), 4.22 (d, 1, J = 0.7), 5.93 (dd, 1, J = 2.0, 1.3); ^{13}C NMR ($CDCl_3$) 14.3 (q), 17.9 (t), 19.5 (q), 19.5 (q), 24.8 (t), 27.6 (t), 29.2 (d), 63.1 (t), 74.4 (d), 95.2 (s), 123.2 (d), 161.2 (s), 190.4 (s); mass spectrum, *m/z* (relative intensity) 224 (M^+, 0.34), 181 (2), 151 (2), 124 (39), 109 (100), 101 (8), 81 (8).

(2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-5-one (25). Spiroketal **24** (528 mg, 2.36 mmol) and 5% Pd/C (75 mg) in ethanol (25 mL) were stirred under a hydrogen atmosphere for 1.5 h. The reaction mixture was filtered, washed with Et_2O (50 mL), and concentrated in vacuo. Flash chromatography (30-mm diameter, 6 in.,

silica; 6:1 hexane/EtOAc) afforded 452 mg (85%) of spiroketal **25** as an oil: IR (CCl_4) 2950 (s), 2860 (s), 1735 (s), 1150 (s); ^1H NMR ($CDCl_3$) 0.87 (d, 3, J = 6.7), 0.92 (d, 3, J = 6.7), 1.12 (d, 3, J = 6.9), 1.62 (m, 4), 1.95 (m, 2), 2.12 (m, 1), 2.30 (dd, 1, J = 13.6, 4.5), 2.54 (dd, 1, J = 13.6, 12.2), 3.59 (dd, 1, J = 10.0, 2.4), 3.69 (m, 1), 3.83 (m, 1); ^{13}C NMR ($CDCl_3$) 14.2, 17.7, 18.1, 20.8, 25.0, 28.1, 28.5, 37.0, 43.4, 61.1, 77.2, 96.7, 204.6; mass spectrum, m/z (relative intensity) 226 (M^+, 1), 198 (7), 183 (3), 101 (100), 83 (15), 69 (8), 55 (19).

Toluenesulfonhydrazone of Spiroketal 25. p-Toluenesulfonhydrazide (439 mg, 2.36 mmol) was added at room temperature to a solution of spiroketal **25** (508 mg, 2.25 mmol) in THF (50 mL). The reaction mixture was stirred at room temperature for 15 h. Concentration in vacuo followed by crystallization from methanol/water afforded 460 mg (52%) of the hydrazone as plates: mp 137.0–137.5 °C; IR (Nujol) 3120 (m), 2910 (s), 2840 (s), 1590 (w), 1450 (s), 1340 (s), 1160 (s); ^1H NMR ($CDCl_3$) 0.78 (d, 3, J = 6.9), 0.85 (d, 3, J = 6.5), 1.05 (d, 3, J = 6.9), 1.48 (m, 3), 1.65 (m, 3), 1.89 (m, 3), 2.40 (s, 3), 2.62 (dd, 1, J = 14.0, 4.1), 3.37 (dd, 1, J = 10.2, 2.2), 3.49 (m, 1), 3.73 (m, 1), 7.34 (m, 2), 7.75 (m, 2). Anal. Calcd for $C_{20}H_{30}N_2O_4S$: C, 60.89; H, 7.66; N, 7.10. Found: C, 60.60; H, 7.76; N, 7.19.

(2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-4-ene (10). p-Toluenesulfonhydrazide (337 mg, 1.81 mmol) was added at room temperature to a solution of spiroketal **25** (390 mg, 1.73 mmol) in THF (10 mL). The reaction mixture was stirred at room temperature for 18 h, and then 2.12 mL of 2.44 M (5.18 mmol) n-butyllithium was added slowly. The reaction mixture was stirred for 1 h, water (10 mL) was added, and the reaction mixture was stirred for 0.25 h. Et_2O (25 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 25 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (20-mm diameter, 6 in., silica; 15:1 hexane/EtOAc) afforded 257 mg (71%) of spiroketal **10** as an oil: IR (neat) 2940 (s), 2860 (s), 1445 (m), 1340 (m), 990 (s); ^1H NMR ($CDCl_3$) 0.91 (d, 6, J = 7.1), 1.10 (d, 3, J = 6.9), 1.60 (m, 5), 1.93 (m, 2), 2.18 (m, 1), 3.33 (dd, 1, J = 9.9, 2.3), 3.60 (m, 1), 3.88 (m, 1), 5.54 (dd, 1, J = 9.9, 2.4), 5.66 (dd, 1, J = 9.9, 1.7); ^{13}C NMR ($CDCl_3$) 14.9, 16.6, 18.6, 21.1, 25.2, 28.6, 31.1, 35.2, 60.9, 76.8, 93.2, 129.4, 134.8; mass spectrum, m/z (relative intensity) 210 (M^+, 15), 167 (31), 158 (62), 138 (100), 127 (61), 101 (99), 82 (81), 71 (64); mass spectrum, m/z 210.1640 (M^+; calcd for $C_{13}H_{22}O_2$: 210.1620).

