Synthetic Studies on Terpenoids. Part 20.† Stereospecific Synthesis of Pseudoclovene-B

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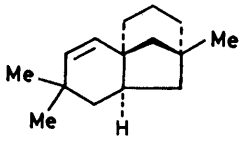
A stereospecific synthesis of pseudoclovene-B (1), a rearranged sesquiterpene artifact, is reported. 1-Methyltricyclo[6.3.1.$0^{3,8}$]dodeca-3,6-dien-5-one (6), an advanced intermediate in this synthesis and a skeletal representative of many other natural products, has been prepared by two different routes utilising Winstein's Ar_{1-6} solvolytic cyclisation as the key step.

PSEUDOCLOVENE-B (1), a rearranged sesquiterpene artifact incorporating a novel tricyclo[6.3.1.$0^{3,8}$]-dodecane ring, is formed [1] along with a number of other tricyclic olefins when caryolan-1-ol is treated with polyphosphoric acid or phosphorus pentaoxide in dimethylformamide; this paper reports a stereospecific synthesis of this novel hydrocarbon. The basic carbon framework present in (1) also represents the skeleton of



(1)

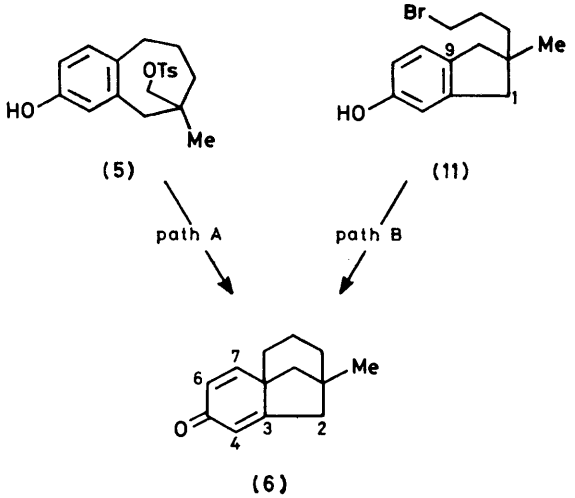
many other natural products, *e.g.*, stemodin [2a] and aconitine.[2b] A synthetic entry into the bridged carbon skeleton of (1) could, in principle, be achieved through Winstein's cyclisation [3] of either a suitably substituted benzosuberane precursor (5) (path A) or an indane derivative (11) (path B), as outlined in the Scheme. Both pathways, indeed, led to the formation of the tricyclic dienone (6).

RESULTS AND DISCUSSION

Path A.—The suitably functionalised benzosuberanone (2), a precursor for this approach, was available from earlier studies.[2c] The corresponding tetrahydropyranyl ether of (2), prepared by the addition of 2,3-dihydropyran and *p*-toluenesulphonic acid to (2), was subjected to Wolff–Kishner reduction and the resulting deoxopyranyl ether hydrolysed [4] in the presence of acetic acid. During hydrolysis, the liberated alcohol was partly converted into the corresponding acetate, as was evident from the i.r. and n.m.r. data (see Experimental section). The product was, therefore, heated with methanolic potassium hydroxide solution. The neutral part from the work-up was characterised as (3), and was obtained in 62% overall yield from (2). Treatment of (3) with toluene-*p*-sulphonyl chloride in pyridine afforded the tosylate (4) which, on hydrogenolysis over Pd–C (10%) in ethanol, yielded the phenolic tosylate (5).

Winstein's high-dilution [5] solvolytic cyclisation of this tosylate, employing a 0.01M-solution in anhydrous t-butyl alcohol in the presence of 1.2 equiv. of potassium t-butoxide, furnished the dienone (6), albeit in 11% yield. The low yield in this reaction probably results from the fact that the functionalised methylene carbon atom (C-12), attached to C-6, represents a neopentyl system and displacement reactions of neopentyl tosylates are generally difficult. Nevertheless, this is an intramolecular cyclisation and operates through an anchimerically assisted concerted process. It is to be expected that close proximity of C-12 and C-10, and a possible internal assistance [6] by the adjacent aryl group, should have facilitated the desired cyclisation in spite of the neopentyl character of C-12. Utilising Winstein's cyclisation as the key step, the dienone (6) has, however, been obtained by an altogether different route in much improved yield.

