The above data indicate that simple electron transfer from **1** initiates a cascade of reactions that afford as initial detectable species complexes **2** and **3**. Since the coupling of methylidene ligands to coordinated ethylene is a very general reaction,[14] we anticipate that the formation of a displaceable ethylene ligand may be possible from a variety of other methyl complexes. The nature of the dimeric intermediate formed from $\mathbf{1}^{\bullet+}$ is not presently known. However, the dimethyl diosmium complex *cis*-$Os_2(CO)_8(CH_3)_2$ has been previously shown by Norton to eliminate CH_4 at 120 °C and form the bridging methylidene complex $Os_2(CO)_8(\mu\text{-}CH_2)$.[15] In conclusion, we speculate that this simple but previously unrecognized methyl ligand activation might aid the development of an efficient method for homogeneous methane functionalization. This study also demonstrates the enhanced capability possible by the complementary use of chemical and electrochemical electron-transfer methods that cannot be achieved with either alone.

Acknowledgment. We thank the Norwegian Research Council for Science and Humanities, Statoil (VISTA program administered by the Norwegian Academy of Science and Letters), the U.S. Department of Energy, and NATO for support of this research.

Supplementary Material Available: Additional data and a figure for double potential step chronoamperometry experiments (2 pages).[9] Ordering information is given on any current masthead page.

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A Convergent General Synthetic Protocol for Construction of Spirocyclic Ketal Ionophores: An Application to the Total Synthesis of (-)-A-23187 (Calcimycin)

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The ionophore antibiotics encompass a class of biologically important molecules whose members are structurally quite diverse and often stereochemically complex.[1] A-23187 (calcimycin), cezomycin, and X-14885A (**1a-c**),[2-4] isolated from cultures of various strains of *Streptomyces*, are representatives of a growing class of these ionophores known to selectively transport divalent cations, particularly calcium ions (Scheme I).[5] The important biological activity and unusual structural features of this group, including a 1,7-dioxaspiro[5,5]undecane ring system on which seven stereogenic centers are arrayed and α-keto pyrrole and benzoxazole residues, have stimulated a number of synthetic studies.[6,7]

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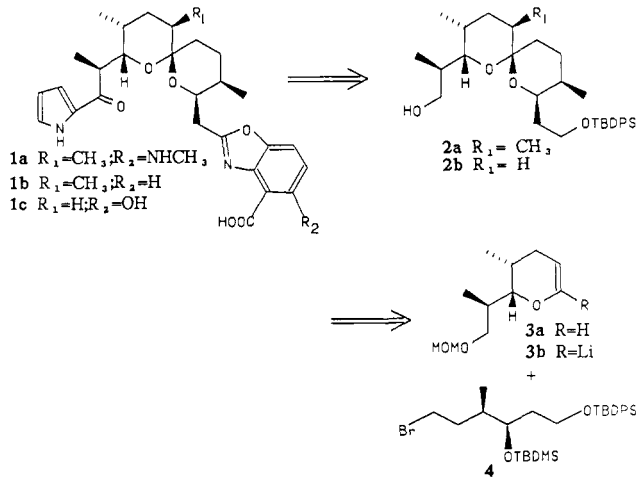
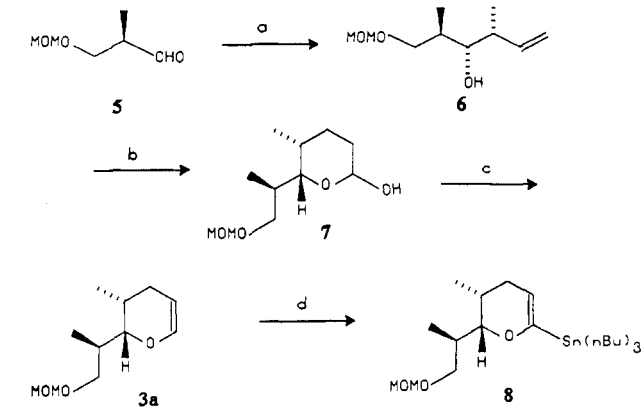
Scheme I

