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Approaches to sesquiterpenes containing three contiguous quaternary carbon atoms. Synthesis of 3-methoxythapsene

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Synthetic approach to 3-alkoxythapsane, comprising of the carbon framework of a small group of sesquiterpenes containing three contiguous quaternary carbon atoms has been described. A combination of alkylation, orthoester Claisen rearrangement and intramolecular diazoketone cyclopropanation has been employed for the creation of the three requisite contiguous quaternary carbon atoms.

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The medicinal properties of the plants belonging to the umbelliferous genus *Thapsia*, mostly distributed in the Mediterranean region and in the Iberian peninsula, were recognized as early as 300 B.C. For centuries, preparations containing resin from the root of *Thapsia garganica* L. have been used in Arabian and European medicine for the treatment of pulmonary diseases, catarrh and as counter-irritants for the relief of rheumatic pains. Phytochemical investigations of *Thapsia garganica* led to the isolation of two major active principles, sesquiterpene lactones (guaianolides) thapsigargin and thapsigargicin, which were found to be responsible for the medicinal activity[1]. Even though, thapsigargin and thapsigargicin were absent in *Thapsia villosa*, it contains a large number of sesquiterpenes belonging to guaianolides, germacranes, cadinenes and caryophyllenes, and in addition a new group of sesquiterpenes named as Thapsanes, which are unique to *Thapsia villosa*. In 1984, Rasmussen and co-workers reported[2] isolation of the first member of this new group of sesquiterpenes, from the ethanolic extract of the roots of *Thapsia villosa* L, whose structure was established as the ester **1** from its spectral data and confirmed by single crystal X-ray analysis. Simultaneously (1985), Grande and co-workers[3,4] reported the isolation of the corresponding senecioate ester **2** from the benzene extract of the roots of *Thapsia villosa* L. var. *minor* (Hoff. and Link) Cout., along with five other hemiacetalic[5] **3-7** and four non-acetalic[5] **8-11** minor components, having the same carbon framework. In 1990, Christensen and co-workers[6] have reported the isolation of three more thapsanes, two nonacetalic **12** and **13**, and one hemiacetalic **14** from *Thapsia villosa* var. *minor* collected near Capo Espichel. The trivial name "*thapsane*" was suggested[4] for the bicyclic carbon framework *cis*-1,2,2,6,8,9-hexamethylbicyclo[4.3.0]-nonane **15** present in these compounds. Structures of all the thapsanes isolated so far are given in **Chart I**.

Presence of three contiguous quaternary carbon atoms makes thapsanes interesting and challenging synthetic targets. The first synthesis of the carbon framework of thapsane was reported[7] in 1989 starting from cyclogeraniol. The strategy has been further extended to the total synthesis[8] of the hemiacetalic thapsane **14** in its racemic form. Recently, enantio-specific synthesis of the thapsanes **6** and **14** had also been accomplished[8]. Herein, we report the details[9] of the first total synthesis of a thapsane containing a oxygen functionality at the C-3 position starting from the Hagemann's ester.

Retrosynthetic analysis of thapsane **16**, (**Scheme I)**, identified the bicyclic ketone **17** as the key intermediate, which could be obtained from the tricyclic ketone **18**. It was contemplated that by employing an intramolecular cyclopropanation reaction the tricyclic ketone **18** could be generated from the ketal acid **19**, which could be obtained from Hagemann's ester **20** *via* the allyl alcohol **21**.

Accordingly, first attention was focused on the conversion of the Hagemann's ester **20** into the ketal acid **19** *via* the allyl alcohol **21**, (**Scheme II**). Thus, treatment of Hagemann's ester **20** with sodium

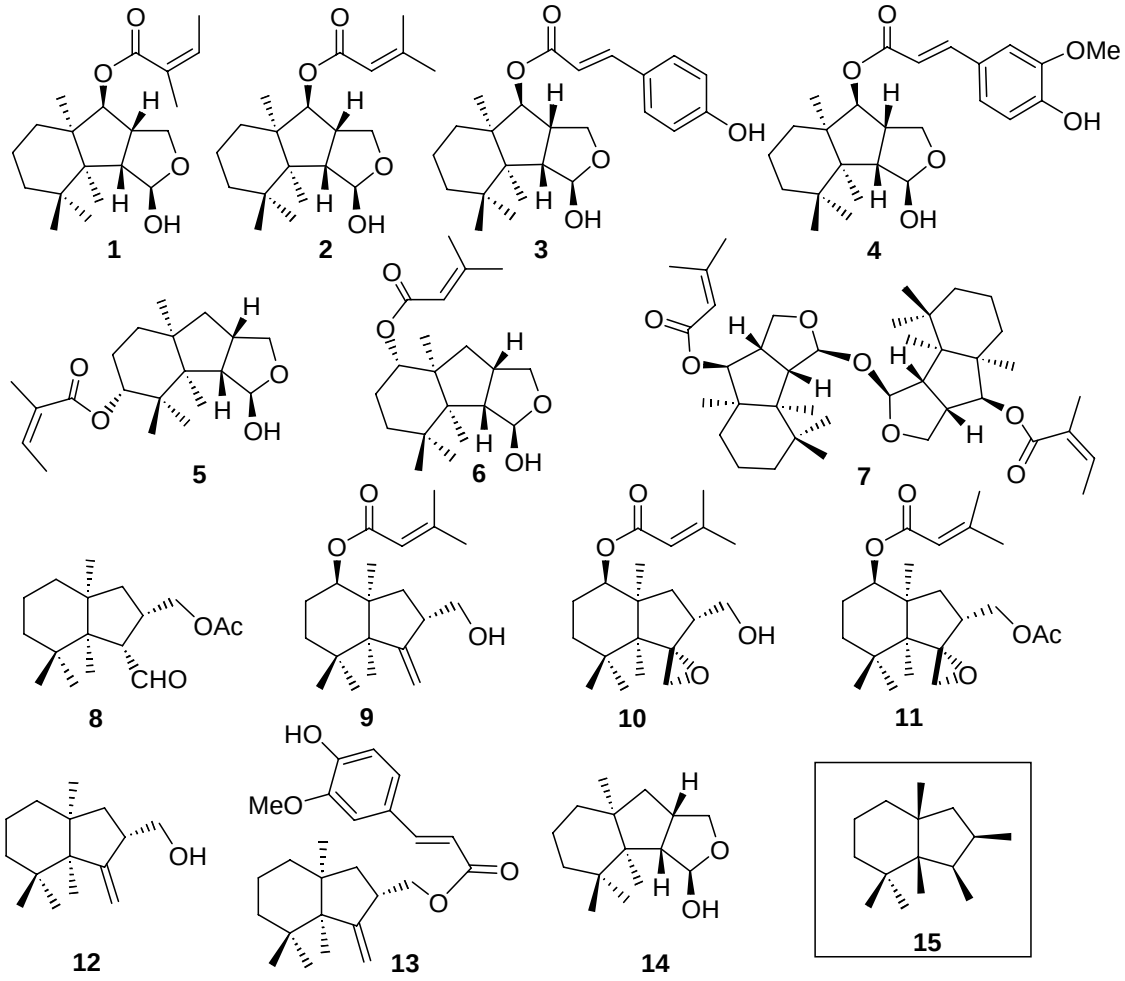
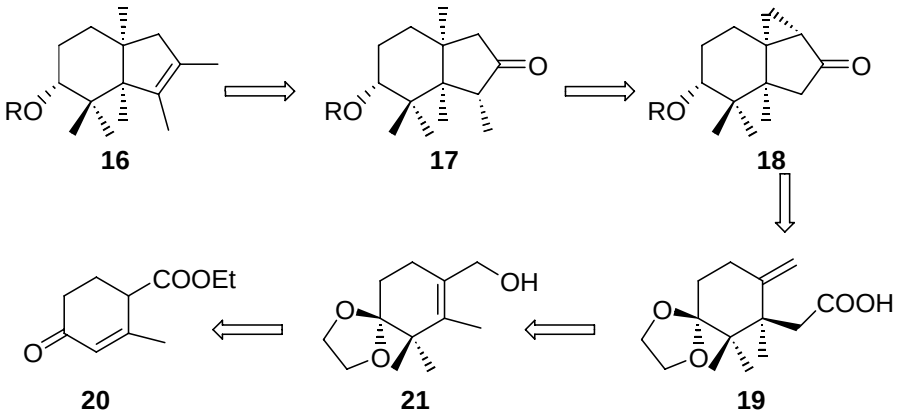
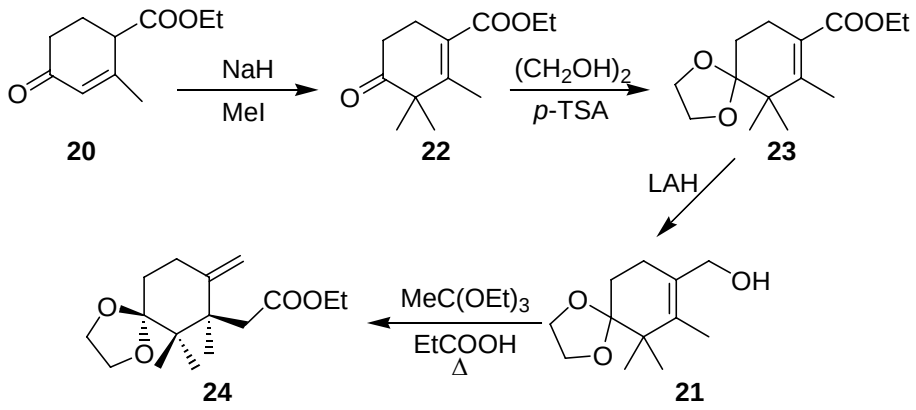


