Indian Journal of Chemistry
Vol. 47B, September 2008, pp. 1423-1429

Construction of spiro[4.5]decane *via* ring-closing metathesis reaction: Formal synthesis of acorone and isoacorones

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Received 29 May 2008; accepted (revised) 4 July 2008

A Claisen rearrangement and RCM reaction based sequence has been developed for formal total synthesis of acorone and isoacorones starting from cyclohexane-1,4-dione. It has been further modified and avoided the protection-deprotection sequence in the second strategy.

Keywords: Spiro[4.5]decane, acorones, RCM reaction, Claisen rearrangement, sesquiterpenes

The creativity of nature in devising varied molecular architecture is revealed through the isolation of a wide range of natural products with remarkable skeletal build-up and multifarious functionalities. Among the natural products, terpenoids (isoprenoids) occupy a special position on account of their widespread occurrence and the bewildering array of carbocyclic skeleta that they embody. Sesquiterpenes comprising of three isoprene units, biogenetically derived from farnesyl pyrophosphate, are assembled in acyclic, monocyclic, bicyclic, tricyclic and even tetracyclic as well as spirofused structures containing small, medium and large rings with a wide range of functionalities[1]. Because of this phenomenal structural diversity this class of natural products holds special appeal to synthetic chemists and provide a fertile ground for developing and testing new synthetic strategies. As a result, synthetic activity in this area continues to flourish[2].

Sorm and coworkers, in 1948, reported the isolation[3] of two sesquiterpene ketones, acorone and isoacorones from the oil of Sweet Flag, *Acorus calamus L.*, whose interconversion in basic media suggested their epimeric relationship. Presence of the novel spiro[4.5]decane carbon framework in acorone and isoacorones (**1** and **2**) was established in 1958 based on the interpretation of extensive degradation experiments by Sorm and coworkers[4]. On the basis of the ORD curves of acorones and their chemically modified derivatives, they concluded the con-formational structures of acorone **1** and isoacorone **2**. The absolute configuration of acorones was established by correlation with cedrene, a tricyclic sesquiterpene isolated along with acorones from the same source, and was finally confirmed by single crystal X-ray analysis of a derivative of acorone. Further investigations[5] led to the isolation and characterisation of a number of acorane derivatives (**Figure 1**).

The most important aspect in the synthesis of acorane sesquiterpenes is the stereocontrolled construction of the spirocyclic carbon skeleton[6]. A successful synthesis of these spiro sesquiterpenes depends critically, therefore, upon the generation of a quaternary carbon centre which is suitably substituted for the annulation to form a functionalized spiro[4.5]decane that may be subsequently elaborated into the target natural products. Since the discovery of acoranes, several research groups have reported synthesis of acoranes[7-9]. In 1977, Dolby and McCrae reported[7] the synthesis of acorone and isoacorones (**1** and **2**) starting from the isoprene-acrolein Diels-Alder adduct *via* the spirodienone **3**. A similar strategy was reported[8] in 1978 by Martin and Chou for the total synthesis of (±)-acorone and isoacorones (**1** and **2**) *via* the spirodienone **3**.

The last decade had witnessed growth of RCM reaction as one of the powerful synthetic tools in organic synthesis[10]. However, its use in the synthesis of spiro systems was under- explored. There are very few reports on the synthesis of spirocyclic compounds based on RCM reaction. It was conceived that a

