α-Bromo Spiroketals: Stereochemistry and Elimination Reactions

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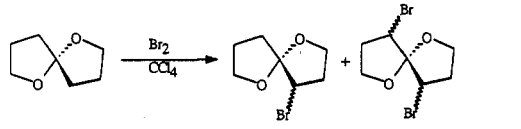
The simple spiroketals, 1,6-dioxaspiro[4.4]nonane (**2**), 1,6-dioxaspiro[4.5]decane (**5**), 1,7-dioxaspiro-[5.5]undecane (**6**), and (*E*,*E*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (**7**), have been brominated by bromine in carbon tetrachloride/calcium carbonate or acetic acid, and a number of mono-, di-, and tribromo derivatives have been characterized. The relative stereochemistries have been established by correlated ^1H and ^{13}C NMR spectroscopy and X-ray crystal structure determinations. Dehydrobromination with potassium *tert*-butoxide in either dimethyl sulfoxide or tetrahydrofuran is facile for the axial monobromides, although both axial and equatorial bromides derived from 1,6-dioxaspiro[4.5]decane (**5**) and 1,7-dioxaspiro[5.5]undecane (**6**) dehydrobrominate to provide 1,6-dioxaspiro[4.5]dec-9-ene (**35**) and 1,7-dioxaspiro[5.5]undec-4-ene (**26**), respectively. Hydration of these readily acquired alkenes furnishes the corresponding 9- and 4-ols, respectively, with the latter being components of the rectal glandular secretion of *Bactrocera oleae* (olive fly), *Bactrocera cacuminatus*, and *Bactrocera distincta*. These studies indicate that α-bromination of suitable spiroketals may be a viable later step in the synthesis of α-bromine-containing spiroketal metabolites such as obtusin and neoobtusin.

Introduction

In contrast to the wide range of methods reported for the assembly of the spiroketal moiety, reactions of the intact system have been less developed.[1] Given that under the appropriate conditions the general spiroketal (**1**) will be in equilibrium with a monocyclic enol or enol ether equivalent, reactions and equilibrations[2] at the α-carbon atom become possible (eq 1).

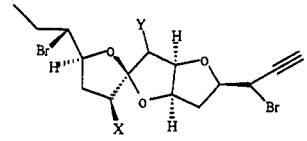
(1) (1)

A significant study of this type described the bromination of the steroidal sapogenin system by Marker and Rohrmann,[3] and subsequently other studies of steroidal spiroketals were reported. Most of this data has been summarized by Kutney.[4] Bromination of simple spiroketals has been restricted to 1,6-dioxaspiro[4.4]nonane (**2**), and Trška and Dědek[5] isolated the 4-bromo- and 4,9-dibromo derivatives, but no stereochemical information was available (eq 2).



(2) (2)

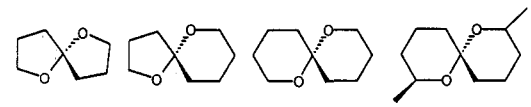
Our interest in the α-bromo derivatives of relatively simple spiroketals was kindled by two considerations: (a) the easy introduction and manipulation of bromine α to the spirocarbon would permit access to functionalized spiroketals and in particular to olefinic derivatives (by dehydrobromination) which in principle could furnish regioisomeric alcohols, diols, and allylic oxidation products, etc.[6] and (b) the recent characterization[7] of α-bromo derivatives of the 1,6-dioxaspiro[4.4]nonane system as marine metabolites, e.g., the cooccurring obtusin (**3**) and neoobtusin (**4**) suggested that α-bromination of a suitable spiroketal may be a viable later step in the total synthesis of these systems.



(3) X = Br, Y = H

(4) X = H, Y = Br

For these reasons we have conducted a study of the bromination of the spiroketals below and characterized a number of mono-, di-, and tribromo derivatives and established their relative stereochemistries. Dehydrobromination has also been studied and in several cases can be managed to provide the corresponding olefinic spiroketals, some of which have been converted to alcohols.



(2) (5) (6) (7)

(1) For an overview see: Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617.

(2) (a) Evans, D. A.; Sacks, C. E.; Whitney, R. A.; Mandel, N. G. *Tetrahedron Lett.* **1978**, 727. (b) Nakahara, Y.; Fujita, A.; Beppa, K.; Ogawa, T. *Tetrahedron* **1986**, *42*, 6465.

(3) Marker, R. E.; Rohrmann, E. *J. Am. Chem. Soc.* **1939**, *61*, 846.

(4) Kutney, J. P.; Cretney, W.; Pettit, G. R.; Knight, J. C. *Tetrahedron* **1964**, *20*, 1999. For recent studies of bromination of ketals see: Giordano, C.; Coppi, L. *J. Org. Chem.* **1992**, *57*, 2765.

(5) Trška, P.; Dědek, V. *Collect. Czech. Chem. Commun.* **1970**, *35*, 661 and references cited therein.

(6) In this connection see: (a) Brimble, M. A.; Edmonds, M. K.; Williams, G. M. *Tetrahedron Lett.* **1990**, *31*, 7509. (b) Brimble, M. A.; Nairu, M. R.; Wu, Y. *Tetrahedron Lett.* **1991**, *32*, 4049.

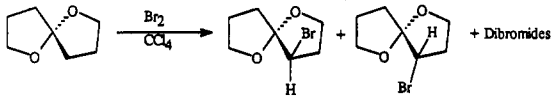
(7) (a) Howard, B. M.; Fenical, W.; Arnold, E. V.; Clardy, J. *Tetrahedron Lett.* **1979**, 2841. (b) Gonzalez, A. G.; Martinl, J. D.; Norte, M.; Perez, R.; Rivera, P.; Rvano, J. Z.; Rodnguez, M. L.; Fayos, J.; Perales, A. *Tetrahedron Lett.* **1983**, *24*, 4143. (c) Caccamese, S.; Toscano, R. M. *Gazz. Chimica Ital.* **1986**, *116*, 177.

0022-3263/93/1958-2501$04.00/0

Results and Discussion

Bromination of spiroketals **2**, **5**, **6**, and **7** was conducted by adding the appropriate amount of bromine dissolved in CCl_4 to a rapidly stirred solution of the spiroketal in CCl_4 (at ca. 20 °C) in which was suspended an excess of fine $CaCO_3$. Several brominations were conducted using bromine in acetic acid, but this procedure had no advantages. The isomeric bromides were generally separable by HPLC, with the monobromides being oils and several of the di- and tribromides being crystalline.

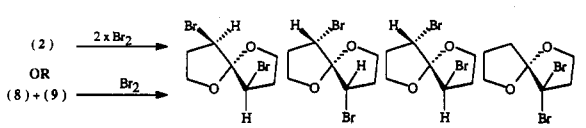
Treatment of spiroketal **2** with 1 molar equiv of bromine provided two monobromo derivatives (69:25) on the basis of GC–MS examination and ca. 6% of a dibromide mixture (eq 3).



(2) (8) (69%) (9) (25%) ....(3)

The separated bromides retained the spiroketal structure on the basis of ^{13}C NMR signals at 116.37 ppm (major isomer) and 112.20 ppm (minor isomer), mass spectral behavior, and IR spectra which exhibited strong ether C–O absorption in the 1000–1100 cm^{-1} region, but no carbonyl bands. Correlated ^1H and ^{13}C NMR spectra required the monobromides to be the epimeric 4-bromo derivatives **8** (E-isomer) and **9** (*Z*-isomer).[29] The ^1H NMR signal for >C*H*Br in the major isomer was a clean doublet (δ 4.25, J = 5.25 Hz) but was a doublet of doublets (δ 3.62, J = 10.8 and 8.4 Hz) in the minor isomer. Consideration of likely conformations (Dreiding models) indicated that only in the trans-isomer **8** was one of the vicinal H-3 unlikely to couple with H-4 (90° dihedral angle). On this basis the major isomer was assigned as **8** and the minor as **9**, and this conclusion was confirmed when a crystalline dibromide was characterized by ^1H NMR and X-ray diffraction methods. The complete assignment of the ^{13}C NMR spectra of **8** and **9** enabled substituent effects to be calculated for the two bromine orientations as in **8** and **9**, so that chemical shifts for the various 4,9-dibromo isomers could then be estimated, assuming additivity of chemical shifts.

