Synthesis based on cyclohexadienes. Part 34.[1] A tandem cationic rearrangement–ene cyclisation route to 2-pupukeanone

P. John Biju, Krishna Kaliappan, M. S. Laxmisha and G. S. R. Subba Rao *

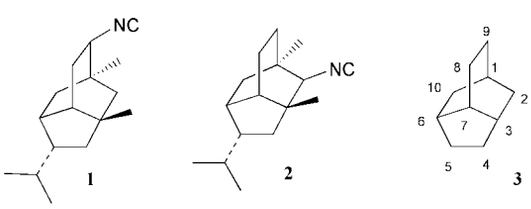
Department of Organic Chemistry, Indian Institute of Science, Bangalore-560012, India

Received (in Cambridge, UK) 27th April 2000, Accepted 4th September 2000
First published as an Advance Article on the web 19th October 2000

A new strategy for the construction of the isotwistane skeleton is reported from easily available cyclohexadienes, which involves a one-pot cationic skeletal rearrangement and ene cyclisation of a bicyclo[2.2.2]octenone derivative and a cationic rearrangement of a tricyclo[5.3.0.$0^{4,8}$]decane to a [4.3.1.$0^{3,7}$]decane skeleton as the key steps in the synthesis of 2-pupukeanone.

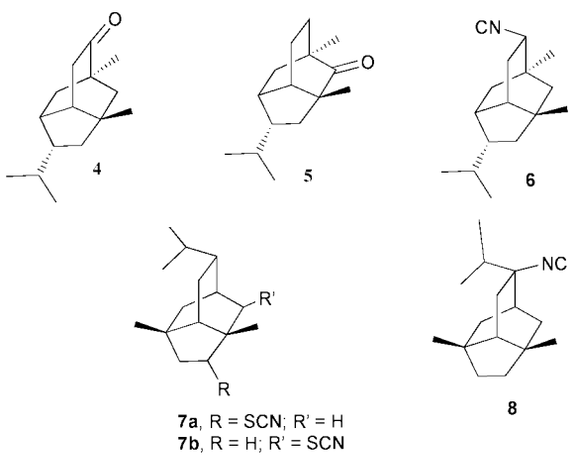
Introduction

A number of marine organisms secrete some toxic or very strongly smelling compounds from their skin glands as a part of their self-defence mechanism in order to protect themselves from their predators. Johannes[2] observed that the nudibranch *Phyllidia varicosa* Lamarck, 1801 secretes from its skin glands a strong and (usually) smelly, heat-stable, volatile substance, which is lethal to fish and crustaceans, to protect the delicate, shell-less, brightly coloured opisthobranch mollusk from its predators. In 1975, Scheuer and co-workers[3] reported the isolation of a metabolite, 9-isocyanopupukeanane **1**, the first member of the isotwistane carbon framework, from *P. varicosa* and also from its prey, a sponge, *Hymeniacidon* sp. In 1979, an isomeric substance, 2-isocyanopupukeanane **2** was also isolated[4] from the same source by the same group. These compounds were named as pupukeananes after the place where the mollusk and sponge were collected.



The structure of the metabolites incorporating the novel isotwistane carbon framework **3** was established by chemical degradation to the corresponding ketones **4** and **5** respectively and confirmed by a single-crystal X-ray analysis; the absolute configuration of the two compounds was also established in the latter study. Since then several other pupukeananes have been isolated from various other sources. These include thiocyanato-neopupukeananes **7a** and **7b** from the sponges *Phycopsis terpnis* and an unidentified species; and 9-isocyanoneopupukeanane **8** from the sponge *Ciocalypta* species.[5,6]

The total synthesis of these sesquiterpenes is challenging since they possess i) a new rearranged isoprenoid skeleton with a unique tricyclo[4.3.1.$0^{3,7}$]decane framework having a bicyclo-[2.2.2]octane subunit with a methyl group at the bridgehead position and ii) an isopropyl group in a thermodynamically unfavourable position. Owing to their unique molecular architecture, several syntheses of these tricyclic sesquiterpenes have been reported.[7,8] In continuation of our interest[9] in the total synthesis of sesquiterpenes having a bicyclo[2.2.2]octane



subunit with a bridgehead methyl group, we report herein a formal synthesis of 2-pupukeanone **5**, a degradation product of 2-isocyanopupukeanane **2**, employing a tandem cationic rearrangement and ene cyclisation as the key step. A preliminary account of this work has been reported.[10]

