137.69, 128.26, 128.10, 127.87, 127.63, 77.63, 76.00, 75.96, 53.84, 36.14, 34.83, 31.41, 25.13, 19.06, 12.37; IR (neat) 1730 cm^{-1}. Anal. Calcd: C, 73.25; H, 9.56. Found: C, 73.14; H, 9.48.

exo-**4c**: ^1H NMR (360 MHz, $CDCl_3$) δ 7.35 (5 H, m), 5.84 (1 H, s), 4.58 (2 H, s), 4.44 (1 H, d, J = 18 Hz), 4.09 (1 H, d, J = 18 Hz), 2.69 (1 H, dd, J = 6 Hz, 9 Hz), 2.28 (1 H, s), 1.77 (3 H, s), 1.75–1.29 (6 H, m), 1.03 (2 H, s); ^{13}C NMR (90 MHz, $CDCl_3$) δ 209.70, 141.84, 137.66, 131.29, 128.56, 128.35, 127.97, 127.74, 77.69, 73.15, 52.33, 35.05, 31.57, 29.77, 25.36, 18.39, 13.40; IR (neat) 1730 cm^{-1}.

5-Methyl-1-(triisopropylsiloxy)bicyclo[2.2.2]oct-5-ene-2-carboxaldehyde (*endo*-3d, 4d). *endo*-**3d**: R_f = 0.71 (SiO_2, 2:1 hexanes–ether); ^1H NMR (300 MHz, $CDCl_3$) δ 9.65 (1 H, d, J = 2.9 Hz, CHO), 5.79 (1 H, s, H-6), 2.62 (1 H, m, H-2), 2.34 (1 H, br s, H-4), 1.79 (3 H, d, J = 1.4 Hz, CH_3), 1.18–1.45 (6 H, m), 104 (21 H, s, $Si(C_3H_7)_3$); IR (neat) 1724.0 cm^{-1}; MS (CI, positive ion) m/e (323 (MH^+, 100), 279 (M – C_3H_7, 8); MS (EI) m/e 322.2351 (322.2378 calcd for $C_{19}H_{34}O_2Si$). Anal. Calcd: C, 70.75; H, 10.62; Found: C, 70.56, H, 10.61.

exo-**4d**: R_f = 0.71 (SiO_2, 2:1 hexanes–ether); ^1H NMR (300 MHz, $CDCl_3$) δ 10.05 (1 H, d, J = 1.4 Hz, CHO), 5.92 (1 H, s, H-6), 2.53 (1 H, ddd, J = 9.0, 2.1, 4.3 Hz, H-2), 2.29 (1 H, br s, H-4), 2.01 (1 H, ddd, J = 13.1, 2.3, 2.4 Hz, H-3), 1.79 (3 H, d, J = 1.4 Hz, -CH_3), 1.74 (1 H, td, J = 11.6, 2.8 Hz), 1.58 (1 H, m), 1.5–1.3 (3 H, m), 1.08 (21 H, s, $Si(C_3H_7)_3$); IR (neat) 1721.4 cm^{-1}; MS (CI) m/e 323 (MH^+, 100), 279 (M – isopropyl, 20); MS (EI) m/e 322.2306 (322.2328 calcd for $C_{19}H_{34}O_2Si$), 279.1768 (M – C_3H_7).

***N*-[[5-Methyl-1-(triisopropylsiloxy)bicyclo[2.2.2]oct-5-en-2-yl]carbonyl]-2-oxazolidinone (3e and 4e).** *endo*-**3e**: R_f = 0.68 (SiO_2, ether); R_f = 0.35 (SiO_2, 1:2 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 5.79 (1 H, s, H-6), 4.3 (2 H, m, OCH_2), 3.94 (2 H, t, J = 8.03 Hz, NCH_2), 2.31 (1 H, br s, H-4), 191 (1 H, ddd, J = 3.0, 10.0, 12.4 Hz), 1.82 (3 H, d, J = 1.1 Hz, CH_3), 1.75 (1 H, m), 1.64 (1 H, m), 1.55–1.35 (2 H, m), 1.03 (21 H, s, Si $(C_3H_7)_3$), 1.95 (2 H, m); IR ($CHCl_3$) 1779.4, 17005 cm^{-1}; MS (CI, positive ion) m/e 408 (MH^+, 100), 364 (M – isopropyl, 5); MS (EI) m/e 407.2515 (407.24916 calcd for $C_{22}H_{37}NO_4Si$, 9.2), 364.1948 (M – C_3H_7, 100).

exo-**4e**: R_f = 0.85 (SiO_2, ether); R_f = 0.44 (SiO_2, 1:2 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 5.93 (1 H, s, H-6), 4.3 (2 H, m, OCH_2), 4.02 (2 H, m, NCH_2), 2.30 (2 H, br s, H-4, H-2), 1.78 (3 H, d, J = 1.6 Hz, CH_3), 1.66 (2 H, m), 1.5–1.2 (2 H, m), 1.04 (21 H, s, $Si(C_3H_7)_3$), 1.95 (2 H, m); IR (neat) 1760.4, 1693.3 cm^{-1}.

