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HIGHLY STEREOCONTROLLED SYNTHESIS OF [3.3.3] PROPELLANE SESQUITERPENES. (±)-MODHEPHENE AND (±)-EPIMODHEPHENE

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Abstract—Stereospecific total synthesis of (±)-modhephene (2) and (±)-epimodhephene (3) are reported. Conjugate addition of 1-trimethylsilyl-1-butyn-4-yl cuprate (BF_3-etherate catalysis) to bicyclic ketone **6**, fluoride ion-promoted deblocking of the terminal acetylene, and ene reaction, gave tricyclic enone **11**. Sequential Wittig methylenation, regiocontrolled epoxidation, and Lewis acid catalyzed isomerization afforded ketone **14** whose double bond relocation and Wolff-Kishner reduction led exclusively to **2**. In a still shorter route to **3**, 3-butenyl cuprate addition to **6** was utilized to gain access to **7**. Thermolysis of this intermediate, methylenation, and double bond isomerization were found to deliver pure **3** successfully.

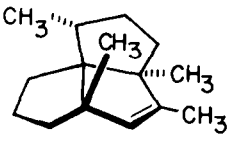
Ingestion by higher animals of rayless goldenrod (*Isocoma wrightii*) was recognized more than a century ago to lead to a disease known as "trembles". The toxic constituent passes into the animal's milk which when ingested by humans can result in death and disability ("milksickness").[1] In their investigation of the ethanol extract of this plant, Zalkow and his coworkers uncovered a host of secondary metabolites of diverse structure.[2] Their more recent examination of the hexane soluble fraction has led them to a rich source of unusually structured sesquiterpenes which includes isocomene (**1**)[3] and modhephene (**2**).[4] While either of these constituents is quite certainly not the toxic principle,[5] their unique carbon skeletons have attracted considerable synthetic interest.

Prior to the isolation of isocomene, no substance based upon a tricyclo[6.3.0.$0^{4,8}$]undecane ring system had been isolated from natural sources except for retigeranic acid.[6] In 1977, Bohlmann independently described the successful efforts of his group in isolating **1** from the roots of *Berkheya radula*.[7] In the few intervening years, a remarkable number of additional triquinanes[8] of related type have been characterized.[9] Several imaginative synthetic approaches to isocomene have already been devised.[10–13]

Modhephene (**2**) is one of only two carbocyclic [3.3.3]propellanes to be identified from natural sources.[14] Although the hydrocarbon contains a single chiral center,[15] its synthesis acquires special significance by virtue of the need to introduce stereochemistry in one bridge in a manner which is unambiguous relative to the other two (differently substituted) members. Although the last two decades have witnessed explosive developments in the propellane field,[16] purposeful stereochemical strategies have been given scant attention.[17] In this paper, we describe short, efficient, and fully stereocontrolled approaches to both **2** and epimodhephene (**3**).[18] In the alternative schemes designed by Smith and Jerris[19] and by Karpf and Dreiding[20] to deliver **2**, serious epimer contamination resolvable only by chromatographic means was encountered. The present methodology is devoid of such complications.

Although the complexity of **2** and **3** is not such that a convergent synthesis is necessary, a distinct advantage would be gained if bicyclic enone **6** could be readily acquired. Previously, we described the ready Friedel–Crafts acylation of 1-trimethylsilylcyclopentene (**4a**) with β,β-dimethylacryloyl chloride and subsequent Nazarov cyclization of the resulting crystalline dienone **5** to **6**.[21] The need to prepare vinylsilane **4a** could be obviated by the direct acylation of cyclopentene. In combination with the acid chloride and $AlCl_3$,[22] **4b** is readily transformed into **5** in good yield. More spectacularly, reaction of cyclopentene with β,β-dimethylacrylic acid in polyphosphoric acid at 40°[23] leads directly to **6**, although with lesser efficiency. In view of the satisfactory nature of these procedures, the availability of **6** was no longer an issue.

