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Stereochemistry of terpene derivatives. Part 4:☆ Fragrant terpenoid derivatives with an unsaturated *gem*-dimethylbicyclo[3.1.0]hexane system

Bożena Frąckowiak,[a] Teresa Olejniczak,[b] Rafał Latajka,[a] Agata Białońska,[c] Zbigniew Ciunik[c] and Stanisław Lochyński[a,*]

[a]*Department of Bioorganic Chemistry, Faculty of Chemistry, Wrocław University of Technology, Wybrzeże Wyspiańskiego 27, 50-370 Wrocław, Poland*
[b]*Department of Chemistry, Agricultural University, Norwida 25, 50-375 Wrocław, Poland*
[c]*Faculty of Chemistry, University of Wrocław, F. Joliot-Curie 14, 50-383 Wrocław, Poland*

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Abstract—Starting from (+)-3-carene **1** several chiral fragrant compounds with the bicyclo[3.1.0]hexane system **4**–**6** and **10**–**20** were synthesized. These compounds are structural analogues of naturally occurring fragrant compounds, such as ionones and damascones, and possess either an *endo*- or an *exo*-cyclic double bond in the bicyclo[3.1.0]hexane moiety. The absolute configuration of selected products was confirmed by X-ray crystallography and circular dichroism analysis.

1. Introduction

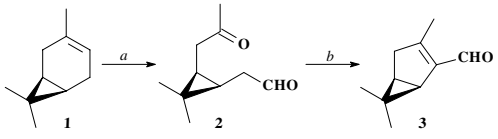
The optically active monoterpene (+)-3-carene **1** is a convenient substrate in the syntheses of chiral derivatives displaying interesting fragrant properties, in which the bicyclo[4.1.0]heptane system is preserved.[2,3] The chemical properties of this monoterpene allowed the formation of compounds with the bicyclo[3.1.0]hexane system possessing an *endo*-cyclic double bond.[4–6] Recently, derivatives obtained from (+)-3-carene with the bicyclo[3.1.0]hexane moiety have been investigated as chiral auxiliaries in a variety of reactions.[7–10]

Compounds with the bicyclo[3.1.0]hexane system possess a valuable sandalwood odour in the perfume industry.[2] In our previous studies, we obtained a series of derivatives with a saturated 6,6-dimethylbicyclo[3.1.0]-hexane moiety substituted at the C-3 position possessing various groups: hydroxyl, carbonyl or ester (especially acetates).[11] The double bond present in this system makes it unstable and in some cases drives its conversion to other systems, for example, to monocyclic compounds in the Horner–Wadsworth–Emmons (HWE) reaction catalyzed by sodium hydride.[12] Herein, we report syntheses of fragrant derivatives, in which the bicyclic fragment was preserved with an *endo*- or *exo*-cyclic double bond.

2. Results and discussion

The key compound, α,β-unsaturated aldehyde **3**, was synthesized in a two-step procedure from the monoterpene hydrocarbon (+)-3-carene **1** via condensation of the ketoaldehyde **2**.[5]

This reaction was carried out in acetic acid–morpholine (1:1) with azeotropic removal of water and led to the desired product (1*R*,5*S*)-(−)-3,6,6-trimethylbicyclo[3.1.0]-hex-2-en-2-carboaldehyde **3** (Scheme 1).



Scheme 1. Reagents: (a) (1) O_3, (2) Zn; (b) AcOH.

☆ See Ref. 1.

* Corresponding author. Tel.: +48 71 320 2400; fax: +48 71 347 7175; e-mail: stanislaw.lochynski@pwr.wroc.pl

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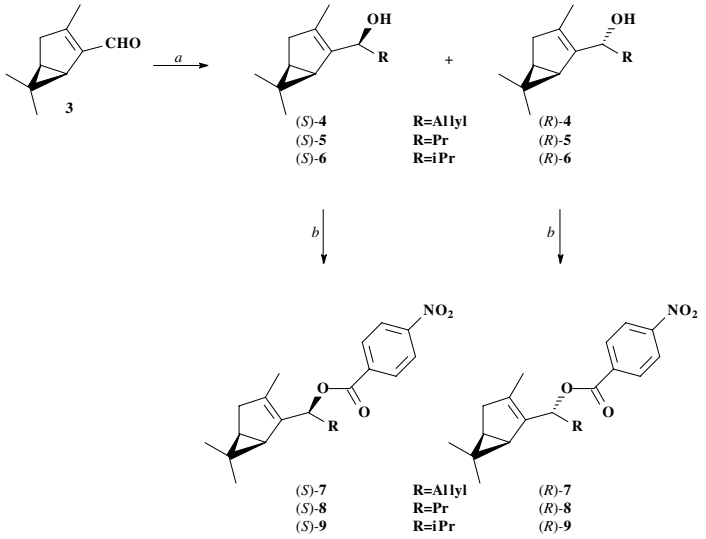


Scheme 2. Reagents: (a) RI or RBr, Mg, Et_2O; (b) *p*-$NO_2PhCOCl$, Py.

Aldehyde **3** was subjected to a Grignard reaction with three–carbon units of alkylmagnesium halides: allylmagnesium bromide, *n*-propylmagnesium bromide and isopropylmagnesium iodide, to give the appropriate unsaturated secondary alcohols (*RS*)-**4**–(*RS*)-**6**[†] as a mixture of diastereoisomers (Scheme 2). Only the reaction with allylmagnesium bromide afforded a mixture of diastereoisomeric alcohols (*R*)-**4** and (*S*)-**4** in a 1:1 ratio. In the case of alcohols obtained from *n*-propylmagnesium bromide, diastereoisomer (*S*)-**5**, which possesses a higher R_f value in a TLC analysis, was predominant in the mixture (68%). The same effect was observed in the reaction with isopropylmagnesium iodide [73% of isomer (*S*)-**6**].

The separation of these diastereoisomeric mixtures of alcohols by preparative column chromatography afforded pure diastereoisomers of (*R*)-**4**–(*R*)-**6** and (*S*)-**4**–(*R*)-**6**. The enantiopure (*R*)-**7**–(*R*)-**9** and (*S*)-**7**–(*S*)-**9** were obtained in their crystalline forms. The crystal structure of (*S*)-**9** was determined and its (*S*)-configuration at the stereogenic centre in the side chain was assigned on the basis of the known absolute configuration at the C-1 and C-5 atoms (Fig. 1). In the CD spectra obtained for methanolic solutions of the *p*-nitrobenzoates for isomers (*S*)-**7**–(*S*)-**9**, the Cotton effect was positive, whereas for diastereoisomers (*R*)-**7**–(*R*)-**9** the effect was negative (Fig. 2).

With the crystal structure of (*S*)-**9**, the observed Cotton effects for (*R*)-**7**–(*R*)-**9** and (*S*)-**7**–(*S*)-**9** and the analysis of ^{1}H NMR spectra of alcohols (*R*)-**4**–(*R*)-**6** and (*S*)-**4**–(*S*)-**6**, we assigned the absolute configurations in their side chains.

The α- and β-damascone and damascenone, known as 'rose ketones', belong to the most famous fragrant compounds.[13] Many of their analogues have already been synthesized.[14] We obtained three more analogues by the oxidation of alcohols (*RS*)-**6** with the Dess–Martin periodinane[15] to the appropriate ketones **10**–**12** (Scheme 3). Earlier reactions with oxidizing agents, such as PCC, PDC or MnO_2, gave mixtures of products, from which we could not separate the desired ketones **10**–**12** in high yields. The crude ketone **10** was converted to compound **13** with a double bond conjugated to the carbonyl group in the side chain—a close analogue of β-damascone (Scheme 3).

