Notes

Synthesis of Cyclohex-1-ene-1,6-dicarbaldehydes via Diels–Alder Reactions with Furans

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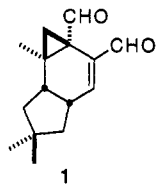
Introduction

A considerable number of terpenoid natural products containing an unsaturated 1,4-dialdehyde functionality has been isolated from various natural sources such as fungi, plants, insects, and molluscs. Examples are isovelleral (**1**),[1] merulidial (**2**),[2] polygodial (**3**),[3] and scalaradial (**4**).[4] Many of these compounds have been shown to possess potent biological activities,[5,6] which appear to be strongly connected to the unsaturated dialdehyde functionality,[7,8] although large qualitative and quantitative activity differences have been observed. Small structural changes, like stereoisomerization, may affect the biological activity dramatically.[9,10]



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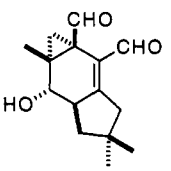

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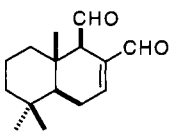

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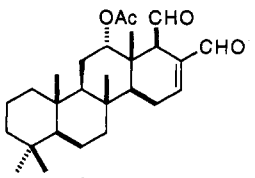

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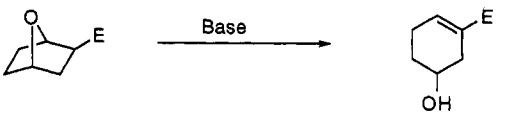
Most of the natural unsaturated dialdehydes have been prepared synthetically,[11] but surprisingly few synthetic studies on simpler derivatives containing the cyclohex-1-ene-1,6-dicarbaldehyde part of compounds **1**–**4** have been reported. The only example is, to our knowledge, 4,4-dimethylcyclohex-1-ene-2,3-dicarbaldehyde, prepared by regioselective formylation of 4,4-dimethylcyclohex-2-enone.[12] In an on-going study of the relationship between structure and activity for unsaturated dialdehydes, the lipophilicity of the compounds appears to influence some of their activities.[10,13] In order to investigate this effect we required a set of similar unsaturated dialdehydes which mainly differ in their lipophilicity, e.g., a series of cyclohex-1-en-1,6-dicarbaldehydes substituted with an alkyl group of variable length. It was also desirable[14] that the target compounds are functionalized in a way to facilitate their transformation to the corresponding cyclopropane derivatives (i.e., 6-alkylbicyclo[4.1.0]hept-2-ene-1,2-dicarbaldehydes).

The usefulness of 7-oxabicyclo[2.2.1]heptane or heptene derivatives as key intermediates in the syntheses of several natural products has recently been demonstrated,[15] and the number of selective transformations of the 7-oxabicyclo[2.2.1]heptene system reported also reflects its benefits.[15,16] Especially interesting to us was the base-induced opening of the oxygen bridge via the β-elimination shown below, previously used in stereospecific syntheses of a number of shikimic acid derivatives[17] and other cyclohexenes[18] (eq 1).



(1)

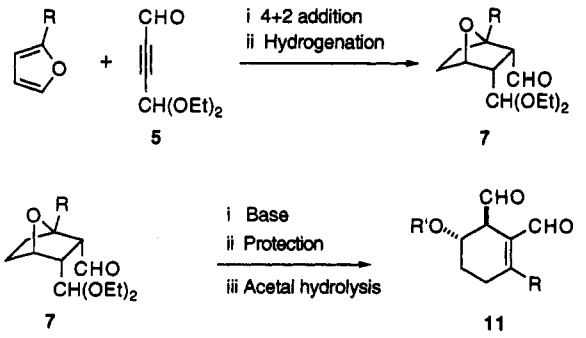
E=CO_2R, CN, SO_2Ph, COR

The use of 4,4-diethoxybut-2-ynal (**5**) as a acetylenedicarbaldehyde synthon facilitates the simple introduc-

