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SYNTHESIS OF (±)-HIRSUTENE BY A CATALYTIC ALLYLPALLADIUM-ALKYNE CYCLIZATION/CARBONYLATION CASCADE

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Abstract: The tricyclic terpenoid (±)-hirsutene (1) has been synthesized starting from 2-hydroxy-4,4-dimethyltetrahydropyrane (8). In the key step, acyclic enynyl carbonate 7 afforded bicyclooctenone 2 *via* a 85% diastereoselective palladium catalyzed metallo-ene/carbonylation reaction cascade. The third ring was closed by a radical/alkene addition 19 → 20.

Introduction

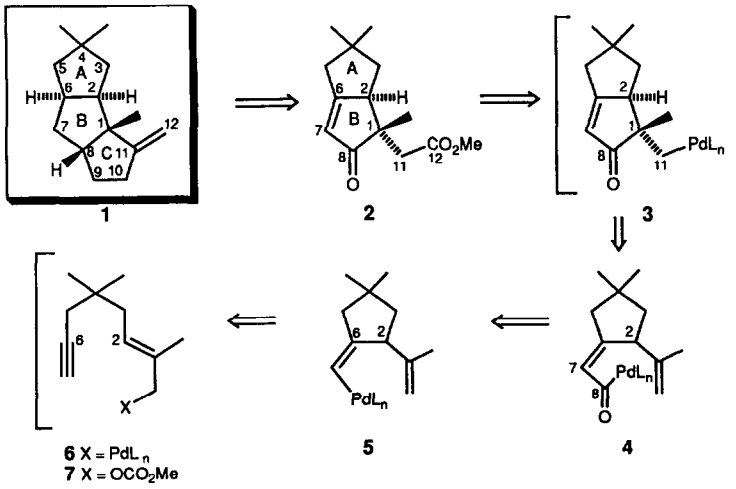
The intramolecular insertion of allyl-palladium and -nickel species into alkene and alkyne bonds (*metallo-ene type cyclization*) has evolved into a synthetically powerful process.[1] Most critically, this insertion becomes part of a catalytic cycle when combined with initiation and termination steps (allylmetal generation and metal catalyst recovery, respectively).[1,2]

Combinations of palladium- and nickel-ene cyclizations with carbonylation reactions are particularly attractive since they permit the stereoselective formation of four carbon-carbon bonds in a single process.[3] This has been illustrated by the syntheses of pentalenolactone E methyl ester, [4] (+)-3-isorauniticine, [5] coriolin [6] and [5.5.5.5]fenestranes.[7] We present here a further rational application of this reaction cascade in a synthesis of the triquinane terpenoid hirsutene.

Hirsutene, a metabolite of the Basidiomycete *Coriolus consors* was assigned structure 1 based on spectroscopic evidence and total synthesis.[8] The synthesis of 1 has become a popular test case to evaluate new methods of five-membered carbocycle annulation.[8,9]

Our approach to hirsutene (1) is summarized by the disconnective analysis depicted in Scheme 1.[10]

Scheme 1

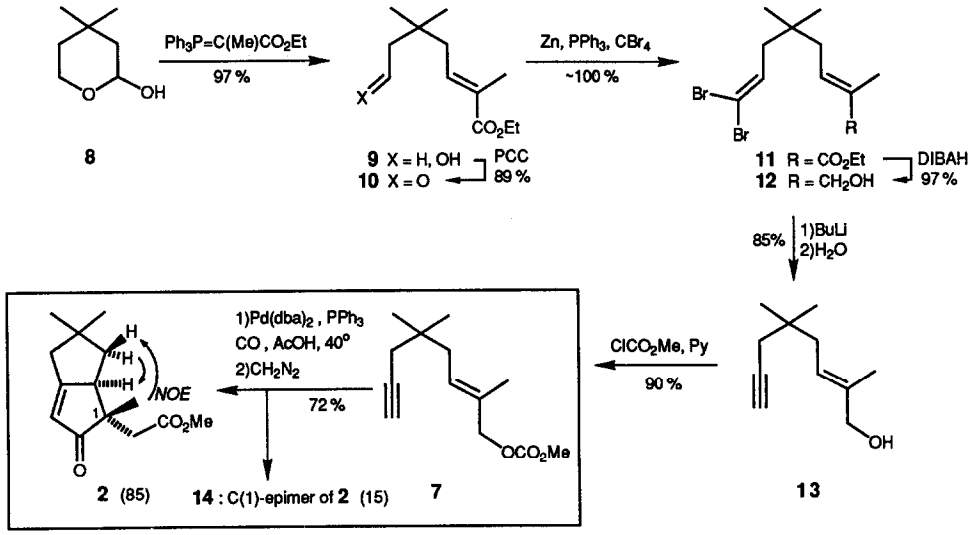


Hence, it was envisaged that oxidative addition **7** → **6** (initiation), allylpalladium/alkyne insertion **6** → **5** (metallo-ene cyclization) and CO insertions **5** → **4** → **3** → **2** (termination) would allow creation of the bonds between C(2)-C(6), C(7)-C(8), C(8)-C(1) and C(11)-C(12) in a single operation. The direction and extent to which the stereocenter C(2) would bias the generation of quaternary center C(1) in the acylpalladium/alkene insertion step **4** → **3** was an intriguing aspect of this strategy.

Synthesis.

In order to implement this plan (Scheme 2), lactol **8** [11] was treated with (carbethoxyethylidene)-triphenylphosphorane affording hydroxyenoate **9** (97%) as a 93:7-mixture of *E*/*Z*-isomers.

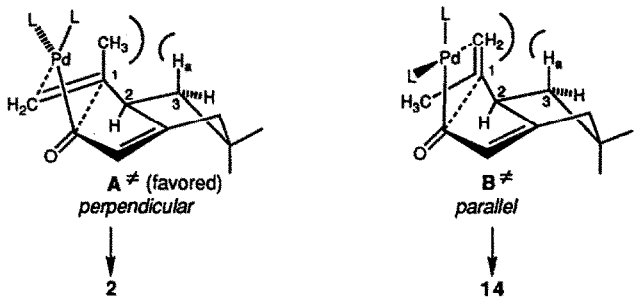
Scheme 2



Expecting *Z*/*E* isomerization of the allylpalladium intermediate **6** to occur faster than cyclization **6** → **5**, [12] enoate **9** (*E*/*Z* = 93:7) was converted to carbonate **7** without separation of *E*/*Z*-isomers. However, for characterization purposes, separated (*E*)-**9** was also transformed into pure (*E*)-**7**. Thus, oxidation of **9** with PCC and treatment of resulting aldehyde with zinc powder, PPh_3 and CBr_4 [13] furnished dibromodienoate **11** (89% from **9**) which was reduced with diisobutylaluminum hydride to dibromodienol **12** (97%). Treatment of dibromodienol **12** with BuLi (4 mol-equiv.) [13] and aq. workup gave enynol **13** (85%). Acylation of **13** with methyl chloroformate/pyridine provided carbonate **7** (90%), the key cyclization precursor.

Stirring acyclic enynyl carbonate **7** (*E*/*Z* = 93:7) with $Pd(dba)_2$ [14] (dba = dibenzylideneacetone, 0.1 mol-equiv.), PPh_3 (0.3 mol-equiv.) in AcOH at 40° under CO (1 atm) for 21 h, followed by treatment with CH_2N_2, afforded the epimeric bicyclooctenones **2** and **14** in a 83:17-ratio (78% yield). Subjecting pure (*E*)-carbonate **7** to identical cyclization conditions furnished a 85:15-mixture of **2** and **14** (72%) from which the major isomer **2** was isolated in 61% yield. NOE-measurements on **2** clearly revealed the desired *trans*-disposition of the C(1)-methyl group and the C(2)-hydrogen atom. The observed stereodirecting effect of center C(2) on the acylpalladium/alkene insertion **4** → **3** can be rationalized as follows. Inspection of Dreiding models reveals two transition state conformations $A^{\neq}$, $B^{\neq}$ (Scheme 3) which are free of strain and which accommodate a suprafacial 4-center insertion of the alkene into the palladium-carbon bond. [15]

