the enzymatic reaction, and both enantiomers were recovered almost quantitatively. Accordingly, the substrates must be the free acids, and additional studies are now under way.

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Synthesis of (±)-11,*O*(3)-Dihydropseudopterolide

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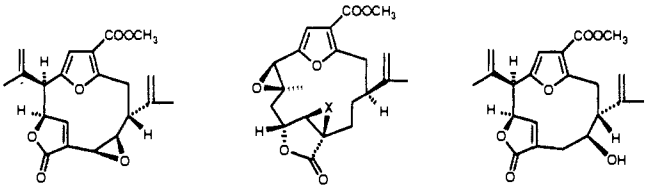
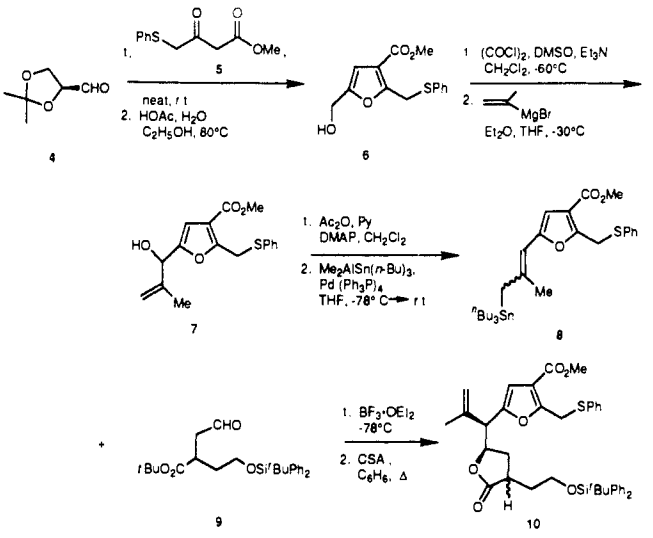
Pseudopterolide (**1**), a potent cytotoxic furanocembranolide that inhibits cell cleavage but not nuclear division much like cytochalasin D, was isolated and characterized in 1982.[2] Its 12-carbon macrocyclic ring is shared by the lesser oxygenated analogues kallolide A and B.[3] Pukalide (**2a**),[4] epoxypukalide (**2b**),[5] and lophotoxin,[6] on the other hand, are characterized by a somewhat larger (14C) central core.[7] Despite the biomedical importance of many of these marine products,[8] synthetic accomplishments in the area have been few and mostly preliminary in nature.[9] Herein we describe the first successful approach to a pseudopterane, viz., **3**, and detail a concise scheme for effecting the interlinking of sensitive, highly oxygenated functional groups in close transannular proximity.

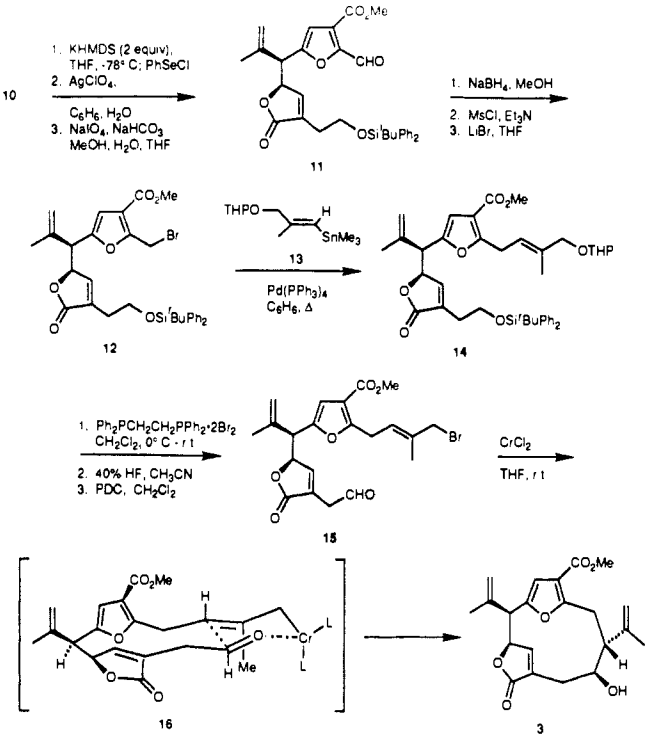


In light of the dismal prospects for arrival at a suitably functionalized furan by direct acylation methods,[10] 2,3-*O*-isopropylidene-D-glyceraldehyde (**4**)[11] was condensed with **5**[12] in an adaptation of the procedure developed by Aparicio for glucose[13] and then heated in aqueous acetic acid to give **6** (60%, Scheme I). Swern oxidation of **6** was most effective (98%) in making