(1) Magnusson, G.; Thoren, S.; Wickberg, B. *Tetrahedron Lett.* **1972**, 1105.
(2) Giannetti, B.; Steffan, B.; Steglich, W.; Quack, W.; Anke, T. *Tetrahedron* **1986**, *42*, 3579.
(3) Barnes, C. S.; Loder, J. W. *Austr. J. Chem.* **1962**, *15*, 322.
(4) Cimino, G.; De Stefano, S.; Minale, L. *Experientia* **1974**, *30*, 846.
(5) Kubo, I.; Ganjian, I. *Experientia* **1981**, *31*, 1063.
(6) Anke, H.; Sterner, O. *Planta Medica* **1991**, *57*, 344.
(7) Sterner, O.; Carter, R. E.; Nilsson, L. M. *Mutat. Res.* **1987**, *188*, 169.
(8) Fritz, G. L.; Mills, G. D.; Warthen, J. D.; Waters, R. M. *J. Chem. Ecol.* **1989**, *15*, 2607.
(9) Caprioli, V.; Cimino, G.; Colle, R.; Gavagnin, M.; Sodano, G.; Spinella, A. *J. Nat. Prod.* **1987**, *50*, 146.
(10) Andersson, M.; Bocchio, F.; Sterner, O.; Forsby, A.; Lewan, L. *Toxicol. in Vitro* **1993**, *7*, 1.
(11) Synthesis of isovelleral: (a) Thompson, S. K.; Heathcock, C. H. *J. Org. Chem.* **1992**, *57*, 5979. (b) Bergman, R.; Hansson, T.; Sterner, O.; Wickberg, B. *J. Chem. Soc., Chem. Commun.* **1990**, 865. Synthesis of merulidial: Trost, B. M.; Hipskind, P. A. *Tetrahedron Lett.* **1992**, *33*, 4541. Synthesis of polygodial, waburganal, cinnamodial, and related drimanes. For a review, see: de Groot, A.; van Beek, T. A. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 1. (c) Kutney, J. P.; Piotrowska, K.; Chen, Y.-H.; Cheng, K.-P. N.; Gao, Z.; Rettig, S. J. *Can. J. Chem.* **1990**, *68*, 1699. (d) Jansen, B. J. M.; Sengers, H. W. J. M.; Bos, H. J. T.; de Groot, A. *J. Org. Chem.* **1988**, *53*, 855. (e) He, J.-F.; Wu, Y.-L. *Tetrahedron* **1988**, *44*, 1933. (f) Mori, K.; Takaishi, H. *Liebigs Ann. Chem.* **1989**, 695. Synthesis of marasmic acid: (g) Woodward, R. B.; Greenlee, W. J. *Tetrahedron* **1980**, *36*, 3361. (h) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1980**, *102*, 7146. (i) Tobe, Y.; Yamashita, D.; Takahashi, T.; Inata, M.; Sato, J.-I.; Kakiuchi, K.; Kobiro, K.; Odaira, Y. *J. Am. Chem. Soc.* **1990**, *112*, 775. Synthesis of velleral: Froborg, J.; Magnusson, G. *J. Am. Chem. Soc.* **1978**, *100*, 6728.
(12) Guillerm, D.; Boussac, G.; Lalande, J.; Lemaitre, P.; Lallemand, J.-Y. *Synthetic communications*, **1981**, *11*(8), 627.
(13) Forsby, A.; Walum, E.; Sterner, O. *Chem.-Biol. Interact.* **1992**, *84*, 85.
(14) The presence of a cyclopropane ring in these systems, as in isovelleral (**1**) and merulidial (**2**), has been suggested to enhance the mutagenic activity of these compounds (see ref 7), and it is our intention to study this in the future.
(15) For a review, see: Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173.
(16) For a review, see: Ager, D. J.; East, M. B. *Tetrahedron* **1993**, pp 5707–5713.
(17) (a) Campbell, M. M.; Mahon, M. F.; Sainsbury, M.; Searle, P. A. *Tetrahedron Lett.* **1991**, *32*, 951 and references cited therein. (b) Koreeda, M.; Jung, K.-Y.; Ichita, J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2129. See also: Moore, S. M.; Cho, H.; Casati, R.; Kennedy, E.; Reynolds, K. A.; Mocek, U.; Beale, J. M.; Floss, H. G. *J. Am. Chem. Soc.* **1993**, *115*, 5254.
(18) (a) Brion, F. *Tetrahedron Lett.* **1982**, *23*, 5299. (b) Keay, B. A.; Rajapaksa, D.; Rodrigo, R. *Can. J. Chem.* **1984**, *62*, 1093. (c) Yang, W.; Koreeda, M. *J. Org. Chem.* **1992**, *57*, 3836. (d) Guildford, A. J.; Turner, R. W. *J. Chem. Soc., Chem. Commun.* **1983**, 466.