Methyl 3,5-Dimethyl-1-(triisopropylsiloxy)bicyclo-[2.2.2]oct-5-ene-2-carboxylates (3f, 4f). *endo*-**3f**: R_f = 0.60 (SiO_2, 4:1 hexanes–ether); ^1H NMR (300 MHz, $CDCl_3$) δ 5.74 (1 H, s, H-6), 3.60 (3 H, s, CH_3), 2.20 (1 H, d, J = 6.6 Hz, H-2), 1.94 (1 H, br s, H-4), 1.82 (3 H, d, 1.3 Hz, CH_3), 1.80 (1 H, m, H-3), 1.57 (1 H, dt, J = 3.9, 10.9 Hz), 1.45 (1 H, dt, J = 4.3, 11.17 Hz), 1.25 (2 H, m), 1.03 (24 H, s, CH_3, $Si(C_3H_7)_3$); IR (neat) 1740.7 cm^{-1}; MS (EI) m/e 366.2570 (366.2590 calcd for $C_{21}H_{38}O_3Si$), 323.2029 (322.2042 calcd for M – C_3H_7).

exo-**4f**: R_f = 0.67 (SiO_2, 4:1 hexanes–ether); ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (1 H, br s, H-6), 3.64 (3 H, s, OCH_3), 2.23 (1 H, dt, J = 3.1, 10.3 Hz, H-4), 2.05 (3 H, m, H-2, H-3), 1.79 (3 H, d, J = 1.4 Hz, CH_3), 1.73 (1 H, tdd, J = 10.4, 1.5, 3.8 Hz), 1.37 (1 H, tt, J = 12.0, 3.5 Hz), 1.22 (1 H, m), 1.08 (21 H, s, $SiC_3H_7)_3$), 0.85 (3 H, d, J = 6.34 Hz, CH_3); IR (neat) 1734.4 cm^{-1}; MS (EI) m/e 366.2614 (366.2590 calcd for $C_{21}H_{38}O_3Si$).

Methyl 3-(Bromoethyl)-5-methyl-1-(triisopropylsiloxy)-bicyclo[2.2.2]oct-5-ene-2-carboxylates (3g and 4g). *endo*-**3g**: R_f = 0.39 (SiO_2, 4:1 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 5.78 (1 H, s, H-6), 3.62 (3 H, s, OCH_3), 3.48 (1 H, dd, J = 7.4, 10.1 Hz, CHBr), 3.33 (1 H, dd, J = 8.6, 10.1 Hz, CHBr), 2.40 (2 H, br s, H-4), 2.31 (1 H, d, J = 6.6 Hz, H-2), 2.22 (1 H, m, H-3), 1.86 (3 H, d, J = 1.6 Hz, CH_3), 1.70 (1 H, m), 1.55 (2 H, d-quintet, J = 4.7, 11.7 Hz), 1.30 (1 H, m), 1.04 (21 H, br s, $Si(C_3H_7)_3$); IR (neat) 2946, 2858, 1737 cm^{-1}; MS (CI) m/e 447 (MH^+, 100), 445 (Br – isotope, 96.8); MS (EI) m/e 446 (M^+, 8.3, 403 (M – C_3H_7, 100), 401 (Br – isotope, 100).

exo-**4g**: R_f = 0.46 (SiO_2, 4:1 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 5.92 (1 H, s, H-6), 3.67 (3 H, s, OCH_3), 3.08 (2 H, d of AB quartet, J = 8.1 Hz, J_{AB} = 9.8 Hz, ν_{AB} = 11.6 Hz, CH_2Br), 2.49 (1 H, br s, H-4), 2.44 (1 H, m, H-3), 2.18 (1 H, dt, J = 3.7, 10.7 Hz), 2.13 (1 H, dd, J = 2.0, 5.6 Hz), 1.81 (3 H, d, J = 1.6 Hz, CH_3), 1.79 (1 H, m), 1.44 (1 H, tt, J = 3.5, 12.3 Hz, H-8), 1.26 (1 H, m), 1.05 (21 H, br s, $Si(C_3H_7)_3$); MS (CI, a positive ion) m/e 447 (MH^+, 100), 445 (Br – isotope, 97.4), 403 (M – C_3H_7, 16.2), 401 (Br – isotope, 15.1); MS (EI) m/e 446 (M^+, 8.2), 444 (Br – isotope, 8.2), 403 (M – C_3H_7, 100), 401 (Br – isotope, 98.7).