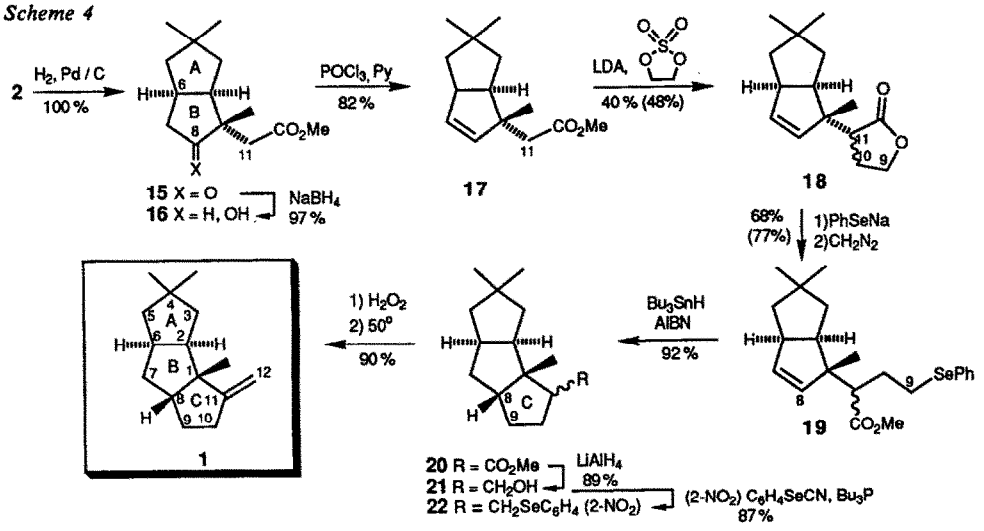
Scheme 3



Whereas a parallel orientation of the C=C and C-Pd bonds (transition state $B^{\neq}$) should lead to the minor product **14**, a perpendicular alignment (transition state $A^{\neq}$) should result in the formation of major isomer **2**. Assuming repulsions CH_3-C(1)/H_a (in $A^{\neq}$) and CH_2=C/H_a (in $B^{\neq}$) to be comparable, it seems that the acylpalladium/alkene insertion **4** → **3** favors a perpendicular over a parallel C-Pd/C=C orientation in the transition state. [16]

Catalytic hydrogenation of **2** proceeded, as expected, from the *exo*-face thus securing the *cis*-fusion of rings A and B in product **15** (Scheme 4).

Scheme 4



To set the stage for the annulation of ring C, the C(8)-carbonyl group of **15** was reduced with $NaBH_4$ giving a single alcohol **16** (97% from **2**) which underwent smooth elimination to alkene **17** (82%) when treated with $POCl_3$/pyridine. Attachment of the remaining carbon atoms C(9) and C(10) to the sterically hindered C(11) by alkylation of the lithium enolate of ester **17** with cyclic ethylene sulfate [17] afforded lactone **18** as a 1.3:1-mixture of C(11)-epimers in 40% yield (48% based on recovered **17**). Since the configuration at C(11) should be irrelevant for the synthesis of **1**, the following steps were carried out with C(11)-epimer mixtures. Opening of lactone **18** with (*in situ* prepared) sodium phenylselenolate [18] and esterification of the non-isolated carboxylic acid with CH_2N_2 furnished selenide esters **19** (68%, 77% based on recovered **18**).

Ring C was then efficiently closed by a radical chain reaction [19] of olefinic selenides **19**. Adding toluene solutions of AIBN (0.14 mol-equiv.) and Bu_3SnH (1.5 mol-equiv.) simultaneously over 18 h to a refluxing solution of selenides **19** in toluene furnished tricyclic esters **20** in 92% yield.

Finally, the carbomethoxy group of **20** was converted to the *exo*-methylene group of **1**: Reduction with $LiAlH_4$, treatment of the primary alcohol **21** with *o*-nitrophenylselenocyanate and tributylphosphine [20], oxidation of selenide **22** with H_2O_2 and thermal selenoxide elimination (50°) provided pure hirsutene (**1**) in 70% overall yield from esters **20**. The IR, ^{1}H-NMR and ^{13}C-NMR spectra of thus obtained **1** are in perfect accord with published data.[9]

In summary, (±)-hirsutene (**1**) has been prepared from lactol **8** by a sequence of 16 steps in 7.4% overall yield. The strategic allylation/carbonylation step which forms four C-C bonds with 85% diastereocontrol of a quaternary center demonstrates once more the value of this method in organic synthesis.

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EXPERIMENTAL

General.- All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O, THF, toluene (Na), CH_2Cl_2, DMF, pyridine, HMPA (CaH_2), EtOH (Mg). Workup denotes addition of sat. aq. NH_4Cl, extraction with an org. solvent, washing of the org. phase with sat. aq. NH_4Cl soln., drying ($MgSO_4$) and evaporation *in vacuo*. Column flash chromatography (FC): SiO_2 (*Merck, Kieselgel 60*, 0.040-0.060 mm). GC: *Hewlett-Packard 5790 A*, integrator *HP 3390 A*, capillary column (fused silica, *OV-1*, 0.2 mm i.d., 12 m), 10 psi H_2; t_R in min. (area -%). IR: *Polaris Matteson Instruments or Perkin-Elmer 681* in $CHCl_3$, unless otherwise specified. NMR spectra (*Bruker AMX-400* or *Varian XL-200*), in $CDCl_3$, unless otherwise specified; standard $CHCl_3$ (δ = 7.27 ppm), *J* in Hz. MS: *Varian CH-4* or *Finnigan 4023* at 70 eV, m/z (rel.-%). HR-MS: *VG 7070-E*.

Synthesis.-*Ethyl 7-Hydroxy-2,5,5-trimethyl-hept-2-enoate* (**9**) : A mixture of lactol **8** [11] (1.0 g, 7.7 mmol) and (carbethoxyethylidene)triphenylphosphorane (4.17 g, 11.5 mmol) in CH_2Cl_2 (30 ml) was heated under reflux. After 100 h, further phosphorane (1.4 g, 3.8 mmol) was added and the mixture was heated under reflux for 16 h. Workup (CH_2Cl_2) and FC gave hydroxyenoate **9** (1.60 g, 97%) as a 93:7 *E/Z* mixture (^{1}H-NMR). IR: 3620, 3500 (broad), 2960, 1700, 1645, 1470, 1390, 1370, 1260, 1180, 1110, 1090, 1025. (*E*)-isomer: ^{1}H-NMR (200 MHz) : 6.84 (*tq*, *J* = 7.8, 1.4, 1 H); 4.19 (*q*, *J* = 7.1, 2 H); 3.71 (*t*, *J* = 7.5, 2 H); 2.10 (*d*, *J* = 7.8, 2 H); 1.81 (*d*, *J* = 1, 3 H); 1.56 (*t*, *J* = 7.5, 2 H); 1.29 (*t*, *J* = 7.1, 3 H); 0.96 (*s*, 6 H). ^{13}C-NMR (50 MHz): 168.2 (*s*); 138.8 (*d*); 129.2 (*s*); 60.5 (*t*); 59.7 (*t*); 44.3 (*t*); 41.3 (*t*); 33.6 (*s*); 27.3 (*q*); 14.3 (*q*); 12.6 (*q*). MS: 215 (12, $C_{12}H_{22}O_3 + H^{+\cdot}$), 214 (1.7, $C_{12}H_{22}O_3^{+\cdot}$), 169 (39), 168 (13), 128 (55), 123 (22), 100 (44), 95 (12), 82 (24), 69 (100), 57 (15), 56 (11), 55 (20), 54 (10), 53 (13), 45 (15). HR-MS: 214.1570 ($C_{12}H_{22}O_3^{+\cdot}$, calc. 214.1569). Characteristic ^{1}H-NMR signals of (*Z*)-isomer: 5.96 (*tq*, *J* = 7.6, 1.3, 1 H); 2.40 (*dq*, *J* = 7.6, 1.3, 1 H); 1.86 (*q*, *J* = 1.3, 3 H); 0.86 (*s*, 3 H).

Ethyl 7-Oxo-2,5,5-trimethyl-hept-2-enoate (**10**) : A soln. of alcohol **9** (1.49 g, 6.95 mmol, (*E/Z*) = 93:7) in CH_2Cl_2 (5 ml) was added at r.t. to a stirred suspension of Celite (2.25 g) and PCC (2.25 g, 10.4 mmol) in CH_2Cl_2 (10 ml). Stirring for 1.5 h, filtration through Florisil, evaporation and FC (pentane/Et_2O 95:5) of the filtrate gave (*E*)-aldehyde **10** and its more polar (*Z*)-isomer (1.307 g total, 89 %). (*E*)-Isomer: IR: 2961, 2939, 2904, 2874, 2836, 2741, 1716, 1704, 1647, 1468, 1446, 1390, 1370, 1311, 1265, 1174, 1155, 1111, 1082, 1030. ^{1}H-NMR (400 MHz): 9.84 (*t*, *J* = 2.9, 1 H); 6.82 (*tq*, *J* = 7.8, 1.5, 1 H); 4.20 (*q*, *J* = 7.0, 2 H); 2.32 (*d*, *J* = 2.9, 2 H); 2.23 (*d* br. *J* = 7.8, 2 H); 1.84 (*s* br. 3 H); 1.31 (*t*, *J* = 7.0, 2 H); 1.12 (*s*, 6 H). ^{13}C-NMR: 202.6 (*d*); 167.9 (*s*); 137.3 (*d*); 130.2 (*s*); 60.6 (*t*); 54.6 (*t*); 41.1 (*t*); 34.5 (*s*); 27.4 (*q*); 14.3 (*q*); 12.6 (*q*). MS: 212 (19, $C_{12}H_{20}O_3^{+\cdot}$), 171 (12), 169 (25), 168 (100), 167 (23), 166 (39), 155 (27), 154 (10), 153 (56), 139 (12), 128 (96), 127 (26), 125 (27), 123 (32), 113 (12), 111 (19), 100 (100), 99 (11), 97 (17), 95 (51), 85

(30), 83 (77), 82 (45), 79 (11), 71 (19), 69 (34), 67 (18), 59 (19). HR-MS: 212.14197 ($C_{12}H_{20}O_3^{+\cdot}$, calc. 212.14123).

