Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 1544–1548

Chiral synthons from α-pinene: enantioselective syntheses of bicyclo[3.3.0] and [3.2.1]octanones

Adusumilli Srikrishna,* B. Beeraiah and Gedo Satyanarayana

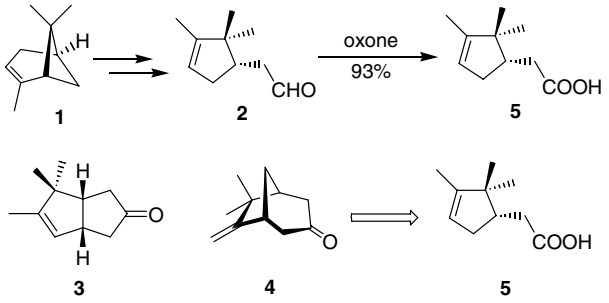
Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

Received 19 April 2006; accepted 29 May 2006

Abstract—Enantioselective syntheses of bicyclo[3.3.0]octan-3-one, bicyclo[3.2.1]octan-3-one and bicyclo[3.2.1]octan-2-one derivatives were accomplished by employing a chiron based approach, using intramolecular rhodium carbenoid C–H insertion, acid catalysed cyclisation of α-diazo ketone and intramolecular type II carbonyl ene reactions as key steps.

1. Introduction

Monoterpenes are widely used as chiral auxiliaries, but their potential as chiral synthons has not been properly exploited.[1] The overwhelming emphasis on carbohydrates as chirons[2] during the 1980s and 1990s in natural product synthesis has somewhat marginalised the importance of the abundantly available monoterpenes as chiral building blocks for the synthesis of natural products in their optically active form. This has come about despite the fact that monoterpenes are inexpensive, readily available (in several cases, in both enantiomeric forms unlike carbohydrates and amino acids) and are endowed with only one or two stereogenic centres with modest functionality, which means that it does not require recourse to wasteful manoeuvres to dispense with excess chirality or functionality as in some carbohydrate based approaches. More interestingly, terpenes can be readily restructured into cyclic and acyclic fragments that can be directly incorporated into carbocyclic frameworks of complex target molecules. Utilization of the readily and abundantly available chiral natural products, such as monoterpenes, is very advantageous in organic synthesis, as the derived compounds can be obtained in enatiopure forms. Among the monoterpenes, pinenes are relatively less exploited as chirons in total synthesis.[1] As α-pinene **1** is one of the most abundantly available monoterpenes, its conversion to a variety of enantiopure compounds, which have the potential to be used as chirons in the synthesis of complex natural products and their analogues as well as hybrid systems, enhances the repertoire of synthetic chemists in many ways, such as drug development. The presence of bicyclo[3.3.0]octane (diquinane) and bicyclo[3.2.1]octanes as part structures is frequently encountered in a variety of natural products, in particular terpenoids.[3] Herein, we report the enantioselective generation of some bicyclic octanes starting from camphelenaldehyde **2**, which is readily available from α-pinene **1** in two steps via the corresponding epoxide.[4]



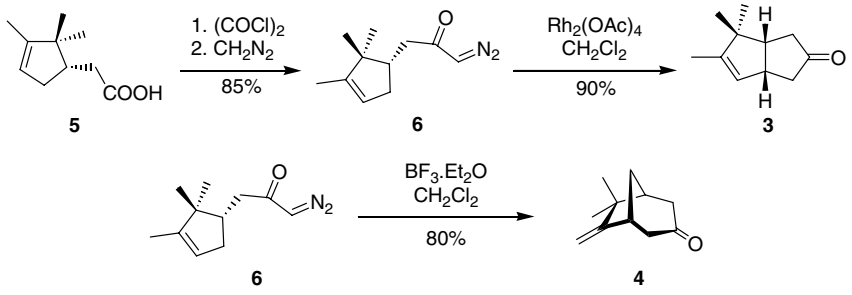
2. Results and discussion

Initially, the generation of bicyclo[3.3.0]octanone **3** and bicyclo[3.2.1]octanone **4** from aldehyde **2** via acid **5** was investigated. Regio- and stereoselective insertion of α-keto rhodium carbenoids into a γ-CH sigma bond is a convenient reaction for the generation of cyclopentanones from acids, via the corresponding α-diazo ketones.[5] For the generation of bicyclo[3.3.0]octanone **4**, a regio- and