(2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecane (11). Method A. Spiroketal **10** (63 mg, 0.30 mmol) and tris(triphenylphosphine)rhodium(I) chloride (10 mg) in benzene (3 mL) were stirred under a hydrogen atmosphere for 6 h. Concentration in vacuo and microdistillation (0.4 mmHg, 63–67 °C) afforded 61 mg (96%) of spiroketal **11** as an oil: IR (CCl_4) 2940 (s), 2860 (s), 1160 (s), 1025 (s); ^1H NMR ($CDCl_3$) 0.80 (d, 3, J = 6.0), 0.85 (d, 3, J = 6.9), 1.05 (d, 3, J = 6.9), 1.47 (m, 10), 1.85 (m, 2), 3.13 (dd, 1, J = 9.2, 2.1), 3.56 (m, 2); ^{13}C NMR ($CDCl_3$) 14.2, 17.3, 18.9, 20.8, 25.6, 28.2, 28.5, 31.8, 36.1, 36.2, 60.2, 77.7, 94.9; mass spectrum, m/z (relative intensity) 212 (M^+, 2), 169 (4), 140 (25), 111 (8), 98 (100), 83 (111), 55 (26); mass spectrum, m/z 212.1785 (M^+; calcd for $C_{13}H_{24}O_2$: 212.1776). **Method B.** Spiroketal **27** (14.9 mg, 0.05 mmol) and W-2 Raney nickel (100 mg) in ethanol (15 mL) were refluxed under a hydrogen atmosphere for 24 h. The reaction mixture was filtered and washed with Et_2O (50 mL), and the residue was passed through silica (5 g) with Et_2O, affording 9.3 mg (89%) of spiroketal **11** as an oil.

(2α,3α,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undec-4-ene (26). p-Toluenesulfonhydrazide (332 mg, 1.79 mmol) was added at room temperature to a solution of spiroketal **24** (381 mg, 1.70 mmol) in THF (10 mL). The reaction mixture was stirred at room temperature for 28 h and then concentrated in vacuo. To the crude tosylhydrazone in $CHCl_3$ (25 mL) at 0 °C was slowly added 1.97 mL of 1.0 M (1.97 mmol) catecholborane. The reaction mixture was stirred for 3 h, $NaOAc{\cdot}3H_2O$ (694 mg, 5.1 mmol) was added, and the reaction mixture was refluxed for 2 h. Water (25 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (20-mm diameter, 6 in., silica; 8:1 hexane/EtOAc) furnished 26 mg (7%) of spiroketal **26** as an oil: IR (neat) 2940 (s), 2860 (s), 1200 (s), 990 (s); ^1H NMR ($CDCl_3$) 0.84 (d, 3, J = 6.6), 0.86 (d, 3, J = 6.9), 1.09 (d, 3, J = 6.6), 1.78 (m, 5), 1.90 (m, 2), 2.03 (m, 1), 3.41 (dd, 1, J = 10.2, 2.9), 3.59 (m, 1), 3.89 (m, 1), 5.51 (dd, 1, J = 9.9, 1.1), 5.91 (dd, 1, J = 9.9, 5.8); mass spectrum, m/z (relative intensity) 210 (M^+, 38), 167 (35), 152 (55), 138 (100), 111 (84), 98 (83), 82 (92), 71 (99).

Spiroketal 27. 1,2-Ethanedithiol (20 mg, 0.21 mmol) was added at room temperature to a solution of spiroketal **25** (39 mg, 0.17 mmol) and zinc triflate (75 mg, 0.21 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was refluxed for 21 h and then concentrated in vacuo. Flash chromatography (10-mm diameter, 6 in., silica; 20:1 hexane/EtOAc) afforded 33 mg (63%) of spiroketal **27** as an oil: IR (CCl_4) 2945 (s), 2855 (s), 1055 (s), 1025 (s); ^1H NMR ($CDCl_3$) 0.81 (d, 3, J = 6.4), 0.88 (d, 3, J = 6.9), 1.05 (d, 3, J = 6.9), 1.97 (m, 9), 2.39 (m, 1), 3.20 (m, 5), 3.62 (m, 2); ^{13}C NMR ($CDCl_3$) 14.2, 16.8, 19.2, 20.7, 24.8, 28.4, 29.2, 32.3, 39.0, 39.4, 46.7, 61.6, 77.4, 100.2, quaternary thioketal carbon not observed; mass spectrum, m/z (relative intensity) 302 (M^+, 5), 202 (3), 174 (19), 145 (5), 118 (100), 83 (7), 55 (15).

(1α,2β,4α,5β,6α)-5-Methyl-4-(1-methylethyl)spiro[3,7-dioxabicyclo-[4.1.0]heptane-2,2′-[2H]pyran] (28) and (1β,2β,4α,5β,6β)-5-Methyl-4-(1-methylethyl)spiro[3,7-dioxabicyclo[4.1.0]heptane-2,2′-[2H]pyran (29). m-CPBA (80–85%, 130 mg, 0.60 mmol) was added to a 0 °C solution containing spiroketal **10** (127 mg, 0.60 mmol) and Na_2HPO_4 (114 mg, 0.80 mmol) in 10 mL of CH_2Cl_2. After 12 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (10 mL), saturated aqueous $NaHSO_3$ (10 mL), and saturated aqueous $NaHCO_3$ (10 mL). The organic layer was then dried (Na_2SO_4) and concentrated in vacuo. Separation of the resulting 1:1 mixture of spiroketals **28** and **29** (185 °C, R_f = 6.94, 5.93) by flash chromatography (20-mm diameter, 6 in., silica; 4:1 hexane/EtOAc) gave 46 mg (33%) of **28** and 46 mg (33%) of **29** as oils. **Spiroketal 28:** IR (neat) 2940 (s), 2860 (s), 1450 (m), 1370 (m), 1010 (s); ^1H NMR ($CDCl_3$) 0.84 (d, 3, J = 6.9), 0.96 (d, 3, J = 7.3), 1.02 (d, 3, J = 6.9), 1.50 (m, 8), 2.80 (dd, 1, J = 3.9, 0.6), 2.96 (d, 1, J = 3.9), 3.13 (dd, 1, J = 10.2, 2.5), 3.60 (m, 1), 3.78 (m, 1); ^{13}C NMR ($CDCl_3$) 15.0, 15.9, 17.9, 21.2, 25.4, 29.1, 29.3, 32.3, 53.6, 56.8, 60.9, 74.8, 93.7; mass spectrum, m/z (relative intensity) 226 (M^+, 1), 183 (9), 154 (100), 125 (36), 111 (33), 101 (47), 98 (52), 83 (33). **Spiroketal 29:** IR (neat) 2940 (s), 2860 (s), 1450 (m), 1370 (m), 1010 (s); ^1H NMR ($CDCl_3$) 0.81 (d, 3, J = 6.9), 1.01 (d, 6, J = 6.9), 1.60 (m, 4), 1.80 (m, 4), 3.08 (d, 1, J = 4.0), 3.18 (dd, 1, J = 4.0, 1.6), 3.29 (dd, 1, J = 10.1, 2.1), 3.67 (m, 1), 3.85 (m, 1); ^{13}C NMR ($CDCl_3$) 13.6, 14.1, 18.3, 21.4, 25.3, 27.8, 31.5, 34.9, 57.1, 61.0, 72.2, 92.7; mass spectrum, m/z (relative intensity) 226 (M^+, 1), 183 (7), 154 (62), 125 (40), 111 (71), 101 (100), 83 (62).

