Enantioselective Synthesis of Cuparane Sesquiterpenes. Synthesis of (−)-Cuparene and (−)-δ-Cuparenol

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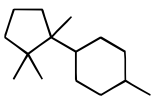
(−)-Cuparene and (−)-δ-cuparenol, two cuparane-type sesquiterpenoids, were synthesized from β-cyclogeraniol in 47% and 27% overall yield, respectively, using a Katsuki−Sharpless asymmetric epoxidation, a pinacollic rearrangement, and a Robinson annulation as key synthetic steps.

Introduction

A family of sesquiterpenes sharing the hypothetical cuparane skeleton (**1**) has been isolated from several natural sources.[1] Most of them show important biological activity such as antifungal and antibiotic properties.



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Their syntheses have attracted the attention of numerous organic synthetic chemists, due to the difficulty associated with the construction of the vicinal quaternary centers on the five-membered ring. Although several basic approaches have been reported for the construction of the cuparane skeleton,[2] few of them can be adapted to the enantioselective synthesis of these compounds. We have recently described a procedure for the enantioselective construction of the 1,2,2-trimethylcyclopentane nucleus common to all the cuparane-type sesquiterpenoids.[3] As a continuation of this work, we now wish to report the enantioselective synthesis of two representative members of this type of sesquiterpenes, (−)-cuparene (**2**) and (−)-δ-cuparenol (**3**).

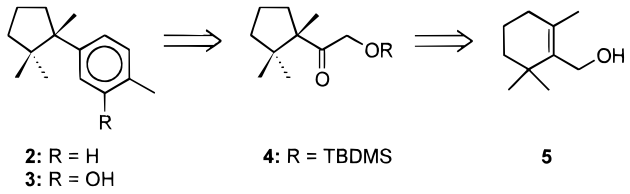
Our approach to these cuparane sesquiterpenoids employs enantiomerically pure (−)-(*S*)-**4** as chiral synthon (Scheme 1), which is prepared from readily available β-cyclogeraniol[4] (**5**) using a Katsuki−Sharpless asymmetric epoxidation and a pinacollic rearrangement as key synthetic steps.

Results and Discussion

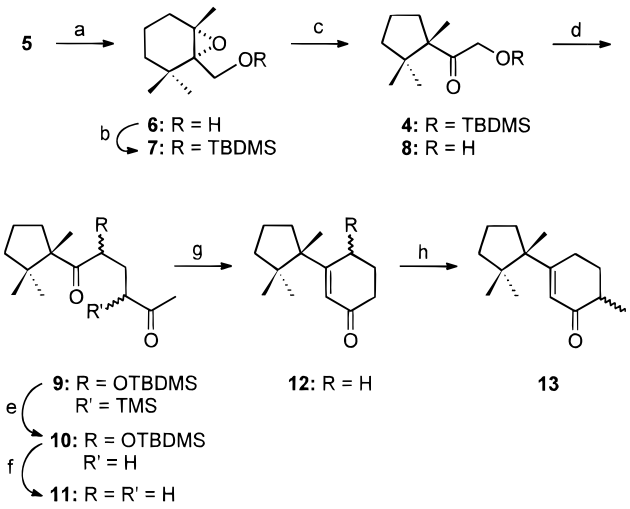
As described in our previous work,[3] epoxidation of β-cyclogeraniol (**5**) with the Sharpless L-(+)-DET reagent gave the (1*S*,2*S*)-epoxy alcohol **6** in 89% yield with high enantiomeric purity (98% ee)[5] (Scheme 2). Conversion of the hydroxyl group of **6** in the corresponding *tert*-butyldimethylsilyl ether **7**, followed by tin(IV) chloride-promoted pinacollic rearrangement, afforded the α-(silyloxy) ketone **4** in 90−95% yield.[6]

For the construction of the cyclohexane ring we adopt the classical Robinson annulation methodology. Michael addition of the lithium enolate obtained by treatment of **4** with LDA to α-(trimethylsilyl) vinyl ketone[7] gave a mixture of the expected adduct **9** and desilylated com-

