Mononuclear η^2(4e)-Bonded Phosphaalkyne Complexes; Selective Formation of a 1,2-Diphosphacyclobutadiene Tantalum Complex**

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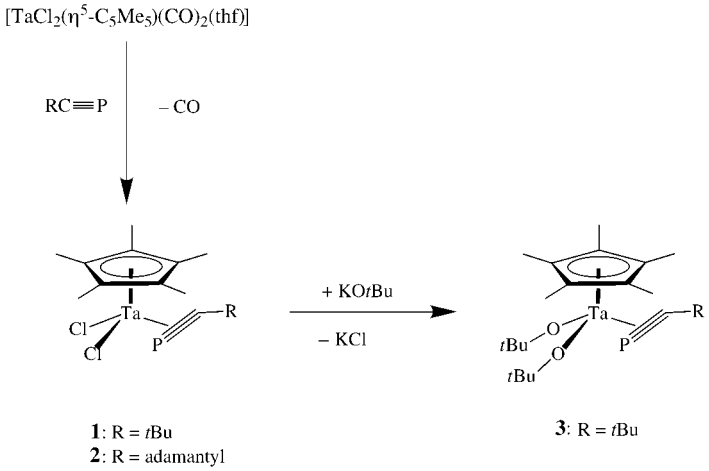
Dedicated to Professor Paul Binger

An interest in η^2(4e)-bonded alkyne complexes[1] together with the recognition that the chemistry of coordinated *t*BuC≡P frequently mirrors that of alkynes[2] led us to explore the possibility that phosphaalkynes might also adopt a η^2(4e) bonding mode in mononuclear complexes. Here we describe the synthesis and structural characterization of the d^2 tantalum complex $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2(4e)\text{-}t\text{BuC}{\equiv}P\}]$ and its reaction with an excess of *t*BuC≡P to selectively form the 1,2-diphosphacyclobutadiene complex $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\sigma,\sigma,\pi\text{-}1,2\text{-}P_2C_2t\text{Bu}_2\}]$.

In seeking to establish whether phosphaalkynes (RC≡P) can adopt a η^2(4e) bonding mode involving $\pi_{\parallel}\rightarrow M(\sigma)$, $M(d_\pi)\rightarrow\pi^*_{\parallel}$, $\pi_{\perp}\rightarrow M(d_\pi)$, and possibly $M(d_\delta)\rightarrow\pi^*_{\perp}$ orbital interactions, we sought to prepare analogues of η^2(4e)-bonded mononuclear alkyne complexes in which the alkyne is replaced by a η^2-bonded *t*BuC≡P ligand. We reasoned that a comparison of the structural data for the two complexes would provide an insight into the nature of the bond between the metal center and the phosphaalkyne. In this study we focused on the report that the well-characterized (NMR, X-ray) d^2 complex $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2(4e)\text{-}PhC_2Ph\}]$[3] can be synthesized by reaction of PhC≡CPh with the labile complex $[TaCl_2(\eta^5\text{-}C_5Me_5)(CO)_2(thf)]$.[4] This suggested that the tantalum dicarbonyl complex might also react with *t*BuC≡P to form a novel η^2(4e)-bonded phosphaalkyne complex.

When *t*BuC≡P (1.1 mol equiv) was added at room temperature to a stirred solution of $[TaCl_2(\eta^5\text{-}C_5Me_5)(CO)_2(thf)]$ in THF, both CO ligands were readily (5 min) displaced (IR), and the reaction mixture changed color from yellow to deep purple. Removal of the solvent in vacuo and extraction of the residue with hexane afforded the air-sensitive complex **1** (Scheme 1) in 85% yield as a deep purple powder, which



Scheme 1. Synthesis of η^2(4e)-bonded phosphaalkyne complexes.

could be recrystallized from hexane or pentane at −30 °C. Complex **1** was characterized by elemental analysis, NMR spectroscopy, and single-crystal X-ray crystallography as the phosphaalkyne-substituted d^2 complex $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2(4e)\text{-}t\text{BuC}{\equiv}P\}]$. The corresponding reaction with the adamantyl-substituted phosphaalkyne afforded in a similar fashion **2** in high yield (Scheme 1), and it was also found that KO*t*Bu readily (RT, 12 h) reacted in toluene with **1** to form in good yield the bis-alkoxy complex **3** (Scheme 1).