Treatment of **2** with 2 equiv of bromine, or the purified mixture of **8** (65%) and **9** (25%) with 1 equiv of bromine, furnished a mixture of isomeric dibromides which were separated by HPLC. The proportions were 60:17:13:10. On one occasion, it was possible to isolate low levels of a tribromide shown by HRMS, NMR, and IR spectra to be 1,3,7-tribromoheptan-4-one,[8] which presumably results from bromination of the corresponding α-bromo ketodiol.



(E,E) (60%) (10) (Z,Z) (17%) (11) (Z,E) (13%) (12) (10%) (13) (4)

The major component (60%) was crystalline (mp 102–103 °C) and exhibited four ^{13}C NMR signals, as did the next most abundant isomer (17%). Consequently, these

(8) We are grateful to Dr. J. K. McLeod, Research School of Chemistry, Australian National University, for the high-resolution mass spectral measurements on this compound.

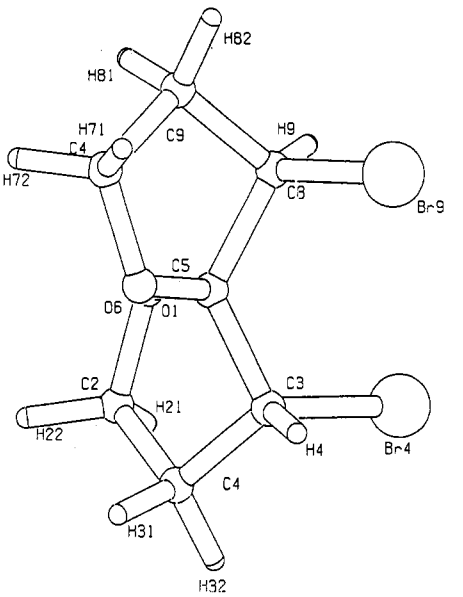
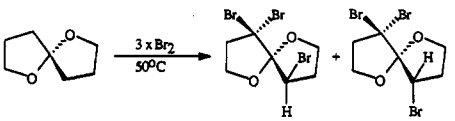


Figure 1. PLUTON plot of one molecule of **10**. Selected mean bond lengths (Å): Br(4)–C(4), 1.957; (9)–C(9), 1.986; O(1)–C(2), 1.42; O(1)–C(5), 1.426; O(6)–C(5), 1.388; O(6)–C(7), 1.40; C(2)–C(3); 1.52; C(3)–C(4), 1.51; C(4)–C(5), 1.51; C(5)–C(9), 1.55; C(7)–C(8), 1.55; C(8)–C(9), 1.52. Selected mean bond angles (deg): C(2)–O(1)–C(5), 109.4; C(1)–C(2)–C(3), 106.5; C(2)–C(3)–C(4), 103.7; Br(4)–C(4)–C(3), 110.3; C(3)–C(4)–C(5), 101.2; O(1)–C(5)–O(6), 110.9; O(1)–C(5)–C(4), 104.6; O(1)–C(5)–C(9), 103.7; C(4)–C(5)–C(9), 125.5; Br(4)–C(4)–C(5), 109.8.

were the *E,E* and the *Z,Z* isomers, which were distinguished by the multiplicity of the >C*H*Br resonances, with that for the major isomer being a doublet at δ 4.28 (J = 4.9 Hz) and for the other isomer being a doublet of doublets at δ 3.94 (J = 11.2 and 8.5 Hz). These values are similar to those discussed above for the monobromides and led to the assignments shown in eq 4 for **10** and **11**. The ^{13}C NMR chemical shifts strongly support these assignments, and there is good agreement between the calculated (based on the data for **8** and **9**) and observed shifts for **10–13**. The isomer in 13% abundance was unsymmetrical (seven ^{13}C NMR signals), and other NMR data required structure **12**. The minor isomer (10%) was also unsymmetrical (seven ^{13}C NMR signals) but lacked >C*H*Br absorption in the ^1H NMR spectrum. The ^{13}C NMR signal at δ 67.19 was shown to be quaternary, and the chemical shift required the *gem*-dibromo arrangement as in **13**. An interesting feature is that both >C*H*Br signals of **12** are apparent triplets (2 × 8.1 Hz and 2 × 6.4 Hz) despite the presence of *E*- and *Z*-rings, requiring that the conformational features are different from isolated *E*- and *Z*-rings as in **8** and **9**.

The X-ray structure[30] of the crystalline isomer, concluded above to be **10**, was obtained and confirmed this conclusion. A PLUTON drawing is shown in Figure 1, and this structure confirms the self-consistency of ^1H and ^{13}C NMR data for **8**, **9**, **10**, and **11**.

Bromination of **2** with 3-equiv of bromine at 50 °C provided the two tribromides (GC–MS) (60:40) as shown in eq 5.



(2) (14) (E) (40%) (15) (Z) (60%) (5)

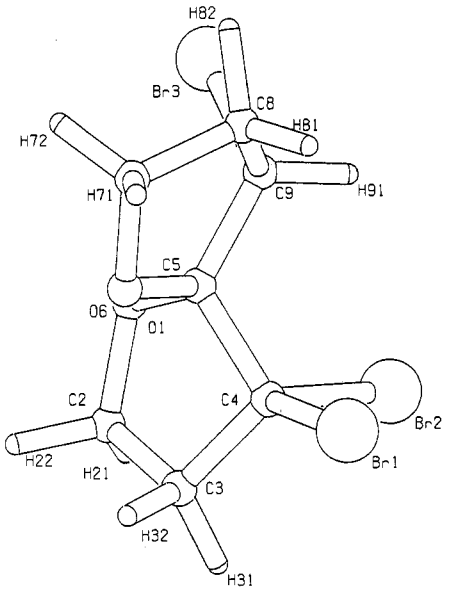
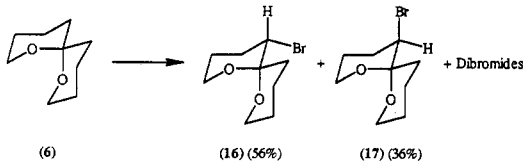


Figure 2. PLUTON plot of one molecule of **15**. Selected mean bond lengths (Å): Br(1)–C(4), 2.015; Br(2)–C(4), 1.948; Br(3)–C(9), 1.901; O(1)–C(2), 1.43; O(1)–C(5), 1.433; O(6)–C(5), 1.41; O(6)–C(7), 1.45; C(2)–C(3), 1.49; C(3)–C(4), 1.50; C(4)–C(5), 1.52; C(5)–C(9), 1.50; C(7)–C(8), 1.48; C(8)–C(9), 1.50. Selected mean bond angles (deg): C(2)–O(1)–C(5), 110.3; C(5)–O(6)–C(7), 108.7; O(1)–C(2)–C(3), 106.2; C(2)–C(3)–C(4), 102.9; Br(1)–C(4)–Br(2), 104.7; Br(1)–C(4)–C(3), 114.8; Br(1)–C(4)–C(5), 113.2; Br(2)–C(4)–C(3), 111.5; Br(2)–C(4)–C(5), 110.7; C(3)–C(4)–C(5), 102.2; O(1)–C(5)–C(6), 108.2; O(1)–C(5)–C(4), 100.4; O(1)–C(5)–C(9), 112.5; O(6)–C(5)–C(4), 107.5; O(6)–C(5)–C(9), 108.6; C(4)–C(5)–C(9), 118.9; O(6)–C(7)–C(8), 106.0; C(7)–C(8)–C(9), 104.0; Br(3)–C(9)–C(5), 115.6; Br(3)–C(9)–C(8), 108.9; C(5)–C(9)–C(8), 103.9.

The minor oily isomer showed >C*H*Br as a doublet (δ 4.28, J = 5.2 Hz) indicating the *E*-isomer, whereas the major crystalline isomer (mp 73–74 °C) showed >C*H*Br as a doublet of doublets (pseudo triplet) at δ 4.56 (2 × 9.3 Hz). Both showed ^{13}C NMR signals in the δ 63–65 range for carbon bearing two bromines, and the X-ray crystal structure[30] of the major isomer confirmed the *Z*-geometry as in **15** (Figure 2).

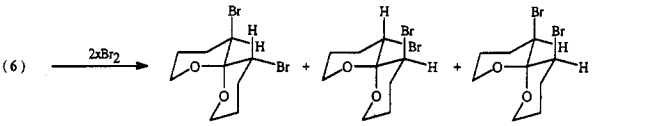
Bromination of 1,7-dioxaspiro[5.5]undecane (**6**) in the described way provided two monobromides (56:36) and a dibromide mixture (~8%). The monobromides were separated and the >C*H*Br ^{1}H NMR patterns established that the major isomer was the equatorial bromide **16** (>C*H*Br, δ 3.80, dd, J = 12.46 and 4.46 Hz) and the minor the axial isomer **17** (>C*H*Br, δ 3.97, J = 2.68, 2.93 Hz) as shown in eq 6.



