70 °C for 20 h, equimolar amounts of **18a** and **18b** were obtained (70% yield). The stereochemistry at C-15 and -20 was shown by transforming **18a** and **18b** separately into (−)-**4** and (+)-**5** via the three-step sequence described above ($NaCNBH_3$, Raney Ni, and $LiAlH_4$), in 57% and 55% overall yields, respectively. (−)-**4**: $[\alpha]^{20}_D$ −81° (*c* 0.35, EtOH) [lit.[8c] $[\alpha]^{21}_D$ −79.2° (*c* 0.35, EtOH)]. (+)-**5**: $[\alpha]^{20}_D$ +190° (*c* 0.4, pyridine) [lit.[8c] $[\alpha]^{23}_D$ +190.4° (*c* 0.4, pyridine)]. Reduction of **18a** with 1.2 equiv of $NaCNBH_3$ in AcOH at 50 °C gave an 82% yield of **19** [$[\alpha]^{22}_D$ +241° (*c* 0.85, CH_2Cl_2)] and **20** [$[\alpha]^{22}_D$ +129° (*c* 0.15, CH_2Cl_2)] in a 2:1 ratio, while rotamer **18b** provided an 80% yield of **19** and **20** in a 1:2.[25] The stereochemistry shown for C-14 of **19** and **20** is presumed on the basis of the coupling constant $J_{3,14}$ = 1 Hz for **19** and 7 Hz for **20** (equatorial–axial coupling).

In summary, highly efficient constructions of functionalized chiral indolizidines have been explored. The stereoselective reduction of β-sulfinyl enamides offers a new arena for further investigation. The synthetic methodology used to prepare the indolizidines and yohimbanoid alkaloids is facile and should be applicable to the construction of (+)-castanospermine,[2] (+)-swansonine,[26] and other biologically active alkaloids.[27] Related asymmetric induction in the reactions of **1** with β-substituted-α,β-unsaturated esters, aldehydes, and other electrophiles will be reported shortly.

Acknowledgment. We gratefully acknowledge financial support from the National Institute of General Medical Sciences (Grant GM36336) and the National Science Foundation (Grant CHE-8800654). This project is in part funded by Wesley Foundation, Wichita, KS (Grant 8802041). The Wesley Foundation is an independent, nonprofit organization dedicated to improving the quality of life in Kansas through financial support for health related programs. We are indebted to Mr. Ken Walsh, Coal Research Center, Southern Illinois University at Carbondale, for obtaining mass spectra.

Supplementary Material Available: Optical rotations and ^1H and ^{13}C NMR spectral data for compounds **1–22**, fractional coordinates and equivalent isotropic thermal parameters (Table 1), anisotropic thermal parameters (Table 2), bond distances and bond angles (Tables 3 and 4), and torsion angles (Table 5) for sulfoxide **12** (14 pages); F_o and F_c lists (Table 6) (7 pages). Ordering information is given on any current masthead page.

(26) For a review: Grundon, M. F. *Nat. Prod. Rep.* **1985**, 235.

(27) These studies are being actively pursued.

Articles

Total Synthesis of Furanether B

Mary E. Price and Neil E. Schore*

Department of Chemistry, University of California, Davis, California 95616

Received March 1, 1989

The first total syntheses of furanether B, a member of the lactarane class of sesquiterpenes, have been completed starting from 1-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**3**). After ketone reduction, Pauson–Khand cycloaddition (propyne–$Co_2(CO)_6$, benzene, heat) gives rise to a 75% yield of stereoisomeric tricyclic enones **5** and **6**. Reduction and methylation of enone **5**, removal of the ketone (Barton), and oxidation of the remaining alcohol function give **13**. The natural product is obtained upon regiospecific formylation, conversion to the *S*-butyl derivative, and generation of the furan via a modification of Garst's procedure using a thiomethylene ylide under phase-transfer conditions. A similar sequence beginning with **6** also provides access to **13**, but most of the steps proceed in somewhat lower yields.

Introduction

In a previous publication we reported an efficient synthetic entry into the highly functionalized 11-oxatricyclo[5.3.1.$0^{2,6}$]undecane ring system that would be potentially useful in the synthesis of natural products of the lactarane type, which are found in mushrooms of the genera Lactarius and Russula.[1] Synthetic work in this area has been very limited, with only a small number of total syntheses involving one subclass of compounds,[2] together with a few demonstrations of interconversion of naturally occurring compounds.[3,4] Herein we report the first total synthesis of furanether B (**1**), a fungal metabolite isolated by Vita-Finzi in 1980, utilizing our earlier methodology.[5]

Results and Discussion

Our general entry to the ring system involved octacarbonyldicobalt-catalyzed cycloaddition of 8-oxabicyclo-

(1) LaBelle, B. E.; Knudsen, M. J.; Olmstead, M. M.; Hope, H.; Yanuck, M. D.; Schore, N. E. *J. Org. Chem.* **1985**, *50*, 5215.

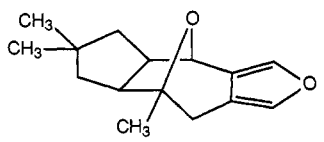
(2) (a) Froborg, J.; Magnusson, G. *J. Org. Chem.* **1975**, *40*, 1595. (b) Fex, T.; Froborg, J.; Magnusson, G. *J. Org. Chem.* **1976**, *41*, 3518. (c) Froborg, J.; Magnusson, G. *J. Am. Chem. Soc.* **1978**, *100*, 6728. (d) Christensen, J. R.; Reusch, W. *Can. J. Chem.* **1984**, *62*, 1954.

(3) For example: (a) Kihlberg, J.; Bergman, R.; Nilsson, L.; Sterner, O.; Wickberg, B. *Tetrahedron Lett.* **1983**, *24*, 4631. (b) Sterner, O.; Bergman, R.; Kihlberg, J.; Oluwadiya, J.; Wickberg, B.; Vidari, G.; De Bernardi, M.; De Marchi, F.; Fronza, G.; Vita Finzi, P. *J. Org. Chem.* **1985**, *50*, 950.

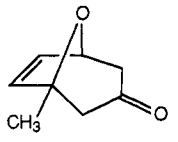
(4) General reference: DeBernardi, M.; Fronza, G.; Scilingo, A.; Vidari, G.; Vita-Finzi, P. *Tetrahedron* **1986**, *42*, 4277, and references therein.

(5) Battaglia, R.; DeBernardi, M.; Fronza, G.; Mellerio, G.; Vidari, G.; Vita-Finzi, P. *J. Nat. Prod.* **1980**, *43*, 319.