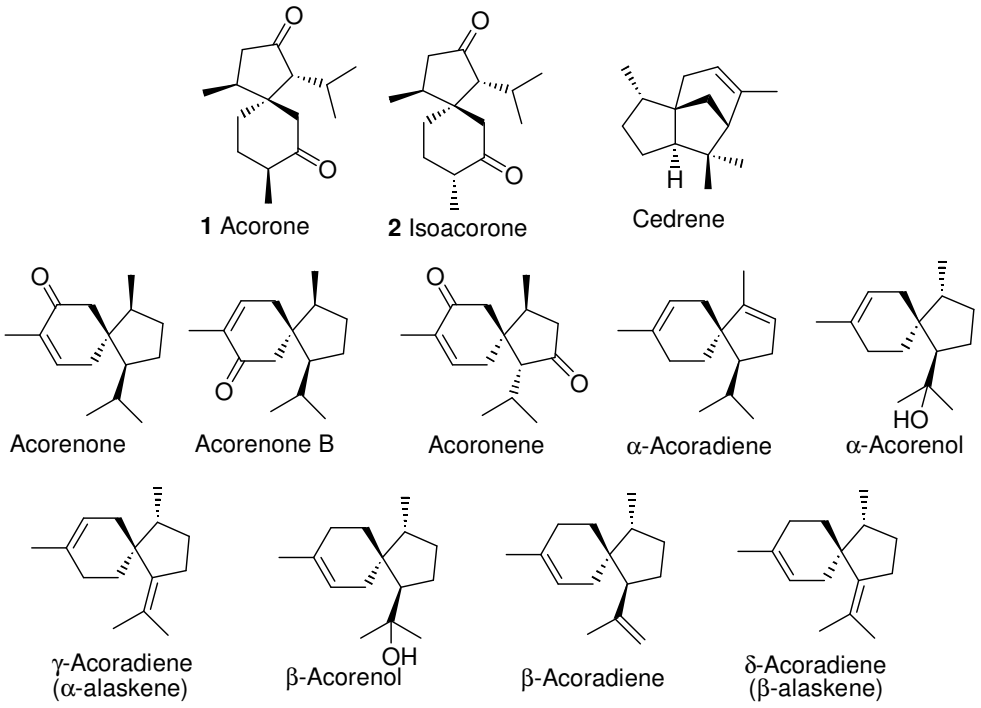
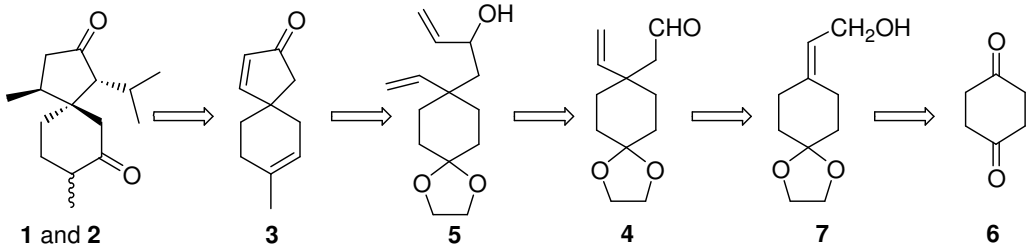