* Corresponding author. Tel.: +91 80 22932215; fax: +91 80 23600683; e-mail: ask@orgchem.iisc.ernet.in

0957-4166/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2006.05.028

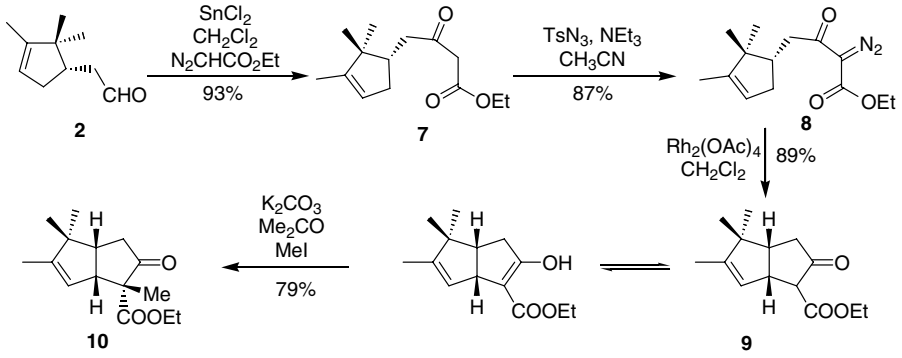
stereospecific intramolecular rhodium carbenoid CH insertion strategy was investigated via diazo ketone **6**. Accordingly, the oxidation of aldehyde **2** with oxone in DMF at room temperature generated acid[6] **5** in 93% yield. Treatment of acid **5** with oxalyl chloride in benzene at room temperature, followed by the reaction of the resultant acid chloride with an excess of diazomethane in ether, generated diazo ketone **6**. Treatment of diazo ketone **6** with a catalytic amount of rhodium acetate in refluxing methylene chloride cleanly furnished bicyclo[3.3.0]octanone **3** via the regio- and stereospecific insertion of an intermediate rhodium carbenoid into the allylic CH bond. The structure of the bicyclic ketone was established from its spectral data. In particular, the presence of a strong carbonyl absorption band at 1741 cm^{-1} in the IR spectrum and presence of a quaternary carbon resonance at δ 219.2 ppm in the eleven lines (three quaternary carbons, three methines, two methylenes and three methyl carbons) ^{13}C NMR spectrum clearly established the presence of cyclopentanone moiety.

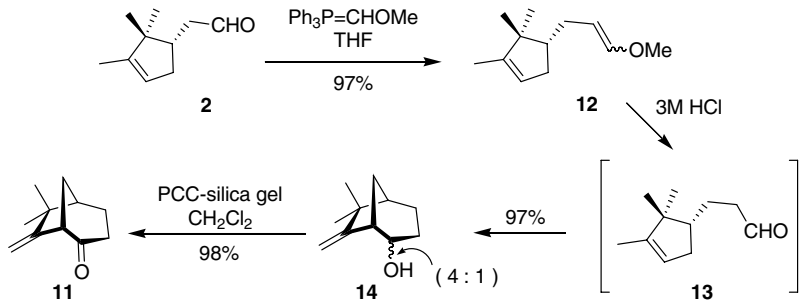


After successfully accomplishing the synthesis of diquinane **3**, attention was focused on the synthesis of a bicyclo[3.2.1]octane, and acid catalysed cyclisation reaction of the diazo ketone **6** was considered. Consequently, the reaction of a 0.1 M methylene chloride solution of diazo ketone **6** with boron trifluoride etherate at ice cold temperature for 10 min furnished bicyclo[3.2.1]octanone **4** in 80% yield, whose structure was established from its spectral data. In particular, the presence of a strong carbonyl absorption band at 1713 cm^{-1} in the IR spectrum and presence of a quaternary carbon resonance at δ 210.2 ppm in the 11 lines (three quaternary carbons, two methines, four methylenes and two methyl carbons) ^{13}C NMR spectrum clearly established the presence of the cyclohexanone moiety. It was further supported by the presence of two singlets at δ 4.84 and 4.94 ppm, due to the *exo*-methylene protons, in the ^{1}H NMR spectrum and at 106.3 ppm, due to the olefinic methylene carbon, in the ^{13}C NMR spectrum.

