A formal total synthesis of (±)-α-pinguisene and (±)-pinguisenol

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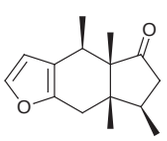
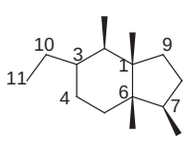
Formal total synthesis of (±)-α-pinguisene and (±)-α-pinguisenol, containing a *cis*-1,2,6,7-tetramethylbicyclo[4.3.0]-nonane skeleton incorporating two vicinal quaternary carbon atoms and four *cis* oriented methyl groups on four contiguous carbon atoms, isolated from liverworts is described. Thus, an orthoester Claisen rearrangement of the allyl alcohol **14**, obtained from the Hagemann's ester **15**, afforded the ene ester **18**. Hydrolysis of the ketal and ester moieties transformed the ene ester **18** into keto acid **23**. Intramolecular cyclopropanation of the diazo ketone **24** derived from the keto acid **23** afforded a 3:2 mixture of chromatographically separable tricyclic diones **25** and **26**. Simultaneous regioselective reductive cyclopropane-ring cleavage and reduction of the cyclohexanone carbonyl in the dione **25** with lithium in liquid ammonia furnished the keto alcohol **27**, which on Wolff–Kishner reduction followed by oxidation of the alcohol afforded the bicyclic ketone **11**, Schinzer's precusor of pinguisenol **9** and α-pinguisene **10**.

Liverworts are endowed with a rich and wide variety of sesquiterpenoids, such as acoranes, aristolanes, azulenes, caryophyllanes, cedranes, chamigrenes, himachalanes, longifolanes, pinguisanes, *etc*.[1] An important endogenous character of the Hepaticae family is that most of the sesquiterpenoids from liverworts are enantiomeric to those found in higher plants. In 1969 Benesova and co-workers[2a–c] isolated the crystalline furanosesquiterpene pinguisone **1** from the essential oil obtained from the pentane extract of liverwort *Aneura pinguis* (L.) Dum. The structure of pinguisone **1** was established on the basis of spectral studies, and the absolute structure by single-crystal X-ray diffraction analysis of its 8-*p*-bromobenzylidene derivative.[2d] Since the isolation of pinguisone **1**, more than two dozen pinguisanoid sesquiterpenes have been isolated from various liverworts such as *Lejeuneaceae*, *Porellaceae*, *Triichocoleaceae*, *Ptilidiaceae* and *Aneuraceae*.[2] A few representative examples of pinguisanes are depicted in Chart 1. A notable structural feature of these sesquiterpenes is that almost all these compounds have a *cis*-fused 1,2,6,7-tetramethylbicyclo[4.3.0]-nonane framework **2** incorporating two vicinal quaternary carbon atoms and four methyl groups attached to four contiguous carbon atoms, in an all-*cis* orientation. Biosynthetically these compounds are interesting. Earlier[3a] the biosynthesis of these compounds was explained to be from farnesyl pyrophosphate **3** *via* the formation of, first, bisabolanyl and then acoranyl carbonium ion followed by a series of 1,2 migrations eventually leading to the pinguisane skeleton. Recently, Tazaki *et al*.[3b] on the basis of labelling studies, postulated the plausible biosynthetic pathway which is depicted in Scheme 1. The carbenium ion **4**, was obtained from farnesyl pyrophosphate **3** *via* C^6–C^{11} bond formation. 1,2-Hydride migration on **4** followed by a 1,2-methyl shift furnishes **5**. Formation of the C^3–C^9 bond in **5** with the elimination of pyrophosphate leads to the bicyclic cation **6**. Isomerisation of the bicyclo[3.3.1]nonane to bicyclo-[4.3.0]nonane *via* bond migration led to hydrindane skeleton **7**, which on 1,2-methyl shift generates the pinguisane system **8**.



Pinguisone **1**



2

The pinguisanes pinguisenol[2f] **9** and α-pinguisene[2g] **10** were isolated from the liverwort *Porella vernicosa* and *Porella elaguntala*, respectively, and their structures were unambiguously determined by Asakawa *et al*. on the basis of spectral and chemical studies. Recently, the relative stereostructures of α-pinguisene **10** and pinguisenol **9** were established by the total synthesis of the racemic compounds, employing an amberlyst (A15)-catalysed cyclisation of a propargylsilane(prop-2-ynylsilane) as the key reaction.[4] Interesting structural features, namely the *cis*-fused 1,2,6,7-tetramethylbicyclo[4.3.0]nonane

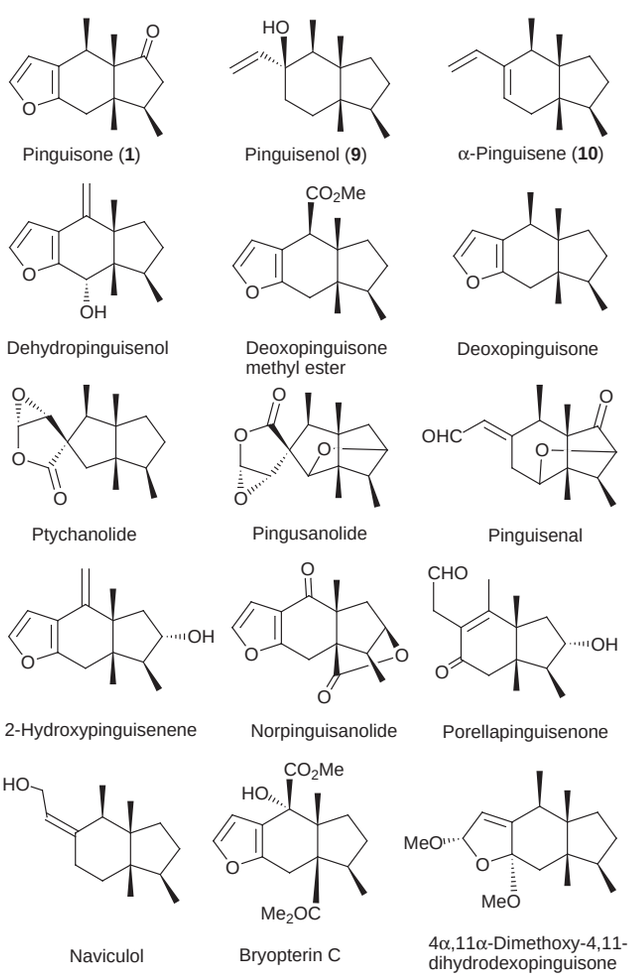
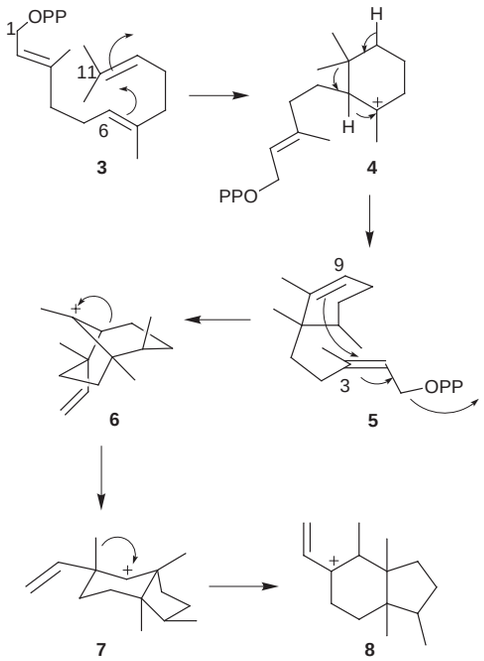
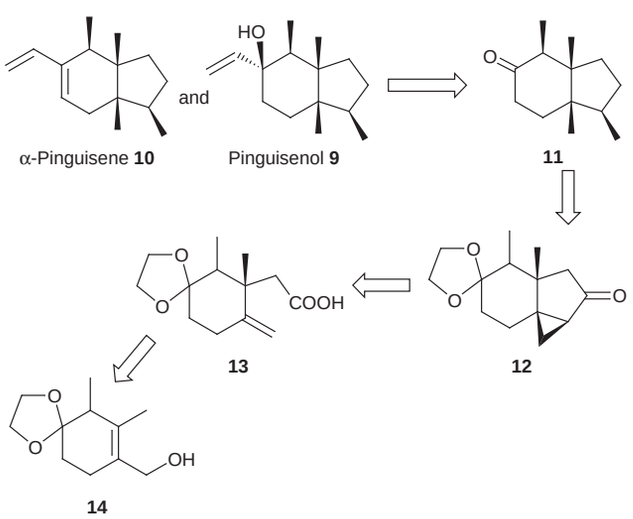