For elaboration of the third cyclopentane ring, our plan focused on the application of an intramolecular ene reaction between the cyclic ketone functionality and a remote center of unsaturation.[24] At the mechanistic level, such thermal processes proceed by hydrogen atom transfer from an enol tautomer to the tethered double or triple bond. In the first instance, therefore, the newly formed methyl substituent necessarily becomes positioned syn to the carbonyl group. With **3** in mind as the first target molecule, the conjugate addition of a suitable



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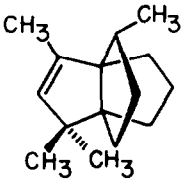

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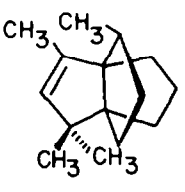

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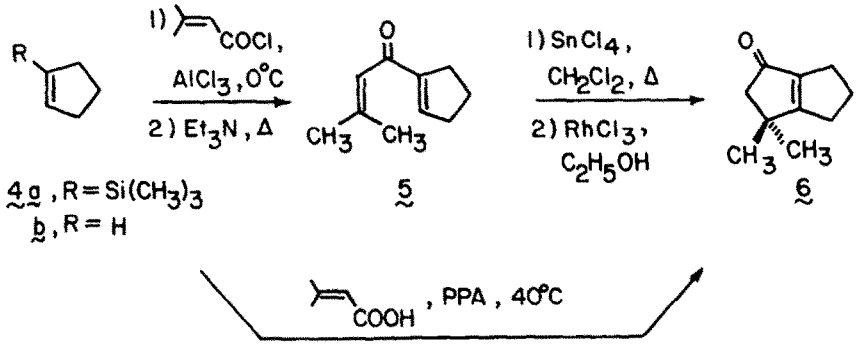
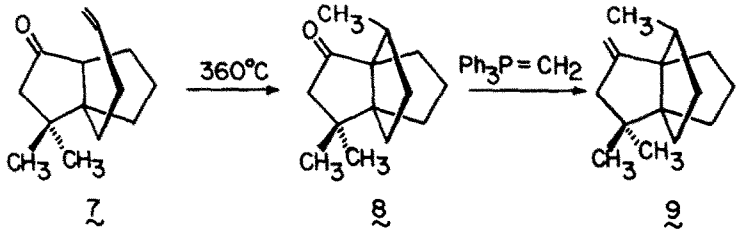


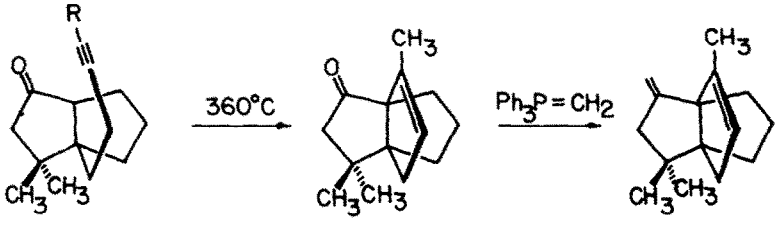
cuprate reagent to **6** was next studied. It is immediately recognized that the β carbon of the enone moiety in **6** is quite hindered. Nonetheless, it was soon determined that proper reaction with the reagent prepared from 3-butenylmagnesium bromide and cuprous iodide could be efficaciously promoted by boron trifluoride etherate catalysis.[25] An 81% yield of **7** was realized. When heated in decalin solution at 360° for 4 hr, **7** was smoothly converted into **8** (85%). The previously discussed mechanistic constraints serve to deliver an epimerically pure product as determined by both ^1H and ^{13}C NMR spectroscopy.