Methyl 3-[(Benzyloxy)methyl]-5-methyl-1-(triisopropylsiloxy)bicyclo[2.2.2]oct-5-ene-2-carboxylates (3h and 4h). *endo*-**3h**: R_f = 0.41 (SiO_2, 4:1 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 7.33 (5 H, m, Ph), 5.79 (1 H, s, H-6), 4.50 (2 H, AB q, ν_{AB} = 13.0 Hz, J_{AB} = 12.1 Hz), 3.59 (3 H, s, OCH_3), 3.50 (1 H, dd, J = 6.8, 9.4 Hz, CHO), 3.40 (1 H, t, J = 8.9 Hz, CHO) 2.33 (1 H, br s, H-4), 2.27 (1 H, d, J = 6.7 Hz, H-2), 2.14 (1 H, qt, J = 8.2, 1.6 Hz, H-3), 1.85 (3 H, d, J = 1.5 Hz, (1 H, td, J = 11.03, 4.32 Hz, H-7), 1.25 (1 H, m, H-8), 1.04 (21 H, br s, $Si(CH_3H_7)_3$); IR (neat) 2925, 2860, 1740 cm^{-1}; MS (CI, positive ion) m/e 473 (MH^+, 100), 429 (M^+ – C_3H_7, 20); MS (EI) m/e 472.2993 (472.3009 calcd for $C_{28}H_{44}O_4Si$).

exo-**4h**: R_f = 0.51 (SiO_2, 4:1 hexanes–ether); ^1H NMR (250 MHz, $CDCl_3$) δ 7.32 (5 H, m, H-6), 4.45 (2 H, AB q, ν_{AB} = 11.7 Hz, J_{AB} = 12.1 Hz, OCH_2Ph), 3.64 (3 H, s, CH_3), 3.10 (2 H, d, J = 7.5 Hz, CH_2O), 2.39 (1 H, br s, H-4), 2.33 (1 H, dq, J = 3.9, 10.9 Hz, H-3), 2.07 (1 H, d, J = 4.9 Hz, H-2), 1.79 (1 H, m, H-7), 1.76 (3 H, d, J = 1.6 Hz, =CH_2), 1.40 (1 H, m, H-7), 1.26 (2 H, m, H-8), 1.05 (21 H, br s, $Si(C_3H_7)_3$); IR (neat) 2950, 2870, 1730 cm^{-1}; MS (CI, isobutane) m/e 473 (MH^+, 100) 429 (M^+ – C_3H_7, 21); MS (EI) m/e 472.3019 (472.3009 calcd for $C_{28}H_{44}O_4Si$).

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Supplementary Material Available: ^1H NMR spectra for **3a–h**, **4a**, and **4d–h** (14 pages). Ordering information is given on any current masthead page.

Synthesis and Molecular Structure of Two New Crystalline 6,8-Dioxabicyclo[3.2.1]octanes

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The ever-growing number of natural products possessing the 6,8-dioxabicyclo[3.2.1]octane skeleton[1-4] spurs a con-

(1) Brevicomin: (a) Mikami, K.; Nakai, T. *Chem. Lett.* **1982**, 1349. (b) Singh, S.; Oehlschlager, A. *Can. J. Chem.* **1988**, *66*, 209 and references therein. (c) Giese, B.; Rupaner, R. *Synthesis* **1988**, 219. (d) Bartelt, K.; Mundy, B. *Synth. Commun.* **1989**, *19*, 2915.

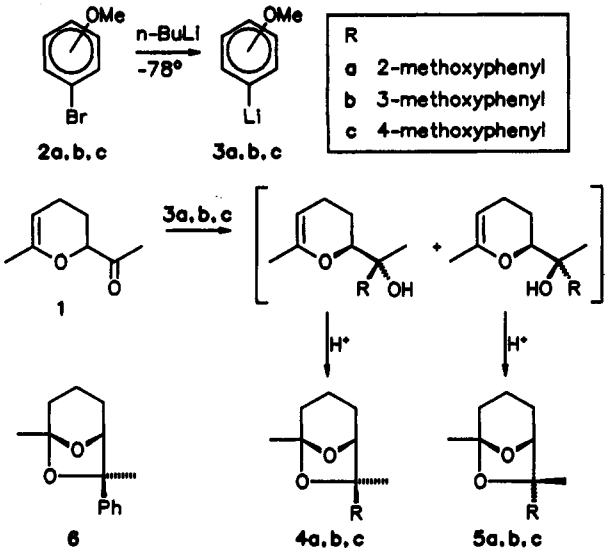
(2) Multistriatin: Larcheveque, M.; Henrot, S. *Tetrahedron* **1987**, *43*, 2302 and references therein.