Since it is not easy to carry out the regio controlled reactions on the two methylenes α to the ketone group in diquinane **3**, and also in order to develop more functionalised diquinanes, intramolecular rhodium carbenoid insertion reaction of the α-diazo ester derived from the β-keto ester **7** was also investigated. A Lewis acid mediated coupling[7] of aldehyde **2** with ethyl diazo acetate was chosen for the generation of β-keto ester **7**. Thus, reaction of aldehyde **2** with ethyl diazoacetate in the presence of a catalytic amount of stannous chloride in methylene chloride at room temperature furnished β-keto ester **7** in 93% yield. β-Keto ester **7** was then converted into α-diazo-β-keto ester **8** via diazo transfer reaction with *p*-toluenesulfonyl azide in acetonitrile in the presence of triethylamine. Treatment of diazo ester **8** with a catalytic amount of rhodium acetate in refluxing methylene chloride furnished diquinane **9** in 90% yield, which was found to exist as a mixture of keto and enol forms. In order to generate a single isomer, alkylation was carried out using potassium carbonate and methyl iodide in refluxing acetone to transform diquinane **9** into β-keto ester **10**, whose structure was established from its spectral data, in particular the IR, ^{1}H and ^{13}C NMR (given in Section 4).

After successfully accomplishing the synthesis of bicyclooctanones **3**, **4** and **10**, generation of an isomeric bicyclo[3.2.1]octanone **11** was investigated via the homologation of aldehyde **2**, followed by an intramolecular type II





carbonyl ene reaction.[8] Accordingly, the Wittig reaction of aldehyde **2** with methoxymethylenetriphenylphosphorane[9] in THF furnished a 1:1 *E*,*Z*-mixture of enol ether **12** in a near quantitative yield. The attempted hydrolysis of enol ether **12** to generate aldehyde **13**, directly furnished a 4:1 diastereomeric mixture of homoallyl alcohol **14**, obviously via the intramolecular ene reaction of the initially generated aldehyde **13**, in a near quantitative yield. Oxidation of the mixture of alcohols **14** with pyridinium chlorochromate (PCC) and silica gel in methylene chloride at room temperature furnished bicyclo[3.2.1]octanone **11** in quantitative yield, whose structure was established from its spectral data. In particular, the presence of a strong carbonyl absorption band at 1716 cm^{-1} in the IR spectrum and presence of a quaternary carbon resonance at δ 208.3 ppm in the ^{13}C NMR spectrum clearly established the presence of a cyclohexanone moiety. This was further supported by the presence of two singlets at δ 4.91 and 5.00 ppm, due to the *exo*-methylene protons, in the ^{1}H NMR spectrum and at 106.7 ppm, due to the olefinic methylene carbon in the ^{13}C NMR spectrum.

3. Conclusion

In conclusion, we have developed convenient chiron based enantioselective methods for the synthesis of bicyclo[3.3.0] and [3.2.1]octanes by employing intramolecular rhodium carbenoid C–H insertion, intramolecular acid catalysed diazo ketone cyclisation and intramolecular type II carbonyl ene reaction as key steps. Further elaboration of these and related chiral synthons in the synthesis of diterpenoids is currently in progress.

4. Experimental

Melting points were recorded using Mettler FP1 melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a JNM λ-300 spectrometer. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^{1}H) or the central line (77.0 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses. Low-resolution mass spectra were recorded using Shimadzu QP-5050A GCMS instrument using direct inlet mode. Relative intensities are given in parentheses. High-resolution mass spectra were recorded using Micromass Q-TOF micromass spectrometer using electrospray ionisation. Optical rotations were measured using a Jasco DIP-370 digital polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}.