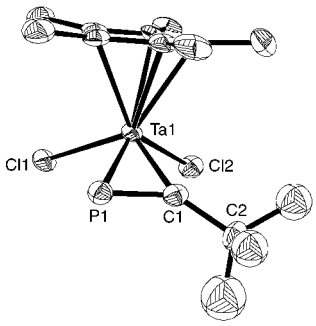


Figure 1. ORTEP represention of **1**. Thermal ellipsoids shown at the 30% probability level. Selected bond lengths [Å] and angles [°]: P1-C1 1.694(10), P1-Ta1 2.438(3), C1-Ta1 2.079(9), Ta1-Cl1 2.346(2), Ta1-Cl2 2.378(2); P1-C1-C2 131.5(7).

An X-ray crystallographic study[5] on a suitable single crystal of **1** obtained from pentane (−30 °C) established the three-legged piano-stool structure illustrated in Figure 1, which closely resembles that reported for $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2(4e)\text{-}PhC_2Ph\}]$. In **1** an η^2-bonded *t*BuC≡P replaces the alkyne ligand: both PhC_2Ph and *t*BuC≡P adopt the same orientation in these complexes. Since a characteristic feature of η^2(4e)-bonded alkyne complexes is a short metal–carbon bond[6] it is especially interesting that in complex **1** the Ta–C1 distance is also short (2.079(9) Å) and is of similar length to the Ta–C(alkyne) bond length of 2.067(6) Å in $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2(4e)\text{-}PhC_2Ph\}]$. In contrast, a long Ti–C(phosphaalkyne) distance (2.187(6) Å) is observed in the d^2 complex $[Ti(\eta^5\text{-}C_5H_5)_2\{\eta^2(2e)\text{-}t\text{BuC}{\equiv}P\}(PMe_3)]$,[7] in which the metal center has 18 electrons and cannot accept more than two electrons from the phosphaalkyne triple bond.

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Similarly, there is a difference in the P–C bond lengths and P-C-R "bend-back" angles, which are larger in the Ta complex (1.694(10) Å, 131.5(7)°) than in the titanium complex (1.636(2) Å, 133.4(7)°). All of these observations, but especially the short Ta–C(phosphaalkyne) bond, are consistent with involvement of the phosphaalkyne $\pi_\perp$ orbital in bonding to the tantalum atom in **1**.

This conclusion is also supported by Extended Hückel MO (EHMO) calculations[8] using the bond parameters found for complex **1**. The complex was divided into Ta(η^5-C_5Me_5)Cl_2 and *t*BuC≡P fragments, and the orbital interactions between the two were examined. The frontier orbitals on the *t*BuC≡P ligand[9] corresponding to $\pi_\parallel$, $\pi_\parallel^*$, and $\pi_\perp$ all showed significant interactions with the $TaCl_2(\eta^5$-$C_5Me_5)$ fragment; the electron populations of these orbitals were 1.81, 1.02, and 1.85 respectively, and the population of the $\pi_\perp^*$ orbital of 0.04 implies little or no interaction with the metal center. These results compare well with those reported (EHMO calculation) by Curtis et al.[10] for [$NbCl_2(\eta^5$-$C_5H_5)\{\eta^2$(4e)-HC_2H}] ($\pi_\parallel$ 1.74, $\pi_\parallel^*$ 0.81, $\pi_\perp$ 1.68, and $\pi_\perp^*$ 0.02) and indicate that, as in the alkyne complex, the phosphaalkyne ligand in **1** is a four-electron donor. A similar calculation on [$Ti(\eta^5$-$C_5H_5)_2\{\eta^2$(2e)-*t*BuC≡P}(PMe_3)] showed orbital populations consistent with the proposed bonding mode of the phosphaalkyne ($\pi_\parallel$ 1.87, $\pi_\parallel^*$ 1.02, $\pi_\perp$ 1.94, and $\pi_\perp^*$ 0.04).