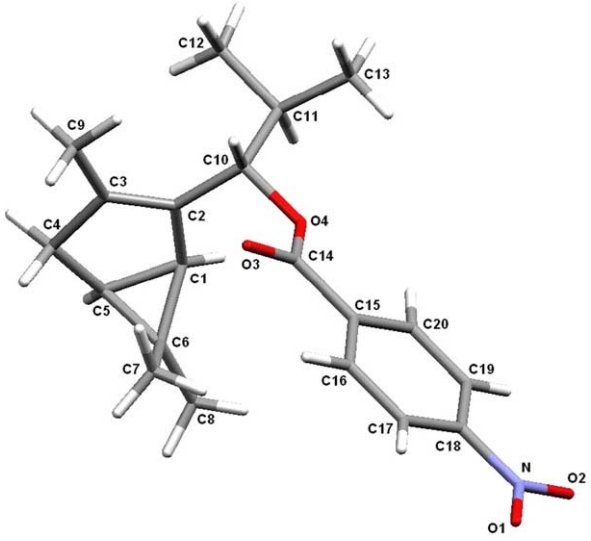


Figure 1. Crystal structure of (*S*)-**9**.

We also synthesized the structural analogue **14** of another important fragrance compound—the ionone[13] from the aldehyde **3** in a Horner–Wadsworth–Emmons (HWE) reaction with the barium-hydroxide-promoted modification[16] (Scheme 4). This modification of the HWE reaction provided only one product **14** from substrate **3**. Earlier attempts to obtain compound **14** in the

[†] In compounds: (*R*)-**4**–(*R*)-**9** and (*S*)-**4**–(*S*)-**9** the letters: (*R*)- and (*S*)- apply to absolute configurations of the carbon atom C-10 in the said chain in each of them.

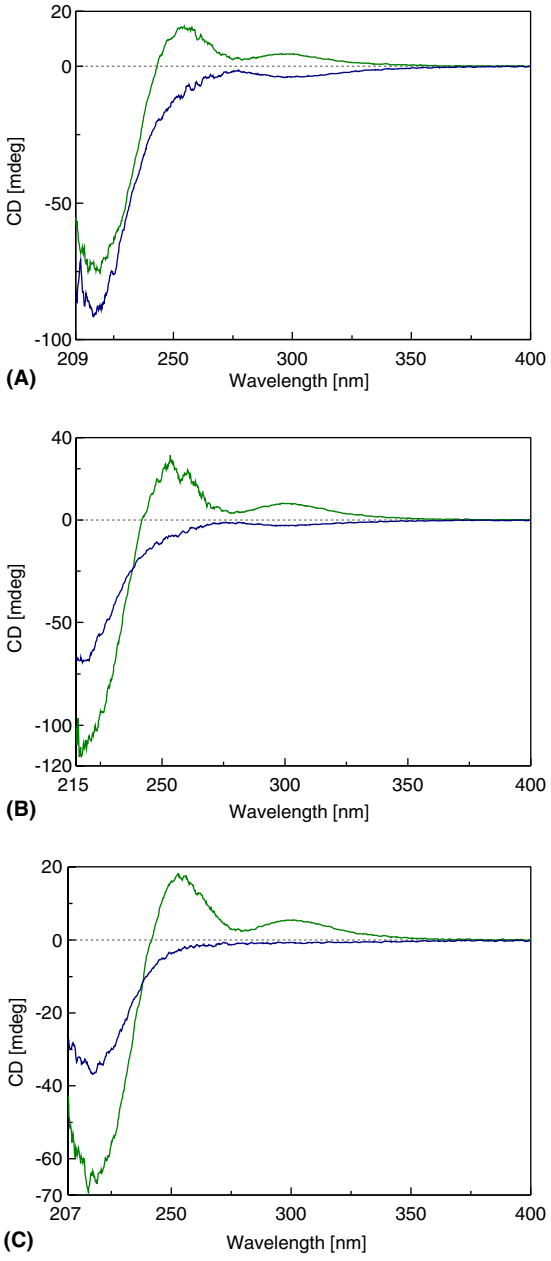
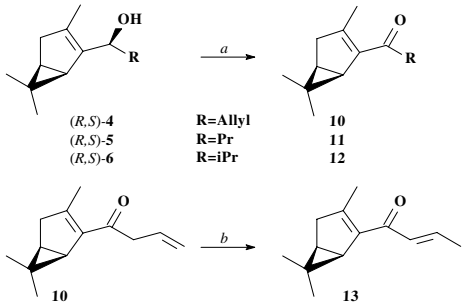


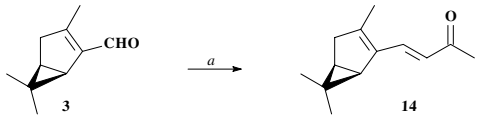
Figure 2. CD spectra of the purified diastereoisomeric benzoates: A—(*S*)-**7** (green line) and (*R*)-**7** (blue line); B—(*S*)-**8** (green line) and (*R*)-**8** (blue line); C—(*S*)-**9** (green line) and (*R*)-**9** (blue line).

Wittig–Horner reaction with triphenylphosphineacetylmethylene failed.

The next fragrant compounds **17**–**20** were obtained from alcohol **15**. The α,β-unsaturated aldehyde **3** was reduced with LAH to give allyl alcohol **15**, which was purified by crystallization of the *p*-nitrobenzenoate **16** and then hydrolyzed under alkaline conditions to furnish alcohol **15** (98% purity by GC). Compound **15** was the key substrate for the syntheses of the derivatives with the bicyclo[3.1.0]hexane system which possess an *exo*-cyclic double bond. The Claisen rearrangement (*ortho*-acetate modification)[17] of **15** afforded the enantiomerically pure γ,δ-unsaturated ester **18**. The steric hindrance created by the *gem*-dimethylcyclopropyl group in the molecule of



Scheme 3. Reagents: (a) Dess–Martin periodinane, CH_2Cl_2; (b) DBU, CH_2Cl_2.



Scheme 4. Reagents: (a) $CH_3COCH_2PO(OC_2H_5)_2$, $Ba(OH)_2{\cdot}0.8H_2O$, THF–H_2O (40:1).

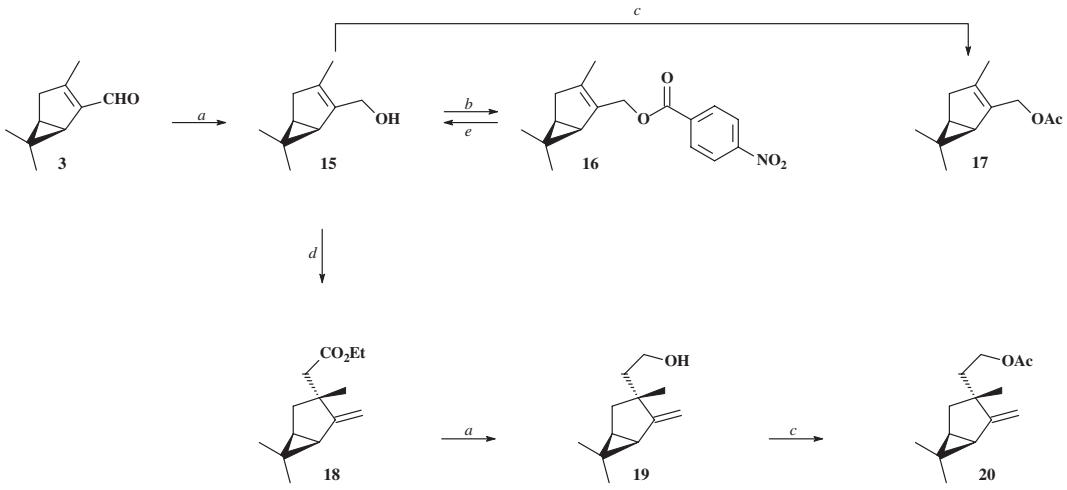
alcohol **15** provided only one diastereoisomer of the ester **18**. Reduction of **18** with LAH gave the primary alcohol **19**, which after esterification with acetyl chloride was converted into acetate **20**. The acetyl derivative **17**, with an *endo*-cyclic double bond, was obtained in the same manner from **15** (Scheme 5).

