[5] a) S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137; b) S. E. Denmark, J. J. Cottell in *The Chemistry of Heterocyclic Compounds: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products* (Eds.: A. Padwa, W. H. Pearson), Wiley-Interscience, New York, **2002**, pp. 83–167.

[6] S. E. Denmark, D. S. Middleton, *J. Org. Chem.* **1998**, *63*, 1604.

[7] a) D. Seebach, G. Calderari, P. Knochel, *Tetrahedron* **1985**, *41*, 4861; b) P. Knochel, D. Seebach, *Tetrahedron Lett.* **1982**, *23*, 3897.

[8] D. L. J. Clive, C. C. Paul, Z. Wang, *J. Org. Chem.* **1997**, *62*, 7028.

[9] a) E. Vedejs, D. Gapinski, J. P. Hagen, *J. Org. Chem.* **1981**, *46*, 5451; b) E. Vedejs, D. W. Powell, *J. Am. Chem. Soc.* **1982**, *104*, 2046.

[10] a) F. Bohlmann, M. Ganzer, M. Krüger, E. Nordhoff, *Tetrahedron* **1983**, *39*, 123; b) W. F. Bailey, Y. Tao, *Tetrahedron Lett.* **1997**, *38*, 6157.

[11] T. K. Chakraborty, S. Chandrasekaran, *Synth. Commun.* **1980**, *10*, 951.

[12] a) D. H. R. Barton, S. W. McCombie, *J. Chem. Soc. Perkin Trans. 1* **1975**, 1574; b) D. H. R. Baron, J. Dorchak, J. C. Jaszberenyi, *Tetrahedron* **1992**, *48*, 7435; c) M. J. Robins, J. S. Wilson, F. Hansske, *J. Am. Chem. Soc.* **1983**, *105*, 4059.

[13] Data for **1**: b.p.: 40 °C (0.1 Torr); ^{1}H NMR (500 MHz, CHCl$_3$, TMS): $\delta = 1.33$ (m, 4 H, HC(5), HC(4)), 1.46 (m, 2 H; HC(2)), 1.78 (m, 4 H; HC(5), HC(4)), 1.89 (m, 2 H; HC(2)), 2.02 (m, 1 H; HC(6)), 2.18 (m, 2 H; HC(3)), 2.70 (dt, $J = 10.5$, 6.2 Hz, 2 H; HC(1)), 2.92 ppm (dt, $J = 10.5$, 6.4 Hz, 2 H; HC(1)); ^{13}C NMR (126 MHz, CHCl$_3$): $\delta = 29.6$, 30.3, 30.5 (C(2), C(4), C(5)), 50.9 (C(3)), 51.9 (C(6)), 52.4 (C(1)), 93.1 ppm (C(7)); IR (CH$_2$Cl$_2$): $\tilde{\nu} = 2945$ (s), 2864 (m), 1454 (w), 1269 (vw), 1209 (vw), 1173 (vw), 1119 (vw); MS (FAB): m/z (%): 178 (M^++1, 100); TLC (CHCl$_3$/MeOH 20:1, Al$_2$O$_3$): $R_f = 0.64$; C,H,N analysis (%): calcd for C$_{12}$H$_{19}$N: C 81.30, H 10.80, N 7.90; found: C 81.02, H 10.95, N 7.97.

[14] X-ray crystal structure analysis of **1**·BH$_3$. A single crystal deposited from Et$_2$O solution at −25 °C: formula C$_{12}$H$_{22}$BN. $M_r = 191.12$, crystal size $0.2 \times 0.2 \times 0.02$ mm^3, $a = 6.2685(13)$ Å, $b = 12.773(3)$ Å, $c = 7.5043(15)$ Å, $\beta = 111.517(4)°$, $V = 558.93(19)$ Å^3, $\rho_{calcd} = 1.136$ g cm^{-3}, $\mu = 0.064$ mm^{-1}, absorption correction by integration, $Z = 2$, monoclinic space group $P2_1$, Siemens 3-circle platform diffractomer with a molybdenum (K$_\alpha = 0.71073$ Å) X-ray source and CCD area detector, $T = 193(2)$ K, 5835 measured reflections ($\pm h$, $\pm k$, $\pm l$), 1074 independent and 722 observed reflections with $I > 2\sigma(I)$, $R = 0.0423$, $wR = 0.0494$ (against $|F^2|$), residual electron density 0.12 e Å^3; programs used: SHELXTL V6. CCDC-189803 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+ 44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[15] A similar twist has been established by electron diffraction (12.4°) in the parent hydrocarbon that gives rise to an overall D_2 symmetry: J. Brunvoll, R. Guidetti-Grept, I. Hargittai, R. Keese, *Helv. Chim. Acta* **1993**, *76*, 2838.