Scheme I



Scheme II



available the aldehyde, reaction of which with 2-propenylmagnesium bromide produced **7** efficiently. Direct acetylation of this allylic alcohol was followed by conversion to **8** (64%) according to the method of Trost.[14] The 82:18 *E*/*Z* distribution of isomeric allylstannanes was not expected to be of stereochemical consequence in the ensuing condensation reaction.[15]

With maximum convergency as our goal, aldehyde **9** was next prepared. This objective was conveniently realized by silylation of 2-bromoethanol with *tert*-butyldimethylsilyl chloride and conversion to the iodide for the purpose of enhancing electrophilicity. Sequential alkylation of this halide with *tert*-butyl lithioacetate and allyl bromide in a THF-HMPA solvent system proceeded well (71% overall) to provide an ester, ozonolysis of which delivered **9** (90%). In this instance, it was imperative that the ozonide be degraded with triphenylphosphine.

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Advantage was now taken of the erythro-selective course of BF_3-catalyzed allylstannane–aldehyde condensations.[15] Treatment of a mixture of **8** and **9** with this Lewis acid gave, after heating with a catalytic quantity of CSA to effect lactonization, a difficulty separable mixture of **10** and its diastereomer in a 7.5:1 ratio (78%). The major constituent was assigned the indicated stereochemistry on the basis of extensive precedent set by less substituted congeners and X-ray crystallographic analysis of a lower homologue.[16]

Expediency and brevity were best served by concurrent chemoselective oxidation of the γ-lactone ring and (phenylthio)methyl side chain. For this purpose, the dianion of **10** was generated with 2 equiv of potassium hexamethyldisilazide. This dianion smoothly underwent 2-fold phenylselenenylation, thereby allowing for subsequent controlled hydrolysis with aqueous silver perchlorate to unmask the aldehyde, and periodate oxidation to produce the butenolide unit. The efficiency of this three-step sequence for acquiring **11** was 63% (Scheme II). Although selenoacetals are well-established intermediates,[17] little use has been made previously of selenothioacetals in synthesis. The feasibility of effecting selenoxide generation and elimination in the presence of a very reactive aldehyde carbonyl group is also noteworthy.

Once **11** had been converted into bromide **12** (99%), introduction of the remaining framework carbons was addressed. Cuprate-based displacement reactions were unsatisfactory for this purpose because of competing rapid conjugate addition to the butenolide ring. In the event, appendage of various side chains to **12** by means of Pd(0)-catalyzed vinylstannane coupling[18] proved especially general and serviceable. The pivotal macrocyclization step was probed in turn with all of these[19] and proved nonworkable in every example save one. Interconnective bonding between **12** and **13**[20] as duly promoted by Pd(0) furnished **14** (56%), a colorless oil. Reliable replacement of a tetrahydropyranyloxy substituent by bromide rested on the unique properties of 1,2-bis(diphenylphosphino)ethane tetrabromide.[21] In CH_2Cl_2, rapid interchange occurs without perturbation of the other structural elements in yields routinely in excess of 75%. This satisfying result made possible deprotection of the primary hydroxyl (62%) and its oxidation to the aldehyde level as in **15** (52%).