(3) Frontalin: (a) Kinzer, G.; Fentiman, A.; Page, T.; Foltz, J.; Vite, J.; Pitman, G.; *Nature* **1969**, *221*, 477. (b) D'Silva, T.; Peck, D. *J. Org. Chem.* **1972**, *37*, 1828. (c) Hicks, D.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1976**, 869. (d) Sato, T.; Yamaguchi, S.; Kaneko, H. *Tetrahedron Lett.* **1979**, *20*, 1863. (e) Sakito, Y.; Mukaiyama, T. *Chem. Lett.* **1979**, 1027. (f) Jarosz, S.; Hicks, D.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 935. (g) Utaka, M.; Makimo, H.; Oota, Y.; Tsuboi, S.; Takeda, A. *Tetrahedron Lett.* **1983**, *24*, 2567.

(4) Selected other 6,8-dioxabicyclo[3.2.1]octanes: (a) Mundy, B.; Lipkowitz, K.; Dirks, G. *Heterocycles* **1977**, *6*, 51 and references therein. (b) Cole, R.; Dorner, J.; Lansden, J.; Cox, R.; Pape, C.; Cunfer, B.; Bedell, D. *J. Agric. Food Chem.* **1977**, *25*, 1197. (c) Ayer, W.; McCaskill, R. *Can. J. Chem.* **1987**, *65*, 15. (d) Copp, R.; Mundy, B. *Synth. Commun.* **1989**, *19*, 2851. (e) Amico, V.; Cunsolo, F.; Piatettelli, M.; Ruberto, G. *Phytochemistry* **1987**, *26*, 1719.

0022-3263/91/1956-1958$02.50/0

Scheme I



tinuing interest in a detailed analysis of the structural features of these compounds. Most early structural work on compounds of this type relied on ^{1}H NMR shifts and coupling constants[4a,5a,b] or mass spectral fragmentation patterns.[5c] The first crystalline ketal in this series, *exo*-7-phenyl-5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octane (**6**), provided an initial analysis of this system.[6]

We endeavored to synthesize a series of crystalline 6,8-dioxabicyclo[3.2.1]octanes to provide a more complete database on the structural features of these important compounds. We report here the details of the syntheses of six of these compounds, pertinent structural data, and the results of the crystal structure work on **4a** and **4c**.

Results and Discussion

The ketone 2-acetyl-6-methyl-3,4-dihydro-2*H*-pyran (**1**) is a useful precursor in the synthesis of substituted 6,8-dioxabicyclo[3.2.1]octanes. Previous studies have dealt with the addition to the carbonyl of **1** by Grignard reagents,[4a,5c] organoalanes,[1d] cuprates,[1b] and organolithium reagents.[1b,4a,d] Stabilized organolithium reagents are relatively easy to prepare,[7] and it was thought that a large lithium reagent might be employed to synthesize a solid 6,8-dioxabicyclo[3.2.1]octane. By the procedure of Parham and Piccirilli[7] the 2-, 3-, and 4-bromoanisoles were converted to their organolithium reagents by halogen–metal exchange. Ketone **1** was added to each lithium reagent at −78 °C. The intermediate alcohols were not isolated,[8] and after acid workup the 7-(2-, 7-(3-, and 7-(4-methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octanes (**4a–c**; **5a–c**) were recovered in good to excellent yield. (Scheme I).

All three ketal pairs were initially recovered as light yellow oily liquids. Over a period of 2 weeks, crystals were observed in the 2-methoxyphenyl (**4a**, **5a**) and 4-methoxyphenyl (**4c**, **5c**) functionalized ketals. The crystals were separated from the supernatant liquid and then recrystallized, and X-ray analyses were performed. Both solid forms were found to have the methoxyphenyl group in the exo-7 position (Figures 1 and 2). All exo/endo ketal pairs **4a–c**/**5a–c** were analyzed separately by GCMS, ^{13}C NMR, and ^{1}H NMR. Only slight differences were noted in the mass spectra and NMR spectra of the respective exo/endo isomers. However, isomer pairs **4a**/**5a**, **4b**/**5b**, and **4c**/**5c** showed significantly different retention times on a DB-5 column. The elution order—exo eluting after endo— is opposite that seen in other 7,7-disubstituted 6,8-dioxabicyclo[3.2.1]octanes having groups smaller than "phenyl" at C-7[9].