The fifteenth and final carbon atom was introduced by reaction of **8** with methylenetriphenylphosphosium bromide and potassium *tert*-butoxide in diisopropyl ether.[26] Although the syn orientation of the methyl substituent causes this transformation to occur somewhat sluggishly, **9** was nevertheless obtained in 67% yield. Upon treatment with iodine in refluxing benzene solution for 10 hr, **9** underwent complete double bond isomerization to give epimodhephene (**3**) exclusively. Associated with this double bond migration is a significant alteration in the chemical shifts of the geminate methyl groups. While the pair of singlets are well separated in **9** (δ0.99 and 0.90), those in **3** are rather tightly spaced at 90 MHz (δ1.02 and 1.00), more reminiscent of the situation in modhephene (singlet of area 6 at δ0.92 in CCl_4).

Having in hand an expedient synthesis of **3**, we next sought to approach modhephene (**3**) with equal control of the methyl group configuration. Although a somewhat less direct synthetic entry was mandated, it appeared to us that the requisite methyl orientation could be installed by a modified ene cyclization scheme. Toward this end, **6** was reacted with the Grignard reagent of 4 - chloro - 1 - trimethylsilyl - 1 - butyne,[27] cuprous iodide, and boron trifluoride etherate in tetrahydrofuran solution as before. The catalyzed 1,4-addition culminates in the formation of **10a** which upon deprotection with tetra-n-butyl-ammonium fluoride afforded **10b**. Thermal activation of this terminal acetylene at 360° in decalin for 100 min led to the isolation of tricyclic enone **11** in 56% yield. Although the corresponding exocyclic olefin is undoubtedly the product of kinetic control, its formation proved difficult to achieve because of the ease of isomerization to **11**. Because **11** was the desired end product, conditions designed to generate the exocyclic isomer reproducibly were neither actively sought nor developed. Subsequent treatment of **11** with methylenetriphenylphosphorane in the predescribed manner delivered diene **12** and set the stage for proper stereochemical disposition of the trigonally-bonded methyl group.

Due to the different substitution plans of the double bonds in **12**, complete discrimination in favor of the endocyclic site of unsaturation could be achieved during





peroxidation with m-chloroperbenzoic acid in dichloromethane solution at 0°. To the best of our knowledge, the formation of **13** (91% yield) was highly regio- and stereoselective. The ^{1}H NMR spectrum, for example, shows only three methyl singlets at δ 1.34, 0.93, and 0.89. This valued stereocontrol presumably arises because of steric shielding provided by the β-methyl group of the geminate pair. The anti stereochemistry assigned to **13** was based on the independent observation that catalytic hydrogenation of **11** produced only **8**. Evidently, insofar as catalyst approach to the π bond is concerned, the access route of least steric resistance lies in the area above the unsubstituted cyclopentane bridge. Our conclusion that peracid attack was subject to the same factors was substantiated by controlled exposure of **13** to boron trifluoride etherate in dichloromethane solution at 0°. As expected on the basis of ample literature precedent,[28] oxirane bond reorganization occurred with in-plane 1,2-hydrogen shift to give epimerically homogeneous **14**. As will be shown below, this product is in the [3.3.3]propellane series isomeric to that in which **8** finds itself.

Studies of molecular models suggested that strategy designed to preserve the anti-methyl stereochemistry present in **14** would be better guaranteed if allylic isomerization of the double bond were first implemented. In essence, a vinyl methyl group as is present in **15** was seen to play a greater space-filling role than an exo-methylene substituent and consequently be expected to exert greater oriental dominance. In line with this analysis, **14** was exposed to iodine in benzene.[29] This afforded a 73% yield of epimerically uncontaminated **15**. Wolff–Kishner reduction of this intermediate with potassium carbonate and hydrazine hydrate in hot diethylene glycol[30] gave modhephene (**2**) as a colorless oil (84%), the IR and ^{1}H NMR spectra of which were superimposable upon those of the authentic sample.[31]