0022-3263/89/1954-5662$01.50/0

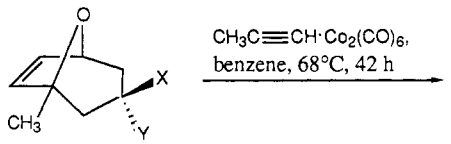


1

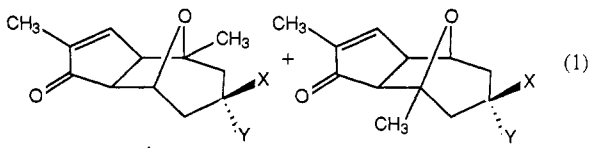


2

[3.2.1]oct-6-ene derivatives with alkynes (Pauson–Khand reaction).[6] The starting material for this synthesis was 1-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**2**), prepared by the method of Noyori from 2-methylfuran and tetrabromoacetone.[7] Reduction of **2** was done to differentiate the carbonyl from one produced later in the synthesis. A 2:1 exo:endo ratio of isomeric alcohols **3** and **4** was produced in 94% yield by reduction of **2** with lithium aluminum hydride. Pauson–Khand cycloaddition of propyne and the mixture of stereoisomeric alcohols **3** and **4** gave a 75% yield of a mixture of four isomeric tricyclic ketones (**5a**, **5b** and **6a**, **6b**, eq 1). The regiochemistry of the



3, X = OH, Y = H
4, X = H, Y = OH



(1)

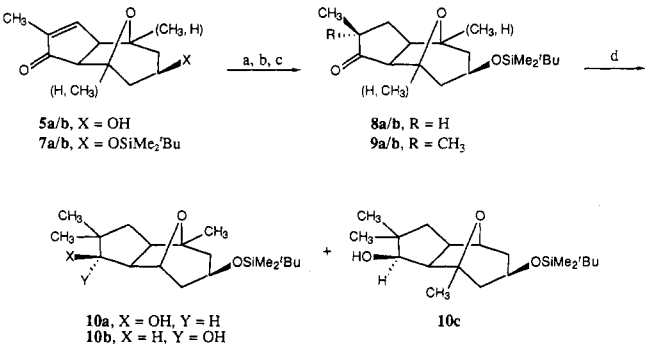
anti **5a**, X = OH, Y = H; **6a**, X = H, Y = OH

syn **5b**, X = OH, Y = H; **6b**, X = H, Y = OH

products was inferred from well-established proton NMR correlations.[1] The products in which the new enone carbonyl ends up anti to the bridgehead methyl group show resonance positions for the remaining bridgehead proton about 0.2–0.3 ppm downfield of the corresponding resonance for the syn regioisomers (e.g., δ 4.48 for **5a** and δ 4.42 for **6a**, vs δ 4.23 for **5b** and δ 4.17 for **6b**). Consistent with earlier results in similar systems, little regioselectivity was obtained in the cycloaddition: both the **5a**:**5b** and **6a**:**6b** ratios approximated 1.5:1. In all four compounds the newly formed ring fusion possesses the exo configuration, based on the lack of any measurable coupling between ring-fusion and bridgehead protons. This is the result expected from Pauson–Khand-type cycloadditions involving bicyclic alkenes.[1,6] The exclusive presence of exo stereochemistry at this ring fusion is the outcome required for ultimate access to furanether B, which, unique among the furanoid lactaranes, possesses this feature (i.e., a cis relationship between the bridgehead methyl and the ring-fusion hydrogens).

We initially had hoped that all four isomers could be taken to a common intermediate further along in the synthesis, as the target molecule possesses neither the stereocenter at C-9 nor the ketone on the five-member ring to give rise to anti and syn isomers with respect to the bridgehead methyl group. However, complications in spectral interpretation and difficulty in judging completeness of reactions led us to separate the stereoisomeric alcohols into exo and endo pairs of anti and syn regioisomers (a 2:1 ratio of **5a** + **5b** to **6a** + **6b**). Recrystallization was generally not found to be effective at separating regioisomers from the mixtures in these series of compounds. Although it is possible to separate anti from syn regioisomers by using MPLC, the separations are tedious and therefore were not attempted for preparative purposes. Therefore each regioisomeric pair was carried through as a mixture, to subsequently be transformed synthetically to a common intermediate. Details concerning the further transformations of the *exo*-9-alcohols **5a** and **5b** are presented first (Scheme I), followed by the chemistry of the *endo*-9-alcohols **6a** and **6b**.

Scheme I



5a/b, X = OH
7a/b, X = OSiMe$_2$^{t}Bu

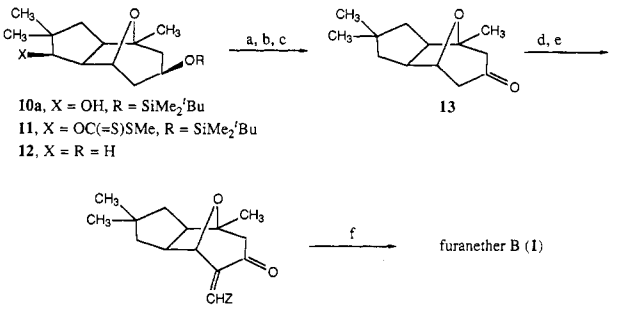
8a/b, R = H
9a/b, R = CH$_3$

10a, X = OH, Y = H
10b, X = H, Y = OH

10c

[a] ^{t}BuMe$_2$SiCl, imidazole, DMF, 25 °C, 18 h (94%). [b] H_2, Pd/C, EtOAc, MeOH, 25 °C, 10 h (100%). [c] MeI, KO^{t}Bu, ^{t}BuOH, C_6H_6, 25 °C, 20 min → 38 °C, 35 min, (100%). [d] $LiAlH_4$, Et_2O, 25 °C, 1.5 h (100%).

Scheme II



10a, X = OH, R = SiMe$_2$^{t}Bu
11, X = OC(=S)SMe, R = SiMe$_2$^{t}Bu
12, X = R = H

13

21, Z = OH
22a and **b**, Z = S^{n}Bu (*E* and *Z* isomers)

[a] NaH, THF, 66 °C, 1 h, then NaH, CS_2, THF, 66 °C, 0.5 h, then MeI, 66 °C, 0.5 h (100%). [b] ^{n}Bu$_3$SnH, toluene, 111 °C, 16 h, then ^{n}Bu$_3$SnH, AIBN, toluene, 111 °C, 6 h (50%). [c] PCC, CH_2Cl_2, 25 °C, 70 min (60%). [d] HCO_2Et, NaOMe, C_6H_6, 25 °C, 18 h (67%). [e] ^{n}BuSH, *p*-TsOH, C_6H_6, 80 °C, 1 h (100%). [f] $Me_3S^+MeSO_4^-$, CH_2Cl_2, 50% aqueous NaOH, 48 °C, 24 h, then concentration, 25 °C, 24 h, then aqueous HCl, THF, 25 °C, 3 h (70%).

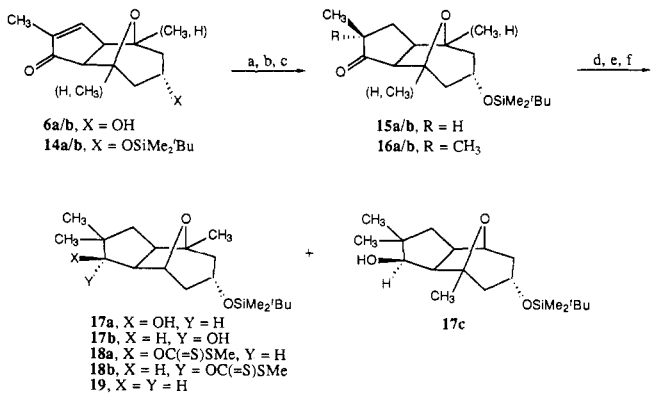
Protection of the regioisomeric alcohol pair **5a** and **5b** provided **7a** and **7b** in 94% combined yield. Catalytic hydrogenation gave a quantitative yield of saturated ketones **8a** and **8b**. Alkylation to give **9a** and **9b** was also achieved in quantitative yield.[8] Reduction of **9a** and **9b** with lithium aluminum hydride provided a mixture of three easily separable isomeric alcohols **10a**, **10b**, and **10c** (1.75:1:1.25, 100%). Alcohol **10a** was then taken further in the synthesis, using the methodology of Barton (Scheme II).[9] The dithiocarbonate **11** was prepared in quantitative

(6) Reviews: (a) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Pauson, P. L. In *Organometallics in Organic Synthesis. Aspects of a Modern Interdisciplinary Field*; de Meijere, A., tom Dieck, H., Eds.; Springer: Berlin, 1988; p 233.