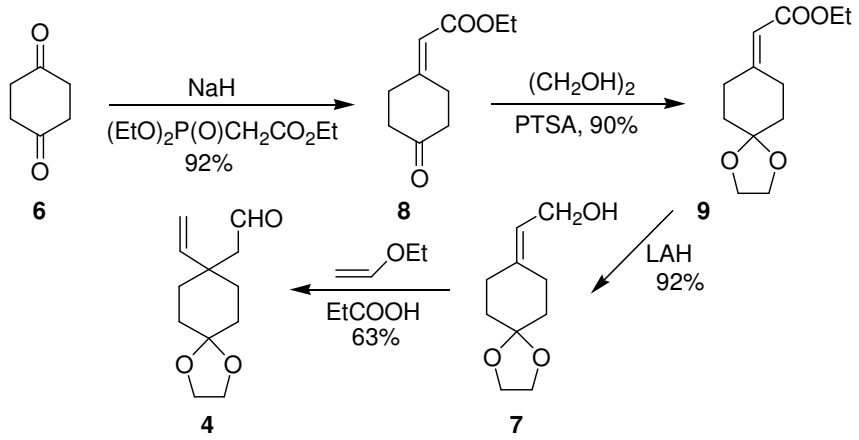
Figure 1



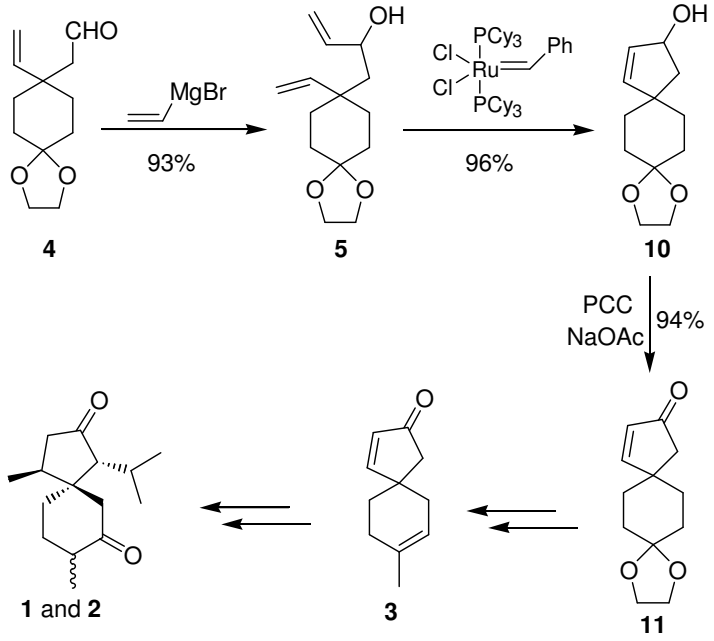
Scheme I

combination of Claisen rearrangement and RCM reaction based methodology developed[11] for the construction of cyclopentane based sesquiterpenes could be extended to the spirocyclic sesquiterpenes, acorone and isoacorones[12]. The retrosynthetic strategy is depicted in **Scheme I**. The dienone **3**, a precursor employed by Dolby and McCrae[7]; and Martin and Chou[8] in their syntheses of acorones, was identified as the target molecule for the formal synthesis of acorones **1** and **2**. It was contemplated that the spirodienone **3** could be obtained from the γ,δ-unsaturated aldehyde **4** *via* the RCM reaction of the hydroxydiene **5**. The aldehyde **4** could be obtained from cyclohexane-1,4-dione **6** *via* the allyl alcohol **7**.

The synthetic sequence is depicted in **Schemes II** and **III**. Conversion of cyclohexane-1,4-dione **6** into the allyl alcohol **7** was carried out employing a methodology developed earlier[9h]. Thus, Horner-Wadsworth-Emmons reaction of cyclohexane-1,4-dione **6** with sodium hydride and triethyl phosphonoacetate in THF generated the ketoester **8** in 92% yield. The ketone in the ketoester **8** was protected as its ethylene ketal by reaction with ethylene glycol in the presence of a catalytic amount of PTSA in refluxing benzene using a Dean-Stark water trap to furnish the ketalester **9** in 90% yield. Regioselective reduction of the ester **9** with LAH in ether at –70 °C gave the allyl alcohol **7** in 92% yield. One-pot Claisen rearrangement[13] of the allyl alcohol **7** with ethyl vinyl ether in the presence of a catalytic amount of propionic acid in a sealed tube at 175 °C furnished the γ,δ-unsaturated aldehyde **4** in 63% yield. Grignard reaction of the aldehyde **4** with vinylmagnesium bromide in THF at RT for 1 hr