Path B.—We have developed an alternative approach starting from the indanone (7) [2c,7] whose synthesis has been reported from this laboratory. It was necessary to eliminate the carbonyl group in (7) at this stage because our earlier studies [2c,7] had disclosed that the key solvolytic cyclisation step fails to produce the tricyclic



SCHEME

intermediate (Scheme) if the phenol (11) has a carbonyl group present at C-1. The successful formation of the hydrazone of (7) was found to be critical owing to the steric congestion around the carbonyl group. This was overcome by employing the modified conditions of Nagata [8] and the subsequent Wolff–Kishner reduction gave a mixture of (8) and the demethylated derivative (9) in 75% and 16% overall yields, respectively. Formation of the corresponding bromide (10) was achieved by

† Part 19, T. K. Das, P. C. Dutta, G. Kartha, and J. M. Bernassan, *J.C.S. Perkin I*, 1977, 1287.

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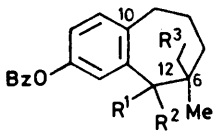
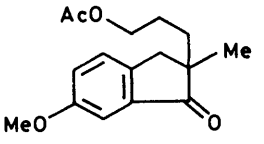
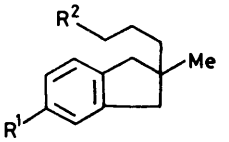
treatment of (8) with phosphorus tribromide and benzene. No accompanying demethylation due to the generated hydrogen bromide could be detected. Treatment of (10) in cold methylene chloride with boron tribromide resulted in a smooth demethylation [9] leading to the formation of (11). Alternatively, the dihydroxy-compound (9) was converted directly into (11) by reaction with phosphorus tribromide in ether–tetrahydrofuran (1 : 1). Both samples of the bromide (11), obtained by different routes, were shown to be completely identical in all respects. Winstein's solvolytic cyclisation of (11) under similar condition gave the dienone (6) in 72% yield. Samples of the tricyclic ketone (6) obtained by paths A and B were found to be completely identical in all respects.





(2) R^1 R^2 = O, R^3 = OH
(3) R^1 = R^2 = H, R^3 = OH
(4) R^1 = R^2 = H, R^3 = OTs

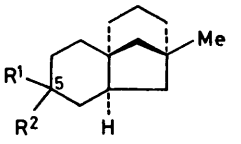
(7)



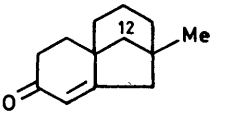
(8) R^1 = OMe, R^2 = OH
(9) R^1 = OH, R^2 = OH
(10) R^1 = OMe, R^2 = Br

Catalytic hydrogenation of (6) over Pd–C (10%) in ethanol quantitatively afforded the saturated ketone (12). The rate of uptake of the first mol of hydrogen was rapid while that of the second was relatively slow. The product was found to be >95% homogeneous by g.l.c. analysis. It is evident [10] from steric considerations in similar systems that during hydrogenation of (6), the latter is first reduced relatively rapidly to an intermediate enone (13), which is further reduced slowly to (12). In fact, analysis of the n.m.r. spectrum of the half-hydrogenated product (13) revealed that the C-4 proton centred at δ 5.96 remained intact as a singlet, while the C-7 proton resonating at δ 6.88 had completely disappeared. It has been shown [11a] that catalytic hydrogenation of systems analogous to that of (13) stereoselectively yields the *cis* isomer as the major, if not the only product. In the light of the high polarity and protic nature of the solvent, it is to be expected [11b] that hydrogenation of (13) takes place through a Horiuti–Polanyi mechanism [12] involving a 1,2-adsorbed species (13a). On rigorous examination of models of (13a) in both *cis* and *trans* forms, and considering their initial and half-hydrogenated states, it is apparent that hydrogen must approach from a face which is opposite to the C-12 methylene bridge.