0022-3263/94/1959-3994$04.50/0

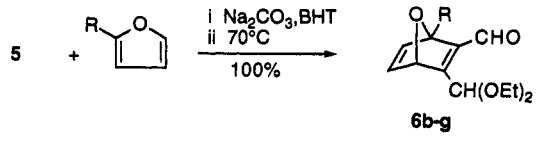
Scheme 1



tion of a 1,4-dialdehyde functionality into different ring systems.[19] Cycloaddition of **5** with furan or 2-alkylfurans, followed by the hydrogenation of the double bonds, base-induced β-elimination (*vide supra*), and hydroxyl group protection (according to Scheme 1) would after final acetal hydrolysis give a suitable product.

Results and Discussion

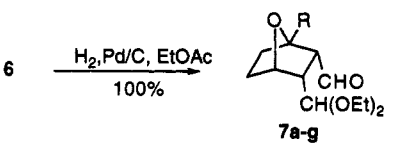
The Diels–Alder reaction between furan and the acetylene **5** to produce the diene **6a** has been reported previously.[20] The same reaction with various 2-alkylfurans to produce dienes **6b–g** (eq 2) proceeded smoothly, in quantitative yields and with complete regioselectivity.



(2)

b: R =CH_3, c: R=C_2H_5, d: R=n-C_4H_9, e: R=n-C_5H_{11}, f: R=n-C_7H_{15}, g: R=n-C_8H_{19}

The addition of small amounts of Na_2CO_3 and of the antioxidant 2,6-di-*tert*-butyl-4-methylphenol (BHT) to the dienophile before adding the furan prevented the formation of polymers and side products.[21] Increasing the chain length of the alkyl group increased the reaction time somewhat, while the use of a solvent (methylene chloride or toluene) made the reaction very slow (only traces of the product are formed after 24 h). The hydrogenation was accomplished in quantitative yield by using Pd–C as catalyst and ethyl acetate as solvent (eq 3). The solvent was of great importance; methanol or acetone gave no hydrogenation product while ethanol or 2-propanol resulted in the formation of side products.

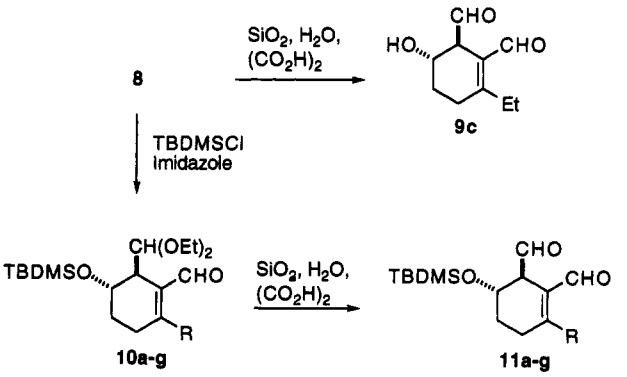


(3)

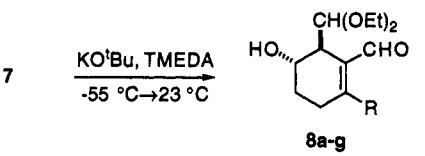
a: R=H, b: R =CH_3, c: R=C_2H_5, d: R=n-C_4H_9, e: R=n-C_5H_{11}, f: R=n-C_7H_{15}, g: R=n-C_8H_{19}

Only the endo isomer was obtained, and the stereochemistry was confirmed by comparing the experimental coupling constants with theoretical values.[22,23] For compound **7a**, J_{1-2} = 5.2 Hz (calculated value 5.04 Hz for the endo isomer and 0.32 Hz for the exo isomer) and J_{2-3} = 11.8 Hz. The ring opening of the 7-oxabicyclo[2.2.1]-heptane derivatives **7a–g** was performed by using KO^t-Bu[24] (3–5 equiv) in neat TMEDA,[25] giving the corresponding alcohols **8a–g** as the unique products in 80–90% yield (eq 4).