Efficient Synthesis of a Tricyclic BCD Analogue of Ouabain: Lewis Acid Catalyzed Diels–Alder Reactions of Sterically Hindered Systems**

Michael E. Jung* and Pablo Davidov

The naturally occurring cardenolide ouabain (**1a**) and its aglycone ouabagenin (**1b**) are members of a class of highly oxygenated cardiotonic steroids (digitalis glycosides) used in the treatment of congestive heart failure.[1] Ouabain has been synthesized starting from other natural steroids,[2] however, no total synthesis[3] has been reported to date although an excellent synthetic route has been described.[4] We have reported some preliminary results on an approach to the bicyclic CD ring system of ouabain in which we attempted to use an anionic [1,3] sigmatropic shift of a 7-alkenylbicyclo[3.2.1]heptane-1,7-diol, which afforded products from an unusual anion-accelerated retroene reaction.[5] We report here a completely different route that allowed us to prepare a tricyclic BCD ring system analogue of ouabain in a very efficient manner. In this route we have developed a novel Diels–Alder reaction of sterically hindered enones and dienes to afford heavily substituted cyclohexene systems extremely easily.
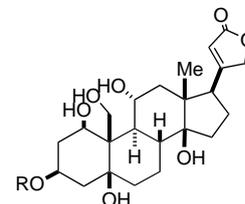
1a R = L-rhamnose
1b R = H

Initially, we decided to investigate a possible Diels–Alder approach for the synthesis of the CD ring system of ouabain. Cycloaddition of a 1-(alkoxyvinyl)cyclohexene **2** with the enone **3** followed by conversion of the ketone to an acetate by a Baeyer–Villiger oxidation and final hydrolysis and reduction of the cyclic ketone would give the diol **4**, which has the required five contiguous asymmetric centers of the BCD ring system of ouabain (Scheme 1). The anticipated difficulty of carrying out a Diels–Alder reaction with a hindered dienophile such as **3** made us first investigate a simpler model system. All attempts at effecting the cycloaddition of 2-trimethylsilyloxybutadiene (**5**) with the known dienophile **6**
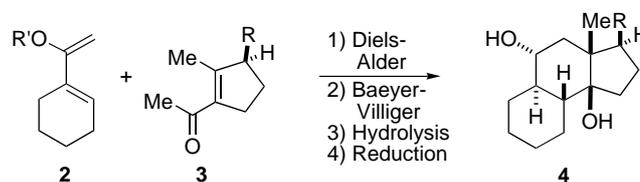
Scheme 1. Diels–Alder approach to the diol **4**, which contains the BCD ring system of ouabain (**1a**).

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(see Scheme 2; prepared in one step from cyclohexane)[6] were unsuccessful; thermal conditions (toluene, 110°C) returned the starting materials, and Lewis acid catalysis (AlCl₃ or TiCl₄) resulted in decomposition of the diene.[7] Even the highly reactive Danishefsky's diene (*trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene) did not give the expected product with the enone **6**, either at 23°C for seven days or at 110°C for several hours, thus implicating the unreactivity of the dienophile **6**.