Scheme II

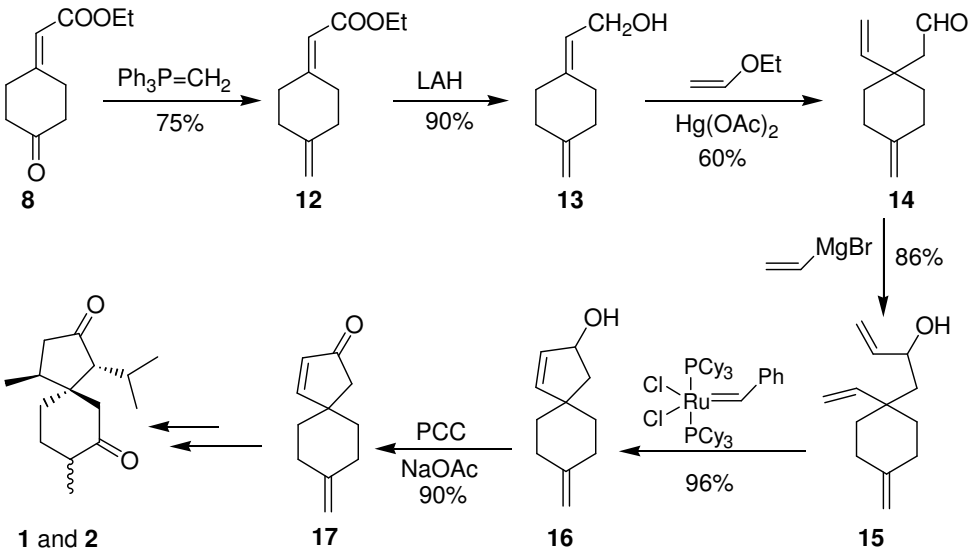


Scheme III

furnished the hydroxydiene **5** in 93% yield. RCM reaction of the hydroxydiene **5** on treatment with 6 mole% of the Grubbs' catalyst in methylene chloride for 5 hr at RT furnished the spiro alcohol **10** in 96% yield. Oxidation of the spiro enol **10** with PCC and sodium acetate in methylene chloride for 1 hr furnished the spiroenone **11** in 94% yield. The enone **11** was identified by comparison of the ^{1}H and ^{13}C NMR spectral data with that of the sample prepared earlier[9h]. The spiroenone **11** has already been transformed into the dienone **3** employing a three step protocol, *viz* hydrolysis of the ketal moiety, Wittig methylenation followed by acid catalysed isomerisation of the olefin.

Subsequently, to reduce the length of the sequence and also to eliminate the protection-deprotection protocol, an alternative strategy was considered (**Scheme IV**). It was conceived that there is no need to protect the ketone in ketoester **8**, and instead it could be converted into an exomethylene. Thus, Wittig reaction of the ketoester **8** in benzene with methylenetriphenylphosphorane at RT for 1 hr furnished the diene ester **12** in 75% yield, whose structure was established from its spectral data.

Regioselective reduction of the ester **12** with LAH in ether at low temperature furnished the allyl alcohol **13** in 90% yield. One pot Claisen rearrangement[13b] of the allyl alcohol **13** with ethyl vinyl ether in the



Scheme IV

presence of a catalytic amount of mercuric acetate in a sealed tube at 175°C furnished the γ,δ-unsaturated aldehyde **14** in 60% yield, whose structure was established from its spectral data. Treatment of the aldehyde **14** with vinylmagnesium bromide in THF at RT for 1 hr furnished the hydroxytriene **15** in 86% yield. The allyl alcohol **15**, although it has three olefinic groups, underwent a smooth RCM reaction in a highly regioselective manner. Thus, reaction of the hydroxytriene **15** with 6 mole% Grubbs' catalyst in methylene chloride for 5 hr at RT furnished the spiroalcohol **16** in near quantitative yield. Oxidation of the spiro alcohol **16** using PCC and sodium acetate in methylene chloride for 1 hr generated the spiroenone **17** in 90% yield. Presence of the molecular ion peak at *m/z* 162 ($C_{11}H_{14}O$) in the mass spectrum and in the IR spectrum, presence of carbonyl absorption band at 1715 cm^{-1} due to the enone revealed the formation of the dienone **17**. It was further confirmed by comparison of the ^1H and ^{13}C NMR spectral data with that of sample prepared earlier[9h].

In conclusion, two convenient and efficient strategies have been developed based on RCM reaction for the formal synthesis of spirocyclic sesquiterpenes acorone and isoacorones **1** and **2** starting from cyclohexane-1,4-dione, demonstrating the utility of RCM reaction for the synthesis of natural products containing spiro systems.

Experimental Section

IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^1H (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 ^1H) 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 a 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 micro mass spectrometer using electro-spray ionisation. The alcohol **7** was prepared as reported earlier[9h].

2-(8-Vinyl-1,4-dioxaspiro[4.5]decan-8-yl)acetaldehyde 4. A solution of the allyl alcohol **7** (200 mg, 1.09 mmoles), ethyl vinyl ether (1.56 mL, 16.3 mmoles) and propionic acid (catalytic) was heated to 175°C for 48 hr in a Carius tube under nitrogen atmosphere. The reaction mixture was then cooled, diluted with ether, washed with aqueous $NaHCO_3$ solution and brine, and dried (anhyd. 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 the aldehyde **4** (143 mg, 63%) as oil[9h]. IR (neat): 2933, 2734 (H-C=O), 1720 (C=O), 1639, 1445, 1373, 1339, 1276, 1109, 1035, 944, 920 ($CH=CH_2$), 873, 659 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 9.68 (1 H, t, J = 3.0 Hz, CH_2CHO), 5.84 (1 H, dd, J = 17.7 and 10.8 Hz,