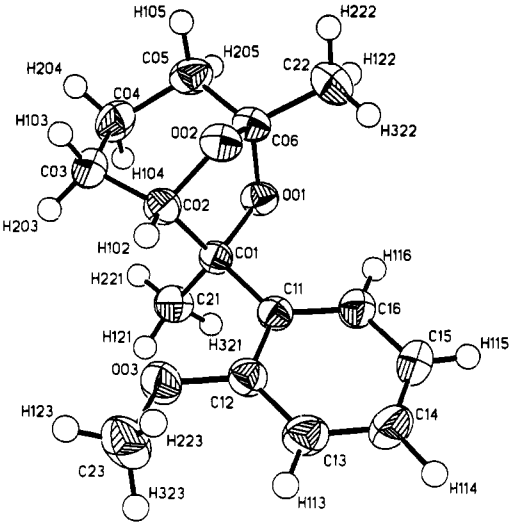


Figure 1. Thermal ellipsoid plot for **4a**. Isotropic thermal parameters for hydrogen atoms were fixed at a constant value for clarity; thermal ellipsoids were at the 50% level for all other atoms. Aromatic C–H averaged 0.97 (4) Å, methyl C–H distances averaged 0.98 (6) Å, and the other aliphatic C–H distances averaged 1.00 (5) Å. Esds for the C–C and C–O distances were 0.004 and 0.003 Å, respectively. The numbering is arbitrary.

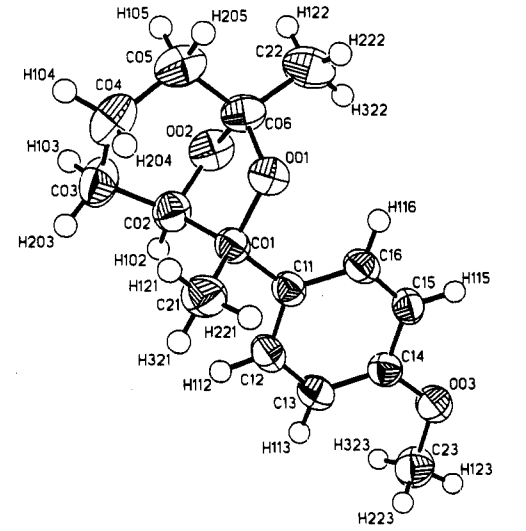


Figure 2. Thermal ellipsoid plot for **4c**. Isotropic thermal parameters for all hydrogen atoms were fixed at a constant value for clarity; thermal ellipsoids were drawn at the 50% probability level for all other atoms. Aromatic C–H distances averaged 0.94 (2) Å, methyl C–H distances averaged 0.97 (3) Å, and the other aliphatic C–H distances averaged 1.02 (5) Å. Esds for C–C and C–O distances were 0.005 and 0.004 Å, respectively. The numbering is arbitrary.

X-ray Crystallographic Study of 4a and 4c

The X-ray analysis of **4a** and **4c** confirms the basic skeletal features reported previously for *exo*-7-phenyl-

(5) (a) Gore, W.; Armitage, I. *J. Org. Chem.* **1976**, *41*, 1926. (b) Cologne, J.; Buendia, J.; Guignard, H. *Bull. Soc. Chim. Fr.* **1969**, *3*, 956. (c) Lipkowitz, K.; Scarpone, S.; Mundy, B.; Bornmann, W. *J. Org. Chem.* **1979**, *44*, 486.

(6) Mundy, B.; Dirks, G.; Larsen, R.; Caughlan, C. *J. Org. Chem.* **1978**, *43*, 2347.

(7) Parham, W.; Piccirilli, R. *J. Org. Chem.* **1977**, *42*, 257.

(8) Alcohols are difficult to isolate. See refs. 4a, 5c, and Mundy, B.; Lipkowitz, K.; Dirks, G. *Synth. Commun.* **1975**, *5*, 7.

(9) Bartelt, K. Ph.D. Dissertation, Montana State University, 1988.

Table I. Contents of Planes and Dihedral Angles in 4a, 4c, and 6

atoms used in least-squares plane	plane no.
C01, C11, C12, C13, C14, C15, C16	1
C11, C01, O01	2
C02, C01, O01, C06	3
C02, O02, C06	4
C02, C03, C05, C06	5
C03, C04, C05	6
C12, O03, C23 (4a)	7
C14, O03, C23 (4c)	

Dihedral angles (deg)

	plane				
compd	1–2	3–4	4–5	5–6	1–7
4a	10.0	45.5	66.6	35.1	11.1
4c	2.5	45.6	66.8	36.5	4.8
6	11.5	46.0	66.1	34.1	

5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octane (6).[6] In both 4a and 4c the pyran ring adopts a distorted chair conformation. The smallest angle, C02–O02–C06, averages 102.5°; the largest angle, C03–C04–C05, averages 112.4°. The five-membered ring is quite distorted with only C06–O01–C01 approaching 109° and the remaining angles ranging from 100 to 104.5°. Carbon–carbon bond lengths within the pyran ring and C01–C21 are within ranges observed for glycopyranosides. A wide variety of glycopyranosides have been studied by X-ray analysis and serve as reasonable models for the pyran portions of 4a and 4c.[10]