Scheme 1



Scheme 2[a]



[a] Reaction conditions, reagents, and yields: (a) Ti(O-*i*-Pr)$_4$, (+)-DET, *t*-BuOOH, CH_2Cl_2, 4 Å mol sieves, −20 °C, 89%; (b) TBDMSOTf, Et_3N, CH_2Cl_2, −78 °C, 93%; (c) $SnCl_4$, CH_2Cl_2 from −60 to −20 °C, 90%; (d) LDA, −78 °C then 3-TMS-3-butene-2-one, −78 °C to rt, 83%; (e) KOH, H_2O−MeOH, 83%; (f) SmI_2, MeOH−THF, −78 °C to rt, 99%; (g) KOH, H_2O−MeOH, 150 °C, 93%; (h) LDA, THF, −50 °C then HMPA, MeI, 96%.

[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1996.

(1) Connolly, J. D.; Hill, R. A. In *Dictionary of Terpenoids*, 1st ed.; Chapman and Hall: London, 1991; Vol. 1; pp 295−298. Also see: Fraga, B. M. *Nat. Prod. Rep.* **1992**, *9*, 217; **1993**, *10*, 397; **1994**, *11*, 536; **1995**, *12*, 306.

(2) For previous synthesis of cuparane-type sesquiterpenoids, see: (a) Schuda, P. F.; Potlock, S. J.; Ziffer, H. *Tetrahedron* **1987**, *43*, 463 and references cited therein. (b) Nakatani, H.; So, T. S.; Ishibashi, H.; Ikeda, M. *Chem. Pharm. Bull.* **1990**, *38*, 1233 and references cited therein. (c) Schwarz, J. B.; Meyers, A. I. *J. Org. Chem.* **1995**, *60*, 6511.

(3) Abad, A.; Agulló, C.; Arnó, M.; Cuñat, A. C.; Zaragozá, R. J. *Synlett* **1993**, 895.

(4) β-Cyclogeraniol (**5**) was obtained by reductive ozonization of commercial β-ionone (O_3, MeOH, −78 °C, then $NaBH_4$, −78 °C to rt; 56% yield).

(5) In the same way, the use of the Sharpless D-(−)-DET reagent afforded enantiomeric (1*R*,2*R*)-**6**, which can be used as chiral template for the construction of cuparane terpenoids belonging to the antipodal series of that described here.

(6) A slight loss of optical purity occurs during the rearrangement of **7** to **4**. See ref 3.

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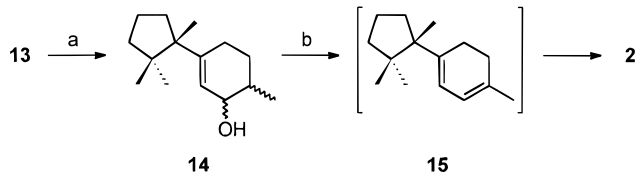
pound **10**. Further treatment of this crude mixture with 1% potassium hydroxide in methanol at room temperature for 6 h completed the cleavage of the trimethylsilyl moiety, affording the compound **10** as a diastereomeric mixture in 83% overall yield.[8]

In order to complete the annulation process, the mixture of diastereomeric *tert*-butyldimethylsilyl ethers **10** was subjected to a variety of basic conditions, but unfortunately, we were unsuccessful in finding conditions to effect the intramolecular aldol reaction. In the hope that the difficulties encountered to complete the ring closure in **10** could be overcome by removal of the (trimethylsilyl)oxy moiety, the mixture of *tert*-butyldimethylsilyl ethers **10** was treated with SmI_2 in THF and MeOH at −78 °C. Smooth reductive elimination of the (trialkylsilyl)oxy moiety occurred upon warming to room temperature to afford the diketone **11** in nearly quantitative yield. With the diketone **11** in hand new attempts were made to complete the cyclohexane ring. After several unsuccessful trials using standard base- and acid-catalyzed[9] aldol reaction conditions, it was found that complete and clean conversion of **11** into **12** could be effected by treatment of **11** with 4% aqueous KOH in MeOH at 150 °C in a sealed tube for 5 h. Under these conditions cyclohexenone **12** was obtained, after chromatographic purification, in an excellent 93% yield.[10]

The final stage of the synthesis was the elaboration of the cyclohexane-ring functionality. First, introduction of the methyl group α to the carbonyl group of **12**, necessary for the completion of the cuparane system, was effected in 96% yield by treatment of the kinetically generated lithium enolate of **12** with methyl iodide at low temperature.