Since the trimethylsilyl enol ether did not withstand the Lewis acidic conditions, we decided to study the more stable diene **7** (see Scheme 2). We have shown that this diene is quite useful in various cycloadditions.[8] Again thermal conditions (110°C/48 h) did not effect cycloaddition and starting materials were returned. However, use of mixed Lewis acid systems afforded a mixture containing the desired product in good yield. Thus treatment of **7** and **6** in toluene with 50 mol% of a 10:1 AlCl₃ and AlMe₃ mixture at 0°C for 2 h furnished a 1.2:1:0.3 mixture of the desired *exo* isomer **8x**, the *endo* isomer **8n,** and an unknown impurity tentatively assigned structure **9**[9] in 73% yield (Scheme 2).[10–12] However, we
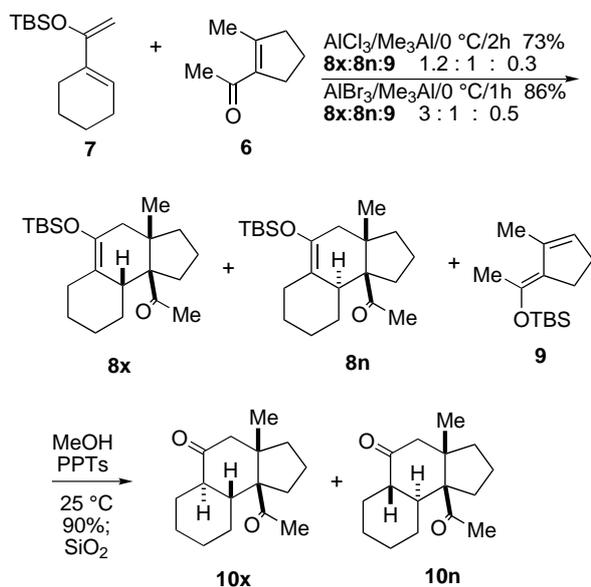
Scheme 2. Reaction between the dienophile **6** and hindered diene **7** in the presence of the mixed Lewis acid system 10:1 AlCl₃/AlMe₃. TBS = *tert*-butyldimethylsilyl, PPTs = pridinium *p*-toluenesulfonate.

found that AlBr₃ is much easier to work with[13] than AlCl₃ and was thus preferable as a catalyst. Use of 50 mol% of a 10:1 mixture of AlBr₃/AlMe₃ in a toluene/dichloromethane mixture at 0°C for 1 h afforded the same three products **8x**, **8n**, and **9** in 86% yield in a 3:1:0.5 ratio. We propose that the small amount of AlMe₃ eliminates any trace of HX in the medium thereby extending the stability of the silyloxy diene. The two diastereomeric products were inseparable by column chromatography but conversion of the silyl enol ethers proceeded in excellent yield under mildly acidic conditions[14] to give the two diastereomeric ketones, **10x** and **10n**, which were separable by simple column chromatography. The structures of these ketones were assigned by NOE NMR

experiments; the undesired minor isomer **10n** was highly crystalline and was characterized by X-ray crystal structure analysis.[15] The last stereocenter was introduced by Li/NH₃ reduction of the cyclic ketone **10x**, which yielded the expected equatorial alcohol and a 1:1 diastereomeric mixture of secondary alcohols from the acetyl group (Scheme 3). The
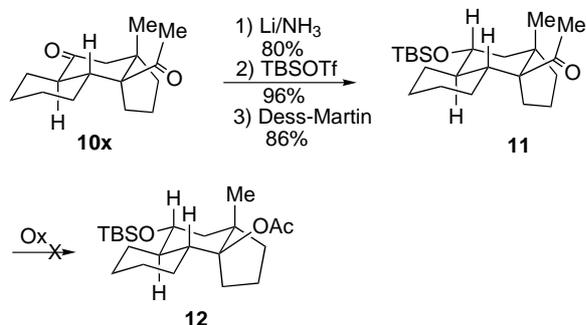
Scheme 3. Conversion of **10x** to the silyl ether ketone **11** as a proposed route to **12**.

two alcohols were easily differentiated by selective protection of the equatorial alcohol with a *tert*-butyldimethylsilyl (TBS) group. The acetyl moiety was regenerated in quantitative yield by exposure to the Dess–Martin periodinane to give the silyl ether ketone **11**. At this point we were ready to attempt the second key step of the route, the Baeyer–Villiger oxidation. Unfortunately, the acetyl moiety is so sterically hindered that all attempts to effect this oxidation failed to yield any of the desired product **12**.[16] This result seemed to doom this attempt at the preparation of a tricyclic BCD ring system analogue of ouabain by this route.