Scheme 2



a: R=H, b: R =CH_3, c: R=C_2H_5, d: R=n-C_4H_9, e: R=n-C_5H_{11}, f: R=n-C_7H_{15}, g: R=n-C_8H_{19}



(4)

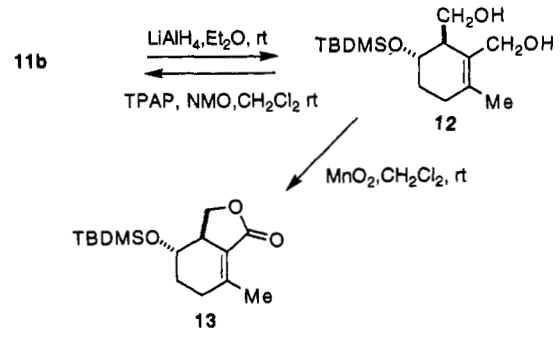
a: R=H, b: R =CH_3, c: R=C_2H_5, d: R=n-C_4H_9, e: R=n-C_5H_{11}, f: R=n-C_7H_{15}, g: R=n-C_8H_{19}

The alcohols **8** obtained from the ring opening were in a first attempt hydrolyzed directly to their corresponding dialdehydes **9** with wet silica gel[26] or Amberlyst 15.[27] However, the yields were poor (30–50% after chromatography), and the dialdehyde alcohols were somewhat unstable. The transformation of the alcohols to the corresponding silyl ethers **10a–g** using TBDMSCl/imidazole prior to the hydrolysis of the acetals with SiO_2/H_2O/oxalic acid[26] gave the more stable dialdehyde silyl ethers **11a–g**.

The yields for the five steps described above were in most cases quantitiative (i.e., TLC and NMR analyses of the crude products indicated that all starting material was consumed and that only one product was formed). The intermediate products were therefore normally used directly for the next step, and only the final products

(19) Gorgues, A. *Janssen Chim. Acta* **1986**, *4*, 21.
(20) Gorgues, A.; Simon, A.; Le Coq, A.; Hercouet, A.; Corre, F. *Tetrahedron* **1986**, *42*, 351.
(21) If care is not taken to remove traces of acid from the acetylene **5**, the 2-alkylfurans give Michael reaction products.
(22) MM calculations were performed with the MacMimic (v. 2.9)/MM2(91) (v. 1.0) software package for Macintosh Quadra, obtained from InStar Software AB (Lund, Sweden).
(23) Vicinal proton–proton coupling constants were calculated according to the 3JHHM extended Karplus program: Imai, K.; Osawa, E. *Magn. Reson. Chem.* **1990**, *28*, 668.
(24) The choice of base is crucial and the bases used previously for similar openings such as NaOMe, LDA, and LiHMDS (see refs 17 and 18) resulted in lower yields and/or side products.
(25) A number of different solvents (DMSO, t-BuOH, THF, toluene, heptane) were investigated, and neat TMEDA gave the best results.
(26) Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 63.
(27) Coppola, G. M. *Synthesis* **1984**, 1021.

Scheme 3



(**11a–g**) were purified by chromatography, giving the cyclohexene-1,6-dialdehydes in overall isolated yields of over 70%.

In order to determine the relative stereochemistry of the products, the dialdehyde **11b** was reduced to the corresponding diol **12** (which upon oxidation with TPAP/NMO[28] reverted to **11b**) and converted to the unsaturated lactone **13** by oxidation with MnO_2.

^{1}H NOE experiments with the lactone **13** showed enhancements of 5-H when 7-H_a was irradiated and of 6-H when 7-H_b was irradiated, confirming the configuration shown in structure **11b**. J_{5-6} is small in all the dialdehydes **11a–g** (less than 1 Hz), and it is reasonable to assume that they all have the same configuration. The magnitude of J_{5-6} in the dialdehydes **11** suggests that the 5-TBDMSO and the 6-aldehyde substituents are in a transdiaxial position, and this was confirmed by MM2 calculations.[22] The steric energy of the transdiaxial conformer was almost 3 kcal/mol lower compared to the *trans-diequatorial conformer*, and the dihedral angles for 5-H/C-5/C-6/6-H was found to be 70° in the former and 25° in the latter.

Conclusions

Cyclohexene-1,6-dicarbaldehydes are readily available in good yields from simple starting materials with the method described here. In addition to a facile preparation of new derivatives for QSAR studies of unsaturated dialdehydes, these multifunctional cyclohexene derivatives may serve as useful building blocks in organic synthesis. Efforts are now made to employ this methodology for the synthetic preparation of natural unsaturated dialdehydes and their isomers.