The pair of syntheses delineated herein not only provide independent confirmation of the structure and configuration of modhephene, but may find utily in other settings where stereochemical control of isolated alkyl groups requires solution.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin–Elmer Model 467 spectrophotometer. The ^{1}H NMR spectra were determined with a Varian EM-390 instrument and apparent splittings are given in all cases. The ^{13}C NMR spectra were recorded on a Bruker HX-90 instrument. Mass spectra were measured with an AEI-MS9 spectrometer at an ionizing energy of 70 eV. Microanalytical determinations were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

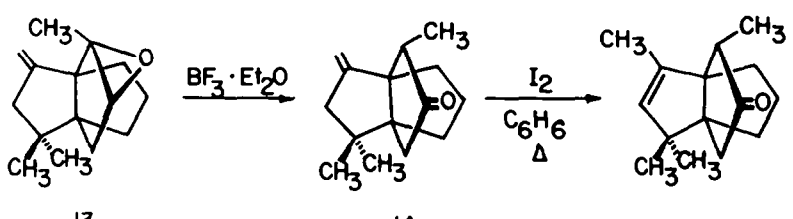
1 - (3,3 - *Dimethylacryloyl*)*cyclopentene* (**5**). (*a*) *From* **4a**. To a cold (−78°C) well-stirred slurry of anhydrous aluminum chloride (1.9 g, 14 mmol) in dichloro-methane (10 ml) was added 3,3-dimethylacryloyl chloride (1.6 g, 14 mmol) dropwise and the mixture was stirred for an additional 5 min. A solution of **4a**[21] (2.0 g, 14 mmol) in dichloromethane (2 ml) was introduced slowly via syringe, the mixture was stirred for 15 min, and the flask contents were poured into cold (0°) 3N hydrochloric acid. After 45 min of vigorous stirring, the product was extracted into dichloromethane and the combined organic layers were washed with saturated sodium bicarbonate and brine solutions prior to drying. The concentrated filtrate was chromatographed on silica gel (elution with ether–pentane, 1:1) and the isolated dienone was recrystallized from pentane to give 650 mg (28%) of **5**[21] as a quite unstable white crystalline substance, mp 48–49.5°C; IR (CCl_4, cm^{-1}) 2940, 1655, 1610, 1440, 1380, 1355, 1250, and 1155; ^{1}H NMR (CCl_4, δ) 6.60 (m, 1H), 6.47 (m, 1H), 2.67–2.47 (m, 4H), 2.17 (s, 3H), 2.13–1.80 (m, 2H), and 1.98 (s, 3H); *m/e* calc. 150.1044, obs 150.1040.

(*b*) *From* **4b**. Treatment of cyclopentene (1.00 g, 14.7 mmol) with aluminum chloride (1.96 g, 14.7 mmol) and 3,3-dimethylacryloyl chloride (1.74 g, 14.7 mmol) as above gave an oil which was immediately taken up in triethylamine (20 ml) and heated for 48 hr at the reflux temperature. Following solvent evaporation, the dark solid residue was recrystallized from pentane and sublimed at 25°C and 0.1 torr. There was obtained 480 mg (22%) of **5**.

3,3,6 - *Trimethyl* - 4,5,6 - *trihydro* - 2H - *pentalen* - 1 - *one* (**6**). (*a*) *Nazarov Cyclization of* **5**. A 14 g (0.21 mol) sample of cyclopentene was acylated with 3,3 - dimethylacryloyl chloride (25 g, 0.21 mol) and aluminum chloride (28 g, 0.21 mol) in dichloromethane (50 ml) in the predescribed manner and the dark oil so produced was heated at the reflux temperature with triethylamine (150 ml) for 48 hr. The resulting dark crystalline **5** was immediately taken up in dichloromethane (50 ml) and stannic chloride (109 g, 0.42 mol) was slowly added to the solution. The reaction mixture was heated at reflux for 24 hr, cooled, and poured into ice water. The product was extracted into dichloromethane and the combined organic layers were washed with saturated sodium bicarbonate solution and brine before drying. Solvent evaporation left a thick black oil which was dissolved in deoxygenated 95% ethanol (100 ml) to which rhodium trichloride hydrate (10 mg) was added. The reaction mixture was heated at reflux for 2 hr, filtered through Celite, and concentrated *in vacuo*. Double distillation of the residue afforded 12.5 g (40%) of **6**, b.p. 55–65° at 0.2 torr, as a clear colorless oil which yellowed on standing. Its spectra were superimposable upon those of the authentic sample.[21]