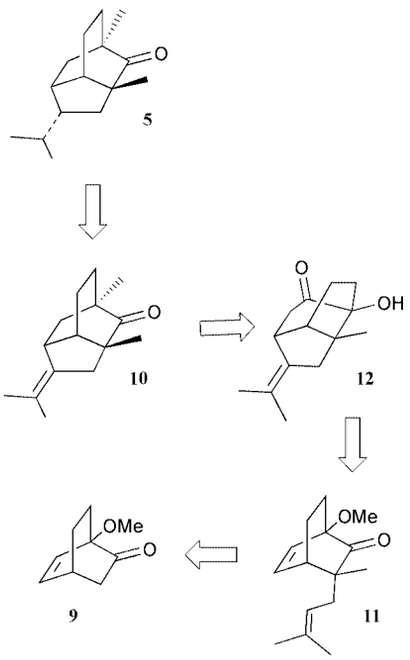
Results and discussion

The synthesis of 2-pupukeanone **5** was devised employing a one-pot tandem acid-catalysed rearrangement and an ene cyclisation as depicted in Scheme 1. Our retrosynthetic analysis indicated that 2-pupukeanone **5** could be obtained from the tricyclic ketone **10**, which in turn could be prepared from the ketone **12** by employing a skeletal rearrangement. The hydroxy ketone **12** can be obtained from the bicyclic ketone **11** by making use of a one-pot tandem rearrangement–ene cyclisation reaction. The bicyclic ketone **11** can in turn be prepared from the known bicyclic ketone **9**.[11]

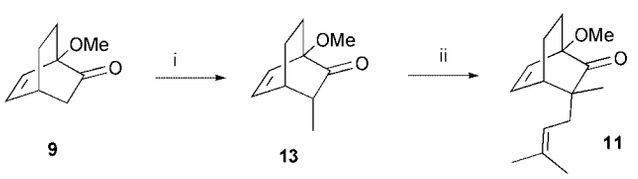
Synthesis of the bicyclic ketone 11

The bicyclic ketone **9** upon alkylation with lithium diisopropyl-amide (LDA) and MeI afforded the ketone **13** having the methyl group in the *endo* position (Scheme 2), as evidenced by the spectral data. Stereoselective alkylation[12] with prenyl bromide (prenyl = 3-methylbut-2-enyl) was achieved by treating the ketone **13** with LDA at −78 °C and quenching of the resultant enolate with prenyl bromide in tetrahydrofuran (THF)–hexamethylphosphonic triamide (HMPA). The structure of the ketone **11** was established from its spectral characteristics,

 DOI: 10.1039/b003409f



Scheme 1



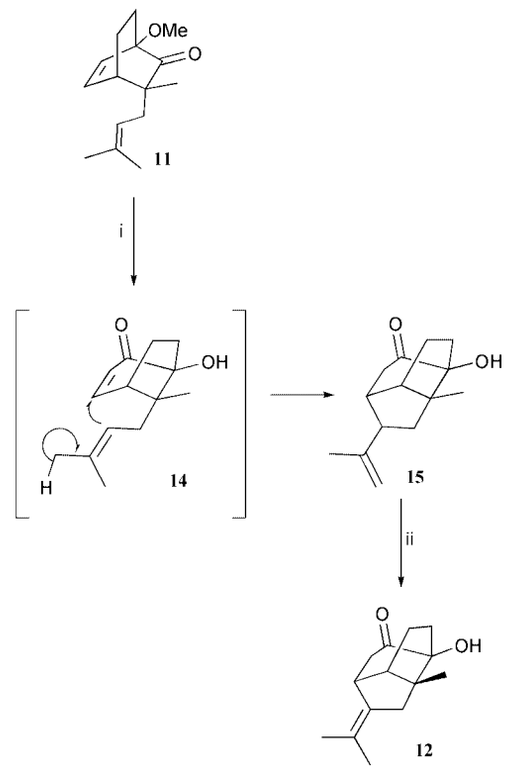
Scheme 2 *Reagents and conditions* (*and yields*): i) LDA, MeI, THF (80%); ii) LDA, prenyl bromide, THF, HMPA, −78 °C (75%).

especially from its ^{1}H NMR spectrum, which showed signals at δ 1.08 (s, Me), 1.59 and 1.73 (two s, allylic Me) and 5.12 (prenyl olefinic H).

Having obtained the bicyclic ketone **11** in good yield, a one-pot tandem acid-catalysed rearrangement–ene cyclisation reaction was next investigated. It is known that bicyclo[2.2.2]-octenones having a bridgehead methoxy group undergo a skeletal rearrangement to give bicyclo[3.2.1]octenones.[13] It was anticipated that the bicyclic ketone **11** upon a similar rearrangement would furnish the enone **14**, which has both the ene and the enophile properly oriented for an intramolecular ene reaction. Thus, a tandem acid-catalysed rearrangement and an ene reaction would furnish the tricyclic ketone **12**. The tricyclic ketone **12** is convertible into 2-pupukeanone **5**.

With this background, we investigated a one-pot tandem acid-catalysed rearrangement and ene cyclisation of the bicyclic ketone **11**. Thus, treatment of the bicyclic ketone **11** with Lewis acid BF_3·MeOH at room temperature gave only the starting material, whilst for reactions at higher temperatures the product decomposed. Treatment of the ketone **11** with $SnCl_4$, BF_3·OEt_2 and HCO_2H failed to produce the desired compound, as did heating it with toluene-*p*-sulfonic acid (PTSA) in refluxing benzene.

