group would weaken a metal–arene bond, which should if anything lead to a more facile decomposition.

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Synthesis of (±)-$\Delta^{(9,12)}$-Capnellene Using Titanium Reagents

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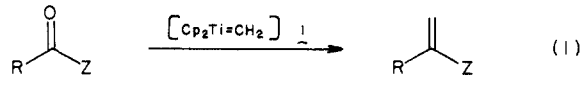
Titanaethylene **1** reacts with organic carbonyls and with olefins. The dominant reaction with carbonyls is "Wittig" methylenation (eq 1),[1] whereas olefins react to form metallacycles **2**[2] that can



Z = H, R', OR', NR'2, NR'COR"

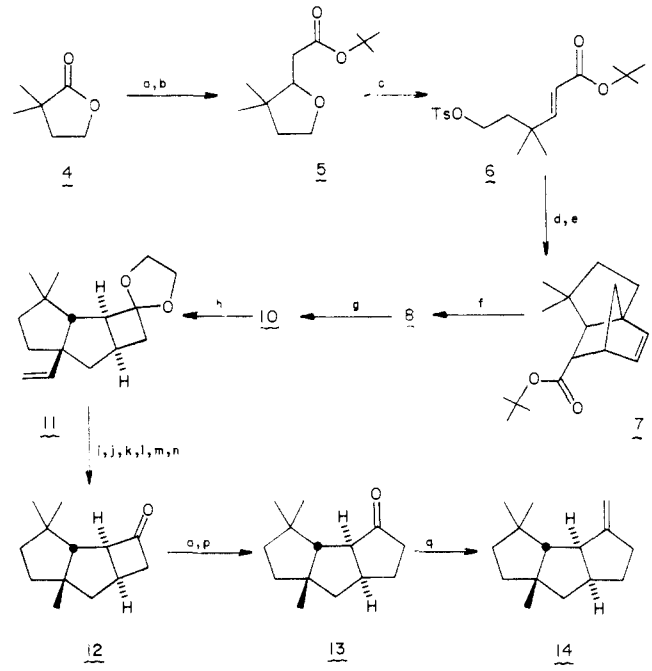
Cp = η^5-cyclopentodienyl

be used as catalysts in olefin metathesis.[3] The use of the "Tebbe Reagent" (**3**)[4] as a source of the titanaethylene fragment has

2 **3**

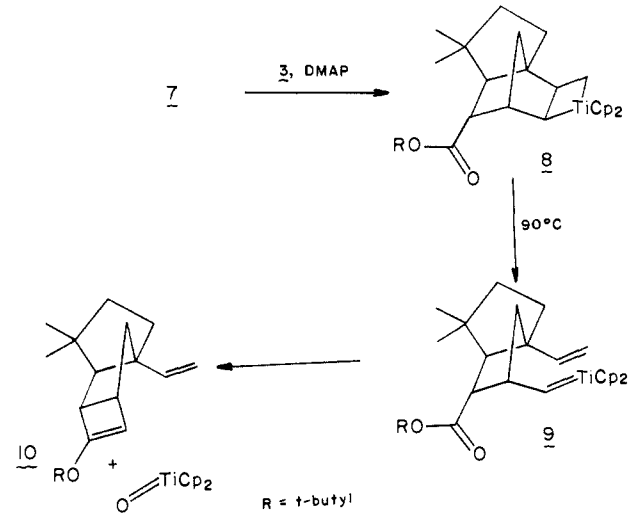
already found several applications in synthetic transformations and the synthesis of natural products.[1c,5] New applications are developing in polymer synthesis. Strained rings can be ring-open polymerized by using **1** as a catalyst.[6] These reactions proceed through the substituted alkylidene resulting from productive cleavage of the intermediate metallacyclobutane.[7] A molecular rearrangement that takes advantage of these two types of reactivity has been investigated and has been demonstrated to be an efficient route to $\Delta^{(9,12)}$-capnellene (**14**, Scheme I).[8] Capnellene is the presumed biosynthetic precursor to the capnellane family of nonisoprenoid sesquiterpenes. This natural product has received significant synthetic attention due to the challenging cis-anti-cis tricyclo(6.3.0.$0^{2,6}$)undecane skeletal framework. Although the details of the biological function of the capnellanes are not known,

Scheme I[a]



[a] (a) DiBAl, −78 °C, toluene; (b) NaH, $(EtO)_2POCH_2CO_2C(CH_3)_3$, benzene, 25 °C (89%); (c) LDA, *p*-TsCl, THF, −78 to 25 °C (83%); (d) CpMgCl, THF, 25 °C; (e) benzene, 75 °C (81%); (f) **3**, DMAP, benzene, 25 °C; (g) 90 °C; (h) $HOCH_2CH_2OH$, *p*-TsOH·H_2O, benzene, reflux (81%); (i) O_3, $MeOH/CH_2Cl_2$, −78 °C; (j) $NaBH_4$, −78 to 25 °C (91%); (k) *n*-BuLi, $[(CH_3)_2N)_2POCl$, NEt_3, DME, 25 °C; (l) Li, *t*-BuOH, $EtNH_2$, THF, −50 to −40 °C; (m) H_2O/CH_3COCH_3, *p*-TsOH·H_2O, benzene, reflux; (n) 0.15 equiv of PDC, CH_2Cl_2, 25 °C (68%); (o) BF_3·Et_2O, N_2CHCO_2Et, Et_2O, −28 °C; (p) NaCl, Me_2SO, H_2O, 150 °C (73%); (q) **3**, DMAP, Et_2O, −40 to 25 °C (93%).