Chart 1



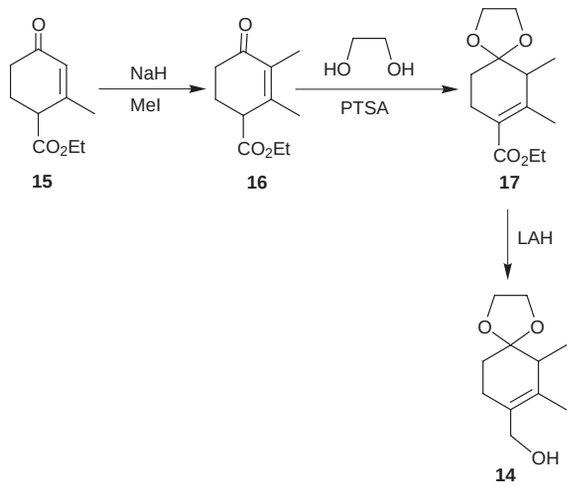
Scheme 1

system incorporating two vicinal quaternary carbon atoms and four methyl groups on four contiguous carbon atoms oriented in an all-*cis* manner, have made pinguisanes attractive and challenging synthetic targets.[5] In continuation of the ongoing research work in our laboratory[6] on the synthesis of sesquiterpenes containing multiple contiguous quaternary carbon atoms, we embarked on the synthesis of (±)-α-pinguisene **10** and (±)-pinguisenol **9**.[7]



Scheme 2

A cursory look at the molecular architecture of pinguisanes reveals that the important task should be the construction of the *cis*-bicyclo[4.3.0]nonane carbocyclic framework, with stereocontrolled generation of four *cis*-oriented methyl groups on four contiguous carbon atoms for the synthesis of pinguisanes. A retrosynthetic analysis of (±)-α-pinguisene **10** and (±)-pinguisenol **9**, based on a combination of Claisen rearrangement[8] and intramolecular diazo ketone cyclopropanation[9] reactions, is depicted in Scheme 2. The Schinzer's precursor[4] **11** was readily identified as the target molecule for the formal total synthesis of (±)-α-pinguisene **10** and (±)-pinguisenol **9**. It was envisaged that the reductive alkylation of the tricyclic keto ketal **12** followed by deoxygenation of the ketone and hydrolysis of the ketal moiety would lead to the target molecule **11**. The tricyclic keto ketal **12** could be obtained by an intramolecular



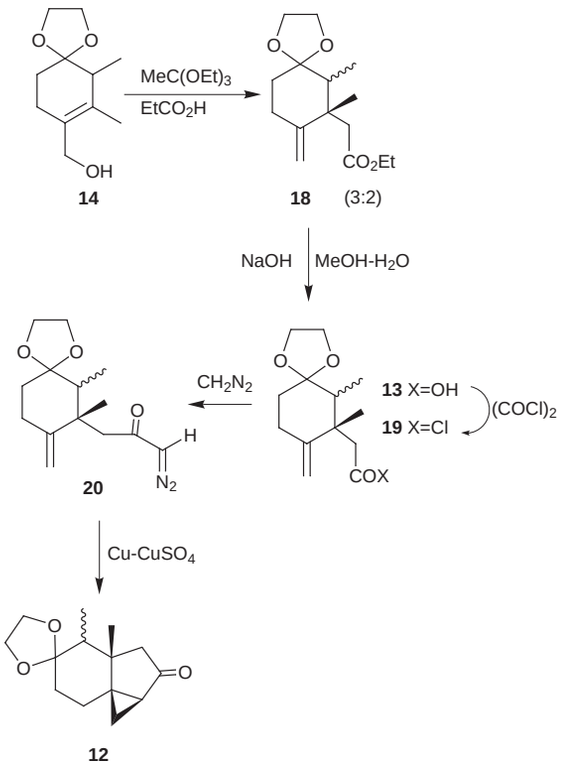
cyclopropanation reaction of the diazo ketone derived from the ene acid **13**, which in turn could be obtained from the allyl alcohol **14** *via* a Claisen rearrangement.

To begin with, the allyl alcohol **14** was synthesised starting from Hagemann's ester **15**.[10] Thus, low-temperature (−50 °C) alkylation of the sodium dienolate of Hagemann's ester, generated at 0 °C using sodium hydride in dry THF, with methyl iodide furnished the γ-methylated ester **16** in almost quantitative yield with high degree of regioselectivity (>20 : 1). For the conversion of the ester **16** into the allyl alcohol **14**, in addition to protection of the ketone as its ketal, the isomerisation of the olefin was also required, and this was achieved by exploiting the well established fact that the double bond isomerises to the β,γ-position from the α,β-position during the ketalisation of a cyclohexenone.[11] Thus, refluxing a benzene solution of the ester **16** and ethylene glycol and a catalytic amount of toluene-*p*-sulfonic acid (PTSA) using a Dean–Stark water trap furnished the ketal **17**. Regioselective reduction of the ketal ester **17** with lithium aluminium hydride in diethyl ether at −70 °C furnished the requisite allyl alcohol **14** in 97% yield.

The regio- and stereospecific formation of γ,δ-unsaturated carbonyl systems, coupled with the ease of creation of a quaternary center from a γ,γ-disubstituted allyl alcohol, prompted us to choose the Claisen rearrangement[8] for the generation of the first quaternary carbon atom. An orthoester variant of the Claisen rearrangement, developed by Johnson *et al.*[8b] was employed as it leads to a γ,δ-unsaturated ester which is more appropriate for the generation of a diazo ketone (Scheme 3). Thus, thermal activation of a solution of the allyl alcohol **14** in triethyl orthoacetate in the presence of a catalytic amount of propionic acid in a sealed tube at 180 °C furnished a 3 : 2 inseparable epimeric mixture of the ene ester **18** in 75% yield, whose structure was derived on the basis of its spectral data. Since separation of the epimers was found to be difficult, the resolution of the epimers was thus deferred to a later stage.

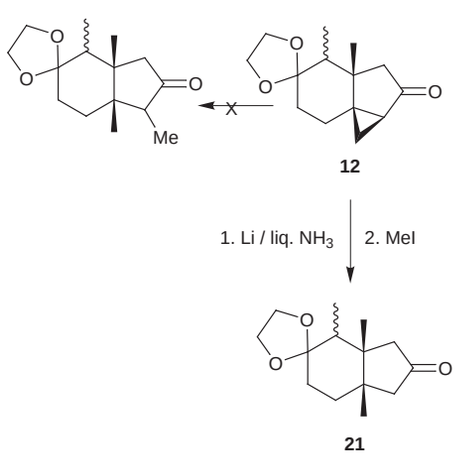
For the annulation of a five-membered ring as well as the creation of the second quaternary carbon atom, an intramolecular diazo ketone cyclopropanation reaction[9] was contemplated. Thus, hydrolysis of the ene ester **18** with aqueous methanolic sodium hydroxide followed by careful acidification gave the ketal acid **13**. Treatment of the acid **13** with oxalyl dichloride in benzene followed by reaction of the resulting acid chloride **19** with an excess of ethereal diazomethane furnished the diazo ketone **20**. Anhydrous copper sulfate–copper-catalyzed decomposition of the diazo ketone **20** in refluxing cyclohexane furnished a 3 : 2 mixture of the tricyclic ketone **12** *via* stereoselective insertion of the intermediate ketocarbenoid into the olefin. The structure of the tricyclic keto ketal **12** was delineated from its spectral data.