However, when the ketone **11** was treated with $HClO_4$ in CH_2Cl_2,[14] it underwent a smooth rearrangement followed by an ene cyclisation to afford the tricyclic ketone **15** in good yield (Scheme 3). The structure of **15** was delineated from its spectral characteristics. The IR spectrum showed absorptions at ν_{max} 3460 and 1700 cm^{-1} due to the hydroxy and the carbonyl groups, respectively. The ^{1}H NMR showed the absence of methoxylic protons at δ 3.52, and the exocyclic olefinic protons appeared at δ 4.68 and 4.90. The stereochemistry of the isopropenyl side chain was not confirmed since it is inconsequential for the synthesis of 2-pupukeanone. The exocyclic double bond in



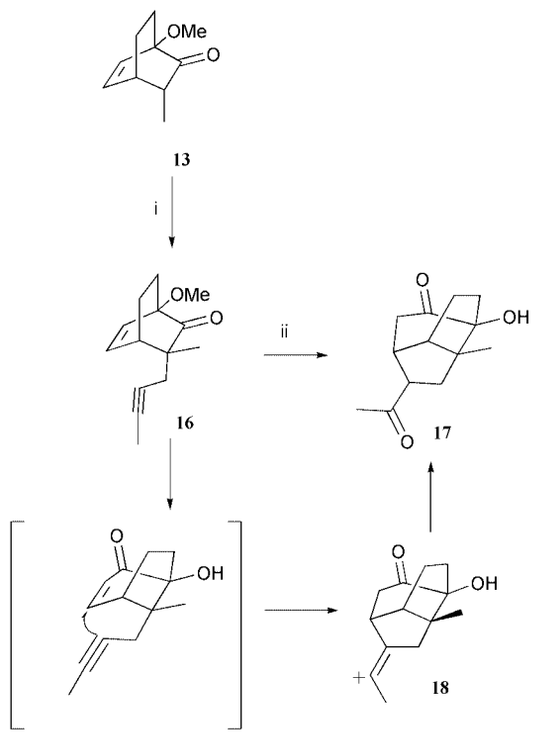
Scheme 3 *Reagents and conditions* (*and yields*): i) $HClO_4$ (catalytic), CH_2Cl_2, room temp. (57%); ii) PTSA, benzene, reflux, 1 h (95%).

15 was isomerised to the tetrasubstituted position by refluxing the ketone **15** with PTSA in benzene to afford the ketone **12**.

The formation of **15** from **11** presumably involves i) acid-catalysed rearrangement[13] of **11** having a bicyclo[2.2.2]octenone subunit to the hydroxy enone **14**, possessing the bicyclo[3.2.1]-octenone framework and ii) an intramolecular ene reaction of **14** to afford the hydroxy ketone **15**.

Having succeeded in the tandem rearrangement–ene cyclisation of the bicyclic ketone **11** having a prenyl subunit, we next investigated a similar reaction on the corresponding alkyne system **16**. The literature is replete with reports[15] which have employed alkynes as the ene component in ene reactions. Thus, alkylation of the lithium enolate of the ketone **13**, generated from LDA, with 1-bromobut-2-yne in the presence of HMPA afforded the *endo*-alkylated product **16** exclusively[12] (Scheme 4). The structure of **16** was established from its spectral data. The IR spectrum showed absorptions at ν_{max} 2240 and 1730 cm^{-1} due to the alkyne and carbonyl functionalities, respectively. The ^{1}H NMR spectrum showed a triplet at δ 1.81 (J = 2.4 Hz) due to the methyl group attached to the alkyne, and two quartets of doublets at δ 2.08 and 2.34 (J = 13.8 and 2.7 Hz) due to the methylene protons on the carbon attached to the acetylenic moiety.

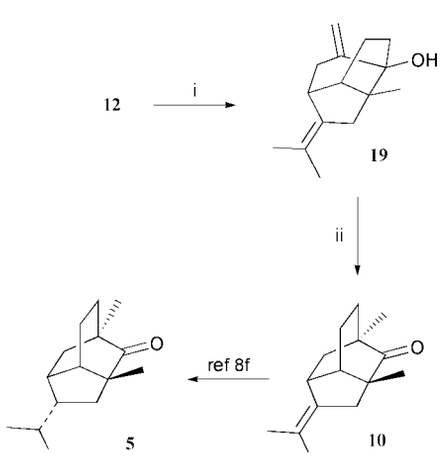
The ketone **16**, having been obtained in good yield, was subjected to the tandem rearrangement–ene cyclisation conditions. All attempts to bring about this transformation employing reagents used in similar transformations[15] were unsuccessful. However, when the ketone **16** was stirred with a catalytic amount of $HClO_4$[14] in dichloromethane, it smoothly underwent a tandem rearrangement followed by an ene cyclisation, resulting in the dione **17**. The structure of the dione **17** was established from its spectral data. The IR spectrum showed the absence of absorptions due to the acetylenic moiety, and the carbonyl absorptions appeared at ν_{max} 1710 and 1700 cm^{-1}. The ^{1}H NMR spectrum showed a signal at δ 2.18 due to the protons of the acetyl group. The structure of **17** was further confirmed from its ^{13}C NMR spectrum, which showed a 13-line spectrum, with characteristic peaks at δ_C 203.8 and 209.7 due to the two carbonyl carbons.