The C06-C22 bond in 4a, 4c, and 6 averages 1.498 Å, much shorter than an sp^3-sp^3 C-C bond.[11] In their X-ray crystallographic analysis of 3α,5-epoxy-6β-iodo-3β-methyl-A-homo-4-oxa-5α-cholestane (a modified steroid containing a 6,8-dioxabicyclo[3.2.1]octane fragment), Furusaki et al reported an even shorter (1.46 Å) bond distance between a methyl group and a carbon geminal to two ether oxygens.[12] X-ray studies of similar systems containing bridgehead-methyl-substituted bicyclo[3.2.1]octane fragments report values closer to 1.54 Å, the accepted mean sp^3-sp^3 C-C bond distance.[13] Thus the presence of an aectal group correlates with the shortening of the C06–C22 bond. While the lengths of the C06–C22 bonds in 4a and 4c are in the range reported for sp^3–sp^2 C–C bonds (1.50 Å),[11] the angles about C06 are 104–114.3 ° and fall in the range for non-acetal sites of glycopyranosides.[10] No additional π character is in evidence. Shortening of the bonds by inductive effects has been noted in pyranose sugars[14] and is presumed to account for the somewhat shortened C06–C22 in 4a, 4c, and 6 as well.

Examination of the calculated angles between the various planes in the molecules (Table I) illustrates several points. First, the system is apparently quite rigid in order to account for the observed close agreement in the angular values calculated for the various planes found in the bicyclic portion of each molecule. Second, the *exo*-phenyl group rotation relative to the C11–C01–001 plane varies over a range of only 9.0°. This suggests that molecular steric considerations are more important than any packing interactions. The sizes of the methyl group, C21, and the doubly substituted ring carbon, C02, would both be expected to be larger than the O01 ether oxygen atom. Consequently, the phenyl group is found in an eclipsed conformation relative to O01. In all three cases the conformation of choice is the one with the lowest energy eclipsed interaction.[15] Any other orientation of the phenyl group would produce substantially larger interactions with the larger methyl groups C21 or C02. Bondi[16] reported the intermolecular contact distance for an ether-type oxygen atom to be 1.47 Å, and the corresponding distances for methyl groups and aliphatic carbons to be 1.67–1.70 Å.

Conclusions

Six new 7,7-disubstituted-6,8-dioxabicyclo[3.2.1]octanes were synthesized by a previously unexplored route. X-ray crystallographic analysis of the two crystalline ketals 4a and 4c determined that in each case the methoxyphenyl group was in the exo position. From the X-ray structural data of 4a and 4c, earlier results regarding the rigidity of this bicyclic ketal system were confirmed. Although some C–C bonds were much shorter than 1.54 Å, these bond distances were not considered unusual when compared to those of other substituted pyrans such as glycopyranosides.

Experimental Section

General Methods. Melting points are uncorrected. Infrared spectra were measured in Nujol mulls. All ^{13}C and ^1H NMR spectra were recorded in $CDCl_3$. Mass spectra were recorded on a Hewlett Packard Model 5790A gas chromatograph equipped with a DB-5 capillary column and interfaced with a Model 5970 mass selective detector. All retention times refer to a temperature program of 150 °C for 3 min, increasing to 280 °C at the rate of 10 °C/min. High resolution mass spectra for accurate mass were obtained on exo/endo isomer pairs on a Varian Model 3700 gas chromatograph equipped with a 30-m DB-1 column and interfaced with a VG Model 7070 mass spectrometer.

Preparation of *exo*- and *endo*-7-(2-Methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octane (4a and 5a). To a solution of 2-bromoanisole (35.7 mmol, 4.45 mL) under a nitrogen atmosphere in 25 mL of freshly distilled THF at −78 °C was added *n*-BuLi (36.0 mmol, 14.3 mL of 2.5M) by a pressure equalizing dropping funnel over the period of 1 h. Ketone 1 (35.7 mmol, 5.00 g) in THF was added rapidly via syringe. The solution was stirred at room temperature for 1 h, quenched at 0 °C with 25 mL of 5% HCl, and stirred for 1 h. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were dried with $MgSO_4$. Distillation of the crude product gave 8.297 g (33.4 mmol, 93.6%) of ketals 4a/5a in the ratio 48/52. The capillary GC retention times were 10.22 and 8.93 min, respectively. Over the period of a week at room temperature, small clear crystals appeared. After separation from the supernate, the crystals were recrystallized from cyclohexane and submitted for X-ray analysis. This solid isomer was determined to be the *exo* isomer 4a and matched both capillary GC retention times and mass spectral data of the later eluting isomer. 4a: mp 134 °C; ^1H NMR (250 Hz) δ 1.54 (s, 3 H), 1.66 (s, 3 H), 1.5–1.9 (m, 5 H), 2.09 (m, 1 H), 3.80 (s, 3H), 4.74 (br s, 1 H), 6.85 (d, 1 H, J = 7.4 Hz), 6.99 (dd, 1 H, J = 7.4, 1 Hz), 7.23 (dd, 1 H, J = 7.4, 1 Hz), 7.67 (dd, 1 H, J = 7.4, 1 Hz); ^{13}C NMR δ 154.71, 135.78, 127.90, 127.00, 120.22, 110.83, 107.17, 83.88, 80.20, 54.90, 34.31, 24.91, 23.97, 20.26, 17.19; IR 1598, 1582, 1240, 1035, 754; EIMS, m/e (rel intensity) 248 (31), 205 (3), 187 (32), 135 (35), 98 (100), 43 (86); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1407. 5a: ^1H NMR (60 MHz) δ 1.0–2.0 (m, 6 H), 1.52 (s, 3 H), 1.55 (s, 3 H), 2.13, (s, 1 H), 3.80 (s, 3 H), 4.58 (br s, 1 H), 7.03 (m, 3 H), 7.75 (dd, 1 H, J = 6.2 Hz); EIMS, m/e (rel intensity) 248 (28), 233 (23), 187 (50), 135 (70), 98 (100), 43 (100); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1410.