C*H*=CH_2), 5.24 (1 H, d, *J* = 10.8 Hz) and 5.13 (1 H, d, *J* = 17.7 Hz) [CH=CH_2], 3.90 (4 H, s, OCH_2CH_2O), 2.35 (2 H, d, *J* = 3.0 Hz, CH_2CHO), 1.90-1.25 (8 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 201.6 (CH, CHO), 143.1 (CH, *C*H=CH_2), 115.0 (CH_2, CH=*C*H_2), 108.4 (C, C-5'), 64.2 (2 C, CH_2, C-2' and 3'), 53.3 (CH_2, C-2), 38.4 (C, C-8'), 33.2 (2 C, CH_2), 30.9 (2 C, CH_2).

8-(2-Hydroxybut-3-en-1-yl)-8-vinyl-1,4-dioxaspiro[4.5]decane 5. To a magnetically stirred solution of the aldehyde **4** (120 mg, 0.57 mmole) in THF (2 mL) was added vinylmagnesium bromide [prepared from magnesium (88 mg, 3.66 mmoles) and bromoethylene (0.5 mL, 7.3 mmoles) in THF (2 mL)] and stirred for 1 hr at RT. The reaction was quenched with aqueous NH_4Cl solution and extracted with ether (3 × 4 mL). The organic layer was washed with water and brine, and dried (anhyd. Na_2SO_4). Evaporation of the solvent and purification over a silica gel column using ethyl acetate-hexane (1:10) as eluent gave a 1:1 diastereomeric mixture of the hydroxydiene **5** (126 mg, 93%) as oil. IR (neat): 3452 (OH), 3078, 2930, 1637 (C=C), 1444, 1372, 1273, 1106, 1034, 1000, 916 (CH=CH_2), 875 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.85-5.70 (2 H, m), 5.20 (1 H, d, *J* = 11.4 Hz), 5.16 (1 H, d, *J* = 17.4 Hz), 5.09 (1 H, d, *J* = 16.8 Hz), 5.00 (1 H, d, *J* = 10.5 Hz), 4.28-4.15 (1 H, m), 3.89 (4 H, s, H-2 and 3), 1.85-1.30 (11 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 145.4 (CH, C-1''), 142.3 (CH, C-3'), 114.2 (CH_2), 113.5 (CH_2), 109.0 (C, C-5), 70.1 (CH, C-2'), 64.1 (2 C, CH_2, C-2 and 3), 48.3 (CH_2, C-1'), 38.8 (C, C-8), 33.7 (CH_2), 32.6 (CH_2), 31.1 (CH_2), 31.0 (CH_2); MS: *m/z* (%) 238 (M^+, 8), 237 (5), 223 (12), 181 (23), 168 (100), 167 (77), 112 (17), 100 (51); HRMS: *m/z* Calcd. for $C_{14}H_{22}O_3Na$ (M+Na): 261.1467. Found: 261.1481.

1,4-Dioxadispiro[4.2.4.2]tetradec-11-en-10-ol 10. To a magnetically stirred solution of a 1:1 diastereomeric mixture of the hydroxydiene **5** (30 mg, 0.13 mmole) in anhydrous CH_2Cl_2 (2 mL) was added a solution of Grubbs' catalyst (7 mg, 6 mole%) in anhydrous CH_2Cl_2 (3 mL) and the reaction mixture was stirred at RT for 5 hr. Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished a 1:1 diastereomeric mixture of the cyclopentenol **10** (25 mg, 96%) as oil. IR (neat): 3417 (OH), 2930, 2890, 1443, 1368, 1285, 1267, 1177, 1100, 1034, 963, 882, 769 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.89 (1 H, d, *J* = 5.7 Hz, H-12), 5.72 (1 H, dd, *J* = 5.7 and 2.4 Hz, H-11), 4.90-4.80 (1 H, m, H-10), 3.91 (4 H, s, H-2 and 3), 2.13 (1 H, dd, *J* = 13.8 and 7.5 Hz), 1.85-1.40 (10 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 143.1 (CH, C-12), 131.9 (CH, C-11), 108.5 (C, C-5), 76.8 (CH, C-10), 64.2 (2 C, CH_2, C-2 and 3), 48.2 (C, C-8), 45.4 (CH_2, C-9), 36.4 (CH_2), 35.2 (CH_2), 32.6 (CH_2), 32.3 (CH_2); MS: *m/z* (%) ($C_{12}H_{18}O_3$) 192 (M–H_2O, 1), 149 (2), 130 (1), 99 (100); HRMS: *m/z* Calcd. for $C_{12}H_{17}O_2$ (M–OH): 193.1229. Found: 193.1224.

