on methane concentration, while that proceeding via path 4 should not. Although there appears to be no dependence of k_{obsd} on $[CH_4]$, changes of 10–15% in the rate are at the limits of the precision of our rate measurements.[9]

An experiment which probably does distinguish between paths 4 and 7 is as follows. It can be seen from Scheme II that in thermolysis of $[(CD_3)_3P]_4Os(H)Np$, **1**-d_{36}, there will be a primary kinetic isotope effect only in the step of k_5. If methane activation proceeds through intermediate **4** (path 4), then there will be an increase in the ratio of **7**/**6** which results from path 3, i.e., an increase in k_4/k_5 because of the primary isotope effect on k_5. If **7** forms via intermediate **9** (path 7), then the **7**/**6** ratio should be unchanged since it is determined by k_7/k_3 and not k_5. The average of four pyrolyses of **1**-d_{36} yielded **7**-d_{36}/**6**-d_{36} corresponding to $k_4/k_5 = 1/2.7$ (compared to 1/6.6 for the average of four thermolyses of **1**-d_0), consistent with an isotope effect of 2.4 on k_5. Independent measurement of this isotope effect yields a value close to 2.5.[5]

Knowing $k_5/k_{4(SiMe_4)}$[5] and $k_5/k_{4(CH_4)}$ one can calculate the per-hydrogen relative reactivity of the C–H bonds in CH_4 and $SiMe_4$ to be 1.5/1.

Thus, this non-cyclopentadienyl-containing osmium system effects intermolecular oxidative additions of C–H bonds of both sp^2 and sp^3 carbon centers, the former to five-coordinate Os(II)[3] and the latter to three-coordinate Os(0). Investigations of reactions with other hydrocarbons and the effects of other phosphine and phosphite ligands on this chemistry are under way.

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(9) Free L forms in these reactions at concentrations of 7×10^{-4}–3×10^{-3} molar and the ratio of paths 1 and 6 depends on [L]. Thus, detection of a dependence on $[CH_4]$ for a 10–15% component of the total reaction means determining [L] with high precision. It is not possible to do this by NMR at these low concentrations.

New Strategies for Annulations: A Highly Convergent and Stereoselective Synthesis of an Octahydronaphthalene Synthon for Dihydrocompactin

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For some time, synthetic chemists have sought efficient and stereospecific methods for carbocyclic annulations. Our recent reports on the fluoride-induced cleavage of 1-(trimethylsilyl)-oxy-2-carbalkoxycyclopropanes have demonstrated the synthetic utility of γ-oxo-α-ester enolates or homoenolates in intermolecular pentannulations.[1,2] At this time we wish to describe a new strategy for annulations based on intramolecular trapping of homoenolates with a Michael acceptor (Scheme I). The protocol begins with a conjugate addition of a chain A containing a potential Michael acceptor and the in situ trapping of the enolate to form the silyl enol ether B. A crucial cyclopropanation of the enol ether sets the trans stereochemistry of the ring juncture in the eventual bicyclic system D. One of the inherent uncertainties in this strategy lies in the stereochemical disposition of the substituents E and CH_2W in various ring systems D.

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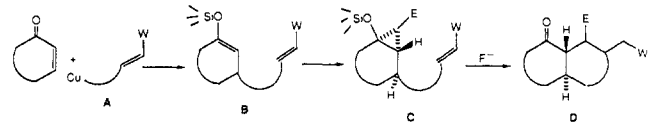
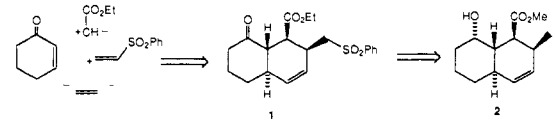
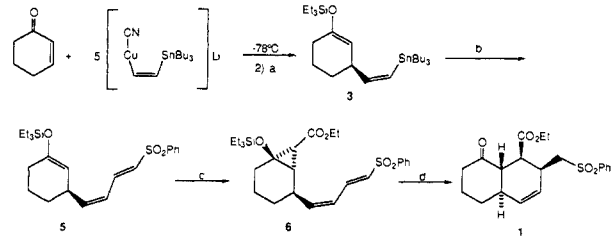
Scheme I



Scheme II



Scheme III[a]



[a] a. 5 equiv of Et_3SiCl, 6 equiv of Et_3N, THF, −78 °C to 0 °C; b. 1 equiv of *trans*-$PhSO_2CH{=}CHOTs$ (**4**) 2–3 mol% $PdCl_2(PPh_3)_2$, 6–10 mol% CuI, 3 equiv of LiCl, THF, 67 °C; c. N_2CHCO_2Et, 2 M solution in PhH, 0.5 mol% bis(*N*-benzylsalicylaldiminato)copper(II), 85 °C; d. 5 equiv of CsF, CH_3CN, 80 °C.