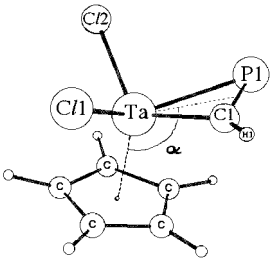


Figure 2. Calculated lowest energy geometry for complex **A**. Selected bond lengths [Å] and angles [°]: P1-C1 1.672, P1-Ta 2.486, C1-Ta 2.086, Ta-Cl1 2.339, Ta-Cl2 2.337, C1-H1 1.099; $\alpha = 114.8$, P1-C1-H1 135.73.

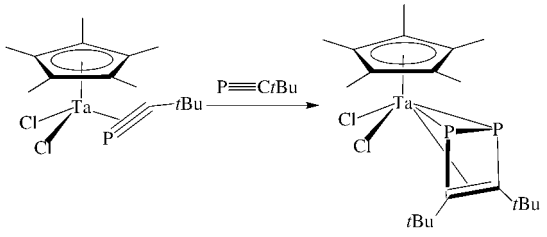
Further insight into the nature of complex **1** was provided by ab initio calculations on the model complexes [$TaCl_2(\eta^5$-$C_5H_5)\{\eta^2$(4e)-RC≡P}] (R = H (**A**), Me (**B**)) with the Gaussian 98 package of programs; the structure depicted in Figure 2 was obtained.[11–13] The geometrical parameters of **A** and **B** are in reasonable agreement with those of **1** in the crystal. Due to a low barrier to rotation of the phosphaalkyne ligand (< 20 kJ mol^{-1}; see Supporting Information) various geometries were considered in the GIAO calculation of the NMR parameters.[14, 15] Based on ECP/DFT calculations on **B**, ^{31}P NMR chemical shifts of $\delta = 492$, when the phosphaalkyne lies parallel to the Cl–Cl vector, and of $\delta = 525$, when it is perpendicular to the Cl–Cl axis with the methyl group away from the η^5-C_5H_5 ligand, are predicted. This is in agreement with the experimental values for **1** and **2** ($\delta = 509.0$ and 515.3 in C_6D_6, respectively). The ^{13}C chemical shifts of the phosphaalkyne C atom in **B**, calculated at the same level of theory, were $\delta = 299$ (P–C parallel to Cl–Cl) and $\delta = 327$ (P–C perpendicular to Cl–Cl). The difference of $\Delta\delta \approx 10-37$ between δ_{calcd}(^{13}C) and δ_{exp}(^{13}C) of the corresponding carbon atoms in **1** and **2** could be due to the different substituents.

The observed and calculated low-field ^{31}P NMR chemical shifts are consistent with our earlier finding that the complex [$Mo(\eta^5$-$C_5H_5)\{\eta^2$(4e)-*t*BuC≡P}{η^2-$P(OMe)_2OBF_2OP(OMe)_2$}][16] shows a low-field ($\delta = 467.8$) ^{31}P chemical shift for the coordinated phosphaalkyne, and it was argued on the basis of isolobal analogies that such a shift is characteristic of a η^2(4e) bonding mode. In contrast, higher field ^{31}P chemical shifts were reported for the d^2 titanium ($\delta = 122.7$) and zirconium ($\delta = 196.9$) complexes [$M(\eta^5$-$C_5H_5)_2\{\eta^2$(2e)-*t*BuC≡P}(PMe_3)] (M = Ti, Zr),[7] in which the phosphaalkyne cannot donate more than two electrons to the metal center. Similarly, the ^{31}P chemical shift of the phosphaalkyne P atom in [$Pt\{\eta^2$(2e)-*t*BuC≡P}(PPh_3)$_2$][16, 17] is $\delta = 84.1$, characteristic of a 2e donor and to much higher field than the signals of the tantalum complexes **1**, **2**, and **3**. The ^{31}P chemical shift ($\delta = 416.3$) of complex **3** can be rationalized by a decrease in $\pi_\perp$ donation from the phosphaalkyne ligand and implies that the two *t*BuO ligands donate more π-electron density to the tantalum atom than the chloro ligands in **1** and **2**.

