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TOTAL SYNTHESIS OF THE TRIQUINANE MARINE SESQUITERPENE (±)$\Delta^{9(12)}$ CAPNELLENE USING A PALLADIUM-CATALYZED BIS-CYCLIZATION STEP.

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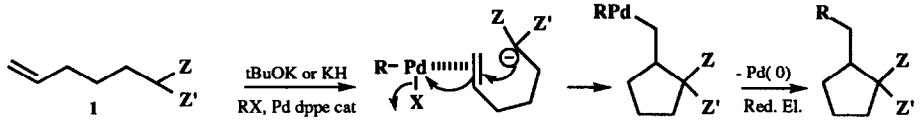
Abstract : Details of a novel palladium catalyzed cyclization approach to linear condensed cyclopentanoids are reported. The mechanism of this reaction which involves a δ-ethylenic (or δ-acetylenic) carbon nucleophile and an unsaturated halide is a "Wacker type process" i.e, an attack by the nucleophile onto the unsaturation electrophilically activated by an *organopalladium(II)* species. In this paper, we will show the intramolecular version of this reaction which then leads to the tricyclic framework of the sesquiterpene (±)$\Delta^{9(12)}$ capnellene, the total synthesis of which is described.

Introduction and Background

In recent years, both radical cyclizations reactions especially those involving Tin-promoted cyclizations of organic halides [1] and intramolecular Heck reactions (palladium catalyzed cyclization) [2] have been developped as powerful tools for the preparation of carbocycles and heterocycles. Although these two methodologies display some similar features, they are also complementary to each other in many other respects.

Palladium(0) catalyzed cyclization processes are currently attracting much attention because of significant progress in extending the intramolecular Heck reaction to the construction of bridged, fused and spirocyclic systems [3] as well as developments in metallo-ene [4] cyclization processes.

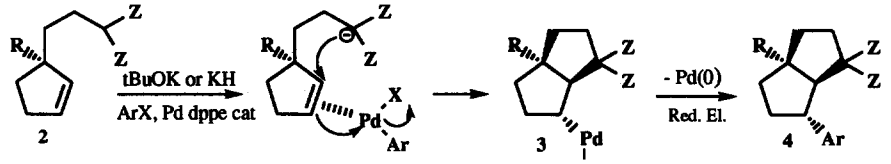
As part of our ongoing interest in palladium chemistry [5], particularly for the construction of various carbocycles [6], we reported a new palladium mediated **cyclopentanation** of alkenes [7] bearing a nucleophilic substituent.



Z, Z' = CO_2Me, CN, COMe or SO_2Ph
R = vinyl, aryl

The stereoselectivity of the same reaction effected on the substrate **2** clearly indicates that the mechanism is a "Wacker type process", i.e an attack, by the nucleophile (here an enolate) onto the unsaturation electrophilically activated by the σ-aryl or σ-vinyl palladium species. Finally, a reductive elimination from the

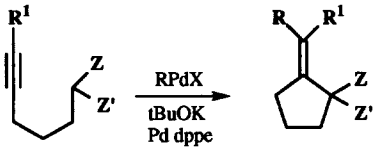
resulting σ-bonded palladium species **3** leads to the reaction product **4** [8].



Scheme 1

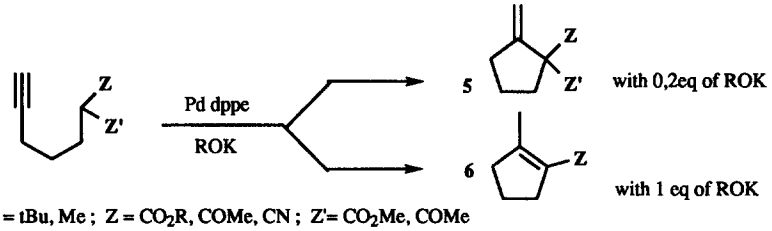
This reaction is unique when compared to the best known palladium(II)-mediated nucleopalladations of alkynes or alkenes [9] because an **organo**palladium(II) halide, not a palladium dihalide or dicarboxylate, acts as the electrophilic mediator of the cyclization.

This new cyclopentannulation method was applied to the acetylenic homologs of **1** and it must be emphasized that stereodefined exocyclic double bonds are formed [10] even in the case of substituted triple bonds ($R^1 \neq H$)



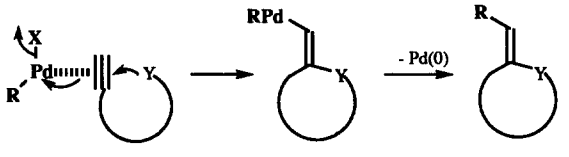
R = vinyl, aryl, alkynyl
R^1 = TMS, CH_3,vinyl, CH_2OTHP
Z = CO_2Me, Z' = CO_2Me, COMe, SO_2Ph

We have also shown [11] that this cyclization of stabilized enolates onto a triple bond can be promoted by a palladium hydride species (produced in situ by insertion of a Pd(0) complex into the C-H bond of the acetylenic starting material) leading either to **5** or **6** depending on the reaction conditions and particularly on the amount (stoichiometric or catalytic) of the potassium alkoxide used to deprotonate the starting malonate.