(*b*) *One-step formation from cyclopentene*. To a warm (40 ± 2°), well stirred mass of polyphosphoric acid (prepared from 30 g of phosphorus pentoxide and 12 ml of 85% phosphoric acid) was added cyclopentene (2.9 g, 43 mmol) and crotonic acid (4.3 g, 43 mmol). This mixture was stirred for 1 hr, poured into ice (100 g), and extracted with ether (3 × 50 ml). The combined ether layers were washed with water (20 ml), saturated sodium bicarbonate solution (20 ml), and brine (20 ml) prior to drying. Medium pressure liquid chromatography of the residue after evaporation on silica gel (elution with ethyl acetate-petroleum ether, 1:3) afforded 1.0 g (16%) of **6**.

4,4 - *Dimethyl* - 5 - (3 - *butenyl*) *bicylo*[3.3.0]*octan* - 2 - *one* (**7**). A cold (−78°), magnetically stirred slurry of cuprous iodide (10.7 g, 56 mmol) in tetrahydrofuran (10 ml) was slowly treated with a solution of the Grignard reagent from 4 - bromo - 1 - butene (80 ml, 0.7 M in THF, 56 mmol) during 1 h. After an additional hr, boron trifluoride etherate (6.9 ml, 56 mmol) was introduced slowly by syringe. This mixture was stirred for 1 hr and 3.0 g (20 mmol) of **6** was added over 8 hr. The reaction



13 14 15

mixture was kept at −78°C for another 4 hr, allowed to warm to room temperature (*ca.* 2 hr), and stirred for 3 hr. Basic ammonium chloride solution was introduced and the product was extracted into ether. The combined organic layers were dried and evaporated to leave a residue which was purified by high pressure liquid chromatography (Waters Prep 500) on silica gel (elution with 5% ethyl acetate in petroleum ether). There was obtained 3.35 g (81%) of **7**; IR (neat, cm^{-1}) 3080, 2980, 2880, 1740, 1640, 1460, 1415, 1390, 1370, 1280, 1220, and 910; ^1H NMR ($CDCl_3$, δ) 5.97–5.41 (m, 1H), 5.08–4.75 (m, 2H), 2.43–1.35 (series of m, 13H), 1.15 (s, 3H), and 1.10 (s, 3H); *m/e* calcd 206.1671, obs 206.1675. Calc for $C_{14}H_{22}O$: C, 81.51; H, 10.75. Found: C, 81.51; H, 10.74%

Thermal Cyclization of **7**. The thermolysis of **7** (536 mg, 2.60 mmol) was carried out using the Conia procedure[27] at 360° for 4 hr. Column chromatography on silica gel served to remove decalin (petroleum ether elution) from ketonic product (ether elution). The ether fraction was further purified by medium pressure liquid chromatography (silica gel, elution with 5% ethyl acetate in petroleum ether). Tricyclic ketone **8** (454 mg, 85%) was obtained as a clear colorless oil; IR (neat, cm^{-1}) 2960, 2880, 1730, 1460, 1410, 1390, 1380, and 1370; ^1H NMR (CCl_4, δ) 2.50–1.17 (series of m, 13H), 1.03 (s, 3H), 1.00 (s, 3H), and 0.99 (d, $J = 7$ Hz, 3H); ^{13}C NMR ($CDCl_3$, ppm) 220.29, 70.21, 66.75, 55.89, 46.36, 38.72, 36.90, 36.78, 35.80, 35.62, 26.64 (2C), 26.15, and 16.02; *m/e* calcd 206.1670, obs 206.1675. Calc. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.49; H, 10.79%.