(*Z*)-Isomer: IR: 2981, 2963, 2933, 2898, 2874, 2838, 2742, 1715, 1644, 1465, 1456, 1372, 1315, 1298, 1231, 1177, 1111, 1023. ^{1}H-NMR (400 MHz): 9.84 (*t*, *J* = 2.9, 1 H); 5.87 (*tq*, *J* = 7.7, 1.5, 1 H); 4.20 (*q*, *J* = 7.0, 2 H); 2.55 (*d* br. *J* = 7.7, 2 H); 2.29 (*d*, *J* = 2.9, 2 H); 1.94 (*d*, *J* = 1.5, 3 H); 1.30 (*t*, *J* = 7.0, 3 H); 1.09 (*s*, 6 H). ^{13}C-NMR (100 MHz): 203.2 (*d*); 167.9 (*s*); 137.0 (*d*); 129.9 (*s*); 60.1 (*t*); 54.5 (*t*); 41.4 (*t*); 34.1 (*s*); 27.3 (*q*); 21.0 (*q*); 14.2 (*q*). MS: 212 (0.2, $C_{12}H_{20}O_3^{+\cdot}$), 197 (1.6), 169 (17), 168 (60), 167 (18), 166 (14), 153 (32), 128 (94), 125 (21), 123 (41), 100 (100), 99 (10), 97 (13), 95 (40), 85 (22), 83 (24), 82 (41), 69 (15), 67 (16), 57 (37), 56 (14), 55 (41). The subsequent transformation of **10** into **2** and **14** was carried out with the *E*/*Z*-mixture as well as with pure (*E*)-**10**.

Ethyl 8,8-Dibromo-2,5,5-trimethyl-octa-2,7-dienoate (**11**) : A mixture of zinc powder (578 mg, 8.84 mmol), triphenylphosphine (2.32 g, 8.84 mmol) and CBr_4 (2.93 g, 8.84 mmol) was stirred at r.t. in CH_2Cl_2 (25 ml) for 40 h [13]. Addition of a soln. of aldehyde **10** (*E*/*Z*= 93:7, 939.6 mg, 4.43 mmol) in CH_2Cl_2 (5 ml), stirring of the dark-red mixture for 1 h, partial evaporation of the solvent *in vacuo*, adsorption of the soln. on SiO_2 and elution (hexane/AcOEt 95:5) gave **11** (1.629 g, ~100%, *E*/*Z* = 93:7). IR: 2960, 2940, 2900, 2880, 1700, 1645, 1620, 1470, 1395, 1370, 1270, 1115, 1085. ^{1}H-NMR (*E*-isomer,400 MHz): 6.83 (*tq*, *J* = 7.9, 1.7, 1 H); 6.43 (*t*, *J* = 7.6, 1 H); 4.20 (*q*, *J* = 7.1, 2 H); 2.11 (*d* br. *J* = 7.9, 2 H); 2.06 (*d*, *J* = 7.6, 2 H); 1.84 (*s*, 3 H); 1.30 (*t*, *J* = 7.1, 3 H); 0.98 (*s*, 6 H). ^{13}C-NMR (*E*-isomer, 100 MHz): 168.0 (*s*); 138.0 (*d*); 135.6 (*d*); 129.9 (*s*); 90.0 (*s*); 60.5 (*t*); 45.2 (*t*); 40.7 (*t*); 35.4 (*s*); 27.0 (*q*); 14.3 (*q*); 12.6 (*q*). MS (*E*/*Z* = 93:7): 370 (1, $C_{13}H_{20}Br_2O_2^{+\cdot}$), 368 (2), 366 (1), 201 (10), 199 (22), 197 (12), 169 (38), 141 (13), 128 (100), 123 (51), 113 (22), 109 (10), 100 (51), 99 (17), 96 (10), 95 (63), 85 (14), 82 (20), 81 (26), 80 (29), 79 (42), 77 (23), 69 (25), 67 (21), 65 (12), 56 (22), 55 (57), 54 (18), 53 (42). Characteristic ^{1}H-NMR signals of (*Z*)-isomer: 6.41 (*t*, *J* = 7.3, 1 H); 5.93 (*tq*, *J* = 7.7, 1.2, 1 H); 4.19 (*q*, *J* = 7.0, 2 H); 2.41 (*d* br. *J* = 7.7, 2 H); 2.10 (*d*, *J* = 7.3, 2 H); 1.93 (*q*, *J* = 1.3, 3 H); 1.26 (*t*, *J* = 7.0, 3 H); 0.87 (*s*, 6 H). Following the same protocol, pure (*E*)-**10** (4.93 g, 23.23 mmol) gave pure (*E*)-**11** (8.045 g, 94 %).

(E)-8,8-Dibromo-2,5,5-trimethyl-octa-2,7-dien-1-ol (**12**) : A 1M soln. of DIBAH in hexane (66 ml) was added over 2 h to a soln. of pure (*E*)-ester **11** (8.009 g, 21.75 mmol) in CH_2Cl_2 (100 ml) at -78°. Stirring of the reaction mixture at -78° for 1 h, addition of sat. aq. NH_4Cl (50 ml) and of a 30% aq. soln. of sodium potassium tartrate (50 ml), workup (Et_2O) and FC (hexane/AcOEt 9:1) gave allylic alcohol **12** (oil, 6.85 g, 97 %). IR: 3605, 3460 (broad), 3020, 2960, 2935, 2875, 1620, 1470, 1385, 1370, 1110, 1055, 1000, 895. ^{1}H-NMR (400 MHz): 6.43 (*t*, *J* = 7.3, 1 H); 5.48 (*tq*, *J* = 7.7, 1.3, 1 H); 4.04 (*s* br. 2 H); 2.025 (*d*, *J* = 7.3, 2 H); 1.98 (*dq*, *J* = 7.7, 1, 2 H); 1.67 (*s* br. 3 H); 1.41 (br. 1 H); 0.93 (*s*, 6 H). ^{13}C-NMR (100 MHz): 136.9 (*s*); 136.2 (*d*); 121.9 (*d*); 89.4 (*s*); 69.1 (*t*); 44.9 (*t*); 39.6 (*t*); 35.1 (*s*); 26.9 (*q*); 13.9 (*q*). MS: 313 (0.1, $[C_{11}H_{18}Br_2O - CH_3]^{+\cdot}$), 311 (0.3), 309 (0.2), 241 (15), 240 (18), 201 (12), 199 (25), 197 (12), 165 (20), 162 (12), 161 (15), 160 (13), 159 (13), 109 (100), 107 (11), 81 (28), 80 (33), 79 (30), 77 (13), 71 (32), 69 (100), 68 (55), 67 (40), 59 (20), 57 (36), 55 (34). Characteristic ^{1}H-NMR signals of (*Z*)-isomer: 5.31 (*t*, br. *J* = 7.5, 1 H); 4.09 (*s*, br. 2 H); 1.80 (*s*, br. 3 H). Following the same protocol, **11** (*E*/*Z* = 92:8, 1.625 g, 4.41 mmol) gave **12** (*E*/*Z* = 93:7, 1.086 g, 75 %).