Experimental Section

General ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded at 23 °C in $CDCl_3$ solutions, the chemical shifts are given in δ (ppm) with the solvent peaks (7.26 and 77.0 ppm, respectively) as reference. Air- and/or moisture-sensitive reactions were carried out in oven-dried glassware under argon atmosphere with dry solvents. EIMS analyses were performed at 70 keV. Melting points are uncorrected.

General Procedure for the Diels–Alder Reaction. A total of 1.2 equiv of the respective furan, a few milligrams of Na_2CO_3, and 0.1 equiv of BHT was added to 1.0 equiv of 4,4-diethoxy-2-butyn-1-al (prepared according to Gorgues[29]) in a high-pressure glass tube. The tube was filled with argon and sealed. The mixture was heated in an oil bath at 70 °C for 5–20 h (depending on the chain length). After the mixture was cooled to rt and excess furan was evaporated, the product was obtained in quantitative yield as a yellow oil. (For preparation of **6a** see ref 20.) Removal of BHT was accomplished by flash chromatography, although it was not necessary for the following steps.

2-Formyl-3-(diethoxymethyl)-1-methyl-7-oxabicyclo[2.2.1]-hepta-2.5-diene (6b): ^{1}H NMR 1.90 (s, 1 H), 1.22 (dt, 6 H, J = 7.1 Hz), 3.45–3.65 (m, 4 H), 5.37 (d, 1 H, J = 2.1 Hz), 5.51 (s, 1 H), 6.90 (d, 1 H, J = 5.2 Hz), 7.02 (dd, 1 H, J = 2.1, 5.2 Hz), 10.16 (s, 1 H); ^{13}C NMR 15.1, 15.1, 16.3, 61.7, 62.0, 82.6, 92.3, 97.7, 143.1, 146.6, 152.0, 171.4, 187.5; HREIMS *m/z* calcd for $C_{14}H_{18}O_4$ $(M)^+$ 238.1205, obsd 238.1221.

General Procedure for Hydrogenation. The substrate dissolved in ethyl acetate (80 mg/mL) and 10% by weight of 10% palladium on carbon was stirred vigorously for 15–30 min under hydrogen gas at atmospheric pressure. Filtering through Celite and removal of the solvent gave the product in quantitative yield as a pale yellow oil. **Note: On a larger scale, cooling is necessary due to heat generated from the exothermic reaction.**

2-*endo*-Formyl-3-*endo*-(diethoxymethyl)-1-methyl-7-oxabicyclo[2.2.1]heptane (7b): ^{1}H NMR 1.13 (dt, 6 H, J = 7.0 Hz), 1.41–1.46 (m, 2 H), 1.44 (s, 3 H), 1.76–2.04 (m, 2 H), 2.80–2.93 (m, 2 H), 3.35–3.68 (m, 4 H), 4.40–4.46 (m, 1 H), 4.78 (d, 1 H, J = 9.3 Hz), 9.71 (d, 1 H, J = 3.9 Hz); ^{13}C NMR 15.1, 15.4, 21.0, 26.7, 31.6, 49.0, 59.2, 61.0, 61.3, 78.6, 86.9, 100.3, 201.7; HREIMS *m/z* calcd for $C_{11}H_{17}O_3$ $(M - EtO)^+$ 197.1178, obsd 197.1153.

General Procedure for Ring Opening. KO^{t}Bu (3–5 equiv) and 0.1 equiv of BHT were added to approximately 100 equiv of freshly destilled TMEDA, and the mixture was cooled to −75 °C at which time TMEDA solidified, whereafter vacuum was applied to remove all traces of oxygen and the flask was filled with argon. The temperature was raised to −50 °C, and the substrate was added dropwise via syringe. After the addition was complete, the temperature of the solution was allowed to rise to rt and kept there for 1–3 h. The reddish solution was cooled to −20 °C, quenched with saturated NH_4Cl, and extracted with EtOAc. Washing, drying, and evaporation of the EtOAc solution afforded the alcohol as an oil which was directly subjected to silylation. The alcohols were isolated by flash chromatography in 80–90% yield but for the purpose of preparing the dialdehydes it was more convenient to purify the corresponding TBDMS ether.