Chart I

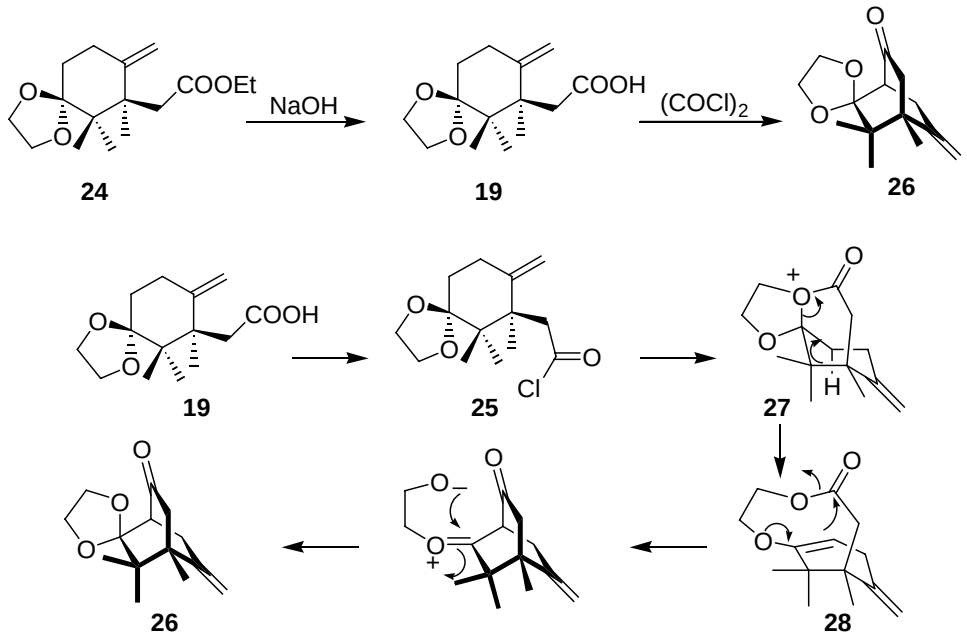


Scheme I

hydride and methyl iodide at low temperature furnished predominantly the γ,γ-dimethylated product, the ketoester **22** in 64% yield. Reaction of the ketoester **22** with ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene with a Dean-Stark apparatus furnished the ketalester **23** in 89% yield. Low temperature reduction of the ester **23** with lithium aluminium hydride (LAH) in ether generated the allyl alcohol **21** in 92% yield. An ortho-ester variant of Claisen rearrangement[10], developed by



Scheme II

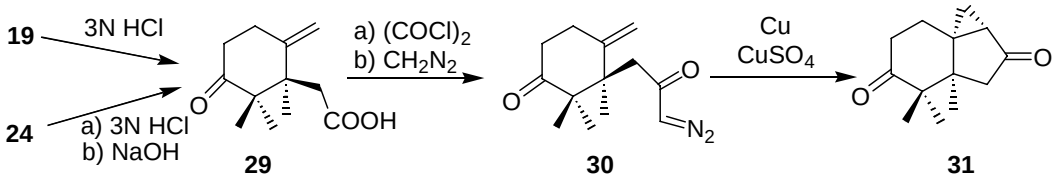


Scheme III

Johnson was employed for the creation of the second quaternary carbon atom. Thermal activation of the allyl alcohol **21** with triethyl orthoacetate and a catalytic amount of propionic acid in a sealed tube at 180 °C furnished the γ,δ-unsaturated ester **24** in 84% yield, whose structure was established from the spectral data. Hydrolysis of the ketalester **24** with 5% sodium hydroxide in 1:1 methanol-water followed by careful acidification generated the ketal acid **19**.

Next, conversion of the ketal acid **19** into the corresponding diazoketone was addressed. However, reaction of the ketal acid **19** with oxalyl chloride in benzene, contrary to the expected acid chloride **25**, both in the presence as well as in the absence of triethylamine furnished the bicyclic ketoketal **26**, m.p. 61°C, in 65% yield, whose structure was deduced from the ^{1}H and ^{13}C NMR spectral data. Formation of the bicyclic ketoketal **26** from the ketal acid **19** could be explained as depicted in **Scheme III**. First reaction of the acid **19** forms the acid chloride **25**. Intramolecular *O*-acylation of the ketal oxygen generates the oxonium ion **27** which loses a proton to generate the enol ether **28**. Intramolecular reaction of the enol ether with the lactone followed by ketal formation transforms the enol ether **28** into the bicyclic ketoketal **26**.