Some of the obtained optically active compounds exhibited various interesting odours.[18] The comparative analysis of the fragrant properties of alcohols (*R*)-**4**–(*R*)-**6** and (*S*)-**4**–(*S*)-**9** showed that diastereoisomers *S* were more intense than the alcohols with the opposite *R* absolute configuration in the side chain. The diastereoisomer (*R*)-**4** also displayed odour different from (*S*)-**4**. The scents of compounds **11**–**14** are also distinct from damascone and ionone, their structural analogues. Odour characteristics for all fragrant compounds are given in Table 1.

3. Experimental

3.1. General

(+)-3-Carene was purchased from Sigma–Aldrich. The course of all reactions, composition of products and their purities were checked by thin-layer chromatography (TLC) and gas chromatography (GC). TLC was carried out on silica gel DC-Alufolien Kieselgel 60 (Merck). Plates were developed in a mixture of hexane, diethyl ether and acetone in various ratios and visualized with 20% ethanolic H_2SO_4, containing 0.1% of anisaldehyde. Preparative column chromatography was carried out on silica gel (230–400 mesh, Merck) with a mixture of hexane, diethyl ether and acetone (various ratios) as eluent. Analytical GC was performed on a Hewlett Packard 5890 (seria II) instrument using the capillary column HP-1 (length 25 m, temperature 120–180 °C). Melting points (uncorrected) were determined on a Boetius apparatus. IR spectra were taken from



Scheme 5. Reagents: (a) LAH, Et_2O; (b) *p*-$NO_2PhCOCl$, C_5H_5N; (c) AcCl, Py; (d) $CH_3C(OC_2H_5)_3$, $C_2H_5CO_2H$; (e) KOH, C_2H_5OH.

Table 1.

Compound	Odour characteristic
(*S*)-**4**	Medium intensive, agreeable, floral with tansy (*Tanacetum vulgare*) note
(*R*)-**4**	Medium intensive, agreeable, floral-fruity, with dried apple and weak mushroom note
(*S*)-**5**	Medium intensive, agreeable, fresh, floral-woody, more intensive then (*R*)-**5**
(*R*)-**5**	Medium intensive, agreeable, fresh, floral-woody
(*S*)-**6**	Intensive, resinous resembling bornyl acetate, camphen with fir oil note, more intensive than (*R*)-**6**
(*R*)-**6**	Medium intensive, fresh, floral with fir oil note
11	Intensive, woody-balsamic
13	Medium intensive, woody-balsamic
14	Medium intensive, floral-woody
15	Medium intensive, fruity-herbal with fresh note
17	Intensive, penetrating, sweet, fruity with woody and dry mandarin's skin note
18	Intensive, woody with spice note
19	Medium intensive, floral, linalol and citronellol-like
20	Balsamic, medium turpentine with fruity note

liquid films or in KBr on a Perkin–Elmer 621 spectrometer. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard on a Bruker Avance DRX 300 instrument. Chemical shifts (δ) are reported in parts per million and coupling constants (J) are given in Hertz. ^{13}C–H substitution was determined with a DEPT-135 experiments. Optical rotation measurements were obtained on an Autopol IV automatic polarimeter (Rudolph). X-ray data were collected at 100 K using an Oxford Cryosystem device on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated MoKα radiation. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Diffraction (Wrocław) programs.[19] The structure was solved by direct methods and refined by the full-matrix least-squares method on all F^2 data using programs.[20] Non-hydrogen atoms were refined with anisotropic thermal parameters; hydrogen atoms were included from the $\Delta\rho$ maps and refined with isotropic thermal parameters. Crystallographic data for structures reported herein have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 273888. CD spectra were recorded on a Jasco J-715 spectropolarimeter at room temperature, over the range 200–400 nm in a 1 mm path length cell. Compounds were dissolved in methanol at concentrations 0.15–0.25 mg/ml.

3.1.1. (1*R*,5*S*)-(−)-3,6,6-Trimethylbicyclo[3.1.0]hex-2-en-2-carboaldehyde 3. Aldehyde **3** was synthesized according to a known procedure.[5] The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate 30:1) to give **3** as an oil: $[\alpha]_D^{26} = -192.75$ (c 0.99, $CHCl_3$); IR (film, cm^{-1}): 3029(m), 2946(m), 2888(m), 1667(vs), 1622(m), 1421(m), 1376(m), 1238(m); ^1H NMR ($CDCl_3$): 0.69 (s, 3H at C-7 or C-8), 1.05 (s, 3H at C-7 or C-8), 1.25 (td, $J = 7.2$, 1.5 Hz, 1H at C-5), 2.04 (s, 3H at C-9), 2.07 (d, $J = 2.8$ Hz, 1H at C-1), 2.59 (d, $J = 20.0$ Hz, 1H at C-4), 2.70 (dd, $J = 20.1$, 7.5 Hz, 1H at C-4), 9.91 (br s, 1H at C-10); ^{13}C NMR ($CDCl_3$): 13.14 (C-7 or C-8), 13.41 (C-7 or C-8), 20.06 (C-6), 25.73 (C-5), 25.87 (C-9), 34.61 (C-1), 40.16 (C-4), 138.66 (C-3), 162.11 (C-2), 187.54 (C-10).

3.2. General procedure for the Grignard reaction

Aldehyde **3** (15 mmol) in anhydrous diethyl ether (20 ml) was added dropwise to the Grignard reagent formed from the appropriate halide (18 mmol) and

magnesium (18 mmol) in anhydrous diethyl ether (60 ml). The mixture was stirred until TLC monitoring showed the absence of substrate **3**. Then NH_4Cl solution was added dropwise and the aqueous layer extracted with diethyl ether. The organic solution was washed with saturated NaCl solution and dried over $MgSO_4$. Each of the crude diastereoisomeric mixtures (*RS*)-**4**–(*RS*)-**6** were separated by column chromatography (eluent: hexane–diethyl ether 9:1) to give pure compounds (*R*)-**4**–(*R*)-**6** and (*S*)-**4**–(*S*)-**6**.

3.2.1. (1*S*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]but-3-en-1-ol (*S*)-4. $[\alpha]_D^{25} = -56.2$ (*c* 0.76, $CHCl_3$); IR (film, cm^{-1}): 3402(s), 3077(m), 2923(vs), 1641(w), 1433(m), 1375(s), 1037(s), 914(s); ^1H NMR ($CDCl_3$): 0.72 (s, 3H at C-7 or C-8), 0.98 (s, 3H at C-7 or C-8), 1.13 (t, $J = 7.2$ Hz, 1H at C-5), 1.55 (s, 3H at C-9), 1.62 (d, $J = 6.7$ Hz, 1H at C-1), 1.93 (d, $J = 17.9$ Hz, 1H at C-4), 2.21–2.38 (m, 2H at C-11), 2.42 (dd, $J = 18.4$, 8.1 Hz, 1H at C-4), 4.34 (t, $J = 6.9$ Hz, 1H at C-10), 5.02 (d, $J = 5.6$ Hz, 1H at C-13), 5.10 (d, $J = 13.1$ Hz, 1H at C-13), 5.67–5.81 (m, 1H at C-12); ^{13}C NMR ($CDCl_3$): 12.98 (C-7 or C-8), 13.65 (C-7 or C-8), 20.44 (C-6), 26.22 (C-9), 26.27 (C-5), 36.26 (C-1), 38.07 (C-4), 40.43 (C-11), 67.90 (C-12), 117.22 (C-13), 134.94 (C-10), 135.23 (C-3), 136.44 (C-2). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.01; H, 10.67.