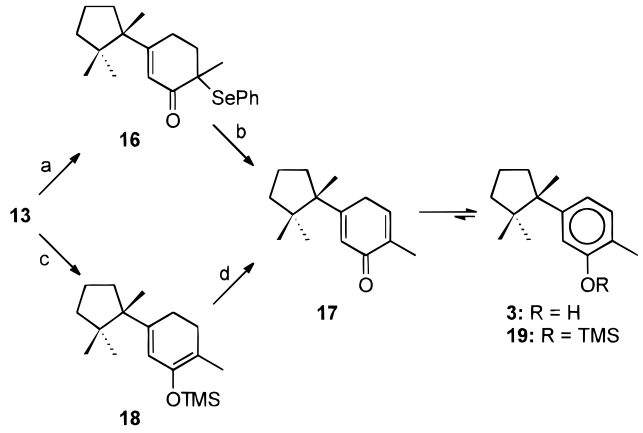
For the synthesis of cuparene (**2**), the enone **13**[11] was reduced in 96% yield to a mixture of diastereomeric allylic alcohols **14** by treatment with DIBALH in THF (Scheme 3). Final aromatization of the cyclohexene ring was achieved in 93% yield by treatment of **14** with selenium dioxide and trimethylsilyl polyphosphate (PPSE)[12] in CCl_4 at reflux overnight, via the cyclohexadiene **15**.[13] The overall yield of (−)-cuparene (**2**) from β-cyclogeraniol (**5**) was 47% in nine synthetic steps. The spectroscopic properties of the synthetic material were identical in all respects with those of the naturally occurring compound.[14]

Scheme 3[a]



[a] Reaction conditions, reagents, and yields: (a) DIBALH, THF, −78 °C, 96%; (b) SeO_2−PPSE, CCl_4 reflux, 93%.

Scheme 4[a]

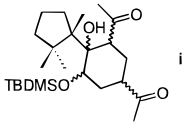


[a] Reaction conditions, reagents, and yields: (a) LDA, THF, −40 °C; PhSeBr; (b) H_2O_2, Py, CH_2Cl_2−H_2O, 20% from **13**; (c) TMSOTf, Et_3N, CH_2Cl_2, −78 °C; $Pd(OAc)_2$, CH_3CN, 51% from **13**.

For the synthesis of δ-cuparenol (**3**) the formation of the phenolic system was achieved by the following two methods (Scheme 4). Reaction of the lithium enolate obtained by treatment of the enone **13** with LDA at low temperature with benzeneselenenyl bromide afforded the corresponding selenated ketone **16**. Subsequent oxidation of **16** with 30% hydrogen peroxide in aqueous methylene dichloride containing pyridine at room temperature provided, after column chromatography, the target compound **3** in 20% overall yield, via the tautomeric form **17**. More conveniently, treatment of **13** with trimethylsilyl triflate and triethylamine in dichloromethane at −78 °C, followed by reaction of the resulting silyl enol ether **18** with palladium(II) acetate in acetonitrile, also afforded δ-cuparenol (**3**) in an improved 51% overall yield, also identical in spectral characteristics to the natural product.[15] The overall yield of (−)-δ-cuparenol (**3**) from β-cyclogeraniol (**5**) was 27% in nine synthetic steps.

(7) Boeckmam, R. K., Jr.; Blum, D. M.; Ganem, B.; Halvey, N. *Organic Syntheses;* Wiley: New York, 1988; Collect. Vol. VI, p 1033.