(6) (16) (56%) (17) (36%) (6)

Full ^{1}H and ^{13}C NMR assignments are presented in Table I. IR bands for the C–Br stretching vibration are assigned at 744 cm^{-1} for **16** and 694 cm^{-1} for **17**, such values being consistent with equatorial and axial C–Br bonds, respectively.[9] However, treatment of axial bromide **17** with trifluoroacetic acid in toluene provided an epimeric mixture of **16** and **17** almost identical with that obtained by direct bromination of **6**, as shown in eq 6. Thus, the product distribution reported herein for the direct brominations of the spiroketals is thermodynamically regulated.

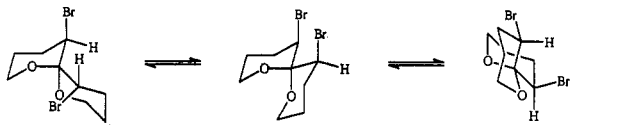
Treatment of spiroketal **6** with ca. 2 equiv of bromine led to a dibromide mixture (eq 7). Two of the dibromides



(18) (22%) (19) (68%) (20) (10%) (7)

each exhibited five ^{13}C NMR signals, and these were the symmetrical diaxial (**18**) and diequatorial (**19**) isomers, whereas the isomer exhibiting nine signals was assigned as the axial–equatorial isomer **20**. The preliminary X-ray crystal structure determination of **19** confirms the arrangement shown.[10]

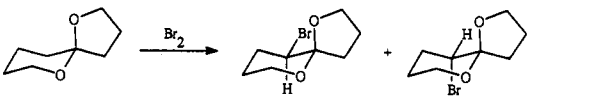
Dibromide **20**, in the conformation shown with maximized anomeric stabilization,[1] has a 1,3-diaxial type of bromo–bromo interaction. Relief would require one chair reversal which would reduce the favorable anomeric effects from two to one (eq 8).



(20) (8)

This conformational inhomogeneity is indicated by the coupling constants for H-11 (7.10 and 3.4 Hz) and H-5 (4.20 Hz) which are smaller and greate, respectively, than would have been expected if **20** were very dominant. This is also indicated by comparison of the calculated and observed ^{13}C NMR chemical shifts, particularly at positions where γ-effects of axial and equatorial bromine are operative.[11]

Bromination of 1,6-dioxaspiro[4.5]decane (**5**) was conducted to determine ring selectivity in bromination. Reaction with 1 molar equiv of bromine led to two monobromo isomers (GC–MS), and consideration of the >C*H*Br coupling patterns in the ^{1}H NMR spectra suggested axial and equatorial bromo groups in the six-membered ring (eq 9). This was confirmed by elimination



(5) (21) (22) (9)

reactions (vide infra) to provide 1,6-dioxaspiro[4.5]dec-9-ene. This ring selectivity may be traced to the highly preferential cleavage of the axial C–O bond of the five-membered ring in the electrophile-induced spiroketal

(9) Barton, D. H. R.; Page, J. E.; Shoppee, C. W. *J. Chem. soc.* **1956**, 331. Equatorial carbon–bromine linkages for 2- and 3-bromosteroids are reported in the ranges 754–708 and 708–704 cm^{-1}, respectively, and the corresponding axial isomers at about 662 and 692–591 cm^{-1}, respectively.

(10) Structure determination by Dr. C. H. L. Kennard and Mr. K. Byriel of the Molecular Structural Unit of the Department of Chemistry, The University of Queensland.

(11) See, for example: Wehrli, F. W.; Wirthlin, F. *Interpretation of Carbon-13 NMR Spectra*; Heyden; London, 1976; p 45.