Reductive alkylation[12] of the cyclopropyl ketone **12** using Birch reduction conditions was contemplated for the simul-

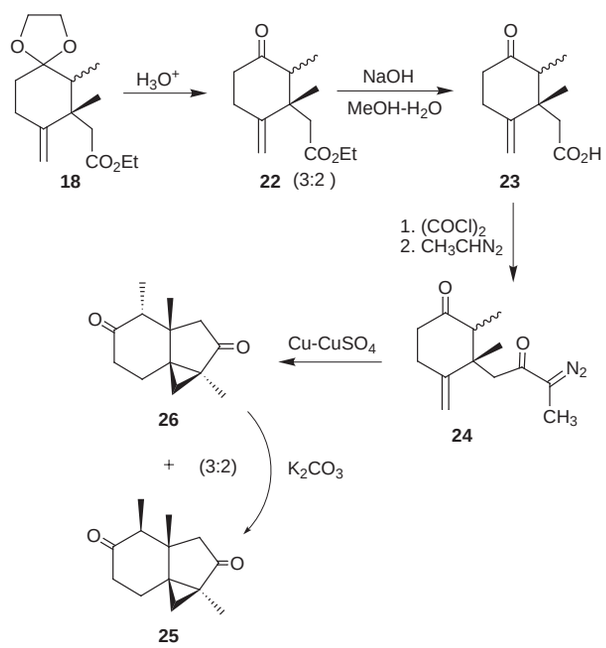


Scheme 3

taneous generation of the tertiary methyl group at the ring junction and the introduction of the secondary methyl group at C-7. However, in contrast to our anticipation, reduction of the cyclopropyl ketone **12** using lithium in liquid ammonia followed by quenching of the intermediate enolate with an excess of methyl iodide gave only the reduced product **21**, perhaps due to the neopentylic nature of the carbon. The keto ketal **21** was not elaborated further due to the anticipated regiochemical problems in introducing the fourth methyl group, *e.g.*, alkylation of the keto ketal **21** under standard conditions would generate both regioisomers.



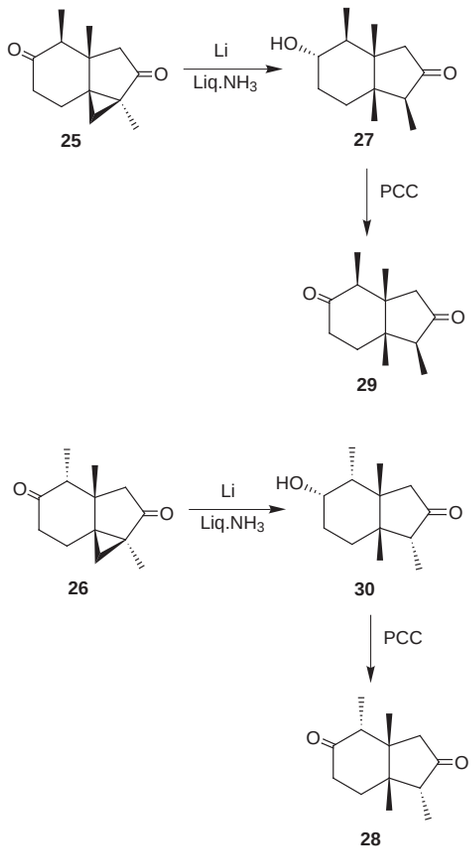
Since the introduction of the fourth methyl group *via* reductive alkylation reaction was not successful, an alternative strategy of introducing the methyl group at an earlier stage of the sequence, *i.e.*, the cyclopropanation stage, by employing diazoethane in the place of diazomethane was conceived. As the reaction of the acid chloride **19** with diazoethane failed to generate the requisite diazo ketone, the sequence was carried out without the ketal protection (Scheme 4). Thus, acid-catalysed hydrolysis of the ketal ester **18** furnished a 3 : 2 epimeric mixture of the keto ester **22** in 96% yield. Hydrolysis of the ester **22** in refluxing 10% aqueous sodium hydroxide and methanol furnished a 3 : 2 epimeric mixture of the keto acid **23** in 90% yield. Reaction of the keto acid **23** with oxalyl dichloride in benzene at room temperature followed by treatment of the resulting acid chloride with an excess of ethereal diazoethane furnished the diazo ketone **24**. Thermal decomposition of a solution of the diazo ketone **24** in refluxing cyclohexane in the presence of anhydrous copper sulfate and copper[13] furnished a 3 : 2 diastereomeric mixture of the tricyclic diketones **25** and **26**, in 24% yield (from acid **23**), which were separated by employing silica gel column chromatography. The structures of the tricyclic ketones **25** and **26** were established on the basis of their interrelated spectral data. In the major isomer **25** of the tricyclic diones, the stereochemistry at the secondary methyl group was assigned as β, *i.e.*, *cis* to the adjacent tertiary methyl group, on the basis of thermodynamic considerations. Equilibration of the minor dione **26** with potassium carbonate in methanol at room temperature cleanly furnished the major dione **25**, establishing the thermodynamic orientation of the secondary methyl group in the major dione **25**. Final confirmation was obtained by the conversion of the major dione **25** into Schinzer's ketone **11**.



Scheme 4

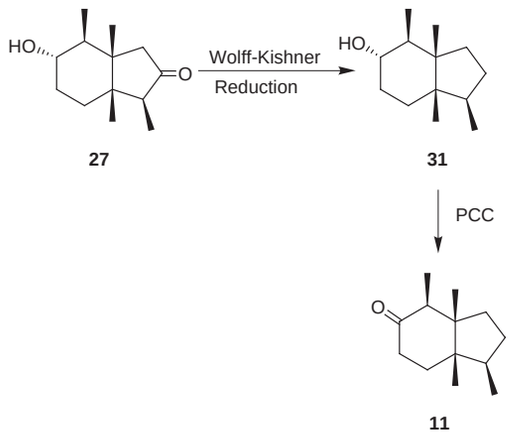
It can be readily visualised that regioselective cleavage of the cyclopropane ring and deoxygenation of the cyclopentanone carbonyl group transforms the tricyclic dione **25** into the Schinzer's ketone **11**. Regioselective cleavage of the cyclopropane ring is straightforward,[14] but deoxygenation of the cyclopentanone carbonyl poses regiochemical problems, as it would be difficult to differentiate between the two carbonyl groups. To overcome this problem, simultaneous cleavage of the cyclopropane ring and reduction of the cyclohexanone carbonyl was contemplated employing the alkali metal in liquid ammonia reduction conditions. Thus, controlled reduction of the tricyclic dione **25** using lithium in liquid ammonia furnished the keto alcohol **27**, achieving both the regioselective cyclopropane cleavage and differentiation of the two ketone functionalities. The structure of the keto alcohol **27** was delineated from its spectral data. The stereochemistry of the hydroxy group in **27** was assigned as equatorial based on the observed *trans* diaxial couplings of the methine attached to the hydroxy group with the vicinal axial protons.