(8) The use of methyl vinyl ketone (MVK) in the Michael reaction afforded the expected adduct **10** in very low yield. LDA (1 equiv), MVK (1 equiv), −78 to +25 °C; 5−10% yield. The use of an excess of MVK gave a complex reaction mixture from which compound **i** was obtained as the only identified compound. This compound, obtained as a mixture of diastereomers, was formed by two consecutive Michael reactions with MVK, followed by aldol ring closure.



i

(9) Jung, M. E. *Tetrahedron* **1976**, *32*, 3.

(10) Treatment of the *tert*-butyldimethylsilyl ether **10** under the same conditions described for **11** afforded a complex mixture that was impractical for our purposes. The failure of this aldol reaction seems to be related to the lability of the (*tert*-butyldimethylsilyl)oxy moiety to the reaction conditions used. In fact, removal of the *tert*-butyldimethylsilyl group of **10** and protection of the hydroxy group as the tetrahydropyranyl ether gave a diastereomeric mixture of tetrahydropyranyl ethers (**11**, R = OTHP, R′ = H), which when heated for 17 h under the conditions described above for **11** (R = R′ = H) afforded the corresponding cyclohexenone (**12**, R = OTHP) in 75% yield. This compound was also converted by us into δ-cuparenol (**3**) by methylation α to the carbonyl group (LDA, THF, −78 °C and then MeI, HMPA, −78 to −15 °C, 98%), followed by acid treatment (PTSA, C_6H_6, 100 °C, 70%). However, the global yield for the conversion of β-cyclogeraniol (**5**) into **3** through this route was lower (*ca.* 22%) than that obtained with the route described in the discussion section (*vide infra*).

(11) Obtained as a chromatographically homogeneous 1:1 mixture of diastereomers with respect to the newly created quiral centre.

(12) Lee, J. G.; Kim, K. C. *Tetrahedron Lett.* **1992**, *42*, 6363.

(13) Heating for only 30 min allowed the isolation of dehydrated compound **15**. Conversion of the allylic alcohol **14** to **15** was also possible by treatment of the former with BF_3Et_2O in pentane at −78 °C. Cyclohexadiene **15**, which was obtained accompanied by variable amounts of dienic regioisomers (*ca.* 20%), is also a naturally occurring cuparane sesquiterpene. See: Dauben, W. G.; Oberhänsly, P. *J. Org. Chem.* **1966**, *31*, 315.

(14) Matsuo, A.; Nakayama, N.; Nakayama, M. *Phytochemistry* **1985**, *24*, 777.

(15) Asakawa, Y.; Takeda, R.; Toyota, M.; Takemoto, T. *Phytochemistry* **1981**, *20*, 858.

In summary, we have established a general synthetic route for the enantioselective synthesis of cuparane-type sesquiterpenoids, which allowed the preparation of two representatives members of this family, (−)-cuparene (**2**) and (−)-*δ*-cuparenol (**3**), to be completed in 47% and 27% overall yield, respectively, from *β*-cyclogeraniol. This strategy is distinctively different from previous approaches and should also allow, with minor modifications, the preparation of related herbertane-type sesquiterpenoids.[16] These studies are being pursued in our laboratory and will be reported on in due course.

Experimental Section

General Procedures. For general experimental information see ref.[17] ^{1}H and ^{13}C NMR assignments were made on the basis of a combination of DEPT and inverse-detected heteronuclear multiple quantum coherence (HMQC) and NOE experiments. Spectroscopic data and experimental details for the preparation of *β*-cyclogeraniol (**5**), epoxy alcohol **6**, *tert*-butyldimethylsilyl ether **7**, and α-siloxy ketone **4**, which were partially given in ref 3, are included in the supporting information.