R = tBu, Me ; Z = CO_2R, COMe, CN ; Z'= CO_2Me, COMe

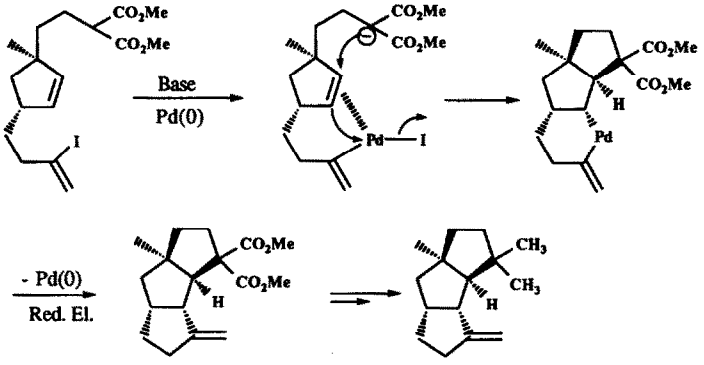
It should be observed that since the pioneering work of Tsuda and Saegusa [12] in 1988, the organopalladic species catalyzed cyclization of alkynes bearing carboxyl [13] hydroxy [14] and nitrogen [15] groups was further developed by us and other groups. This methodology provides a new useful entry to stereodefined allylidene, arylidene, alkynylidene and allenylidene heterocycles.



Y = OCOO, N, O, COO
R = aryl, vinyl, alkynyl, allyl or allenyl
X = OAc, Br, I or OTf

The development of routes for the synthesis of five membered rings continues to attract attention due largely to the wide variety of natural products containing this structural unit.

In scheme 1, we reported that functionalized diquinanes are easily and stereoselectively obtained from a new palladium catalyzed cyclisation **2** → **4**. By using the intramolecular version of this strategy, a triquinane should be directly produced in a single step by construction of the two outer rings around the central ring (scheme 2).



(±)-$\Delta^{9(12)}$-Capnellène

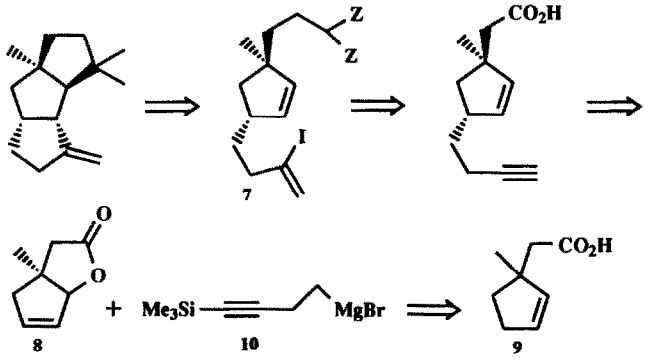
Scheme 2

Based on this concept, we now report the total synthesis of (±) $\Delta^{9(12)}$ capnellene.

Results and discussion

The hydrocarbon (-) $\Delta^{9(12)}$ capnellene, isolated from the soft coral *Capnellena imbricata* has been shown to possess a *cis-transoid-cis* tricyclo [6.3.0.$0^{2,6}$] undecane skeletal framework. The synthesis of this structurally interesting natural product has received significant attention and a number of syntheses via a variety of efficient approaches have been recently reported [16].

The envisaged approach to compound **7** is outlined retrosynthetically in scheme 3.