Whereas the ^{31}P chemical shifts exhibit a diagnostically useful wide range ($\delta = 84-515$) which spans the η^2(2e) to η^2(4e) phosphaalkyne bonding modes, the corresponding ^{13}C chemical shifts, in contrast to those of η^2(2e)- to η^2(4e)-alkynes,[6] show a much narrower and hence less useful range ($\delta = 240-337$) for two- to four-electron donor phosphaalkynes. Thus, the ^{13}C{^{1}H} NMR spectra of **1**, **2**, and **3** recorded in C_6D_6 at room temperature showed signals at $\delta = 337.2$ (d, $^1J_{P,C} = 113.3$ Hz, P≡C), $\delta = 335.6$ (d, $^1J_{P,C} = 110.5$ Hz, P≡C), and $\delta = 326.5$ (d, $^1J_{P,C} = 108.5$ Hz, P≡C), respectively, which are similar to the signal of [$Mo(\eta^5$-$C_5H_5)\{\eta^2$(4e)-*t*BuC≡P}{η^2-$P(OMe)_2OBF_2OP(OMe)_2$}] ($\delta = 328.5$, d, $^1J_{P,C} = 114$ Hz, P≡C),[16] but only to slightly lower field than those of [$M(\eta^5$-$C_5H_5)_2\{\eta^2$(2e)-*t*BuC≡P}(PMe_3)] (M = Ti: $\delta = 298.6$, $^1J_{P,C} = 83.4$ Hz; M = Zr: $\delta = 310.6$, $^1J_{P,C} = 97.7$ Hz)[7] and [$Pt\{\eta^2$(2e)-*t*BuC≡P}(PPh_3)$_2$] ($\delta = 240.8$).[18]

The lack of reactivity of the complexes [$MCl_2\{\eta^2$(4e)-alkyne}(η^5-C_5Me_5)] (M = Nb, Ta) towards alkynes has been rationalized in terms of the large (2 eV) HOMO–LUMO gap.[10] A similar EHMO calculation on **1** also showed a HOMO–LUMO gap of 2 eV, which implies that this complex would also be unreactive towards alkynes. Interestingly **1** is reactive towards an excess of *t*BuC≡P.

A solution of **1** in C_6D_6 was treated with *t*BuC≡P (ca. 1.6 mol equiv), and the subsequent reaction was monitored by ^{31}P{^{1}H} NMR spectroscopy. Over a period of three weeks the signal at $\delta = 509.0$ for **1** decreased in intensity and was replaced by a new singlet at $\delta = 31.8$, with no evidence for any phosphorus-containing intermediates. The color of the solution changed from purple to red. Removal of the C_6D_6 in vacuo and extraction of the residue with hexane gave a deep red solution of complex **4** [Eq. (1)]. Concentration of the solution and cooling to −20 °C afforded crystals of **4**, but due to the high solubility of **4** in hexane, the amount isolated was



1 **4** (1)

  1433-7851/01/4017-3222 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2001**, *40*, No. 17

relatively low, even though the conversion of **1** to **4** was essentially quantitative. Complex **4** was characterized by elemental analysis, NMR spectroscopy, and single-crystal X-ray crystallography as the 1,2-diphosphacyclobutadiene complex $[TaCl_2(\eta^5\text{-}C_5Me_5)(\sigma,\sigma,\pi\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$.[19] This is especially interesting since there is only one previously reported example of a 1,2-diphosphacyclobutadiene complex: $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$ was formed (30% yield) along with $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,3\text{-}P_2C_2t\text{Bu}_2)]$ (30% yield) in an unselective reaction (1/1) between tBuC≡P and $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}C_8H_8)]$.[20] In all other studies on the formation of diphosphacyclobutadiene ligands, only the 1,3-isomer has been observed, even though calculations on the free ligand have predicted that the 1,2-isomer is thermodynamically more stable.[21, 22]

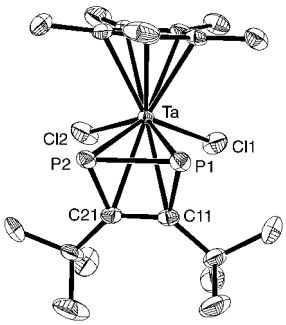


Figure 3. ORTEP represention of complex **4**. Thermal ellipsoids shown at the 30% probability level. For selected bond lengths and angles, see Table 1.