(1′*S*,2*RS*)-2-[(*tert*-Butyldimethylsilyl)oxy]-1-(1′,2′,2′-trimethylcyclopentyl)-1,5-hexanedione (10). A stirred solution of the α-siloxy ketone **4** (1.11 g, 3.89 mmol) in anhyd THF (2.5 mL) containing a few crystals of anhydrous phenanthroline was treated dropwise with a stock solution of lithium diisopropylamide in THF at −78 °C until persistence of the characteristic rust color of LDA−phenanthroline (approximately 6 mL, 0.7 M, 4.2 mmol). The stirring was continued at the same temperature for 2 h. 3-(Trimethylsilyl)-3-buten-2-one (0.66 mL, 3.99 mmol) was then added dropwise at −78 °C, and the resulting solution was allowed to warm slowly to rt. After a few min, water was added and the mixture was extracted with pentane. Workup as usual afforded an oily residue (a mixture of **9** and **10**, as shown by ^{1}H NMR analysis), which was dissolved in a mixture of methanol (12.5 mL) and 4% aqueous potassium hydroxide (2.5 mL). After being stirred at rt for 6 h, the reaction mixture was poured into water and extracted with pentane. Workup as usual gave a residue that was purified by chromatography using pentane−ether 8:2 as eluent to afford, in order of elution, starting material **4** (39.6 mg, 4%) and diketone **10** (1.139 g, 83%) as a 7:1 mixture of diastereomers.

Spectroscopic data of **10**: IR (film) 1705, 1370, 1260, 835, 755 cm^{-1}; ^{1}H NMR (only signals corresponding to the major diastereomer are given) *δ* 4.58 (1H, dd, *J* 6.6, 4.8 Hz, H-2), 2.60 (1H, ddd, *J* = 18.5, 8.0, 7.4 Hz, H-4), 2.40 (1H, ddd, *J* = 18.5, 4.1, 2.8 Hz, H′-4), 2.11 (3H, s, H_3-6), 1.07 (6H, s, CH_3-1′ and CH_3-2′), 0.87 (3H, s, CH_3-2′), 0.88 (9H, s, $SiC(CH_3)_3$), 0.04 and 0.01 (3H each, each s, $SiC(CH_3)_3$).

(1′*S*)-1-(1′,2′,2′-Trimethylcyclopentyl)hexane-1,5-dione (11). A solution of **10** (1.139 g, 3.21 mmol) in a mixture of anhyd THF (10 mL) and MeOH (3.2 mL) was treated with a solution of SmI_2 in THF (40 mL of a 0.2 M solution in THF, 8 mmol) at −78 °C. The reaction mixture was kept at the same temperature for 30 min, and then it was allowed to warm slowly to rt over 3 h. The resulting dark greenish mixture was diluted with pentane and washed with brine. Chromatography of the residue left after evaporation of the solvent (gradient elution, from 90 to 70% pentane in ether) furnished the diketone **11** as a colorless oil (713.6 mg, 99%): $[\alpha]^{20}_D$ −17.5° (*c* 6.0, $CHCl_3$); IR (film) 1715, 1700, 1460, 1370, 1160 cm^{-1}; ^{1}H NMR *δ* 2.58−2.3 (5H, m, H-5′+ H_2-2 + H_2-4), 2.10 (3H, s, H_3-6), 1.08 (3H, s, CH_3-1′), 1.04 and 0.80 (3H each, each s, 2 × CH_3-2′); MS (EI) *m*/*z* 225 (M^+ + 1, 0.7), 224 (M^+, 0.8), 168 (1.5), 155 (16), 115 (17), 113 (47), 111 (100); HRMS calcd for $C_{14}H_{24}O_2$ 224.1776, found 224.1773.

(1′*S*)-3-(1′,2′,2′-trimethylcyclopentyl)-2-cyclohexen-1-one (12). A solution of ketone **11** (433.2 mg, 1.93 mmol) in a mixture of methanol (7.8 mL) and 3.3% aqueous potassium hydroxide (1.6 mL) was heated at 150 °C in a sealed tube for 5 h. The mixture was poured into water and extracted with ether. Workup as usual afforded an oily residue, which was purified by chromatography using pentane−ether 8:2 as eluent to provide the enone **12** (369 mg, 93%) as a colorless oil: $[\alpha]^{20}_D$ −56.6° (*c* 4.8, $CHCl_3$); IR (KBr) 1680, 1615, 1270, 970, 900 cm^{-1}; ^{1}H NMR *δ* 5.95 (1H, br s, H-2), 2.35 (4H, m, H_2-4 and H_2-6), 1.93 (2H, m, H_2-5), 1.07 (3H, s, CH_3-1′), 1.04 and 0.80 (6H each, each s, 2 × CH_3-2′); MS (EI) *m*/*z* 207 (M^+ + 1, 6), 206 (M^+, 35), 191 (7), 163 (6), 150 (62), 137 (100); HRMS calcd for $C_{14}H_{22}O$ 206.1671, found 206.1674.