Wittig olefination of **8**. To a cold (0°), well stirred mixture of methyl-triphenylphosphonium bromide (0.70 g, 1.9 mmol) and potassium t-butoxide (0.21 g, 1.9 mmol) in diisopropyl ether (5 ml) was added 80 mg (0.4 mmol) of **8** dissolved in 2 ml of the same solvent. The reaction mixture was heated at reflux for 10 hr, cooled, treated with saturated oxalic acid solution, and extracted with ether. The combined ethereal layers were washed with brine, dried, and evaporated. Preparative thin layer chromatography of the residue on silica gel (elution with ether-pentane, 1:9) gave 60 mg (84%) of **9** as a clear, colorless oil; IR (neat, cm^{-1}) 3070, 2950, 2880, 1660, 1460, 1380, 1370, 1360, and 880; ^1H NMR (CCl_4, δ) 4.77 (m, 1H), 4.53 (m, 1H), 2.45–1.10 (series of m, 13H), 0.99 (s, 3H), 0.92 (s, 3H), and 0.92 (d, $J = 7$ Hz, 3H); *m/e* calc. 204.1878, obs 204.1882.

Epimodhephen (**3**). A solution containing 74 mg (0.36 mmol) of **9** and a few crystals of iodine in 5 ml of benzene was heated at reflux for 10 hr, cooled, washed with 10% sodium thiosulfate solution, dried, and concentrated. Medium pressure liquid chromatography of the residue on silica gel (elution with 2% ethyl acetate in petroleum ether) afforded 68 mg (92%) of **3** as a clear colorless oil; IR (CCl_4, cm^{-1}) 2950, 2860, 1460, 1375, and 840; ^1H NMR (CCl_4, δ) 4.88 (m, 1H), 2.08–1.06 (series of m, 11H), 1.60 (d, $J = 1.5$ Hz, 3H), 1.02 (s, 3H), and 0.88 (d, $J = 7$ Hz, 3H). Calc. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.13; H, 11.83%.

4,4 - *Dimethyl* - 5(3 - *butynyl*)*bicyclo*[3.3.0]*octan* - 2 - *one* (**10b**). To a well stirred slurry of cuprous iodide (5.7 g, 30 mmol) in dry tetrahydrofuran (10 ml) cooled to −78°C was added the Grignard reagent from 4 - chloro - 1 - trimethylsilyl - 1 - butyne (67 ml, 0.45M in THF, 30 mmol) during 1 hr. Boron trifluoride etherate (3.7 ml, 30 mmol) was introduced via syringe, and after 30 min a solution of **6** (1.5 g, 10 mmol) in tetrahydrofuran (10 ml) was slowly added over an 8 hr period. The reaction mixture was stirred for an additional 4 hr at −78°, allowed to warm to room temperature during 2 hr, and kept at 25°C for 3 hr. Basic ammonium chloride solution was added and the product was extracted into ether. The combined organic extracts were dried and evaporated and the residue was subjected to high pressure chromatography (Waters Prep 500) on silica gel (elution with ethyl acetate-petroleum ether, 1:19). There was isolated 1.4 g (52%) of **10a** as a faintly yellow oil; IR (neat, cm^{-1}) 2960, 2160, 1740, 1450, 1405, 1370, 1250, 1040, 840, and 755; ^1H NMR (CCl_4, δ) 2.30–1.30 (series of m, 13H), 1.03 (s, 6H), and 0.03 (s, 9H); *m/e* calc. (M^+–CH_3) 261.1674, obs 261.1679.