Scheme 4 *Reagents and conditions* (*and yields*): i) LDA, 1-bromobut-2-yne, THF, HMPA, −78 °C (84%); ii) $HClO_4$ (catalytic), CH_2Cl_2, 30 min (42%).

The formation of the dione **17** from the bicyclic ketone **16** presumably involves a similar type of rearrangement and an ene cyclisation as described for compound **11**, except that the vinyl cation **18**, formed after the ene cyclisation,[15] undergoes hydration under the reaction conditions to furnish the diketone **17** as shown in Scheme 4.

The next task in the synthetic sequence was to convert the tricyclic intermediates **12** and **17** into 2-pupukeanone. An acid-catalysed rearrangement[9] was contemplated for the conversion of the tricyclo[5.3.0.$0^{4,8}$]decane framework to the tricyclo[4.3.1.$0^{3,7}$]decane framework. Thus, Wittig olefination of the ketone **12** with (triphenyl)methylphosphonium iodide and potassium *tert*-amylate in refluxing benzene furnished the diene-alcohol **19** (Scheme 5). Although other bases such as

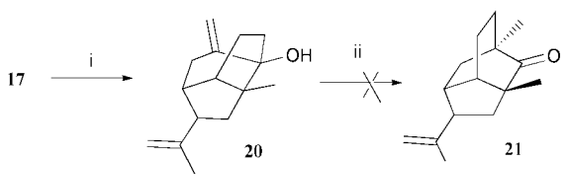


Scheme 5 *Reagents and conditions* (*and yields*): i) Ph_3PMeI, pent^{t}OK, PhH, reflux (83%); ii) $BF_3{\cdot}OEt_2$ (catalytic), CH_2Cl_2 (80%).

n-BuLi, KO^{t}Bu and NaH have been used in the Wittig reaction of the tricyclic ketone **12**, consistent yields of the product were obtained only with $KOC_5H_{11}{}^t$, which may perhaps be due to its solubility in the organic solvent.

The diene **19**, on treatment with catalytic $BF_3{\cdot}OEt_2$ in dry dichloromethane, underwent the expected skeletal rearrangement[9] to furnish the isotwistane ketone **10**, whose spectral characteristics were identical with those reported earlier.[8f] The ketone **10** has been converted into 2-pupukeanone **5** earlier in our laboratory,[8f] and thus the present synthesis constitutes a formal synthesis of 2-pupukeanone **5**.

The same sequence of reactions was attempted on the dione **17**. Thus, Wittig methylenation of the dione **17** furnished the diene **20** (Scheme 6), whose structure was deduced from its



Scheme 6 *Reagents and conditions* (*and yields*): i) Ph_3PMeI, pent^{t}OK, PhH, reflux, 12 h (73%); ii) $BF_3{\cdot}OEt_2$ (cat.), CH_2Cl_2.

spectral data. The IR spectrum showed the absence of carbonyl absorptions. The ^{1}H NMR spectrum showed four olefinic protons at δ 4.67, 4.80, 4.83 and 4.93 due to the four exocyclic olefinic protons. The diene **20** was expected to furnish the isotwistane **21** upon acid-catalysed skeletal rearrangement, similar to the aforementioned rearrangement. Thus, treatment of **20** with catalytic $BF_3{\cdot}OEt_2$ in dry dichloromethane furnished a complex mixture of products, from which the isotwistane **21** could not, however, be isolated. Changing the acid catalyst also did not alter the outcome of the reaction. The failure of this rearrangement was surprising considering the structural similarity between the dienes **19** and **20**.

In conclusion, an efficient method for the construction of the isotwistane skeleton present in pupukeananes is reported from readily available cyclohexadienes, which involved a tandem acid-catalysed rearrangement–ene cyclisation of a bicyclo-[2.2.2]octenone to a tricyclo[5.3.0.$0^{4,8}$]decane skeleton as the key step. This methodology was successful on the corresponding alkyne system also. An acid-catalysed rearrangement to the tricyclo[4.3.1.$0^{3,7}$]decane skeleton culminated in the formal synthesis of 2-pupukeanone **5**.

Experimental

All mps and bps are uncorrected. Mps were recorded on a Mettler FP1 instrument. IR spectra were recorded on Perkin-Elmer 78 and JASCO FT/IR-410 spectrophotometers. NMR spectra were recorded on a JEOL FX-90Q, a Bruker ACF-200, or a JEOL JNM LA-300 spectrometer. The chemical shifts (δ/ppm) and coupling constants (J/Hz) are reported for standard tetramethylsilane (for ^{1}H) or the central line of $CDCl_3$ (for ^{13}C). Mass spectra were recorded on a JEOL MS-DX 303 with inbuilt direct-inlet system, and relative intensities of the ions are given in parentheses. Microanalysis was carried out using a Carlo Erba 1106 instrument. Analytical and preparative TLC were performed on glass plates coated with Acme's silica gel G containing 13% calcium sulfate as binder. Visualisation of the spot was accomplished by exposure to iodine vapour. Acme's silica gel (60–120 mesh) was used for column chromatography. 'Hexane' refers to petroleum spirit fraction boiling at 60–80 °C, and ether refers to diethyl ether. All dry solvents were prepared by standard procedures. Liquid ammonia was distilled over sodamide before use. All reactions involving air- and moisture-sensitive reagents were performed under either a blanket of nitrogen or argon-filled balloons. Wherever it is mentioned, 'the usual work-up' means the reaction mixture was washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in a rotary evaporator

at aspirator pressure for the isolation of the product mixture. Unless otherwise stated, all starting materials were obtained from commercial suppliers and were used without further purification.