1,4-Dioxadispiro[4.2.4.2]tetradec-11-en-10-one 11. To a magnetically stirred suspension of PCC (39 mg, 0.18 mmole) and sodium acetate (15 mg, 0.18 mmole) in CH_2Cl_2 (1 mL) was added a solution of a 1:1 diastereomeric mixture of the alcohol **10** (18 mg, 0.09 mmole) in CH_2Cl_2 (2 mL) in one portion. The reaction mixture was stirred at RT for 1 hr, filtered through a silica gel column, and the column eluted with more CH_2Cl_2. Evaporation of the solvent furnished the enone **11** (17 mg, 94%) as oil[9h]. IR (neat): 3068, 2940, 2884, 2853, 1714 (C=O), 1585, 1441, 1399, 1365, 1360, 1254, 1207, 1170, 1117, 1078, 1032, 970, 885, 818, 660 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 7.53 (1 H, d, *J* = 5.7 Hz, H-12), 6.06 (1 H, d, *J* = 5.7 Hz, H-11), 3.94 (4 H, s, OCH_2CH_2O), 2.25 (2 H, s, H-9), 1.95-1.45 (8 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 208.4 (C, C=O) 171.6 (CH, C-12), 132.1 (CH, C-11), 107.8 (C, O-C-O), 64.3 (2 C, CH_2, OCH_2CH_2O), 46.2 (CH_2, C-9), 45.1 (C, C-8), 34.3 (2 C, CH_2) 32.4 (2 C, CH_2); HRMS: *m/z* Calcd. for $C_{12}H_{16}O_3Na$ (M+Na): 231.0997. Found: 231.0986.

Ethyl (4-methylenecyclohexylidene)acetate 12. To a cold (0°C), magnetically stirred solution of methyltriphenylphosphonium iodide (1.60 g, 3.96 mmoles) in benzene (3 mL) was added potassium *tert*-amyloxide (4 mmoles) [prepared from potassium (156 mg, 4 mmoles) and 2 mL *tert*-amyl alcohol] in benzene (2 mL) and the resultant yellow reaction mixture was stirred for 20 min at RT. To methylenetriphenylphosphorane thus formed, was added a solution of the ketoester **8** (400 mg, 2.20 mmoles) in benzene (2 mL) and stirred at RT for 1 hr. The reaction was quenched with water (3 mL) and extracted with ether (2 × 4 mL). The ether extract was washed with brine and dried (anhyd. 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 the diene ester **12** (296 mg, 75%) as oil. IR (neat): 3073, 2982, 2939, 2846, 1714 (OC=O), 1650, 1445, 1377, 1294, 1270, 1248, 1209, 1169, 1138, 1096, 1063, 1037, 891

(C=CH_2), 863, 797, 704 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.64 (1 H, s, H-2), 4.71 (1 H, s) and 4.70 (1 H, s) [C=CH_2], 4.13 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$$CH_3$), 2.92 (2 H, t, *J* = 6.3 Hz), 2.30 (6 H, br s), 1.28 (3 H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 166.2 (C, OC=O), 160.8 (C, C-1'), 146.9 (C, C-4'), 114.3 (CH, C-2), 108.8 (CH_2, C=*C*H_2), 59.4 (CH_2, O*C*$H_2$$CH_3$), 38.5 ($CH_2$), 35.8 ($CH_2$), 35.0 ($CH_2$), 30.1 ($CH_2$), 14.4 ($CH_3$, OCH_2*C*H_3); MS: *m/z* (%) ($C_{11}H_{16}O_2$) 180 (M^+, 26), 179 (27), 167 (16), 149 (50), 135 (40), 107 (54), 105 (58), 99 (60), 91 (100).