(2α,3β,5α,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-5-ol (30). Spiroketal **28** (22 mg, 0.10 mmol) was stirred with 1.0 mL of 1.0 M (1.0 mmol) lithium triethylborohydride in THF at room temperature. After 12 h, 5% aqueous NaOH (10 mL), 3% H_2O_2 (5 mL), and Et_2O (20 mL) were added. The layers were separatedf and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by PLC (0.50 mm, 4:1 hexane/EtOAc) afforded 17 mg (76%) of spiroketal **30** as an oil: IR (CCl_4) 3590 (sharp, w), 2940 (s), 2860 (s), 1240 (s), 1200 (s), 1110 (s), 1070 (s), 1040 (s), 970 (s); ^1H NMR ($CDCl_3$) 0.81 (d, 3, J = 6.9), 0.90 (d, 3, J = 6.9), 1.07 (d, 3, J = 6.9), 1.64 (broad m, 11), 3.21 (m, 1), 3.41 (m, 1), 3.62 (m, 2); ^{13}C NMR ($CDCl_3$) 14.3, 17.0, 18.6, 20.6, 25.3, 25.5, 28.4, 31.7, 35.5, 60.0, 70.7, 96.3; mass spectrum, m/z (relative intensity) 229 (M^+ + 1, 4), 228 (M^+, 1), 211 (8), 193 (2), 167 (2), 144 (9), 114 (14), 101 (100), 83 (10); mass spectrum, m/z 228.1741 (M^+; calcd for $C_{13}H_{24}O_3$: 228.1725).

(2α,3β,5β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-5-ol (31). Method A. $NaBH_4$ (32 mg, 0.85 mmol) was added to a solution of spiroketal **25** (183 mg, 0.81 mmol) in methanol (10 mL) at room temperature. After 30 min, 3% aqueous NaOH (15 mL) and Et_2O (15 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (10-mm diameter, 6 in., silica; 6:1 hexane/EtOAc) afforded 175 mg (95%) of spiroketal **31** as an oil: IR (neat) 3570 (s), 3400 (broad, w), 2940 (s), 2860 (s); ^1H NMR ($CDCl_3$) 0.80 (d, 3, J = 6.4), 0.83 (d, 3, J = 6.8), 1.04 (d, 3, J = 6.8), 1.48 (m, 6), 1.84 (m, 5), 3.06 (dd, 1, J = 9.8, 2.2), 3.21 (m, 1), 3.64 (m, 2); ^{13}C NMR ($CDCl_3$) 13.9, 16.8, 18.3, 20.8, 25.2, 28.0, 30.7, 32.0, 37.1, 60.3, 72.1, 77.0, 96.0; mass spectrum, m/z (relative intensity) 228 (M^+, 3), 144 (9), 114 (6), 101 (100), 83 (10), 69 (9), 55 (18); mass spectrum, m/z 228.1707 (M^+; calcd for $C_{13}H_{24}O_3$: 228.1725).

Method B. Spiroketal **29** (18 mg, 0.08 mmol) was stirred with 1.0 mL of 1.0 M (1.0 mmol) lithium triethylborohydride in THF at room temperature. After 12 h, 5% aqueous NaOH (10 mL), 3% H_2O_2 (5 mL), and Et_2O (20 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by PLC (0.50 mm, 4:1 hexane/EtOAc) afforded 15 mg (83%) of spiroketal **31**.

(2α,3β,4α,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-4-ol (32) and (2α,3β,4β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-4-ol (9). Spiroketal **10** (85 mg, 0.40 mmol) was added to a solution of mercuric acetate (130 mg, 0.41 mmol) in water (1 mL) and THF (1 mL) at room temperature. After 12 h, 3 M NaOH (1 mL) was added followed by $NaBH_4$ (30 mg, 0.80 mmol) in 3 M NaOH (1