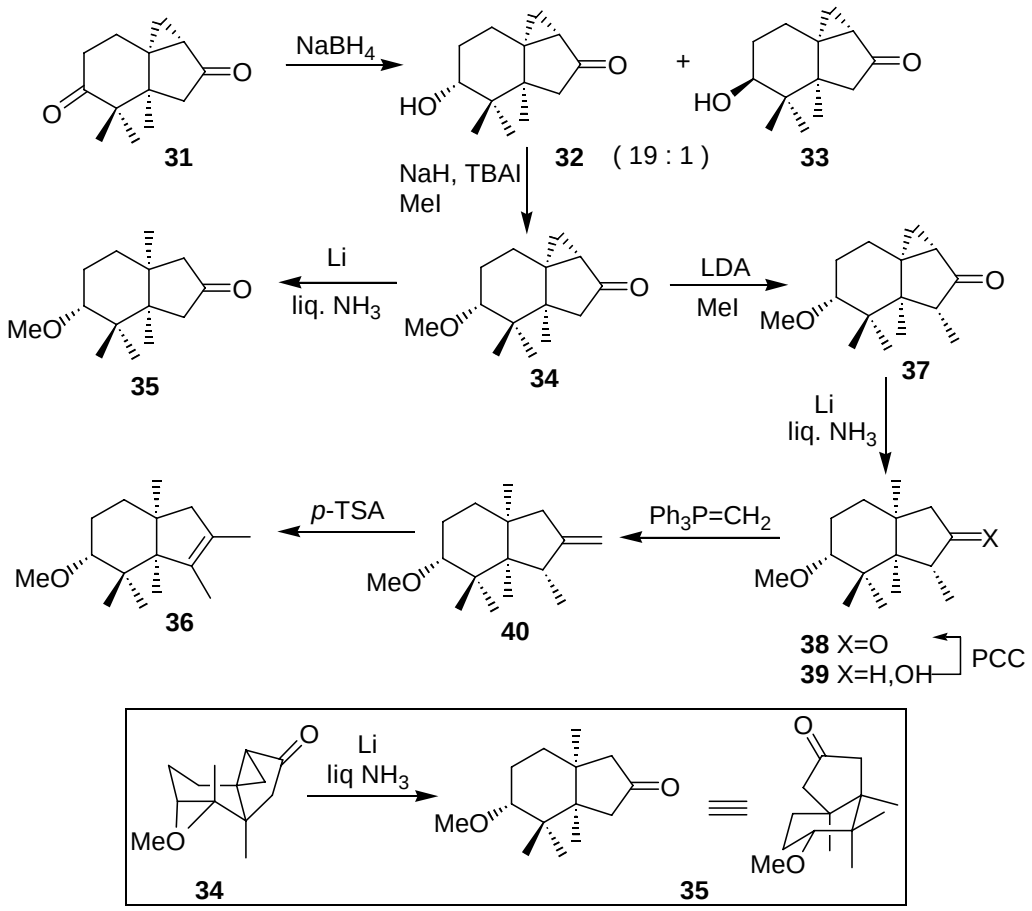
To overcome the problem, ketal moiety in **19** was hydrolysed. Treatment of the ketal acid **19** with 3*N* aqueous hydrochloric acid in THF furnished the keto acid **29**. Alternately, hydrolysis of the ketal moiety in the ketal ester **24** with 3*N* aqueous hydrochloric acid in THF followed by hydrolysis of the ester moiety in



the resultant ketoester with sodium hydroxide in refluxing aqueous methanol also furnished the keto acid **29**. Reaction of the keto acid **29** with oxalyl chloride in benzene at room temperature followed by treatment of the resultant acid chloride with an excess of ethreal diazomethane furnished the diazoketone **30**. It was envisaged that in the intramolecular cyclopropanation reaction[11], the intermediate ketocarbenoid derived from the diazoketone **30** inserts into the olefin exclusively from the *syn* face of the olefin (due to steric reasons) thereby resulting the cyclopropane methylene and the tertiary methyl at C-6 *cis* to each other as required for thapsanes. As expected, intramolecular cyclopropanation of the diazoketone **30** with a mixture of copper powder and anhydrous copper sulphate in refluxing cyclohexane created the third quaternary carbon furnishing exclusively the tricyclic dione **31**, m.p. 199°C, in 74% yield, whose structure was established from its spectral data.

Conversion of the dione **31** into a thapsane *via* differentiation of the two ketones in **31** was then explored. Preferred reduction of a cyclohexanone when compared to cyclopentanone was exploited[12]. Thus, regio- and stereo-selective reduction of the dione **31** with one equivalent of sodium borohydride in methanol at -15°C for 10 min furnished a 19:1 mixture of the hydroxy-ketones **32** and **33** in almost quantitative yield, which were separated by column chromatography on silica gel. Stereochemistry of the hydroxy group in the major and minor hydroxy-ketones **32** and **33** was tentatively assigned based on the coupling constants of the proton attached to the hydroxy bearing carbon. In the major isomer **32**, the signal appeared as a triplet with 2 Hz coupling constant, whereas in the minor isomer **33** it appeared as a doublet of a doublet with 10.8 and 4.8 Hz coupling constants (typical *trans*-diaxial and axial-equatorial couplings of cyclohexane) establishing clearly that the hydroxy group is axial in the major isomer **32** and equatorial in the minor isomer **33**. Hence, based on the preferred conformation of the tricyclo[4.4.0.0^{1,3}]decane system, the structures of the hydroxyketones were assigned as given in **32** and **33**. The good stereoselectivity of the reaction can be readily explained *via* the approach of the hydride from the less crowded equatorial side of the dione **31**. For further confirmation of the stereo- and regio-structures of the hydroxyketones **32** and **33**, it was contemplated to protect the hydroxy group and cleave the cyclopropane ring in the major isomer **32**. Consequently, etherification of the hydroxyketone **32** with sodium hydride and methyl iodide in the presence of a catalytic amount of tetrabutylammonium iodide (TBAI) in *N*,*N*-dimethylformamide (DMF) and THF at room temperature furnished the methoxyketone **34** in 94% yield. Reaction of the methoxyketone **34** with lithium in liquid ammonia furnished the ketone **35**. The stereochemistry of the methoxy group in **35** was assigned as equatorial based on the observed coupling constants of 11.0 (*trans*-diaxial) and 3.3 Hz (axial-equatorial) for the axial proton attached to the methoxy bearing carbon. Based on the molecular mechanics calculations (PCMODEL) in the most preferred conformation of the bicyclic ketone **35** the methoxy group will be equatorial oriented supporting the assigned structure.

Attention was then turned towards the conversion of the methoxyketone **35** into thapsane **36**, which requires introduction of one carbon each at the C-8 and C-9 positions in the methoxyketone **35**. Introduction of one carbon at C-8 could be easily achieved *via* Wittig reaction. But for the introduction of one carbon at C-9, it was quite obvious, that alkylation of the methoxyketone **35** is not practical due to the regiochemical problems associated with the reaction, as alkylation at both the C-7 and C-9 positions are equally feasible. To overcome the regiochemical problems, introduction of the methyl group prior to the cyclopropane ring cleavage, *i.e.* alkylation of the tricyclic ketone **34** was explored. Thus, alkylation of the tricyclic ketone **34** with LDA and methyl iodide in THF and HMPA furnished the methylated ketone **37**, m.p. 78-80°C, in 87% yield in a highly stereoselective manner. Stereochemistry of the secondary methyl group in **37** was assigned on the basis of the approach of the electrophile from the less hindered *exo* face of the hydrindane part of the ketone **34**. Reaction of the tricyclic ketone **37** with lithium in liquid ammonia and THF for 15 min furnished a 2:1 mixture of the bicyclic ketone **38**, m.p. 62°C, and the



alcohol **39**, m.p. 93°C, in 81% yield, which were separated by column chromatography on silica gel. Oxidation of the alcohol **39** with PCC and silica gel in methylene chloride at room temperature furnished the ketone **38**. The regiospecificity of the cyclopropane ring cleavage can be readily explained. It is well established[13] that in the reaction of cyclopropyl ketones using lithium in liquid ammonia conditions, the cyclopropane bond which has better overlap with carbonyl π-orbital will be cleaved. In the tricyclic ketone **37**, it is clear that the π-orbital of the carbonyl group will have better overlap with the C-2 C-3 bond than the C-1 C-3 bond (which is orthogonally oriented) of the cyclopropane ring. Stereochemistry of the secondary methyl group was assigned based on the thermodynamic considerations. As expected, the methyl group in the bicyclic ketone **38** did not isomerise when treated with potassium carbonate in methanol at room temperature. Molecular mechanics calculations (PCMODEL) indicated that the *exo* isomer **38** is 4.90 kcal/mole more stable than the corresponding *endo* isomer. Finally, reaction of the ketone **38** with methylenetriphenylphosphorane in benzene at room temperature furnished 3-methoxythaps-8(11)-ene **40** in 84% yield. Isomerisation of the exomethylene of the thaps-8(11)-ene **40** with a catalytic amount of *p*-TSA in methylene chloride at room temperature furnished 3-methoxythaps-8-ene **36** in 76% yield. Structures of the thapsenes **40** and **36** were established from their spectral data.