1-Methoxy-3-*endo*-methylbicyclo[2.2.2]oct-5-en-2-one 13

To a freshly prepared LDA solution [prepared from 1 M solution of *n*-BuLi (14.4 ml, 14.4 mmol) and diisopropylamine (2 ml, 15.8 mmol) in 40 ml of THF] at −78 °C under argon was added a solution of the ketone **9** (2.38 g, 13.14 mmol) in 40 ml of THF dropwise. After stirring of the reaction mixture at −78 °C for 1 h, methyl iodide (2 ml, 30 mmol) as a solution in 10 ml of THF was added and the mixture was stirred for 1 h. The reaction mixture was poured into saturated aq. ammonium chloride and extracted with ether. The ether layer was washed successively with water, aq. sodium thiosulfate, water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent followed by column chromatography over silica gel [ether–pentane (1 : 49)] as eluent afforded the *ketone* **13** as a colourless oil (2.1 g, 80%); ν_{max}/cm^{-1} 3005, 2925, 1715 and 1640; δ_H (90 MHz) 1.09 (3H, d, *J* 7.2, CH*Me*), 1.6–2.2 (5H, m), 2.73 (1H, m, bridgehead H), 3.52 (3H, s, OMe) and 6.1–6.5 (2H, m, olefinic); δ_C (22.5 MHz) 16.7, 24.4, 25.0, 37.6, 43.4, 52.3, 83.6, 129, 134.2 and 210.3; *m*/*z* 166 (M^+, 55%), 138 (100), 122 (100) and 110 (60) (Found: M^+, 166.0994. $C_{10}H_{14}O_2$ requires *M*, 166.0994).

1-Methoxy-3-methyl-3-*endo*-(3-methylbut-2-enyl)bicyclo[2.2.2]-oct-5-en-2-one 11

To a freshly prepared LDA solution [prepared from 1 M solution of *n*-BuLi (8 ml, 8 mmol) and diisopropylamine (1.04 ml, 7.4 mmol) in 20 ml of THF] at −78 °C under argon was added a solution of the ketone **13** (0.66 g, 2.0 mmol) in THF (10 ml) dropwise. The resultant solution was stirred for 1 h at −78 °C and quenched with prenyl bromide (1.48 g, 10 mmol) followed by the addition of HMPA (0.7 ml, 4 mmol). The reaction mixture was stirred overnight, poured into ice-cold water, and extracted with ether (4 × 25 ml). The combined organic layer was washed successively with 2 M HCl, water and brine and dried over anhydrous Na_2SO_4. Removal of the solvent followed by column chromatography on silica gel [ethyl acetate–'hexane' (1 : 24)] afforded the *ketone* **11** (0.7 g, 75%) as an oil; ν_{max}/cm^{-1} 3020, 2940, 1720 and 1640; δ_H (90 MHz) 1.08 (3H, s, Me), 0.85–2.18 (6H, m), 1.59 (3H, s, Me), 1.73 (3H, s, Me), 2.61 (1H, m, bridgehead H), 3.52 (3H, s, OMe), 5.12 (1H, t, *J* 7.1, olefinic), 6.17 (1H, dd, *J* 6.7 and 1.7, olefinic) and 6.45 (1H, dd, *J* 8.2 and 6.7, olefinic); δ_C (22.5 MHz) 17.6, 21.0, 21.1, 25.7, 26.2, 36.5, 39.5, 47.0, 52.8, 84.2, 118.7, 127.4, 134.6, 136.5 and 213.1; *m*/*z* 234 (M^+, 90%), 206 (25), 175 (26), 150 (75), 136 (100) and 110 (100) (Found: M^+, 234.1616. $C_{15}H_{22}O_2$ requires *M*, 234.1620).