Thus, we decided to try to effect an inverse electron demand in the key cycloaddition, namely the coupling of an electron-poor diene with an electron-rich dienophile (Scheme 4). The desired 2-acetyl-1,3-diene **14** was prepared
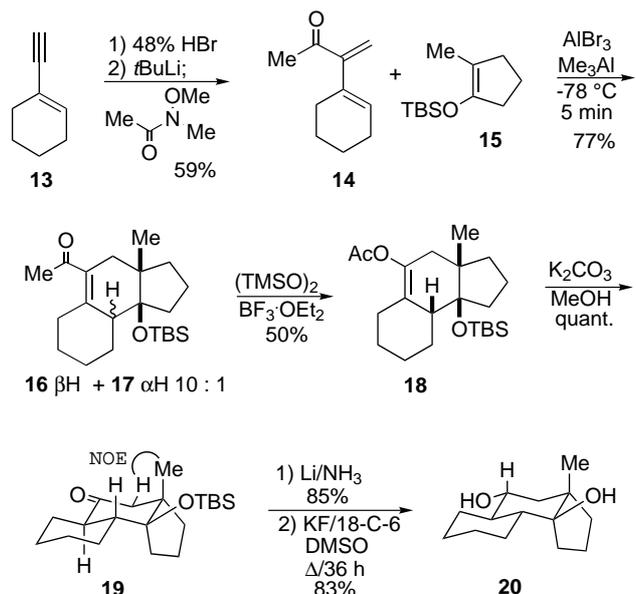
Scheme 4. Synthesis of the desired ketone **19** and its conversion to the diol **20**, a BCD ring system analogue of ouabain (**1a**). 18-C-6 = [18]crown-6.

from ethynylcyclohexene (**13**) in two steps (addition of HBr[17] and coupling of the derived organometallic compound with the Weinreb amide).[18] This enone was then treated with the TBS-protected enol ether **15** under the same conditions as before—50 mol% of a 10:1 mixture of $AlBr_3$ and $AlMe_3$ in toluene/dichloromethane at $-78\,°C$ for 5 min—to afford a 10:1 diastereomeric mixture of the desired *exo* adduct **16** and the *endo* adduct **17** in 77% yield, which were easily separable by chromatography, affording **16** in 72% yield. Baeyer–Villiger oxidation of this mixture of enones was effected by using bis(trimethylsilyl) peroxide and $BF_3\cdot OEt_2$ to furnish the desired acetate **18** in 50% yield. This enol acetate was hydrolyzed in quantitative yield under mildly basic conditions to yield the desired ketone **19**. The structure of this ketone was assigned based on a strong NOE between the quaternary methyl group and the equatorial proton α to the ketone group (Scheme 4). Reduction of the ketone **19** with Li/NH_3 yielded the desired equatorial alcohol in 85% yield. Finally deprotection of the TBS group required forcing conditions,[19] namely heating with KF in DMSO for 36 h, to cleanly remove the protecting group and yield the desired diol **20** in 83% yield along with 15% of the recovered hydroxy silyl ether. The structure of **20** was confirmed by a single-crystal X-ray structure analysis (Figure 1).[16]
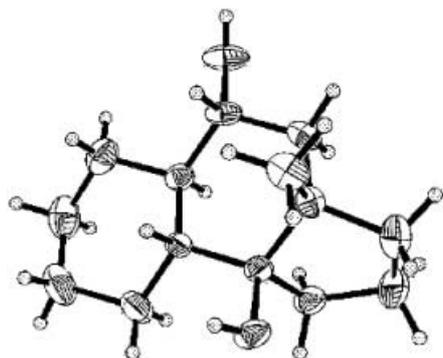
Figure 1. X-ray structure analysis of diol **20**.

Finally, we have some preliminary results that indicate that more functionalized silyl enol ethers can be used as ring D precursors in this process (Scheme 5). A racemic mixture of the silylfuran **21** was synthesized by using a modified version of the procedure developed by Kim and Park.[20] Treatment of the diene **14** and the dienophile **21** with 0.5 equivalents of $AlBr_3$ and 0.05 equivalents of $AlMe_3$ at $-78\,°C$ for 5 min furnished a 10:1 mixture of the *exo* adduct **22** and the *endo* adduct **23** in 28% yield. The structures were assigned based on our previous results (for the *exo/endo* stereocenter) and NOE experiments which displayed a through-space interaction between the protons of the quaternary methyl group and a proton from the furyl group, thus implying that the two groups were *syn* to each other. Although this unoptimized reaction provided low yields of the desired *exo* adduct **22**, it demonstrated the feasibility of this approach to obtain advanced tricyclic adducts containing four correct contiguous stereocenters plus a butenolide-equivalent moiety.
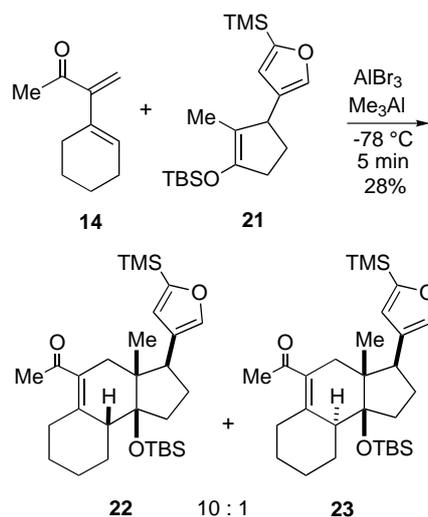
Scheme 5. Synthesis of **22** and **23** by using the highly functionalized silyl enol ether **21** as ring D precursor.