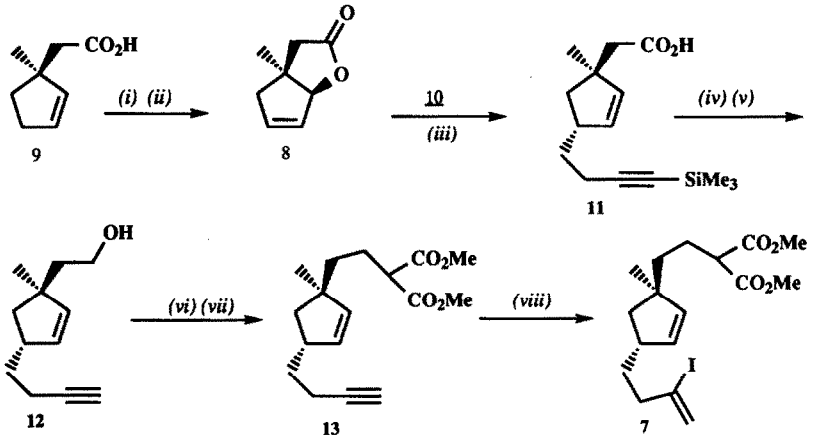
Scheme 3

In fact, our plan to reach the compound **7** was inspired by the elegant racemic route described by Curran and Chen [16j] which involved the regio and stereoselective opening of a vinyl lactone by the Grignard reagent of 2(2-Bromomethyl)-1.3 dioxane. With regard to our strategy, we chose to open the readily available lactone **8** (vide infra) by the well known 1-trimethylsilyl-4 butynyl magnesium bromide **10** [17].

Vinyl lactone **8** is obtained by standard iodolactonization of acid **9** [18] followed by a base-promoted elimination. Addition of Grignard reagent **10** in the presence of a stoichiometric amount of CuBr.Me_2S to lactone **8** provided acid **11** as a single regio and stereoisomer in near quantitative yield. This acid was reduced with lithium aluminium hydride, and then, removal of the trimethylsilyl group with KF, H_2O produced **12** in high yield . After mesylation of the resulting alcohol, product **13** was obtained by the reaction of the sodium enolate of methyl malonate.

The remaining task is to convert regio and chemoselectively the acetylenic unit of **13** to internal alkenyl iodide.

Several methods are known to effect this stereoselective synthesis of alkenyl iodide in a Markonikov fashion from terminal alkynes. For this purpose, the haloboration of 1-alkynes by B-bromo or B-iodo-9-boracyclo [3.3.1] nonane [19] has been developed. Attempted bromoboration of the carbon-carbon triple bond of **13** with commercial B-Br-9-BBN followed by protonolysis with CH_3CO_2H gave poor yields (17%) of the expected bromide. It has also been reported that the hydroiodination of 1-alkynes with I_2 on Al_2O_3 [20] produces 2-iodo-1-alkenes. However, in our hands, the lack of selectivity encountered between the double bond of the cyclopentene and the triple bond as well as the separation problems led us to abandon this approach. We then turned our attention to a recent alternative method : the hydroiodination of alkynes via an in-situ generation of HI from $Me_3SiCl/NaI/H_2O$ system [21]. In our case, the reaction proceeds with total chemoselectivity leading to **7** but with some amounts of starting material (about 30%) which can be fully consumed by repeating the procedure on the mixture of **7** and **13** previously obtained. The alkenyl iodide is then isolated in 68% yield.

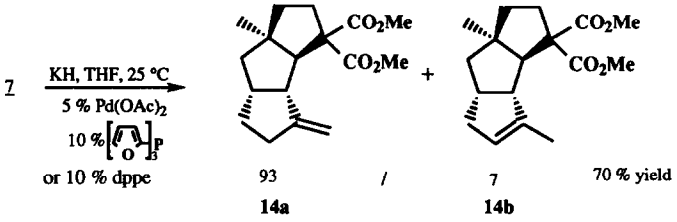


Reagents : *(i) I_2, KI, $NaHCO_3$, H_2O, 20 °C; (ii) DBU, toluene, 110 °C (iii) CuBr-Me_2S,THF/Me_2S, -20°C; (iv) LAH, Et_2O, 0°C; (v) KF, H_2O, DMF; (vi) $ClSO_2Me$, NEt_3, CH_2Cl_2, 0°C; (vii) NaH, $CH_2(CO_2Me)_2$, 10 % KI, THF/DMF 1/1, Δ; (viii) Me_3SiCl, NaI, 0,5 H_2O, CH_3CN.*

Scheme 4

With **7** in hand, the required *cis-transoid-cis* stereochemistry of the capnellane system can be now generated in one step through the key step of our strategy : the tandem-palladium cyclization outlined in scheme 2.

After some unsuccessful attempts using different catalysts and (or) solvents, we finally found that by treating bifunctional compound **7** at room temperature, in THF, with one equivalent of potassium hydride in the presence of $Pd(OAc)_2$ as the catalyst and tri(2-furyl) phosphine [22] or dppe as the ligand the starting material was completely consumed while two compounds were simultaneously formed in a ratio of 93/7 as indicated by GC and ^1H NMR . These two compounds were isolated by flash chromatography and identified as **14a** and **14b** (yield 70%).