mL). The reaction mixture was stirred for 1 h, the resulting mercury was allowed to settle, and saturated aqueous NaCl (15 mL) and Et_2O (15 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification and separation of the resulting 1:1 mixture of alcohols (185 °C, R_f = 6.18, 6.43) by flash chromatography (10-mm diameter, 6 in., silica; 6:1 hexane/EtOAc) afforded 66 mg (72%) of spiroketals **32** and **9**. **Spiroketal 32**: low R_f, plates recrystallized from MeOH/H_2O; mp 84–85 °C; IR (Nujol) 3280 (broad, m), 2910 (s), 2850 (s), 1215 (s), 1175 (s), 1160 (s), 1000 (s); ^{1}H NMR ($CDCl_3$) 0.86 (d, 3, J = 6.9), 0.94 (d, 3, J = 6.5), 1.07 (d, 3, J = 6.9), 1.2 (m, 10), 1.97 (m, 2), 3.17 (dd, 1, J = 10.2, 2.2), 3.59 (m, 2); ^{13}C NMR ($CDCl_3$) 12.2, 14.0, 18.7, 20.9, 25.3, 28.2, 35.7, 40.7, 44.9, 60.3, 70.2, 75.9, 96.4; mass spectrum, m/z (relative intensity) 228 (M^+, 3), 185 (9), 167 (12), 156 (31), 127 (12), 113 (16), 98 (100), 84 (13), 69 (12). Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.39; H, 10.59. Found: C, 68.59; H, 11.00. **Spiroketal 9**: oil; IR (CCl_4) 3500 (sharp, m), 3400 (broad (w), 2920 (s), 2860 (s), 1170 (s), 1040 (s); ^{1}H NMR ($CDCl_3$) 0.84 (d, 3, J = 6.8), 0.98 (d, 3, J = 6.9), 1.06 (d, 3, J = 6.9), 1.50 (m, 8), 1.87 (m, 3), 3.42 (dd, 1, J = 10.7, 2.3), 3.70 (m, 3); ^{13}C NMR ($CDCl_3$) 13.7, 14.0, 18.3, 20.6, 25.1, 28.1, 35.5, 36.3, 41.5, 60.5, 70.3, 71.8, 97.3; mass spectrum, m/z (relative intensity) 228 (M^+, 8), 210 (10), 192 (45), 167 (48), 138 (86), 121 (48), 109 (66), 98 (100), 83 (62), 69 (61); mass spectrum, m/z 228.1736 (M^+; calcd for $C_{13}H_{24}O_3$: 228.1725).

(2α,3β,6β)-3-Methyl-2-(1-methylethyl)-1,7-dioxaspiro[5.5]undecan-4-one (33). From 32. PCC (194 mg, 0.90 mmol) was added at room temperature to a solution of spiroketal **32** (102 mg, 0.45 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 7 h and Et_2O (25 mL) was added. The reaction mixture was vacuum filtered through Florosil and washed with Et_2O (25 mL). Concentration in vacuo followed by flash chromatography of the residue (10-mm diameter, 6 in., silica; 4:1 hexane/EtOAc) afforded 90 mg (89%) of spiroketal **33** as an oil.

From 9. Employing the same procedure as used for the oxidation of **32**, spiroketal **9** (21 mg, 0.09 mmol) also afforded 19 mg (91%) of spiroketal **33** as an oil: IR (neat) 2930 (s), 2860 (s), 1712 (s), 1190 (s), 1070 (s); ^{1}H NMR ($CDCl_3$) 0.94 (d, 3, J = 6.5), 0.95 (d, 3, J = 6.9), 1.10 (d, 3, J = 6.9), 1.53 (m, 6), 1.80 (m, 2), 1.91 (septet of doublets, 1, J = 6.9, 2.2), 2.36 (dq, 1, J = 10.4, 6.5), 2.39 (s, 2), 3.42 (dd, 1, J = 10.4, 2.2), 3.56 (m, 2); ^{13}C NMR ($CDCl_3$) 8.8, 13.9, 18.8, 20.6, 24.7, 29.0, 35.2, 46.9, 52.1, 60.9, 77.6, 98.8, 208.1; mass spectrum, m/z (relative intensity) 226 (M^+, 1), 183 (5), 154 (24), 126 (38), 111 (15), 98 (100), 83 (19); mass spectrum, m/z 226.1590 (M^+; calcd for $C_{13}H_{22}O_3$: 226.1569).

3-(2-Furyl)propan-1-ol (8). 3-(2-Furyl)acrolein (10.0 g, 82 mmol) in MeOH (50 mL) was added over 0.5 h to a solution of $NaBH_4$ (3.12 g, 82 mmol) in MeOH (200 mL) and 5% aqueous NaOH (10 mL). The reaction mixture was stirred at room temperature for 1 h, and then acetone (10 mL) was added. The reaction mixture was concentrated in vacuo, aqueous 10% acetic acid (100 mL) and Et_2O (100 mL) were added, and the layers were separated. The organic layer was washed with saturated aqueous NaCl (50 mL), dried ($MgSO_4$), and concentrated in vacuo. MeOH (100 mL) and 20% $Pd(OH)_2/C$ (125 mg) were added, and the reaction mixture was stirred under a hydrogen atmosphere for 12 h. Vacuum filtration through celite, concentration in vacuo, and fractional distillation of the resulting oil (43–44 °C (0.2 mmHg)) afforded 5.10 g (49%) of alcohol **8** as an oil: IR (neat) 3340 (broad, s), 2930 (s), 2860 (s), 1595 (m), 1030 (s); ^{1}H NMR ($CDCl_3$) 1.87 (m, 2), 2.70 (t, 2, J = 7.5), 3.06 (s, 1), 3.63 (t, 2, J = 6.4), 5.98 (dd, 1, J = 3.0, 0.7), 6.26 (dd, 1, J = 3.0, 2.0), 7.28 (m, 1).

1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-(2-furyl)propane (34). A solution of 3-(2-furyl)-propanol (**8**) (3.45 g, 27.4 mmol) in DMF (10 mL) was added slowly to a 0 °C solution of *tert*-butyldimethylsilyl chloride (5.06 g, 33.6 mmol) and imidazole (4.83 g, 70.9 mmol) in DMF (10 mL). The reaction mixture was stirred at room temperature for 2 h. Water (50 mL) was added, the layers were partitioned, and the aqueous layer was extracted with hexane (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification of the oily residue by flash chromatography (45-mm diameter, 2 in., silica; 1:1 hexane/EtOAc) afforded 6.56 g (99%) of silyl ether **34** as an oil: IR (neat) 2940 (s), 2920 (s), 2880 (s), 2845 (s), 1590 (m), 1240 (s), 1080 (s); ^{1}H NMR ($CDCl_3$) 0.06 (s, 6), 0.91 (s, 9), 1.88 (m, 2), 2.70 (t, 2, J = 7.5), 3.66 (t, 2, J = 6.2), 5.98 (m, 1), 6.27 (dd, 1, J = 3.1, 1.9), 7.29 (dd, 1, J = 1.9, 0.7); ^{13}C NMR ($CDCl_3$) −5.4, 18.3, 24.4, 25.9, 31.1, 62.2, 104.7, 110.0, 140.7, 156.0; mass spectrum, m/z (relative intensity): 225 (M^+ − 15, 3), 183 (100), 155 (60), 108 (10), 75 (34); mass spectrum, m/z 225.1319 (M^+ − 15; calcd for $C_{12}H_{21}O_2Si$: 225.1310).