(1′*S*,6*RS*)-6-Methyl-3-(1′,2′,2′-trimethylcyclopentyl)-2-cyclohexen-1-one (13). To a solution of **12** (100 mg, 0.485 mmol) in THF (5 mL) was added dropwise a solution of LDA in THF (0.750 mL of a 0.7 M solution, 0.525 mmol) at −50 °C. The mixture was stirred for 30 min, and HMPA (0.26 mL) and MeI (0.3 mL, 4.82 mmol) were successively added. The solution was allowed to warm gradually to −20 °C over 1 h, and saturated aqueous NH_4Cl solution was added. Usual workup afforded the crude product, which was purified by chromatography using pentane−ether 8:2 as eluent to give the methyl ketone **13** (102 mg, 96%) as a 1:1 mixture of epimers at C-6 (^{1}H NMR analysis): IR (KBr) 1660, 1610, 1370, 1215, 880 cm^{-1}; ^{1}H NMR *δ* 5.93 (1H, br s, H-2 of both epimers at C-6), 1.12 and 1.11 (3H, each d, *J* = 6.8 Hz, CH_3-6 of both epimers at C-6), 1.061 and 1.058 (3H, each s, CH_3-1′ of both epimers at C-6), 1.037 and 1.033 (3H, each s, CH_3-2′ of both epimers at C-6), 0.79 (3H, s, CH_3-2′ of both epimers at C-6); EM (EI) *m*/*z* 221 (M^+ + 1, 9), 220 (M^+, 48), 205 (11), 192 (5), 177 (7), 164 (60), 151 (100); HRMS calcd for $C_{15}H_{24}O$ 220.1827, found 220.1825.

(1*RS*,1′*S*,6*RS*)-6-Methyl-3-(1′,2′,2′-trimethylcyclopentyl)-2-cyclohexen-1-ol (14). The mixture of epimeric α-methyl ketones **13** (83.7 mg, 0.38 mmol) in THF (2.4 mL) was treated with DIBALH (0.95 mL of a 1 M solution in cyclohexane, 0.95 mmol) at −78 °C. The solution was stirred for 80 min, water (1.5 mL) was added and the solution was extracted with ether. Workup as usual gave a residue, which was purified by chromatography using pentane-ether 8:2 as eluent to afford alcohol **14** (81 mg, 96%) as a mixture of four diastereomers: IR (film) 3300, 3020, 1630, 1360, 1015, 880 cm^{-1}; ^{1}H NMR *δ* 5.61 and 5.41 (1H, each m), 4.00 and 3.76 (1H, each m), 1.02−0.94 (9H, m), 0.76 (3H, m).

(1′*S*)-1 -Methyl-4-(1′, 2′,2′-trimethylcyclopentyl)benzene [(−)-Cuparene (2)]. Hexamethyldisiloxane (0.45 mL, 2.13 mmol) was added to a stirred suspension of P_2O_5 (153 mg, 1.08 mmol) in CCl_4 (0.75 mL).[12] The resulting solution was heated at reflux for 2 h until a homogeneous solution was formed. Then SeO_2 (76.6 mg, 0.69 mmol) was added followed by a solution of the above-obtained mixture of diastereomeric alcohols **14** (66.5 mg, 0.3 mmol) in CCl_4 (1.5 mL). The resulting reaction mixture was heated at reflux overnight and poured into water. Extraction with pentane and workup as usual afforded an oil, which was purified by chromatography, using pentane as eluent, to give cuparene (**2**) (57 mg, 93%): $[\alpha]^{20}_D$ −59.6° (*c* 1.9, $CHCl_3$) (lit.[14] $[\alpha]_D$ −63°); IR (film) 1510, 1460, 1370, 810 cm^{-1}; ^{1}H NMR *δ* 7.25 (2H, d, *J* = 8 Hz, H-3 and H-5), 7.09 (2H, d, *J* = 8 Hz, H-2 and H-6), 2.48 (1H, m, H-5′), 2.31 (3H, s, CH_3-1), 1.25, 1.05 and 0.55 (3H each, each s, CH_3-1 and 2 × CH_3-2); MS (EI) *m*/*z* 203 (M^+ + 1, 5), 202 (M^+, 30), 187 (6), 159 (8), 146 (10), 145 (38), 132 (100); HRMS calcd for $C_{15}H_{22}$ 202.1721, found 202.1721.