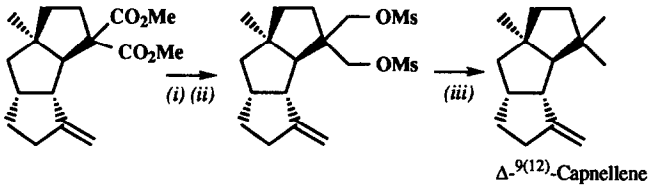


When we used tBuOK as base, the triquinane was accompanied by minor amounts of an alkyne coming from elimination of HI from the substrate ; a similar reaction was observed recently by Piers [23].Use of the triphenylphosphine ligand or DMSO as solvent decreased the yield of triquinanes.

Mass spectra and elementary analysis confirmed the $C_{17}H_{24}O_4$ expected formula and ^1H NMR showed clearly the presence, for the major product, of two methylene protons (broad singlet at δ 4.92) and for the minor endocyclic isomer, the presence of one vinylic proton (broad singlet at δ 5.14) and one methyl singlet at δ 1.69.

The structural assignment of the triquinane **14a** based on the spectral evidence was confirmed by the synthesis of $\Delta^{9(12)}$ capnellene.

Completion of this synthesis was then accomplished according to the procedure of Zimmerman [24] : treatment of the malonate unit with lithium aluminium hydride led to the expected diol in high yield, transformation to the dimesylate was performed with methanesulfonyl chloride in dichloromethane, in the presence of triethylamine and treatment of the latter with lithium triethylborohydride followed by careful medium pressure liquid chromatography with 100% pentane gave $\Delta^{9(12)}$ capnellene accompanied by small amounts of its endo isomer (50% yield for this last step).



(i) LAH, Et_2O ; (ii) $ClSO_2Me$, Et_3N, CH_2Cl_2 ; (iii) $LiEt_3BH$, THF, reflux

Scheme 5

A comparison of spectral data (IR, ^1H NMR, ^{13}C NMR, GC, MS) with those of authentic material kindly supplied to us by Professor Curran verified the structure of the product obtained by our total synthesis.

It is noteworthy that although Palladium catalyzed zipper mode cyclization using Heck reaction conditions have recently attracted widespread attention for the construction of polycyclic system, this methodology is not suitable for the construction of the requiered *cis-anti-cis* stereochemistry of the capnellane system. Indeed, since the Heck reaction proceeds via *syn* addition of an organopalladium species to the carbon-carbon double bond followed by the *syn* elimination of a palladium hydride, only the *cis-syn-cis* triquinane was obtained by this method [25]. In the same way, palladium catalyzed cascade carbometallation of alkynes and alkenes was not, for instance, an efficient route to the capnellane structure as indicated by a recent paper of Negishi et al. [26].

Aknowledgements. We wish to thank Professor *J.Gore* for valuable discussion. We are very grateful to Professor *D.Curran* for a sample of synthetic (±) capnellene and for copies of its spectra as well as for his interest in this work. We also express our sincere appreciation to *C.Traversa* for preliminary synthetic studies.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer 337 instrument. ^1H-NMR spectra were obtained on a Brucker AC 200 instrument (^1H : 200MHz or ^{13}C : 75MHz) using TMS as an internal standard. Chemical shifts were expressed in ppm downfield from TMS and coupling constants (J) in Hertz. G.C.-MS was measured on a NERMAG R10-10 spectrograph (ionization potential Ei = 70eV) coupled to a DELSI DI 700 chromatograph (equipped with a OV-1 (25 m column). Microanalysis were performed by le Service Central d'Analyse du CNRS, Solaize, France.

4-Bromo-1-trimethylsilyl-but-1-yne.

Methanesulfonylchloride (3.06 ml, 39.3 mmol) was added dropwise to a stirred solution of 4-trimethylsilyl-3-butyn-1-ol (5.25 g, 37.5 mmol) in a mixture of CH_2Cl_2 (132 ml) and triethylamine (15.72 ml, 112 mmol) maintained at 0°C. After stirring for 2h at 0°C and 3h at room temperature, Et_2O was added and the mixture was washed with a saturated aqueous NH_4Cl solution, water, dried and concentrated in vacuo. LiBr (112.5 mmol) was added during 3 min to a solution of the residue so obtained in acetone (80 ml) and the mixture was stirred for 15h under reflux. It was then poured into water (200 ml) and extracted with Et_2O. The organic extract was washed with an aqueous $NaHCO_3$ solution, water, dried and concentrated in vacuo. The residue was purified by flash-chromatography (petroleum ether) to give 4-bromo-1-trimethylsilyl-but-1-yne (6.1 g - 80% yield).
IR : 2960, 2180, 1250, 1210, 850, 760, 680, 635 cm^{-1}. **^1H NMR** ($CDCl_3$; 200MHz) : δ, 3.43 (t, 2H, J=7.6Hz) ; 2.76 (t, 2H, J=7.6Hz) ; 0.16 (s, 9H).

Iodolactonization of acid 9 .