5-Hydroxy-1-methyl-6-(diethoxymethyl)-1-cyclohexenecarbaldehyde (8b): ^{1}H NMR 1.07 (t, 3 H, J = 7.0 Hz), 1.22 (t, 3 H, J = 7.0 Hz), 1.48–1.61 (m, 1 H), 1.95–2.07 (m, 1 H), 2.17 (s, 3 H), 2.24–2.31 (m, 2 H), 2.85–2.90 (m, 1 H), 3.25–3.37 (m, 1 H), 3.54, 3.80 (m, 3 H), 4.28–4.35 (m, 1 H), 4.86 (d, 1 H, J = 3.4 Hz), 10.06 (s, 1 H); ^{13}C NMR 15.3, 15.4, 18.9, 27.3, 31.6, 46.0, 64.5, 64.7, 65.6, 103.9, 131.1, 158.8, 191.2; HREIMS *m/z* calcd for $C_{13}H_{22}O_4$ $(M)^+$ 242.1518, obsd 242.1522.

2-Ethyl-5-hydroxycyclohex-1-ene-1,6-dicarbaldehyde (9c). Acetal hydrolysis according the general procedure (see below) and flash chromatography afforded the dialdehyde as a pale yellow oil in 50% yield: R_f 0.23 (heptane/EtOAc (1:3)); ^{1}H NMR 1.22 (t, 3H, J = 7.6 Hz), 1.68–1.90 (m, 2 H), 2.19–2.72 (m, 6H), 3.42–3.52 (m, 1H), 4.18–4.24 (m, 1H), 9.40 (d, 1H, J = 1.6 Hz), 10.12 (s, 1H); ^{13}C NMR 14.6, 25.7, 27.3, 28.2, 54.1, 65.0, 128.2, 165.9, 189.8, 200.8; HREIMS *m/z* calcd for $C_{10}H_{12}O_2$ $(M - H_2O)^+$ 164.0837, obsd 164.0821.

General Procedure for Silylation. To a mixture of *tert*-butyldimethylsilyl chloride (2 equiv) of imidazole (2.5 equiv) in CH_2Cl_2 (4 mL/g of alcohol) was added the alcohol in one portion. A suspension was quickly formed which was stirred at rt until TLC revealed that no starting material was left. Methanol was added, and the solution was stirred for 10 min, diluted with EtOAc, washed twice with 1 M $NaHSO_4$, dried with Na_2SO_4, and concentrated *in vacuo*. Purification of the product by flash chromatography on silica gel afforded the silyl ethers as colorless oils in over 80% yield from **5**.

5-[(tert-Butyldimethylsilyl)oxy]-2-methyl-6-(diethoxymethyl)-1-cyclohexenecarbaldehyde (10b): R_f 0.30 (heptane/EtOAc (9:1)); ^{1}H NMR 0.029 (s, 3 H), 0.036 (s, 3 H), 0.82 (s, 9 H), 1.09 (t, 3 H, J = 7.0 Hz), 1.22 (t, 3 H, J = 7.0 Hz), 1.55–1.67 (m, 1 H), 1.95–2.11 (m, 2 H), 2.17 (s, 3 H), 2.35–2.51 (m, 1 H), 2.80–2.90 (m, 1 H), 3.22–3.34 (m, 1 H), 3.54–3.72 (m, 3 H), 4.38–4.43 (m, 1 H), 4.47 (d, 1 H, J = 4.0 Hz), 10.10 (s, 1 H); ^{13}C NMR −4.9, −4.8, 15.1, 15.3, 18.0, 18.9, 25.8, 26.7, 29.7,

(28) Griffith, W. P.; Ley, S. V.; Whitecombe, G. P.; White, A. D. *Chem. Commun.* **1987**, 1625.

(29) Gorgues, A.; Stephan, D.; Belyasmine, A.; Khanous, A.; Le Coq, A. *Tetrahedron* **1990**, *46*, 2817.

44.2, 63.8, 64.0, 64.0, 103.2, 130.2, 158.5, 191.6; HREIMS *m/z* calcd for $C_{19}H_{36}O_4Si(M)^+$ 356.2383, obsd 356.2366.

General Procedure for Acetal Hydrolysis.[26] A 0.1-mL portion of 10% solution of oxalic acid in water was added to a suspension of 0.9 g of silica gel in 10 mL of CH_2Cl_2. After the mixture was stirred for 2–3 min, the acetal (0.1 g) was added and stirring was continued at rt for 1–2 h. The reaction was stopped by adding solid $NaHCO_3$ and further stirring for 10 min. The suspension was filtrated, the silica gel was washed with EtOAc, and the filtrate was concentrated *in vacuo* to give the pure dialdehyde as a pale yellow oil, which after chromatography gave crystalline compounds in 90–95% yield.