In summary, we have been able to prepare the diol **20**, a tricyclic BCD ring system analogue of the steroid ouabain **1a**, by an efficient route that highlights a new procedure for the formation of hindered cyclohexyl systems through the use of a mixed Lewis acid medium for effecting cycloadditions of hindered systems bearing acid-sensitive functionalities. Further studies on this reaction and the synthesis of ouabain **1a** are currently in progress.

Experimental Section

Diels–Alder adducts **8x** and **8n**: The enone **6** (1.5 g, 12 mmol) was dissolved in a solution of toluene (20 mL) and dichloromethane (7 mL), and the mixture was cooled to $-8\,°C$. Trimethylaluminum (0.3 mL of a 2.0 M solution in toluene, 0.6 mmol) was slowly added to the solution, followed after 15 min by aluminum bromide (6 mL of a 1.0 M solution in dibromomethane, 6 mmol). The mixture was stirred 15 min and the silyl enol ether **7** (3.8 g, 16 mmol) in dichloromethane (5 mL) was slowly added to the mixture. The reaction was warmed to $0\,°C$ over 1 h and quenched with pyridine (20 mL) and the mixture warmed to $23\,°C$. The suspension was filtered over a small pad of silica gel, and the solvent removed in vacuo. The product was purified by column chromatography over silica gel (94:6 hexanes/ethyl acetate) to yield the desired compound (3.724 g, 10.3 mmol, 86%) as a 3:1 mixture of the diastereomers **8x** and **8n**. The diastereomers were inseparable by column chromatography. **8x**: ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.92$ (bd, 1H), 2.73 (bd, 1H), 2.19 (s, 3H), 1.99 (m, 1H), 1.55–1.81 (m, 8H), 1.03–1.48 (m, 6H), 1.00 (s, 3H), 0.93 (s, 9H), 0.10 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (125.75 MHz, $CDCl_3$): $\delta = 214.8$, 138.2, 113.3, 64.1, 44.2, 42.1, 40.0, 38.6, 31.5, 30.7, 30.1, 29.5, 25.9, 25.6, 22.6, 20.1, 18.2, 14.1, -3.8, -3.9 ppm. **8n**: ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.98$ (bd, 1H), 2.12 (s, 3H), 1.55–1.81 (m, 8H), 1.03–1.48 (m, 8H), 0.95 (s, 9H), 0.90 (s, 3H), 0.13 (s, 3H), 0.11 ppm (s, 3H); ^{13}C NMR (125.75 MHz, $CDCl_3$): $\delta = 214.1$, 140.0, 113.9, 63.8, 43.2, 41.2, 39.3, 38.8, 31.7, 30.9, 30.2, 29.3, 25.8, 25.7, 22.7, 20.0, 18.4, 14.3, -3.7, -4.0 ppm; IR of mixture (thin film on NaCl): $\tilde{\nu}$: 2955 (s), 2930 (s), 2857 (m), 1696 (m), 1471 (m), 1361 (m), 1251 (m), 851 (s), 777 cm^{-1} (m); MS of mixture (m/z): 362.29 [M^+], 319.26, 239.20, 182.12.