Scheme II



these compounds display biological effects similar to those of their terrestrial counterparts, hirsutanes, which possess promising antibacterial and antitumor properties.[9] The key step requires the rearrangement of **7** to the corresponding cyclobutene enol ether **10**, which was then transformed into the desired product by using standard group manipulations. The regiochemistry of the (2 + 2) cycloaddition of titanaethylene to **1** (Scheme II) and the corresponding cycloreversion of **8** to **9** has been established in model studies.[10] All of the stereochemistry of the final product

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is set in the Diels-Alder reaction used to produce **7**.

For the purposes of this synthesis, direct alkylation of the tosylate **6** with a cyclopentadienyl anion was the most efficient route (Scheme I). Because alkylations with the cyclopentadienyl anions of lithium and sodium resulted in base-catalyzed intramolecular conjugate addition of the functionalized cyclopentadiene,[11] the reagent of choice was the cyclopentadienyl Grignard reagent.[12]

The preparation of the tosylate 6 was achieved starting from lactone **4**.[13] Reduction of **4**, followed by treatment of the corresponding lactol with the anion of $(EtO)_2POCH_2CO_2C(CH_3)_3$, resulted in condensation with the aldehyde and subsequent intramolecular conjugate addition to produce ester **5** in 89% isolated yield. Deprotonation of **5** by LDA, followed by the addition of *p*-TsCl, resulted in formation of **6** in 83% isolated yield.

Alkylation of **6** proceeded smoothly in THF, using CpMgCl to produce the corresponding functionalized cyclopentadiene. Intramolecular cycloaddition was complete within 2 h at 75 °C in benzene to produce **7** (81% isolated yield). Through this single cycloaddition reaction, the relative stereochemistry of all four asymmetric centers of **14** was established.

The generation of **1**, by the addition of a solution of Tebbe reagent to a solution of 4-(dimethylamino)pyridine, in the presence of **7**, resulted in the formation of the metallacycle **8**. Heating of this mixture to 90 °C initiated ring opening to the alkylidene **9**. Subsequent intramolecular trapping of **10** resulted in the complete conversion of **7** to **9**. Due to the sensitivity of the cyclobutene enol ether to hydrolysis and upcoming reaction conditions, the cyclobutanone functionality was protected and isolated as the 1,3-dioxolane **11**. The ketal was isolated in 81% yield based on **7**. This rearrangement established the skeletal framework of capnellene without affecting the asymmetric centers established during the cycloaddition. Completion of the synthesis required only the manipulation of existing functionality.

Transformation of the vinyl substituent to a methyl group was achieved through the use of standard techniques. Cleavage of the olefin using ozonolysis removed the excess carbon and workup with $NaBH_4$[14] reduced the angular substituent to a hydroxyl methyl group. Further reduction to the methyl group was achieved by using a reported procedure involving lithium reduction of the tetramethylphosphorodiamidate ester of the alcohol.[15] Unfortunately, even at −50 °C, reduction of the protected cyclobutanone functionality occurred to a small extent producing the corresponding cyclobutanol of **12**. After removal of the protecting group from the desired product, the mixture was treated with pyridinium dichromate (0.15 equiv) to produce a single organic product, **12**, isolated in 68% yield based on **11**.

Ring expansion of the cyclobutanone to the cyclopentanone resulted in the known capnellene ketone precursor. Although this system appeared similar in nature to that reported to exhibit 100% regiochemical ring expansion,[16] we were able to obtain only a 83:17 ratio of **13** to that of its regiochemical isomer. The use of ethyl diazoacetate, catalyzed by boron trifluoride etherate,[17] produced optimal results. Following decarbonylation,[18] **13** was isolated by flash chromatography in 73% overall yield from **12**. Methylenation of **13** using the Tebbe reagent produced a 93% yield of capnellene.[19] The Tebbe reagent, which can be isolated as a solid[4] or prepared in situ,[20] provides an attractive alternative to Ph_3PCH_2 in the final step. Previous use of this tempermental reagent for the transformation of **13**, formed by hydrogenation of α,β-unsaturated **13**, to **14** has led to inconsistent product yields of 36–80% for these two combined steps.[8] This efficient synthesis (20% overall from **4**) demonstrates the utility of the multifunctional reactivity of titanaethylene in synthetic transformations.

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Cobalt-Catalyzed One-Step Assembly of B-Ring Aromatic Steroids from Acyclic Precursors

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Because of their varied physiological activity, steroids are important testing grounds on which to explore the utility of novel synthetic methodology.[1] We have used cobalt, in the form of $CpCo(CO)_2$, as a matrix around which to assemble natural and unnatural polycyclic products, including the steroid nucleus.[2] In this way, the total synthesis of A-ring aromatic systems of the estrone type was achieved via the D → ABCD[3] and A → ABCD strategies.[4] We now report an approach in which all four rings are assembled (0 → ABCD) in one step to give B-ring aromatic derivatives with complete control of the crucial stereochemistry of the C,D-ring juncture. To our knowledge, this strategy has been accomplished previously only by employing biomimetic cyclizations[5] and not en route to the rare[6] target class of compounds which has never been constructed by total synthesis.

Our retrosynthetic analysis is shown in Scheme I and relies in the first step on a previously unexplored[2] intramolecular alkyne cyclization to form a cyclobutahydronaphthalene **2**, in turn to be converted to product by an intramolecular Diels-Alder cycloaddition via **3**. On the basis of a model study,[7] the C,D-ring junction was hoped to emerge trans. The convergent and efficient

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