5-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-1-cyclohexene-1,6-dicarbaldehyde (11b): R_f 0.14 (heptane/EtOAc (9:1)); mp 44–45 °C; ^{1}H NMR 0.05 (s, 3 H), 0.07 (s, 3 H), 0.85 (s, 9 H), 1.54–1.80 (m, 2 H), 2.13–2.30 (m, 1 H), 2.25 (s, 3 H), 2.40–2.56 (m, 1 H), 3.54–3.62 (m, 1 H), 4.32–4.40 (m, 1 H), 9.69 (d, 1 H, J = 1.2 Hz), 10.14 (s, 1 H); ^{13}C NMR −5.0, −4.7, 18.0, 18.7, 25.7, 27.4, 30.2, 54.4, 65.0, 129.1, 159.8, 190.0, 200.6; HREIMS *m/z* calcd for $C_{11}H_{17}O_3Si$ (M − *t*-Bu)$^+$ 225.0947, obsd 225.0931.

5-[(*tert*-Butyldimethylsilyl)oxy]-1,6-bis(hydroxymethyl)-2-methyl-1-cyclohexene (12). To a suspension of $LiAlH_4$ (excess) in ether at 0 °C was added a solution of the dialdehyde (**11b**) (12.4 mg, 0.044 mmol) in either dropwise. After the addition was complete, the ice bath was removed and the reaction was allowed to reach rt. The reaction was complete in less than 5 min and was quenched with EtOAc and a few drops of 6 M NaOH. Filtration of the resulting precipitate through Na_2SO_4/Celite and concentration *in vacuo* gave the diol as a colorless oil in quantitative yield: ^{1}H NMR 0.076 (s, 3 H), 0.085 (s, 3 H), 0.88 (s, 9 H), 1.51–1.64 (m, 1 H), 1.68–1.83 (m, 1 H), 1.75 (s, 3 H), 2.02–2.12 (m, 2 H), 2.12–2.22 (m, 1 H), 2.7 (bs, 1 H), 2.9 (bs, 1 H), 3.75–3.92 (m, 3 H), 3.97 (d, 1 H, J = 11.4 Hz), 4.36 (d, 1 H, J = 11.4 Hz); ^{13}C NMR −4.8, −4.3, 18.0, 19.0, 25.8, 30.2, 30.2, 50.2, 61.4, 62.0, 68.9, 127.6, 136.0; HREIMS *m/z* calcd for $C_{11}H_{19}O_2Si$ (M − *t*-Bu - H_2O)$^+$ 211.1154, obsd 211.1146.

5-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-9-oxo-8-oxabicyclo[4.3.0]non-1-ene (13). The diol **12** (13.5 mg, 0.047 mmol) was stirred in a suspension of MnO_2 (excess) in CH_2Cl_2 at rt for 24 h. Filtration, concentration, and chromatography of the resulting residue (heptane/EtOAc (9:1–2:1)) afforded the lactone as a white crystalline solid (6.5 mg, 50% yield): R_f 0.57 (heptane/ethyl acetate (2:1)); mp 76–78 °C; ^{1}H NMR 0.051 (s, 3 H), 0.069 (s, 3 H), 0.88 (s, 9 H), 1.60–1.73 (m, 1 H), 1.85–1.95 (m, 1 H), 2.11 (d, 3 H, J = 2.7 Hz), 2.22–2.49 (m, 2 H), 2.93–3.07 (m, 1 H), 3.57–3.66 (m, 1 H), 3.83 (dd, 1 H, J = 8.5, 9.9 Hz), 4.54 (apparent t, 1 H, J = 8.5 Hz); ^{13}C NMR −4.8, −4.2, 17.5, 17.9, 25.7, 31.6, 33.4, 45.4, 70.9, 72.1, 118.9, 148.9, 170.1; HREIMS *m/z* calcd for $C_{15}H_{26}O_3Si$ (M)$^+$ 282.1651, obsd 282.1654.

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Supplementary Material Available: ^{1}H NMR spectra for compounds **6b**, **7b**, **8b**, **9c**, **10b**, **11b**, **12**, and **13**, and NMR data and ^{1}H NMR spectra for compounds **6c–g**, **7a,c–g**, **8a,c–g** **9a,c–g**, **10a,c–g**, and **11a,c–g** (45 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.