4.1. (1*R*,5*R*)-7,8,8-Trimethylbicyclo[3.3.0]oct-6-en-3-one 3

To the magnetically stirred, ice-cold solution of aldehyde[4] **2** (500 mg, 3.29 mmol) in DMF (5 ml) was added oxone (2.02 g, 3.29 mmol) and stirred for 4 h at room temperature. Filtration using a sintered funnel furnished acid **5** (515 mg, 93%).[5]

To a magnetically stirred solution of acid **5** (300 mg, 1.8 mmol) in dry benzene (1 ml) was added oxalyl chloride (0.5 ml, 5.4 mmol) and stirred for 2 h at room temperature. Evaporation of the excess oxalyl chloride and solvent under reduced pressure gave the acid chloride, which was taken in dry ether (5 ml) and added to a cold, magnetically stirred ether solution of diazomethane (excess, prepared from *N*-nitroso-*N*-methylurea (400 mg, 7.14 mmol), 20 ml of 60% aqueous KOH solution and 10 ml of ether) and the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 2 h. Careful evaporation of the excess diazomethane and solvent on a hot water bath, followed by purification of the residue over a silica gel column using CH_2Cl_2 as eluent, furnished diazoketone **6** (291 mg, 85%) as yellow oil. [IR (neat): ν_{max}/cm^{-1}: 2102, 1637]. To a magnetically stirred and refluxed solution of $Rh_2(OAc)_4{\cdot}2H_2O$ (3 mg) in dry CH_2Cl_2 (5 ml) was added a solution of diazoketone **6** (57 mg, 0.3 mmol) in dry CH_2Cl_2 (25 ml, 0.01 M) dropwise over a period of 50 min. Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:10) as eluent furnished the bicyclic ketone **3** (46 mg, 90%) as an oil. $[\alpha]_D^{25} = -42.5$ (*c* 2.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 1741; ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 5.14 (1H, br s, H-6), 3.40–3.25 (1H, m, H-5), 2.55 (1H, q, *J* 8.4 Hz, H-1), 2.36 (1H, dd, *J* 18.3 and 9.0 Hz), 2.23–2.10 (3H, m), 1.62 (3H, s, olefinic CH_3), 1.06 (3H, s) and 0.97 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 219.2 (C, C=O), 147.8 (C, C-7), 126.0 (CH, C-6), 50.8 (CH), 48.1 (C, C-8), 42.83 (CH), 42.78 (CH_2), 39.9 (CH_2), 26.8 (CH_3), 22.3 (CH_3), 12.5 (CH_3); HRMS: *m*/*z* calcd for $C_{11}H_{16}ONa$ (M+Na): 187.1099; found: 187.1104.

4.2. (1*S*,5*R*)-7,7-Dimethyl-6-methylenebicyclo[3.2.1]octan-3-one 4

To a magnetically stirred, ice-cold solution of diazo ketone **6** (55 mg, 0.29 mmol) in dry CH_2Cl_2 (15 ml, 0.1 M) was added $BF_3{\cdot}Et_2O$ (0.1 ml) and stirred for 10 min at the same temperature. This was then quenched with saturated aqueous $NaHCO_3$ solution (10 ml) and extracted with CH_2Cl_2 (2×5 ml). The combined organic extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:10) as eluent furnished the bicyclic ketone **4** (40 mg, 80%) as an oil. $[\alpha]_D^{26} = -30.0$ (*c* 3.6, $CHCl_3$); IR (neat): ν_{max}/cm^{-1}: 1713, 886; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 4.94 (1H, s) and 4.84 (1H, s) [C=CH_2], 3.03–2.95 (1H, br s, H-5), 2.60 (1H, dq, *J* 16.8 and 2.4 Hz), 2.47 (1H, dd, *J* 15.9 and 3.9 Hz), 2.40–2.15 (3H, m), 2.12–2.05 (1H, br s), 1.73 (1H, d, *J* 12.0 Hz), 1.10 (3H, s) and 1.07 (3H, s) [$2 \times$ *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 210.2 (C, C=O), 162.7 (C, C-6), 106.3 (CH_2, C=*C*H_2), 51.6 (CH_2), 46.3 (CH_2), 45.4 (CH), 44.7 (C, C-7), 42.6 (CH), 35.2 (CH_2), 31.6 (CH_3) and 24.8 (CH_3) [$2 \times$ *tert*-CH_3]; HRMS: *m*/*z* calcd for $C_{11}H_{16}ONa$ (M+Na) 187.1099; found: 187.1092.