Geminal bis-methylation in place of the 5-ketone in (12) and introduction of the $\Delta^{6,7}$-double bond would complete the synthesis of (1). Recent approaches to geminal alkylation [13] would be of no practical use in this synthesis, because none of them will lead to a stage where the $\Delta^{6,7}$-double bond could be re-introduced. Based on this consideration, it was decided to convert the 5-ketone into the corresponding α,β-unsaturated nitrile (15) by cyanohydrin formation and subsequent dehydration. This method of forming [14] the cyanohydrin from (12), using acetone cyanohydrin and triethylamine, afforded a mixture of (14) and the unreacted ketone, as was evident from the i.r. spectrum of the product. In view of the close boiling-points of (12) and (14), it was difficult to effect complete separation of them by fractional distillation. In t.l.c., the mixture resolved as two spots of equal intensity (sulphuric acid spray). To improve the yield of cyanohydrin, the ketone (12) was subjected to an alternative reaction [15] using hydrogen cyanide, generated *in situ* by the reaction of aqueous sodium cyanide and concentrated hydrochloric acid in the cold. A gas chromatogram of the reaction product indicated the formation of (14) in 80% yield mixed with unreacted (12). The product was dehydrated directly [16] by



(12) R^1 R^2 = O
(13) R^1 = OH, R^2 = CN



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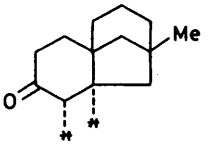
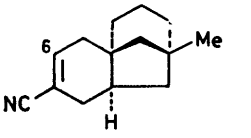
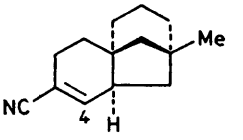


(13a)



(15)



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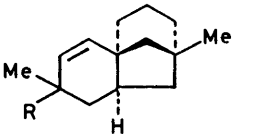

(17) R = $CONMe_2$
(17a) R = $C(NMe_2)=N^- Na^+$
(18) R = CN
(19) R = CHO

treatment with phosphorus oxychloride in pyridine to furnish the mixture of the isomeric nitriles (15) and (16), along with unreacted starting ketone (cyanohydrin formation is known to be an equilibrium process). Dehydration with the mixture was carried out with the idea of removing (14) from the resulting equilibrium mixture of (12) and (14). Repeating the process of

cyanohydrin formation and subsequent dehydration with the mixture resulted in almost complete conversion of (12) into the isomeric nitriles (15) and (16). The desired nitrile (15) was identified by the n.m.r. spectrum, which showed a complex triplet (J 4 Hz) centred at δ 6.59 (0.4 H) for the C-6 proton of (15); a broad doublet (J 4 Hz) at δ 6.25 (0.6 H) was attributed to the C-4 proton in (16). This was confirmed by g.l.c. analysis which indicated that the ratio of (15) : (16) was 2 : 3. The formation of the latter as the major isomer, analogous[17] with the simple hydroindane or decalin systems, indicates that the A–B ring junction in (12) is *cis*. Complete separation of the isomeric nitrile mixture by column chromatography [over silica gel impregnated with silver nitrate (15%)] was found to be unsatisfactory. Resorting to the inverted dry-column chromatography technique,[18] the desired nitrile (15) was completely separated from (16) on a column packed with silica gel of t.l.c.-grade impregnated with silver nitrate (15%) and using azobenzene as the reference.

Although ester enolates have previously been generated by the reaction of relatively unreactive esters with 1 and 2 equiv. of lithium amide in liquid ammonia,[19] and with the alkali-metal salts of triphenylmethane,[20] we considered that sodium hydride might be the appropriate base to effect the methylation of (15). In an attempted methylation, this nitrile was treated with 1.5 equiv. of sodium hydride in dimethylformamide. The resulting mixture was heated under nitrogen to generate the corresponding anion of the nitrile. Refluxing with an excess of methyl iodide yielded a mixture which showed characteristic absorptions due to the tertiary amide (1 670 cm^{-1}) and the α,β-unsaturated nitrile (2 220 cm^{-1}) in the i.r. spectrum. From the mixture was isolated a pure compound in 23% yield, *via* extensive column chromatography over alumina, which was characterised as the amide (17) by its analytical and spectroscopic data. Sharp singlets at δ 2.9 (6 H) and 1.32 (3 H) were assigned to the N-dimethyl and the 5-methyl groups, respectively, in the n.m.r. spectrum. That the double bond had migrated to the $\Delta^{6,7}$-position was also evident from n.m.r. signals due to two olefinic protons. In the mass spectrum of the amide, the base peak was located at m/e 189; this arises from the extrusion of 72 mass units of a dimethylamido-group, which is a characteristic fragmentation pattern of amides. The formation of (17) may be explicable in the light of the following considerations. Dimethylformamide decomposes[21] to carbon monoxide and dimethylamine under acid or base catalysis. Therefore, the presence of dimethylamine and thus formation of $Na^+NMe_2^-$ is easily justified. The 5-cyano-group, being susceptible[22] to nucleophilic attack by this species, undergoes transformations into (17a) and finally to a trimethylamidine (by N-methylation), which can be subsequently hydrolysed on work-up to the dimethylamide (17).