Table I. Characterization of Bromo Spiroketals

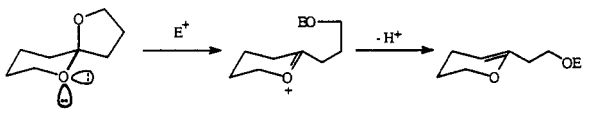
compd	MS/microanalysis	^{13}C NMR (C_6D_6, δ)	^{1}H NMR (C_6D_6, δ, J in Hz)
8[a,b]	$C_7H_{11}O_2{}^{81}Br$ requires 207.9923, found 207.9931. $C_7H_{11}O_2{}^{79}Br$ requires 205.9942, found 205.9944	24.9 (C8), 34.4 (C9), 35.2 (C3), 53.5 (C4), 65.5 (C2), 69.0 (C7), 116.4 (C5)	1.65–2.09 (2 H, m, 2 × H8), 2.15–2.77 (4 H, m, 2 × H9, 2 × H3), 3.84 (1 H, td, J = 15.5, 8.4, H2), 4.25 (1 H, d, J = 5.25, H4)
9[a,b]	$C_7H_{11}O_2{}^{81}Br$ requires 207.9923, found 207.9909. $C_7H_{11}O_2{}^{79}Br$ requires 205.9942, found 205.9947	24.9 (C8), 32.1 (C9), 33.4 (C3), 48.7 (C4), 64.8 (C2), 68.9 (C7), 112.2 (C5)	1.48–1.76 (2 H, m, 2 × H8), 1.78–1.93 (3 H, m, 2 × H9, H3), 2.23–2.31 (1 H, m, H3), 3.35–3.37 (1 H, m, H2), 3.62 (1 H, dd, J = 10.8, 8.4, H4), 3.68–3.73 (2 H, m, H7, H2), 3.84 (1 H, td, J = 13, 5.2, H7)
10[c] (mp 102–103 °C)	$C_7H_{10}O_2{}^{81}Br_2$ requires 287.9009, found 287.8996. $C_7H_{10}O_2{}^{81,79}Br_2$ requires 285.9028, found 285.9033.	35.1 (C3, 8), 53.1 (C4,9) 67.5 (C2, 7), 117.9 (C5)	1.71–1.76 (2 H, dd, J = 6.6, 13.9, 1 × H3, 1 × H8), 2.32–2.41 (2 H, m, 1 × H3), 3.74–3.79 (2 H, m, H2), 3.95–4.00 (2 H, m, H2, H7), 4.28 (2 H, d, J = 4.9, H4, H9)
11[c]	$C_7H_{10}O_2{}^{81}Br_2$ requires 287.9009, found 287.9010. $C_7H_{10}O_2{}^{81,79}Br_2$ requires 285.9028, found 285.9018. Anal. Calcd for $C_7H_{10}Br_2$: C, 29.4; H, 3.5. Found: C, 28.7; H, 3.4.	33.7 (C3,8), 45.2 (C4,9), 65.8 (C2,7), 109.4 (C5)	1.77–1.85 (2 H, m, H3, H8), 2.08–2.19 (2 H, m, H3, H8), 3.30–3.36 (2 H, m, H2, H7), 3.60–3.65 (2 H, m, H2, H7), 3.94 (2 H, dd, J = 11.2, 8.5, H4, H9)
12[c]	$C_7H_{10}O_2{}^{81}Br_2$ requires 287.9009, found 287.9011. $C_7H_{10}O_2{}^{81,79}Br_2$ requires 285.9028, found 285.9026.	35.3 (C3), 36.1 (C8), 49.1 (C4), 50.7 (C9), 65.6 (C2), 66.5 (C7), 112.6 (C5)	1.77–2.15 (4 H, m, 2 × H3, 2 × H8), 3.20 (1 H, dt, J = 8.3, 2 × 7.3, H2), 3.53–3.65 (2 H, m, H2, H7), 3.74–3.79 (1 H, m, H7), 3.92 (1 H, dd, J = 2 × 6.4, H9), 4.32 (1 H, dd, J = 2 × 8.1, H4)
13	$C_7H_{10}O_2{}^{81}Br_2$ requires 287.9009, found 287.9022. $C_7H_{10}O_2{}^{81,79}Br_2$ requires 285.9028, found 285.9028. Anal. Calcd for $C_7H_{10}O_2Br_2$: C, 29.4; H, 3.5. Found: C, 29.8; H, 3.7.	25.4 (C8), 33.0 (C9), 46.1 (C3), 64.5 (C2), 67.2 (C4), 70.7 (C7), 116.6 (C5)	1.46–1.83 (2 H, m, 2 × H8), 2.26–2.54 (3 H, m, 2 × H9, H3), 2.96–3.04 (1 H, m, H3), 3.64–3.83 (3 H, m, 2 × H2, H7), 3.94–3.99 (H1, m, H7)
14	$C_7H_9O_2{}^{81}Br_3$ requires 367.8095, found 367.8131 $C_7H_9O_2{}^{81,79,79}Br_3$ requires 363.8134, found 363.8144. Anal. Calcd for $C_7H_9O_2Br_3$: C, 23.2; H, 2.5. Found: C, 23.3; H, 2.5.	35.9 (C8), 49.0 (C3), 51.7 (C9), 61.7 (C4), 64.9 (C2), 68.7 (C7), 114.1 (C5)	1.74–2.94 (4 H, m, 2 × H3, 2 × H8), 3.39 (1 H, ddd, J = 9.5, 7.9, 1.5, H2), 3.58 (1 H, ddd, J = 7.9, 6.5, 9.5, H2), 3.77 (1 H, ddd, J = 9.0, 8.0, 1.3, H7), 4.13 (1 H, dddd, J = 10.4, 8.0, 6.2, 0.55, H7), 4.28 (1 H, d, J = 5.2, H9)
15 (mp 73–74 °C)	$C_7H_9O_2{}^{81}Br_3$ requires 367.8095, found 367.8115. $C_7H_9O_2{}^{81,79,79}Br_3$ requires 363.8134, found 363.8144. Anal. Calcd for $C_7H_9O_2{}^{79}Br_3$: C, 23.2; H, 2.5. Found: C, 23.1; H, 2.5.	37.9 (C8), 46.5 (C3), 47.0 (C9), 65.2 (C4), 65.7 (C2), 67.4 (C7), 113.0 (C5)	2.03–2.12 (2 H, m, 2 × H8), 2.39 (1 H, ddd, J = 13.6, 6.7, 2.2 H3), 2.78 (1 H, dt, J = 13.6, 2 × 9.0, H3), 3.42 (1 H, dt, J = 8.3, 2 × 7.0, H7), 3.55 (1 H, td, J = 2 × 9.0, 2.2, H2), 3.68–3.77 (2 H, m, H2, H7), 4.56 (1 H, dd, J = 7.3, H9)
16[a]	$C_9H_{15}O_2{}^{79}Br$ requires 234.0255, found 234.0257.	18.3 (C10), 24.6 (C9), 28.0 (C3), 30.4 (C4), 32.1 (C11), 55.2 (C5), 59.4 (C8), 61.0 (C2), 95.9 (C6)	1.36–1.61 (5 H, m, H3, H10, 2 × H9, H11eq), 1.67–1.79 (2 H, m, H3, H10), 2.0–2.05 (1 H, m, H4eq), 2.08 (1 H, td, J = 2 × 13.2, 4.9, H11ax), 2.28 (1 H, qd, J = 3 × 12.6, 4.3 H4ax), 3.24–3.69 (4 H, m, 2 × H2, 2 × H8), 3.80 (1 H, dd, J = 12.6, 4.6, H5ax)
17[a]	$C_9H_{15}O_2{}^{81}Br$ requires 236.0235, found 236.0243. $C_9H_{15}O_2{}^{79}Br$ requires 234.0255, found 234.0251. Anal. Calcd for $C_9H_{15}O_2Br$: C, 45.9; H, 6.38. Found: C, 48.8; H, 6.6.	18.8 (C10); 19.8 (C3), 24.6 (C9), 28.0 (C4), 34.9 (C11); 55.4 (C5), 60.0 (C2); 61.4 (C8), 95.2 (C6)	1.26 (1 H, td, J = 2 × 13.4, 4.6, H11ax), 1.30–1.35 (1 H, m, H3eq); 1.40–1.58 (3 H, m, 2x, H9, H10eq) 1.67–1.77 (1 H, m, H10ax), 1.83–1.89 (1 H, m, H4eq), 2.04–2.16 (2 H, m, H11eq, H3ax); 2.43–2.52 (1 H, m, H4ax), 3.65–3.60 (3 H, m, 2 × H8, H2eq), 3.75–3.65 (1 H, m, H2ax), 3.97 (1 H, t, J = 2.9, 2.7, H5eq)
18	$C_9H_{14}O_2{}^{81}Br_2$ requires 315.9321, found 315.9317. $C_9H_{14}O_2{}^{81,79}Br$ requires 313.9341, found 313.9344.	19.6 (C3, C9), 27.8 (C4, C10), 54.1 (C5, C11), 60.9 (C2, C8), 95.4 (C6)	0.73–0.76 (1 H, m, H3eq), 1.59–1.66 (1 H, m, H4eq), 1.99–2.02 (1 H, qdd, J = 3 × 13.0, 5.6, 5.4, H3ax), 2.11–2.20 (1 H, m, H4ax), 3.25 (1 H, td, J = 2 × 13.0, 2.9, H2ax), 3.24–3.44 (1 H, m, H2eq), 4.45 (1 H, t, J = 3.17, 2.4, H5eq)
19	$C_9H_{14}O_2{}^{81}Br_2$ requires 315.9321, found 315.9312, $C_9H_{14}O_2{}^{81,79}Br_2$ requires 313.9341, found 313.9344.	27.5 (C3, C9), 30.4 (C4, C10), 50.9 (C5, C11), 60.2 (C2, C8), 96.5 (C6)	0.42–0.93 (2 H, m, H3eq, H9eq), 1.32 (2 H, qdd, J = 3 × 12.7, 5.6, 4.0, H3ax, H9ax), 1.75–1.80 (2 H, m, H4eq, H10eq), 2.19 (2 H, qd, J = 3 × 12.7, 4.2, H4ax, H10ax), 3.21–3.30 (4 H, m, 2 × H2, 2 × H8), 4.55 (2 H, dd, J = 12.7, 4.6, H5ax, H11ax)
20	$C_9H_{14}O_2{}^{81}Br_2$ requires 315.9321, found 315.9321, $C_9H_{14}O_2{}^{79,81}Br_2$ requires 313.9341, found 313.9341.	20.8 (C3), 22.3 (C9), 28.3 (C4), 29.3 (C10), 50.6 (C5), 53.6 (C11), 60.3 (C2), 61.8 (C8), 95.4 (C6)	0.80–0.95 (2 H, m, H3, H9), 1.57–1.68 (2 H, m, H9, H10), 1.81–1.93 (4 H, m, H10, H3, 2 × H4), 2.91–2.97 (1 H, m, H8ax), 3.43–3.51 (2 H, m, H2eq, H8eq), 3.70 (1 H, dt, J = 2 × 15.4, 3.9, H2ax), 4.27 (1 H, dd, J = 2 × 4.2, H5), 4.68 (1 H, dd, J = 7.1, 3.5, H11)
21	$C_8H_{13}O_2{}^{81}Br$ requires 222.0079, found 222.0061 $C_8H_{13}O_2{}^{79}Br$ requires 220.0099, found 220.0099.	24.7 (C3), 28.3 (C8), 32.3 (C9), 36.5 (C4), 53.2 (C10), 60.6 (C7), 68.9 (C2), 106.4 (C5)	0.99–1.04 (1 H, m, H8), 1.34 (1 H, ddq, J = 3 × 13.3, 5.3, 4.0, H8), 1.53–1.62 (1 H, m, H3), 1.67–1.81 (2 H, m, H4, H3), 1.90–1.94 (1 H, m, H9eq), 2.22 (1 H, ddd, J = 12.4, 10, 8.0, H4), 3.24 (1 H, dq, J = 3 × 12.6, 4.3, H9ax), 3.32 (1 H, td, J = 5.1, 3.1, 1.5, H7ax), 3.73–3.81 (3 H, m, 2 × H2, H7eq), 3.91 (1 H, dd, J = 12.6, 4.6, H10)
22	$C_8H_{13}O_2{}^{81}Br$ requires 222.0079, found 222.0142. $C_8H_{13}O_2{}^{79}Br$ requires 220.0099, found 220.0121.	20.7 (C8), 24.7 (C3), 29.6 (C9), 38.9 (C4), 54.1 (C10), 61.0 (C7), 69.1 (C2), 106.1 (C5)	0.89–0.92 (1 H, m, H8), 1.33–1.37 (1 H, m, H3), 1.63 (1 H, td, J = 2 × 9.3, H4), 1.72–1.78 (2 H, m, H3, H9), 2.06–2.28 (3 H, m, H9, H4, H8), 3.46–3.49 (1 H, m, H7), 3.59 (1 H, q, J = 7.5, H2), 3.75–3.80 (2 H, m, H7, H2), 3.90 (1 H, dd, J = 3.1, 2.9 H10)