A solution of **10a** (695 mg, 2.52 mmol) and tetra - n - butylammonium fluoride (7.5 ml of 0.40 M in aqueous tetrahydrofuran, 3.00 mmol) was stirred at room temperature for 30 min, treated with water, and extracted with ether. The combined organic phases were dried and concentrated. Medium pressure liquid chromatography of the residue on silica gel (elution with ethyl acetate-petroleum ether, 1:9) afforded 416 mg (81%) of **10b** as a clear, colorless oil; IR (neat, cm^{-1}) 3290, 2960, 2880, 1740, 1450, and 1370; ^1H NMR (CCl_4, δ) 2.40–1.37 (series of m, 14H), 1.07 (s, 3H), and 1.03 (s, 3H); *m/e* calcd 204.1514, obs 204.1518. Calc. for $C_{14}H_{20}O$: H, 82.30; H, 9.87. Found: C, 81.90; H, 9.91%.

Thermal Cyclization of **10b**. The thermolysis of **10b** (1.0 g, 4.9 mmol) was carried out according to the method of Conia[27] at 360° for 100 min. Separation of the decalin (hexane elution) from product (ether elution) was achieved on a plug of silica gel. Purification of the concentrated ether eluate by medium pressure liquid chromatography (silica gel, 5% ethyl acetate/petroleum ether) gave **11** as a clear, colorless oil (560 mg, 56%); IR (neat, cm^{-1}) 3020, 2960, 2880, 1740, 1460, 1420, 1370, and 780; ^1H NMR (CCl_4, δ) 5.13 (m, 1H), 2.77–1.3 (series of m, 10H), 1.73 (d, $J = 1$ Hz, 3H), 1.05 (s, 3H), and 0.97 (s, 3H); *m/e* calc. 202.1514, obs 202.1518. Calc. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 81.98; H, 9.81%.

Wittig Olefination of **11**. Treatment of **11** (350 mg, 1.7 mmol) with 3.2 g (8.8 mmol) of methyltriphenylphosphonium bromide and 950 mg (8.5 mmol) of potassium t-butoxide in 25 ml of diisopropyl ether in the predescribed manner, followed by bulb-to-bulb distillation (80°, 0.01 torr) and medium pressure liquid chromatography (silica gel, elution with 2% ethyl acetate-petroleum ether) of the crude product furnished 280 mg (81%) of **12** as a clear, colorless oil; IR (neat, cm^{-1}) 3020, 2940, 2840, 1650, 1450, 1380, 1370, 1360, and 870; ^1H NMR (CCl_4, δ) 5.07 (m, 1H), 4.68 (m, 2H), 2.69–1.07 (series of m, 10H), 1.70 (d, $J = 1$ Hz, 3H), 0.95 (s, 3H), and 0.92 (s, 3H); *m/e* calcd 202.1721, obs 202.1716. Calc. for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 89.05; H, 10.95.

Catalytic Hydrogenation of **11**. A solution of **11** (790 mg, 3.8 mmol) in absolute ethanol (20 ml) containing platinum oxide (20 mg) was hydrogenated at 50 psi for 48 hr. The reaction mixture was filtered through Celite and the filtrate was concentrated. Preparative thin layer chromatography of the residue on silica gel (dichloromethane elution) gave 712 mg (89%) of **8** as a clear, colorless oil. The spectral properties of this material were superimposable upon those of the ene product **8** isolated earlier.

Epoxidation of **12**. A cold (0°), magnetically stirred slurry of disodium hydrogen phosphate (550 mg, 3.9 mmol) and **12** (281 mg, 1.39 mmol) in dichloromethane (5 ml) was treated with m-chloroperbenozic acid (270 mg, 1.57 mmol) and allowed to react for 4 hr. Conventional workup followed by medium pressure chromatographic purification on silica gel (elution with 5% ethyl acetate in petroleum ether) afforded 62 mg of recovered **12** and 215 mg (91% based on unreacted starting material) of **13** as a colorless oil; IR (neat, cm^{-1}) 3070, 2980, 2870, 1655, 1440, 1380, 1360, 1070, 880, and 830; ^1H NMR (CCl_4, δ) 4.88 (m, 1H), 4.78 (m, 1H), 3.18 (m, 1H), 2.58–1.18 (series of m, 10H), 1.34 (s, 3H), 0.93 (s, 3H), and 0.89 (s, 3H); *m/e* calc. 218.1670, obs 218.1666.