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Preparation of *exo*- and *endo*-7-(3-Methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.3.1]octane (4b and 5b). The reaction was repeated with 3-bromoanisole (31.6 mmol, 4.00 mL), *n*-BuLi (32.5 mmol, 13 mL of 2.5 M), and ketone 1 (31.6 mmol, 4.42 g). It was unclear by ^{1}H NMR analysis of the mixture whether cyclization was complete, so the crude product was stirred for 18 h in 30 mL of benzene and 0.1 g of *p*-toluenesulfonic acid. The reaction was quenched with Na_2CO_3, extracted into CH_2Cl_2 (3 × 30 mL), dried ($MgSO_4$), concentrated, and filtered through Florisil. Only 2.835 g (11.4 mmol) was recovered (36%). Analysis of the mixture by GCMS indicated two isomers, ratio 56/44, having capillary GC retention times of 9.41 and 10.84 min, respectively. The earlier eluting isomer was tenatively identified as the *endo* isomer **5b** because the 2- and 4-methoxy-substituted ketals eluted in this order. Furthermore, the 2- and 4-methoxy-substituted endo ketals contain a *m/e* 233 peak in the mass spectrum, which is lacking in the mass spectrum of the exo ketal. Neither isomer ever crystallized, and no further separations were performed. NMR assignments are made on the basis of peak integrations for analogous protons or carbons. **4b*/5b#**: ^{1}H NMR (363 MHz) δ 1.2–2.2 (m, 6 H), 1.52# (s, 3 H), 1.53* (s, 3 H), 1.54* (s, 3 H), 1.59# (s, 3 H), 3.81* (s, 3 H), 3.80# (s, 3 H), 4.39* (br s, 1 H), 4.46# (br s, 1 H), 6.76 (td, 1 H, *J* = 8.2, 2.3 Hz), 6.92 (br t, 1 H, *J* = 9.6 Hz), 7.03 (dt, 1 H, *J* = 10.3, 1.8 Hz), 7.23 (td, 1 H, *J* = 8.4, 4.0 Hz); ^{13}C NMR δ 159.13, 150.35, 145.37, 129.28, 128.82 (2 C), 117.90, 116.87, 113.73, 111.51, 111.37, 110.75, 108.15#, 107.91*, 85.32#, 84.56*, 82.26*, 81.88#, 54.98*,#, 34.61*, 34.15#, 31.82#, 25.83#, 24.86*,#, 24.23*, 23.21*, 17.06*, 16.25#. **4b**: EIMS, *m/e* (rel intensity) 248 (25), 205 (7), 187 (30), 161 (32), 135 (20), 98 (80), 43 (100); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1412. **5b**: EIMS, *m/e* (rel intensity) 248 (15), 233 (5), 205 (4), 187 (20), 161 (21), 135 (25), 98 (100), 43 (86); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1407.