In conclusion, we have accomplished the first total synthesis of the thapsenes **40** and **36** containing oxygen functionality at the C-3 position. Incidentally, the relative orientation of the C-3 alkoxy group is identical to those found in natural thapsanes, *e.g.* **5**. A combination of alkylation, orthoester Claisen rearrangement, intramolecular diazoketone cyclopropanation and regiospecific ring cleavage of cyclopropane were employed for the stereospecific generation of the three requisite contiguous quarternary carbon atoms.

Experimental Section

Melting points are recorded using Tempo and Mettler FP1 melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on

Perkin-Elmer 781 and Jasco FTIR 410 spectrophotometers. ^{1}H (300 MHz) and ^{13}C (75 MHz) spectra were recorded on Jeol 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 using DEPT-135, and are given in parentheses. Mass spectra were recorded using Jeol JMS-DX 303 GCMS instrument using direct inlet mode. Relative intensities are given in parentheses. Elemental analyses were carried out using Carlo Erba 1106 CHN analyser. Acme's silica gel (100-200 mesh) was used for column chromatography.

Ethyl 2,3,3-trimethyl-4-oxocyclohex-1-ene-1-carboxylate 22. To a magnetically stirred, ice-cold suspension of NaH (60-65% dispersion in oil, 2.285 g, 59.5 mmoles, washed with dry hexane) in anhydrous THF (150 mL) was added Hagemann's ester **20** (5 mL, 5.38 g, 29.71 mmoles) and stirred for 45 min at the same temperature. The reaction mixture was cooled to -100°C, added methyl iodide (4.64 mL, 10.53 g, 74.32 mmoles) and stirred at -100°C for 1.5 hr. The reaction mixture was slowly warmed up to RT and stirred for 7 hr. Solvent was then evaporated under reduced pressure, 3 *N* aq. HCl (20 mL) was added to the residue and extracted with CH_2Cl_2 (2 × 25 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (0:1 to 1:10) as eluent furnished the ester **22** (4 g, 64%) as oil, IR (neat): 1713, 1626 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 4.20 (2 H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 2.66 (2 H, br t, *J* = 6.9 Hz, H-5), 2.53 (2 H, br t, *J* = 6 Hz, H-6), 2.00 (3 H, t, *J* = 1.8 Hz, olefinic CH_3), 1.32 (3 H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 1.23 (6 H, s, 2 × *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 212.4 (C, C=O), 168.2 (C, OC=O), 149.2 (C, C-2), 124.8 (C, C-1), 60.3 (CH_2, O*C*H$_2$CH$_3$), 48.7 (C, C-3), 35.7 (CH_2, C-5), 26.0 (CH_2, C-6), 23.7 (2 C, CH_3, *C*H$_3$-C-*C*H$_3$), 16.1 (CH_3, C$_2$-CH_3), 14.3 (CH_3, OCH$_2$*C*H$_3$); Mass: m/z 210 (M^+, $C_{12}H_{18}O_3$, 8%), 182 (99), 165 (99), 154 (38), 140 (42), 139 (48), 125 (42), 123 (43), 109 (45), 95 (100), 93 (50).

Ethyl 4,4-(ethylenedioxy)-2,3,3-trimethylcyclohex-1-enecarboxylate 23. A magnetically stirred solution of the ester **22** (1 g, 4.76 mmoles), ethylene glycol (1.5 g, 1.35 mL, 24 mmoles) and a catalytic amount of *p*-TSA in dry benzene (35 mL) was refluxed with a Dean-Stark water trap for 5 hr. Benzene was evaporated under reduced pressure, saturated aq. $NaHCO_3$ solution (5 mL) was added to the residue and extracted with CH_2Cl_2 (2 × 10 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:50 to 1:10) as eluent furnished the ketalester **23** (1.08 g, 89%) as oil, IR (neat): 1712, 1624 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 4.18 (2 H, q, *J* = 6.9 Hz, OC*H*$_2$CH$_3$), 4.05-3.90 (4 H, m, OCH$_2$CH$_2$O), 2.41 (2 H, q of t, *J* = 6.6 and 2.1 Hz), 1.91 (3 H, t, *J* = 1.8 Hz, olefinic CH_3), 1.75 (2 H, t, *J* = 6.6 Hz), 1.29 (3 H, t, *J* = 6.9 Hz, OCH$_2$C*H*$_3$), 1.10 (6 H, s, 2 × *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 169.2 (C, OC=O), 148.1 (C, C-2), 123.7 (C, C-1), 111.4 (C, O-C-O), 64.9 (2 C, CH_2, OCH$_2$CH$_2$O), 59.9 (CH_2, O*C*H$_2$CH$_3$), 44.1 (C, C-3), 26.2 (CH_2), 25.6 (CH_2), 22.1 (2 C, CH_3, *C*H$_3$-C-*C*H$_3$), 16.1 (CH_3, C$_2$-*C*H$_3$), 14.4 (CH_3, OCH$_2$*C*H$_3$); Mass: m/z 254 (M^+, $C_{14}H_{22}O_4$, 20%), 209 (25), 168 (26), 140 (22), 137 (30), 134 (22), 109 (27), 99 (20), 95 (30), 87 (94), 86 (100).

4,4-(Ethylenedioxy)-2,3,3-trimethylcyclohex-1-ene-1-methanol 21. To a magnetically stirred, cold (-70°C) solution of the ester **23** (1.06 g, 4.165 mmoles) in anhydrous ether (25 mL) was added $LiAlH_4$ (158 mg, 4.165 mmoles) and stirred for 2 hr at the same temperature. EtOAc (2 mL) was then added to consume excess $LiAlH_4$, the reaction was quenched with water (10 mL) and extracted with ether (2 × 10 mL). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:10 to 1:2.5) as eluent furnished the allyl alcohol **21** (0.81 g, 92%) as a white solid, m.p. 71°C; IR (thin film): 3430, 1655 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 4.07 (2 H, s, C*H*$_2$OH), 4.05-3.90 (4 H, m, OCH$_2$CH$_2$O), 2.27 (2 H, m), 1.76 (2 H, t, *J* = 6.6 Hz), 1.69 (3 H, s, olefinic CH_3), 1.25 (1 H, br s, OH), 1.05 (6 H, s, 2 × *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 136.6 (C), 128.6 (C), 112.1 (C, O-C-O), 64.9 (2 C, CH_2, OCH$_2$CH$_2$O), 63.4 (CH_2, CH_2OH), 43.1 (C, C-3), 26.8 (CH_2), 26.7 (CH_2), 22.3 (2 C, CH_3, *C*H$_3$-C-*C*H$_3$), 13.4 (CH_3); Mass: m/z 212 (M^+, $C_{12}H_{20}O_3$, 8%), 194 (8), 93 (40), 87 (49), 86 (100).