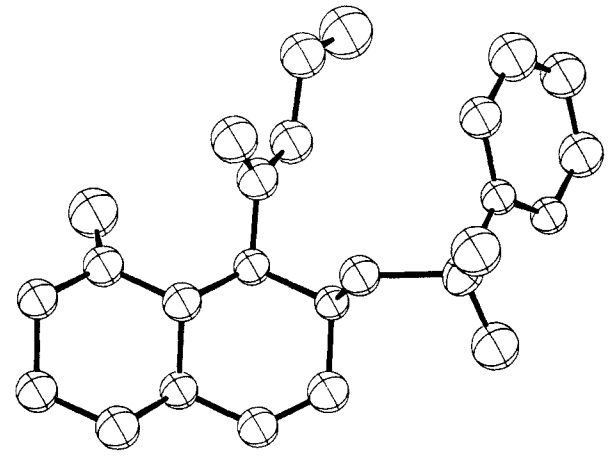


Figure 1. ORTEP drawing of compound **1**.

In this communication we report the successful execution of this strategy in the stereoselective synthesis of an octahydronaphthalene synthon of dihydrocompactin. The clinical importance of the mevinic acids as HMG-CoA reductase inhibitors[3] has prompted a flurry of synthetic activity in recent years.[4] We envisioned a four-step process to the octahydronaphthalene **1** which could easily be transformed into a known synthon **2** for dihydrocompactin.[5] A retrosynthetic analysis is shown in Scheme II with a unique combination of new synthons to introduce the dienyl sulfone chain.

Our synthesis first involved the conjugate addition of a *cis*-2-tri-*n*-butylstannylvinyl cuprate (generated in situ from tri-*n*-bu-

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tylstannyl cyanocuprate and acetylene) to cyclohexenone.[6] The intermediate enolate was trapped in situ with triethylsilyl chloride at −78 °C. The enol ether/vinyl stannane **3** can be isolated in 80–85% yield after flash chromatography (silica gel). The attachment of the vinyl sulfone unit in a stereospecific manner was efficiently achieved by a Stille reaction[7] involving *trans*-2-tosylvinylphenyl sulfone[8] **4** and a Pd(II) complex.[9] The resulting dienyl sulfone **5** was produced in yields of 65–70%. After chemoselective cyclopropanation of the enol ether double bond of **5** [ethyl diazoacetate and bis(*N*-benzylsalicylaldiminato)copper(II) catalyst, 65% yield], the stage was set for the key cyclization process. The reaction of **6** with cesium fluoride in refluxing acetonitrile did in fact trigger a facile cyclopropane cleavage and subsequent Michael addition to the vinyl sulfone, in 75–87% yields, in a completely stereoselective manner to install four contiguous chiral centers! This remarkable stereoselectivity is presumably controlled by the cis double bond of the dienyl sulfone and a preferred approach of the enolate to the geometrically accessible vinyl sulfone double bond.

The stereochemical assignments of the asymmetric centers in adduct **1** were confirmed both by high field ^{1}H NMR[5b,10] and by a single-crystal X-ray analysis[11] (Figure 1, see Supplementary Materials for details). The new synthon **1** was readily converted to a known dihydrocompactin relay compound **2**[5b] by stereospecific reduction of the ketone with L-Selectride (63% yield) and subsequent desulfonylation with concomitant ester exchange with sodium amalgam and disodium hydrogen phosphate in dry methanol (75% yield).[12]

In summary, the salient, new features of this convergent synthesis of the dihydrocompactin synthon **1** are (1) a new *cis*-2-stannylvinyl cuprate reagent, (2) the 2-tosylvinyl sulfone coupling, and most importantly (3) the intramolecular cyclization of an ester enolate on a vinyl sulfone in a stereospecific fashion.

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Supplementary Material Available: Summary of crystal data, fractional coordinates, thermal parameters, and perspective drawings for compound **1** (9 pages). Ordering information is given on any current masthead page.

(6) For a typical procedure: To a stirred solution of 5.25 mmol of LDA in 5 mL of dry THF was added 5.0 mmol of freshly distilled *n*-Bu_3SnH at −78 °C. After 30 min, the solution of anion was transferred via cannula into a stirred solution of 5.5 mmol of CuCN and 12 mmol of dry LiCl[13] in 20 mL of THF at −45 °C, producing a deep red solution of *n*-$Bu_3SnCuCNLi$. After 30 min, acetylene gas, 6.0 mmol (146 mL at 24 °C) was bubbled in. After stirring 30 min at −45 °C to −30 °C, the greenish brown solution was cooled to −78 °C. Successive additions of 6.0 mmol of Et_3N, 5.0 mmol of Et_3SiCl,[14] and 1.0 mmol of cyclohex-2-en-1-one were carried out. The reaction mixture was allowed to warm slowly to 0 °C over 2 h and was quenched by addition to a rapidly stirred mixture of 50 mL of Et_2O and 20 mL of aqueous NH_4Cl/NH_4OH (4:1). Flash column chromatography of the crude product on silica gel, with 1% Et_3N/hexane eluant followed by 1% Et_3N/1% EtOAc/hexane, gave the desired adduct as the silyl enol ether, 437 mg (83%). To the best of our knowledge, this constitutes the first preparation of this *cis*-2-stannylvinyl cuprate.