The regioselectivity in the cleavage of the cyclopropane ring is well established. The cyclopropane bond which has better overlap with the carbonyl π-orbital will be cleaved.[14] The



stereochemistry at the newly created secondary methyl group was assigned on the basis of thermodynamic considerations. Molecular mechanics calculations indicated that compound **27** is ~3.33 kcal mol^{-1}† more stable than its C-7 epimer. The formation of the keto alcohol **27**, in addition to differentiating the two carbonyl groups, also avoided the possible equilibration of the secondary methyl group at C-2. It is interesting to note that in 1,2,6,7-tetramethylbicyclo[4.3.0]nonane-3,8-diones, the *trans-cis-trans* isomer **28** is slightly more stable than the all-*cis* isomer **29** which in turn is more stable than the other two isomers. To further ascertain the stereochemistry of the keto alcohol **27**, the all-*cis* **29** and the *trans-cis-trans* diones **28** were prepared. Thus, the keto alcohol **27** was oxidised using PCC and silica gel in methylene dichloride, to furnish the bicyclic diketone **29**. The *trans-cis-trans* dione **28** was prepared from the tricyclic dione **26** following the same sequence. Thus, Birch reduction of the tricyclic dione **26** followed by oxidation of the resultant keto alcohol **30** furnished the *trans-cis-trans* bicyclic diketone **28**, whose structure was established on the basis of its spectral data. The formation of the diones **28** and **29** established that the orientation of the secondary methyl group controls the stereochemistry of the product in the Birch reduction.

Finally, the keto alcohol **27** was transformed into the Schinzer's ketone **11** *via* a modified Wolff–Kishner reduction and oxidation protocol. Thus, treatment of the keto alcohol **27** with hydrazine hydrate in diethylene glycol and ethylene glycol at 185 °C for two hours, followed by treatment with sodium in diethylene glycol at the same temperature for four hours, furnished the alcohol **31**. Oxidation of the alcohol **31** with PCC and silica gel furnished the Schinzer's ketone[4] **11**, which exhibited spectral data identical with those reported by Schinzer *et al*. The spectral data of ketone **11** were also found to be identical with those reported for the product obtained by ozonolysis of the pinguisane naviculol (see Chart 1).[2p] Since Schnizer *et al*. have already converted the ketone **11** into pinguisenol **9** *via* 1,2-addition of vinylmagnesium bromide and into α-pinguisene **10** *via* coupling of the enol triflate with tributylvinylstannane, the present synthesis of ketone **11** constitutes a formal total synthesis of (±)-pinguisenol and (±)-α-pinguisene.



Experimental

IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ^1H (90, 200, 300 and 400 MHz) and ^{13}C NMR (22.5, 50 and 75 MHz) spectra were recorded on JEOL FX-90Q, JNM λ-300 and Bruker ACF-200 and AMX-400 spectrometers. The chemical shifts (δ/ppm) and the coupling constants (J/Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^1H) or the central line (δ_C 77.1) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra off-resonance multiplicities, when recorded are given in parentheses. Low- and high-resolution mass measurements were carried out using a JEOL JMS-DX 303 GC-MS instrument using a direct inlet mode. Relative intensities of the ions are given in parentheses. Acme's silica gel (100–200 mesh) was used for column chromatography. Low-temperature reactions were conducted in a bath made of alcohol and liquid nitrogen. Dry THF and cyclohexane were obtained by distillation over sodium-benzophenone ketyl. Dry ether (Et_2O) was obtained by distillation over sodium and stored over sodium wire. Dry methylene dichloride was prepared by distilling over calcium hydride. Copper(II) sulfate was dried by irradiation in a microwave oven prior to reaction. Liquid ammonia was obtained in cylinders from Mysore Ammonia Ltd. and distilled over sodium prior to use. Methyl iodide and DMF were filtered through a neutral alumina column prior to use. PCC, *N*-nitroso-*N*-ethylurea and *N*-nitroso-*N*-methylurea were prepared according to literature procedures. Lithium, $LiAlH_4$, 55% NaH dispersed in oil, oxalyl dichloride, copper powder and triethyl orthoacetate were obtained from Fluka. 99% NH_2-NH_2·H_2O was obtained from BDH. Diethylene glycol and ethylene glycol were stored over molecular sieves prior to use.

[2,3-Dimethyl-4,4-(ethylenedioxy)cyclohex-1-enyl]methanol 14

To a magnetically stirred, cold (−70 °C) suspension of LAH (500 mg, 13 mmol) in dry ether (75 ml) was added dropwise a solution of the ketal ester **17**[11] (5 g, 20.8 mmol) in dry ether (15 ml) over a period of 10 min. The reaction mixture was stirred at −70 °C for 2 h and allowed to attain room temperature over a period of 30 min. Ethyl acetate (2 ml) was added to the reaction mixture to consume the excess of reagent and the reaction was quenched by careful addition of water (0.5 ml). The solids were filtered off and the residue was washed with ether (25 ml). The combined organic phase was dried (Na_2SO_4) and solvent was evaporated. Purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 20) as eluent furnished the allyl alcohol **14**[10] (4 g, 97%) as an oil, ν_{max} 3330 cm^{-1}; δ_H(90 MHz; $CDCl_3$) 4.12 (2 H, m, CH_2OH), 4.00 (4 H, s, OCH_2CH_2O), 2.34

† 1 cal = 4.184 J.

(1 H, m, H-3), 1.20–2.20 (4 H, m), 1.76 (3 H, s, olefinic CH_3), 1.10 (3 H, d, *J* 7.2, *sec*-CH_3); δ_C(75 MHz, $CDCl_3$) 133.4 and 128.6 (C-2 and -3), 110.3 (O–C–O), 64.5 (OCH_2), 64.3 and 62.7 (OCH_2CH_2O), 43.9 (C-5), 27.2, 26.7, 17.4 and 15.5 (2 × CH_3).

Ethyl 2-[3,3-(ethylenedioxy)-1,2-dimethyl-6-methylenecyclohexyl]acetate 18

A solution of the allyl alcohol **14** (2 g, 10.1 mmol), triethyl orthoacetate (9 ml, 50 mmol) and a catalytic amount (10 µl) of propionic acid was placed in two sealed tubes and heated to 170 °C for 2 days in an oil-bath. The reaction mixture was cooled, diluted with ether (20 ml), washed successively with 0.5 M aq. HCl, saturated aqueous $NaHCO_3$, and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1 : 40) as eluent furnished a 3 : 2 epimeric mixture of the ester **18** (2.03 g, 75%) as an oil, ν_{max} 1725, 1640, 905 cm^{-1}; δ_H(200 MHz, $CDCl_3$) Peaks due to the major isomer: 4.74 (2 H, s, olefinic H), 3.80–4.10 (6 H, m, OCH_2CH_2O and OCH_2CH_3), 3.07 (1 H, d, *J* 13.0) and 2.18 (1 H, d, *J* 13.0) ($CH_2C{=}O$), 1.35–2.70 (7 H, m), 1.19 (3 H, t, *J* 7.0, OCH_2CH_3), 1.16 (3 H, s, *tert*-CH_3) and 0.93 (3 H, d, *J* 7.0, *sec*-CH_3). Peaks due to the minor isomer: 4.86 (1 H, s) and 4.80 (1 H, s) ($C{=}CH_2$), 2.82 (1 H, d, *J* 18.3), 2.72 (1 H, d, *J* 16.0), 1.28 (3 H, s, *tert*-CH_3), 1.23 (3 H, t, *J* 7.3 Hz, OCH_2CH_3), 0.89 (3 H, d, *J* 7.2, *sec*-CH_3); δ_C(22.5 MHz, $CDCl_3$) Peaks due to the major isomer: 172.2 (O–C=O), 150.2 ($C{=}CH_2$), 110.0 (O–*C*–O), 108.4 ($C{=}CH_2$), 65.3 and 63.8 (OCH_2CH_2O), 59.4 (OCH_2CH_3), 49.1, 43.4, 38.7, 36.1, 30.4, 23.7, 14.2 (OCH_2CH_3), 7.7 ($CHCH_3$). Peaks due to the minor isomer: 152.0 ($C{=}CH_2$), 111.1 (O–*C*–O), 109.4 ($C{=}CH_2$), 64.2, 42.4, 32.2, 30.2, 23.1, 11.3 ($CHCH_3$). Mass: *m*/*z* 268 (M^+, 20%), 239 (48), 223 (18), 181 (100), 153 (66), 99 (59). HRMS: *m*/*z* For $C_{15}H_{24}O_4$ (Calc.: *M*, 268.1674. Found: M^+, 268.1684).