(E)-2,5,5-Trimethyloct-2-en-7-yn-1-ol (**13**) : A 1.55M soln. of BuLi in hexane (54 ml, 83.7 mmol) was added at -78° over 75 min. to a soln. of (*E*)-dibromide **12** (6.808 g, 20.88 mmol) in THF (70 ml). Stirring at -78° for 1 h then at 0° for 2 h, workup (Et_2O) and FC (hexane/AcOEt 4:1) afforded (*E*)-alkyne **13** (oil, 2.943 g, 85 %). IR: 3600, 3450 (broad), 3300, 3005, 2965, 2935, 2870, 2120, 1730, 1470, 1380, 1365, 1250, 1000, 640. ^{1}H-NMR (200 MHz): 5.44 (*tq*, *J* = 7.7, 1.4, 1 H); 3.99 (*s*, br. 2 H); 2.05 (*d*, *J* = 2.7, 2 H); 2.03 (*d*, br. *J* = 7.7, 2 H); 1.97 (*t*, *J* = 2.7, 1 H); 1.70 (br., 1 H); 1.65 (*s* br. 3 H); 0.95 (*s*, 6 H). ^{13}C-NMR (50 MHz): 136.9 (*s*); 122.0 (*d*); 82.6 (*s*); 69.9 (*d*); 68.9 (*t*); 38.7 (*t*); 34.3 (*s*); 31.3 (*t*); 26.5 (*q*); 13.8 (*q*). MS: 166 (5, $C_{11}H_{18}O^{+\cdot}$), 151 (25), 135 (18), 133 (24), 123 (10), 109 (100), 93 (35), 81 (77), 79 (85), 68 (98), 53 (62). Characteristic ^{1}H-NMR signals of (*Z*)-isomer: 5.33 (*t*, br., *J* = 7.5, 1 H); 4.13 (*d*, br. *J* = 5.5, 2 H); 1.82

(*s*,br. 3 H). Following the same protocol, 12 (*E*/*Z* = 93:7, 1.065 g, 3.27 mmol) gave 13 (*E*/*Z* = 93:7, 455.2 mg, 84%).

(E)-2,5,5-Trimethyloct-2-en-7-yn-1-yl Methyl Carbonate (7).- Methyl chloroformate (2.62 ml, 33.9 mmol) was added at r.t. to a soln. of (*E*)-alcohol 13 (3.708 g, 22.3 mmol) in CH_2Cl_2 (50 ml). Addition of pyridine (2.80 ml, 34.6 mmol) over 25 min. while cooling the reaction mixture with cold water, stirring at r.t. for 1 h, evaporation *in vacuo* and FC of the residue (hexane/AcOEt 9:1) provided (*E*)-carbonate 7 (oil, 4.524 g, 90 %). IR: 3300, 2960, 2110, 1750, 1440, 1370, 1280, 950, 630. ^{1}H-NMR (400 MHz): 5.56 (*tq*, *J* = 7.75, 1.2, 1 H); 4.55 (*s*, 2 H); 3.79 (*s*, 3 H); 2.07 (*d*, *J* = 7.75, 2 H); 2.07 (*d*, *J* = 2.8, 2 H); 1.99 (*t*, *J* = 2.8, 1 H); 1.69 (*s*, 3 H); 0.98 (*s*, 6 H). ^{13}C-NMR (50 MHz): 155.7 (*s*); 131.7 (*s*); 126.6 (*d*); 82.4 (*s*); 73.9 (*t*); 70.0 (*d*); 54.7 (*q*); 38.8 (*t*); 34.4 (*s*); 31.3 (*t*); 26.5 (*q*); 14.0 (*q*). MS: 224 (0.3, $C_{13}H_{20}O_3^{+\cdot}$), 209 (0.8), 194 (1.3), 148 (10), 133 (34), 109 (72), 105 (11), 93 (35), 92 (17), 91 (17), 81 (36), 80 (26), 79 (35), 68 (100), 67 (43). HR-MS: 209.11736 ([$C_{13}H_{20}O_3$ CH_3] $^{-+\cdot}$, calc. 209.11775). Characteristic ^{1}H-NMR signals of (*Z*)-isomer: 5.45 (*t*,br. *J* ~ 7, 1 H); 4.66 (*s*, br. 2 H); 1.80 (*q*, *J* = 1.2, 3 H). Following the same protocol, 13 (*E*/*Z* = 93:7, 70 mg, 0.42 mmol) gave carbonate 7 (*E*/*Z* = 93:/7, 86.6 mg, 92%).

(1RS,2SR)-Methyl 2,7,7-Trimethyl-3-oxo-bicyclo[3.3.0]oct-4-en-2-acetate (2): A flask, containing (*E*)-carbonate 7 (1.202 g, 5.35 mmol), $Pd(dba)_2$ [14] (307 mg, 0.53 mmol) and triphenylphosphine (421 mg, 1.61 mmol) was briefly evacuated and then filled with CO. After addition of degassed acetic acid (45 ml), carbon monoxide was bubbled through the mixture *via* a glass sinter plate at 40° for 21 h. Evaporation of the soln. *in vacuo* (oil pump) at -10 to 20°, filtration of a soln. of the residue in AcOEt through Celite and evaporation gave a 5.6:1-mixture (^{1}H-NMR) of diastereoisomeric carboxylic acids. Treatment with CH_2N_2 in Et_2O, evaporation and careful chromatography (hexane/AcOEt 95:5) gave the less polar, minor isomer 14 (106.0 mg, 8.4%). IR: 2958, 2932, 2869, 1736, 1697, 1632, 1456, 1437, 1354, 1280, 1206, 1177, 1090, 1010. ^{1}H-NMR (400 MHz): 5.79 (*s*, br. 1 H); 3.65 (*s*, 3 H); 3.03 (*m*, 1 H); 2.46 (*d*, br. *J* = 18.8, 1 H); 2.45 (*d*, *J* = 16.2, 1 H); 2.37 (*d*, br. *J* = 18.8, 1 H); 2.26 (*d*, *J* = 16.6, 1 H); 1.84 (*dd*, *J* = 7.8, 12.0, 1 H); 1.29 (*s*, 3 H); 1.20 (*s*, 3 H); 1.17 (*m*, 1 H); 1.13 (*s*, 3 H). ^{13}C-NMR (100 MHz): 213.6 (*s*); 188.6 (*s*); 171.8 (*s*); 121.7 (*d*); 57.0 (*d*); 51.5 (*q*); 48.5 (*s*); 42.2 (*t*); 41.7 (*t*); 40.2 (*s*); 38.1 (*t*); 30.8 (*q*); 30.4 (*q*); 22.5 (*q*). MS: 237 (37, $[C_{14}H_{20}O_3 + H]^{+\cdot}$), 236 (32, $C_{14}H_{20}O_3^{+\cdot}$), 208 (10), 205 (31), 204 (20), 193 (19), 189 (12), 177 (23), 176 (100), 163 (40), 162 (49), 161 (32), 149 (23), 148 (23), 147 (34), 135 (57), 134 (30), 133 (41), 121 (42), 120 (18), 119 (39), 117 (11), 109 (12), 108 (15), 107 (56), 105 (38), 95 (18), 93 (56), 92 (41), 91 (94), 83 (13), 81 (16), 80 (12), 79 (51), 78 (22), 77 (76), 69 (46), 67 (37), 66 (12), 65 (38), 63 (10), 59 (54), 55 (69), 53 (59). HR-MS: 236.1366 ($C_{14}H_{20}O_3^{+\cdot}$, calc. 236.1412). Further elution furnished mixed fractions (41.4 mg, 3%), followed by the more polar, major isomer 2 (oil, 766.2 mg, 61%). IR: 3020, 2960, 2875, 1732, 1695, 1631, 1460, 1440, 1305, 1285, 1235, 1195, 1180, 1155, 1010. ^{1}H-NMR (400 MHz) : 5.82 (*s* br. 1 H); 3.66 (*s*, 3 H); 3.27 (*m*, 1 H); 2.62 (*d*, *J* = 16.2, 1 H); 2.57 (*d*, *J* = 16.2, 1 H); 2.49 (*d*, *J* = 18.7, 1 H); 2.38 (*d*, *J* = 18.7, 1 H); 1.71 (*dd*, *J* = 8.5, 12.1, 1 H), spin saturation at 1.71 ppm → NOE effects at 1.30 ppm (+19%) and at 3.27 ppm (+5.5%); 1.32 (*t*, *J* = 12.3, 1 H); 1.20 (*s*, 3 H); 1.15 (*s*, 3 H); 0.98 (*s*, 3 H), spin saturation at 0.98 ppm → NOE effects at 1.30 ppm (+7.5 %) and at 2.60 ppm (+3%). ^{1}H-NMR (400 MHz, C_6D_6): 5.74 (*d*, br. *J* = 1.5, 1 H); 3.32 (*s*, 3 H); 3.20 (*m*, 1 H); 2.69 (*d*, *J* = 16.2, 1 H); 2.54 (*d*, *J* = 16.2, 1 H); 2.02 (*d* br. *J* = 18.4, 1 H); 1.90 (*d* br. *J* = 18.4, 1 H); 1.57 (*dd*, *J* = 8.5, 12.1, 1 H); 1.10 (*t J* = 12.1, 1 H); 0.97 (*s*, 3 H); 0.94 (*s*,3 H); 0.88 (*s*, 3 H). ^{13}C-NMR (100 MHz): 213.3 (*s*); 188.2 (*s*); 172.2 (*s*); 121.4 (*d*); 55.0 (*d*); 51.5 (*q*); 49.1 (*s*); 42.5 (*t*); 40.6 (*t*); 40.1 (*t*); 30.6 (*q*); 30.2 (*q*); 20.6 (*q*). ^{13}C-NMR (100 MHz, C_6D_6): 211.4 (*s*); 186.1 (*s*); 171.8 (*s*); 121.7 (*d*); 55.1 (*d*); 50.9 (*q*); 49.2 (*s*); 42.1 (*t*); 40.8 (*t*); 40.4 (*t*); 40.1 (s); 30.3 (*q*); 29.9 (*q*); 20.3 (*q*). MS: 236 (39, $C_{14}H_{20}O_3^{+\cdot}$), 205 (14), 193 (17), 177 (22), 176 (100), 163 (38), 162 (66), 161 (36), 149 (20), 148 (25), 147 (44), 135 (48), 134 (30), 133 (42), 121 (36), 120 (21), 119 (40), 117 (11), 108 (10), 107 (45), 106 (10), 105 (35), 95 (11), 93 (53), 92 (46), 91 (90), 81 (11), 79 (42), 78 (25), 77 (79), 69 (27), 67 (26), 66 (11), 65 (33), 59 (49), 56 (12), 55 (52). HR-MS: 236.1412 ($C_{14}H_{20}O_3^{+\cdot}$, calc. 236.1412). Following the same protocol, 7 (*E*/*Z* = 93:7, 76.4 mg, 0.34 mmol) gave a 1.6:1-epimer mixture 2/14 (17.4 mg, 22%) and pure epimer 2 (45 mg, 56%).