The single-crystal X-ray structure of **4** (from hexane, −20 °C) is shown in Figure 3, and selected bond parameters, along with those calculated (ECP/DFT geometry optimization) for the model complex $[TaCl_2(\eta^5\text{-}C_5H_5)(\eta^4\text{-}1,2\text{-}P_2C_2H_2)]$ and reported for the titanium complex $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$ are listed in Table 1. Examination of these data shows that the bonding mode adopted by the 1,2-$P_2C_2t\text{Bu}_2$ ligand in the tantalum complex **4** is different from that reported for $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$, which was described as a η^4-bonded delocalized π system. Thus, the P1–P2 distance of 2.204(2) Å in **4** is essentially the same as the P–P single-bond length in 3,4-di-*tert*-butyl-1,2-dihydro-1,2-diiododiphosphete[23] (2.192(4) Å), and perceptibly longer than that in the Ti complex (2.175(1) Å). Although the C11–C21 bond length (1.410(6) Å) in **4** is apparently shorter than that in the Ti complex (1.429(3) Å), the difference is not statistically significant, and the P–C bond lengths (1.820(5) Å, 1.840(5) Å) in **4** are close to the P–C single-bond length (1.827(6) Å) in the 1,2-dihydro-1,2-diiododiphosphete.[23] The corresponding calculated bond lengths for the model complex $[TaCl_2(\eta^5\text{-}C_5H_5)(1,2\text{-}P_2C_2H_2)]$ show the same trend with an even longer P–P bond and shorter C–C bond. An obvious interpretation of these findings is that the 1,2-$P_2C_2t\text{Bu}_2$ ligand in complex **4** adopts a σ,σ,π bonding mode, as illustrated in Equation (1).

Table 1. Observed and DFT-calculated (in square brackets) bond parameters (bond length [Å], angle [°]) for the 1,2-diphosphacyclobutadiene ligand.

Bond or angle	Complex **4**	$[TaCl_2(\eta^5\text{-}C_5H_5)(\eta^4\text{-}1,2\text{-}P_2C_2H_2)]$	$[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$[11]
P1–P2	2.204(2)	[2.250]	2.175(1)
P1–C11	1.820(5)	[1.808]	1.815(5)
P2–C21	1.840(5)	[1.809]	1.806(2)
C11–C21	1.410(6)	[1.385]	1.429(3)
M–P1	2.4992(13)	[2.554]	2.487(1)
M–P2	2.5116(13)	[2.552]	2.494(1)
M–C11	2.684(5)	[2.456]	2.392(2)
M–C21	2.655(5)	[2.454]	2.381(2)
C21-C11-P1	103.0(3)	[103.8]	102.0(1)
C11-P1-P2	77.7(2)	[76.2]	77.8(1)
P2-C21-C11	102.1(3)	[103.9]	101.8(1)
P1-P2-C21	77.3(2)	[76.2]	78.4(1)

As might be expected, the NMR parameters of the 1,2-$P_2C_2t\text{Bu}_2$ ligand in **4** differ from those of the corresponding Ti complex. The $^{31}P\{^1H\}$ NMR spectrum of **4** showed one singlet at $\delta = 31.8$ to high field of that of $[Ti(\eta^8\text{-}C_8H_8)(\eta^4\text{-}1,2\text{-}P_2C_2t\text{Bu}_2)]$ ($\delta = 133.6$), and the $^{13}C\{^1H\}$ NMR spectrum of **4** exhibited an apparent doublet of doublets at $\delta = 168.5$ ($^1J_{P,C} = 23.9$ Hz, $^2J_{P,C} = 18.4$ Hz) not dissimilar to that reported for the Ti complex at $\delta = 153.9$ (app t, $J_{P,C} = 49.5$ Hz) and in the region typical for sp^2 carbon atoms. Again the data are consistent with a σ,σ,π bonding mode for complex **4**.

Neither the selective or the stepwise [**1** → **4**] formation of a 1,2-diphosphacyclobutadiene has been previously observed. In agreement with our previous DFT calculations, it is noteworthy that the recent calculations also show that the observed product has the lowest energy and is the most stable isomer. Therefore, the reaction might be considered to be thermodynamically controlled. However, so far only a tilted 1,3-diphosphabicyclo[1.1.0]butanediyl[22] has been identified as a potential intermediate in the reaction. It is hoped that the progressive replacement of the chloro ligands in **1** followed by a study of the reaction of the resulting phosphaalkyne complexes with further tBuC≡P might enable us to tune the system and thus allow a deeper understanding of this interesting reaction.