2-(4-Methylenecyclohexylidene)ethanol 13. To a cold (–20°C) magnetically stirred solution of the ester **12** (190 mg, 1.05 mmoles) in dry ether (4 mL) was added LAH (20 mg, 0.53 mmole) in one portion. The reaction mixture was stirred at the same temperature for 2 hr and allowed to warm to 0 °C over a period of 30 min. Ethyl acetate (2 mL) was carefully introduced to consume the excess reagent and the reaction was quenched with ice-cold water (5 mL). The solution was filtered through a sintered funnel and the residue thoroughly washed with ether (3 × 5 mL). The ether layer was separated, washed with brine and dried (anhyd. 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 primary alcohol **13** (131 mg, 90%) as oil. IR (neat): 3339 (OH), 3071, 2935, 2842, 1649, 1439, 1315, 1151, 1084, 1060, 997, 889 (C=CH_2), 692 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.41 (1 H, t, *J* = 6.9 Hz, H-2), 4.66 (2 H, s, C=C*H*$_2$), 4.13 (2 H, d, *J* = 6.9 Hz, H-1), 2.50-2.00 (9 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 148.0 (C, C-4'), 142.2 (C, C-1'), 122.0 (CH, C-2), 108.4 (CH_2, C=*C*H_2), 58.5 (CH_2, C-1), 37.7 (CH_2), 36.2 (CH_2), 35.6 (CH_2), 29.5 (CH_2); MS: *m/z* (%) ($C_9H_{14}O$) 120 (M–H_2O, 33), 105 (50), 93 (50), 91 (70), 41 (100).

2-(4-Methylene-1-vinylcyclohexyl)acetaldehyde 14. One pot Claisen rearrangement of the allyl alcohol **13** (130 mg, 0.94 mmole) with ethyl vinyl ether (1.35 mL, 14.1 mmoles) and mercuric acetate (15 mg) at 175°C for 48 hr and work up as described for the aldehyde **4**, followed by purification over a silica gel column using ethyl acetate-hexane (1:20) as eluent furnished the aldehyde **14** (92 mg, 60%) as oil. IR (neat): 3073, 2930, 2731 (H-C=O), 1723 (C=O), 1647, 1444, 1400, 1373, 1320, 1239, 1197, 1041, 916 (CH=CH_2), 889 (C=CH_2), 815 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 9.70 (1 H, t, *J* = 3.0 Hz, CH_2C*H*O), 5.88 (1 H, dd, *J* = 18.0 and 10.8 Hz, C*H*=CH_2), 5.25 (1 H, d, *J* = 10.8 Hz) and 5.13 (1 H, d, *J* = 18.0 Hz) [CH=C*H*$_2$], 4.60 (2 H, s, C=CH_2), 2.37 (2 H, d, *J* = 3.0 Hz, H-2), 2.40-2.00 (4 H, m, H-3' and 5'), 1.95-1.75 (2 H, m), 1.65-1.45 (2 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 201.4 (CH, CHO), 147.6 (C, C-4'), 143.7 (CH, *C*H=CH_2), 114.8 (CH_2, CH=*C*H_2), 107.9 (CH_2, C=*C*H_2), 53.2 (CH_2, C-2), 39.1 (C, C-1'), 37.1 (2 C, CH_2, C-2' and 6'), 30.6 (2 C, CH_2, C-3' and 5').