(7) See: Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630) for the analogous reactions of vinyl triflates.

(8) This compound was readily prepared by LDA deprotonation of methylphenyl sulfone in THF at −20 °C, followed by addition of DMF (see: Kozerski, L., et al. *Tetrahedron* **1986**, *42*, 1469) for the analogous reaction with methylphenyl sulfoxide). Treatment of the filtered solid with 1.05 equiv of TsCl in THF gave the *trans*-2-tosylvinyl sulfone, separable from the minor cis isomer by flash chromatography.

(9) We found it convenient to use a minor modification of the catalyst, the use of 2–3 mol% of $PdCl_2(PPh_3)_2$ and 6–10 mol% of CuI. See: Hagiwara, N. *Synthesis* **1980**, 627.

(10) Key 360 MHz ^{1}H NMR data ($CDCl_3$): δ 2.50 (t, J = 11.5 Hz, 1 H) confirmed the trans ring juncture, and 2.86 (dd, J = 11.5, 5.7 Hz, 1 H) confirmed the configuration at the ester and methylene sulfone groups, with an axial and an equatorial proton, respectively.

(11) Compound **1** crystallized in the monoclinic space group $P2_1$, with a = 14.191 (4) Å, b = 20.835 (16) Å, c = 13.110 (4) Å, and β = 91.12 (4)°; four molecules of composition $C_{20}H_{24}O_5S$ formed the asymmetric unit. The structure was solved with direct methods and refined to a R = 0.089 with a final R_w of 0.075.

(12) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477.

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(14) For conjugate additions in the presence of trimethylsilyl chloride, see: (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047.

The Effect of Substitution and Stereochemistry on Ion Binding in the Polyether Ionophore Monensin

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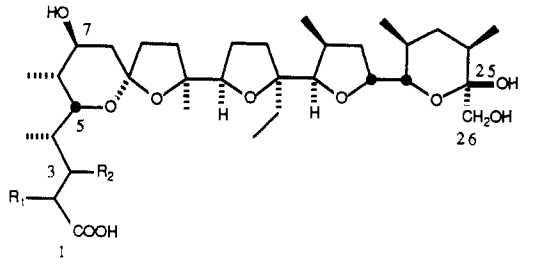
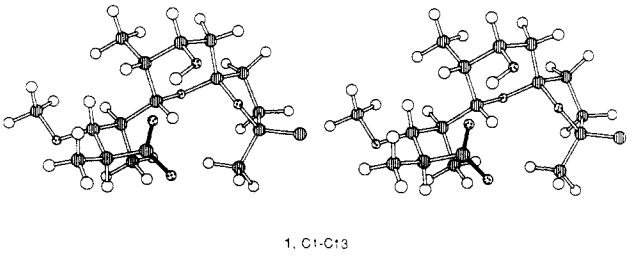
One of the most striking features of the polyether ionophores is their incorporation of specific substitutional and stereochemical arrays which appear to stabilize ion-binding conformations.[1] These conformations in the acyclic segments of the polyethers appear to be rigidified by avoidance of alternative conformers having relatively high-energy +gauche/−gauche (+g/−g) pentane interactions. In monensin[2] (**1**) with its particular substitution and



1, R_1 = β-Me, R_2 = β-OMe
2a, R_1 = H, R_2 = β-iPr
2b, R_1 = H, R_2 = α-iPr
2c, R_1 = H, R_2 = β-Me
2d, R_1 = H, R_2 = H

stereochemical pattern at C2–C7, the avoidance of +g/−g interactions leaves little opportunity for the acyclic C1–C5 segment to adopt conformations other than that found in the crystal structures of monensin and its salts. This conclusion follows from examination of the C1–C13 conformation of monensin shown



1, C1-C13

below in stereo. The reader will note that no rotation about C3–C4, C4–C5, or the C3–OMe is possible without creating new +g/−g interactions and that C2–C3 has at least one +g/−g interaction in all three of its conformations. The C2–C3 conformer shown would appear to be the least strained of the three possibilities since it uniquely places the planar C1 carbon in nonbonded contact with C5, allows formation of stabilizing hydrogen bonds,

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