8,8-(Ethylenedioxy)-6,7-dimethyltricyclo[4.4.0.0^{1,3}]decan-4-one 12

To a magnetically stirred solution of the ester **18** (2 g, 7.46 mmol) in methanol (16 ml) was added 10% aq. NaOH (16 ml) and the reaction mixture was refluxed for 6 h. Methanol was evaporated under reduced pressure, and the residue was taken up in water (15 ml) and washed with CH_2Cl_2 (2 × 10 ml). The aq. phase was acidified with 3 M aq. HCl and extracted with CH_2Cl_2 (2 × 15 ml). The CH_2Cl_2 extract was washed with water (10 ml) followed by brine and dried (Na_2SO_4). Evaporation of the solvent furnished the acid **13** (1.67 g, 92%) as a pale yellow oil (ν_{max} 3000br, 1700, 1635, 910 cm^{-1}).

A solution of the acid **13** (1 g, 4.12 mmol) and oxalyl dichloride (1.08 ml, 12.5 mmol) in dry benzene (5 ml) was magnetically stirred for 2 h at room temperature. Evaporation of the excess oxalyl dichloride and benzene under reduced pressure afforded the acid chloride **19**.

A solution of the acid chloride **19** in anhydrous ether (5 ml) was added dropwise to an ice-cold, magnetically stirred ethereal solution of diazomethane (excess, prepared from 5 g of *N*-methyl-*N*-nitrosourea, 50 ml of 60% aq. KOH solution and 50 ml of ether). The reaction mixture was stirred for 2 h at room temperature and the excess diazomethane and ether were carefully evaporated on a water-bath. Rapid purification by filtration of the product through a silica gel column using ethyl acetate–hexane (1 : 10) as eluent furnished the diazo ketone **20** as a yellow oil (ν_{max} 3100, 2060, 1645, 1360, 895 cm^{-1}).

A mixture of copper powder (1.3 g, 20.6 mmol) and anhydrous $CuSO_4$ (329 mg, 2.06 mmol) was added to a magnetically stirred solution of the diazo ketone **20** in 80 ml of anhydrous cyclohexane under a blanket of nitrogen and refluxed for 3 h. After completion of the reaction, the solids were filtered off and the solvent was evaporated under reduced pressure. Purification of the residue on a silica gel column using ethyl acetate–hexane (1 : 20–1 : 5) as eluent furnished a 3 : 2 epimeric mixture of the tricyclic ketone **12** (324 mg, 33% from the acid **13**) as an oil, ν_{max}(neat): 1715 cm^{-1}; δ_H(200 MHz, $CDCl_3$) Peaks due to the major isomer: 3.70–4.10 (4 H, m), 2.40 and 2.26 (2 H, d of AB q, *J* 15.7 and 5.0), 2.13 (1 H, d, *J* 18), 1.85 (1 H, d, *J* 18), 1.45–2.10 (4 H, m), 1.32 (3 H, s), 1.20–1.30 (2 H, m), 1.00 (3 H, d, *J* 7.3). Peaks due to the minor isomer: 1.11 (3 H, s, *tert*-CH_3), 0.86 (3 H, d, *J* 6.8, *sec*-CH_3); δ_C(22.5 MHz, $CDCl_3$) Peaks due to the major isomer: 213.8, 111.2, 64.2, 63.4, 47.3, 45.5, 41.1, 36.1, 33.5, 28.9, 24.6, 19.6, 16.5, 12.6. Peaks due to the minor isomer: 213.1, 110.0, 65.7, 64.2, 45.9, 42.3, 35.0, 34.4, 26.0, 17.0, 8.0. Mass: *m*/*z* 236 (M^+, 6%), 207 (5), 167 (8), 140 (5), 121 (5), 100 (10), 99 (100), 86 (21); HRMS: *m*/*z* For $C_{14}H_{20}O_3$ (Calc.: *M*, 236.1412. Found: M^+, 236.1417).

3,3-(Ethylenedioxy)-1,2,6-trimethylbicyclo[4.3.0]nonan-8-one 21

To magnetically stirred, freshly distilled (over sodium) ammonia (50 ml) in a three-necked flask equipped with a Dewar condenser was added the tricyclic ketone **12** (60 mg, 0.25 mmol) in dry THF (3 ml) followed by freshly cut lithium (9 mg, 1.3 mmol). The resulting blue coloured solution was stirred at −33 °C for 30 min and the reaction was quenched with excess methyl iodide (1.1 ml, 18.75 mmol). After evaporation of ammonia, the residue was taken up in water (10 ml) and extracted with ether (2 × 10 ml). The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1 : 20) as eluent furnished the keto ketal **21** (50 mg, 84%) as an oil, ν_{max}(neat): 1725 cm^{-1}; δ_H(300 MHz, $CDCl_3$, Peaks due to the major isomer) 3.70–4.00 (4 H, m), 3.02 (1 H, d, *J* 19.2), 2.28 (1 H, d, *J* 18.6), 1.93 (1 H, d, *J* 18.6), 1.79 (1 H, d, *J* 19.7), 1.25–1.80 (5 H, m), 1.06 (3 H, s), 0.94 (3 H, s), 0.81 (3 H, d, *J* 6.9); δ_C(75 MHz, $CDCl_3$, Peaks due to the major isomer) 219.2, 110.0, 65.5, 63.9, 52.4, 47.0, 45.4, 42.2, 39.9, 34.3, 30.8, 24.0, 19.5, 8.5. Mass: *m*/*z* 238 (M^+, 2%), 99 (100), 86 (24); HRMS: *m*/*z* For $C_{14}H_{22}O_3$ (Calc.: *M*, 238.1569. Found: M^+, 238.1558).

Ethyl 2-(1,2-dimethyl-6-methylene-3-oxocyclohexyl)acetate 22

To a magnetically stirred solution of the ketal ester **18** (500 mg, 1.87 mmol) in THF (2 ml) was added 3 M aq. HCl (2 ml) and the reaction mixture was stirred for 3 h. After completion of the reaction, water was added and the mixture was extracted with ether (2 × 10 ml). The ether layer was washed successively with saturated aq. $NaHCO_3$ and brine, and dried (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 keto ester **22** (402 mg, 96%) as an oil, ν_{max} 1735, 1710, 1640, 900 cm^{-1}; δ_H(200 MHz, $CDCl_3$) Peaks due to the major isomer: 4.93 (2 H, s), 4.08 (2 H, q, *J* 7.1), 2.78 (1 H, q, *J* 6.9), 2.30–2.80 (4 H, m), 2.35 (1 H, d, *J* 12.8), 2.27 (1 H, d, *J* 13.0), 1.21 (3 H, t, *J* 7.1) 1.09 (3 H, s), 1.02 (3 H, d, *J* 6.9). Peaks due to the minor isomer: 5.06 (1 H, s) and 5.01 (1 H, s) ($C{=}CH_2$), 4.05 (2 H, q, *J* 7.1, OCH_2CH_3), 1.33 (3 H, s, *tert*-CH_3), 1.19 (3 H, t, *J* 7.1, OCH_2CH_3), 1.04 (3 H, d, *J* 6.9, *sec*-CH_3); δ_C(22.5 MHz, $CDCl_3$) Peaks due to the major isomer: 212.9, 170.5, 148.5, 110.9, 59.8, 51.9, 43.3, 39.0, 38.0, 30.9, 22.5, 13.9, 10.5. Peaks due to the minor isomer: 211.1, 149.2, 110.3, 54.1, 40.3, 31.5, 23.7, 9.3. Mass: *m*/*z* 224 (M^+, 5%), 179 (10), 137 (100), 121 (12), 109 (13), 95 (16). HRMS: *m*/*z* For $C_{13}H_{20}O_3$ (Calc.: *M*, 224.1412. Found: M^+, 224.1406).