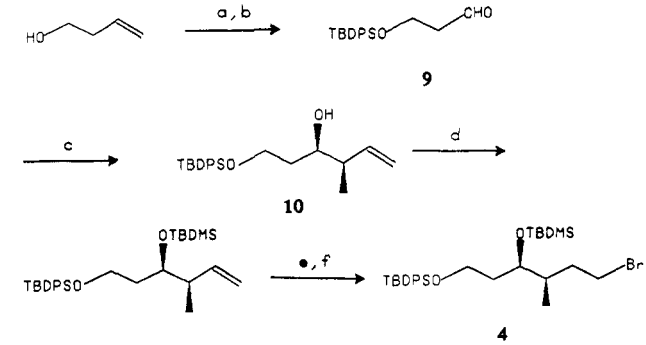


Scheme II[a]



[a] Reagents: (a) crotyltributylstannane (1.4 equiv), $MgBr_2$-Et_2O (2 equiv), CH_2Cl_2, -23 °C, 3 h; (b) BH_3-THF (1 equiv), THF, room temperature, 12 h, then successive addition of CH_3OH (1 equiv), 0 °C → room temperature, 2 h, $LiCH(SPh)OCH_3$ (3 equiv) in THF, -40 °C → -10 °C, 2 h, $HgCl_2$ (3 equiv), -10 °C → room temperature, 3 h, and H_2O_2 (12 equiv), pH 7, room temperature, 3 h; (c) MsCl (1.5 equiv), Et_3N (3 equiv), CH_2Cl_2, 14 h; (d) KO-*t*-Bu (3 equiv), *n*-BuLi (3 equiv), THF, -78 °C, 1 h then Bu_3SnCl (3.2 equiv), -78 °C → room temperature, 45 min.

Scheme III[a]



[a] Reagents: (a) TBDPSCl (1.1 equiv), imidazole (2 equiv), DMF, room temperature, 6 h; (b) O_3, CH_2Cl_2-CH_3OH (7:3), -78 °C; DMS, -78 °C to room temperature, 6 h; (c) (*Z*)-crotyldiisopinocampheylborane (1 equiv), THF, -78 °C, 5 h; H_2O_2, NaOH; (d) TBDMSOTf (1.3 equiv), Et_3N (3 equiv), CH_2Cl_2, room temperature, 1 h; (e) B-H_3-THF (1.5 equiv); H_2O_2, NaOH; (f) Ph_3P (2 equiv), CBr_4 (2 equiv), Et_2O, room temperature, 6 h.

Our interest in exploiting methodology for the generation and coupling of cyclic vinyl ether anions, developed in our labora-