α-(Methylethyl)-5-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propyl]-2-furanmethanol (35). A solution of *n*-butyllithium (35.6 mL of a 0.843 M solution, 30 mmol) was slowly added to a 0 °C solution of silyl ether **34** (6.40 g, 26.7 mmol) and TMEDA (3.13 g, 27 mmol) in ether (50 mL). The reaction mixture was stirred at room temperature for 3 h. The resulting clear yellow solution was cooled to −78 °C, and freshly distilled isobutyraldehyde (2.88 g, 40 mmol) in ether (25 mL) was added dropwise. When addition was complete, the reaction mixture was allowed to warm to 0 °C and was stirred for 2 h. Saturated aqueous NH_4Cl (30 mL) was added and the layers were separated. The aqueous layer was extracted with ether (3 × 50 mL), and the combined ether layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 7 in., silica; 10:1 hexane/EtOAc) afforded 6.99 g (84%) of furan alcohol **35** as an oil: IR (neat) 3400 (broad, m), 2940 (s), 2920 (s), 2880 (s), 2845 (s), 1555 (m), 1240 (s), 1080 (s); ^{1}H NMR ($CDCl_3$) 0.06 (s, 6), 0.86 (d, 3, J = 6.8), 0.91 (s, 9), 1.03 (d, 3, J = 6.8), 1.85 (m, 3), 2.10 (m, 1), 2.68 (t, 2, J = 7.5), 3.66 (t, 2, J = 6.8), 4.32 (m, 1), 5.93 (d, 1, J = 3.0), 6.12 (d, 1, J = 3.0); mass spectrum, m/z (relative intensity): 312 (M^+, 6), 269 (25), 255 (55), 237 (17), 163 (100), 137 (24), 75 (12); mass spectrum, m/z 312.2108 (M^+; calcd for $C_{17}H_{32}O_3Si$: 312.2120).

***trans*-6-[3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]propyl]-6-hydroxy-2-(1-methylethyl)-2*H*-pyran-3(6*H*)-one (36).** *m*-CPBA (80–85%, 0.80 g, ≈3.7 mmol) was added to a 0 °C solution containing furan alcohol **35** (1.15 g, 3.5 mmol) in CH_2Cl_2 (50 mL). After 3 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (25 mL), saturated aqueous $NaHSO_3$ (25 mL), and saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 6 in., silica; 4:1 hexane/EtOAc) afforded 1.06 g (88%) of pyranone **36** as a single isomer of undefined stereochemistry as an oil: IR (neat) 3500–3300 (broad, w), 2940 (s), 2920 (s), 2840 (s), 1690 (vs), 1245 (s), 1070 (s), 1010 (s); ^{1}H NMR ($CDCl_3$) 0.06 (s, 6), 0.79 (d, 3, J = 6.9), 0.87 (s, 9), 0.99 (d, 3, J = 6.9), 1.79 (m, 2), 2.07 (m, 2), 2.40 (septet of doublets, 1, J = 6.9, 2.8), 3.59 (dt, 1, J = 9.1, 2.9), 3.78 (m, 1), 4.34 (d, 1, J = 2.8), 5.70 (s, 1), 5.93 (d, 1, J = 10.1), 6.74 (d, 1, J = 10.1); mass spectrum, m/z (relative intensity) 328 (M^+, 0.27), 271 (21), 256 (43), 199 (38), 179 (100), 124 (77), 75 (92); mass spectrum, m/z 271.1378 (M^+ − 57; calcd for $C_{13}H_{23}O_4Si$: 271.1366).

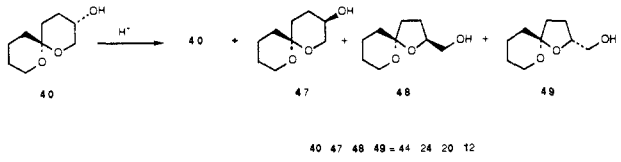
***trans*-7-(1-Methylethyl)-1,6-dioxaspiro[4.5]dec-9-en-8-one (37) and *cis*-7-(1-Methylethyl)-1,6-dioxaspiro[4.5]dec-9-en-8-one (38).** Employing the acetonitrile/HF protocol for the preparation of spiroketal **14**, pyranone **36** (0.840 g, 2.5 mmol) was converted into 490 mg (97%) of an 87:13 (150 °C, R_f = 4.88, 5.56) mixture of **37** and **38**. The mixture was separated by radial chromatography (2 mm, 1 L of hexane, 1 L of 100:1 hexane/EtOAc). **Spiroketal 37**: oil; IR (neat) 2950 (s), 2860 (s), 1690 (vs), 1625 (w), 1010 (s); ^{1}H NMR ($CDCl_3$) 0.83 (d, 3, J = 6.9), 1.00 (d, 3, J = 6.9), 1.99 (m, 2), 2.21 (m, 2), 2.39 (septet of doublets, 1, J = 6.9, 2.9), 3.98 (m, 2), 4.24 (d, 1, J = 2.9), 6.03 (d, 1, J = 10.1), 6.71 (d, 1, J = 10.1); ^{13}C NMR (C_6D_6) 16.3, 19.1, 24.8, 28.6, 38.1, 68.2, 78.9, 102.5, 128.5, 146.6, 196.5; mass spectrum, m/z (relative intensity) 167 (M^+ − 29, 2), 149 (5), 124 (100), 96 (46), 82 (8), 68 (19), 55 (47), 28 (62); mass spectrum, m/z 196.1099 (M^+; calcd for $C_{11}H_{16}O_3$: 196.1100). **Spiroketal 38**: oil; IR (CCl_4) 2945 (s), 2920 (s), 2860 (m), 1690 (s), 1060 (s), 1010 (s); ^{1}H NMR ($CDCl_3$) 0.94 (t, 6, J = 6.7), 1.83 (m, 1), 2.02 (m, 2), 2.29 (m, 2), 3.76 (d, 1, J = 6.1), 4.00 (m, 1), 4.16 (m, 1), 6.03 (d, 1, J = 10.1), 6.71 (d, 1, J = 10.1); ^{13}C NMR (C_6D_6) 18.2, 19.0, 24.5, 30.6, 35.8, 68.9, 83.5, 103.3, 128.5, 147.8, 195.5; mass spectrum, m/z (relative intensity) 196 (M^+, 2), 153 (6), 124 (100), 96 (41), 82 (9), 68 (17), 55 (47); mass spectrum, m/z 196.1116 (M^+; calcd for $C_{11}H_{16}O_3$: 196.1100).