Acid **9** (2.3g, 16.41 mmol) was added to a solution of $NaHCO_3$ (4.13g, 49.33 mmol) in water (40 ml) and the resulting mixture was stirred until it became homogeneous. The flask was then protected from light and the

mixture was treated in one portion with a solution of KI (16.34g, 98.2 mmol) and I_2 (4.6g, 18.05 mmol) in water (40 ml). The reaction mixture was stirred at room temperature for 20h and then extracted with $CHCl_3$ (5x35 ml). The organic extracts were combined, washed with 10% aqueous $Na_2S_2O_3$ (100 ml), 10% aqueous $NaHCO_3$ (100 ml) and water (50 ml) and then dried (Na_2SO_4). Removal of the solvent in vacuo yielded 4.15g of iodolactone (95%).

IR (neat) : 2960, 2920, 2860, 1780, 1455, 1170, 1010, 755 cm^{-1}.**^{1}H NMR** (200MHz) : 4.87 (1H, s) ; 4.35 (1H, d, J=2.8) ; 2.56 (2H, s) ; 1.82-2.22 (4H, m) ; 1.55 (3H, s). **^{13}C NMR** (75MHz) : 175.39, 97.75, 45.53, 43.41, 40.24, 35.74, 28.42, 28.33. **Mass spectrum.** m/z (%) : 266 ($M^{+\cdot}$, 7), 139(73), 121(18), 93(22), 55(100), 43(49), 27(47). **Anal.** Calc. for $C_8H_{11}O_2I$: C, 36.11 ; H, 4.16 ; O, 12.02 ; Found C, 36.22 ; H, 4.07 ; O, 12.07.

Lactone 8.

Iodo-lactone (4.02g, 15.12 mmol) from the previous experiment was dissolved in dry toluene (40 ml) containing freshly distilled 1,3-diazabicyclo [5.4.0] undec-7-ene (DBU) (3.4 ml, 22.7 mmol) and the mixture was heated at reflux for 6h, cooled, and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash-chromatography using a mixture of petroleum ether and Et_2O 7:3 as eluant to give 1.88g of pure **8** (90% yield).

IR (neat) : 3060, 2960, 2920, 2860, 1775, 1450, 1355, 1330, 1275, 1180, 1150, 1110, 1005, 750 cm^{-1}. **^{1}H NMR** (200MHz) $CDCl_3$: 6.04 (1H, m) ; 5.82 (1H, m) ; 5.02 (1H, s) ; 2.54 (1H, s) ; 2.50 (2H, s) ; 2.41-2.48 (1H, m) ; 1.35 (3H, s) ; **^{13}C NMR** (75MHz) : 176.63, 136.77, 128.83, 95.17, 46.33, 44.16, 43.13, 25.37. **Mass spectrum.** m/z (%) : 138 ($M^{+\cdot}$, 32), 109(9), 95(58), 77(37), 53(35), 39(100), 27(52). **Anal.** Calc. for $C_8H_{10}O_2$: C, 69.54 ; H, 7.29 ; Found C, 69.70 ; H, 7.36.

Trans-{1-Methyl-4-[(4-trimethylsilanyl)-3-butynyl]-cyclopent-2-enyl}-acetic acid 11.

To a solution of freshly prepared copper bromide dimethylsulfide complex (3.6g , 17.4 mmol) in dimethyl sulfide (23 ml) was added THF (23 ml). After cooling to -20°C, 4-trimethylsilyl-3-butynylmagnesium bromide (18 ml, 13.05 mmol) was added dropwise. The resulting mixture was stirred for 20 min at this temperature, then lactone **8** (1.20g , 8.7 mmol) was added. After stirring 2h at -20°C, the reaction was quenched with 10% HCl (80 ml). The acid was extracted with Et_2O and the organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash-chromatography using a mixture of petroleum ether and Et_2O 7:3 as eluant to afford an oil (2.18 g , 95% yield).

IR (neat) : 3400-3100, 3020, 2975, 2920, 2860, 2180, 1710, 1250, 845, 760 cm^{-1}. **^{1}H NMR** (200MHz) $CDCl_3$: 5.64 (2H, m) ; 2.82 -2.86 (1H, m), 2.38 (2H, s), 2.2-2.28 (4H, m), 1.64-1.75 (1H, m), 1.47-1.59 (1H, m), 1.24 (3H, s), 0.15 (9H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 178.68, 138.74, 133.58, 107.32, 84.61, 47.40, 45.44, 44.39, 43.75, 35.24, 27.73, 18.47, 0.17. **Mass spectrum.** m/z (%) : 249 (M-15), 205(8), 152(17), 132(33), 107(24), 93(55), 73(100), 55(10), 43(21) ; **Anal.** Calc. for $C_{15}H_{24}O_2Si$: C, 68.13 ; H, 9.15 ; Found C, 68.34 ; H, 9.29.