1-Hydroxy-5-isopropenyl-7-methyltricyclo[5.3.0.0^{4,8}]decan-2-one 15

A solution of the ketone **11** (0.5 g, 2.13 mmol) in CH_2Cl_2 (50 ml) was stirred with $HClO_4$ (70%; 0.1 ml) at room temperature. After 30 min, the reaction mixture was diluted with CH_2Cl_2, washed successively with water, saturated aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the solvent followed by chromatography of the crude product over silica gel [ethyl acetate–'hexane' (1 : 30)] gave the *hydroxy ketone* **15** (0.272 mg, 57%) as a viscous oil; ν_{max}/cm^{-1} 3460, 2920, 1700 and 1640; δ_H (300 MHz) 1.22 (3H, s, Me), 1.67 (3H, s, Me), 1.30–2.50 (10H, m), 2.68–2.75 (1H, m, H-4), 4.68 (1H, s, olefinic) and 4.90 (1H, s, olefinic); *m*/*z* 220 (M^+, 61.5%), 202 (11), 192 (73), 177 (41), 134 (97.5), 123 (100), 109 (67) and 95 (86) (Found: M^+, 220.1466. $C_{14}H_{20}O_2$ requires *M*, 220.1465).

1-Hydroxy-5-isopropylidene-7-methyltricyclo[5.3.0.0^{4,8}]decan-2-one 12

A solution of the hydroxy olefin **15** (0.25 g, 1.14 mmol) and PTSA (catalytic) in dry benzene (5 ml) was refluxed for 1 h. The reaction mixture was cooled, washed successively with saturated aq. $NaHCO_3$ (10 ml) and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified on a silica gel column [ethyl acetate–'hexane' (1 : 30)] to yield the *hydroxy ketone* **12** (0.24 g, 95%) as a solid, which was recrystallised from methylene dichloride; mp 77 °C; ν_{max}/cm^{-1} 3460, 2910 and 1700; δ_H (300 MHz) 1.24 (3H, s, Me), 1.53 (3H, s, vinylic Me), 1.63 (3H, s, vinylic Me), 1.50–2.00 (6H, m), 2.11 and 2.16 (1H, dt, *J* 15.9 and 2.1, H-8), 2.29 (1H, dd, *J* 12.6 and 9.3 Hz, H-3), 2.42 (1H, d, *J* 16.2, H-6) and 3.03 (1H, dd, *J* 9 and 5.4, H-4); δ_C (75 MHz) 17.6 (t), 18.1 (q), 20.6 (q), 20.7 (q), 32.3 (t), 38.0 (t), 41.0 (d), 42.3 (t), 44.8 (d), 53.7 (s), 74.4 (s), 123.6 (s), 136.1 (s) and 221.0 (s); *m*/*z* 220 (M^+, 100%), 202 (7), 192 (37), 177 (48), 159 (16), 134 (66), 119 (39) and 107 (22) (Found: M^+, 220.1452; C, 76.13; H, 9.04. $C_{14}H_{20}O_2$ requires *M*, 220.1453; C, 76.33; H, 9.15%).

3-(But-2-ynyl)-1-methoxy-3-methylbicyclo[2.2.2]oct-5-en-2-one 16

To a solution of LDA [generated from 7 ml of 1.4 M BuLi (10 mmol) and diisopropylamine (1.58 ml, 11.3 mmol) in 40 ml of dry THF] at −78 °C under argon was added a solution of the ketone **13** (1.1 g, 6.6 mmol) in dry THF (20 ml) dropwise. After being stirred at the same temperature for 1 h, the mixture was treated with 1-bromobut-2-yne (1.7 g, 13.2 mmol) and dry HMPA (2 ml) and was stirred at −78 °C for another 30 min and at room temperature for 2 h. Water was added and the product was extracted with ether. The ether layer was washed successively with dil. HCl, water, and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent followed by chromatography [ethyl acetate–'hexane' (1 : 25)] furnished the *ketone* **16** (1.22 g, 84%) as a colourless oil; ν_{max}/cm^{-1} 2240 and 1730; δ_H (300 MHz) 1.2 (3H, s, Me), 1.28–2.02 (4H, m), 1.81 (3H, t, *J* 2.4, acetylenic Me), 2.08 and 2.34 (2H, q of d, *J* 13.8 and 2.7, $C{\equiv}CCH_2$), 2.93 (1H, br s, bridgehead proton), 3.51 (3H, s, OMe), 6.15 (1H, d, *J* 8.4, olefinic) and 6.54 (1H, dd, *J* 8.4 and 6, olefinic); δ_C (75 MHz) 3.4, 19.4, 26.3, 27.6, 30.3, 42.2, 48.9, 52.8, 76.1, 79.2, 83.9, 125.4, 142.2 and 211.4; *m*/*z* 218 (M^+, 14%), 190 (49), 110 (100) and 82 (33) (Found: M^+, 218.1842. $C_{14}H_{18}O_2$ requires *M*, 218.1831).

5-Acetyl-1-hydroxy-7-methyltricyclo[5.3.0.0^{4,8}]decan-2-one 17

A solution of the ketone **16** (0.5 g, 2.3 mmol) in CH_2Cl_2 (20 ml) was stirred with $HClO_4$ (0.1 ml) at room temperature. After 30 min, the reaction mixture was washed successively with water, saturated aq. $NaHCO_3$, and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent followed by column chromatography over silica gel [ethyl acetate–'hexane' (1 : 5)] gave the *hydroxy dione* **17** (0.21 g, 42%) as a viscous oil; ν_{max}/cm^{-1} 3460, 1710 and 1700; δ_H (300 MHz) 1.13 (3H, s, Me), 1.6–2.15 (8H, m), 2.18 (3H, s, $COCH_3$) and 2.34–2.59 (3H, m); δ_C (75 MHz) 16.4, 21.7, 27.2, 33.4, 33.6, 36.4, 38.0, 44.3, 47.8, 48.6, 85.0, 203.8 and 209.7; *m*/*z* 222 (M^+, 6%), 180 (43), 149 (50), 91 (62) and 41 (100) (Found: M^+, 222.1413. $C_{13}H_{18}O_3$ requires *M*, 222.1419.