Equilibration of Spiroketals 37 and 38. Using the acetonitrile/HF procedure for the equilibration of spiroketals **14** and **15**, 38 mg of a 53:47 mixture of spiroketals **37** and **38** was equilibrated to yield 34 mg (89%) of an 87:13 mixture of spiroketals **37** and **38**. Using the same method, 92 mg of pure **37** was equilibrated to afford 88 mg (96%) of an 87:13 mixture of spiroketals **37** and **38**.

Dinitrophenylhydrazone of Spiroketal 37. Spiroketal **37** (220 mg, 1.12 mmol) and 5% Pd/C (25 mg) in ethanol (10 mL) were stirred under a hydrogen atmosphere for 4 h. Vacuum filtration through Celite, concentration in vacuo, and purification by flash chromatography (10-mm diameter, 1 in., silica; Et_2O) afforded 200 mg, (90%) of the ketone as an oil: IR (CCl_4) 2945 (s), 2860 (s), 1720 (s), 1000 (s); ^{1}H NMR ($CDCl_3$) 0.85 (d, 3, J = 6.8), 0.97 (d, 3, J = 6.9), 2.2 (m, 9), 3.94 (m, 3); mass spectrum, m/z (relative intensity) 198 (M^+, 7), 155 (3), 126 (12), 98 (100), 84 (19), 56 (28).

2,4-Dinitrophenylhydrazine (50 mg, 0.25 mmol) was added at room temperature to a solution of the above ketone (50 mg, 0.25 mmol) in ethanol (2 mL) and glacial acetic acid (0.3 mL). The reaction mixture was stirred for 2 h at room temperature and then filtered to yield the crude product. Recrystallization from ethanol/water yielded 80 mg (84%) of the hydrazone as needles: mp 139–140 °C; IR (CCl_4) 3320 (m), 3100 (w), 2950 (s), 2860 (s), 1610 (s); ^{1}H NMR ($CDCl_3$) 0.97 (d,

Scheme XIII



3, J = 6.7), 1.07 (d, 3, J = 6.7), 1.25 (s, 1), 1.79 (m, 2), 2.10 (m, 4), 2.45 (m, 1), 2.66 (m, 1), 3.70 (m, 1), 3.95 (m, 2), 4.26 (d, 1, J = 4.0), 7.92 (d, 1, j = 9.4), 8.32 (dd, 1, J = 9.4, 2.5), 9.14 (d, 1, J = 2.5), mass spectrum, m/z relative intensity) 378 (M^+, 3.6), 335 (100), 307 (17), 97 (66), 82 (35), 55 (37). Anal. Calcd for $C_{17}H_{22}O_6N_4$: C, 53.96; H, 5.86. Found: C, 53.79; H, 5.90.

4-(2-Furyl)butyl 1-Acetate (41). Acetic anhydride (2.45 g, 24 mmol) and 4-(dimethylamino)pyridine (0.50 g, 4 mmol) were added to a 0 °C solution of 4-(2-furyl)butan-1-ol (**7**) (2.77 g, 19.8 mmol) in pyridine (3 mL). The reaction mixture was stirred at room temperature for 8 h and then concentrated in vacuo. Saturated aqueous $CuSO_4$ (50 mL) and ether (50 mL) were added, the layers were partitioned, and the organic layer was washed with saturated aqueous $CuSO_4$ (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 2 in., silica; 8:1 hexane/EtOAc) afforded 3.45 g (96%) of acetate **41** as an oil: IR (neat) 2940 (s), 2860 (s), 1735 (s), 1230 (s); ^{1}H NMR ($CDCl_3$) 1.69 (m, 4), 2.04 (s, 3), 2.66 (t, 2, J = 6.8), 4.08 (t, 2, J = 6.2), 5.99 (dd, 1, J = 3.1, 0.7), 6.27 (dd, 1, J = 3.1, 1.8), 7.29 (dd, 1, J = 1.8, 0.7); ^{13}C NMR ($CDCl_3$) 20.8, 24.4, 27.4, 28.0, 64.1, 104.9, 110.0, 140.8, 155.6, 170.9; mass spectrum, m/z (relative intensity) 182 (M^+, 28), 122 (15), 94 (100), 81 (46), 53 (11), 43 (34); mass spectrum, m/z 182.0940 (M^+; calcd for $C_{10}H_{14}O_3$: 182.0943).