(7) Sato, T.; Watanabe, M.; Noyori, R. *Tetrahedron Lett.* **1979**, 2897.

(8) (a) Sondheimer, F.; Mazur, Y. *J. Am. Chem. Soc.* **1958**, *80*, 6296. (b) Sondheimer, F.; Mazur, Y. *Ibid.* **1958**, *80*, 5220.

Scheme III



6a/b, X = OH
14a/b, X = $OSiMe_2{}^tBu$

15a/b, R = H
16a/b, R = CH_3

17a, X = OH, Y = H
17b, X = H, Y = OH
18a, X = OC(=S)SMe, Y = H
18b, X = H, Y = OC(=S)SMe
19, X = Y = H

17c

[a] $^tBuMe_2SiCl$, imidazole, DMF, 25 °C, 18 h (90%). [b] H_2, Pd/C, EtOAc, MeOH, 25 °C, 10 h (85%). [c] MeI, KO^{t}Bu, ^{t}BuOH, C_6H_6, 25 °C, 20 min → 38 °C, 35 min, (82%). [d] $LiAlH_4$, Et_2O, 25 °C, 1.5 h (92%). [e] NaH, CS_2, THF, 66 °C, 0.5 h, then MeI, 66 °C, 0.5 h (74%). [f] $^nBu_3SnH$, toluene, 111 °C, 20 h (43%).

yield. Its deoxygenation proved to be very slow and was finally realized in 50% yield after subjecting **11** to $(n\text{-}C_4H_9)_3SnH$ in refluxing toluene twice for 8 h and then for 6 h under the same conditions except for the addition of AIBN. The protecting group was also removed during the deoxygenation to give **12** as the final product. Oxidation of **12** with pyridinium chlorochromate gave ketone **13** in 60% yield.

Stereoisomers **6a** and **6b** were also converted into ketone **13** via a similar sequence (Scheme III). Again, regioisomers were not separated until reduction of ketones **16a/b** gave a readily separable mixture of three alcohols **17a–c**.[10] Under the same reaction conditions described for the exo series above, the endo isomers were found to react somewhat more slowly and to give somewhat lower yields. The overall yield from **6** to **17** was 58%, in contrast to 94% for the sequence **6** → **10**. Barton reduction of the anti regioisomers **17a** and **17b** proceeded via the dithiocarbonate in a similar manner to reduction of **11**. The silyl ether, with the less accessible endo stereochemistry, was unaffected by this procedure and was therefore removed in a separate step (HF/CH_3CN), giving the corresponding endo-alcohol **20**. The more hindered syn compound **17c** was also readily converted to a dithiocarbonate, but the latter proved to be very resistant to reduction, proceeding in only very low yield. Oxidation of **20** gave **13**, identical with that produced from the exo series.

A modification of a sequence developed by Garst was used to construct the furan ring.[11] Ketone **13** was formylated regiospecifically to give a 67% yield of **21**.[12] In solution **21** consists of 75–80% intramolecularly hydrogen-bonded (*Z*)-β-hydroxyenone (^1H NMR signal at δ 7.63), the remainder being the *E* isomer (δ 8.05) and traces of ketoaldehyde. The regioselectivity of this process was confirmed by both the clean, unsplit appearance of the NMR signals for the α-protons at C-8 and the successful conversion to the natural product. Ireland's procedure for the preparation of the thiomethylene derivative gave **22a** and **22b** in quantitative yield.[13] Treatment of this mixture with trimethylsulfonium methylsulfate in a two-phase system provided an epoxide that rearranged on standing at room temperature for 24 h.[14] The rearrangement product was subsequently aromatized with hydrochloric acid in THF to provide furanether B (**1**) in 46% yield (70% based upon unrecovered **21**).[15] Spectral data (NMR and mass spectra) for **1** were in agreement with that published at the time of isolation.[16]

Experimental Section

General Procedures. Solvents and Reagents. For procedures carried out under anhydrous conditions, tetrahydrofuran (THF), benzene, and toluene were distilled from sodium benzophenone ketyl and stored over 4-Å molecular sieves under argon. Dimethylformamide (DMF) was vacuum distilled from calcium hydride before use. Dichloromethane was dried over 4-Å molecular sieves. Other solvents were used as received. All reagents were obtained commercially and either distilled if volatile or otherwise used without further purification. All reactions were carried out under an atmosphere of dried argon.

Separation, Purification, and Analysis. Neutral alumina (Mallinckrodt), silica gel (Baker), and Florisil (Sigma) for column chromatography were used as received. Analytic thin-layer chromatography was done on fluorescent indicating silica gel sheets (Merck). Iodine was used to visualize nonchromophoric bands. Analytical samples were purified by recrystallization or flash chromatography. ^1H NMR spectra were recorded at 90 or 300 MHz. High-resolution mass spectral data were determined at the Facility for Advanced Instrumentation (FAI) at the University of California, Davis. Microanalyses were performed at the microanalytical laboratory facility at the University of California, Berkeley. The purity of all title compounds was judged to be ≥95% for solids and ≥90% for liquids on the basis of melting-point (range ≤2 °C), elemental analysis, or 300-MHz NMR analyses. NMR spectra for compounds lacking either a sharp melting point or a satisfactory elemental analysis are included in the supplementary material (see the paragraph at the end of the paper).

(1*R,3*R**,5*S**)- and (1*R**,3*S**,5*S**)-1-Methyl-8-oxabicyclo[3.2.1]oct-6-en-3-ol (3 and 4).** The ketone **2** (1.00 g, 7.3 mmol), prepared by the method of Noyori, dissolved in 10 mL of ether was added to a suspension of 0.29 g of $LiAlH_4$ (7.6 mmol) in 30 mL of ether. The mixture was stirred at 0 °C for 1 h and room temperature for 2 h. Excess hydride was then destroyed by slow successive addition of 0.3 mL of H_2O, 0.3 mL of 15% aqueous NaOH, and 0.9 mL of H_2O. The mixture was filtered through a fritted glass funnel, and the residue was rinsed with 3 × 5 mL of ether. The combined ethereal portions were washed with saturated aqueous NaCl and dried (Na_2SO_4). Concentration yielded 0.96 g of a clear oil (94% yield) that consisted of a 2:1 mixture of exo and endo alcohols **3** and **4**. This crude material was used directly in the following step.