Table I (Continued)

compd	MS/microanalysis	^{13}C NMR (C_6D_6, δ)	^{1}H NMR (C_6C_6, δ, J in Hz)
23	$C_{11}H_{19}O_2{}^{81}Br$ requires 264.0549, found 264.0556. $C_{11}H_{19}O_2{}^{79}Br$ requires 262.0568, found 262.0581.	19.5 (C10), 21.7 (C12), 21.8 (C13), 27.5 (C3), 28.6 (C4), 32.4 (C9), 34.6 (C11), 55.3 (C5), 65.4 (C2), 66.6 (C8), 96.7 (C6)	1.02 (3 H, d, J = 6.3, H13), 1.11 (3 H, d, J = 6.3, H12), 0.89–1.15 (3 H, m, H3, H11ax, H9ax), 1.19–1.24 (1 H, m, H9eq), 1.32–1.39 (1 H, m, H10eq), 1.73–1.88 (3 H, m, H3, H10ax, H4eq), 2.31 (1 H, dddd, J = 13.3, 3.9, 2.7, 1.3, H11eq), 2.46 (1 H, dddd, J = 14.1, 12.8, 4.0, 3.5, H4ax), 3.55 (1 H, ddq, J = 11.3, 3 × 6.3, 2.4, H8), 3.62 (1 H, ddq, J = 12.2, 3 × 6.3, 2.6 H2), 3.92 (1 H, dd, J = 3.3, 2.7, H5)
24	$C_{11}H_{19}O_2{}^{81}Br$ requires 264.0549, found 264.0593, $C_{11}H_{19}O_2{}^{79}Br$ requires 262.0568, found 262.0578.	19.1 (C10), 21.3 (C12), 21.8 (C13), 31.1 (C4), 32.1 (C11), 32.4 (C9), 35.6 (C3), 55.6 (C5), 64.8 (C2), 66.4 (C8), 96.9 (C6)	0.96 (1 H, d, J = 6.3, H12), 0.98–1.09 (1 H, m, H3ax), 1.12 (1 H, d, J = 6.3, H13), 1.10–1.18 (2 H, m, H3eq, H9ax), 1.22–1.29 (1 H, m, H9eq), 1.35–1.41 (2 H,m, H10eq, H11eq), 1.79–1.88 (2 H, m, H10ax, H4eq), 2.18 (1 H, dt, J = 2 × 13.3, 4.6, H11ax), 2.46 (1 H, dq, J = 3 × 12.9, 4.6, H4ax), 3.55–3.64 (2 H, m, H2, H8), 3.66 (1 H, dd, J = 12.5, 4.6, H5)
25	$C_{11}H_{15}O_2{}^{81}Br_2$ requires 363.9634, found 343.9643. $C_{11}H_{18}O_2{}^{81}Br_2$ requires 341.9653, found 341.9656.	20.9, 30.6, 34.9, 51.8 (C5, C11), 66.1 (C2, C8), 96.9 (C6)	0.94 (6 H, d, J = 6.4, H12, H13), 1.02–1.39 (2 H, m, H3eq, H9eq), 1.77–1.83 (2 H, m, H4eq, H10eq), 2.23–2.33 (4 H, m, H3ax, H9ax, H4ax, H10ax), 3.43–3.51 (2 H, m, H2, H8), 4.55 (2 H, dd, J = 12.5, 4.6, H5, H11)

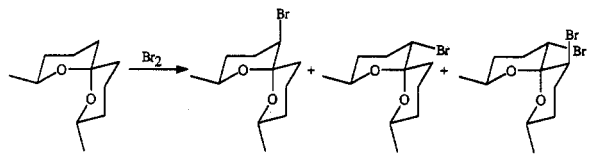
[a] $CDCl_3$ solvent for ^{13}C and ^{1}H NMR spectra. [b] See ref 5 for synthesis and characterization. [c] Compounds 10, 11, and 12 are isomers.

opening, such bond being anti-periplanar to the axial lone pair on the tetrahydropyranyl oxygen atom (eq 10).



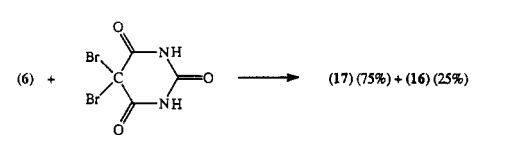
(5) (10)

Monobromination of (*E,E*)-2,8-dimethyl-1,7-dioxaspiro-[5.5]undecane (**7**) provided the expected mixture of axial (**23**) and equatorial (**24**) bromides as shown in eq 11. A mixture of dibromides (~12%) also formed from which the diequatorial dibromide **25** was separated and characterized.



(7) (23) (38%) (24) (50%) (25) (12%) (11)

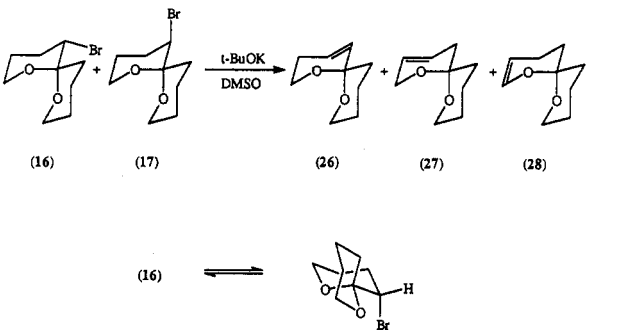
5,5-Dibromobarbituric acid has recently been employed[12] for α-bromination of ketones under mild conditions, and only one bromine is utilized.[13] Reaction of spiroketal **6** in ether, with 1 molar equiv of this reagent, for ca. 4 days at room temperature resulted in precipitation of 5-bromobarbituric acid and the formation of predominantly axial bromide (**17**) as shown in eq 12. This reagent may be useful when mild conditions are required.



(6) + (17) (75%) + (16) (25%) (12)

Dehydrobromination of α-Bromo Spiroketals

Treatment of the epimeric 5-bromo-1,7-dioxaspiro[5.5]-undecanes (**16**) and (**17**) with *t*-BuOK in DMSO at 110 °C resulted in ready reaction of the axial bromide (~2.5 h) and production of a more volatile component lacking bromine and with an apparent $M^{\bullet+}$ = 154, as required for a 1,7-dioxaspiro[5.5]undecene. Further heating (~6 h) led to consumption of the equatorial bromide, with corresponding formation of the same volatile component. ^{1}H and ^{13}C NMR spectra and GC–MS behavior confirmed its identity with the known[14,15] 1,7-dioxaspiro[5.5]undec-4-ene (**26**) (eq 13).



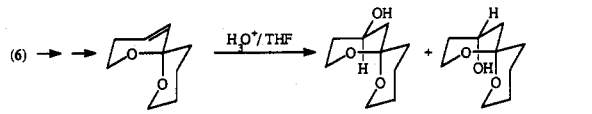
(16) (17) (26) (27) (28)

(16) (29) (13)

We presume that the slower rate of elimination from **16** reflects the advantage of a diaxial arrangement of H and Br for base-induced elimination, and achievement of this conformation (**29**) results in the loss of one anomeric effect. Prolonged reaction (~10 h) results in significant amounts of another olefin (GC–MS) which was different from the known[16] enol ether **28**. Spectroscopic data required this isomer to be 1,7-dioxaspiro[5.5]undec-3-ene (**27**), and its formation (by double-bond migration) could be minimized by stopping the reaction once both bromides were consumed (ca. 6 h at 110 °C). At equilibrium, olefin **27** predominates over **26** by 70:30. These were separable by HPLC.

The desired olefin **26** was converted to the 1,7-dioxaspiro[5.5]undecan-4-ols (**30**) and (**31**) by regiospecific hydration, in the manner reported by Baker[14] (eq 14). Thus, these alcohols, which are minor components of the

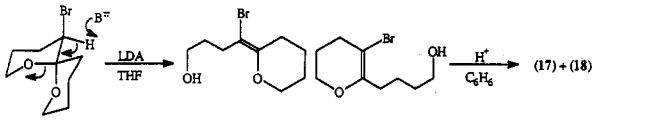
(12) Grundke, G.; Keese, W.; Rimpler, M. *Chem. Ber.* **1985**, *118*, 2488.
(13) Jacobsen, N. W.; Dorr, A. The University of Queensland. Unpublished results. We are grateful to Dr. Jacobsen for information and provision of this reagent.
(14) Baker, R.; Herbert, R. H. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1123.
(15) Kocienski, P.; Whitby, R. *Synthesis* **1991**, 1029.
(16) Ireland, R. E.; Habich, D. *Chem. Ber.* **1981**, *114*, 1418.