2-(1,2-Dimethyl-6-methylene-3-oxocyclohexyl)acetic acid 23

Hydrolysis of the keto ester **22** (1 g, 4.46 mmol) with 10% aq. NaOH (5 ml) and methanol for 6 h, as described for the ketal acid **13**, furnished the acid **23** (787 mg, 90%) as an oil, ν_{max} 3000-br, 1720, 1700, 1640, 900 cm^{-1}; δ_H(300 MHz, $CDCl_3$) Peaks due to the major isomer: 4.96 (2 H, s), 2.88 (1 H, q, *J* 6.9), 2.30–2.80 (6 H, m), 1.11 (3 H, s), 1.05 (3 H, d, *J* 6.9). Peaks due to the

minor isomer: 5.09 (1 H, s) and 5.05 (1 H, s) (C=CH_2), 1.36 (3 H, s, *tert*-CH_3), 1.04 (3 H, d, *J* 7.2, *sec*-CH_3); δ_C(22.5 MHz; $CDCl_3$) Peaks due to the major isomer: 214.2, 176.7, 148.8, 111.4, 54.2, 43.4, 40.1, 39.3, 31.6, 22.9, 10.6. Peaks due to the minor isomer: 212.0, 176.4, 148.4, 110.9, 51.7, 44.3, 38.2, 31.1, 23.9, 9.9; Mass: *m*/*z* 196 (M^+, 10%), 181 (6), 151 (10), 137 (100), 121 (15), 109 (17), 95 (24); HRMS: *m*/*z* For $C_{11}H_{16}O_3$ (Calc.: *M*, 196.1100. Found: M^+, 196.1092).

(3α,6β,7β)-3,6,7-Trimethyltricyclo[4.4.0.0^{1,3}]decane-4,8-dione 25 and (3α,6β,7α)-3,6,7-trimethyltricyclo[4.4.0.0^{1,3}]decane-4,8-dione 26

A solution of the keto acid **23** (1.2 g, 6.12 mmol) and oxalyl dichloride (2.6 ml, 30.6 mmol) in dry benzene (6 ml) was magnetically stirred for 2 h at room temperature. Evaporation of the excess oxalyl dichloride and benzene under reduced pressure afforded the acid chloride, which was taken up in anhydrous ether (5 ml) and added dropwise to an ice-cold, magnetically stirred ethereal solution of diazoethane (excess, prepared from 7 g of *N*-nitroso-*N*-ethylurea and 75 ml of 60% aq. KOH solution and 75 ml of ether). The reaction mixture was stirred for 2 h at room temperature and the excess diazoethane and ether were carefully evaporated on a water-bath. Rapid purification by filtration of the product through a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the diazo ketone **24** as a yellow oil (ν_{max} 2080, 1710, 1640, 900 cm^{-1}).

A mixture of copper powder (1.9 g, 29.9 mmol) and anhydrous $CuSO_4$ (480 mg, 3 mmol) was added to a magnetically stirred solution of the diazo ketone **24** in 100 ml of anhydrous cyclohexane under a blanket of nitrogen, and the mixture was refluxed for 1.5 h. After completion of the reaction, the solids were filtered off and the solvent was evaporated under reduced pressure. Purification of the residue on a silica gel column using ethyl acetate–hexane (1:20 to 1:5) as eluent furnished the two diketones **25** (180 mg, 14.2% from the acid **23**) and **26** (122 mg, 9.7% from the acid **23**) as oils. ***For the dione 25:*** ν_{max} 1715 cm^{-1}; δ_H(400 MHz; $CDCl_3$) 2.25–2.45 (3 H, m), 2.23 (1 H, q, *J* 6.7), 2.07 (1 H, d, *J* 17.5), 1.99 (1 H, d, *J* 17.5), 1.60–1.72 (1 H, m), 1.39 (1 H, d, *J* 5.1), 1.34 (3 H, s), 0.98 (3 H, s), 0.97 (3 H, d, *J* 6.7), 0.84 (1 H, d of d, *J* 5.1 and 1.1); δ_C(22.5 MHz, $CDCl_3$) 213.3, 210.8, 52.0, 46.4, 45.0, 42.8, 40.7, 38.2, 27.0, 25.1, 16.6, 10.3, 8.7; Mass: *m*/*z*, 206 (M^+, 20%), 163 (8), 135 (20), 121 (10), 107 (20), 69 (100); HRMS: *m*/*z* For $C_{13}H_{18}O_2$ (Calc.: *M*, 206.1307. Found: M^+, 206.1316). ***For the dione 26:*** ν_{max}(neat): 1715 cm^{-1}; δ_H(400 MHz, $CDCl_3$) 2.57 (1 H, d of t, *J* 13.5 and 6.9), 2.45 (1 H, d of t, *J* 13.5 and 5.6), 2.38 (1 H, q, *J* 7.4), 2.26 (1 H, dd, *J* 13.9 and 5.7), 2.02 (1 H, d, *J* 18.1), 1.97 (1 H, d, *J* 18.1), 1.64 (1 H, dd, *J* 13.7 and 6.7), 1.31 (3 H, s), 1.20 (1 H, d, *J* 5.0), 1.18 (3 H, s), 1.03 (3 H, d, *J* 7.4), 0.72 (1 H, d, *J* 5.0); δ_C(22.5 MHz, $CDCl_3$) 213.7 (2 C), 54.7, 43.9, 43.2, 39.3, 38.2, 35.9, 25.3, 23.3, 22.9, 13.5, 10.6; Mass: *m*/*z*, 206 (M^+, 26%), 178 (8), 135 (18), 121 (10), 107 (20), 69 (100); HRMS: *m*/*z* For $C_{13}H_{18}O_2$ (Calc.: *M*, 206.1307. Found: M^+, 206.1310).

Equilibration of the (3α,6β,7α)-3,6,7-trimethyltricyclo[4.4.0.0^{1,3}]-decane-4,8-dione 26

To a magnetically stirred solution of the minor tricyclic ketone **26** (50 mg, 0.23 mmol) in MeOH (1 ml) was added anhydrous K_2CO_3 (64 mg, 0.46 mmol) and the reaction mixture was stirred at room temperature for 48 h. The solvent was removed *in vacuo*, and the residue was taken up in water and extracted with ether (2 × 5 ml). The ether extract was washed successively with 1 M HCl, water and brine, and dried (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 dione **25** (41 mg, 86%), which was identified by comparison (TLC, IR and ^{1}H NMR spectra) with the sample obtained in the previous experiment.

1β,2β,3α,6β,7β-3-Hydroxy-1,2,6,7-tetramethylbicyclo[4.3.0]-nonan-8-one 27

To magnetically stirred, freshly distilled (over sodium) ammonia (50 ml) in a three-necked flask equipped with a Dewar condenser was added the tricyclic ketone **25** (50 mg, 0.23 mmol) in dry THF (3 ml) followed by freshly cut lithium (8 mg, 1.15 mmol). The resulting blue coloured solution was stirred at −33 °C for 1 h and the reaction was quenched with solid NH_4Cl. After evaporation of ammonia, the residue was taken up in water (10 ml) and extracted with ether (2 × 10 ml). The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1:20) as eluent furnished the keto alcohol **27** (32 mg, 67%) as an oil, ν_{max}(neat): 3420, 1730 cm^{-1}; δ_H(400 MHz, $CDCl_3$) 3.45 (1 H, d of t, *J* 11.3 and 4.4), 2.76 (1 H, q, *J* 6.9), 2.35 (1 H, d, *J* 19.2), 1.96 (1 H, d, *J* 19.2, 1.80–1.90 (1 H, m), 1.40–1.65 (4 H, m), 1.0 (3 H, d, *J* 6.5), 0.97 (3 H, s), 0.92 (3 H, d, *J* 6.9), 0.74 (3H, s); δ_C(75 MHz, $CDCl_3$) 220.2, 72.5, 48.8, 47.2, 43.9, 43.5, 42.4, 30.8, 29.0, 19.9, 15.1, 13.0, 7.8. Mass: *m*/*z*, 210 (M^+, 25%), 195 (66), 177 (15), 136 (21), 124 (56), 109 (26), 95 (87), 41 (100); HRMS: *m*/*z* For $C_{13}H_{22}O_2$ (Calc.: *M*, 210.1619. Found: M^+, 210.1605).