(1RS,2SR,5RS)-Methyl 2,7,7-Trimethyl-3-oxo-bicyclo[3.3.0]octan-2-acetate (**15**): A soln. of enone **2** (367 mg, 1.55 mmol) in ethanol (6 ml) was shaken in the presence of Pd/C (5%, 50 mg) under H_2 (1 atm.) at r.t. for 13 h. Filtration through Celite, evaporation of the filtrate and chromatography (pentane/Et_2O 85:15) yielded ketoester **15** (oil, 368.4 mg, 99.5 %). IR: 3030, 2960, 2860, 1735, 1470, 1430, 1350, 1230, 1200, 1170, 1030. ^{1}H-NMR (400 MHz) : 3.65 (*s*, 3 H); 2.83-2.70 (3 H); 2.49 (*d*, *J* = 14.8, 1 H); 2.40 (*d*, *J* = 14.8, 1 H); 2.02 (*m*, 1 H); 1.91 (*m*, 1 H); 1.51 (*m*, 1 H); 1.27-1.17 (2 H); 1.08 (*s*, 3 H); 1.04 (*s*, 3 H); 0.99 (*s*, 3 H). ^{13}C-NMR (100 MHz): 221.7 (*s*); 171.6 (*s*); 51.5 (*q*); 49.9 (*s*); 49.3 (*d*); 49.2 (*t*); 43.8 (*t*); 43.6 (*t*); 42.9 (*t*); 40.5 (*s*); 35.0 (*d*); 29.9 (*q*); 28.4 (*q*); 19.4 (*q*). MS: 238 (0.6, $C_{14}H_{22}O_3^{+\cdot}$), 166 (12), 165 (100), 121 (16), 109 (30), 107 (13), 95 (27), 93 (11), 69 (22), 67 (30), 55 (74). HR-MS: 238.1555 ($C_{14}H_{22}O_3^{+\cdot}$, calc. 238.1569).

(1RS,2SR,3SR,5RS)-Methyl 2,7,7-Trimethyl-3-hydroxy-bicyclo[3.3.0]octan-2-acetate (**16**): Solid $NaBH_4$ (132 mg, 3.49 mmol) was added at -18° to a soln. of ketoester **15** (755.6 mg, 3.17 mmol) in ethanol (20 ml). Stirring of the mixture at -18° for 0.5 h, successive addition of Et_2O, 1M aq. soln. of HCl (until gas evolution ceased, ~8 ml) and aq. buffer soln. (40 ml), workup (Et_2O) and chromatography (hexane/AcOEt 85:15) gave alcohol **16** (oil, 738.5 mg, 97%). IR: 3463 (broad), 3005, 2954, 2867, 1716, 1466, 1439, 1351, 1235, 1118, 1079, 1014. ^{1}H-NMR (400 MHz) : 3.97 (*ddd*, *J* = 3.1, 6.2, 10.3, 1 H); 3.68 (*s*, 3 H); 3.26 (*d*, *J* = 3.1, 1 H); 2.46 (*m*, 1 H); 2.40 (*d*, *J* = 14.5, 1 H); 2.31 (*d*, *J* = 14.5, 1 H); 2.28 (*dt*, *J* = 11.2, 9.1, 1 H); 2.15 (*ddd*, *J* = 6.2, 8.3, 12.5, 1 H); 1.66 (*ddd*, *J* = 1.7, 7.9, 12.2, 1 H); 1.44-1.31 (3 H); 1.07 (*dd*, *J* = 10.8, 12, 1 H); 1.06 (*s*, 3 H); 0.90 (*s*, 6 H). ^{13}C-NMR (100 MHz): 174.4 (*s*); 82.0 (*d*); 51.7 (*q*); 51.3 (*d*); 49.3 (*t*); 46.8 (*t*); 44.0 (*s*); 42.8 (*s*); 40.6 (*t*); 38.3 (*t*); 37.6 (*d*); 29.0 (*q*); 27.3 (*q*); 15.4 (*q*). MS: 241 (0.3, $[C_{14}H_{24}O_3 + H]^{+\cdot}$), 207 (10), 181 (13), 167 (14), 166 (100), 165 (50), 149 (23), 121 (14), 109 (74), 107 (13), 95 (16). HR-MS: 222.16600 ($[C_{14}H_{24}O_3 - H_2O]^{+\cdot}$, calc. 222.16197).

(1RS,2RS,5RS)-Methyl 2,7,7-Trimethyl-bicyclo[3.3.0]oct-3-en-2-acetate (**17**).- Freshly distilled $POCl_3$ (1.4 ml, 15.1 mmol) was added over 5 min. at -17° to a soln. of alcohol **16** (729.3 mg, 3.03 mmol) in pyridine (7 ml). The reaction mixture was stirred at -17° for 5 min., then at r.t. for 0.5 h, then at 35° for 72 h, diluted with pentane (10 ml) and Et_2O (10 ml) and H_2O (20 ml) was added slowly at 0°. Acidification with conc. aq. HCl, extraction with pentane/Et_2O (1:1), washing of the combined org. phases (sat aq. $NaHCO_3$, sat. aq. NaCl), drying ($MgSO_4$), evaporation and chromatography (pentane/Et_2O 98:2) afforded alkene **17** (oil, 550.7 mg, 82 %). IR: 3032, 2953, 2935, 2864, 1727, 1461, 1438, 1383, 1365, 1315, 1118, 1012. ^{1}H-NMR (400 MHz) : 5.53 (*dd*, *J* = 1.9, 5.6, 1 H); 5.37 (*dd*, *J* = 2.2, 5.6, 1 H); 3.65 (*s*, 3 H); 3.23 (*m*, 1 H); 2.68 (*dt*, *J* = 11, 7.8, 1 H); 2.35 (*d*, *J* = 13.8, 1 H); 2.29 (*d*, *J* = 13.8, 1 H); 1.68 (*ddd*, *J* = 1.9, 9.0, 12.5, 1 H); 1.40 - 1.19 (2 H); 1.11 (*dd*, *J* = 7.2, 12.5, 1 H); 1.10 (*s*, 3 H); 1.03 (*s*, 3 H); 0.93 (*s*, 3 H). ^{13}C-NMR (50 MHz): 172.6 (*s*); 136.2 (*d*); 134.5 (*d*); 51.2 (*d*) 51.2 (*q*); 49.1 (*d*); 48.3 (*s*); 47.6 (*t*); 45.9 (*t*); 42.4 (*t*); 40.8 (*s*); 29.3 (*q*); 27.5 (*q*); 21.1 (*q*). MS: 222 (5, $C_{14}H_{22}O_2^{+\cdot}$), 208 (2), 207 (7), 150 (14), 149 (100), 148 (27), 133 (10), 121 (6), 107 (27), 93 (31), 92 (26), 91 (17), 77 (10). HR-MS: 222.16151 ($C_{14}H_{22}O_2^{+\cdot}$, calc. 222.16197).