Ethyl 2-[3,3-(ethylenedioxy)-1,2,2-trimethyl-6-methylenecyclohexyl]acetate 24. A solution of the

allyl alcohol **21** (5 g, 23.6 mmoles), triethyl ortho-acetate (17.8 g, 109 mmoles) and propionic acid (≈50 µl) was placed in a sealed tube and heated to 180°C for 7 days in an oil-bath. The reaction mixture was then cooled, diluted with CH_2Cl_2 (25 mL), washed with 1 *N* aq. HCl (5 mL) followed by saturated aq. $NaHCO_3$ solution (5 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:50 to 1:10) as eluent furnished the ester **24** (5.575 g, 84%) as colourless oil, IR (neat): 1729, 1639, 904 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ [4.84 (1 H, br s), 4.68 (1 H, br s), C=CH_2], 4.10-3.90 (4 H, m, OCH_2CH_2O), 3.95-3.75 (2 H, m, O*C*$H_2$$CH_3$), 3.48, 2.14 (2 H, 2 × d, *J* = 12.9 Hz, *C*H_2COOEt), 2.63 (1 H, m), 2.15 (1 H, m), 1.70-1.50 (2 H, m), 1.19 (3 H, t, *J* = 7.2 Hz, OCH_2C*H*$_3$), [1.18 (3 H, s), 0.95 (3 H, s), 0.88 (3 H, s), 3 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 172.5 (C, OC=O), 150.1 (C, *C*=CH_2), 113.0 (C, O-C-O), 110.6 (CH_2, C=*C*H_2), 65.5 (CH_2), 63.8 (CH_2, OCH_2CH_2O), 59.5 (CH_2, O*C*H_2CH_3), 46.3 (C), 46.2 (C), 40.8 (CH_2, *C*H_2C=O), 31.8 (CH_2), 30.6 (CH_2), 21.7 (CH_3), 19.0 (CH_3), 15.8 (CH_3), 14.4 (CH_3, OCH_2*C*H_3); Mass: m/z 282 (M^+, $C_{16}H_{26}O_4$, 5%), 239 (100), 237 (11), 195 (16), 167 (29), 99 (32).

2-[3,3-(Ethylenedioxy)-1,2,2-trimethyl-6-methyl-enecyclohexyl]acetic acid 19. A magnetically stirred solution of the ester **24** (826 mg, 2.93 mmoles) in methanol (6.6 mL) and 10% aq. NaOH (6.6 mL, 16.5 mmoles) was refluxed in an oil-bath for 7 hr. The reaction mixture was cooled and washed with CH_2Cl_2 (2 mL). The *p*H of the reaction mixture was adjusted to 7 by dropwise addition of 3 *N* aq. HCl, and extracted with CH_2Cl_2 (3 × 10 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent furnished the ketalacid **19** (603 mg, 81%) as a solid, m.p. 162°C; IR (thin film): 3100, 1700, 1640, 900 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ [4.91 (1 H, d, *J* = 1.5 Hz), 4.75 (1 H, br s), C=C*H*$_2$], 4.00 (2 H, d of t, *J* = 6.3 and 2.1 Hz), 3.89 (1 H, m), 3.80 (1 H, m, OCH_2CH_2O), 3.55, 2.24 (2 H, 2 × d, *J* = 12.9 Hz, C*H*$_2$COOH), 2.60 (1 H, t of d, *J* = 13.5 and 9.9 Hz), 2.19 (1 H, t of d, *J* = 13.5 and 3.6 Hz), 1.67 (2 H, m), [1.20 (3 H, s), 0.97 (3 H, s), 0.90 (3 H, s), 3 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.3 (C, OC=O), 149.4 (C, *C*=CH_2), 112.7 (C, O-C-O), 110.9 (CH_2, C=*C*H_2), 65.4 (CH_2), 63.7 (CH_2, OCH_2CH_2O), 46.1 (C), 46.0 (C), 40.8 (CH_2, *C*H_2COOH), 31.6 (CH_2), 30.3 (CH_2), 21.5 (CH_3), 18.7 (CH_3), 15.6 (CH_3); Mass: m/z 254 (M^+, $C_{14}H_{22}O_4$, 2%), 211 (100), 195 (20), 167 (44), 125 (20), 113 (20), 99 (85).

6,6-(Ethylenedioxy)-4,5,5-trimethyl-8-methylene-bicyclo[2.2.2]octan-2-one 26. To a magnetically stirred solution of the acid **19** (200 mg, 0.79 mmole) in dry benzene (1 mL) and one drop of DMF, was added triethylamine (0.1 mL, 0.786 mmole), and stirred for 5 min at RT. Oxalyl chloride (0.68 mL, 7.86 mmoles) was added to the reaction mixture and stirred for 1 hr. It was then diluted with ether (10 mL), washed with saturated aq. $NaHCO_3$ solution (2 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:20 to 1:5) as eluent furnished the ketoketal **26** (120 mg, 65%) as a white solid, which was recrystallised from hexane, m.p. 61°C; IR (thin film): 1728, 1646, 878 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ [4.91 (1 H, br s), 4.87 (1 H, br s), C=CH_2], 4.10-3.75 (4 H, m, OCH_2CH_2O), 2.77 (1 H, d, *J* = 16.5 Hz), 2.55 (1 H, d, *J* = 19.0 Hz), 2.47 (1 H, m), 2.43 (1 H, m of d, *J* = 16.5 Hz), 1.85 (1 H, d, *J* = 19.0 Hz), [1.05 (3 H, s), 0.96 (3 H, s), 0.94 (3 H, s), 3 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 210.1 (C, C=O), 148.1 (C, *C*=CH_2), 110.8 (C, O-C-O), 108.0 (CH_2, C=*C*H_2), 64.9 (CH_2), 64.4 (CH_2, OCH_2CH_2O), 54.2 (CH, C-1), 46.9 (CH_2, C-3), 45.0 (C), 43.5 (C), 28.4 (CH_2), 21.6 (CH_3), 19.9 (CH_3), 17.2 (CH_3); Mass: m/z 236 (M^+, $C_{14}H_{20}O_3$, 58%), 221 (10), 194 (10), 193 (28), 179 (10), 167 (14), 121 (12), 115 (19), 114 (60), 113 (100), 107 (14), 99 (70).

2-[1,2,2-Trimethyl-6-methylene-3-oxocyclohexyl]-acetic acid 29. Hydrolysis of the ester group in the ketalester **24** (400 mg, 1.42 mmoles) with 10% aq. NaOH (5 mL, 12.5 mmoles) in methanol (5 mL) for 12 hr furnished the ketalacid **19**. Hydrolysis of the ketal moiety in the ketalacid **19** with 3 *N* aq. HCl (5 mL, 15 mmoles) in THF (5 mL) for 1 hr at RT furnished the ketoacid **29** (290 mg, 97% from the ketalester **24**) as a solid, which was recrystallised from hexane, m.p. 127°C; IR (thin film): 3200, 1733, 1705, 1642, 904 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 10.00 (1 H, br s, COOH), [5.09 (1 H, s), 4.95 (1 H, s), C=CH_2], 2.82-2.25 (6 H, m), [1.29 (3 H, s), 1.07 (3H, s), 1.03 (3 H, s), 3 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 214.0 (C, C=O), 177.2 (C, OC=O), 147.0 (C, *C*=CH_2), 113.2 (CH_2, C=*C*H_2), 52.5 (C, C-2'), 47.5 (C, C-1'), 41.0 (CH_2, C-2), 37.5 (CH_2, C-4'), 31.6 (CH_2, C-5'), 22.8 (CH_3), 17.9 (CH_3),

17.7 (CH_3); Mass: m/z 210 (M^+, $C_{12}H_{18}O_3$, 25%), 151 (82), 135 (25), 125 (40), 123 (60), 122 (86), 121 (60), 109 (50), 108 (55), 107 (65), 93 (44), 41 (100).