Trans-3-methyl-3-(2-hydroxyethyl)-5-(4-trimethylsilyl-3-butynyl)cyclopent-1-ene.
To a cold (0°C) stirred suspension of $LiAlH_4$ (0.54g , 14.2 mmol) in 19 ml of dry Et_2O was added a solution of acid **11** (2.1g , 7.9 mmol) in 19 ml of dry Et_2O. The mixture was stirred at 0°C for 2h. Water (0.540 ml), 1N NaOH (0.540 ml) then water (5.8 ml) were successively added until a precipitate appeared. The slurry was filtered through celite (Et_2O). The eluate was dried (Na_2SO_4) and concentrated. Flash-chromatography with petroleum ether/Et_2O 3:2 gave 1.71g of alcohol (95% yield).
IR (neat) : 3350, 3015, 2950, 2920, 2860, 2170, 1250, 1050, 1015, 845, 760 cm^{-1}. **^{1}H NMR** (200MHz) $CDCl_3$: 5.51-5.60 (2H, m), 3.66 (2H, t, J=7.4), 2.77-2.85 (1H, m), 2.24(2H, t, J=7.5), 2.05 (1H, dd, J=13, 8.2), 1.15-1.69 (6H, m), 1.10 (3H, s), 0.14 (9H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 139.69, 132.90, 107.41, 84.54, 60.52, 47.45, 44.92, 44.38, 43.73, 35.58, 28.87, 18.43, 0.2. **Anal.** Calc. for $C_{15}H_{26}OSi$: C, 71.94 ; H, 10.46 ; Found C, 71.86 ; H, 10.70.

Trans-3-methyl-3-(2-hydroxyethyl-5-(3-butynyl)cyclopent-1-ene 12.
To a solution of the acetylenic compound prepared above (1.64g , 6.56 mmol) and potassium fluoride (0.572g, 9.84 mmol) in DMF (12 ml) was added water (0.531 ml , 29.52 mmol). The mixture was stirred overnight at room temperature, then petroleum ether (12 ml) and Et_2O (12 ml) were added. After washing with water and brine, drying over $MgSO_4$, the organic phase was concentrated in vacuo. Flash-chromatography with petroleum ether/ Et_2O 3:2 gave alcohol **12** (1.1g, 95% yield).
IR (neat) : 3350, 3015, 2920, 2850, 2120, 1450, 1250, 1060, 1015, 750 cm^{-1}. **^{1}H NMR** (200MHz $CDCl_3$) 5.53-5.61 (2H, m), 3.66 (2H, t, J=7.3), 2.81-2.88 (1H, m), 2.17 (2H, td, J=7.2, 2.6), 2.06 (1H, dd, J=13, 8.2), 1.96 (1H, t, J=2.6), 1.14-1.74 (6H, m), 1.11 (3H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 139.83, 132.72, 84.47, 68.36, 60.51, 47.46, 44.70, 44.33, 43.73, 35.43, 28.84, 16.96. **Anal.** Calc. for $C_{12}H_{18}O$: C, 80.85 ; H, 10.17 ; Found C, 80.70 ; H, 10.04.

Trans-3-methyl-3-(2-methanesulfonyloxyethyl)-5-(3-butynyl)-cyclopent-1-ene.
Prepared as above. The crude product was used without purification.

Trans-3-methyl-3-(3-dimethoxycarbonylpropyl)-5-(3-butynyl)-cyclopent-1-ene. 13
A suspension of 60% NaH in mineral oil (0.472g, 11.8 mmol) was washed with pentane (2x10 ml) and then suspended in a mixture of THF and DMF (19 ml , 1/1). KI was added (0.196g , 1.18 mmol), then dimethylmalonate (1.48 ml , 13 mmol) was added dropwise at 0°C. After the resulting solution of sodium malonate was allowed to warm at room temperature, the crude above mesylate (2.24g , 11.8 mmol) was added in one portion. The resulting mixture was warmed at 70°C for 14h, cooled, dilued with Et_2O and washed with 3% HCl, water, saturated aqueous NaCl and dried (Na_2SO_4). The crude product obtained after removal of solvent by rotary evaporation was purified by flash-chromatography using petroleum ether/Et_2O 7:3 to provide **13** (1.6g , 78% yield).
IR (neat) : 3290, 3030, 2950, 2860, 2120, 1750, 1430 cm^{-1}. **^{1}H NMR** (200MHz $CDCl_3$) 5.57 (1H, dd, J=5.6, 1.6), 5.47 (1H, dd, J=5.6 ; 2.1Hz), 3.74 (6H, s), 3.29 (1H, t, J=5), 2.81 (1H, m), 2.21 (2H, td, J=7.3, 2.5), 1.98-2.05 (1H, m), 1.95 (1H, t, J=2.5), 1.87 (2H, t, J=8.3), 1.11-1.79 (5H, m), 1.08 (3H, s).