(1*R,7*S**,9*S**)- and (1*R**,7*S**,9*R**)-9-Hydroxy-4,7-dimethyl-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (5a and 6a) and (1*R**,7*S**,9*R**)- and (1*R**,7*S**,9*S**)-9-Hydroxy-1,4-dimethyl-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (5b and 6b).** To 80 mL of benzene that had been flushed with propyne was added 4.12 g of dicobalt octacarbonyl (12.1 mmol). A balloon full of propyne was attached, and the mixture was stirred at room temperature for 2 h. To the brown solution was added 1.67 g (11.9 mmol) of the alcohols **3** and **4** in 5 mL of benzene. The flask was flushed with 50:50 CO:propyne and then maintained under a 50:50 CO:propyne atmosphere for 42 h at 68 °C. The brown solution was then concentrated onto 60 g of silica gel and transferred to the top of a 150-g silica gel column previously made in hexane. The column was eluted with 1 L of hexane, 1 L of ether, and portions of ethyl acetate. The products began to elute after 400 mL of ethyl acetate. The regioisomeric

(9) Barton, D. H.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.
(10) An X-ray crystal structure determination has been carried out on compound **17c**, providing confirmation for the stereo- and regiochemical assignments described herein: Olmstead, M. M., unpublished results.
(11) Garst, M. E.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 250.
(12) Johnson, W. S.; Posvic, H. *J. Am. Chem. Soc.* **1947**, *69*, 1361.
(13) Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615.
(14) Mosset, P.; Gree, R. *Synth. Commun.* **1985**, *15*, 749.
(15) Jessen, B.; Schroder, G.; Tochtermann, W. *Chem. Ber.* **1985**, *118*, 3287.
(16) Since the completion of the work described in this paper an alternative, complementary approach to this system has been successfully developed: Price, M. E.; Schore, N. E. *Tetrahedron Lett.*, in press.

endo-alcohols **6a** and **6b** eluted first (0.66 g), followed by *exo*-alcohols **5a** and **5b** (1.39 g). Passing each pair of regioisomers through a short silica gel column gave colorless liquids, free of cobalt impurities: 0.60 g of isomers **6a** and **6b** and 1.26 g of isomers **5a** and **5b** (75% yield total).

5a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30 (s, 3 H), 1.37–1.73 (series of m, 3 H), 1.80 (d, J = 0.9 Hz, 3 H), 2.01–2.20 (m, 2 H), 2.71 (d, J = 5.4 Hz, 1 H), 3.07 (br s, 1 H), 4.06 (m, 1 H), 4.48 (br s, 1 H), 7.18 (m, 1 H); IR (CH_2Cl_2) 3584, 1705, 1640 cm^{-1}. **6a**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (s, 3 H), 1.79 (s, 3 H), 1.83–1.91 (m, 3 H), 2.00–2.12 (m, 2 H), 3.26 (d, J = 5.4 Hz, 1 H), 3.62 (br m, 1 H), 4.24 (br s, 1 H), 4.42 (d, J = 3.6 Hz, 1 H), 7.22 (q, J = 1.5 Hz, 1 H). **5b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 3 H), 1.37–1.73 (series of m, 3 H), 1.77 (d, J = 0.9 Hz, 3 H), 2.01–2.20 (m, 2 H), 2.58 (d, J = 5.4 Hz, 1 H), 3.17 (br s, 1 H), 4.06 (m, 1 H), 4.23 (br s, 1 H), 7.15 (m, 1 H). **6b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29 (s, 3 H), 1.76 (s, 3 H), 1.83–1.91 (m, 3 H), 2.00–2.12 (m, 2 H), 3.20 (d, J = 5.4 Hz, 1 H), 3.72 (br m, 1 H), 4.17 (d, J = 3.6 Hz, 1 H), 4.24 (br s, 1 H), 7.19 (q, J = 1.5 Hz, 1 H); high-resolution MS for a mixture of **5a** and **5b** calcd for $C_{12}H_{16}O_3$ m/e 208.1099, found m/e 208.1108. For a mixture of **6a** and **6b**, found m/e 208.1107.

(1*R,7*S**,9*S**)-4,7- and (1*R**,7*S**,9*R**)-1,4-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo-[5.3.1.0^{2,6}]undec-4-en-3-one (7a and 7b).** To 0.79 g (3.8 mmol) of *exo*-alcohols **5a** and **5b** dissolved in 1.25 mL of DMF were added 0.65 g (9.5 mmol) of imidazole and 0.69 g (4.6 mmol) of *tert*-butyldimethylsilyl chloride. The mixture was stirred for 18 h at room temperature. The mixture was poured into 10 mL of H_2O and extracted with 4 × 15 mL of ether. The combined ether extracts were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to yield 1.3 g of an oil. This material was chromatographed by flash on silica gel to yield 1.15 g of a white solid (94% yield). Recrystallization from methanol–H_2O yielded a colorless solid, mp 64.0–65.0 °C.

7a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 6 H), 0.87 (s, 9 H), 1.26 (s, 3 H), 1.41–1.75 (m, 2 H), 1.78 (s, 3 H), 1.85–1.96 (m, 2 H), 2.65 (d, J = 5.4 Hz, 1 H), 3.03 (br s, 1 H), 3.99 (m, 1 H), 4.42 (br s, 1 H), 7.15 (m, 1 H); IR (CH_2Cl_2) 1703, 1639 cm^{-1}. **7b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 6 H), 0.87 (s, 9 H), 1.29 (s, 3 H), 1.41–1.75 (m, 2 H), 1.75 (s, 3 H), 1.85–1.98 (m, 2 H), 2.53 (d, J = 5.4 Hz, 1 H), 3.13 (br s, 1 H), 3.91 (m, 1 H), 7.13 (m, 1 H). Anal. Calcd for $C_{18}H_{30}O_3Si$: C, 67.03; H, 9.38. Found: C, 66.79; H, 9.28.

(1*R,4*S**,7*S**,9*S**)-4,7- and (1*R**,4*S**,7*S**,9*R**)-1,4-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-one (8a and 8b).** To a solution of 1.15 g (3.6 mmol) of **7a** and **7b** in 35 mL of a 1:1 mixture of ethyl acetate and methanol was added ca. 110 mg of 5% palladium on carbon. The mixture was stirred under 1 atm of hydrogen for 10 h. Filtration through Celite and concentration afforded 1.16 g (100%) of a clear oil that solidified on standing. Recrystallization from methanol–H_2O afforded a colorless solid, mp 53.5–55.5 °C.

8a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.06 (d, J = 6.6 Hz, 3 H), 1.30 (s, 3 H), 1.31–1.72 (m, 3 H), 1.86–1.93 (m, 2 H), 2.11–2.74 (m, 4 H), 3.86 (m, 1 H), 4.53 (br s, 1 H); IR (CH_2Cl_2) 1740 cm^{-1}. **8b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.06 (d, J = 6.6 Hz, 3 H), 1.35 (s, 3 H), 1.31–1.72 (m, 3 H), 1.86–1.93 (m, 2 H), 2.11–2.74 (m, 4 H), 3.86 (m, 1 H), 4.13 (br s, 1 H). Anal. Calcd for $C_{18}H_{32}O_3Si$: C, 66.62; H, 9.94. Found: C, 66.47; H, 9.98.