6, 7, 7-Trimethyltricyclo[4.4.0.0^{1,3}]decane-4, 8-dione 31. A solution of the ketoacid **29** (2.45 g, 11.66 mmoles) and oxalyl chloride (5 mL, 57.5 mmoles) in dry benzene (10 mL) was magnetically stirred for 2 hr at RT. Evaporation of the excess oxalyl chloride and solvent under reduced pressure afforded the acid chloride, which was taken in ether (10 mL), added to a magnetically stirred ice-cold solution of ethereal diazomethane [prepared from *N*-nitroso-*N*-methylurea (10 g) and 60% aq. KOH solution (100 mL) in ether (50 mL)] and stirred for 2 hr at RT. Careful evaporation of the excess diazomethane and solvent on a water-bath and purification of the residue over a silica gel column using EtOAc-hexane (1:20 to 1:1) as eluent furnished the diazoketone **30** (2.64 g, 97% from the keto-acid **29**) as oil, IR (neat): 3080, 2980, 2100 (diazo), 1700 (C=O), 1630 (O=CCHN$_2$), 1350, 1150, 1080, 1050, 900 (C=CH$_2$) cm^{-1}.

To a magnetically stirred, refluxing (by placing two 100 W tungsten lamps near the reaction flask) suspension of copper powder (3.4 g, 53.5 mmoles) and anhydrous copper sulfate (1.13 g, 7.08 mmoles) in dry cyclohexane (215 mL) was added dropwise a solution of the diazoketone **30** (2.64 g, 11.3 mmoles) in dry cyclohexane (25 mL) over a period of 45 min and the reaction mixture was refluxed for 5 hr. It was cooled and copper and copper sulfates were filtered off using a sintered funnel. Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using EtOAc-hexane (1:20 to 1:1) as eluent furnished the tricyclic dione **31** (1.72 g, 74%) as a solid, which was recrystallised from a mixture of hexane - EtOAc, m.p. 198-200°C; IR (thin film): 1728, 1706 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.88 (1 H, d of t, *J* = 14.0 and 7.5 Hz), 2.47 (1 H, d of t, *J* = 14.4 and 5.7 Hz), 2.26 (1 H, d of d of d, *J* = 13.5, 5.7 and 2.0 Hz), 2.11 (1 H, d, *J* = 18.0 Hz), 2.08 (1 H, d of d, *J* = 7.8 and 2.4 Hz), 1.87 (1 H, d of d, *J* = 18.0 and 1.0 Hz), 1.62 (1 H, d of d of d, *J* = 13.5, 7.8 and 1.5 Hz), 1.19 (3 H, s, *tert*-CH_3), 1.09 (1 H, d of d, *J* = 5.1 and 3.0 Hz), 1.07 (3 H, s, *tert*-CH_3), 0.98 (3 H, s, *tert*-CH_3), 1.00-0.90 (1 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 213.0 (C), 211.2 (C), 51.8 (C, C-7), 46.9 (C, C-6), 43.0 (CH_2, C-5), 37.0 (CH, C-3), 35.5 (C and CH_2, C-1 and 9), 28.5 (CH_2, C-10), 23.2 (CH_3), 20.1 (CH_3), 19.0 (CH_3), 16.7 (CH_2, C-2); Mass: m/z 206 (M^+, $C_{13}H_{18}O_2$, 25%), 178 (13), 163 (15), 151 (36), 137 (28), 121 (100), 109 (20), 107 (42), 93 (42).

(1*R,3*S**,6*R**,8*R**)-8-Hydroxy-6,7,7-trimethyltricyclo[4.4.0.0^{1,3}]decan-4-one 32**. To a cold (ice-salt), magnetically stirred solution of the dione **31** (265 mg, 1.29 mmoles) in dry methanol (1.3 mL) was added $NaBH_4$ (48 mg, 1.28 mmoles) in small portions and stirred for 10 min at the same temperature. The reaction was quenched with water (1 mL) followed by 3 *N* aq. HCl (2 mL) and extracted with CH_2Cl_2 (2 × 8 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:4 to 1:1) as eluent furnished the major hydroxyketone **32** (255 mg, 95%) as a white solid, which was recrystallised from a mixture of hexane - CH_2Cl_2, m.p. 255-57°C; IR (thin film): 3450, 1700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62 (1 H, t, *J* = 2.0 Hz, C*H*OH), 2.47 (1 H, d of t, *J* = 14.4 and 4.8 Hz), 2.08 (1 H, d, *J* = 18.0 Hz), 1.98 (1 H, d of d of t, *J* = 14.4, 5.1 and 2.7 Hz), 1.84 (1 H, br d, *J* = 8.7 Hz), 1.70 (1 H, d, *J* = 18.0 Hz), 1.70-1.50 (2 H, m), 1.63 (1 H, br s, OH), 1.36 (3 H, s, *tert*-CH_3), 1.08 (1 H, d of d, *J* = 4.8 and 3.0 Hz), 1.00 (3 H, s, *tert*-CH_3), 1.00-0.85 (1 H, m), 0.88 (3 H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.7 (C=O), 77.0 (CHOH), 45.5, 42.3, 40.3, 37.1, 36.9, 27.0, 24.4, 22.4, 22.3, 21.2, 17.8; Mass: m/z 208 (M^+, $C_{13}H_{20}O_2$, 4%), 156 (36), 147 (23), 135 (47), 123 (65), 122 (35), 121 (41), 112 (40), 109 (50), 107 (67), 105 (35), 97 (42), 95 (50), 93 (61). Further elution of the column with the same solvent furnished the minor hydroxyketone **33** (14 mg, 5%) as a solid, which was recrystallised from a mixture of hexane - CH_2Cl_2, m.p. 224-26 °C; IR (thin film): 3430, 1711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.70 (1 H, d of d, *J* = 10.8 and 4.8 Hz, C*H*OH), 2.13 (1 H, d of t, *J* = 14.7 and 6.0 Hz), 2.06 (1 H, d, *J* = 18 Hz), 2.00 (1 H, br s, OH), 1.78 (1 H, br d, *J* = 9 Hz), 1.75-1.50 (3 H, m), 1.14 (1 H, d of d of d, *J* = 17.7, 5.1 and 2.7 Hz), 1.09 (3 H, s, *tert*-CH_3), 0.92 (1 H, d of d, *J* = 5.1 and 2.7 Hz), 0.89 (3 H, s, *tert*-CH_3), 0.81 (3 H, s, *tert*-CH_3), 0.77 (1 H, d of d of d, *J* = 9.0, 5.4 and 1.5 Hz); ^{13}C NMR (75 MHz**,** $CDCl_3$ + CCl_4): δ 213.4 (C, C=O), 72.9 (CH, CHOH), 44.1 (CH_2, C-5), 44.0 (C, C-6), 41.7 (C, C-7), 37.1 (CH, C-3), 36.2 (C, C-1), 28.8 (CH_2), 27.0 (CH_2), 22.2 (CH_3), 19.1 (CH_3), 17.0 (CH_2, C-2), 15.4 (CH_3).