3-[(1RS,2RS,5RS)-2,7,7-Trimethyl-bicyclo[3.3.0]oct-3-en-2-yl]-tetrahydro-2-furanone (**18**).- A 1.6M soln. of BuLi in hexane (291 µl, 0.466 mmol) was added to diisopropylamine (69 µl, 0.486 mmol) in THF (0.1 ml) at 0° and the mixture was stirred for 15 min. Then a soln. of ester **17** (90 mg, 0.405 mmol) in THF (0.6 ml) was added to the such prepared soln. of LDA at -78° over 2 h. The reaction mixture was stirred at -78° for 1 h, then warmed to -12° and a solution of cyclic ethylene sulfate [17] (158 mg, 1.27 mmol) in THF (0.45 ml) was added. Stirring of the mixture at 0° for 66 h, addition of H_2O (5 drops), evaporation, stirring of the residue with dioxane (3 ml) and conc. aq. H_2SO_4 (3 drops) at r.t. for 20 h, workup (AcOEt) and chromatography furnished recovered ester **17** (15.4 mg, 17%) and lactones **18** (oil, 38.0 mg, 40%) as a 1.3:1 mixture (GC) of epimers including a sample of the major, less polar epimer. Major epimer: IR: 3042, 2954, 2938, 2863, 1764, 1464, 1372, 1172, 1130. ^{1}H-NMR (400 MHz) : 5.65 (*dd*, *J* = 2.0, 5.5, 1 H); 5.28 (*dd*, *J* =

2.3, 5.5, 1 H); 4.26 (*ddd*, *J* = 3.0, 8.8, 9.0, 1 H); 4.09 (*ddd*, *J* = 7.0, 9.0, 9.3, 1 H); 3.21 (*m*, 1 H); 2.89 (*ddd*, *J* = 7.3, 8.0, 11.3, 1 H); 2.52 (*dd*, *J* = 8.8, 10.5, 1 H); 2.24 (*dddd*, *J* = 3.0, 7.0, 8.8, 12.6, 1 H); 2.10 (*dddd*, *J* = 8.8, 9.3, 10.5, 12.6, 1 H); 1.69 (*ddd*, *J* = 2.0, 9.0, 12.2, 1 H); 1.42 (*ddd*, *J* = 2.0, 7.3, 12.0, 1 H); 1.30 (*dd*, *J* = 11.3, 12.0, 1 H); 1.17 (*s*, 3 H); 1.10 (*dd*, *J* = 7.2, 12.2, 1 H); 1.04 (*s*, 3 H); 0.95 (*s*, 3 H). ^{13}C-NMR (100 MHz): 177.4 (*s*); 136.4 (*d*); 133.9 (*d*); 65.8 (*t*); 50.6 (*s*); 50.2 (*d*); 49.8 (*d*); 49.1 (*d*); 46.0 (*t*); 42.5 (*t*); 40.8 (*s*); 29.3 (*q*); 27.3 (*q*); 25.4 (*t*); 18.1 (*q*). Minor epimer: ^{13}C-NMR (100 MHz): 177.8 (*s*); 135.6 (*d*); 134.6 (*d*); 66.0 (*t*); 51.0 (*s*); 50.3 (*d*); 50.0 (*d*); 49.5 (*d*); 46.3 (*t*); 42.6 (*t*); 41.0 (*s*); 29.2 (*q*); 27.2 (*q*); 26.0 (*t*); 19.6 (*q*). Mixture of epimers: MS: 234 (0.8, $C_{15}H_{22}O_2^{+\cdot}$), 150 (13), 149 (100), 148 (22), 133 (13), 121 (18), 107 (61), 105 (15), 93 (61), 92 (51), 91 (42), 79 (18), 77 (31), 69 (22), 65 (13), 55 (29), 53 (17). HR-MS: 234.16235 ($C_{15}H_{22}O_2^{+\cdot}$, calc. 234.16197).

Methyl 4-Selenophenyl-2[(1RS,2RS,5RS)-2,7,7-trimethyl-bicyclo[3.3.0]oct-3-en-2-yl]-butanoate (**19**).- Solid $NaBH_4$ (19.7 mg, 0.52 mmol) was added to an oxygen-free soln. of PhSeSePh (74 mg, 0.237 mmol) in dry DMF (2.4 ml) and the mixture was heated slowly to 80° and kept at 80° for 5-10 min. The thus prepared 0.2M soln. of $PhSeNa.BH_3$ [18] (1.3 ml, 0.26 mmol) was added to lactones **18** (1.3:1-epimer mixture, 55.3 mg, 0.236 mmol) and the mixture was stirred at 120° for 2 h. Dilution with Et_2O (25 ml), washing with 1M aq. soln. of HCl, extraction of the aq. phase with Et_2O, washing of the combined org. phases with sat. aq. NaCl soln., drying ($MgSO_4$), evaporation, treatment of the residue with CH_2N_2 in Et_2O and chromatography (hexane/AcOEt 95:5 → 7:3) gave recovered lactones **18** (6.8 mg, 12%) and selenides **19** (oil, 64.8 mg, 68%) as a 1.17:1-epimer mixture (GC). IR: 2953, 2935, 2863, 1724, 1579, 1478, 1462, 1437, 1383, 1365, 1258, 1235, 1202, 1167, 1147, 1108, 1074, 1023. ^{1}H-NMR (400 MHz): 7.49-7.45 (2 H_a + 2 H_b); 7.29-1.20 (3 H_a + 3 H_b); 5.55 (*dt*, *J* = 1.8, 6.0, 1 H_a + 1 H_b); 5.31 (*dd*, *J* = 1.8, 5.5, 1 H_a); 5.09 (*dd*, *J* = 2.2, 5.5, 1 H_b); 3.66 (*s*, 3 H_b); 3.65 (*s*, 3 H_a); 3.18-3.06 (1 H_a+ 1 H_b); 2.95-2.86 (1 H_a+ 1 H_b); 2.77-2.57 (2 H_a+ 2 H_b); 2.52 (*dd*, *J* = 2.8, 11.6, 1 H_a); 2.40 (*dd*, *J* = 2.6, 11.4, 1 H_b); 2.16-2.04 (1 H_a+ 1 H_b); 1.81-1.69 (1 H_a+ 1 H_b); 1.67-1.57 (1 H_a+ 1 H_b); 1.30-1.19 (2 H_a+ 2 H_b); 1.16-0.98 (1 H_a+ 1 H_b); 1.01 (*s*, 3 H_a+ 6 H_b); 0.98 (*s*, 3 H_a); 0.91 (*s*, 3 H_b); 0.89 (*s*, 3 H_a). ^{13}C-NMR (100 MHz): 175.15 (*s*); 175.1 (*s*); 135.4 (*d*); 135.1 (*d*); 135.0 (*d*); 134.9 (*d*); 132.7 (*d*); 132.6 (*d*); 130.1 (*s*); 130.0 (*s*); 129.0 (*2 C*, *d*); 126.9 (*d*); 57.1 (*d*, a); 55.8 (*d*, b); 52.1 (*s*); 52.0 (*s*); 51.2 (*q*, b); 51.0 (*q*, a); 50.3 (*d*, a); 50.1 (*d*, b); 49.3 (*d*, a); 48.1 (*d*, b); 46.2 (*t*, a); 46.15 (*t*, b); 42.6 (*t*, a); 42.59 (*t*, b); 41.0 (2 C, *s*); 29.22 (*q*, b); 29.19 (*q*, a); 28.5 (*t*, b); 28.4 (*t*, a); 27.3 (*q*, b); 27.1 (*q*, a); 26.3 (*t*, b); 26.2 (*t*, a); 20.8 (*q*, a); 19.7 (*q*, b). MS: 406 (2, $C_{22}H_{30}O_2Se^{+\cdot}$ for Se^{80}), 249 (9), 150 (13), 149 (100), 121 (16), 107 (56), 105 (11), 93 (47), 91 (37), 79 (11), 77 (27), 69 (23), 55 (20). HR-MS: 406.14166 ($C_{22}H_{30}O_2Se^{+\cdot}$, calc. 406.14107).