(26) (30) (95%) (31) (5%) (14)

rectal gland secretions of olive flies (*Bactrocera oleae*),[14,17] *Bactrocera cacuminatus*,[18] and *Bactrocera distincta*[17] are easily available from the simple spiroketal **6**. This bromination–dehydrobromination–hydration sequence can be conducted sequentially in a "one-pot" way without purification of the intermediate bromides or olefin, with satisfactory overall yield (53%). This route to **30** and **31** is more direct than those currently available.[19]

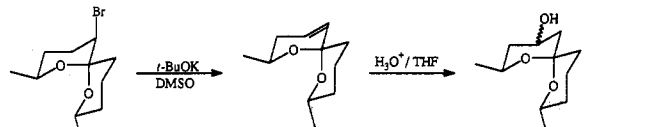
Dehydrobromination of the **16**, **17** mixture was attempted using other base systems. For example, *t*-BuOK in THF was clean and effective for the axial bromides and had some advantages in the workup procedures. However, the use of LDA in THF led to an unexpected result, as now the axial bromide **17** reacted quickly, but the product, after aqueous quenching, was less volatile than **17** and contained bromine (GC–MS). Spectroscopic studies demonstrated that the tetrahydropyran **32** or **32a** had been formed, and since the axial bromide reacted structure **32** is favored on stereoelectronic grounds, as shown in eq 15.



(17) (32) (32a) (15)

Similar considerations would favor **32a** forming from the equatorial bromide **16**, but base approach and axial-hydrogen removal in this case is not competitive.[20] Treatment of the product with a catalytic amount of *p*-toluenesulfonic acid in benzene reformed a mixture of the monobromides **16** and **17**, such behavior being expected for either **32** or **32a** (eq 15).

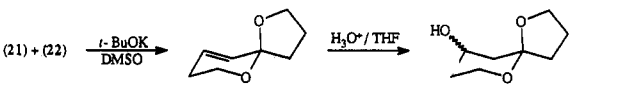
The monobromides formed from (*E*,*E*)-2,8-dimethyl-1,7-dioxaspiro[5.5]undecane (**23** and **24**) were treated with *t*-BuOK in DMSO, and as anticipated, the axial bromide furnished the olefin, with the equatorial epimer unable to access the high energy conformation conductive to elimination. Olefin **33** was isolated by preparative TLC (silica), fully characterized, and converted (eq 16) to the 2,8-



(23) (33) (34) (16)

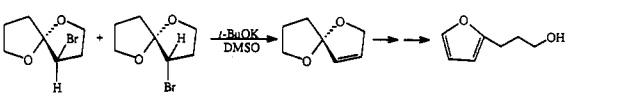
dimethyl-1,7-dioxaspiro[5.5]undecan-4-ols (**34**), which have been prepared previously[21] by another route (eq 16).

The monobromides derived from 1,6-dioxaspiro[4.5]-decane (eq 9), concluded to be **21** and **22**, on treatment with *t*-BuOK in DMSO at 80 °C resulted in rapid dehydrobromination of the axial-bromide **22** and a much slower reaction of the equatorial isomer **21**, a reactivity trend observed by the monobromides **16** and **17**. A more volatile component was formed and shown by GC–MS examination of lack bromine and have apparent $M^{\bullet+}$ = 140. This product was isolated, characterized as the olefin **35**, and converted to the 1,6-dioxaspiro[4.5]decan-9-ols (**36**) which were separated and characterized (eq 17). Some slight isomerization of **35** to 1,6-dioxaspiro[4.5]dec-8-ene was also observed.



(35) (36) (17)

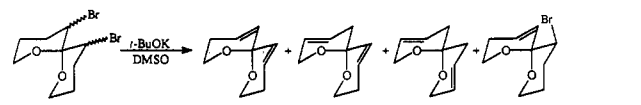
Dehydrobromination of the monobromides **8** and **9** from 1,6-dioxaspiro[4.4]nonane (**2**) (eq 18) was less successful



(8) (9) (37) (38) (18)

in terms of isolating the expected olefin, 1,6-dioxaspiro-[4.4]non-3-ene (**37**). On standard workup, the presumed elimination product, which was characterized by GC–MS ($M^{\bullet+}$ = 126 (2.2%), 81 (100)) underwent facile aromatization to provide 3-(2-furyl)propanol (**38**), identical with an authentic sample.[22] This type of behavior has been noted by Trška and Dědek[5] and more recently by Kocienski[23] and Elsley[24] in similar systems. However, when the elimination reaction was conducted using DMSO-d_6 as solvent, direct ^1H and ^{13}C NMR examination confirmed the ready formation of **37** which was relatively stable in the basic DMSO-d_6 medium. Compound **37** showed a spirocarbon resonance at 118.24 ppm and olefinic signals at 127.64 and 130.53 ppm. For the homologous 1,6-dioxaspiro[4.5]dec-3-ene,[23] the corresponding shifts are 110.0, 130.07, and 130.46 ppm, and there are the expected similarities in the ^1H NMR spectra of the two compounds. A natural product incorporating the 1,6-dioxaspiro[4.4]non-3-ene system has been characterized, but this has a 2,2-dimethyl grouping preventing aromatization.[25]

Double elimination from an isomeric mixture of 5,11-dibromo-1,7-dioxaspiro[5.5]undecanes (see eq 7) also occurred, as shown in eq 19, but was accompanied by



(39) (41%) (40) (34%) (41) (8%) (42) (5%) (19)

(17) The absolute stereochemistry of the 1,7-dioxaspiro[5.5]undecan-3- and 4-ols present in the fruit fly species *B. oleae*, *B. cacuminatus*, and *B. distincta* has been determined. See: Fletcher, M. T.; Jacobs, M. F.; Kitching, W.; Krohn, S.; Drew, R. A. I.; Haniotakis, G.; Francke, W. *J. Chem. Soc., Chem. Commun.* **1992**, 1457.

(18) Krohn, S.; Fletcher, M. T.; Kitching, W.; Drew, R. A. I.; Moore, C. J.; Francke, W.; Schurig, V. *J. Chem. Ecol.* **1991**, *17*, 485.

(19) See, for example: (a) De Shong, P.; Rybczynski, P. J. *J. Org. Chem.* **1991**, *56*, 3207. (b) Marko, I. E.; Mekhalfia, A.; Bayston, D. J.; Adams, H. *J. Org. Chem.* **1992**, *57*, 2211.

(20) For a discussion of similar features see ref 15.

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substantial double-bond migration. The major dienes **39** and **40** were obtained pure by HPLC and fully characterized.

In summary, the ready installation of a double bond in the tetrahydropyran ring by bromination–dehydrobromination provides simple access to the 1,7-dioxaspiro[5.5]undec-4-ene and 1,6-dioxaspiro[4.5]dec-9-ene systems, with the former being a substructure in a number of important polyether natural products.[26] These alkenes are precursors to a variety of alcohols by regiospecific hydration and allylic functionalization and to 1,2-diols by syn-hydroxylation.[6] A potential drawback in some systems containing an unsaturated linkage would be that addition of bromine was more facile than α-substitution. However, in such cases, iodide-induced debromination is much faster than reaction of the α-bromo group, so that regeneration of unsaturation proceeds.[27]

Experimental Section

General Procedure for Bromination. Brominations were routinely conducted using molecular bromine in carbon tetrachloride; this procedure was simpler than using *N*-bromosuccinimide as the brominating agent. The detailed procedure is described for 1,6-dioxaspiro[4.4]nonane (**2**).[5] Spiroketals **2**, **5**, **6**, and **7** have been described previously.[1]

Bromination of Spiroketal 2. Bromine (1.25 g, 7.8 mmol) in CCl_4 (10 mL) was added dropwise to a solution of **2** (1 g, 7.8 mmol) in CCl_4 (10 mL) in which was suspended $CaCO_3$ (1.17 g, 11.7 mmol). After addition of bromine was complete, the mixture was filtered, and the solution washed with 5% $NaHCO_3$. The organic layer was dried ($MgSO_4$) and concentrated in vacuo (rotary evaporator) to provide the crude product (ca. 90%) which by GC–MS examination consisted of two monobromides (69:25) and a mixture of dibromides, together representing 6%. The isomers were generally easily separated by (HPLC, silica, (1:20) ether/hexane). The separated bromides were fully characterized by LRMS (from GC–MS examination), ^1H and ^{13}C NMR spectra, HRMS, and/or microanalytical data, which are presented in Table I.