4.3. Ethyl 4-[(1*S*)-2,2,3-trimethylcyclopent-3-enyl]-3-oxobutanoate 7

To a magnetically stirred solution of aldehyde **2** (200 mg, 1.32 mmol) and ethyl diazoacetate (0.25 ml, 2.4 mmol) in methylene chloride was added $SnCl_2{\cdot}2H_2O$ (30 mg, 0.13 mmol) in portions over a period of 50 min and stirred for 3 h at room temperature. Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:10) as eluent furnished the β-keto ester **7** (292 mg, 93%) as an oil. $[\alpha]_D^{25} = -1.7$ (*c* 14, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 1746, 1717, 1649; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 5.20 (1H, s, *H*C=C), 4.22–4.14 (2H, m, OCH_2CH$_3$), 3.42 (2H, s, H-2), 2.70–2.20 (4H, m), 1.87–1.70 (1H, m), 1.60 (3H, s, olefinic CH_3), 1.29 (3H, t, *J* 7.2 Hz, OCH$_2$CH_3), 0.99 (3H, s) and 0.77 (3H, s) [$2 \times$ *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 202.2 (C, C=O), 167.0 (C, OC=O), 147.5 (C, C-3′), 121.9 (CH, C-4′), 61.2 (CH_2, O*C*H$_2$CH$_3$), 49.5 (CH_2, C-2), 46.8 (C, C-2′), 45.0 (CH_2), 44.0 (CH), 35.6 (CH_2), 25.6 (CH_3), 20.1 (CH_3), 14.2 (CH_3, OCH$_2$*C*H$_3$), 12.7 (CH_3); HRMS: *m*/*z* calcd for $C_{14}H_{22}O_3Na$ (M+Na): 261.1467; found: 261.1468.

4.4. Ethyl (1*S*,2*R*,5*R*)-2,6,6,7-tetramethyl-3-oxobicyclo-[3.3.0]cyclopent-7-ene-2-carboxylate 10

To a magnetically stirred solution of β-keto ester **7** (267 mg, 0.89 mmol) in acetonitrile (1 ml) were added tosyl azide (133 mg, 0.8 mmol) and triethylamine (0.12 ml, 0.89 mmol) and stirred at room temperature for 4 h. The solvent was evaporated and the residue was purified over a neutral alumina column using ethyl acetate–hexane (1:20) as eluent to furnish the α-diazo-β-keto ester **8** (235 mg, 87%) as a yellow solid. IR (neat): ν_{max}/cm^{-1} 2133, 1718, 1656, 1464. Further elution of the column with ethyl acetate–hexane (1:10) furnished the β-keto ester (23 mg) as an oil.

To a refluxed suspension of $Rh_2(OAc)_4{\cdot}2H_2O$ (1 mg) in methylene chloride (5 ml), was added a solution of the α-diazo-β-keto ester **8** (50 mg, 0.19 mmol) in methylene chloride (15 ml, 0.01 M) over 45 min. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished β-keto ester **9** (40 mg, 89%) as an oil. IR (neat): ν_{max}/cm^{-1} 3437, 1753, 1725.

To a solution of β-keto ester **9** (200 mg, 0.85 mmol) in acetone (5 ml) were added K_2CO_3 (1.17 g, 8.5 mmol) and methyl iodide (0.53 ml, 8.5 mmol) and refluxed for 4 h. It was cooled to room temperature, diluted with water (5 ml) and extracted with ether (3×5 ml). The combined ether extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the keto ester **10** (168 mg, 79%) as oil. $[\alpha]_D^{26} = -31.7$ (*c* 0.6, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 1749, 1731; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 5.01 (1H, s, H-8), 4.30–4.10 (2H, m, OCH_2CH$_3$), 3.21–3.15 (1H, m, H-1), 2.50–2.38 (2H, m, H-4), 2.32–2.21 (1H, m), 1.62 (3H, s, olefinic CH_3), 1.32 (3H, s, *tert*-CH_3), 1.26 (3H, t, *J* 6.9 Hz, OCH$_2$CH_3), 1.05 (3H, s) and 1.02 (3H, s) [$2 \times$ *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 213.8 (C, C=O), 171.4 (C, OC=O), 147.7 (C, C-7), 122.6 (CH, C-8), 60.7 (CH_2, O*C*H$_2$CH$_3$), 58.4 (C, C-2), 56.2 (CH, C-1), 47.9 (CH, C-5), 47.7 (C, C-6), 40.6 (CH_2, C-4), 26.6 (CH_3), 21.7 (CH_3), 21.2 (CH_3), 14.4 (CH_3), 12.6 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{22}O_3Na$ (M+Na): 273.1468; found: 273.1471.