Successful methylation of (15) was carried out[23] using methyl iodide and lithium di-isopropylamide–hexamethylphosphoramide (1 : 1) (1M in tetrahydrofuran) at −78 °C to obtain (18). That the double bond migrated exclusively to the desired position was evident from the n.m.r. spectrum and the sample homogeneity (g.l.c.). In the n.m.r. spectrum of (18), the C-7 and the C-6 protons appeared as doublets (J 5 Hz) at δ 5.47 and 6.21, respectively, while the 5-methyl signal appeared as a singlet at δ 1.34. The 5-cyano-group in (18) was converted[24] into the corresponding aldehyde (19) by reduction of the nitrile with di-isobutylaluminium hydride in hexane, followed by hydrolysis of the intermediate imine. Attempts to convert the 5-cyano-group in (15) to an aldehyde first and then to effect the methylation of the resulting α,β-unsaturated aldehyde were found unsatisfactory, on the basis of low overall yield and undesired bond migration. Wolff–Kishner reduction of (19) resulted in the formation of an olefin whose analytical and spectroscopic data were in complete accord with those of an authentic sample of (1). Remarkably, the C-6 and C-7 olefinic protons[1] in (1) appeared as a singlet (2 H) at δ 5.34 in the n.m.r. spectrum. In g.l.c., co-injection of the samples of (1), obtained from the synthesis and from the rearrangement of caryolan-1-ol, further confirmed their identity. Pseudoclovene-B (1), as obtained above, readily formed a dibromide when treated with bromine in carbon tetrachloride and the m.p. of this bromide was identical with that reported in the literature.[1]

EXPERIMENTAL

M.p.s were taken for samples in open capillaries in a sulphuric acid bath. U.v. spectra were recorded for solutions in 95% ethanol with Beckmann DU (manually operated) and Perkin-Elmer 402 spectrophotometers; i.r. spectra with Perkin-Elmer 21 and 577 instruments for solutions in chloroform. N.m.r. spectra were recorded with the Varian A–60D, T–60 and Perkin-Elmer R32 (90 MHz) instruments (tetramethylsilane as internal reference). Mass spectra were run with a CEC 21–110B double-focusing spectrometer and a Hitachi RM–60 mass spectrometer. G.l.c. were carried out on Varian Aerograph 1864–4 or Perkin-Elmer 900 flame-ionisation instruments. Helium was the carrier gas and the following columns were used: (A), 12 ft × 0.125-in outside diameter (15% Carbowax 20 M on 40/50 Anakrom ABS); (B), 50 ft × 0.02-in internal diameter (10% Apiezon L on 80/90 Anakrom ABS); and (C), 12 ft × 0.125-in outside diameter (10% FFAP on 80/100 chromosorb W). T.l.c. plates were coated (0.2-mm thickness) with either silica gel G (200 mesh) or silica gel (TLC-grade) impregnated with silver nitrate (15%) and, unless stated otherwise, the spots were located either by exposing the dried plates to iodine vapour or by charring. The compounds described are all racemic forms. Usual work-up refers to thorough extraction with the specified solvent, washing the combined extracts with saturated brine solution (pre-washing with dilute solution of acid or base when necessary), and drying the extracts over anhydrous sodium sulphate. Solvents were removed from the filtered extracts under reduced pressure. Light petroleum refers to the fraction boiling at 60—80 °C.

3-Benzyloxy-6-gem-hydroxymethyl-6-methylbenzosuberane (3).—To a stirred solution of the benzosuberanone (2) (9 g) in benzene (210 ml) at room temperature was added 2,3-