Base-Induced Dehydrobromination of Bromo Spiroketals. Several procedures were examined, and potassium *tert*-butoxide in DMSO was generally used. This base in THF was employed but it induced α-deprotonation and spiroketal ring opening as discussed in the text. A representative procedure for dehydrobromination is described.

Dehydrobromination of (*Z*)- and (*E*)-5-Bromo-1,7-dioxaspiro[5.5]undecane (16 and 17). An epimeric mixture of the (*Z*)- and (*E*)-bromo spiroketals **16** and **17** (ca. 2:1) (0.5 g, 2.1 mmol) in DMSO (5 mL) was added to a solution of *t*-BuOK (0.48 g, 4.2 mmol) in DMSO (10 mL). This mixture was heated to 110 °C for 2.5 h after which time the axial-bromide **18** had reacted (VPC monitoring) to provide a more volatile component. Warming (110 °C) for a further 6 h led to reaction of the remaining equatorial bromide (**16**), with increased formation of the more volatile component mentioned above. At this stage, a second volatile component of similar retention time began to appear. Further heating (12 h) provided a 7:3 mixture of elimination products, subsequently shown to be 1,7-dioxaspiro[5.5]undec-3-ene (**27**) and 1,7-dioxaspiro[5.5]undec-4-ene (**26**). The mixture was saturated with salt and extracted with pentane which was separated, dried ($MgSO_4$), and concentrated. This reaction was repeated, but was terminated after 8 h to provide 260 mg (79%) of crude olefin **26** which was purified (HPLC, silica, 1:20 ethyl acetate/hexane). Olefins **26** and **27** were also separated in this manner.

1,7-Dioxaspiro[5.5]undec-4-ene (26): ^1H NMR (400 MHz, $CDCl_3$) δ 1.46–1.66 (5 H, m), 1.78–1.88 (2 H, m), 2.22–2.31 (1 H, m), 3.59–3.62 (1 H, m), 3.71–3.94 (3 H, m), 5.6 (1 H, ddd, J = 10.0, 2.7, 1.4 Hz), 5.89–5.93 (1 H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 24.8, 25.0, 34.8, 57.7, 60.9, 92.9, 127.7, 130.7; MS (EI) *m/z* ($M^{\bullet+}$ 154 (24)), 126 (13), 125 (14), 124 (17), 113 (20), 109 (25), 99 (97), 96 (100), 86 (19); HRMS calcd for $C_9H_{14}O_2$ 154.0993, found 154.0994. These data match those previously reported.[14,15]

1,7-Dioxaspiro[5.5]undec-3-ene (27): ^1H NMR (400 MHz, $CDCl_3$) δ 1.40–1.59 (4 H, m), 1.64–1.69 (1 H, dm), 1.84–1.89 (1 H, m), 1.98–2.05 (1 H, dm), 2.12–2.18 (1 H, dm), 3.65–3.77 (2 H, m), 3.99–4.17 (2 H, m), 5.63–5.74 (2 H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7, 25.1, 34.9, 35.8, 59.8, 61.5, 94.4, 121.4, 124.8; MS (EI) *m/z* ($M^{\bullet+}$ 154 (6.9)), 101 (20), 99 (15), 98 (53), 81 (10), 55 (38), 54 (100); HRMS calcd for $C_9H_{14}O_2$ 154.0993, found 154.1002.

Hydration of olefin **26** in the manner described by Baker,[14] using acidic THF–H_2O, led cleanly to a mixture of the epimeric 1,7-dioxaspiro[5.5]undecan-4-ols **30** and **31**, with the equatorial **30** greatly predominating (95:5). These alcohols exhibited LRMS and ^1H and ^{13}C NMR spectra essentially identical with those reported previously.[14]

Attempted Dehydrobromination of 16 and 17 with Lithium Diethylamide. Addition of a mixture of the monobromides **16** and **17** to a cold solution (−30 °C) of LDA in THF resulted in rapid disappearance of the axial-bromide **17**, with the equatorial-bromide **16** being unreactive. After standard workup, GC–MS examination revealed the product to be less volatile than **17** and to contain bromine. High-resolution ^1H and ^{13}C NMR spectra were consistent with either structure **32** or **32a**, and treatment with a catalytic amount of tosic acid in benzene regenerated a mixture of the bromo spiroketals **16** and **17**. Enol ether **32** or **32a**: ^1H NMR (400 MHz, C_6D_6) δ 1.33–1.36 (2 H, m), 1.49–1.54 (2 H, m), 1.60–1.65 (2 H, m), 2.14–2.17 (2 H, m), 2.38–2.42 (3 H, m), 3.45–3.48 (2 H, m), 3.52–3.55 (2 H, m); ^{13}C NMR (100 MHz, C_6D_6) δ 23.3, 24.6, 31.3, 32.4, 33.0, 62.4, 65.8, 96.8, 152.8; IR (film) ν 2942 (s), 2874 (m), 1440 (w), 1202 (w), 1088 (s), 1067 (s), 1047 (s), 1032 (s), 1000 (s); MS (EI) *m/z* ($M^{\bullet+}$ 236, 234 (16.8, 19.4), 190 (6.1), 188 (6.0), 176 (14), 149 (13), 111 (35), 109 (30), 98 (100), 97 (41), 95 (20); HRMS calcd for $C_9H_{15}O_2{}^{79}Br$ 234.0255, found 234.0255.

1,6-Dioxaspiro[4.5]dec-9-ene (35) was prepared from a mixture of the monobromides **21** and **22** by the standard elimination procedure: ^1H NMR (500 MHz, $CDCl_3$) δ 1.74–1.81 (1 H, m, H4), 1.85 (1 H, dddt, J = 17.7, 5.5, 3.8, 2 × 1.4, H8eq), 1.89–1.94 (1 H, m, H3), 1.94–1.99 (1 H, m, H4), 2.05–2.12 (1 H, m, H3), 2.24 (1 H, dddt, J = 17.7, 11.7, 6.1, 2 × 2.6 Hz, H8ax), 3.37 (1 H, ddt, J = 11.2, 6.1, 2 × 1.2, Hz, H7), 3.86–3.97 (3 H, m, H7, 2 × H2), 5.60 (1 H, ddd, J = 10.5, 2.7, 1.4 Hz, H10), 5.99 (1 H, dddd, J = 10.5, 7.3, 2.4, 1.2 Hz, H9); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4 (C3), 37.4 and 40.9 (C4,C8), 59.0 (C7), 67.3 (C2), 102.5 (C5), 128.4 (C10), 128.8 (C9); MS (EI) *m/z* ($M^{\bullet+}$ 140 (64)), 112 (50), 110 (100), 109 (37), 99 (40), 95 (29), 82 (73), 81 (37), 79 (47); HRMS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0804. Olefin **35** was hydrated in the usual way (HCl, THF–H_2O) to produce two epimeric alcohols (GC–MS) which were separated and purified (HPLC, silica, 1:1 ethyl acetate/hexane).

1,6-Dioxaspiro[4.5]decan-9-ol (36) (equatorial isomer): ^1H NMR (500 MHz, C_6D_6) δ 1.41–1.46 (2 H, m, H4, H3), 1.47–1.56 (1 H, m, H8), 1.65–1.74 (2 H, m, H8, H10), 1.76–1.89 (1 H, m, H3), 1.90–1.96 (1 H, m, H4), 2.06 (1 H, ddd, J = 12.1, 4.6, 1.9 Hz, H10eq), 3.14 (1 H, br s, OH), 3.57 (1 H, ddd, J = 11.4, 5.0, 1.6 Hz, H7eq), 3.65–3.88 (m, 3 H, 2 × H2, H7), 4.16 (1 H, tt, J = 5.2, 2 × 11.1 Hz, H9); ^{13}C NMR (500 MHz, C_6D_6) δ 23.7 (C3), 35.5 (C8), 38.1 (C4), 43.3 (C10), 59.5 (C7), 65.3 (C9), 67.2 (C2), 107.1 (C5); MS (EI) *m/z* ($M^{\bullet+}$ 158 (4)), 117 (21), 87 (100), 86 (16), (85, 59), 72 (34), 71 (15), 57 (27); HRMS calcd for $C_8H_{14}O_3$ 158.0943, found 158.0949.