(1*R,7*S**,9*S**)-4,4,7- and (1*R**,7*S**,9*R**)-1,4,4-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo-[5.3.1.0^{2,6}]undecan-3-one (9a and 9b).** To a suspension of 0.78 g (6.9 mmol) of potassium *tert*-butoxide in a mixture of 5 mL of *tert*-butyl alcohol and 1 mL of benzene was added 0.75 g (2.3 mmol) of ketones **8a** and **8b**. After this stirred briefly, 2.30 g (16.2 mmol) methyl iodide was added. The mixture was stirred for 20 min at 25 °C, during which time a precipitate, presumably KI, appeared. The mixture was then heated at 38 °C (oil bath temperature) for 35 min. When this cooled, 5 mL water was added, and the mixture was stirred to dissolve the precipitate. After addition of 20 mL of ether the layers were separated, and the aqueous layer extracted with 3 × 10 mL of ether. The combined ether extracts were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give 0.78 g (100%) of a light yellow oil that solidified on standing. Recrystallization from methanol–H_2O afforded a colorless solid, mp 74.0–76.0 °C.

9a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.06 (s, 3 H), 1.09 (s, 3 H), 1.28 (s, 3 H), 1.46–1.69 (m, 3 H), 1.75–1.95 (m, 3 H), 2.55–2.80 (m, 2 H), 3.90 (m, 1 H), 4.50 (br s, 1 H); IR (CH_2Cl_2) 1738 cm^{-1}. **9b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.04 (s, 3 H), 1.05 (s, 3 H), 1.34 (s, 3 H), 2.03–2.13 (m, 1 H), 3.90 (m, 1 H), 4.12 (br s, 1 H); high-resolution MS calcd for $C_{15}H_{25}O_3Si$ (M − 57, loss of t-C_4H_9 from Si) m/e 281.1573, found m/e 281.1549.

(1*R,3*R**,7*S**,9*S**)- and (1*R**,3*S**,7*S**,9*S**)-4,4,7-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-ol (10a and 10b) and (1*R**,3*R**,7*S**,9*R**)-1,4,4-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-ol (10c).** To a suspension of 0.10 g (2.6 mmol) of $LiAlH_4$ in 8 mL of dry ether at 0 °C was added dropwise 0.78 g (2.3 mmol) of an ether solution of **9a** and **9b**. The mixture was stirred for 30 min at 0 °C and 1.5 h at 25 °C. Excess hydride was destroyed by successive addition of 0.1 mL of water, 0.1 mL of 15% NaOH, and 0.3 mL of water. The mixture was filtered through a frit, and the residue washed with small portions of ether. The combined filtrates were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give 0.80 g of an oil. Flash chromatography on silica gel (15:85 ethyl acetate:hexane) gave the three isomeric products **10c** (0.25 g, colorless solid, mp 114.5–115.5 °C), **10a** (0.35 g, colorless solid, mp 56.0–58.0 °C), and **10b** (0.20 g, colorless solid, mp 94.0–95.0 °C).

10a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 6 H), 0.89 (s, 9 H), 0.91 (s, 3 H), 1.08 (s, 3 H), 1.23 (s, 3 H), 1.20–1.62 (m, 4 H), 1.76–1.85 (m, 2 H), 2.09 (d, J = 9.6 Hz, 1 H), 2.43–2.53 (m, 1 H), 2.72 (m, 1 H), 3.48 (m, 1 H), 3.93 (m, 1 H), 4.47 (br s, 1 H). **10b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.89 (s, 9 H), 0.92 (s, 3 H), 1.01 (s, 3 H), 1.20 (s, 3 H), 1.25–1.86 (series of m, 9 H), 2.20–2.38 (m, 2 H), 3.37 (m, 1 H), 3.90 (m, 1 H), 4.18 (br s, 1 H). **10c**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 6 H), 0.89 (s, 9 H), 1.08 (s, 3 H), 1.62 (s, 3 H), 1.42–1.93 (m, 8 H), 2.59 (m, 2 H), 2.97 (d, J = 8.4 Hz, 1 H), 3.54 (m, 1 H), 3.96 (m, 1 H), 4.04 (br s, 1 H); IR (CH_2Cl_2) 3530 cm^{-1}; high-resolution MS for **10a** calcd for $C_{15}H_{27}O_3Si$ (M − 57) m/e 283.1729, found m/e 283.1723. **10b**: Found m/e = 283.1724. **10c**: Anal. Calcd for $C_{19}H_{36}O_3Si$: C, 67.01; H, 10.65. Found: C, 66.83; H, 10.74.

***S*-Methyl *O*-[(1*R**,3*R**,7*S**,9*S**)-4,4,7-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo-[5.3.1.0^{2,6}]undecan-3-yl]thiothionocarbonate (11).** Sodium hydride (0.09 g of a 60% mineral oil suspension, 2.3 mmol) was washed with 3 × 1 mL of pentane and aspirated to dryness. The sodium hydride was then suspended in 2.0 mL of THF. Slowly 0.38 g (0.96 mmol) of **10a** in 5 mL of THF was then added along with 2 mg of imidazole. The mixture was stirred at 66 °C (oil bath temperature) for 55 min. The resulting pink suspension was cooled briefly before adding 0.29 mL (0.37 g, 4.8 mmol) of carbon disulfide. After brief stirring, the mixture was again heated at 66 °C for 30 min, during which time it became an orangish brown color. After brief cooling, 0.30 mL (0.68 g, 4.8 mmol) of methyl iodide was added, and the mixture was stirred briefly and then returned to 66 °C for 30 min. The mixture became a pale yellow color and contained a white precipitate. The suspension was then cooled in an ice bath, and 0.4 mL of glacial acetic acid was added very slowly. Water (5 mL) and 8 mL of dichloromethane were then added. After separation of the layers, the aqueous layer was extracted with 2 × 5 mL of dichloromethane. The combined organic extracts were washed twice with saturated aqueous $NaHCO_3$, then water and saturated aqueous NaCl. Upon drying (Na_2SO_4) and concentration 0.42 g (100% yield) of a reddish oil which solidified upon standing was obtained, having mp 104.0–105.0 °C after chromatography on silica gel; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 6 H), 0.89 (s, 9 H), 1.04 (s, 6 H), 1.25 (s, 3 H), 1.24–1.55 (m, 4 H), 1.67–1.88 (m, 2 H), 2.57 (s, 3 H), 2.86 (m, 1 H), 2.48–2.60 (m, 1 H), 3.93 (m, 1 H), 4.03 (br s, 1 H), 5.80 (d, J = 6.0 Hz, 1 H); high-resolution MS calcd for $C_{17}H_{29}O_3S_2Si$ (M − 57) m/e 373.1327, found 373.1308. Anal. Calcd for $C_{21}H_{38}O_3S_2Si$: C, 58.56; H, 8.89; S, 14.9. Found: C, 58.28; H, 8.92; S, 14.6.