dihydropyran (18 ml) and *p*-toluenesulphonic acid (600 mg) and the mixture stirred for 20 h. The usual work-up with benzene gave an oil (10.98 g) which was mixed with hydrazine (102 ml, 99%), hydrazine dihydrochloride (25 g), and diethylene glycol (300 ml). The mixture was heated to 120 °C (inner temperature) for 3 h under a slow stream of nitrogen. The reaction was cooled and after the addition of potassium hydroxide (49.8 g), the temperature was raised to 210 °C for 2 h. The usual work-up with ether afforded a pale brown oil (10.02 g). This was heated with acetic acid (105 ml, 90%) in a boiling water-bath for 30 min. Neutralisation of the acetic acid with sodium hydrogencarbonate and the usual work-up with ether gave an oil; $\nu_{max.}$ 1 725 and 1 600 cm^{-1}; $\delta(CDCl_3)$ 2.08 (1.3 H, s, CO_2Me). The oil was refluxed for 1 h with methanolic potassium hydroxide solution (50 ml, 5%) and the resulting product was diluted with water. Usual work-up with ether gave a concentrate, which on distillation afforded (3) (5.31 g, 62% overall yield), b.p. 168—170 °C at 0.05 mmHg (Found: C, 81.1; H, 8.0. $C_{20}H_{24}O_2$ requires C, 81.0; H, 8.1%); $\nu_{max.}$ 1 600 cm^{-1}; $\delta(CCl_4)$ 7.36 (5 H, s, aromatic), 7.00—6.40 (3 H, m, aromatic), 4.94 (2 H, s, $PhCH_2O$), 3.46 (2 H, s, $HOCH_2$), 3.23 (1 H, s, OH, vanishes on exchange with D_2O), 2.59 (4 H, m, seven-membered ring protons), and 0.76 (3 H, s, 6-Me).

3-Hydroxy-6-gem-(p-tosyloxymethyl)-6-methylbenzosuberane (5).—The alcohol (3) (1.73 g) in dry pyridine (18 ml) was treated with *p*-toluenesulphonyl chloride (1.8 g) and allowed to stand at 0 °C for 20 h. Extraction with ether followed by washing of the combined extracts with copper sulphate solution afforded, on concentration, the oily (4) (2.17 g, 94%), $\nu_{max.}$ 1 600 and 1 180 cm^{-1}. This crude tosylate (4) was hydrogenolysed in ethanol (30 ml) over palladium–charcoal (500 mg, 10%), during 10 h. The catalyst was filtered off, washed with ether, and the combined filtrates on evaporation gave an oil which was chromatographed over alumina (30 g). Elution with benzene–light petroleum (1 : 3) yielded (5) (1.17 g, 68%), m.p. 116 °C (Found: C, 66.4; H, 6.5. $C_{20}H_{24}O_4S$ requires C, 66.6; H, 6.6%); $\delta(CDCl_3)$ 7.80—7.40 (4 H, m, tosyl protons), 6.84—6.50 (3 H, m, aromatic protons), 3.67 (2 H, s, CH_2–OTs), 2.60 (4 H, m, ring protons), 2.39 (3 H, s, tosyl Me), and 0.77 (3 H, s, 6-Me).

2-(3-Hydroxypropyl)-2-methyl-5-methoxyindane (8) *and 5-Hydroxy-2-(3-hydroxypropyl)-2-methylindane* (9).—To a solution of (7) (21.4 g) in diethylene glycol (1 180 ml) was added hydrazine hydrate (316 ml, 99%) and hydrazine dihydrochloride (74 g) and the mixture heated to 130 °C (inner temperature) under nitrogen for 3 h. The reaction was cooled, potassium hydroxide (102 g) was added, and the reaction was heated to 210 °C for 2 h. The reaction mixture was diluted with water and the usual work-up with ether afforded a viscous oil. Fractional distillation of this oil furnished the indane (8) (12.8 g, 75%) as the first fraction, b.p. 138—142 °C at 0.1 mmHg (Found: C, 76.1; H, 9.1. $C_{14}H_{20}O_2$ requires C, 76.3; H, 9.0%); $\nu_{max.}$ 1 612 cm^{-1}; $\delta(CDCl_3)$ 3.73 (3 H, s, OMe), 3.59 (2 H, t, *J* 6 Hz, $HOCH_2$), 2.63 (4 H, broad s, ring CH_2), and 1.06 (3 H, s, Me).

From the above distillation was obtained the indane (9) (2.6 g, 16%) as the second fraction, b.p. 170 °C at 0.2 mmHg, which solidified on standing. This was crystallised from ether–light petroleum (3 : 1) as needles, m.p. 119 °C (Found: C, 75.6; H, 8.7. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.7%); $\delta(CDCl_3)$ 5.31 (1 H, s, phenolic OH, vanishes on exchange with D_2O) and 2.40 (1 H, s, aliphatic OH, vanishes on exchange with D_2O).