1,6-Dioxaspiro[4.5]decan-9-ol (36) (axial isomer): ^1H NMR (500 MHz, C_6D_6) δ 1.22 (1 H, ddd, J = 10.8, 10.3, 8.5 Hz, H4), 1.27–1.34 (1 H, m, H3), 1.49–1.55 (2 H, m, 2 × H8), 1.63–1.71 (3 H, m, 2 × H10, H3), 1.77 (1 H, ddd, J = 11.1, 8.5, 3.0 Hz, H4), 3.40–3.44 (1 H, m, H7eq), 3.50 (1 H, dt, J = 2× 8.0, 6.0, Hz, H2), 3.62 (1 H, dt, J = 2 × 8.2, 5.7 Hz, H2), 3.87 (1 H, d, J = 10.1 Hz, –OH), 3.99–4.02 (1 H, m, H9), 4.07–4.13 (1 H, m, H7ax); ^{13}C NMR (100 MHz, C_6D_6) δ 23.0 (C3), 32.6 (C8), 38.2 (C4), 39.0 (C1O), 56.2 (C7), 64.5 (C9), 67.7 (C2), 106.3 (C5); MS (EI) *m/z* ($M^{\bullet+}$ 158 (0.4)), 117 (15), 113 (12), 87 (100), 84 (37), 72 (37), 57 (23); HRMS calcd for $C_8H_{14}O_3$ 158.0943, found 158.0947.

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(*E,E*)-2,8-Dimethyl-1,7-dioxaspiro[5.5]undec-4-ene (33) was obtained by dehydrobromination of the axial-bromide **23** in the described way and purified by preparative TLC on silica: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (3 H, d, J = 6.9 Hz, C13), 1.14–1.25 (1 H, m, H9ax), 1.34 (3 H, d, J = 5.5 Hz, C12), 1.45–1.51 (1 H, m, H11ax), 1.53–1.58 (2 H, m, H9eq, H10eq), 1.59–1.64 (1 H, m, H11eq), 1.85–1.91 (1 H, m, H10ax), 1.92–1.97 (2 H, m, 2 × H3), 3.86–3.90 (1 H, m, H8ax), 3.99–4.03 (1 H, m, H2ax), 5.6 (1 H, ddd, J = 9.9, 2.6, 1.5 Hz, H5), 5.86 (1 H, ddd, J = 9.9, 5.4, 2.2 Hz, H4); ^{13}C NMR (100 MHz, $CDCl_3$), δ 18.8 (C10), 21.2 (C13), 22.2 (C12), 32.4 (C3), 32.5 (C9), 34.4 (C11), 62.9 (C2), 65.7 (C8), 94.7 (C6), 127.8 (C4), 130.7 (C5); MS (EI) m/z ($M^{\bullet+}$ 182 (5)), 138 (16), 123 (18), 114 (11), 113 (100), 110 (86), 109 (16), 100 (30), 95 (60), 81 (11); HRMS calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1328. Olefin **33** was further characterized by its hydration to the axial and equatorial alcohols **34** which are fully described elsewhere.[21]

1,6-Dioxaspiro[4.4]non-3-ene (37). Dehydrobromination of the monobromides **8** and **9**, when conducted in the normal way and subjected to a standard workup, provided only the known[22] 3-(2-furyl)propanol (**38**), as a result of facile aromatization of **37**. Use of DMSO-d_6 as reaction medium with *t*-BuOK and direct NMR examination of the reaction mixture showed that the title olefin **37** was formed almost quantitatively: ^{1}H NMR (200 MHz, DMSO-d_6) δ (relative to DMSO taken as δ 2.5) 1.77–2.17 (4 H, m), 3.67–4.0 (2 H, m), 3.83–4.07 (2 H, "AB" system with further couplings, J = 14.0, 2.5 and 1.5 Hz in lower-field component; J = 14.0, 2.0, 2.0 Hz in higher field component), 5.76 (1 H, dt, J = 5.9, 2.47 Hz), 6.23 (1 H, dt, J = 5.9, 2 × 1.6 Hz); ^{13}C NMR (50 MHz DMSO-d_6, relative to DMSO at δ 39.1) δ 24.2, 35.1, 66.4, 72.4, 118.2, 127.6, 130.5; MS (EI) m/z ($M^{\bullet+}$ 126 (0.2)), 96 (14), 85 (53), 81 (100), 67 (57), 55 (51). These data compare well with those reported[23] for the homologous 1,6-dioxaspiro[4.5]dec-3-ene, when allowance is made for the ring size difference.

Dehydrobromination of 5,11-Dibromo-1,7-dioxaspiro[5.5]undecanes. Treatment of a mixture of dibromides **18**, **19**, and **20** (eq 7) with potassium *tert*-butoxide in DMSO in the described way led to a mixture of dienes **39**, **40**, and **41** and a minor proportion of the bromoolefin **42**. The major dienes **39** and **40** were separated (HPLC, silica, 1:1 ethyl acetate/hexene) and characterized, but **41** and **42** were obtained as a mixture and characterized by ^{13}C NMR and LRMS. **1,7-Dioxaspiro[5.5]undeca-4,10-diene (39)**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (2 H, dddd, J = 17.8, 7.8, 3.4, 1.2, Hz, H3ax, H9ax), 2.26 (2 H, dddt, J = 17.8, 11.0, 6.2, 2 × 2.7 Hz, H3eq, H9eq), 3.73 (2 H, dd, J = 11.0, 6.2 Hz, H2eq, H8eq), 3.95 (2 H, td, J = 2 × 11.0, 3.42 Hz, H2ax, H8ax), 5.55 (2 H, ddd, J = 10.0, 2.7, 1.2 Hz, H5, H11), 5.96–6.00 (2 H, m, H4, H10); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.40 (C3, C9), 58.32 (C2, C8), 90.76 (C6), 128.35, 128.76 (C5, C11 and C4, C10); MS (EI) m/z ($M^{\bullet+}$ 152 (28)), 124 (28), 123 (20), 122 (100), 121 (45), 94 (40), 93 (25), 91 (32), 79 (47), 77 (27); HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0852. **1,7-Dioxaspiro[5.5]undeca-3,10-diene (40)**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.78–0.85 (m, 1 H), 1.78–1.88 (dm, 1 H), 1.99–2.09 (dm, 1 H), 2.25–2.34 (m, 1 H), 3.74–3.81 (m, 1 H), 3.90–3.97 (m, 1 H), 4.04–4.08 (dm, 1 H), 4.21–4.26 (dm, 1 H), 5.53–5.75 (m, 3 H), 5.95–6.01 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.6, 34.6, 58.4, 60.2, 92.0, 121.2, 124.7, 128.5, 129.6; MS (EI) m/z ($M^{\bullet+}$ 152 (6.2)), 99 (33), 96 (20), 68 (26), 54 (100), 39 (31); HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0839. **1,7-Dioxaspiro[5.5]undeca-3,9-diene (41)**: ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.1, 60.9, 93.7, 121.1, 124.8; MS (EI) ($M^{\bullet+}$ m/z 152 (3.9)), 98 (16), 97 (12), 55 (12), 54 (100). **4-Bromo-1,7-dioxaspiro[5.5]undec-10-ene (42)**: ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 27.8, 30.1, 53.5, 58.3, 59.8, 94.0, 128.2, 130.1; MS (EI) m/z ($M^{\bullet+}$ 176 (10.8), 174 (124)), 153 (100), 126 (13), 125 (34), 99 (50), 81 (13).

X-ray Crystal Structure Determinations. The crystal structures were determined on an Enraf-Nonius CAD 4 four-circle diffractometer[28a] with molybdenum X-radiation (graphite monochromator). The crystal of **10** selected was a clear colorless prism, yielding 832 observed [$I > 3.0\sigma(I)$] reflections out of 2356 collected. The structure was solved by Patterson heavy atom techniques in SHELXS 86. Full-matrix least-squares refinement[28c] was on F's. Scattering factors for C, H, O, and Br[28d] were used; hydrogen positions were calculated. For tribromide **15**, a clear colorless prism yielded 591 observed [$I > 2.5\sigma(I)$] reflections out of the 1183 collected. The structure was solved by the above method.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra (20 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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(30) The author has deposited atomic coordinates for the structures of compounds **10** and **15** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.