Diels–Alder adducts **16**: The dienone **14** (0.793 g, 5.27 mmol) was dissolved in a solution of toluene (7 mL) and dichloromethane (3.5 mL) and the mixture was cooled to $-78\,°C$. Trimethylaluminum (0.125 mL of a 2.0 M solution in toluene, 0.25 mmol) was added as a chemical dessicant. Shortly afterwards (5 min), aluminum bromide (2.5 mL of a 1.0 M solution in dibromomethane, 2.5 mmol) was added dropwise followed immediately by the silyl enol ether **15** (1.27 g, 6 mmol) neat. After 5 min the reaction was quenched by adding pyridine (10 mL) at $-78\,°C$ and warming the mixture to $23\,°C$. The suspension was filtered through a small pad of silica and the

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filtrate was concentrated in vacuo. ^{1}H NMR spectroscopy of the crude product reveals a 10:1 mixture of diastereomers **16** and **17** in favor of the desired *exo* adduct. The residue was purifed by column chromatography on silica gel (95:5 hexanes/ethyl acetate) to yield the desired isomer **16** (1.46 g, 4.03 mmol, 76.5 %). ^{1}H NMR (500 MHz, CDCl$_3$): $\delta = 2.77$ (bd, 1 H), 2.19 (s, 3 H), 2.12 (m, 1 H), 2.05 (m, 2 H), 1.89 (bd, 1 H), 1.72–1.85 (m, 4 H), 1.65 (m, 3 H), 1.40 (m, 2 H), 1.23 (m, 2 H), 1.15 (m, 1 H), 0.92 (s, 3 H), 0.86 (s, 9 H), 0.11 (s, 3 H), 0.10 ppm (s, 3 H); ^{13}C NMR (125.75 MHz, CDCl$_3$): $\delta = 205.8$, 140.8, 129.8, 87.3, 46.1, 44.7, 38.6, 37.0, 33.4, 30.8, 29.9, 29.4, 27.0, 26.1, 25.9, 18.9, 18.3, 18.1, -2.3, -2.8; IR (thin film on NaCl): $\tilde{v} = 2953$ (s), 2928 (s), 2855 (s), 1690 (s), 1471 (m), 1350 (m), 1251 (s), 1226 (m), 1124 (s), 1062 (s), 1005 (m), 833 (s), 770 cm^{-1} (s); high-resolution MS (*m/z*) $[M+H]^+$ 362.2616, calcd for C$_{22}$H$_{38}$O$_2$Si 362.2641.

[1] a) R. Thomas, P. Gray, J. Andrew, *Adv. Drug Res.* **1990**, *19*, 312; b) U. T. Ruegg, *Experientia* **1992**, *48*, 1102; c) P. S. Steyn, F. R. Heerden, *Nat. Prod. Rep.* **1998**, 397; d) N. M. Bigelow, W. A. Jacobs, *J. Biol. Chem.* **1932**, *96*, 647.

[2] J. R. Hanson, *Nat. Prod. Rep.* **1993**, *10*, 313.

[3] a) For the total synthesis of digitoxigenin, see: G. Stork, F. West, Y. H. Lee, R. C. Isaacs, S. Manabe, *J. Am. Chem. Soc.* **1996**, *118*, 10660; b) for the total synthesis of a derivative of 9,11-dehydrodigitoxigenin, see: A. R. Daniewski, M. M. Kabat, M. Masnyk, J. Wicha, W. Wojciechowska, H. Duddeck, *J. Org. Chem.* **1988**, *53*, 4855.

[4] Overman and co-workers have reported significant progress toward the total synthesis of ouabain. a) L. E. Overman, P. V. Rucker, *Heterocycles* **2000**, *52*, 1297; b) S. Laschat, F. Narjes, L. E. Overman, *Tetrahedron* **1999**, *55*, 347; c) L. E. Overman, P. V. Rucker, *Tetrahedron Lett.* **1998**, *39*, 4643; d) J. Hynes, Jr., L. E. Overman, T. Nasser, P. V. Rucker, *Tetrahedron Lett.* **1998**, *39*, 4647; e) W. Deng, M. S. Jensen, L. E. Overman, P. V. Rucker, J. P. Vionnet, *J. Org. Chem.* **1996**, *61*, 6760.

[5] M. E. Jung, P. Davidov, *Org. Lett.* **2001**, *3*, 3025; for earlier work in this area, see: M. E. Jung, P. Davidov, *Org. Lett.* **2001**, *3*, 627.

[6] K. E. Harding, K. S. Clement, *J. Org. Chem.* **1984**, *49*, 2049.

[7] An attempt to effect a tandem Michael–Michael process by treating the silyl enol ether with methyllithium consumed the starting material but no desired bicyclic product was isolated.

[8] For examples, see: M. E. Jung, N. Nishimura, *J. Am. Chem. Soc.* **1999**, *121*, 3529; M. E. Jung, Nishimura, N. *Org. Lett.* **2001**, *3*, 2113.