5-Isopropylidene-7-methyl-2-methylenetricyclo[5.3.0.0^{4,8}]decan-1-ol 19

A solution of potssium *tert*-amylate [prepared from potassium (0.11 g, 2.727 mmol) and *tert*-amyl alcohol (0.5 ml)] was added to a suspension of methyl(triphenyl)phosphonium iodide (1.1 g, 2.727 mmol) in benzene (5 ml) under nitrogen *via* cannula, and the resulting pale yellow solution was stirred

for 20 min at room temperature. A solution of the ketone **12** (100 mg, 0.45 mmol) in dry benzene (5 ml) was added and the mixture was refluxed for 24 h. After cooling of the reaction mixture, water was added and the product was extracted with ether. The extract was subjected to the usual work-up followed by chromatography of the crude mixture over silica gel [ethyl acetate–'hexane' (1 : 30)] to furnish the *hydroxy olefin* **19** (83 mg, 83%) as a colourless oil; ν_{max}/cm^{-1} 3350 and 1420; δ_H (90 MHz) 1.10 (3H, s, Me), 1.58 (3H, s, vinylic Me), 1.64 (3H, s, vinylic Me), 1.70–2.80 (10H, m), 4.54 (1H, t, *J* 2.5, olefinic) and 4.80 (1H, t, *J* 2.5, olefinic); δ_C (22.5 MHz) 19.7, 20.2, 20.5, 21.1, 35.1, 37.2, 37.9, 45.5, 52.6, 52.8, 84.5, 103.4, 120.2, 138.3 and 152.4; *m*/*z* 218 (M^+, 21%), 203 (4), 185 (5), 175 (6), 134 (100), 119 (36), 105 (21) and 91 (24) (Found: M^+, 218.1673. $C_{15}H_{22}O$ requires *M*, 218.1672).

5-Isopropenyl-7-methyl-2-methylenetricyclo[5.3.0.0^{4,8}]decan-1-ol 20

A solution of potassium *tert*-amylate [prepared from potassium (0.21 g, 5 mmol) and *tert*-amyl alcohol (1 ml)] was added to a suspension of methyl(triphenyl)phosphonium iodide (2.1 g, 5.4 mmol) in benzene (10 ml) under nitrogen *via* cannula, and the resulting yellow solution was stirred for 20 min at room temperature. The dione **17** (0.2g, 0.9 mmol) as a solution in dry benzene (5 ml) was added and the mixture was refluxed for 12 h. After cooling of the reaction mixture, water was added and the product was extracted with ether. The extract was subjected to the usual work-up followed by column chromatography of the crude product over silica gel [ethyl acetate–'hexane' (1 : 30)] to furnish the *hydroxy diene* **20** (0.15 g, 73%) as a colourless oil; ν_{max}/cm^{-1} 3350, 1640 and 890; δ_H (300 MHz) 0.81 (3H, s, Me), 1.62 (3H, s, vinylic Me), 1.23–2.66 (11H, m), 4.67 (1H, t, *J* 1.5, olefinic), 4.80 (1H, br s, olefinic), 4.83 (1H, t, *J* 1.5, olefinic) and 4.93 (1H, t, *J* 2.1, olefinic); *m*/*z* 218 (M^+, 56%), 203 (58), 175 (100), 91 (78) and 77 (50) (Found: M^+, 218.1782. $C_{15}H_{22}O$ requires *M*, 218.1672).

5-Isopropylidene-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decan-2-one 10

To a solution of the diene **19** (50 mg, 0.23 mmol) in dry CH_2Cl_2 (1 ml) was added catalytic $BF_3{\cdot}OEt_2$ (one drop) and the solution was stirred for 24 h at room temperature. Saturated aq. Na_2CO_3 was added and the product was extracted with ether. The extract was submitted to the usual work-up followed by chromatography over silica gel [ethyl acetate–'hexane' (1 : 24)] to furnish the *ketone* **10** (40 mg, 80%); ν_{max}/cm^{-1} 2920 and 1712; δ_H (400 MHz) 0.89 (3H, s, Me), 1.17 (3H, s, Me), 0.9–2.4 (9H, m), 1.52 (3H, s, Me), 1.62 (3H, s, Me) and 2.9 (1H, m); δ_C (100 MHz) 17.0, 18.71, 19.88, 20.42, 20.61, 23.25, 27.57, 32.74, 38.39, 40.67, 41.88, 50.6, 122.69, 137.43 and 222.74; *m*/*z* 218 (M^+, 100%), 162 (50) and 134 (80) (Found: M^+, 218.1681. $C_{15}H_{22}O$ requires *M*, 218.1671).