(1*R,3*S**,6*R**,8*R**)-6,7,7-Trimethyl-8-methoxy-tricyclo[4.4.0.0^{1,3}]decan-4-one 34**. To a magnetically stirred, ice-cold suspension of NaH (60-65%

dispersion in oil, 94 mg, 2.45 mmoles, washed with dry hexane) and catalytic amount of TBAI in anhydrous THF (0.5 mL) was added, a solution of the hydroxyketone **32** (340 mg, 1.634 mmoles) in dry THF (1.5 mL) and stirred for 0.5 hr at the same temperature. Methyl iodide (0.52 mL, 7.8 mmoles) and DMF (0.28 mL, 3.61 mmoles) were added to the reaction mixture and stirred for 24 hr at RT. 3 *N* aq. HCl (3 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (2 × 10 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (0:1 to 1:10) as eluent furnished the methoxy-ketone **34** (340 mg, 94%) as oil, IR (neat): 1726 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.30 (3 H, s, OCH_3), 2.94 (1 H, br s, H-8), 2.31 (1 H, d of t, *J* = 14.0 and 5.1 Hz), 2.02 (1 H, d, *J* = 18.0 Hz), 1.90-1.70 (4 H, m), 1.64 (1 H, d, *J* = 18.0 Hz), 1.27 (3 H, s, *tert*-CH_3), 1.04 (1 H, d of d, *J* = 5.0 and 2.7 Hz), 0.96 (3 H, s, *tert*-CH_3), 0.87 (3 H, s, *tert*-CH_3), 0.95-0.75 (1 H, m); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 213.7 (C, C=O), 86.8 (CH, C-8), 57.5 (CH_3, OCH_3), 45.4 (CH_2, C-5), 42.7 (C, C-6), 40.8 (C, C-7), 37.0 (C, C-1), 36.97 (CH, C-3), 24.9 (CH_3), 22.9 (CH_2), 22.5 (CH_3), 21.6 (CH_2), 21.2 (CH_3), 17.7 (CH_2, C-2); Mass: m/z 222 (M^+, $C_{14}H_{22}O_2$, 80%), 207 (22), 190 (40), 179 (44), 152 (46), 151 (51), 147 (64), 135 (87), 125 (50), 121 (90), 120 (55), 109 (50), 107 (93), 99 (58), 93 (70), 91 (55).

(1*R,3*R**,6*S**)-3-Methoxy-1,2,2,6-tetramethylbicyclo[4.3.0]nonan-8-one 35**. To a magnetically stirred, freshly distilled (over sodamide) ammonia (20 mL) in a three necked flask equipped with a Dewar condenser, was added freshly cut lithium (3.3 mg, 0.48 mmole) followed by the ketone **34** (53 mg, 0.238 mmole) in dry THF (0.5 mL). The resulting blue coloured solution was stirred for 5 min at -33°C and then the reaction was quenched with solid NH_4Cl. After evaporation of the ammonia, the residue was taken in water (2 mL) and extracted with CH_2Cl_2 (2 × 5 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (1:20 to 1:5) as eluent furnished the ketone **35** (20 mg, 37.4%) as oil, IR (neat): 1739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.52 (3 H, s, OCH_3), 3.01 (1 H, d of d, *J* = 11.0 and 3.3 Hz, H-3), 2.56, 1.89 (2 H, 2 × d, *J* = 18.3 Hz, H-7), 2.30, 1.91 (2 H, 2 × d, *J* = 18.9 Hz, H-9), 1.88-1.82 (1 H, m), 1.60-1.40 (3 H, m), [1.20 (3 H, s), 1.02 (3 H, s), 0.96 (3 H, s), 0.91 (3 H, s), 4 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 216.8 (C, C=O), 84.0 (CH, C-3), 57.5 (CH_3, OCH_3), 54.1 (CH_2), 49.3 (CH_2), 47.5 (C, C-1), 40.8 (C), 40.5 (C), 35.8 (CH_2), 23.3 (CH_3), 22.53 (CH_2), 22.50 (CH_3), 18.8 (CH_3), 17.6 (CH_3). Further elution of the column with the same solvent furnished the corresponding alcohol (25 mg, 46%) as oil, which was oxidised with PCC (120 mg) and silica gel (120 mg) in CH_2Cl_2 (1.5 mL) at RT to furnish the ketone **35**.

(1*R,3*S**,5*R**,6*R**,8*R**)-8-Methoxy-5,6,7,7-tetramethyltricyclo[4.4.0.0^{1,3}]decan-4-one 37**. To a magnetically stirred, cold (ice-salt) solution of *i*-Pr_2NH (0.25 mL, 1.9 mmoles) in anhydrous THF (1 mL) was added a solution of *n*-BuLi (1.6 *M* in hexane, 1.06 mL, 1.7 mmoles) and stirred for 15 min at the same temperature. To the LDA thus formed was added a solution of the tricyclic ketone **34** (222 mg, 1 mmole) in anhydrous HMPA (0.35 mL, 2 mmoles) and stirred for 1 hr at the same temperature. Methyl iodide (0.3 mL, 4.5 mmoles) was added to the reaction mixture and stirred for 10 hr at same temperature. It was then diluted with CH_2Cl_2 (15 mL) and washed with 3 *N* aq. HCl (3 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (0:1 to 1:5) as eluent furnished the methylated ketone **37** (141 mg, 60%, 87% based on starting material consumed) as a solid, m.p. 78-80 °C; IR (thin film): 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.31 (3 H, s, OCH_3), 2.96 (1 H, br s, H-8), 2.32 (1 H, d of t, *J* = 14.0 and 5.7 Hz), 2.12 (1 H, q, *J* = 8.0 Hz, C*H*CH_3), 1.84 (1 H, br d, *J* = 9 Hz), 1.85-1.65 (3 H, m), 1.21 (3 H, s, *tert*-CH_3), 1.02 (3 H, d, *J* = 8.0 Hz, *sec*-CH_3), 0.92 (3 H, s, *tert*-CH_3), 0.90-0.80 (1 H, m), 0.85 (3 H, s, *tert*-CH_3), 0.74 (1 H, d of d, *J* = 9.0 and 5.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 216.9 (C, C=O), 87.2 (CH, C-8), 57.6 (CH_3, OCH_3), 47.3 (CH, C-5), 44.5 (C, C-6), 41.9 (C, C-7), 37.1 (C, C-1), 36.9 (CH, C-3), 24.8 (CH_3), 23.4 (CH_2), 22.3 (CH_3), 21.5 (CH_2), 17.4 (CH_2), 17.3 (CH_3), 16.5 (CH_3); Mass: m/z 236 (M^+, $C_{15}H_{24}O_2$, 13%), 205 (25), 176 (28), 161 (53), 149 (74), 137 (28), 135 (50), 133 (45), 121 (55), 107 (100), 105 (40), 99 (25), 93 (78), 91 (55). Further elution of the column with the same eluent afforded the unreacted starting material **34** (69 mg).