^{13}C NMR (75MHz , $CDCl_3$) : 169.89, 139.34, 133.80, 84.54, 68.23, 52.46, 52.18, 48.41, 44.73, 43.01, 39.14, 35.54, 28.25, 24.79, 16.95. **Mass spectrum** : 160 (M - 132) (3) ; 133(20) ; 105 (23) ; 93 (41) ; 55 (60) ; 41 (100) ; 27 (37). **Anal.** Calc. for $C_{17}H_{24}O_4$: C, 69.84 ; H, 8.27 ; Found C, 69.38 ; H, 8.33.

Trans-3-methyl-3-(3-dimethoxycarbonylpropyl)-5-(3-iodo-3-butenyl) cyclopent-1-ene.7

At room temperature in acetonitrile (2 ml) was dissolved NaI (0.252g , 1.68 mmol) and then added Me_3SiCl (0.216 ml, 1.68 mmol) followed by H_2O (0.016 ml , 0.84 mmol). After 10 min at ambient temperature, to the solution was added acetylenic **13** (0.400g , 1.37 mmol) and the mixture was allowed to react at this temperature for 3h. The reaction was then quenched by water and extracted with Et_2O (3x15 ml). Drying over $MgSO_4$ and evaporation of Et_2O gave a liquid which was a mixture of starting material and alkenyl iodide **7**.

The same reaction was then repeated on this mixture. The crude product was purified by flash-chromatography with petroleum ether/Et_2O 4:1 yielded iodide **7** (0.424g , 73%).

IR (neat) : 3040, 2960, 2860, 1750, 1620, 1440, 895 cm^{-1}. **^{1}H NMR** (200MHz $CDCl_3$) : 6.01 (1H, d, J=1.2), 5.67 (1H, d, J=1.2), 5.55 (1H, dd, J=5.6 ; 1.7), 5.46 (1H, dd, J=5.6Hz, 2.1), 3.72 (6H, s), 3.29 (1H, t), 2.65-2.76 (1H, m), 2.4 (2H, t, J=7.5), 1.89-2.02 (1H, m), 1.81 (2H, t, J=8), 1.12-1.74 (5H, m), 1.08 (3H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 169.71, 139.42, 132.92, 125.19, 111.28, 52.36, 52.03, 48.33, 44.20, 43.80, 42.93, 39.05, 36.23, 28.22, 24.71. **Mass spectrum** : 420 ($M^{+\cdot}$, 4) ; 261(10) ; 239(12) ; 175(14) ; 145(20) ; 107(100) ; 93(28) ; 79(30) ; 53(33) ; 41(27).

Preparation of the tricyclic compounds 14a and 14b.

On the one hand, a suspension of 35% KH in mineral oil (0.055g , 0.48 mmol) was washed with pentane (2x10 ml) and then suspended in dry THF (2 ml). Malonate **7** (0.195g, 0.46 mmol) was added followed by 18 crown-6 (0.025g, 0.09 mmol) in 2 ml of THF. The resultant mixture was stirred at room temperature for 15mn. On the other hand, the palladium(0) complex was preformed at 50°C in THF (5 ml) by reaction of 1-heptene (10 µl) with palladium acetate (0.054 g, 0.023 mmol) and tri(2-furyl) phosphine (0.012 g, 0.046 mmol). Then, the addition of this Pd(0) solution is made at room temperature via a canula on the malonate anion prepared above. The mixture is stirred at this temperature until the starting material is consumed (G.C). The reaction mixture was then quenched with water and extracted with Et_2O. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by flash-chromatography with petroleum ether/Et_2O 95:5 to give **14a** and **14b** in 70% yield in a ratio of 93/7.

14a

IR (neat) : 3065, 2950, 2860, 1735, 1650, 1450, 1430, 1375, 1265, 1130, 1075, 1025, 880 cm^{-1}.

^{1}H NMR (200MHz $CDCl_3$) : 4.92 (2H, s), 3.73 (3H,s), 3.70 (3H, s), 2.96 (1H, d, J=2.2), 2.10-2.58 (8H, m), 1.31-1.79 (4H, m), 1.16 (3H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 172.59, 171.51, 156.94, 106.58, 66.31, 62.71, 53.82, 53.48, 52.60, 52.27, 47.50, 45.07, 39.44, 34.06, 31.15, 29.55, 28.62. **GC/MS** T_{in} = 180°C for 10 min the T_{fin} = 250°C at 10°C min^{-1}. t_R = 307s. 292 ($M^{+\cdot}$, 16) ; 277(4) ; 261(4) ; 233(18) ; 232(100) ; 204(18) ; 160(21) ; 145(26) ; 133(58) ; 105(14) ; 91(26) ; 77(25) ; 59(30) ; 41(32).