(1*R,7*S**,9*R**)-1,4,4-Trimethyl-*exo*-11-oxatricyclo-[5.3.1.0^{2,6}]undecan-9-ol (12).** To a solution of 0.41 g (0.95 mmol) of **11** in 18 mL of toluene was added 0.60 mL (0.65 g, 2.2 mmol) of tributyltin hydride. The solution was refluxed for 8 h. After

concentration on a rotary evaporator, the residual oil was transferred to an alumina column (30 g) that had been previously prepared with hexane. Gradient elution with hexane and ether and the pure ethyl acetate provided 0.095 g of recovered **11** (mixed with tin-containing organic impurities) and 0.52 g of desilylated **11** also containing organic tin-containing impurities. This desilylated material was redissolved in 15 mL of toluene, and 0.36 mL (0.39 g, 1.3 mmol) of tributyltin hydride was added. This solution was refluxed for 8 h, concentrated, and resubmitted to chromatography on alumina. A mixture of desilylated **11** and **12** (0.23 g) plus organic tin-containing impurities was obtained. This crude mixture was then redissolved in 10 mL of toluene, and 0.30 mL (0.32 g, 1.1 mmol) of tributyltin hydride along with 10 mg of AIBN was added. This solution was then added dropwise to 10 mL of refluxing toluene. AIBN (5 mg) was added to the refluxing solution after 2 and 4 h. After 6 h of total reflux time, the solution was concentrated, and the residue chromatographed on alumina to yield 0.10 g of *exo*-alcohol **12**, a colorless liquid, still containing very small amounts of organic tin-containing impurities (0.48 mmol, 50% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (s, 3 H), 1.06 (s, 3 H), 1.24 (s, 3 H), 1.11–1.74 (series of m, 7 H), 1.89–1.99 (m, 2 H), 2.35–2.58 (m, 2 H), 3.97 (br s, 1 H), 4.01 (br s, 1 H). IR (CH_2Cl_2) 3599 cm^{-1}; high-resolution MS calcd for $C_{13}H_{22}O_2$ *m/e* 210.1620, found *m/e* 210.1615.

(1*R,7*S**,9*R**)-4,7- and (1*R**,7*S**,9*S**)-1,4-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undec-4-en-3-one (14a and 14b).** With the same procedure described for the conversion of **5a/b** into **7a/b**, 0.60 g (2.9 mmol) of a mixture of regioisomeric *endo*-alcohols **6a** and **6b** was converted into 0.85 g of a mixture of **14a** and **14b** (90% yield). Recrystallization from methanol–H_2O yielded a colorless solid, mp 71.0–73.0 °C.

14a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.24 (s, 3 H), 1.65–1.79 (m, 2 H), 1.81 (s, 3 H), 1.84–2.08 (series of m, 2 H), 3.27 (d, J = 5.4 Hz, 1 H), 3.62 (br m, 1 H), 4.12 (br d, J = 3 Hz, 1 H), 4.13 (br d, J = 3 Hz, 1 H), 7.23 (q, J = 1.5 Hz, 1 H). **14b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 6 H), 0.88 (s, 9 H), 1.29 (s, 3 H), 1.65–1.79 (m, 2 H), 1.77 (s, 3 H), 1.84–2.08 (series of m, 2 H), 3.21 (d, J = 5.4 Hz, 1 H), 3.72 (br m, 1 H), 4.13 (br d, J = 3 Hz, 1 H), 4.14 (br d, J = 3 Hz, 1 H), 7.18 (q, J = 1.5 Hz, 1 H); high-resolution MS calcd for $C_{14}H_{21}O_3Si$ (M – 57) *m/e* 265.1260, found *m/e* 265.1276. Anal. Calcd for $C_{18}H_{30}O_3Si$: C, 67.03; H, 9.38. Found: C, 66.64; H, 9.57.

(1*R,4*S**,7*S**,9*R**)-4,7-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-one and (1*R**,4*S**,7*S**,9*S**)-1,4-Dimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-one (15a and 15b).** With the same procedure described for hydrogenation of **7a/b**, 0.85 g (2.6 mmol) of **14a/b** was converted into 0.70 g of **15a/b** (85% yield), a colorless liquid.

15a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.03 (s, 6 H), 0.89 (s, 9 H), 1.05 (d, J = 6.6 Hz, 3 H), 1.26 (s, 3 H), 1.19–1.30 (m, 2 H), 1.63–1.78 (m, 2 H), 1.84–2.03 (m, 2 H), 2.10–2.25 (m, 1 H), 2.32–2.47 (m, 1 H), 3.03 (dd, J = 8.4, 17.7 Hz, 1 H), 3.53 (d, J = 9 Hz, 1 H), 4.08 (br s, 1 H). **15b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.05 (d, J = 6.6 Hz, 3 H), 1.19–1.30 (m, 2 H), 1.32 (s, 3 H), 1.63–1.78 (m, 2 H), 1.84–2.03 (m, 2 H), 2.10–2.25 (m, 1 H), 2.32–2.47 (m, 1 H), 3.15 (dd, J = 8.7, 17.7 Hz, 1 H), 3.32 (d, J = 9 Hz, 1 Hz), 4.50 (br s, 1 H); high-resolution MS calcd for $C_{14}H_{25}O_3Si$ (M – 57) *m/e* 267.1417, found *m/e* 267.1419.

(1*R,7*S**,9*R**)-4,4,7- and (1*R**,7*S**,9*S**)-1,4,4-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-one (16a and 16b).** With the same procedure described for the methylation of ketones **8a** and **8b**, 0.70 g (2.2 mmol) of ketones **15a/b** was converted to 0.60 g of ketones **16a/b** (82% yield). Recrystallization from methanol–H_2O afforded a colorless solid, mp 39.0–41.0 °C.

16a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.35 (s, 6 H), 0.90 (s, 9 H), 1.05 (s, 3 H), 1.08 (s, 3 H), 1.24 (s, 3 H), 1.21–1.31 (m, 2 H), 1.47–2.10 (series of m, 4 H), 3.08 (dd, J = 9 Hz, 1 H), 3.68 (d, J = 9.0, 18.0 Hz, 1 H), 4.07 (br s, 1 H), 4.47 (br s, 1 H). **16b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 6 H), 0.90 (s, 9 H), 1.02 (s, 3 H), 1.04 (s, 3 H), 1.21–1.31 (m, 2 H), 1.31 (s, 3 H), 1.47–2.10 (series of m, 4 H), 3.22 (dd, J = 9.0, 18.0 Hz, 1 H), 3.41 (d, J = 9 Hz, 1 H), 4.07 (br s, 1 H), 4.08 (br s, 1 H); high-resolution MS calcd for $C_{19}H_{34}O_3Si$ *m/e* 338.2277, found *m/e* 338.2288. Anal. Calcd for $C_{19}H_{34}O_3Si$: C, 67.41; H, 10.12. Found: C, 67.01; H, 10.32.

(1*R,3*R**,7*S**,9*R**)- and (1*R**,3*S**,7*S**,9*R**)-4,4,7-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-ol (17a and 17b) and (1*R**,3*R**,7*S**,9*S**)-1,4,4-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy)]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-3-ol (17c).** With the same procedure described for $LiAlH_4$ reduction of **9a** and **9b**, reduction of 0.45 g (1.3 mmol) of **16a/b** gave three isomeric products: **17a/b** (0.30 g) and **17c** (0.11 g), for a total yield of 92%. Compound **17c** was isolated as a colorless, crystalline solid, mp 76.0–77.0 °C.