(1β,2β,6β,7β)-1,2,6,7-Tetramethylbicyclo[4.3.0]nonane-3,8-dione 29

To a magnetically stirred suspension of PCC (61 mg, 0.28 mmol) and silica gel (61 mg) in anhydrous CH_2Cl_2 (0.5 ml) was added a solution of the keto alcohol **27** (50 mg, 0.238 mmol) in dry CH_2Cl_2 (0.5 ml) in one portion. The reaction mixture was stirred at room temperature for 1.5 h, filtered through a silica gel column and the column was eluted with more CH_2Cl_2. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the dione **29** (50 mg, 84%) as an oil, ν_{max}(neat): 1740, 1715 cm^{-1}; δ_H(200 MHz, $CDCl_3$) 3.0 (1 H, q, *J* 6.9), 2.6 (1 H, q, *J* 6.4), 2.15–2.50 (2 H, m), 2.43 (1 H, d, *J* 19.3), 2.08 (1 H, d, *J* 19.2), 1.65–2.05 (2 H, m), 1.04 (3 H, d, *J* 6.9), 0.98 (3 H, d, *J* 6.5), 0.92 (3 H, s), 0.82 (3 H, s); δ_C(75 MHz, $CDCl_3$) 218.6, 211.6, 49.1, 48.7, 48.1, 47.7, 44.3, 37.8, 31.9, 19.5, 15.4, 9.1, 8.3; Mass: *m*/*z*, 208 (M^+, 40%), 180 (9), 153 (10), 139 (16), 124 (18), 111 (56), 69 (100); HRMS: *m*/*z* For $C_{13}H_{20}O_2$ (Calc.: *M*, 208.1464. Found: M^+, 208.1457).

(1β,2α,6β,7α)-Tetramethylbicyclo[4.3.0]nonane-3,8-dione 28

To magnetically stirred, freshly distilled (over sodium) ammonia (50 ml) in a three-necked flask equipped with a Dewar condenser was added the tricyclic ketone **26** (50 mg, 0.23 mmol) in dry THF (3 ml), followed by freshly cut lithium (8 mg, 1.15 mmol) and the resulting blue coloured solution was stirred for 1 h at −33 °C. Work-up and purification as described for **27** furnished the keto alcohol **30** (32 mg, 67%) as an oil.

Oxidation of the keto alcohol **30** with PCC (62 mg, 0.29 mmol) and silica gel (62 mg) in anhydrous CH_2Cl_2 (0.5 ml) as described for **29** furnished the dione **28** (31 mg, 85%) as an oil, ν_{max}(neat): 1735, 1705 cm^{-1}; δ_H(200 MHz, $CDCl_3$) 2.63 (1 H, q, *J* 6.9), 2.51 (1 H, q, *J* 7.0), 2.20–2.55 (2 H, m), 2.0 (2 H, s), 1.77 (1 H, ddd, *J* 14.4, 5.1 and 3.0), 1.46 (1 H, dd, *J* 14.4 and 4.7), 1.36 (3 H, s), 1.21 (3 H, s), 1.02 (3 H, d, *J* 6.7), 0.98 (3 H, d, *J* 7.1); δ_C(50 MHz, $CDCl_3$) 217.2, 211.4, 53.2, 52.8, 49.0, 45.3, 42.8, 37.6, 33.2, 23.3, 18.0, 9.3, 7.4; Mass: *m*/*z*, 208 (M^+, 47%), 180 (10), 138 (14), 137 (14), 124 (28), 111 (53), 69 (100); HRMS: *m*/*z* For $C_{13}H_{20}O_2$ (Calc.: *M*, 208.1463. Found: M^+, 208.1459).

(1β,2β,3α,6β,7β)-1,2,6,7-Tetramethylbicyclo[4.3.0]nonan-3-ol 31

A solution of the hydroxy ketone **27** (28 mg, 0.133 mmol) and hydrazine monohydrate (0.1 ml, 2 mmol) in diethylene glycol (1 ml) and ethylene glycol (0.25 ml) was heated at 180 °C for 2 h.

The reaction mixture was cooled to 70 °C and treated with a solution of sodium (82 mg, 3.56 mmol) in diethylene glycol (1.65 ml). It was then further heated at 180 °C for 4 h before being cooled to room temperature, poured into ice cold water (5 ml) and extracted with ether (2 × 10 ml). The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate–hexane (1 : 20) as eluent furnished the alcohol **31** as an oil, ν_{max}(neat): 3340 cm^{-1}; δ_H(300 MHz, $CDCl_3$) 3.31 (1 H, d of t, *J* 10.8 and 4.5), 2.4 (1 H, q, *J* 6.9), 1.10–1.90 (9 H, m), 0.95 (3 H, d, *J* 6.6), 0.81 (3 H, d, *J* 6.9), 0.77 (3 H, s), 0.62 (3 H, s); δ_C(75 MHz, $CDCl_3$) 73.6, 41.7, 35.0, 34.5, 30.7, 29.2, 28.9, 19.0, 15.5, 14.6, 12.8 (two quaternary carbons not seen); Mass: *m*/*z*, 196 (M^+, 2%), 178 (12), 163 (99), 139 (47), 123 (81), 109 (100), 95 (70); HRMS: *m*/*z* For $C_{13}H_{24}O$ (Calc.: *M*, 196.1828. Found: M^+, 196.1814).

(1β,2β,6β,7β)-1,2,6,7-Tetramethylbicyclo[4.3.0]nonan-3-one 11

To a solution of the bicyclic alcohol **31**, in methylene dichloride (0.5 ml) were added PCC (40 mg, 0.186 mmol) and silica gel (40 mg) and the mixture was stirred for 2 h. The reaction mixture was filtered through a silica gel column and the column was eluted with more CH_2Cl_2. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 40) as eluent furnished the Schinzer's ketone **11** (17.5 mg, for two steps 68%) as an oil, which was identified by comparison of the spectral data with that of an authentic sample **11**, ν_{max}(neat): 1715, 1315, 1165, 1010 cm^{-1}; δ_H(400 MHz, $CDCl_3$) 2.59 (1 H, q, *J* 6.5), 2.35–2.55 (2 H, m), 2.16 (1 H, ddd, *J* 15.5, 5.1 and 3.8), 1.61 (1 H, ddd, *J* 14.1, 12.6 and 5.1), 1.85–2.00 (1 H, m), 1.25–1.50 (3 H, m), 0.95 (3 H, d, *J* 6.6), 0.945 (3 H, d, *J* 6.8), 0.719 (3 H, s), 0.717 (3 H, s); δ_C(50 MHz, $CDCl_3$) 214.1, 48.4, 53.3, 45.6, 37.7, 37.4, 35.5, 32.4, 22.6, 29.2, 18.4, 16.5, 14.8, 8.7; Mass: *m*/*z* 194 (M^+, 20%), 179 (25), 137 (15), 123 (45), 122 (25), 109 (100), 95 (17).

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References

1 Y. Asakawa in *Progress in the Chemistry of Organic Natural Products*, eds. W. Herz, G. W. Kirby, R. E. Moore, W. Steglich and Ch. Tamm, Springer, Wien, New York, 1995, vol. 65, pp. 1–296.