(cis, anti, cis)-Methyl 1,4,4-Trimethyl-tricyclo[6.3.0.0^{2,6}]-undecane-11-carboxylate (**20**).- A soln. of azaisobutyronitrile (3.7 mg, 0.022 mmol) in toluene (3.3 ml) and a soln. of Bu_3SnH (62 µl, 0.234 mmol) in toluene (3.3 ml) were added simultaneously over 18 h using a syringe pump to a boiling soln. of selenides **19** (63.4 mg, 0.156 mmol, 1.17:1-epimer mixture) in toluene (16 ml). Heating the mixture under reflux for further 2 h, evaporation and chromatography (hexane → hexane/AcOEt 95:5) provided a 1.13:1-mixture (GC) of tricyclic esters **20** (36.0 mg, 92%). Traces of tin derived impurities were removed at a later stage *i.e.* during chromatography of **21**. IR (film): 2949, 2865, 1737, 1462, 1432, 1248, 1198, 1163, 1024. ^{1}H-NMR (400 MHz) : 3.68 (*s*, 3 H_a); 3.66 (*s*, 3 H_b); 2.83 (*dt*, *J* = 7.8, 11.5, 1 H_a); 2.72-2.59 (1 H_a + 1 H_b); 2.56 (*dd*, *J* = 8.5, 9.8, 1 H_a); 2.38 (*dt*, *J* = 7.2, 10.4, 1 H_b); 2.20 (*m*, 1 H_b); 2.17-2.02 (2 H_b + 2 H_a); 1.93-1.83 (2 H_a); 1.84-1.72 (2 H_b); 1.70 (*ddd*, *J* = 2, 8.5, 12.7, 1 H_a); 1.59 (*ddd*, *J* = 1.7, 7.9, 12.3, 1 H_b); 1.52 - 1.47 (2 H_a); 1.50-1.26 (4 H_b + 2 H_a); 1.20 (*ddd*, *J* = 1.8, 8.0, 9.7, 1 H_b); 1.16 (*t*, *J* = 11.9, 1 H_a); 1.16 (*s*, 3 H_b); 1.05 (*m*, 1 H_b); 1.04 (*m*, 1 H_a); 1.04 (*s*, 3 H_a); 1.03 (*s*, 3 H_b); 0.92 (*s*, 3 H_a); 0.90 (*s*, 3 H_b); 0.87 (*s*, 3 H_a). ^{13}C-NMR (major epimer **20**, 100 MHz): 175.4 (*s*); 56.4 (*s*); 53.5 (*d*); 52.6 (*d*); 51.2 (*q*); 50.6 (*d*); 48.7 (*t*); 44.0 (*t*); 41.3 (*d*); 40.5 (*s*); 40.0 (*t*); 29.8 (*q*); 28.4 (*t*); 27.3 (*q*); 26.0 (*t*); 18.2 (*q*). ^{13}C-NMR (minor epimer **20**, 100 MHz): 175.3 (*s*); 56.3 (*d*); 55.9 (*d*); 54.7 (*s*); 51.1 (*q*); 48.8 (*d*); 48.6 (*t*); 44.3 (*d*); 42.9 (*s*); 42.2 (*t*); 38.4 (*t*); 30.4 (*t*); 29.9 (*q*); 28.2 (*q*); 27.4 (*t*); 25.0 (*q*). MS: 250 (35, $C_{16}H_{26}O_2^{+\cdot}$), 218 (14), 176 (15), 164 (21), 150 (13), 149 (100), 121 (19), 119 (10), 109 (10), 108 (18), 107 (56), 95 (35), 93 (32), 91 (20), 87 (30),

81 (30), 79 (21), 77 (14), 69 (13), 67 (14), 57 (12), 55 (19). HR-MS: 250.19176 ($C_{16}H_{26}O_2^{+\cdot}$, calc. 250.19327).

(cis, anti, cis)-11-Hydroxymethyl-1,4,4-trimethyl-tricyclo[6.3.0.0^{2,6}]-undecane (**21**): Solid $LiAlH_4$ (33.5 mg, 0.88 mmol) was added to a soln. of esters **20** (7:2-epimer mixture, 88.4 mg, 0.353 mmol) in Et_2O (3.5 ml). Stirring of the mixture at r.t. for 2 h, addition of ice water, Et_2O and 1M aq. H_2SO_4, workup (Et_2O) and chromatography (hexane/AcOEt 85:15) afforded alcohols **21** (4:1-epimer mixture, 70.0 mg, 89%). IR: 3326, 2958, 2868 1461, 1377, 1364, 1023, 1002, 668. ^{1}H-NMR: 3.75 (*dd*, *J* = 5.2, 10.3, 1 H_a); 3.73 (*dd*, *J* = 5.2, 10.5, 1 H_b); 3.53 (*dd*, *J* = 8.9, 10.3, 1 H_a + 1 H_b); 2.72-2.58 (1 H_a + 1 H_b); 2.52 (*ddd*, *J* = 8.0, 8.5, 11.4, 1 H_a); 2.37 (*dt*, *J* = 8.2, 10.3, 1 H_b); 2.33-2.12 (2 H_b); 2.09-1.93 (2 H_a); 1.90-1.75 (2 H_a + 2 H_b); 1.67 (*ddd*, *J* = 2.2, 8.7, 12.7, 1 H_a); 1.62 (*ddt*, *J* = 1.8, 8.0, 13.0, 2 H_b); 1.57-1.46 (2 H_a); 1.48-1.13 (5 H_a + 6 H_b); 1.04 (*s*, 3 H_b); 1.03 (*dd*, *J* = 7.8, 12.2, 1 H_a); 1.03 (s, 3 H_a); 0.93 (*s*, 3 H_b); 0.89 (*s*, 3 H_a); 0.78 (*s*, 3 H_a). ^{13}C-NMR (major epimer, 100 MHz): 65.2 (*t*); 53.7 (*s*); 52.9 (*d*); 50.8 (d); 50.5 (*d*); 48.7 (*t*); 43.9 (*t*); 41.7 (*d*); 40.6 (*s*); 40.3 (*t*); 29.7 (*q*); 28.5 (*t*); 27.9 (*t*); 27.2 (*q*); 16.9 (*q*). ^{13}C-NMR (minor epimer, 100 MHz): 65.5 (*t*); 56.4 (*d*); 54.1 (*d*); 52.5 (*s*); 46.8 (*d*); 44.6 (*d*); 43.3 (*t*); 42.5 (*s*); 38.1 (*t*); 29.8 (*t*); 28.7 (*t*); 28.1 (*q*); 24.7 (*q*); 14.1 (*q*). MS: 223 (5, $[C_{15}H_{26}O + H]^{+\cdot}$), 222 (24, $C_{15}H_{26}O^{+\cdot}$), 204 (20), 191 (24), 189 (18), 165 (19), 164 (19), 150 (17), 149 (84), 148 (12), 147 (20), 135 (21), 123 (29), 121 (30), 119 (16), 109 (50), 108 (56), 107 (81), 106 (14), 105 (25), 96 (14), 95 (79), 94 (51), 93 (97), 91 (53), 81 (100), 80 (24), 79 (69), 77 (42), 67 (50), 55 (60). HR-MS: 222.1984 ($C_{15}H_{26}O^{+\cdot}$, calc. 222.1984).

Hirsutene (**1**).- Tributylphosphine (112.5 µl, 456 µmol) was added dropwise at 0° to a mixture of alcohols **21** (4:1-epimer mixture, 50.6 mg, 228 µmol) and o-nitrophenyl-selenocyanate (101.0 mg, 440 µmol) in THF (1.5 ml). Stirring of the mixture at r.t. for 16 h, evaporation and chromatography of the residue (hexane/Et_2O 95:5) gave the *(cis, anti, cis)-11-(o-nitrophenylseleno)methyl-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]-undecanes* **22** (4:1-epimer mixture, 80.5 mg, 87%). IR (film): 2948, 2931, 2866, 1591, 1566, 1514, 1463, 1378, 1364, 1332, 1304, 1252, 1096, 1038, 852, 782, 729. HR-MS: 407.1358 ($C_{21}H_{29}NO_2Se^{+\cdot}$, calc. 407.1363). A 30% aq. soln. of H_2O_2 (250 µl, 2.44 mmol) was added over 5 min. at 0° to a soln. of thus prepared selenides **22** (80.3 mg, 0.197 mmol) in THF (3.5 ml). Stirring of the reaction mixture at 0° for 15 min., at r.t. for 15 min. and at 50° for 1 h, workup (pentane) and chromatography (pentane) provided hirsutene (**1**) (oil, 36.3 mg, 90%). GC (100°): 6.67 (100). IR (film): 3066, 2948, 2931, 2864, 1650, 1463, 1453, 1435, 1380, 1364, 876. ^{1}H-NMR (400 MHz) : 4.82 (*s* br. 1 H); 4.77 (s, br. 1 H); 2.61 (*dt*, *J* = 11.1, 8.1, 1 H); 2.50 (*m*, 1 H); 2.48 - 2.43 (2 H); 2.15 (*m*, 1 H); 1.73 (*ddt*, *J* = 6.25, 12.9, 8.8, 1 H); 1.63 (*ddd*, *J* = 2.2, 8.4, 12.5, 1 H); 1.49-1.39 (4 H); 1.21 (*t*, *J* = 11.8, 1 H); 1.05 (*s*, 3 H); 1.02 (*dd*, *J* = 7.7, 12.5, 1 H); 0.95 (*s*, 3 H); 0.92 (*s*, 3 H). ^{13}C-NMR (100 MHz): 162.9 (*s*); 103.5 (*t*); 56.0 (*s*); 53.4 (*d*); 49.9 (*d*); 49.0 (*t*); 44.3 (*t*); 41.9 (*d*); 40.9 (*s*); 38.6 (*t*); 30.9 (*t*); 29.7 (*q*); 27.2 (*q*); 26.8 (*t*); 23.2 (*q*). MS: 204 (3.4, $C_{15}H_{24}^{+\cdot}$), 95 (17), 94 (100), 79 (32). HR-MS: 204.1878 ($C_{15}H_{24}^{+\cdot}$, calc. 204.1878). The IR, ^{1}H-NMR and ^{13}C-NMR spectra agree with the published data [9]