In conclusion, single-crystal X-ray crystallography, NMR spectroscopy, and theoretical (EHMO, DFT) studies show that the phosphaalkyne ligand in $[TaCl_2(\eta^5\text{-}C_5Me_5)\{\eta^2\text{-}t\text{BuC}{\equiv}\text{P}\}]$ (**1**) adopts a η^2(4e) bonding mode. Surprisingly, **1** reacts with an excess of tBuC≡P to form the complex $[TaCl_2(\eta^5\text{-}C_5Me_5)(1,2\text{-}P_2C_2t\text{Bu}_2)]$; the X-ray data indicate a σ,σ,π bonding mode for the 1,2-diphosphacyclobutadiene ligand. This is only the second time that the formation of a 1,2-diphosphacyclobutadiene has been observed, but in this case there is no evidence for the formation of the 1,3-isomer.

Experimental Section

Full experimental details (both syntheses and calculations) are provided in the Supporting Information.

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[5] a) Crystal structure data of **1** (173 K) with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å): $M_r = 487.16$, crystal dimensions $0.40 \times 0.35 \times 0.35$ mm, triclinic, space group $P\bar{1}$, $a = 7.555(2)$, $b = 9.712(2)$, $c = 13.263(4)$ Å, $\alpha = 68.626(4)$, $\beta = 80.968(5)$, $\gamma = 77.277(4)^\circ$, $Z = 2$, $\rho_{calcd} = 1.837$ g cm^{-3}, $R1 = 0.057$ for 3340 data ($I > 4\sigma I_o$). b) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-160698 (**1**) and -160699 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
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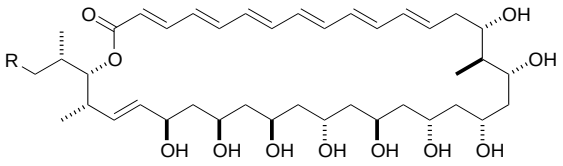
Total Synthesis of Dermostatin A**

Christopher J. Sinz and Scott D. Rychnovsky*

By virtue of their biological activity and structural complexity, the polyene macrolides have attracted a great deal of interest from the synthetic community.[1] We have been engaged in the development of broadly applicable methodology for the stereochemical elucidation and the total synthesis of highly oxygenated natural products. Pursuant to these goals, a recent report from our group described a new approach to the rapid stereochemical assignment of polyol-containing natural products in which 2D-^{13}C acetonide analysis allowed for the stereochemical elucidation of dermostatin A (**1**) and B (**2**).[2] Herein, we disclose studies which have culminated in the first total synthesis of dermostatin A (**1**).



1: R = H
2: R = Me

Dermostatin A (**1**) and B (**2**) are 36-membered macrolides that were isolated from the mycelium of *Streptomyces viridogriseus* Thirum.[3] Their flat structures were determined by Rinehart and Pandey.[4] The dermostatins show potent antifungal activity (comparable to amphotericin B) against a large number of human pathogens,[5] and have been used clinically as a treatment for deep vein mycoses.[6] Additionally, in an evaluation of a variety of polyene macrolides as potential HIV treatments, dermostatin A (**1**) and B (**2**) showed the highest antiproliferative activity against HIV in H9 cells.[7] Although the dermostatins have demonstrated a broad range of biological activities, details of their mode of action remain unknown.

We set out to develop a highly convergent synthetic approach that would be sufficiently flexible to allow the facile generation of analogues for studies of the mode of action (Scheme 1). The central synthetic challenges posed by dermostatin A (**1**) are the complex polyol region and the conjugated hexaene. The acid- and light-sensitivity of the polyene necessitates delaying its introduction until a late stage. We intended to employ a palladium-mediated cross-coupling with vinyl stannane **4** as the penultimate carbon–carbon bond construction. Previous studies from our group have demonstrated the utility of cyanohydrin acetonide

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