Preparation of *exo*- and *endo*-7-(4-Methoxyphenyl)-5,7-dimethyl-6,8-dioxabicyclo[3.2.1]octane (4c and 5c). As previously described, 4-bromoanisole (35.7 mmol, 4.47 mL) was reacted with *n*-BuLi (40.0 mmol, 16.0 mL of 2.5 M) and ketone 1 (35.7 mmol, 5.00 g). The reaction was quenched with 25 mL of 5% HCl, allowed to stir 12 h, and worked up as described in the synthesis of **4a** and **5a**. GCMS analysis showed two components only, ratio 54/46, eluting at 9.83 and 11.11 min. No further purifications were performed. Recovered material totalled 8.689 g (98.0%). After ca. 10 days at room temperature, flaky opaque crystals came out of solution. Capillary GC retention time and the mass spectrum of these crystals corresponded to that of the later eluting ketal. Crystals suitable for X-ray analysis were separated from the supernate and recrystallized from hexane as platelets. By X-ray analysis the platelets were determined to be the exo isomer **4c**. **4c**: mp 101 °C; ^{1}H NMR (250 MHz) δ 1.50 (s, 3 H), 1.58 (s, 3 H), 1.60–2.18 (m, 6 H), 3.78 (s, 3 H), 4.41 (br s, 1 H), 6.85 (d, 2 H, *J* = 8.4 Hz), 7.32 (d, 2 H, *J* = 8.4 Hz); ^{13}C NMR δ 157.99, 140.73, 125.57, (2 C), 113.13 (2 C), 107.82, 84.31, 82.23, 55.01, 34.18, 24.91, 24.26, 23.32, 17.06; EIMS, *m/e* (rel intensity) 248 (25), 205 (20), 187 (30), 161 (55), 135 (68), 98 (100), 43 (43); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1408. **5c**: ^{1}H NMR (250 MHz) δ 1.48 (s, 3 H), 1.53 (s, 3 H), 1.1–1.8 (m, 6 H), 3.80 (s, 3 H), 4.36 (br s, 1 H), 6.85 (d, 2 H, *J* = 8.1 Hz), 7.29 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR δ 157.99, 135.69, 126.37 (2 C), 113.13 (2 C), 107.94, 85.06, 81.93, 55.01, 34.58, 31.90, 25.81, 24.91, 16.08; IR 1511, 1244, 1038, 845; EIMS, *m/e* (rel intensity) 248 (9), 233 (4), 205 (10), 161 (25), 135 (40), 98 (77), 43 (100); exact mass calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1406.

Crystal Structure Analyses: General Remarks. For both crystal structure analyses, intensity data were collected at 23 °C on a Nicolet R3mE four-circle diffractometer equipped with a graphite monochromator (Mo K_α radiation, λ = 0.71069 Å) using the ω-scan method with fixed scan speeds out to a $2\theta_{max}$ of 65.0°. Three standard reflections were collected periodically through the data collections, in both cases, to check for crystal alignment and deterioration. The structures were solved by direct methods.[17] All refinements were done by block-cascade least squares, minimizing $\Sigma w(|F_o| - |F_c|)^2$ with 101 parameters refined in each full-matrix block.[17] Hydrogen atoms were located from difference maps at an intermediate stage of refinement (unit weighing), refining until the hydrogen atom parameters converged (isotropic thermal parameters for the hydrogen atoms and anisotropic thermal parameters for the carbon and oxygen atoms), and held constant during the weighted refinement, which used the weighting scheme $w = k[\sigma^2F_o + 0.0015F_o^2]^{-1}$. The numbering scheme used in the two structures is shown in the thermal ellipsoid plots (Figures 1 and 2). Atomic parameters, bond distances, and unit cell data for both structures are available in the supplementary data.[18]

Ketal 4a. The crystal used for data collection had dimensions of 0.70 × 0.70 × 0.41 mm^3 and was mounted on a glass fiber with epoxy cement. The total data collection included 5084 intensity measurements of which 4759 were considered unique and 2039 were observed at the $6\sigma_F$ level (approximately equivalent to $3\sigma_I$). Lorentz and polarization corrections were applied to the data in the usual manner; no corrections were made for absorption or extinction (μ = 0.80 cm^{-1}). R = 0.048 for the observed data, R_w = 0.055, GOOF = 1.18, and R = 0.151 for the unique data set. The maximum residual electron density $\Delta\rho$ = 0.16 e Å^{-3} and the minimal value was −0.26 e Å^{-3}.

Ketal 4c. The crystal chosen for data collection was approximately 0.87 × 0.56 × 0.24 mm^3 and was mounted in the same manner as **4a**. The total data collection included 5679 intensity measurements of which 4848 were considered unique and 1570 were considered observed at the $6\sigma_F$ level. Lorentz and polarization corrections were applied to the data in the normal manner; no corrections were made for absorption or extinction (μ = 0.78 cm^{-1}). R = 0.046 for the observed data, R_W = 0.051, GOOF = 1.098, and R = 0.104 for the unique data set. The maximum residual electron density $\Delta\rho$ = 0.16 e Å^{-3} and the minimal value was −0.25 e Å^{-3}.

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Supplementary Material Available: Full tables of crystallographic data, unit cell parameters, bond distances and angles, atomic coordinates, isotropic and anisotropic thermal parameters, and hydrogen atom coordinates and ^{1}H and ^{13}C NMR spectra of title compounds (22 pages). Ordering information is given on any current masthead page.

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A Rapid and Efficient Synthesis of Chiral 2-Hydro 2-Oxazolines

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During the course of our studies on asymmetric synthetic methods we required a fast, general, and efficient route to a variety of chiral 2-H oxazolines, **3**. In searching the literature, we found a number of methods[1-7] of varying

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