REFERENCES AND NOTES

1. Reviews: W. Oppolzer, *Angew. Chem.* **1989**, *101*, 39; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 38; W. Oppolzer, *Pure & Appl. Chem.* **1990**, *62*, 1941; W. Oppolzer in 'Comprehensive Organic Synthesis', Ed. B. M. Trost, Pergamon, 1991, Vol 5, p. 29.
2. Cf. W. Oppolzer, R. J. DeVita, *J. Org. Chem.* **1991**, *56*, 6256; R. Grigg, V. Sridharan, S. Sukirthalingam, *Tetrahedron Lett.* **1991**, *32*, 3855. W. Oppolzer, J. Ruiz-Montes, *Helv. Chim. Acta* **1993**, *76*, 1266.
3. W. Oppolzer, M. Bedoya-Zurita, C. Y. Switzer, *Tetrahedron Lett.* **1988**, *29*, 6433; W. Oppolzer, T. H. Keller, M. Bedoya-Zurita, C. Stone, *ibid.* **1989**, *30*, 5883.
4. W. Oppolzer, J.-Z. Xu, C. Stone, *Helv. Chim. Acta* **1991**, *74*, 465.
5. W. Oppolzer, H. Bienaymé, A. Genevois-Borella, *J. Am. Chem. Soc.* **1991**, *113*, 9660.

6. W. Oppolzer, A. Ando, *Chimia* **1992**, *46*, 122.
7. R. Keese, R. Guidetti-Grept, B. Herzog, *Tetrahedron Lett.* **1992**, *33*, 1207.
8. a) S. Nozoe, J. Furukawa, U. Sankawa, S. Shibata, *Tetrahedron Lett.* **1976**, 195; b) D. H. Hua, S. Venkatamaran, R. A. Ostrander, G. Sinai-Zingde, P. J. McCann, M. J. Coulter, M. R. Xu, *J. Org. Chem.* **1988**, *53*, 507.
9. a) K. Tatsuta, K. Akimoto, M. Kinoshita, *J. Am. Chem. Soc.* **1979**, *101*, 6116; b) A.E. Greene, *Tetrahedron Lett.* **1980**, *21*, 3059; c) T. Hudlicky, T. M. Kutchan, S. R. Wilson, D. T. Mao; *J. Am. Chem. Soc.* **1980**, *102*, 6351; d) R. D. Little, R. G. Higby, K. D. Moeller, *J. Org. Chem.* **1983**, *48*, 3139; e) Ph. Magnus, D. A. Quagliato, *Organometallics* **1982**, *1*, 1243; f) P. A. Wender, J. J. Howbert, *Tetrahedron Lett.* **1982**, *23*, 3983; g) S. Misumi, H. Matsushima, H. Shirahama, T. Matsumoto, *Chem. Lett.* **1982**, 855; h) B. A. Dawson, A. K. Gosh, J. L. Jurlina, A. J. Ragauskas, J. B. Stothers, *Can. J. Chem.* **1984**, *62*, 2521; i) R. L. Funk, G. L. Bolton, J. Umstead-Daggett, M. M. Hansen, L. H. M. Horcher, *Tetrahedron* **1985**, *41*, 3479; j) S. V. Ley, P. J. Murray; *J. Chem. Soc. Chem. Comm.* **1982**, 1252; k) B. W. Disanayaka, A. C. Weedon *J. Org. Chem.* **1987**, *52*, 2905; l) A. T. Hewson, D. T. MacPherson, *J. Chem. Soc. Perkin. Trans. I.* **1985**, 2625; m) D. P. Curran, D. M. Rakiewicz, *Tetrahedron*, **1985**, *41*, 3943; n) M. Iyoda, T. Kushida, S. Kitami, M. Oda, *J. Chem. Soc. Chem. Comm.* **1986**, 1049; o) G. Mehta, A. N. Murthy, D. S. Reddy, A. V. Reddy, *J. Am. Chem. Soc.* **1986**, *108*, 3443; p) J. Cossy, D. Belotti, J. P. Pete, *Tetrahedron* **1990**, *46*, 1859; q) M. Franck-Neumann, M. Miesch, E. Lacroix, B. Metz, J. -M. Kern, *Tetrahedron* **1992**, *48*, 1911; r) D. D. Sternbach, C. L. Ensinger, *J. Org. Chem.* **1990**, *55*, 2725; s) J. Castro, H. Sörensen, A. Riera, C. Morin, A. Moyano, M. A. Pericàs, A. E. Greene, *J. Am. Chem. Soc.* **1990**, *112*, 9388; t) T. K. Sarkar, S. K. Ghosh, P. S. V. Subba Rao, V .R. Mamdapur, *Tetrahedron Lett.* **1990**, *31*, 3465; u) L. A. Paquette, K. J. Moriarty, C.-C. Shen, *Isr. J. Chem.* **1991**, *31*, 195; v) K. Ramig, M. A. Kuzemko, K. McNamara, Th. Cohen, *J. Org. Chem.* **1992**, *57*, 1968; w) K. Weinges, H. Reichert, U. Huber-Patz, H. Irngartinger, *Liebigs Ann. Chem.* **1993**, 403.
10. The numbering of 1 is used also for all intermediates; systematic names are given in the experimental part.
11. R. D. Little, G. W. Muller, *J. Am. Chem. Soc.* **1981**, *103*, 2744.
12. W. Oppolzer, T. N. Birkinshaw, G. Bernardinelli, *Tetrahedron Lett.* **1990**, *31*, 6995.
13. E. J. Corey, P. L. Fuchs, *Tetrahedron Lett.* **1972**, 3769.
14. Preparation of $Pd(dba)_2$: M. F. Rettig, P. M. Maitlis, *Inorg. Synth.* **1992**, *28*, 110.
15. Arguments supporting a suprafacial 4-center transition state in acylpalladium/alkene insertions: D. L. Thorn, R. Hoffmann, *J. Am. Chem. Soc.* **1978**, *100*, 2079; E. G. Samsel, J. R. Norton, *Ibid.*, **1984**, *106*, 5505; J. S. Brumbaugh, R. R. Whittle, M. Parvez, A. Sen, *Organometallics* **1990**, *9*, 1735. C.f.: P. DeShong, D. R. Sidler, P. J. Rybczynski, G. A. Slough, A. L. Rheingold, *J. Am. Chem. Soc.* **1988**, *110*, 2575.
16. Under similar cyclization conditions, the "C(1)-desmethyl" analog [10] of 7 gave exclusively a bicyclo[3.3.0]octenone with C(1)-CH_2CO_2Me/C(2)-H *cis*-relation, consistent with a transition state resembling A≠ [4]. For a discussion of "eclipsed" *versus* "twisted" C-Pd/C=C orientations in Heck reactions see: M. M. Abelman, L. E. Overman, V. D. Tran, *J. Am. Chem. Soc.* **1990**, *112*, 6959.
17. Y. Gao, K. B. Sharpless, *J. Am. Chem. Soc.* **1988**, *110*, 7538; preparation of cyclic ethylene sulfate: V. Massoneau, X. Radisson, M. Mulhauser, N. Michel, A. Buforn, B. Botannet, B. Mandard, G. Perrier, S. Lutz, M. Lavigne; *Nouveau J. Chem.* **1992**, *16*, 107; review: B.B. Lohray, *Synthesis* **1992**, 1035.
18. R. M. Scarborough Jr., B. H. Toder, A. B. Smith III, *J. Am. Chem. Soc.* **1980**, *102*, 3904.
19. D. L. J. Clive, T. L. B. Boivin, *J. Org. Chem.* **1989**, *54*, 1997; W. R. Leonard, T. Livinghouse, *Tetrahedron Lett.* **1985**, *26*, 6431.
20. P. A. Grieco, S. Gilman, M. Nishizawa, *J. Org. Chem.* **1976**, *41*, 1485; K. B. Sharpless, M. W. Young, *J. Org. Chem.* **1975**, *40*, 947.

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