3.2.2. (1*R*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]but-3-en-1-ol (*R*)-4. $[\alpha]_D^{25} = -83.1$ (*c* 0.95, $CHCl_3$); IR (film, cm^{-1}): 3434(s), 3079(m), 2978(w), 1641(w), 1446(m), 1384(m), 1112(s), 910(s); ^1H NMR ($CDCl_3$): 0.67 (s, 3H at C-7 or C-8), 0.97 (s, 3H at C-7 or C-8), 1.15 (td, $J = 7.5$, 1.1 Hz, 1H at C-5), 1.55 (s, 3H at C-9), 1.79 (dd, $J = 6.7$, 2.9 Hz, 1H at C-1), 1.92 (d, $J = 18.2$ Hz, 1H at C-4), 2.05–2.13 (m, 1H at C-11), 2.20–2.28 (m, 1H at C-11), 2.40 (dd, $J = 17.9$, 7.6 Hz, 1H at C-4), 4.34 (dd, $J = 8.7$, 4.3 Hz, 1H at C-10), 5.06 (d, $J = 5.4$ Hz, 1H at C-13), 5.10 (d, $J = 13.7$ Hz, 1H at C-13), 5.72–5.86 (m, 1H at 12); ^{13}C NMR ($CDCl_3$): 12.96 (C-7 or C-8), 13.80 (C-7 or C-8), 20.53 (C-6), 26.18 (C-9), 26.52 (C-5), 36.26 (C-1), 38.02 (C-4), 40.36 (C-11), 66.97 (C-12), 117.75 (C-13), 135.12 (C-10), 135.25 (C-3), 136.96 (C-2). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.03; H, 10.65.

3.2.3. (1*S*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]butan-1-ol (*S*)-5. $[\alpha]_D^{25} = -141.5$ (*c* 0.80, $CHCl_3$); IR (film, cm^{-1}): 3418(m), 3019(m), 2956(vs), 1659(w), 1456(m), 1374(m), 1022(m); ^1H NMR ($CDCl_3$): 0.72 (s, 3H at C-7 or C-8), 0.87 (t, $J = 7.3$ Hz, 3H at C-13), 0.97 (s, 3H at C-7 or C-8), 1.13 (t, $J = 6.7$ Hz, 1H at C-5), 1.24–1.30 (m, 2H at C-12), 1.44–1.47 (m, 2H at C-11), 1.54 (s, 3H at C-9), 1.72–1.82 (m, 1H at C-1), 1.92 (d, $J = 16.7$ Hz, 1H at C-4), 2.42 (dd, $J = 17.9$, 7.7 Hz, 1H at C-4), 4.30 (t, $J = 7.0$ Hz, 1H at C-10); ^{13}C NMR ($CDCl_3$): 12.88 (C-7 or C-8), 13.63 (C-7 or C-8), 13.99 (C-13), 18.94 (C-12), 20.36 (C-6), 26.19 (C-5), 35.90 (C-1), 37.89 (C-4), 38.01 (C-11), 68.09 (C-9), 68.12 (C-10), 134.85 (C-3), 136.99 (C-2). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.11; H, 11.68.

3.2.4. (1*R*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]butan-1-ol (*R*)-5. $[\alpha]_D^{25} = -98.5$ (*c* 0.90, $CHCl_3$); IR (film, cm^{-1}): 3358(m), 3019(m), 2958(vs), 1660(w), 1457(m), 1373(m), 1021(s); ^1H NMR ($CDCl_3$): 0.66 (s, 3H at C-7 or C-8), 0.86 (t, $J = 7.1$ Hz, 3H at C-13), 0.96 (s, 3H at C-7 or C-8), 1.13 (t, $J = 6.9$ Hz, 1H at C-5), 1.23–1.27 (m, 2H at C-12), 1.43–1.47 (m, 2H at C-11), 1.541 (s, 3H at C-9), 1.76 (d, $J = 6.8$ Hz, 1H at C-1); 1.92 (d, $J = 17.0$ Hz, 1H at C-4), 2.38 (dd, $J = 17.8$, 7.7 Hz, 1H at C-4), 4.30 (dd, $J = 7.6$, 5.1 Hz, 1H at C-10); ^{13}C NMR ($CDCl_3$): 13.74 (C-7 or C-8), 14.68 (C-7 or C-8), 14.77 (C-13), 19.77 (C-12), 21.39 (C-6), 27.30 (C-5), 36.77 (C-1), 37.04 (C-4), 38.77 (C-11), 68.56 (C-9), 68.57 (C-10), 135.50 (C-3), 138.66 (C-2). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.09; H, 11.62.

3.2.5. (1*S*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]-2-methylpropan-1-ol (*S*)-6. $[\alpha]_D^{25} = -134.2$ (*c* 0.89, $CHCl_3$); IR (film, cm^{-1}): 3464(m), 3019(m), 2954(vs), 1655(w), 1467(m), 1374(s), 1012(s), 999(s); ^1H NMR ($CDCl_3$): 0.76 (s, 3H at C-7 or C-8), 0.78 (d, $J = 6.6$ Hz, 3H at C-12 or C-13), 1.00 (s, 3H at C-7 or C-8), 1.04 (d, $J = 6.0$ Hz, 3H at C-12 or C-13), 1.17 (t, $J = 7.2$ Hz, 1H at C-5), 1.58 (s, 3H at C-9), 1.62 (dd, $J = 7.4$, 2.7 Hz, 1H at C-1), 1.75–1.84 (m, 1H at C-11), 1.97 (d, $J = 17.7$ Hz, 1H at C-4), 2.48 (dd, $J = 17.9$, 7.6 Hz, 1H at C-4), 3.89 (d, $J = 8.8$ Hz, 1H at C-10); ^{13}C NMR ($CDCl_3$): 13.07 (C-7 or C-8), 13.68 (C-7 or C-8), 18.94 (C-13), 19.24 (C-12), 20.36 (C-6), 26.24 (C-9), 26.25 (C-5), 33.14 (C-1), 38.04 (C-4), 36.24 (C-11), 74.30 (C-10), 135.57 (C-3), 136.32 (C-2). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.17; H, 11.71.