14b

^{1}H NMR (200MHz $CDCl_3$) : 5.14 (1H, s), 3.69 (6H, s), 2.85 (1H, d, J=2.7), 2.10-2.58 (6H, m), 1.69 (3H, s), 1.31-1.79 (4H, m), 1.11 (3H, s). **GC/MS** T_{in} = 180°C for 10 min the T_{fin} = 250°C by 10°C min^{-1}. t_R = 300s. 292 (M^+, 27) ; 261(11) ; 233(14) ; 232(81) ; 133(100) ; 93(19) ; 79(39) ; 55(13) ; 41(24).
14a + 14b Anal. Calc. for $C_{17}H_{24}O_4$: C, 69.84 ; H, 8.27 ; Found C, 69.43 ; H, 8.32.

Capnellene synthesis

1 - Reduction of diester 14a + 14b to diol

A solution of triquinanes **14a + 14b** (0.042g, 0.144 mmol) in Et_2O (10 ml) was added to a suspension of $LiAlH_4$ (0.017g, 0.43 mmol) in Et_2O (1 ml) at 0°C. The mixture was then allowed to warm to ambient temperature, stirred 16h and then quenched with water and filtered. Evaporation of solvent, gave diol (0.034g, 100% yield) used without purification.
IR (neat) : 3300, 3060, 3020, 2930, 2860, 1650, 1450, 1120, 1020, 875 cm^{-1}. **^{1}H NMR** (200MHz , $CDCl_3$) : 4.91 (1H, broad, s), 4.85 (1H, broad, s), 3.66-3.77 (4H, m), 3.07 (2H, m), 2.73 (1H, m), 2.27-2.63 (3H, m), 1.89 (1H, d, J=2.4), 1.17-1.75 (8H, m), 1.15 (3H, s). **^{13}C NMR** (75MHz , $CDCl_3$) : 158.26, 105.63, 70.85, 68.59, 62.02, 53.60, 51.18, 51.09, 46.75, 45.86, 39.22, 31.77, 31.28, 30.82, 28.85.

2. Formation of dimesylate

To a stirred solution of the diol prepared above (0.034g , 0.144 mmol) in CH_2Cl_2 (2 ml) was added Et_3N (60 µl, 0.43 mmol). The mixture was cooled to 0°C and methanesulfonylchloride (23 µl, 0.25 mmol) was added dropwise. The mixture was stirred overnight at room temperature. After the reaction mixture was washed with saturated aqueous sodium bicarbonate and dried, solvent was removed in vacuo to give 0.055g (98% yield) of dimesylate. The crude product was used without purification.
IR (neat) : 3060, 3020, 2930, 2860, 1650, 1350, 1175, 950, 835 cm^{-1}.

3. Capnellene

A solution of dimesylate (0.055g , 0.14 mmol) in THF (6 ml) was added during 1.5h to 1.6 ml (1.6 mmol) of 1.0M lithium triethylborohydride in THF at 0°C. After addition was complete, the reaction was refluxed for 18h, cooled and quenched with water (1 ml), 3N aqueous sodium hydroxide (2.1 ml) and 30% hydrogen peroxide were added (2.1 ml). The reaction mixture was extracted with Et_2O, and the organic layers were washed with water and brine and dried over Na_2SO_4. The crude product obtained after removal of solvent by rotary evaporation was purified by careful flash-chromatography. Elution with 100% pentane give 0.014g of $\Delta^{9(12)}$ capnellene accompanied by small amount of its endo isomer. Yield : 50%.
IR (neat) : 3045, 1640, 1450, 1370, 870 cm^{-1}. **^{1}H NMR** (200MHz $CDCl_3$) : 4.89 (1H, s), 4.78 (1H, s), 2.30-2.68 (4H, m), 1.42-1.78 (9H, m), 1.15 (3H, s), 1.07 (3H, s), 0.98 (3H,s). **^{13}C NMR** (75MHz , $CDCl_3$) : 158.96, 104.96, 69.07, 53.33, 52.28, 47.91, 45.99, 42.33, 41.66, 40.55, 31.80, 31.52, 30.80,

29.05, 26.04. **Mass spectrum** : 204 ($M^{+\cdot}$, < 1%) ; 189(2) ; 148(7) ; 135(14) ; 133(13) ; 109(20) ; 91(20) ; 80(100) ; 79(26) ; 55(10) ; 41(28). The chromatographic (GC) behavior of our compound was identical with that of the same material prepared by Professor Curran.

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