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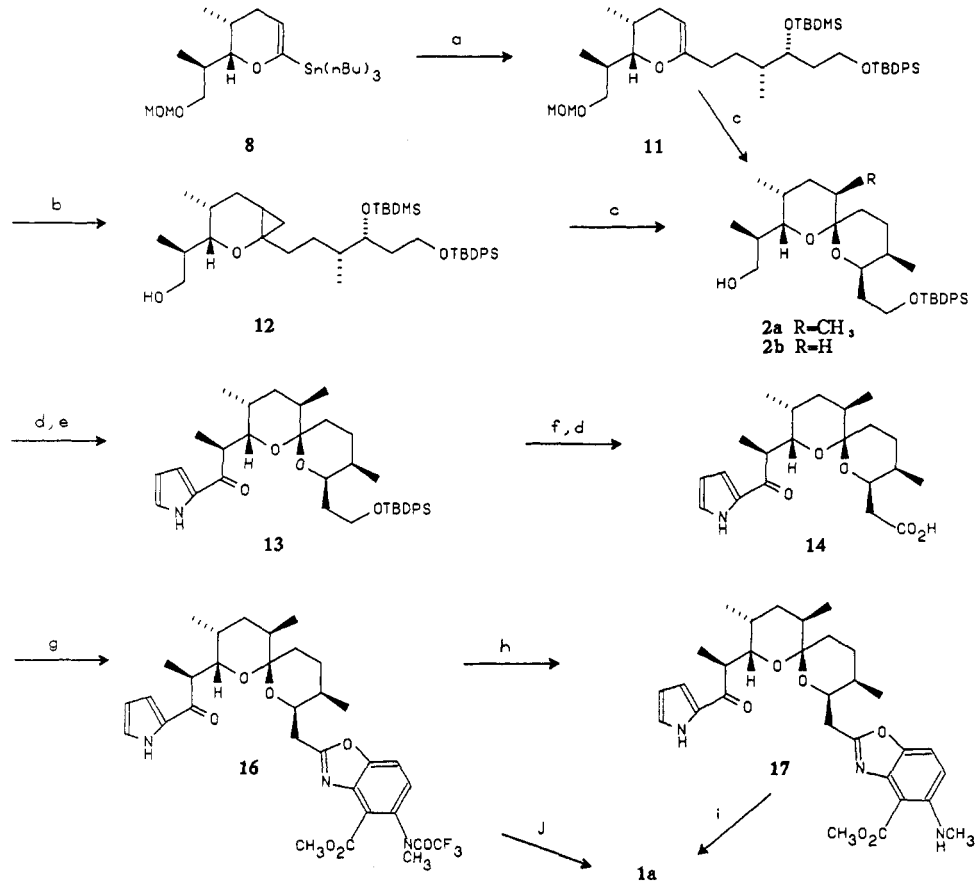
Scheme IV[a]



[a] Reagents: (a) *n*-BuLi (1.1 equiv), THF, −78 °C → 0 °C, 20 min; **4** (1.5 equiv), THF–HMPA, 0 °C → room temperature 16 h; (b) Et_2Zn (5 equiv, 1.0 M in hexanes), CH_2I_2 (10 equiv), ether, room temperature 5 h; (c) *p*-TsOH-H_2O (2 equiv), benzene, 55 °C, 5 h (3 h for **11**); (d) CrO_3, H_2SO_4, acetone, −20 °C → −5 °C, 1 h; (e) Ph_3P (4 equiv), 2,2′-dipyridyldisulfide (4 equiv), CH_2Cl_2, room temperature 16 h; pyrrole magnesium chloride (18 equiv), toluene, −78 °C, 295 h; (f) TBAF (2 equiv), THF, room temperature 2 h; (g) BOP (1 equiv), Et_3N (5 equiv), **15** (1 equiv), DMF, 65 °C, 18 h; PPTS (3 equiv), $ClCH_2CH_2Cl$, 4 A sieves, 80 °C, 24 h; (h) TBAF (2 equiv), THF, room temperature 3 h; (i) LiSPr (3 equiv), HMPA, room temperature 1 h; (j) LiSPr (10 equiv), HMPA, room temperature 3.5 h.

tories,[8-10] and in developing a general synthetic protocol for **1a–c** led to the retrosynthetic analysis for **1a–c** shown in Scheme I. Central to this analysis is the construction of differentially protected spirocyclic diols **2a,b** to which the appropriate pyrrole and benzoxazole residues could be appended. Both **2a,b** should be available from the common intermediates **3a** and **4**, via coupling of the derived anion **3b**.[8,9] We now describe the implementation of this general strategy as exemplified by the construction of (−)-A-23187 (calcimycin, **1a**).