[9] This impurity decomposes on attempted chromatographic purification. It exhibits a TBS group and an olefinic proton in the ^{1}H NMR spectrum of the crude product mixture and thus is most likely compound **9**.

[10] For examples of somewhat hindered cycloadditions of this type, see: a) T. Fujiwara, T. Ohsaka, T. Inoue, T. Takeda, *Tetrahedron Lett.* **1988**, *29*, 6283; b) I. S. Levina, L. E. Kulikova, A. V. Kamernitskii, B. S. El'yanov, E. M. Gonikberg, *Izv. Akad. Nauk, Ser. Khim.* **1992**, 1622; c) R. D. Hubbard, B. L. Miller, *J. Org. Chem.* **1998**, *63*, 4143.

[11] Although this Diels–Alder reaction could be a concerted [4+2] cycloaddition, we propose that the cycloaddition occurs by a stepwise mechanism, namely a double Mukaiyama-type Michael addition rather than a concerted [4+2] cycloaddition and thus produces the *exo* product as the major isomer. For an example of a Diels–Alder reaction of the diene **6** with 2-methylcyclohexenone under Lewis acid catalysis to give mainly the *endo* adduct, see: a) M. Ge, B. M. Stoltz, E. J. Corey, *Org. Lett.* **2000**, *2*, 1927; since the *endo* isomer is the minor isomer in our case, we favor the double Michael process. For examples of Mukaiyama Michael additions, see: b) K. Narasaki, K. Soai, T. Mukaiyama, *Chem. Lett.* **1974**, 1223; c) D. A. Evans, K. A. Scheidt, J. N. Johnston, M. C. Willis, *J. Am. Chem. Soc.* **2001**, *123*, 4480; d) G. Desimoni, G. Faita, S. Filippone, M. Mella, M. G. Zampori, M. Zema, *Tetrahedron* **2001**, *57*, 10203; for examples of double Michael additions to produce [4+2] cycloadducts, see: e) M. E. Jung in *Comprehensive Organic Synthesis, Vol. 4* (Ed.: B. M. Trost), Pergamon, Oxford, **1991**, chap. 1.1, pp. 1–67 (especially pp. 30–32).

[12] It should be pointed out that Diels and Alder just described the reaction of a diene and dienophile to give cyclohexene systems without implying any mechanistic detail and thus this reaction is a Diels–Alder reaction by their definition even if the mechanism is more likely stepwise than concerted.

[13] Aluminum tribromide (AlBr$_3$) is commercially available as a 1 M solution in dibromomethane, while aluminum trichloride (AlCl$_3$) is supplied as a 1 M solution in nitrobenzene. The lower boiling point and lack of a chromophore makes the use of the former preferable. All of the solutions of AlBr$_3$ and AlMe$_3$ were prepared by mixing the commercially available solutions (a 2 M solution of AlMe$_3$ in toluene was used).

[14] Hydrolysis of the silyl enol ether with tetrabutylammonium fluoride (TBAF) gave poor yields, presumably due to retro-Michael reactions.

[15] We thank Dr. Saeed Khan for obtaining the X-ray crystal structures. CCDC-194419 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.ca-n.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Centre, 12 Union Road, Cambridge CB21EZ, UK; Fax: (+ 44) 1223-336033; or deposit@ccdc.cam.ac.uk).

[16] For example, oxidation with *meta*-chloroperoxybenzoic acid (MCPBA) (alone or in the presence of a radical inhibitor at elevated temperatures), trifluoroperacetic acid, 3,5-dintiroperbenzoic acid, hydrogen peroxide, and bis(trimethylsilyl)peroxide in the presence of trimethylsilyl triflate gave only starting material or desilylated starting material under all conditions tried. The addition of several other nucleophiles to this very hindered ketone was also unsuccessful.

[17] J. C. Traynard, *Bull. Soc. Chim. Fr.* **1962**, 19.

[18] a) S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815; b) M. P. Sibi, *Org. Prep. Proced. Int.* **1993**, *25*, 15.

[19] Hydrolysis of the TBS ether could not be effected with TBAF in THF at 23 °C or at reflux. Acidic conditions caused extensive elimination of the silyl ether to give the trisubstituted alkene.

[20] S. Kim, J. H. Park, *Synlett* **1995**, 163.