1-(4-Methylene-1-vinylcyclohexyl)but-3-en-2-ol 15. Grignard reaction of the aldehyde **14** (50 mg, 0.30 mmole) with vinylmagnesium bromide (3.0 mmoles) in dry THF (4 mL) for 1 hr at RT, and work up as described for the hydroxydiene **5**, followed by purification over a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished the hydroxydiene **15** (50 mg, 86%) as oil; IR (neat): 3406 (OH), 3074, 2980, 2928, 2849, 1650, 1443, 1118, 992, 916 (CH=CH_2), 885 (C=CH_2), 736 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.90-5.75 (1 H, m, H-3), 5.82 (1 H, dd, *J* = 17.7 and 11.1 Hz, H-1''), 5.21 (1 H, d, *J* = 12.0 Hz), 5.16 (1 H, d, *J* = 16.8 Hz), 5.10 (1 H, d, *J* = 17.7 Hz), 5.01 (1 H, d, *J* = 11.1 Hz), 4.56 (2 H, s, C=CH_2), 4.30-4.20 (1 H, m, H-2), 2.20-2.05 (4 H, m), 1.90-1.70 (2 H, m), 1.70-1.40 (5 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 148.9 (C, C-4'), 146.1 (CH, C-1''), 142.3 (CH, C-3), 114.3 (CH_2), 113.6 (CH_2), 107.0 (CH_2, C=*C*H_2), 70.1 (CH, C-2), 48.4 (CH_2, C-1), 39.5 (C, C-1'), 38.0 (CH_2) and 36.6 (CH_2) [C-2' and 6'], 31.0 (2 C, CH_2, C-3' and 5'); MS: *m/z* (%) ($C_{13}H_{20}O$) 177 (17), 167 (15), 149 (28), 136 (17), 119 (29), 105 (50), 93 (70), 91 (100); HRMS: *m/z* Calcd. for $C_{13}H_{19}$ (M–OH): 175.1514. Found: 175.1510.

8-Methylenespiro[4.5]dec-3-en-2-ol 16. RCM reaction of the hydroxydiene **15** (30 mg, 0.15 mmole) with Grubbs' catalyst (7 mg, 6 mole%) in anhydrous CH_2Cl_2 (7 mL) for 5 hr at RT as described for the compound **10**, followed by purification over a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished the spiro compound **16** (24 mg, 96%) as oil. IR (neat): 3343 (OH), 3068, 2920, 2847, 1650, 1444, 1360, 1330, 1260, 1145, 1112, 1077, 1041, 957, 887 (C=CH_2), 838, 766 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 5.87 (1 H, d, *J* = 6.0 Hz, H-4), 5.73 (1 H, dd, *J* = 6.0 and 1.8 Hz, H-3), 4.90-4.82 (1 H, m, H-2), 4.60 (2 H, s, C=CH_2), 2.30-2.08 (5 H, m), 1.70-1.30 (6 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 148.2 (C, C-8), 143.3 (CH, C-4), 131.8 (CH, C-3), 107.5 (CH_2, C=*C*H_2), 76.9 (CH, C-2), 49.1 (C, C-5), 45.7

(CH_2, C-1), 40.4 (CH_2) and 39.1 (CH_2) [C-6 and 10], 32.4 (CH_2) and 32.2 (CH_2) [C-7 and 9]; MS: *m/z* (%) ($C_{11}H_{16}O$) 164 (M^+, 5), 149 (15), 131 (35), 117 (30), 106 (100), 95 (90), 91 (98); HRMS: *m/z* Calcd. for $C_{11}H_{17}O$ (M+1): 165.1279. Found: 165.1287.

8-Methylenespiro[4.5]dec-3-en-2-one 17. Oxidation of the spiro alcohol **16** (20 mg, 0.12 mmole) with PCC (52 mg, 0.24 mmole) and sodium acetate (16 mg, 0.24 mmole) in CH_2Cl_2 (2 mL), followed by work up as described for the enone **11**, furnished the spiro enone **17** (18 mg, 90%) as oil[9h]. IR (neat): 2921, 1715 (C=O), 1650, 1440, 1185, 890 (C=CH_2), 797 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 7.48 (1 H, d, *J* = 5.7 Hz, H-4), 6.06 (1 H, d, *J* = 5.7 Hz, H-3), 4.68 (2 H, s, C=CH_2), 2.28 (2 H, s, H-1), 2.45-2.00 (4 H, m, H-7 and 9), 1.80-1.50 (4 H, m, H-6 and 10); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 209.2 (C, C-2), 171.6 (CH, C-4), 146.6 (C, C-8), 132.1 (CH, C-3), 108.6 (CH_2, C=*C*H_2), 46.3 (CH_2, C-1), 45.8 (C, C-5), 37.9 (2 C, CH_2, C-6 and 10), 32.1 (2 C, CH_2, C-7 and 9); MS: *m/z* (%) ($C_{11}H_{14}O$) 162 (M^+, 43), 147 (34), 133 (32), 119 (39), 107 (40), 105 (46), 95 (100), 91 (83).

Acknowledgement

The authors thank the CSIR, New Delhi for financial support.

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