The optically active dihydropyran **3a** was elaborated as shown in Scheme II. Protected aldehyde *R*-(−)-**5**[11-13] ($[\alpha]^{25}_D$ −12.6° (*c* 2.00, $CHCl_3$)) was condensed with tri-*n*-butylcrotylstannane in the presence of $MgBr_2$–Et_2O to establish the required 2,3-anti–3,4-syn relationship between the substituents.[14] A separable mixture of stereoisomers (6.7:1) was obtained in 88% total yield containing stereoisomer **6** as the major component.[15] One carbon homologation of **6** via hydroboration with BH_3–THF and in situ conversion to the dioxaborinane followed by addition rearrangement of lithiated methoxymethyl phenyl sulfide, afforded the desired lactols **7** (1.4:1 α:β) in 52% yield. Dihydropyran **3a** (α^{25}_D +68° (*c* 1.20, $CHCl_3$)) was then obtained in 85% yield upon treatment of the mixture of lactols **7** with CH_3SO_2Cl/Et_3N. Since attempts to deprotonate vinyl ether **3a** using *t*-BuLi (1 equiv) in THF at 0 °C were unsuccessful,[8,16] we converted **3a** to an alternative carbanion precursor, vinyl stannane **8**, in quantitative yield by treatment with *t*-BuOK/*n*-BuLi (3 equiv) at −78 °C and trapping with tri-*n*-butyltin chloride.[8,17]

The second major subunit, bromide **4**, was prepared as shown in Scheme III. Ozonolysis of 3-buten-1-ol *tert*-butyldimethylsilyl (TBDPS) ether and reductive workup provided aldehyde **9** in quantitative yield. Condensation of **9** with (*Z*)-crotyldiisopinocampheylborane (derived from (+)-α-pinene) provided alcohol **10** in 80% yield.[18-20] Conversion to bromide **4** was straightforward

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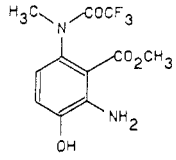
(19) Only one diastereomer was observed by 300-MHz ^{1}H NMR. Mosher ester formation showed the presence of a single diastereomer by 300-MHz ^{1}H NMR.[28]

by using standard methods (three steps, 62% overall from alcohol **10**).

We were then in a position to begin assembly of spirocyclic system. Regeneration of **3b** from **8** with 1 equiv of *n*-BuLi at −78 °C,[17] followed by addition of a solution of bromide **4** (1.5 equiv) in HMPA to the anion **3b** at 0 °C, provided the key alkylated vinyl ether **11** in 70% yield from **3a** (Scheme IV). Subsequent cyclopropanation of **11** using Et_2Zn/CH_2I_2 gave cleanly a mixture of diasteromeric cyclopropanes **12**.[21] The required substrate for the crucial closure to the spiroketal nucleus was now complete. Most pleasingly, direct treatment of the mixture of cyclopropanes **12** with *p*-TsOH–H_2O in benzene at 55 °C for 5 h gave the monoprotected spiroketal **2a** as a *single diastereomer* in 55% overall yield (from **11**).[22] Furthermore, **2b** (required for X-14885A (vide supra)) was obtained in comparable yield from **11** under the same conditions (unoptimized).

With the central spiroketal intermediate **2a** in hand, incorporation of the pyrrole unit was effected by using a variant of the Nicolaou procedure (Scheme IV).[23] Oxidation of **2a** gave the expected carboxylic acid which was converted to the desired α-keto pyrrole **13** in 80% overall yield (from **2a**) via treatment of the 2-thiopyridyl ester with a solution of pyrrole magnesium chloride in toluene. Desilylation of **13** with TBAF in THF followed by oxidation gave the pyrrole acid **14** ($[\alpha]^{23}_D$ +116° (*c* 0.15, $CHCl_3$) lit.[7] $[\alpha]^{25}_D$ +121° (*c* 0.01 $CHCl_3$)) which was identical in all respects (TLC, NMR, HRMS, $[\alpha]_D$) with material obtained by degradation of natural material.[24]

Treatment of acid **14** with aminophenol **15** (prepared by a modification of Evans' protocol[6,25]), benzotriazolyloxy-*tris*-(dimethylamino)phosphonium hexafluorophosphate (BOP),[26] and



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Et_3N in DMF gave the intermediate amide, which was directly closed to benzoxazole **16** by exposure of the crude amide to pyridinium *p*-toluene sulfonate (PPTS) in $ClCH_2CH_2Cl$ (73% overall from **14**).[27] Benzoxazole **16** was identical with authentic material in all respects.[27] Cleavage of the trifluoroacetyl group with TBAF in THF afforded (−)-A-23187 methyl ester **17** identical in all respects with authentic material.[28] Dealkylation to (−)-A-23187 (**1a**) with LiSPr in HMPA proceeded as previously described.[6] More efficiently, treatment of **16** with excess LiSPr in HMPA directly afforded **1a** (98%).