4.5. (4*S*)-2,3,3-Trimethyl-4-[3-methoxyprop-2-enyl]cyclopentene 12

To a magnetically stirred solution of freshly prepared ^{t}AmOK [prepared from potassium (170 mg, 4.34 mmol) and ^{t}AmOH (5 ml), followed by evaporation of ^{t}AmOH under reduced pressure] in dry THF (5 ml) was added methoxymethyltriphenylphosphonium chloride (2.03 mg, 5.92 mmol) and the resulting wine red colored solution stirred for 25 min at room temperature. A solution of aldehyde **2** (300 mg, 1.97 mmol) in dry THF (2 ml) was added at 0 °C to the dark red coloured solution of methoxymethylenetriphenylphosphorane and stirred at RT for 30 min. Saturated aqueous NH_4Cl solution (5 ml) was added to the reaction mixture and extracted with ether (2×10 ml). The combined organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a neutral alumina column using hexane as eluent furnished a 1:1 *E*/*Z* mixture of enol ether **12** (345 mg, 97%) as an oil. IR (neat): ν_{max}/cm^{-1} 1655, 1208, 1110; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$, 1:1 mixture of *E*/*Z* isomers): δ 6.26 (d, *J* 12.3 Hz) and 5.82 (dt, *J* 7.2 and 0.6 Hz) [1H, HC=C*H*OMe], 5.18 (1H, br s, H-1), 4.65 (dt, *J* 12.3 and 6.9 Hz) and 4.30 (q, *J* 7.2 Hz) [1H, *H*C=CHOMe], 3.56 and 3.47 (3H, s, OCH_3), 2.30–1.90 (3H, m), 1.90–1.65 (2H, m), 1.59 and 1.58 (3H, s, olefinic CH_3), 0.99 (3H, s,

tert-CH_3), 0.80 and 0.78 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 148.3 (C), 147.2 and 146.1 (CH), 122.0 and 121.9 (CH), 106.6 and 102.3 (CH), 59.2 and 55.5 (CH), 51.3 and 50.5 (CH_3), 46.8 and 46.7 (C), 35.7 and 35.6 (CH_2), 28.5 and 24.6 (CH_2), 26.2 and 26.1 (CH_3), 19.9 and 19.8 (CH_3), 12.8 and 12.7 (CH_3).

4.6. (1*S*,5*R*)-6,6-Dimethyl-7-methylenebicyclo[3.2.1]octan-2-ol 14

A solution of enol ether **12** (315 mg, 1.75 mmol) in THF (10 ml) and 3 *N* HCl (5 ml) was magnetically stirred for 3 h at room temperature. The reaction mixture was then diluted with water (5 ml) and extracted with ether (2 × 10 ml). The combined organic layer was washed with aqueous $NaHCO_3$ solution and brine, and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:20) as eluent furnished a 4:1 epimeric mixture of the bicyclic alcohol **14** (297 mg, 97%) as a white solid. Mp: 90–92 °C; $[\alpha]_D^{27} = -6.4$ (*c* 1.1, $CHCl_3$); IR (neat): ν_{max}/cm^{-1}: 3383, 1652, 1029, 885; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 4.88 and 4.80 (1H, s), 4.85 and 4.78 (1H, s), 3.66–3.56 and 3.77–3.72 (1H, m), 2.65 (1H, br s), 2.20–1.25 (8H, m), 1.14 and 1.19 (3H, s), 1.07 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$, peaks due to the major isomer): δ 161.0 (C), 104.2 (CH_2), 71.8 (CH), 50.2 (CH), 44.3 (CH), 43.1 (C), 34.8 (CH_2), 32.4 (CH_3), 29.7 (CH_2), 26.9 (CH_2), 21.6 (CH_3); HRMS: *m*/*z* calcd for $C_{11}H_{19}O$ (M+H): 167.1436; found: 167.1445.