5-(4-Acetoxybutyl)-2-furaldehyde (42). Phosphorus oxychloride (1.51 g, 9.9 mmol) and CH_2Cl_2 (5 mL) were added slowly to DMF (0.73 g, 10.0 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h and furan acetate **41** (1.50 g, 8.2 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After addition was complete, the reaction mixture was allowed to warm to room temperature and was stirred for 3 h. Saturated aqueous Na_2CO_3 (30 mL) and CH_2Cl_2 (30 mL) were added and the layers were separated. The organic layer was washed with saturated aqueous NaCl (30 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography (30-mm diameter, 5 in., silica; 2:1 hexane/EtOAc) afforded 1.45 g (84%) of furan aldehyde **42** as an oil: IR (neat) 2950 (s), 2740 (m), 2700 (w), 1735 (s), 1675 (s), 1225 (s), 1005 (s); ^{1}H NMR ($CDCl_3$) 1.74 (m, 4), 2.06 (s, 3), 2.78 (t, 2, J = 6.9), 4.09 (t, 2, J = 6.3), 6.27 (d, 1, J = 3.5), 7.18 (d, 1, J = 3.5), 9.53 (s, 1); ^{13}C NMR ($CDCl_3$) 20.8, 24.0, 27.9, 28.0, 63.7, 108.7, 123.1, 151.9, 163.0, 170.9, 176.8; mass spectrum, m/z (relative intensity) 210 (M^+, 37), 182 (9), 168 (74), 150 (15), 122 (100), 109 (30), 94 (45), 81 (29), 53 (22); mass spectrum, m/z 210.0872 (M^+; calcd for $C_{11}H_{14}O_4$: 210.0892).

5-(4-Hydroxybutyl)-2-furanmethanol (43). Furan aldehyde **42** in MeOH (50 mL) was added slowly to a solution of $NaBH_4$ (0.43 g, 11.3 mmol) and 5% aqueous NaOH (5 mL) in MeOH (50 mL). The reaction mixture was stirred for 6 h at room temperature, and 5% aqueous HOAc was added until the solution was slightly acidic by litmus. The reaction mixture was concentrated in vacuo, and ether (50 mL) and water (50 mL) were added. The layers were separated and the aqueous layer was extracted with ether (3 × 25 mL). The combined organic layers were then dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (45-mm diameter, 6 in., silica; 1:1 hexane/EtOAc) gave 1.66 g (86%) of furan diol **43** as an oil: IR (CCl_4) 3325 (broad, s), 2930 (s), 2860 (s), 1560 (m), 1040 (s), 990 (s); ^{1}H NMR ($CDCl_3$) 1.57 (m, 4), 2.62 (t, 2, J = 7.0), 2.71 (s, 2), 3.59 (t, 2, J = 6.3), 4.50 (s, 2), 5.91 (d, 1, J = 3.1), 6.14 (d, 1, J = 3.1); ^{13}C NMR ($CDCl_3$) 24.2, 27.7, 32.0, 57.4, 62.4, 105.6, 108.4, 152.3, 156.2; mass spectrum, m/z (relative intensity) 170 (M^+, 11), 168 (35), 152 (100), 137 (58), 121 (67), 107 (86), 95 (80), 81 (52); mass spectrum, m/z 170.0953 (M^+; calcd for $C_9H_{14}O_3$: 170.0943).

1,7-Dioxaspiro[5.5]undec-4-en-3-one (44). *m*-CPBA (80–85%, 231 mg, 1.1 mmol) was added to a 10 °C solution of furan diol **43** (173 mg, 1.0 mmol) in benzene (10 mL). The reaction mixture was stirred for 2 h at room temperature, and 10-camphorsulfonic acid (232 mg, 1 mmol) was added. The reaction mixture was stirred for 15 min and concentrated in vacuo. Ether (50 mL) and water (50 mL) were added, the layers were separated, and the aqueous layer was washed with ether (3 × 25 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (20-mm diameter, 6 in., silica; 6:1 hexane/EtOAc) afforded 106 mg (62%) of spiroketal **44** as an oil: IR (CCl_4) 2940 (s), 2860 (s), 1690 (s), 1640 (w), 1060 (s), 1030 (s), 980 (s); ^{1}H NMR ($CDCl_3$) 1.75 (m, 6), 3.77 (m, 2), 4.07 (d, 1, J = 16.8), 4.37 (d, 1, J = 16.8), 6.03 (dd, 1, J = 10.3, 0.5), 6.71 (d, 1, J = 10.3); ^{13}C NMR ($CDCl_3$) 17.8, 24.5, 33.8, 62.6, 65.8, 92.9, 127.0, 149.0, 195.2; mass spectrum, m/z (relative intensity) 168 (M^+, 4), 138 (57), 123 (5), 113 (20), 95 (6), 80 (21); mass spectrum, m/z 168.0786 (M^+; calcd for $C_9H_{12}O_3$: 168.0786).

1,7-Dioxaspiro[5.5]undecan-3-one (45). A solution of spiroketal **44** (439 mg, 2.61 mmol) in methanol (10 mL) was added to a prereduced solution of 5% Pd/C (50 mg) and Na_2HPO_4 (50 mg) in methanol (5 mL) under a hydrogen atmosphere. The reaction mixture was stirred for 2 h. Vacuum filtration through Celite, concentration in vacuo, and purification by flash chromatography (20-mm diameter, 6 in., silica; 6:1 hexane/EtOAc) afforded 429 mg (97%) of spiroketal **45** as an oil: IR (CCl_4) 2940 (s), 2860 (s), 1730 (s), 1060 (s), 1030 (s); ^{1}H NMR ($CDCl_3$) 1.52 (m, 4), 1.73 (m, 2), 1.96 (m, 2), 2.31 (m, 1), 2.55 (m, 1), 3.61 (m, 2), 3.84 (dd, 1, J = 16.7, 1.1), 3.99 (d, 1, J = 16.7); ^{13}C NMR ($CDCl_3$) 18.6, 24.8, 33.7, 34.2, 34.4, 61.8, 67.3, 95.2, 208.6; mass spectrum, m/z (relative intensity) 170 (M^+, 6), 140 (26), 112 (100), 98 (16), 83 (16); mass spectrum, m/z 170.0947 (M^+; calcd for $C_9H_{14}O_3$: 170.0943).