The transition-state model for chromous chloride induced cyclization[22] of **15** contemplated intramolecular π-facially selective attack at the aldehyde carbonyl by the flanking π-bond such that both large groups are equatorially disposed on the oxachromium six-membered ring (see **16**). Indeed, it seems that this trajectory is favored, since cyclization product **3** does form stereoselectively in 20–25% yield when admixed with 10 equiv of $CrCl_2$ and 4-Å molecular sieves in deoxygenated THF (25 °C, 5.5 h). Since two threo-selective processes are available to **15** and only one operates, the stereogenicity of the newly formed chiral centers in **3** is interlinked in a significant way with the configuration of those already present in the bromo aldehyde. The overall stereochemistry of **3** was firmly established by 2-D $^1H/^{13}C$ correlation studies.[23] Still and Mobilio's approach to asperdiol was the first to utilize the Heathcock–Hiyama allylchromium process for the stereoselective closure of a macrocycle.[24] The tolerance of yet additional functional groups to these organometallic conditions is herein demonstrated.

This method of assembling furanocembranolide systems, as demonstrated by the present direct total synthesis of **3**, should be amenable to the preparation of other members of this class. Such investigations are currently underway in this laboratory.[25]

(16) The X-ray work was performed on the crystalline triol obtained by $LiAlH_4$ reduction of the des(*tert*-butyldimethylsiloxy)ethyl system. We emphasize that ^1H NMR correlations are especially useful and diagnostic in delineating specific diastereomers in this series.

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(19) Included in this group are various modifications of the ene reaction, allylsilane–carboxaldehyde condensations, and Cr(II)-promoted cyclization of the *Z* isomer of **15**.

(20) Prepared from the known 1,1,3-tribromo-2-methyl-1-propene (Fischetti, W.; Mak, K. T.; Stakem, F. G.; Kim, J.-L.; Rheingold, A. L.; Heck, R. F. *J. Org. Chem.* **1983**, *48*, 948) via the following sequence of steps: (a) K_2CO_3, H_2O, Δ; (b) DHP, (TsOH); (c) CH_3Li, LiBr, Et_2O, pentane, −100 °C, then CH_3OH; (d) *t*-BuLi, DME, then Me_3SnCl.

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(23) The significant signals in **3** determined in $CDCl_3$ at 500 MHz compare very closely to those of **1** (see ref 2 for numbering):

	δ		ppm
β-H-2	2.67 (dd, *J* = 2.9, 15.1 Hz)	C-1	30.4
α-H-2	3.65 (dd, *J* = 13.2, 15.0 Hz)	C-2	47.7
H-1	2.87 (dd, *J* = 2.6, 13.2 Hz)	C-3	69.3
H-12	3.01 (br m)	C-4	35.3
α,β-H-11	2.55 (d, *J* = 7.4 Hz)	C-6	150.5
H-9	7.23 (s)	C-7	80.7
H-8	5.39 (s)	C-8	49.4
H-7	3.75 (s)	C-9	111.4
H-5	6.42 (s)		

The mass spectrum of **3** was scanned to *m/z* 800 to guard against the substance actually being a dimer of the structure shown.

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A Stable η^2-Silene Complex of Iridium: $(\eta^5\text{-}C_5Me_5)(PMe_3)Ir(\eta^2\text{-}CH_2{=}SiPh_2)$

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The ability of transition metals to stabilize reactive species by ligation has recently allowed isolation of silylene,[1] silene,[2] and disilene[3] coordination complexes. Such complexes have often been invoked in mechanistic proposals,[4] and recently Berry and Procopio have obtained good evidence for the participation of an osmium silene complex in a catalytic cycle.[5] We recently isolated the first stable silene complexes, $Cp^*(PR_3)Ru(H)(\eta^2\text{-}CH_2{=}SiPh_2)$ ($Cp^* = \eta^5\text{-}C_5Me_5$; **1**, R = ^{i}Pr; **2**, R = Cy), which are apparently stabilized by the electron-rich ruthenium center.[2] Reactivity studies with **1** and **2** so far indicate only processes involving migration of hydride to the silene ligand to produce reactive 16-electron alkyl or silyl derivatives.[2] Here we report the synthesis of a second type of η^2-silene complex, $Cp^*(PMe_3)Ir(\eta^2\text{-}CH_2{=}SiPh_2)$ (**3**), its X-ray structure, and preliminary reactivity studies that demonstrate direct interaction of reactants with the coordinated silene ligand.

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