2-(3-Bromopropyl)-2-methyl-5-methoxyindane (10.)—To a solution of (8) (25.6 g) in dry benzene (60 ml) was added dropwise phosphorus tribromide (13.4 ml). After heating to reflux for 2 h, the resulting mixture was poured into crushed ice and the organic layer separated. Extraction of the aqueous part with benzene and concentration of the combined organic extracts gave an oil, which on distillation afforded the bromoindane (10) (30 g, 91%), b.p. 145 °C at 0.1 mmHg (Found: C, 59.5; H, 6.6. $C_{14}H_{19}BrO$ requires C, 59.3; H, 6.7%); $\delta(CDCl_3)$ 3.73 (3 H, s, OMe), 3.28 (2 H, t, *J* 6 Hz, CH_2Br), 2.59 (4 H, broad s, ring CH_2), and 1.03 (3 H, s, Me).

2-(3-Bromopropyl)-5-hydroxy-2-methylindane (11).—(*a*) To a stirred solution of the indane (10) (30 g) in dry methylene chloride (250 ml) at 0 °C was added dropwise a solution of boron tribromide (15 ml) in dry methylene chloride (40 ml). At the end of the addition, the reaction mixture was stirred at room temperature for 20 h, and the boron complexes were then hydrolysed by shaking with cold water (200 ml). The organic part was separated, the aqueous part extracted with methylene chloride and the combined organic extracts concentrated. The residue was taken up in ether, washed with cold aqueous sodium hydroxide solution (5%), and the aqueous washings acidified in the cold. The usual work-up of the acidified residue with ether, followed by distillation, afforded (11) (25.6 g, 90%), b.p. 170—173 °C at 0.1 mmHg (Found: C, 57.8; H, 6.4. $C_{13}H_{17}BrO$ requires C, 57.9; H, 6.3%); $\delta(CDCl_3)$ 6.96—6.36 (3 H, m, aromatic protons), 5.31 (1 H, s, phenolic OH, vanishes on exchange with D_2O), 3.28 (2 H, t, *J* 6 Hz, CH_2Br), 2.59 (4 H, broad s, ring CH_2), and 1.03 (3 H, s, Me).

(*b*) The indane (9) (4 g) in dry ether–tetrahydrofuran (1 : 1, 20 ml) was treated with phosphorus tribromide (2.1 ml) according to the method for the preparation of (10). The product (4 g, 80%) was identical with the indane (11), obtained by the above method, on the basis of spectroscopic and analytical data.

1β-Methyltricyclo[6.3.1.0^{3,8}]dodeca-3,6-dien-5-one (6).—(*a*) To a stirred solution (0.01M) of potassium t-butoxide in t-butyl alcohol [prepared by dissolving potassium (117 mg) in dry t-butyl alcohol (300 ml)] under nitrogen was added dropwise the benzosuberane (5) (1 g), dissolved in dry t-butyl alcohol (10 ml). After refluxing for 22 h, the solvent was removed by distillation, and the residue diluted with water and extracted with ether. The combined organic extract was washed with aqueous sodium hydroxide solution (4%) and water, dried over sodium sulphate, and concentrated. Short-path distillation gave (6) (7 mg, 11%), b.p. 95—97 °C at 0.1 mmHg (Found: C, 82.9; H, 8.4. $C_{13}H_{16}O$ requires C, 82.9; H, 8.5%); *m/e* 188 (M^+); $\lambda_{max.}$ 246 nm (ε 14 350); $\nu_{max.}$ 1 652 and 1 620 cm^{-1}; $\delta(CCl_4)$ 6.88 (1 H, d, *J* 9 Hz, C-7 proton), 5.96 (2 H, d and s, *J* 9 Hz, C-6 and C-4 protons), 2.63 (1 H, d, *J* gem 17 Hz, C-2 proton), 2.16 (1 H, d, *J* gem 17 Hz, C-2 proton), and 1.06 (3 H, s, Me). This ketone was found to be 99% homogeneous in g.l.c. (column A).

(*b*) The indane (11) was cyclised using the same procedure as above except that the reaction mixture was heated to reflux for 16 h. The cyclisation was easily monitored by the precipitate of potassium bromide formed during the reaction. The product (72% yield) was identical with the sample of (6), obtained above, in all respects.