(1*R,3*R**,6*S**,9*R**)-3-Methoxy-1,2,2,6,9-pentamethylbicyclo[4.3.0]nonan-8-one 38**. To a magnetically stirred, freshly distilled (over sodamide)

ammonia (20 mL) in a three necked flask equipped with Dewar condenser was added, freshly cut lithium (3.7 mg, 0.534 mmole) followed by the tricyclic ketone **37** (63 mg, 0.266 mmole) in anhydrous THF (0.5 mL). The resulting blue coloured solution was stirred for 15 min at -33°C and then the reaction was quenched with solid NH_4Cl. After evaporation of ammonia, the residue was taken in water (3 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using EtOAc-hexane (0:1 to 1:5) as eluent furnished the bicyclic ketone **38** (34 mg, 53.5%) as a solid, m.p. 62 °C; IR (thin film): 1737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.34 (3 H, s, OCH_3), 3.10-3.00 (1 H, m of d, *J* = 8 Hz, H-3), 2.56 (1 H, q, *J* = 7.2 Hz, H-9), 2.22 (1 H, d, *J* = 18.3 Hz), 1.90 (1 H, d of d, *J* = 18.3 and 1.5 Hz, H-7), 1.85-1.75 (1 H, m), 1.55-1.40 (3 H, m), 1.22 (3 H, s, *tert*-CH_3), 1.10 (3 H, d, *J* = 7.2 Hz, *sec*-CH_3), 0.98 (3 H, s, *tert*-CH_3), 0.94 (3 H, s, *tert*-CH_3), 0.91 (3 H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 219.8 (C, C=O), 84.4 (CH, C-3), 57.6 (CH_3, OCH_3), 53.4 (CH_2, C-7), 49.7 (C, C-1), 49.0 (CH, C-9), 41.8 (C, C-2), 39.8 (C, C-6), 35.6 (CH_2), 24.9 (CH_3), 23.0 (CH_3), 22.6 (CH_2), 18.0 (CH_3), 13.8 (CH_3), 13.4 (CH_3); Mass: m/z 238 (M^+, $C_{15}H_{26}O_2$, 38%), 206 (28, M - MeOH), 195 (37), 167 (48), 125 (35), 124 (60), 113 (33), 97 (90), 86 (22), 81 (70), 71 (100). Further elution of the column with EtOAc-hexane (1:3) as eluent furnished the bicyclic alcohol **39** (18 mg, 28%) as a solid, m.p. 93°C; IR (thin film): 3236 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.80-3.65 (1 H, m, H-8), 3.34 (3 H, s, OCH_3), 3.17 (1 H, d of d, *J* = 11.5 and 3.6 Hz, H-3), 2.28 (1 H, quintet, *J* = 6.9 Hz, H-9), 2.03 (1 H, d of t, *J* = 13.5 and 3.6 Hz), 1.94 (1 H, d of d, *J* = 14.5 and 9 Hz), 1.85-1.70 (1 H, m), 1.50-1.20 (3 H, m), 1.12 (3 H, d, *J* = 6.9 Hz, *sec*-CH_3), [1.02 (3 H, s), 0.94 (3 H, s), 0.83 (3 H, s), 0.75 (3 H, s), 4 × *tert*-CH_3].

Oxidation of the alcohol 39. To a magnetically stirred solution of the bicyclic alcohol **39** (75 mg, 0.312 mmole) in dry CH_2Cl_2 (2 mL) were added PCC (340 mg, 1.57 mmoles) and silica gel (340 mg) and stirred for 3 hr at RT. The reaction mixture was then filtered through a silica gel column using EtOAc-hexane (1:50 to 1:10) as eluent to furnish the bicyclic ketone **38** (70 mg, 94%).

(1*R,3*R**,6*S**,9*S**)-3-Methoxy-8-methylene-1,2,2,6,9-pentamethylbicyclo[4.3.0]nonane (3-Methoxythaps-8(11)-ene 40)**. To a magnetically stirred solution of freshly prepared $K^{+\,t}AmO^-$ (95 mg, 0.756 mmole) in dry benzene (0.5 mL) was added methyltriphenylphosphonium iodide (320 mg, 0.793 mmole) and the resulting yellow colour solution was stirred for 30 min at RT. To the dark yellow coloured solution of methylenetriphenylphosphorane was added the ketone **38** (30 mg, 0.126 mmole) and stirred for 9 hr at RT. Saturated aq. NH_4Cl solution (4 mL) was added to the reaction mixture and extracted with ether (2 × 5 mL). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using hexane as eluent furnished 3-methoxythaps-8(11)-ene **40** (25 mg, 84%) as colourless oil, IR (neat): 3070, 1650, 880 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ [4.82 (1 H, m), 4.77 (1 H, m), C=CH_2], 3.33 (3 H, s, OCH_3), 3.04 (1 H, d of d, *J* = 11.4 and 4.0 Hz, H-3), 2.82-2.70 (1 H, m, H-9), 2.38 (1 H, q of d, *J* = 16.0 and 2.7 Hz), 1.84 (1 H, d, *J* = 16.0 Hz), 1.80-1.60 (1 H, m), 1.60-1.15 (3 H, m), 1.08 (3 H, d, *J* = 6.6 Hz, *sec*-CH_3), [1.06 (3 H, s), 0.96 (3 H, s), 0.86 (3 H, s), 0.79 (3 H, s), 4 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 156.3 (C, *C*=CH_2), 106.3 (CH_2, C=*C*H_2), 84.8 (CH, C-3), 57.6 (CH_3, OCH_3), 51.0 (C, C-1), 49.1 (CH_2, C-7), 42.6 (C, C-2), 42.58 (CH, C-9), 41.7 (C, C-6), 34.6 (CH_2), 24.7 (CH_3), 23.1 (CH_3), 22.8 (CH_2), 18.4 (CH_3), 17.7 (CH_3), 13.4 (CH_3); Mass: m/z 236 (M^+, $C_{16}H_{28}O$, 1%), 205 (15), 189 (20), 167 (21), 149 (27), 135 (76), 125 (40), 123 (55), 121 (100), 113 (45), 107 (49), 95 (30), 93 (34).

(1*S,3*R**,6*S**)-3-Methoxy-1,2,2,6,8,9-hexamethylbicyclo[4.3.0]non-8-ene (3-Methoxythaps-8-ene 36)**. To a magnetically stirred solution of thaps-8(11)-ene **40** (17 mg, 0.072 mmole) in dry CH_2Cl_2 (2 mL) was added a catalytic amount of *p*-TSA and stirred for 6 hr at RT. The reaction mixture was then diluted with CH_2Cl_2 (5 mL) and washed with saturated aq. $NaHCO_3$ solution (1 mL) and brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using hexane as eluent furnished 3-methoxythaps-8-ene **36** (13 mg, 76%) as colourless oil, IR (neat): 1376, 1361, 1138, 1093, 1017, 983 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 3.25 (3 H, s, OCH_3), 2.81 (1 H, d of d, *J* = 6.0 and 3.0 Hz, H-3), 2.18 (1 H, d, *J* = 15.3 Hz), 1.70-1.50 (3 H, m), [1.55 (3 H, s), 1.54 (3 H, s), 2 × olefinic CH_3], 1.40-1.20 (2 H, m), [0.94 (3 H, s), 0.90 (3 H, s), 0.86 (3 H, s), 0.77 (3 H, s), 4 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ 137.2 (C, C-9), 129.8 (C,

C-8), 86.5 (CH, C-3), 57.0 (CH_3, OCH_3), 55.6 (C, C-1), 51.4 (CH_2, C-7), 43.2 (C, C-6), 41.8 (C, C-2), 30.0 (CH_2), 29.0 (CH_3), 26.6 (CH_3), 24.5 (CH_3), 20.9 (CH_2), 17.1 (CH_3), 14.5 (CH_3), 13.6 (CH_3); Mass: m/z 236 (M^+, $C_{16}H_{28}O$, 0.5%), 161 (24), 135 (44), 124 (23), 123 (99), 122 (100), 121 (36), 120 (40), 113 (22), 107 (36), 91 (20).

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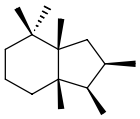

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