3.2.6. (1*R*)-(−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]-hex-2-en-2-yl]-2-methylpropan-1-ol (*R*)-6. $[\alpha]_D^{25} = -146.0$ (*c* 1.13, $CHCl_3$); IR (film, cm^{-1}): 3402(m), 3018(m), 2955(vs), 1655(w), 1462(m), 1373(m), 1168(w), 1011(m); ^1H NMR ($CDCl_3$): 0.72 (s, 3H at C-7 or C-8), 0.80 (d, $J = 6.6$ Hz, 3H at C-12 or C-13), 0.97 (s, 3H at C-7 or C-8), 0.99 (d, $J = 6.7$ Hz, 3H at C-12 or C-13), 1.21 (t, $J = 10.6$, Hz, 1H at C-5), 1.59 (s, 3H at C-9), 1.83 (dd, $J = 6.8$, 2.8 Hz, 1H at C-1), 1.71–1.74 (m, 1H at C-11), 2.00 (d, $J = 17.7$ Hz, 1H at C-4), 2.41 (dd, $J = 17.9$, 8.0 Hz, 1H at C-4), 4.02 (d, $J = 7.8$ Hz, 1H at C-10); ^{13}C NMR ($CDCl_3$): 13.30 (C-7 or C-8), 14.21 (C-7 or C-8), 18.56 (C-13), 19.03 (C-12), 20.84 (C-6), 26.34 (C-9), 26.93 (C-5), 33.06 (C-1), 38.13 (C-4), 37.03 (C-11), 73.75 (C-10), 136.02 (C-3), 136.99 (C-2). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.13; H, 11.73.

3.3. General procedure for the syntheses of *p*-nitrobenzoates

The appropriate alcohol (*R*)-**4**–(*R*)-**6** and (*S*)-**4**–(*S*)-**6** or **15** (6.6 mmol) was dissolved in anhydrous pyridine. *p*-Nitrobenzoic chloride (7.5 mmol) was added to the solution in portions and the mixture stirred overnight. If the substrate was detected in the TLC analysis, the reaction was warmed up to 60 °C and stirred for 2 more hours. The mixture was then diluted with water (20 ml), saturated $NaHCO_3$ solution (7 ml) added and the product extracted with diethyl ether. The combined organic

layers were washed with a 5% H_2SO_4 solution, then with water and dried over $MgSO_4$. The crude product was purified by column chromatography (if necessary) and recrystallized from hexane for compounds (*R*)-**7**–(*R*)-**9** and (*S*)-**7**–(*S*)-**9** and from hexane–acetone 4:1 for compound **15**.

3.3.1. (1*S*)-(−)-1-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.0]hex-2-en-2-yl]but-3-en-1-yl *p*-nitrobenzoate (*S*)-7. $[\alpha]_D^{20} = -25.4$ (*c* 0.88, $CHCl_3$); mp = 97–100 °C; ^{1}H NMR ($CDCl_3$): 0.53 (s, 3H at C-7 or C-8), 0.99 (s, 3H at C-7 or C-8), 1.21 (t, $J = 7.2$ Hz, 1H at C-5), 1.72 (s, 3H at C-9), 1.80 (dd, $J = 6.7$, 2.7 Hz, 1H at C-1), 1.99 (d, $J = 18.7$ Hz, 1H at C-4), 2.47–2.71 (m, 1H at C-4 and 2H at C-11), 5.06–5.10 (m, 1H at C-13), 5.13–5.20 (m, 1H at C-13), 5.71–5.84 (m, 1H at C-10 and 1H at C-12), 8.19–8.29 (m, 4H at C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.30 (C-5), 13.52 (C-7 or C-8), 20.58 (C-6), 26.27 (C-1), 26.34 (C-7 or C-8), 36.63 (C-9), 37.48 (C-4), 38.04 (C-11), 72.02 (C-10), 117.91 (C-13), 123.55 (C-17 and C-19), 130.53 (C-16 and C-20), 132.42 (C-3), 133.39 (C-12), 136.34 (C-2), 138.43 (C-15), 150.48 (C-18), 163.85 (C-14). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.11; H, 6.81; N, 4.12.

3.3.2. (1*R*)-(−)-1-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.0]-hex-2-en-2-yl]but-3-en-1-yl *p*-nitrobenzoate (*R*)-7. $[\alpha]_D^{20} = -57.9$ (*c* 1.04, $CHCl_3$); mp = 72–73 °C; ^{1}H NMR ($CDCl_3$): 0.79 (s, 3H at C-7 or C-8), 1.07 (s, 3H at C-7 or C-8), 1.23 (t, $J = 7.$ 4 Hz, 1H at C-5), 1.74 (s, 3H at C-9), 1.79 (dd, $J = 6.9$, 2.7 Hz, 1H at C-1), 2.03 (d, $J = 18.1$ Hz, 1H at C-4), 2.30–2.38 (m, 1H at C-11), 2.48 (dd, $J = 18.1$, 7.7 Hz, 1H at C-4), 2.57–2.65 (m, 1H at C-11), 5.07–5.08 (m 1H at C-13), 5.10–5.18 (m 1H at C-13); 5.73–5.87 (m, 1H at C-10 and 1H at C-12), 8.19–8.29 (m, 4H at C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.26 (C-5), 13.96 (C-7 or C-8), 20.72 (C-6), 26.22 (C-1), 26.87 (C-7 or C-8), 36.80 (C-9), 37.85 (C-4), 37.98 (C-11), 71.69 (C-10), 117.83 (C-13), 123.50 (C-17 and C-19), 130.70 (C-16 and C-20), 132.77 (C-3), 133.69 (C-12), 136.30 (C-2), 138.65 (C-15), 150.47 (C-18), 163.98 (C-14). Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.08; H, 6.84; N, 4.11.

3.3.3. (1*S*)-(−)-1-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.0]hex-2-en-2-yl]but-1-yl *p*-nitrobenzoate (*S*)-8. $[\alpha]_D^{20} = -28.0$ (*c* 0.60, $CHCl_3$); mp = 45–49 °C; ^{1}H NMR ($CDCl_3$): 0.52 (s, 3H at C-7 or C-8), 0.97 (t, $J = 7.3$ Hz, 3H at C-13), 0.98 (s, 3H at C-7 or C-8), 1.20 (t, $J = 7.2$ Hz, 1H at C-5), 1.35–1.42 (m, 2H at C-12), 1.73 (s, 3H at C-9), 1.78 (dd, $J = 6.9$, 1.6 Hz, 1H at C-1), 1.99 (d, $J = 16.5$ Hz, 1H at C-4), 2.50 (dd, $J = 18.1$, 7.8 Hz, 1H at C-4), 5.79 (t, $J = 7.3$ Hz, 1H at C-10), 8.17–8.30 (m, 4H at C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.25 (C-13), 13.49 (C-7 or C-8), 13.86 (C-5), 18.84 (C-12), 20.53 (C-6), 26.20 (C-7 or C-8), 26.35 (C-1), 34.98 (C-4), 36.56 (C-9), 38.03 (C-11), 72.70 (C-10), 123.52 (C-17 and C-19), 130.69 (C-16 and C-20), 132.92 (C-3), 136.53 (C-2), 137.97 (C-15), 150.45 (C-18), 163.99 (C-14). Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.59; H, 7.41; N, 4.10.

3.3.4. (1*R*)-(+)-1-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.0]hex-2-en-2-yl]but-1-yl *p*-nitrobenzoate (*R*)-8. $[\alpha]_D^{20} = +19.05$ (*c* 0.60, $CHCl_3$); mp = 56–59 °C; ^{1}H NMR ($CDCl_3$): 0.78 (s, 3H at C-7 or C-8), 0.96 (t, $J = 7.3$ Hz, 3H at C-13), 1.06 (s, 3H at C-7 or C-8), 1.22 (t, $J = 7.7$ Hz, 1H at C-5), 1.32–1.43 (m, 2H at C-12), 1.77 (dd, $J = 6.9$, 2.9 Hz, 1H at C-1), 1.86–1.93 (m, 2H at C-11), 2.02 (d, $J = 18.4$ Hz, 1H at C-4), 2.47 (dd, $J = 18.2$, 7.8 Hz, 1H at C-4), 5.78 (dd, $J = 8.1$, 5.3 Hz), 8.20–8.30 (m, 4H at C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.21 (C-13), 13.86 (C-7 or C-8), 13.88 (C-5), 18.86 (C-12), 20.70 (C-6), 26.25 (C-7 or C-8), 26.86 (C-1), 35.48 (C-4), 36.88 (C-9), 37.98 (C-11), 72.49 (C-10), 123.49 (C-17 and C-19), 130.70 (C-16 and C-20), 133.31 (C-3), 136.44 (C-2), 138.10 (C-15), 150.45 (C-18), 164.28 (C-14). Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.57; H, 7.42; N, 4.11.