1β-Methyl-3αH-cis-tricyclo[6.3.1.0^{3,8}]dodecan-5-one (12).—The ketone (6) (2.8 g) in ethanol (60 ml) was hydrogenated over palladium–charcoal (300 mg, 10%). Half the theoreti-

cal uptake was complete in 15 min and an aliquot (2 ml) was drawn from the reaction flask at this stage. This was filtered and concentrated to give an oil (13) which was 94% homogeneous in g.l.c. (column A); $\delta(CCl_4)$ 5.96 (1 H, s, C-4 proton). The hydrogenation was finally complete in 80 min. The catalyst was filtered off, washed with ether, and the combined filtrates on evaporation gave an oil, which on distillation gave (12) (2.67 g, 95%), b.p. 100 °C at 0.1 mmHg (Found: C, 81.2; H, 10.3. $C_{13}H_{20}O$ requires C, 81.2; H, 10.4%); the red 2,4-*dinitrophenylhydrazone* had m.p. 164 °C (from benzene–methanol) (Found: C, 61.3; H, 6.1. $C_{19}H_{24}N_4O_4$ requires C, 61.4; H, 6.2%). The ketone was found to be 95% homogeneous in g.l.c. (columns A and C); $\nu_{max.}$ 1 720 cm^{-1}; $\delta(CCl_4)$ 0.99 (3 H, s, Me).

5-*Cyano*-1β-*methyl*-3αH-cis-*tricyclo*[6.3.1.$0^{3,8}$]*dodec*-5-*ene* (15) *and the* $\Delta^{4,5}$-*Isomer* (16).—(*a*) The ketone (12) (2.1 g) in redistilled acetone cyanohydrin (9 ml) was treated with ten drops of triethylamine. After stirring for 18 h at room temperature, the deep brown solution was diluted with water, acidified in the cold with concentrated hydrochloric acid, and extracted with ether. The residue, after removal of ether, was concentrated at 75 °C and 10 mmHg, and distillation *in vacuo* afforded a mixture of (12) and (14) (2.2 g), b.p. 102—103 °C at 0.1 mmHg; $\nu_{max.}$ 3 460, 2 245, and 1 720 cm^{-1}. In t.l.c. [benzene–light petroleum (6 : 4)], this mixture showed two spots of equal intensity (sulphuric acid spray).

To the crude cyanohydrin mixture (2 g) in anhydrous pyridine (14.4 ml) was added freshly distilled phosphorus oxychloride (3.6 ml) and stirred for 16 h at room temperature. The reaction mixture was carefully hydrolysed over crushed ice. The usual work-up followed by distillation furnished an oil (1.1 g), b.p. 110 °C (bath temperature) at 0.1 mmHg, shown to be a mixture of (15), (16), and (12); $\nu_{max.}$ 2 220, 1 720, and 1 630 cm^{-1}; $\delta(CCl_4)$ 6.59 (0.2 H, complex triplet, *J* 4 Hz, C-6 proton) and 6.25 (0.3 H, broad doublet, *J* 4 Hz, C-4 proton). A gas chromatogram (column C) of this mixture indicated that the isomeric nitrile mixture was formed in the ratio of 2 : 3.

(*b*) The ketone (12) (3 g) in ether (100 ml) and sodium cyanide (9 g) in water (80 ml) was stirred vigorously at 10—15 °C while a slow stream of nitrogen was passed through the solution. Concentrated hydrochloric acid (20 ml) was added dropwise during 2 h. The organic part was separated, concentrated, and finally distilled to obtain a mixture of (12) and (14) (3.12 g), b.p. 102—104 °C at 0.1 mmHg; $\nu_{max.}$ 3 460, 2 245, and 1 720 cm^{-1}. In g.l.c. (column C), this oil was found to be a mixture of (14) and (12) in the ratio of 4 : 1, respectively.

Using the procedure as described in (*a*), this oil was dehydrated, and the resulting material [a mixture of (14), (15), and (12) from g.l.c. (column C)] was re-subjected to cyanohydrin formation [method (*b*)] and finally dehydrated once again, following the same procedure, to obtain a brown oil which on distillation (bath temperature 110 °C) at 0.1 mmHg gave a colourless oil (2.5 g, overall 80% yield); $\nu_{max.}$ 2 229 and 1 630 cm^{-1}; $\delta(CCl_4)$ 6.59 (0.4 H, complex triplet, *J* 4 Hz, C-6 proton), 6.25 (0.6 H, complex doublet, *J* 4 Hz, C-4 proton). A gas chromatogram (column C) indicated that the two components were present in the ratio 2 : 3.