17a: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 6 H), 0.87 (s, 3 H), 0.89 (s, 9 H), 1.05 (s, 3 H), 1.19 (s, 3 H), 1.20–2.22 (series of m, 9 H), 3.14 (m, 1 H), 3.34 (m, 1 H), 3.43 (br s, 1 H), 4.04 (br s, 1 H), 4.25 (br s, 1 H). **17b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.03 (s, 6 H), 0.88 (s, 3 H), 0.90 (s, 9 H), 0.99 (s, 3 H), 1.49 (s, 3 H), 1.22–2.22 (series of m, 9 H), 2.89 (m, 2 H), 3.30 (br s, 1 H), 4.05 (br s, 1 H), 4.15 (br s, 1 H). **17c**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 6 H), 0.87 (s, 3 H), 0.91 (s, 9 H), 1.07 (s, 3 H), 1.38–1.41 (m, 2 H), 1.59 (s, 3 H), 1.57–1.72 (m, 2 H), 1.80–1.97 (m, 2 H), 2.87 (dd, J = 4.8, 9.0 Hz, 1 H), 2.98 (d, J = 5.4 Hz, 1 H), 3.54 (dd, J = 4.8, 8.1 Hz, 1 H), 3.61 (q, J = 9.0 Hz, 1 H), 3.99 (br s, 1 H), 4.03 (br d, J = 4.8 Hz, 1 H); high-resolution MS for **17c** calcd for $C_{19}H_{36}O_3Si$ *m/e* 340.2433, found *m/e* 340.2425. Anal. Calcd for $C_{19}H_{36}O_3Si$: C, 67.01; H, 10.65. Found: C, 66.51; H, 10.69.

(1*R,7*S**,9*S**)-1,4,4-Trimethyl-9-[(*tert*-butyldimethylsilyl)oxy]-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecane (19) and (1*R**,7*S**,9*S**)-1,4,4-Trimethyl-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-9-ol (20).** With the procedure described for the conversion of alcohol **10a** into dithiocarbonate **11**, the mixture of stereoisomeric alcohols **17a/b** (0.129 g, 0.38 mmol) was converted into 0.12 g (74% yield) of a mixture of dithiocarbonates **18a/b**, suitable for use without further purification; the regioisomeric alcohol **17c** (0.114 g, 0.34 mmol) was likewise converted into dithiocarbonate **18c** (0.115 g, 79% yield). To a solution of 0.12 g (0.28 mmol) of the dithiocarbonate mixture **18a/b** in 10 mL of toluene was added 0.12 mL (0.13 g, 0.44 mmol) of tributyltin hydride. The solution was refluxed for 20 h. Concentration and chromatography on an alumina column as for **12** provided 0.064 g of recovered **18** together with 0.018 g of **19** (0.05 mmol, 18% yield, 43% based on unrecovered starting material), a colorless crystalline solid, mp 52.0–53.0 °C. This material was used directly in the next step; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 6 H), 0.89 (s, 3 H), 0.91 (s, 9 H), 1.05 (s, 3 H), 1.17 (s, 3 H), 1.25–1.34 (m, 3 H), 1.54–1.68 (m, 3 H), 1.78–1.95 (series of m, 2 H), 2.95 (dd, J = 8.7, 18.6 Hz, 1 H), 3.23 (dd, J = 8.7, 18.3 Hz, 1 H), 3.88 (br d, J = 2.7 Hz, 1 H), 4.05 (br t, J = 3.9 Hz, 1 H); high-resolution MS calcd for $C_{15}H_{27}O_2Si$ (M – 57) *m/e* 267.1781, found *m/e* 267.1780.

Desilylation of **19** was achieved as follows. To a solution of **19** (0.023 g, 0.07 mmol) in 1 mL of acetonitrile was added 2 drops of 48% aqueous HF. After stirring for 3 h at room temperature, the solution was diluted with 1 mL of chloroform and 1 mL of water. After separation of layers and extraction of the aqueous layer with 1 mL of chloroform, the combined organic layers were washed with saturated NaCl and dried (Na_2SO_4). Concentration gave a quantitative yield (0.015 g) of *endo*-alcohol **20**, a colorless liquid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (s, 3 H), 1.06 (s, 3 H), 1.20 (s, 3 H), 1.23–1.76 (series of m, 7 H), 1.86–2.04 (series of m, 2 H), 2.91 (dd, J = 8.7, 18.6 Hz, 1 H), 3.17 (dd, J = 8.7, 18.3 Hz, 1 H), 3.91 (d, J = 3.3 Hz, 1 H), 4.17 (br s, 1 H); high-resolution MS calcd for $C_{13}H_{22}O_2$ *m/e* 210.1620, found *m/e* 210.1620.

1,4,4-Trimethyl-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-9-one (13). To a suspension of 0.14 g (0.64 mmol) of pyridinium chlorochromate in 1.5 mL of dichloromethane was added 0.085 g (0.4 mmol) of **12** in 1.5 mL of dichloromethane. The blackened mixture was stirred at room temperature for 70 min. Ether (5 mL) was added and the solution was filtered through a short column of Florisil. The black residue was washed with 3 × 5 mL of ether, and the washes were also filtered through the Florisil column. Concentration afforded 0.50 g of **13** as an oil (60%). Similar reaction of **20** gave essentially the same result. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (s, 3 H), 1.07 (s, 3 H), 1.34 (s, 3 H), 1.18–1.49 (m, 4 H), 2.27–2.66 (series of m, 6 H), 4.26 (d, J = 4.8 Hz, 1 H); IR (CH_2Cl_2) 1718 cm^{-1}; high-resolution MS calcd for $C_{13}H_{20}O_2$ *m/e* 208.1463, found *m/e* 208.1469.

1,4,4-Trimethyl-8-(hydroxymethylene)-*exo*-11-oxatricyclo[5.3.1.0^{2,6}]undecan-9-one (21). To 0.047 g (0.23 mmol) of **13** in 2 mL of benzene was added 0.037 g (0.68 mmol) of sodium methoxide and 0.18 mL (0.17 g, 2.3 mmol) of ethyl formate. The mixture was stirred at room temperature for 18 h. Ice and water (5 mL) were then added along with 0.5 mL of 5% aqueous NaOH. After separation of the layers, the organic phase was washed with 3 × 1 mL of aqueous NaOH. The combined aqueous portions were washed once with 2 mL of ether and then brought to pH 3 with concentrated HCl after cooling in ice. This acidic aqueous mixture was then extracted with 4 × 2 mL ether. The combined ether extracts were washed with water and saturated aqueous NaCl, and dried (Na_2SO_4). Concentration afforded 0.022 g (0.09 mmol) of **21** as a yellow oil (42% yield). The original organic mixture (after NaOH wash above) was washed with water and saturated aqueous NaCl and dried (Na_2SO_4). Concentration afforded 0.018 g (0.09 mmol) of **13**. The yield based on recovered **13** is 67%. Crude **21**, a mixture of β-hydroxyenone stereoisomers and ketoaldehyde, was used without further purification; ^{1}H NMR ($CDCl_3$, 300 MHz, major component) δ 0.88 (s, 3 H), 1.07 (s, 3 H), 1.34 (s, 3 H), 1.19–1.51 (series of m, 4 H), 2.37 (d, J = 19.2 Hz, 1 H), 2.46–2.76 (m, 2 H), 2.61 (d, J = 19.2 Hz, 1 H), 4.37 (s, 1 H), 7.63 (s, 1 H), 13.40 (br s, 1 H); IR (CH_2Cl_2) 3056, 1644, 1619 cm^{-1}; high-resolution MS calcd for $C_{14}H_{20}O_3$ m/e 236.1412, found m/e 236.1420.