3.3.5. (1*S*)-(−)-1-[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.0]hex-2-en-2-yl]-2-methylprop-1-yl *p*-nitrobenzoate (*S*)-9. $[\alpha]_D^{20} = -10.1$ (*c* 1.60, $CHCl_3$); mp = 126–128 °C; ^{1}H NMR ($CDCl_3$): 0.46 (s, 3H at C-7 or C-8), 0.93 (d, $J = 6.7$ Hz, 3H at C-12 or C-13), 0.94 (s, 3H at C-7 or C-8), 1.03 (d, $J = 6.6$ Hz, 3H at C-12 or C-13), 1.18 (t, $J = 7.2$ Hz, 1H at C-5), 1.73 (s, 3H at C-9), 1.72–1.76 (m, 1H at C-1), 1.98 (d, $J = 18.5$ Hz, 1H at C-4), 2.16–2.28 (m, 1H at C-11), 2.52 (dd, $J = 18.1$, 7.8 Hz, 1H at C-4), 5.42 (d, $J = 9.4$ Hz, 1H at C-10), 8.19–8.31 (m, 4H at C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.31 (C-7 or C-8), 13.42 (C-5), 18.66 (C-12 or C-13), 19.26 (C-12 or C-13), 20.44 (C-6), 26.14 (C-7 or C-8), 26.33 (C-1), 30.94 (C-9), 36.86 (C-11), 38.01 (C-4), 78.28 (C-10), 123.55 (C-17 and C-19), 130.52 (C-16 and C-20), 132.25 (C-2), 136.51 (C-3), 138.68 (C-15), 150.46 (C-18), 163.98 (C-14). Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.65; H, 7.40; N, 4.09. Crystal data: $C_{20}H_{25}NO_4$, $M_w = 343.41$, $T = 100(2)$ K, Mo-K$_\alpha$ radiation, monoclinic, space group $P2_1$, $a = 11.254(2)$ Å, $b = 7.4550(10)$ Å, $c = 11.404(2)$ Å, $\beta = 105.27(3)°$, $V = 923.0(3)$ Å^3, $Z = 2$, $D_c = 1.236$ Mg^{-3}, $\mu = 0.086$ mm^{-1}, $F(000) = 368$, crystal size $0.27 \times 0.25 \times 0.20$, $3.30 \leqslant \theta \leqslant 28.47$, $R = 0.100$, $wR = 0.089$ (2715 reflections, all data) for 326 parameters.

3.3.6. *p*-Nitrobenzenoate (1*R*)-(+)-[(1*S*,5*R*)-6,6-dimethylbicyclo[3.1.0]hex-2-en-2-yl]-2-methylprop-1-yl (*R*)-9. $[\alpha]_D^{20} = +100.0$ (*c* 0.20, $CHCl_3$); mp = 90–94 °C; ^{1}H NMR ($CDCl_3$): 0.83 (s, 3H at C-7 or C-8), 0.94 (d, $J = 6.7$ Hz, 3H at C-12 or C-13), 1.02 (d, $J = 6.7$ Hz, 3H at C-12 or C-13), 1.05 (s, 3H at C-7 or C-8), 1.22 (t, $J = 6.7$ Hz, 1H at C-5), 1.73 (s, 3H at C-9), 1.77 (dd, $J = 7.1$, 2.8 Hz, 1H at C-1), 1.98 (d, $J = 19.3$ Hz, 1H at C-4), 2.06–2.11 (m, 1H at C-11), 2.44 (dd, $J = 18.4$, 7.8 Hz, 1H at C-4), 5.53 (d, $J = 7.9$ Hz, 1H at C-10), 8.21–8.31 (m, 4H C-16, C-17, C-19 and C-20); ^{13}C NMR ($CDCl_3$): 13.49 (C-7 or C-8), 14.32 (C-5), 18.56 (C-12 or C-13), 19.93 (C-12 or C-13), 20.91 (C-6), 26.35 (C-7 or C-8), 27.25 (C-1), 31.78 (C-9), 37.69 (C-11), 38.02 (C-4), 77.45 (C-10), 123.54 (C-17 and C-19), 130.69 (C-16 and C-20), 132.42 (C-2), 136.51 (C-3), 139.24 (C-15), 150.46 (C-18), 163.94 (C-14). Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.62; H, 7.39; N, 4.10.

3.3.7. (−)-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]hex-2-en-2-yl]methyl *p*-nitrobenzoate 16. $[\alpha]_D^{20} = -51.5$ (*c* 5.10, $CHCl_3$); mp = 88–90 °C; IR (KBr, cm^{-1}): 3414(m), 3015(w), 2958(m), 1714(s), 1528(s), 1269(s), 1099(s), 726(m); ^1H NMR ($CDCl_3$): 0.75 (s, 3H at C-7 or C-8), 1.04 (s, 3H at C-7 or C-8), 1.22–1.28 (m, 1H at C-5), 1.74 (s, 3H at C-9), 1.78 (dd, $J = 6.9$, 2.9 Hz, 1H at C-1), 2.08 (d, $J = 6.0$ Hz, 1H at C-4), 2.56 (dd, $J = 18.1$ Hz, 7.6 Hz, 1H at C-4), 4.91 (s, 2H at C-10), 8.21–8.26 (m 4H at C-13, C-14, C-16 and C-17); ^{13}C NMR ($CDCl_3$): 13.02 (C-7 or C-8), 13.42 (C-5), 20.66 (C-6), 26.27 (C-1), 26.61 (C-7 or C-8), 38.01 (C-4), 38.99 (C-9), 62.20 (C-10), 123.53 (C-14 and C-16), 129.74 (C-12), 130.65 (C-13 and C-17), 136.05 (C-3), 140.08 (C-2), 150.51 (C-15), 164.69 (C-11). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.49; H, 6.45; N, 4.68.

3.4. General procedure for the oxidation of alcohols to ketones

The commercially available (Aldrich) Dess–Martin periodinane (1.24 mmol) was added to the appropriate alcohol (*RS*)-**4**–(*RS*)-**6** (1.03 mmol) in anhydrous dichloromethane (2.5 ml). The reaction was stirred at room temperature for 30 min. Then a 1:1 mixture of saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ was added and the reaction stirred until a clear mixture was obtained. The aqueous phase was extracted with CH_2Cl_2 three times and the combined organic phases washed with brine and dried with $MgSO_4$. The crude products **11** and **12** were purified by column chromatography (eluent: hexane–diethyl ether 30:1). The crude product **10** was used in the next reaction.