2 (*a*) V. Benesova, Z. Samek, V. Herout and F. Sorm, *Collect. Czech. Chem. Commun.*, 1969, **34**, 582; (*b*) V. Benesova, V. Herout and F. Sorm, *Collect. Czech. Chem. Commun.*, 1969, **34**, 1810; (*c*) S. M. Krutov, Z. Samek, V. Benesova and F. Sorm, *Phytochemistry*, 1973, **12**, 1405; (*d*) A. Corbella, P. Gariboldi and G. Jommi, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1875; (*e*) Y. Asakawa, M. Toyota, M. Uemoto and T. Aratani, *Phytochemistry*, 1976, **15**, 1929; (*f*) Y. Asakawa, M. Toyota and T. Aratani, *Tetrahedron Lett.*, 1976, 3619; (*g*) Y. Asakawa, M. Toyota and T. Takemoto, *Phytochemistry*, 1978, **17**, 457; (*h*) Y. Asakawa, M. Toyota, T. Takemoto and C. Suire, *Phytochemistry*, 1979, **18**, 1349; (*i*) Y. Asakawa, M. Toyota, M. Kano and T. Takemoto, *Phytochemistry*, 1980, **19**, 2651; (*j*) Y. Asakawa, M. Toyota and T. Takemoto, *Phytochemistry*, 1981, **20**, 257; (*k*) Y. Asakawa, A. Yamamura, T. Waki and T. Takemoto, *Phytochemistry*, 1980, **19**, 603; (*l*) Y. Asakawa, M. Toyota, R. Takeda, C. Suire and T. Takemoto, *Phytochemistry*, 1981, **20**, 725; (*m*) Y. Asakawa, R. Matsuda and C. Suire, *Phytochemistry*, 1981, **20**, 1427; (*n*) R. Takeda, H. Naoki, T. Iwashita and Y. Hirose, *Tetrahedron Lett.*, 1981, **22**, 5307; (*o*) Y. Fukuyama, M. Tori, M. Wakamatsu and Y. Asakawa, *Phytochemistry*, 1988, **27**, 3557; (*p*) M. Toyota, F. Nagashima and Y. Asakawa, *Phytochemistry*, 1989, **28**, 1661; (*q*) M. Toyota, H. Koyama, T. Hashimoto and Y. Asakawa, *Chem. Pharm. Bull.*, 1995, **43**, 714; (*r*) M. S. Buchanan, J. D. Connolly and D. S. Rycroft, *Phytochemistry*, 1996, **43**, 1249; (*s*) D. S. Rycroft and W. J. Cole, *J. Chem. Res.* (*S*), 1998, 600.

3 (*a*) M. Tori, H. Arbiyanti, Z. Taira and Y. Asakawa, *Phytochemistry*, 1993, **32**, 335; (*b*) H. Tazaki, H. Soutome, Z. Iwasaki, K. Babeta and D. Arigoni, *Chem. Commun.*, 1997, 1101.

4 (*a*) D. Schinzer, K. Ringe, P. G. Jones and D. Doring, *Tetrahedron Lett.*, 1995, **36**, 4051; (*b*) D. Schinzer and K. Ringe, *Tetrahedron*, 1996, **52**, 7475.

5 S. Bernasconi, P. Gariboldi, G. Jommi, S. Montanari and M. Sisti, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2394; T. Uyehara, Y. Kabasawa, T. Kato and T. Furuta, *Tetrahedron Lett.*, 1985, **26**, 2343; T. Uyehara, Y. Kabasawa and T. Kato, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 2521; A. Gambacorta, M. Botta and S. Turuchetta, *Tetrahedron Lett.*, 1988, **29**, 4846; R. Baker, D. L. Selwood, C. J. Swain, N. M. H. Webster and J. Hirshfield, *J. Chem. Soc., Perkin Trans. 1*, 1988, 471; A. F. Mateos, O. F. Barrueco and R. R. Gonzalez, *Tetrahedron Lett.*, 1990, **31**, 4343; A. Srikrishna and D. Vijaykumar, *Tetrahedron Lett.*, 1998, **39**, 5833.

6 A. Srikrishna and K. Krishnan, *Tetrahedron Lett.*, 1989, **30**, 6577; A. Srikrishna and G. Sundarababu, *Tetrahedron*, 1990, **46**, 3601; A. Srikrishna and K. Krishnan, *Indian J. Chem., Sect. B*, 1990, **29**, 879; A. Srikrishna and G. Sundarababu, *Tetrahedron*, 1991, **47**, 481; A. Srikrishna and S. Nagaraju, *J. Chem. Soc., Perkin Trans. 1*, 1991, 657; *Indian J. Chem., Sect. B*, 1991, **30**, 1006; A. Srikrishna and K. Krishnan, *J. Chem. Soc., Chem. Commun.*, 1991, 1693; *Tetrahedron*, 1992, **48**, 3429; *J. Chem. Soc., Perkin Trans. 1*, 1993, 667; *J. Org. Chem.*, 1993, **58**, 7751; A. Srikrishna, K. Krishnan and S. Nagaraju, *J. Indian Inst. Sci.*, 1994, **74**, 157; A. Srikrishna, C. V. Yelamaggad, K. Krishnan and M. Nethaji, *J. Chem. Soc., Chem. Commun.*, 1994, 2259; A. Srikrishna and S. Nagaraju, *Phytochemistry*, 1995, **40**, 1699; A. Srikrishna, T. J. Reddy, P. Praveen Kumar and D. Vijaykumar, *Synlett*, 1996, 67; A. Srikrishna and R. Viswajanani, *Tetrahedron Lett.*, 1996, **37**, 2863; *Indian J. Chem., Sect. B*, 1996, **35**, 521; A. Srikrishna and P. Praveen Kumar, *Tetrahedron Lett.*, 1997, **38**, 2005.

7 *Preliminary communication*: A. Srikrishna and D. Vijaykumar, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3295.

8 (*a*) L. Claisen, *Ber. Dtsch. Chem. Ges.*, 1912, **45**, 3157; (*b*) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-t. Li, D. J. Faulkner and M. R. Petersen, *J. Am. Chem. Soc.*, 1970, **92**, 741; (*c*) W. S. Johnson, T. J. Brocksom, P. Loew, D. H. Rich, L. Werthemann, R. A. Arnold, T.-t. Li and D. J. Faulkner, *J. Am. Chem. Soc.*, 1970, **92**, 4463; (*d*) F. E. Ziegler, *Acc. Chem. Res.*, 1977, **10**, 227; (*e*) G. B. Bennett, *Synthesis*, 1977, 589; (*f*) R. P. Lutz, *Chem. Rev.*, 1984, **84**, 205; (*g*) F. E. Ziegler, *Chem. Rev.*, 1988, **88**, 1423.

9 (*a*) G. Stork and J. Ficini, *J. Am. Chem. Soc.*, 1961, **83**, 4678; (*b*) S. D. Burke and P. A. Grieco, *Org. React.*, 1979, **26**, 361; (*c*) L. N. Mander, *Synlett*, 1991, 134; (*d*) A. Padwa and K. E. Krumpe, *Tetrahedron*, 1992, **48**, 5385.

10 A. Srikrishna, S. Nagaraju and S. Venkateswarlu, *Tetrahedron Lett.*, 1994, **35**, 429.

11 G. Buchi and J. D. White, *J. Am. Chem. Soc.*, 1964, **86**, 2884.

12 G. Stork, S. Uyeo, T. Wakamatsu, P. Grieco and J. Labovitz, *J. Am. Chem. Soc.*, 1971, **93**, 4949.

13 J. E. McMurry and L. C. Blaszczak, *J. Org. Chem.*, 1974, **39**, 2217.

14 (*a*) T. Norin, *Acta Chem. Scand.*, 1963, **17**, 738; (*b*) W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, 1966, **31**, 3794; (*c*) W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 374; (*d*) *J. Org. Chem.*, 1970, **35**, 2361; (*e*) T. Norin, *Acta Chem. Scand.*, 1965, **19**, 1289; (*f*) A. Srikrishna, K. Krishnan and C. V. Yelamaggad, *Tetrahedron*, 1992, **48**, 9725.

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