Furanether B (1). To a solution of 0.02 g (0.14 mmol) of butanethiol in 3.5 mL of benzene was added 0.022 g (0.9 mmol) of **21** and 8 mg *p*-TsOH. The solution was refluxed, with removal of water, for 1 h. Upon cooling the mixture was washed twice with 1 mL of 2.5% aqueous NaOH, 2 × 1 mL of water, and saturated aqueous NaCl and dried (Na_2SO_4). Concentration afforded 0.033 g of yellow oil that was used directly in the next reaction.

The crude thiomethylene ketone was dissolved in 0.6 mL of dichloromethane. To this solution was added 0.035 g (0.19 mmol) of trimethylsulfonium methylsulfate and 0.25 mL of 50% aqueous NaOH. The mixture was stirred at reflux (48 °C oil bath) for 24 h. After this cooled, 0.5 mL dichloromethane was added and the organic layer was separated from the aqueous layer. The aqueous layer was then diluted with 0.25 mL of water and extracted with 3 × 1 mL of ether. The combined organic layers were washed with water, and saturated aqueous NaCl and dried (Na_2SO_4). Concentration afforded a lemon yellow oil that was let stand at room temperature for 24 h. The oil was then dissolved in 0.5 mL of THF, and 0.25 mL of 2 N HCl was added. This mixture was stirred at room temperature for 3 h. After saturation with solid $CaCO_3$, the organic layer was diluted with 1 mL of ether, and the layers were separated. The aqueous layer was extracted with 2 × 1 mL of ether. The combined organic portions were washed with water and saturated aqueous NaCl, and dried (Na_2SO_4). Concentration yielded 0.029 g of yellow oil. Flash chromatography on silica gel (2:98 ethyl acetate:hexane) yielded 0.010 g of unreacted thiomethylene ketone and 0.010 g of furanether B (46% yield based on **21**, 70% based on unrecovered starting material); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.877 (s, 3 H), 1.091 (s, 3 H), 1.271–1.400 (m, 2 H), 1.404 (s, 3 H), 1.474 (m, 2 H), 2.531–2.619 (m, 2 H), 2.695–2.830 (m, 2 H), 4.797 (s, 1 H), 7.131 (s, 1 H), 7.172 (s, 1 H); high-resolution MS calcd for $C_{15}H_{20}O_2$ m/e 232.1463, found m/e 232.1475.

Acknowledgment. We wish to express our appreciation to Professor Paola Vita-Finzi for providing us with spectra of natural furanether B. We also thank Jon Strutzel for performing some preliminary experiments associated with this work. This work was supported by a grant from the National Institutes of Health (GM 26294). We are also grateful for support from the Chevron Research Corp. Mass spectrometric data were obtained from the Facility for Advanced Instrumentation of the University of California, Davis.

Registry No. (±)-**1**, 123164-81-8; (±)-**2**, 89920-04-7; (±)-**3**, 99327-50-1; (±)-**4**, 99327-49-8; (±)-**5a**, 123099-16-1; (±)-**5b**, 123099-27-4; (±)-**6a**, 123164-82-9; (±)-**6b**, 123164-90-9; (±)-**7a**, 123099-17-2; (±)-**7b**, 123099-28-5; (±)-**8a**, 123099-18-3; (±)-**8b**, 123099-29-6; (±)-**9a**, 123099-19-4; (±)-**9b**, 123099-30-9; (±)-**10a**, 123099-20-7; (±)-**10b**, 123164-91-0; (±)-**10c**, 123164-97-6; (±)-**11**, 123099-21-8; (±)-**11** (R = H), 123099-31-0; (±)-**12**, 123099-22-9; (±)-**13**, 123099-23-0; (±)-**14a**, 123164-83-0; (±)-**14b**, 123164-93-2; (±)-**15a**, 123164-84-1; (±)-**15b**, 123164-94-3; (±)-**16a**, 123164-85-2; (±)-**16b**, 123164-95-4; (±)-**17a**, 123164-86-3; (±)-**17b**, 123164-96-5; (±)-**17c**, 123099-33-2; (±)-**18a**, 123164-87-4; (±)-**18b**, 123237-24-1; (±)-**18c**, 123099-32-1; (±)-**19**, 123099-24-1; (±)-**20**, 123164-88-5; (±)-(*E*)-**21**, 123164-92-1; (±)-(*Z*)-**21**, 123099-25-2; (±)-(*E*)-**22**, 123164-89-6; (±)-(*Z*)-**22**, 123099-26-3; $CH_3C{\equiv}CH{\cdot}Co_2(CO)_8$, 41026-24-8.

Supplementary Material Available: NMR spectra for **5a/b**, **6a/b**, **12**, **13**, **15a/b**, **17a**, **17b**, **20**, and **1** (9 pages). Ordering information is given on any current masthead page.

Synthesis of 1,4-, 2,4-, and 3,4-Dimethylphenanthrenes: A Novel Deoxygenation of Arene 1,4-Endoxides with Trimethylsilyl Iodide

Kee-yong Jung and Masato Koreeda*

Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109

Received May 24, 1989

A mild, efficient synthesis of the carcinogen 1,4-dimethylphenanthrene (**2**) and its bay-region methyl-bearing regioisomers 2,4-dimethyl- and 3,4-dimethylphenanthrenes (**3** and **4**) is described. The synthesis involves a generally applicable strategy that features a furan/dimethyl-1-naphthyne cycloaddition reaction followed by a convenient direct deoxygenation of the resulting endoxide with excess trimethylsilyl iodide generated in situ. The Friedel–Crafts cyclization of *p*-xylene with γ-butyrolactone/$AlCl_3$ or γ-(2,5-dimethylphenyl)butyric acid via its trifluoromethanesulfonic anhydride derivative results in the formation of a mixture of 5,8-, 6,8-, and 5,7-dimethyl-1-tetralones (**17**, **20**, and **21**, respectively) through migration of aromatic methyl groups. The precursor to 6,8-dimethyl-1-naphthyne (**10**) was prepared from tetralone **20**, isolable only as a 5:1 inseparable mixture with **17** from the direct Friedel–Crafts cyclization of *p*-xylene with γ-butyrolactone, by α-dibromination with $CuBr_2$, dehydrobromination, and tosylation. The precursors to 5,8-dimethyl-1-naphthyne (**9**) and 7,8-dimethyl-1-naphthyne (**11**) were synthesized from the corresponding 1-naphthols **15** and **31**, respectively. The synthesis of these naphthols involved cycloaddition between the corresponding dimethylated benzyne and furan followed by acid-catalyzed isomerization.

Introduction

Methylated polycyclic aromatic hydrocarbons (PAHs) are of considerable interest since they have frequently been shown to possess biological activity that would not have been predicted based on studies of their parent hydrocarbons.[1] There appears to be a general rule regarding

0022-3263/89/1954-5667$01.50/0