3.4.1. (−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]hex-2-en-2-yo]butan-1-one 11. $[\alpha]_D^{25} = -85.4$ (*c* 0.96, $CHCl_3$); IR (film, cm^{-1}): 3022(m), 2960(s), 1678(s), 1607(s), 1455(m), 1375(m), 1179(m); ^1H NMR ($CDCl_3$): 0.77 (s, 3H at C-7 or C-8), 0.92 (t, $J = 7.4$ Hz, 3H at C-13), 1.08 (s, 3H at C-7 or C-8), 1.21 (t, $J = 7.3$ Hz, 1H at C-5), 1.55–1.67 (m, 2H at C-12), 1.93 (d, $J = 6.8$ Hz, 1H at C-1), 1.98 (s, 3H at C-9), 2.14 (d, $J = 20.7$ Hz, 1H at C-4), 2.41–2.51 (m, 2H at C-11), 2.59 (dd, $J = 20.7$, 9.0 Hz, 1H at C-4); ^{13}C NMR ($CDCl_3$): 13.24 (C-7 or C-8), 13.87 (C-7 or C-8), 17.06 (C-12) 20.13 (C-6), 25.84 (C-5), 26.15 (C-9), 38.77 (C-1), 39.96 (C-4), 44.39 (C-11), 135.83 (C-3), 153.75 (C-2), 200.60 (C-10). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.89; H, 10.59.

3.4.2. (−)-1-[(1*R*,5*S*)-3,6,6-Trimethylbicyclo[3.1.0]hex-2-en-2-yl]-2-methylpropan-1-one 12. $[\alpha]_D^{25} = -120.0$ (*c* 0.90, $CHCl_3$); IR (film, cm^{-1}): 3021(m), 2970(s), 1674(s), 1596(s), 1466(m), 1381(m), 971(m); ^1H NMR ($CDCl_3$): 0.73 (s, 3H at C-7 or C-8), 0.98 (s, 3H at C-7 or C-8), 1.01 (d, $J = 2.1$ Hz, 3H at C-12 or C-13), 1.03 (d, $J = 2.7$ Hz, 3H at C-12 or C-13), 1.16 (t, $J = 5.5$, Hz, 1H at C-5), 1.94 (s, 3H at C-9), 1.91 (d, $J = 2.8$ Hz, 1H at C-1), 2.89 (m, 1H at C-11), 2.10 (d, $J = 19.7$ Hz, 1H at C-4); 2.58 (dd, $J = 18.8$, 7.9 Hz, 1H at C-4); ^{13}C NMR ($CDCl_3$): 13.33 (C-7 or C-8), 14.21 (C-7 or C-8), 15.92 (C-13), 18.07 (C-12), 20.19 (C-6), 26.34 (C-9), 25.78 (C-5), 38.12 (C-1), 38.62 (C-11), 40.00 (C-4), 135.00 (C-3), 155.27 (C-2), 200.84 (C-10). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.91; H, 10.56.

3.5. Synthesis of (−)-1-[(1*R*,5*S*)-3,6,6-trimethylbicyclo-[3.1.0]hex-2-en-2-yl]but-2-en-1-one 13

DBU (0.05 mmol) was added to the solution of the crude ketone **10** (0.16 mmol) in anhydrous dichloromethane (3 ml). The reaction mixture was stirred overnight, saturated aqueous $CuSO_4$ then added and the mixture extracted with CH_2Cl_2 three times. The combined organic layers were washed with brine and dried over $MgSO_4$. The crude product **13** was purified by column chromatography (eluent: hexane–diethyl ether 30:1). $[\alpha]_D^{25} = -38.4$ (*c* 0.50, $CHCl_3$); IR (film, cm^{-1}): 3025(m), 2971(s), 1668(s), 1585(s), 1458(m), 1379(m), 970(m); ^1H NMR ($CDCl_3$): 0.82 (s, 3H at C-8 or C-9), 0.89–0.94 (m, 1H at C-5), 1.10 (s, 3H at C8 or C-9), 1.18–1.28 (m, 1H at C-1), 1.91 (dd, $J = 6.9$, 1.4 Hz, 3H at C-13), 1.97 (s, 3H at C-9), 2.17 (d, $J = 19.5$ Hz, 1H at C-4), 2.68 (dd, $J = 19.5$, 7.8 Hz, 1H at C-4), 6.42 (dd, $J = 15.4$, 1.5 Hz, 1H at C-11), 6.84–6.96 (m, 1H at C-12). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.88; H, 9.74.

3.6. Synthesis of (−)-4-[(1*R*,5*S*)-3,6,6-trimethylbicyclo-[3.1.0]hex-2-en-2-yl]but-3-en-2-one 14

Diethyl (2-oxopropyl)phosphonate (39.92 mmol) was added to the pulverized $Ba(OH)_2{\cdot}8H_2O$ (8.02 mmol) (earlier warmed at 130 °C for 4 h) in tetrahydrofuran (130 ml). The suspension was stirred at room temperature for 30 min. Next the solution of aldehyde **3** (13.34 mmol) in THF–H_2O 40:1 (140 ml) was added and stirring continued at room temperature for 15 h. The reaction mixture was diluted with dichloromethane and washed with water. The aqueous layer was extracted three times with CH_2Cl_2 and the combined organic phases washed with saturated aqueous $NaHCO_3$, brine and dried over $MgSO_4$. The crude product **13** was purified by column chromatography (eluent: hexane–diethyl ether 30:1). $[\alpha]_D^{25} = -52.5$ (*c* 1.77, $CHCl_3$); IR (film, cm^{-1}): 3021(m), 2944(s), 1685(vs), 1588(vs), 1360(s), 1279(s), 1169(m), 969(m). ^1H NMR ($CDCl_3$): 0.69 (s, 3H at C-7 or C-8), 1.09 (s, 3H at C-7 or C-8), 1.28 (t, $J = 6.7$ Hz, 1H at C-5), 1.81-1-83 (m, 1H at C-1), 1.84 (s, 3H at C-9), 2.17 (d, $J = 19.7$ Hz, 1H at C-4), 2.31 (s, 3H at C-13), 2.65 (dd, $J = 19.9$, 7.5 Hz, 1H at C-4), 6.17 (d, $J = 15.6$ Hz, 1H at C-11), 7.42 (d, $J = 15.6$ Hz, 1H at C-10); ^{13}C NMR ($CDCl_3$): 13.05 (C-7 or C-8), 13.94 (C-5), 20.43 (C-6), 26.27 (C-7 or C-8), 27.37 (C-13), 36.56 (C-9), 39.60 (C-4), 127.20 (C-11), 134.39 (C-3), 137.34 (C-10), 150.24 (C-2), 199.28 (C-12). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.84; H, 9.76.

3.7. Synthesis of (−)-[(1*R*,5*S*)-3,6,6-trimethylbicyclo-[3.1.0]hex-2-en-2-yl]methanol 15

Aldehyde **3** (0.12 mol) in anhydrous diethyl ether (180 ml) was added to the suspension of lithium aluminium

hydride (0.14 mol) in anhydrous diethyl ether (60 ml). The reaction mixture was stirred until the TLC monitoring did not show the presence of the substrate, and then quenched with distilled water. The precipitate was filtered off, the organic layer collected and the water layer extracted three times with diethyl ether. The combined organic layers were dried over $MgSO_4$, the crude product converted to *p*-nitrobenzoate **16** and after recrystallization (the procedure and spectroscopic data described above) compound **16** (0.05 mol) was diluted in methanol (120 ml) and potassium hydroxide (0.06 mol) added. The reaction mixture was stirred overnight and after TLC analysis did not show the presence of *p*-nitrobenzoate **16**, the solvent was removed. Next water was added and the aqueous phase extracted three times with diethyl ether and the organic phase dried over $MgSO_4$. After removing the solvent the alcohol **15** was 94% pure (GC). $[\alpha]_D^{20} = -208.4$ (*c* 5.10, $CHCl_3$); bp = 72–73 °C/0.5 mmHg; $n_D^{20} = 1.4878$; IR (film, cm^{-1}): 3334(s), 3019(m), 2876(vs), 1445(m), 1373(m), 997(s); ^1H NMR ($CDCl_3$): 0.77 (s, 3H at C-7), 1.05 (s, 3H at C-8), 1.21 (td, $J = 7.2$, 1.2 Hz, 1H at C-5), 1.63 (s, 3H at C-9), 1.75 (dd, $J = 6.0$, 2.8 Hz, 1H at C-1), 2.01 (d, $J = 18.1$ Hz, 1H at C-4), 2.49 (dd, $J = 17.9$, 7.6 Hz, 1H at C-4), 4.14 (s, 2H at C-10); ^{13}C NMR ($CDCl_3$): 13.06 (C-7 or C-8), 13.46 (C-5), 20.60 (C-6), 26.56 (C-7 or C-8), 31.77 (C-9), 38.00 (C-4), 38.59 (C-1), 59.18 (C-10), 136.26 (C-3), 137.78 (C-2). Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.63; H, 10.67.