4.7. (1*S*,5*R*)-6,6-Dimethyl-7-methylenebicyclo[3.2.1]octan-2-one 11

To a magnetically stirred solution of alcohol **14** (400 mg, 2.41 mmol) in dry CH_2Cl_2 (5 ml) was added a homogeneous mixture of PCC (1.56 g, 7.3 mmol) and silica gel (1.56 g) and stirred vigorously for 4 h at room temperature. The reaction mixture was then filtered through a small silica gel column with an excess of CH_2Cl_2. Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:5) as eluent furnished the bicyclic ketone **11** (387 mg, 98%) as a white solid. Mp: 98–99 °C; $[\alpha]_D^{26} = -34.0$ (*c* 4.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 1716, 1651, 888; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 5.00 (1H, s) and 4.91 (1H, s) [C=CH_2], 3.25 (1H, d, *J* 5.4 Hz, H-1), 2.52–2.25 (2H, m), 2.20–2.00 (2H, m), 2.00–1.95 (1H, m, H-5), 1.85–1.65 (2H, m), 1.29 (3H, s) and 1.16 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 208.3 (C, C=O), 158.3 (C, C-7), 106.7 (CH_2, H_2C=C), 59.3 (CH, C-1), 44.8 (CH, C-5), 43.7 (C, C-6), 34.8 (CH_2), 34.3 (CH_2), 32.1 (CH_3), 27.0 (CH_2), 24.3 (CH_3); HRMS: *m*/*z* calcd for $C_{11}H_{17}O$ (M+H): 165.1279; found: 165.1284.

Acknowledgements

We thank the Council of Scientific and Industrial Research, New Delhi for the award of research fellowships to B.B. and G.S. We are grateful to Organica Aromatics (Bangalore) Pvt. Ltd, for the generous gift of campholenaldehyde.

References

1. Ho, T.-L. *Enantioselective Synthesis: Natural Products from Chiral Terpenes*; John Wiley: Chechester, 1992.
2. Hannesian, S. *Total Synthesis of Natural Products. The Chiron Approach*; Pergamon Press: Oxford, 1983.
3. Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671; Singh, V.; Thomas, B. *Tetrahedron* **1998**, *54*, 3647; Heathcock, C. H. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1973; Vol. 2; Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1983; Vol. 5; *The Total Synthesis of Natural Products*; Pirrung, M. C., Morehead, A. T., Eds. Acyclic and Monocyclic Sesquiterpenes, Part A; Wiley: New York, 1997; Vol. 10; *The Total Synthesis of Natural Products*; Pirrung, M. C., Morehead, A. T., Young, B. G., Eds. Bicyclic and Tricyclic Sesquiterpenes, Part B; Wiley: New York, 1999; Vol. 11.
4. Lewis, J. B.; Hedrick, G. W. *J. Org. Chem.* **1965**, *30*, 4271.
5. Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 109; Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: New York, 1995; Vol. 12, Chapter 5.2; Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Wiley and Sons: New York, 1998; Doyle, M. P. *Aldrichim. Acta* **1996**, *29*, 3.
6. Walling, C.; Buckler, S. A. *J. Am. Chem. Soc.* **1955**, *77*, 6039.
7. Holmquist, C. R.; Roskamp, E. J. *J. Org. Chem.* **1989**, *54*, 3258; Holmquist, C. R.; Roskamp, E. J. *Tetrahedron Lett.* **1992**, *33*, 1131.
8. Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556; Keung, E. C.; Alper, H. *J. Chem. Educ.* **1972**, *49*, 97; Snider, B. B.; Rodini, D. J.; Straten, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 5872; Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476; Taber, D. F. *Intramolecular Diels–Alder and Alder Ene Reactions*; Springer: Berlin, 1984; Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1992; Vol. 5; p 1; Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426; Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927.
9. Hudlicky, T.; Sinai, G.-Z.; Natchus, M. G.; Ranu, B. C.; Papadopolous, P. *Tetrahedron* **1987**, *43*, 5685.