Spiroketal 46. 1,2-Ethanedithiol (214 mg, 1.98 mmol) was added at room temperature to a solution of spiroketal **45** (281 mg, 1.65 mmol) and zinc triflate (720 mg, 1.98 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was refluxed for 16 h and concentrated in vacuo. Flash chromatography of the residue (20-mm diameter, 6 in., silica; 6:1 hexane/EtOAc) followed by recrystallization from hexane at −5 °C afforded 346 mg (85%) of spiroketal **46** as prisms: mp 94–95 °C; IR (CCl_4) 2910 (s), 2860 (s), 1160 (s), 1075 (s), 1040 (s); ^{1}H NMR (C_6D_6) 1.28 (m, 4), 1.60 (m, 2), 1.86 (m, 2), 2.02 (m, 1), 2.65 (m, 1), 2.72 (d, 4, J = 1.3), 3.47 (m, 2), 3.77 (d, 1, J = 11.0), 4.09 (d, 1, J = 11.0); ^{13}C NMR (C_6D_6) 18.9, 25.5, 35.1, 35.5, 36.5, 38.2, 38.3, 60.6, 66.1, 70.1, 94.4; mass spectrum, m/z (relative intensity) 246 (M^+, 6), 216 (52), 188 (53), 131 (13), 118 (100), 98 (32). Anal. Calcd for $C_{11}H_{18}O_2S_2$: C, 53.62; H, 7.36. Found: C, 53.80; H, 7.60.

1,7-Dioxaspiro[5.5]undecane (39). Spiroketal **46** (123 mg, 0.50 mmol) and W-2 Raney nickel (500 mg) in ethanol (15 mL) were refluxed under a hydrogen atmosphere for 36 h. The reaction mixture was filtered, water (100 mL) and pentane (50 mL) were added, and the layers were separated. The aqueous layer was extracted with pentane (3 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo at 0 °C. Purification by flash chromatography (10-mm diameter, 6 in., silica; 100 mL of pentane, 200 mL of 100:1 pentane/Et_2O) afforded 61 mg (78%) of spiroketal **39** as an oil: IR (neat) 2950 (s), 2880 (s), 1470 (w), 1455 (m), 1440 (m), 1385 (m), 1370 (m), 1290 (m), 1255 (m), 1230 (m), 1205 (m), 1180 (m), 1110 (m), 1095 (s), 1065 (s), 1040 (s), 990 (s), 930 (m), 910 (m), 875 (s), 795 (s); ^{1}H NMR (C_6D_6) 1.30 (m, 8), 1.64 (m, 2), 1.93 (m, 2), 3.60 (m, 4); ^{13}C NMR (C_6D_6) 19.1, 25.8, 36.2, 60.2, 94.9.

***cis*-1,7-Dioxaspiro[5.5]undecan-3-ol (40) and *trans*-1,7-Dioxaspiro[5.5]undecan-3-ol (47).** $NaBH_4$ (71 mg, 1.88 mmol) was added to a solution of spiroketal **44** (315 mg, 1.88 mmol) and $CeCl_3 \cdot 8H_2O$ (735 mg, 1.88 mmol) in methanol (10 mL) at room temperature. The reaction mixture was stirred for 30 min and then 2% aqueous NaOH (25 mL) and EtOAc (25 mL) were added. The layers were separated, the aqueous layer was extracted with EtOAc (3 × 25 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The resulting oil was dissolved in MeOH (5 mL) and then added to a prereduced solution of 5% Pd/C (40 mg) and Na_2HPO_4 (100 mg) in MeOH (10 mL) under a hydrogen atmosphere. The reaction mixture was stirred for 4 h. Vacuum filtration through Celite, concentration in vacuo, and purification by flash chromatography (20-mm diameter, 6 in., silica; 3:2 hexane/EtOAc) of the resulting 14.5:1 mixture of spiroketals **40** and **47** (150 °C, R_f = 6.66, 6.23) afforded 229 mg (71%) of **40** and 20 mg (6%) of **47** (contaminated with **40**) as oils. **Spiroketal 40**: IR (neat) 3400 (broad, s), 2940 (s), 2860 (s), 1220 (s), 1170 (s), 1090 (s), 1050 (s), 1020 (s), 1000 (s), 970 (s) 880 (s); ^{1}H NMR (C_6D_6) 1.2–2.2 (m, 11), 3.60 (m, 5); ^{13}C NMR (C_6D_6) 19.1, 25.5, 28.6, 35.0, 35.2, 60.4, 65.0, 66.3, 94.4; mass spectrum, m/z (relative intensity) 172 (M^+, 5), 142 (13), 117 (13), 98 (100). **Spiroketal 47**: ^{13}C NMR (C_6D_6) partial data, recorded as a 1:3 mixture with **40**; 18.8, 25.7, 30.2, 35.5, 60.7, 64.5, 64.8, 95.2.

Acknowledgment. We thank the Public Health Service, National Institutes of Health (Grant AI 23688) for generous financial support. Support by the National Science Foundation (Grant CHE-84-02155) for purchase of the X-ray diffractometer/computer system is gratefully acknowledged.

Supplementary Material Available: General experimental procedures, description of X-ray crystallographic analyses, tables of atomic coordinates, and temperature factors for the tosylhydrazone of ketone **25** and alcohol **32** (10 pages). Ordering information is given on any current masthead page.