3.8. Synthesis of ethyl (+)-[(1*R*,5*S*)-3,6,6-trimethyl-2-mehtylenebicyclo[3.1.0]hex-3-yl]acetate 18

The mixture of alcohol (0.05 mol), triethyl orthoacetate (0.04 mol) and propionic acid (one drop) was heated at 138 °C until TLC analysis did not show the presence of the substrate **15**. The unreacted orthoacetate was then distilled off and the crude product **18** was purified by column chromatography (eluent: hexane–diethyl ether from 100:1 to 50:1). $[\alpha]_D^{20} = +151.2$ (*c* 5.50, $CHCl_3$); bp = 70 °C/0.5 mmHg; $n_D^{20} = 1.4697$; IR (film, cm^{-1}): 3076(w), 2957(s), 1735(vs), 1646(m), 1452(m), 1367(m), 1185(s). ^1H NMR ($CDCl_3$): 0.85 (s, 3H at C-7 or C-8), 1.03 (s, 3H at C-7 or C-8), 1.12 (s, 3H at C-9), 1.26 (t, $J = 7.1$ Hz, 3H at C-14), 1.29–1.36 (m, 1H at C-5), 1.58–1.68 (m, 1H at C-1), 1.80 (d, $J = 6.7$, 1H at C-4), 2.11 (dd, $J = 14.5$, 7.5 Hz, 1H at C-4), 2.24 and 2.37 (AB, 2d, $J = 13.1$ Hz, 2H at C-11), 4.1 (q, $J = 7.1$ Hz, 2H at C-13), 4.76 (s, 1H at C-10), 4.86 (s, 1H at C-10); ^{13}C NMR ($CDCl_3$): 14.31 (C-7 or C-8), 16.23 (C-5), 22.53 (C-7 or C-8), 24.42 (C-6), 27.09 (C-14), 29.35 (C-9), 36.69 (C-4), 37.51 (C-1), 48.17 (C-11), 53.18 (C-3), 59.95 (C-13), 106.02 (C-10), 157.84 (C-2), 171.75 (C-12). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.37; H, 10.01.

3.9. Synthesis of (+)-2-[(1*R*,5*S*)-3,6,6-trimethylbicyclo-[3.1.0]hex-3-yl]ethanol 19

The procedure was analogous as in the reduction of aldehyde **3** to alcohol **15**. The crude product **19** was purified by column chromatography (eluent: hexane–acetone 10:1). $[\alpha]_D^{20} = +251.5$ (*c* 2.20, $CHCl_3$); IR (film, cm^{-1}): 3322(vb), 3074(v), 3015(v), 1644(m), 1054(s); ^1H NMR ($CDCl_3$): 0.84 (s, 3H at C-7), 1.00 (s, 3H at C-8), 1.02 (s, 3H at C-9), 1.25–1.34 (m, 2H at C-1 and C-5), 1.47 (s, 1H at –OH), 1.52–1.62 (m, 1H at C-4), 1.70–1.85 (m, 2H at C-4 and 2H at C-11), 3.64–3.79 (m, 2H at C-12), 4.76 (s, 1H at C-10), 4.88 (s, 1H at C-10); ^{13}C NMR ($CDCl_3$): 16.56 (C-5), 23.46 (C-7 or C-8), 24.25 (C-6), 27.09 (C-7 or C-8), 29.70 (C-9), 38.22 (C-1), 38.31 (C-4), 47.50 (C-11), 52.47 (C-3), 60.33 (C-12), 105.61 (C-10), 158.92 (C-2). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.65; H, 11.26.

3.10. General procedure for the esterification of alcohols to acetates

Acetyl chloride (0.2 ml) was added dropwise to a cooled (water-ice bath) mixture of the appropriate alcohol (3.28 mmol) and anhydrous pyridine (0.5 ml) in anhydrous diethyl ether (15 ml). The reaction was stirred overnight, then diluted with diethyl ether and washed with an HCl solution. The ethereal solution was then collected. The product was additionally extracted from the aqueous layer with diethyl ether. The combined organic layers were washed with a 5% H_2SO_4 solution, saturated $NaHCO_3$ solution, brine and dried ($MgSO_4$). The crude product was purified by vacuum column chromatography (eluent: hexane–acetone from 100:1 to 70:1).

3.10.1. Methyl (−)-[(1*R*,5*S*)-3,6,6-trimethylbicyclo[3.1.0]-hex-2-en-2-yl]acetate 17. $[\alpha]_D^{20} = -111.6$ (*c* 3.15, $CHCl_3$); IR (film, cm^{-1}): 3021(v), 2942(vb), 1742(vs), 1445(m), 1234(vb), 956(v); ^1H NMR ($CDCl_3$): 0.74 (s, 3H at C-7), 1.04 (d, $J = 7.4$ Hz, 2H at C-4), 1.21 (td, $J = 17.3$, 1.9 Hz, 1H at C-5), 1.65 (s, 3H at C-9), 1.71 (dd, $J = 6.8$, 2.7 Hz, 1H at C-1), 2.06 (s, 3H at C-12), 2.51 (dd, $J = 18.1$, 7.6 Hz, 2H at C-4), 4.59 (s, 2H at C-10). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.97; H, 9.52.

3.10.2. Ethyl (+)-2-[(1*R*,3*S*,5*S*)-3,6,6-trimethyl-2-methylene-bicyclo[3.1.0]hex-3-yl]acetate 20. $[\alpha]_D^{20} = +243.3$ (*c* 1.95, $CHCl_3$); IR (film, cm^{-1}): 3322(vb), 3074(v), 3015(m), 1453(m), 1239(vs), 1031(m); ^1H NMR ($CDCl_3$): 0.84 (s, 3H at C-7), 1.00 (s, 3H at C-8), 1.02 (s, 3H at C-9), 1.25–1.35 (m, 2H at C-1 and C-5), 1.57–1.87 (m, 4H at C-4 and C-11), 2.03 (s, 3H at C-14), 4.03–4.20 (m, 2H at C-12), 4.72 (s, 1H at C-10), 4.89 (s, 1H at C-10); ^{13}C NMR ($CDCl_3$): 16.33 (C-5), 21.08 (C-7 or C-8), 23.35 (C-4), 24.28 (C-6), 27.06 (C-7 or C-8), 29.64 (C-9), 37.99 (C-4), 38.18 (C-1), 42.89 (C-11), 52.24 (C-3), 62.32 (C-12), 105.90 (C-10), 157.72 (C-2), 171.16 (C-13). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.31; H, 10.04.

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