Acknowledgements

We thank the UGC, New Delhi for the award of a fellowship to M. S. L. We thank CSIR, New Delhi for a fellowship to K. K. and for financial assistance (Emeritus Scientist to G. S. R. S. R.).

References

1 For earlier parts see: Part 30, H. K. Hariprakasha, P. Sathya Shanker and G. S. R. Subba Rao, *Indian. J. Chem.*, *Sect. B*, 2000, **39**, 94; Part 31, P. J. Biju and G. S. R. Subba Rao, *Tetrahedron Lett.*, 1999, **40**, 2405; Part 32, P. J. Biju and G. S. R. Subba Rao, *Tetrahedron Lett.*, 1999, **40**, 9379; Part 33, M. S. Laxmisha and G. S. R. Subba Rao, *Tetrahedron Lett.*, 2000, **41**, 3759.

2 R. E. Johannes, *Veliger*, 1963, **5**, 104.

3 B. J. Burreson, P. J. Scheuer, J. Finer and J. Clardy, *J. Am. Chem. Soc.*, 1975, **97**, 4763.

4 M. R. Hegadone, B. J. Burreson, P. J. Scheuer, J. S. Finer and J. Clardy, *Helv. Chim. Acta*, 1979, **62**, 2484.

5 N. Fusetani, H. J. Wolstenholme and S. Matsunaga, *Tetrahedron Lett.*, 1990, **31**, 5623.

6 (*a*) A. T. Pham, T. Ichiba, W. Y. Yoshida, P. J. Scheuer, T. Uchida, J. I. Tanaka and T. Higa, *Tetrahedron Lett.*, 1991, **32**, 4843; (*b*) P. Karuso, A. Poiner and P. J. Scheuer, *J. Org. Chem.*, 1989, **54**, 2095.

7 (*a*) E. J. Corey, M. Behforouz and M. Ishiguro, *J. Am. Chem. Soc.*, 1979, **101**, 1608; (*b*) S. L. Hseih, C. T. Chiu and N. C. Chang, *J. Org. Chem.*, 1989, **54**, 3820; (*c*) H. Yamamoto and H. L. Sham, *J. Am. Chem. Soc.*, 1979, **101**, 1609; (*d*) E. Piers and M. Winter, *Justus Liebigs Ann. Chem.*, 1982, 973; (*e*) G. A. Schiesher and J. D. White, *J. Org. Chem.*, 1980, **45**, 1864.

8 (*a*) E. J. Corey and M. Ishiguro, *Tetrahedron Lett.*, 1979, 2745; (*b*) G. Frater and J. Wenger, *Helv. Chim. Acta*, 1984, **67**, 1702; (*c*) N. C. Chang and C. K. Chang, *J. Org. Chem.*, 1996, **61**, 4967; (*d*) K. Kaliappan and G. S. R. Subba Rao, *Tetrahedron Lett.*, 1997, **38**, 2185; (*e*) K. Kaliappan and G. S. R. Subba Rao, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3387; (*f*) K. Kaliappan and G. S. R. Subba Rao, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3393; (*g*) A. Srikrishna and T. J. Reddy, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3293; (*h*) A. Srikrishna, D. Vijayakumar and G. V. R. Sharma, *Tetrahedron Lett.*, 1997, **38**, 2003.

9 P. Sathya Shanker and G. S. R. Subba Rao, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 539.

10 P. J. Biju and G. S. R. Subba Rao, *Tetrahedron Lett.*, 1999, **40**, 181.

11 D. A. Evans, W. L. Scott and L. K. Truesdale, *Tetrahedron Lett.*, 1972, 121.

12 G. Stork and N. H. Baine, *Tetrahedron Lett.*, 1985, **26**, 5927.

13 (*a*) I. Alfaro, W. Ashton, K. L. Rabone and N. A. J. Rogers, *Tetrahedron*, 1974, **30**, 559; (*b*) T. Uyehara, K. Osanai, M. Sugimoto, I. Suzuku and Y. Yamamoto, *J. Am. Chem. Soc.*, 1989, **111**, 7264.

14 (*a*) F. H. Koster and H. Wolf, *Tetrahedron Lett.*, 1981, **22**, 3937; (*b*) J. A. Marshall and P. G. Wuts, *J. Org. Chem.*, 1977, **42**, 1794.

15 (*a*) J. A. Amupitan, E. G. Scovell and J. K. Sutherland, *J. Chem. Soc.*, *Perkin. Trans. 1*, 1983, 755; (*b*) E. E. Tamelen and J. R. Hwu, *J. Am. Chem. Soc.*, 1983, **105**, 2490; (*c*) B. E. McCarry, R. L. Markezich and W. S. Johnson, *J. Am. Chem. Soc.*, 1973, **95**, 4416; (*d*) B. M. Trost, *Comprehensive Organic Synthesis*, 1991, vol. 3, pp. 341–377.