(1′*S*)-2-Methyl-5-(1′, 2′,2′-trimethylcyclopentyl)phenol [(−)-*δ*-Cuparenol (3)]. Triethylamine (0.095 mL, 0.69 mmol) was added to a solution of diastereomeric ketones **13** (55.4 mg, 0.251 mmol) in CH_2Cl_2 (1.2 mL) was added triethylamine (0.095 mL, 0.69 mmol) and TMS triflate (0.066 mL, 0.34 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 3 h and then poured into water and extracted with ether. Workup as usual afforded an oily residue, which was taken up in CH_3CN (0.70 mL) and treated with palladium (II) acetate (64 mg, 0.28 mmol). The resulting mixture was stirred overnight at rt, poured into water, and extracted with

(16) Connolly, J. D.; Hill, R. A. In *Dictionary of Terpenoids*, 1st ed.; Chapman and Hall: London, 1991; Vol. 1, pp 299−300.

(17) Abad, A.; Agulló, C.; Arnó, M.; Cuñat, A. C.; Zaragozá, R. J. *J. Org. Chem.* **1992**, *57*, 50.

ether. The residue obtained after workup was purified by chromatography (gradient elution, from 90 to 70% pentane in ether) to provide in order of elution silyl ether **19** (5.1 mg, 7%), δ-cuparenol (**3**) (28 mg, 51%), and starting material **13** (4.1 mg, 7%).

δ-Cuparenol (3): colorless oil; $[\alpha]^{20}_D$ −59.46° (*c* 2.6, $CHCl_3$) (lit.[15] $[\alpha]_D$ −64°); IR (film) 3340, 1625, 1585, 1510, 815 cm^{-1}; ^1H NMR δ 7.00 (1H, d, *J* = 8 Hz, H-3), 6.83 (1H, dd, *J* = 8.0, 2.0 Hz, H-4), 6.77 (1H, d, *J* = 2.0 Hz, H-6), 2.43 (1H, m, H-5′), 2.20 (3H, s, CH_3-2), 1.22, 1.04 and 0.56 (3H each, each s, CH_3-1′ and 2 × CH_3-2′); MS (EI) *m*/*z* 219 (M^+ + 1, 8), 218 (M^+, 56), 204 (3), 203 (3), 175 (5), 161 (30), 149 (33), 148 (82), 136 (100); HRMS calcd for $C_{15}H_{22}O$ 218.1671, found 218.1673.

Silyl ether **19**: colorless oil; ^1H NMR 7.01 (1H, d, *J* = 8.0 Hz, H-3), 6.83 (1H, dd, *J* = 8.0 and 1.6 Hz, H-2), 6.76 (1H, d, *J* = 1.6 Hz, H-6), 2.40 (1H, m, H-5′), 2.13 (3H, s, CH_3-2), 1.21, 1.03 and 0.55 (3H each, each s, CH_3-1′ and 2 × CH_3-2′), 0.24 (9H, s, $SiC(CH_3)_3$).

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Supporting Information Available: Supporting Information Available: Copies of ^1H NMR spectra of compounds **2**−**8** and **11**−**13**, tables of ^{13}C NMR data of compounds **5**−**7** (Table I), **4**, **8**, **10**, and **11** (Table II), and **2**, **3**, **12**, and **13** (Table III), and spectroscopic data and experimental procedures for the preparation of compounds **4**−**7** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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