Isomerization of **13**. A cold (0°C), well stirred solution of **13** (75 mg, 0.34 mmol) in dichloromethane (3 ml) was treated with boron trifluoride etherate (0.10 ml, 0.85 mmol) in one portion and the red solution was stirred for 5 min, poured into water, and extracted with ether. The combined organic extracts were dried and evaporated. Medium pressure liquid chromatography of the residue on silica gel (elution with 4% ethyl acetate-petroleum ether) led to the isolation of 44 mg (59%) of **14** as a colorless oil; IR ($CHCl_3$, cm^{-1}) 3040, 2980, 2880, 1735, 1660, 1460, 1370, 910, and 890; ^1H NMR (CCl_4, δ) 4.80–4.67 (m, 2H), 2.80–1.20 (series of m, 11H), 1.08 (d, $J = 7$ Hz, 3H), 1.07 (s, 3H), and 0.95 (s, 3H); ^{13}C NMR ($CDCl_3$, ppm) 221.02, 162.09, 104.14, 63.11, 61.67, 53.77, 49.63, 46.24, 40.42, 38.90, 36.05, 26.46, 26.22, 24.09, and 11.77; *m/e* calc 218.1670, obs 218.1668. Calc. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.57; H, 10.19%.

Iodine-promoted rearrangement of **14**. A magnetically stirred solution of **14** (60 mg, 0.28 mmol) and iodine (single crystal) in benzene (5 ml) was heated at the reflux temperature for 10 hr. The cooled reaction mixture was washed with 10% sodium thiosulfate solution and brine, dried, and evaporated. Following medium pressure liquid chromatography of the residue on silica gel (elution with 3% ethyl acetate-petroleum ether), there was obtained 44 mg (73%) of **15** as a colorless oil; IR (neat, cm^{-1})

2960, 2880, 1725, 1420, 1340, and 1100; ^{1}H NMR (CCl_4, δ) 4.95 (m, 1H), 2.87–1.21 (series of m, 9H), 1.67 (d, J = 1 Hz, 3H), 1.07 (d, J = 7 Hz, 3H), 1.07 (s, 3H), and 1.01 (s, 3H); *m/e* calc 218.1670, obs 218.1666.

Modhephene (2). A well stirred slurry of **15** (60 mg, 0.28 mmol), hydrazine hydrate (126 mg, 2.5 mmol) and potassium carbonate (480 mg, 3.4 mmol) in diethylene glycol (2 ml) was heated at reflux (160°) for 2 hr. Following distillation of the volatile components at 230° for 2.5 hr, the reaction mixture was heated at this temperature for a further 1.5 hr and allowed to cool. The distillate and reaction mixture were taken up in ether and the organic phase was washed with 10% hydrochloric acid and saturated sodium bicarbonate solutions, dried, and concentrated. Chromatography (petroleum ether) of the residue on silica gel furnished 47 mg (84%) of modhephene (**2**) as a colorless oil; IR (CCl_4, cm^{-1}) 2950, 2870, 1455, 1375, and 840; ^{1}H NMR ($CDCl_3$, δ) 4.80 (m, 1H), 2.18–1.08 (series of m, 8H), 1.58 (d, J = 1.5 Hz, 3H), 0.97 (d, J = 6 Hz, 3H), and 0.96 (s, 9H); ^{13}C NMR ($CDCl_3$, ppm) 139.92, 134.78, 72.09, 65.10, 44.81, 42.92, 37.67, 34.81, 33.30, 28.84, 28.26, 26.17, 25.29, 14.56, and 12.72; *m/e* calc. 204.1878, obs 204.1883.

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