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Supplementary Material Available: NMR and analytical data (including spectra) for compounds **2a, 2b, 3a, 4, 6, 8, 10–14,** and **16** (14 pages). Ordering information is given on any current masthead page.

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(22) Both diastereomeric cyclopropanes **12** were transformed to **2a** by equilibration of the methyl group adjacent to the spiro ring junction,[6] presumably via the intermediate oxonium ion. The major byproduct was the spirocyclic diol arising from loss of the TBDPS group (30%), whose formation can presumably be avoided by modification of the TBDMS protecting group.

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(24) We thank the Eli Lilly Co., Indianapolis, IN, for their generous gift of the magnesium salt of (−)-A-23187.

(25) Aminophenol **15** was prepared in four steps from methyl 2-trifluoroacetamido-5-hydroxybenzoate: (1) TBDMSCl (1.1 (equiv), imidazole (2 equiv), DMF (70%); (2) CH_3I (20 equiv), K_2CO_3, acetone, Δ, 5 h (98%); (3) HNO_3, HF, CH_3NO_2 (70%); (4) H_2, 10% Pd–C, CH_3OH (90%).

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(28) Synthetic (−)-A-23187 (**1a**) (mp 185–187 °C, $[\alpha]^{25}_D$ −48.4° (*c* 0.3, $CHCl_3$)) and synthetic (−)-A-23187 methyl ester (**17**) were identical (TLC, mmp (free acids), IR, NMR (300 MHz), and MS) with authentic samples of natural (−)-A-23187 (mp 186–187 °C, $[\alpha]^{23}_D$ −45.1° (*c* 0.3, $CHCl_3$)) and (−)-A-23187 methyl ester (prepared by methylation (CH_2N_2) of natural A-23187).[24]

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Discovery of a New, Metallic (but Not Superconducting) Compound in the La–Sr–Cu–O System: $La_5SrCu_6O_{15}$

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The discovery of high-temperature superconductivity, first[1] near 40 K and later[2] near 90 K, has generated enormous interest in copper oxide compounds. From a materials perspective, the 90 K system $RBa_2Cu_3O_{7-\delta}$ (R = rare earth, Y), represented a new compound.[3,4] The superconductors with $T_c \sim 40$ K turned out[5,6] to be one of the phases studied earlier by Raveau and co-workers:[7,8] $La_{2-x}Sr_xCuO_4$ ($x \sim 0.15$) and the Ba analogue. As shown schematically in Figure 1, the stable compounds in the La-Sr-Cu-O system include: (1) the superconducting phase[7,8] (noted above) which has the K_2NiF_4-type structure of single sheets of corner sharing CuO_6 octahedra; (2) the $La_{2-x}Sr_{1+x}Cu_2O_{7-\delta}$ phase[9] having the $Sr_3Ti_2O_7$-type structure with double sheets of octahedra; and (3) two linear CuO chain compounds[10] $SrCuO_2$ and Sr_2CuO_3. We report here the discovery of a new highly conducting phase: $La_5Sr_1Cu_6O_{15}$. It is the first compound related to the cubic perovskite in this system and has metallic conductivity but does not become superconducting down to 5 K.

The samples were prepared by solid-state reaction in alumina crucibles from appropriate mixtures of La_2O_3, $SrCO_3$, and CuO. The powders were mixed and ground in an alumina mortar and pestle, fired in flowing oxygen at 900 °C for 6 h; followed by 3 cycles of regrinding, firing in flowing oxygen at 1025 °C for 16 h, and cooling slowly to room temperature (over 6 h).

The new phase is identified by its X-ray powder diffraction pattern, shown in Figure 2 together with the pattern of the related compound[11,12] $La_4BaCu_5O_{13}$. The composition $La_5SrCu_6O_y$ was

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