T.l.c. (silver nitrate–silica gel) of this oil was studied [benzene–light petroleum–ethyl acetate (2 : 4 : 1)] and the isomeric nitriles showed good resolution, solvent front 15 cm, ΔR_F *ca.* 0.1. The position of the reference dye [25] (azobenzene) was also determined on the same chromatogram; it had an R_F value, 0.2 units higher than the fast-moving nitrile (16). The nitrile mixture with the dye was subjected to inverted dry-column chromatography [18] [silver nitrate (15%) silica gel (500 g) column, 25 × 6.6 cm, internal diameter] using the same solvent system and the nitriles were separated. The desired nitrile (15) was distilled (short-path, bath temperature 105 °C) at 0.1 mmHg to obtain the homogeneous (>99%, g.l.c. column C) oil (1 g); $\delta(CCl_4)$ 6.59 (1 H, complex triplet, *J* 4 Hz, C-6 proton) and 0.99 (3 H, s, Me); *m/e* 201 (M^+) (Found: C, 83.6; H, 9.4. $C_{14}H_{19}N$ requires C, 83.5; H, 9.4%).

5-(NN-*Dimethylamido*)-1β,5-*dimethyl*-3αH-cis-*tricyclo*-[6.3.1.$0^{3,8}$]*dodec*-6-*ene* (17).—To oil-free sodium hydride (34 mg) overlaid with dry dimethylformamide (5 ml) under nitrogen was added a solution of (15) (200 mg) in dry dimethylformamide (2 ml). The mixture was heated to 80 °C for 2 h, cooled to 0 °C, and methyl iodide (3 ml) added. The reaction was then heated to reflux for 5 h, cooled, and diluted with water. The usual work-up with ether gave a gummy oil; $\nu_{max.}$ 2 220, 1 670, and 1 640w cm^{-1}. This was successively chromatographed over alumina (5 g) and elution with benzene–ethyl acetate (8 : 2) gave a pure oil which was evaporatively distilled (120 °C at 0.01 mmHg) to afford (17) (60 mg); $\nu_{max.}$ 1 670 and 1 640w cm^{-1}; $\delta(CCl_4)$ 5.50 (1 H, d, *J* 5 Hz, C-7 proton), 6.19 (1 H, d, *J* 5 Hz, C-6 proton), 2.90 (6 H, s, NMe_2), 1.32 (3 H, s, 5-Me), and 0.94 (3 H, s, 1-Me); *m/e* 261 (M^+), 219, 189 (base peak), and 147 (Found: C, 78.1; H, 10.3. $C_{17}H_{27}ON$ requires C, 78.1; H, 10.3%); single spot on t.l.c. [benzene–ethyl acetate (8 : 2)].

5β-*Cyano*-1β,5α-*dimethyl*-3αH-cis-*tricyclo*[6.3.1.$0^{3,8}$]*dodec*-6-*ene* (18).—To a solution (7.5 ml, 1M) of lithium di-isopropylamide (from n-butyl-lithium and di-isopropylamine) in tetrahydrofuran, under nitrogen and cooled to −78 °C, was added anhydrous hexamethylphosphoramide (1.3 g); the mixture was stirred for 30 min. A solution of the nitrile (15) (1.5 g) in tetrahydrofuran (1 ml) was then introduced dropwise followed, after 15 min, by methyl iodide (1.25 g). After stirring for 10 min at −78 °C, the reaction temperature was raised to −30 °C and stirring was continued at this temperature for 2 h. Addition of a saturated solution of ammonium chloride, removal of the solvent and excess of methyl iodide under reduced pressure, and the usual work-up of the residue with ether furnished an oil, which gave on evaporative distillation (110 °C at 0.1 mmHg) the nitrile (18) (1.4 g, 87%) (Found: C, 83.8; H, 9.6. $C_{15}H_{21}N$ requires C, 83.7; H, 9.7%); $\nu_{max.}$ 2 240, 1 640w, 1 510, and 1 460 cm^{-1}; $\delta(CCl_4)$ 6.21 (1 H, d, *J* 5 Hz, C-6 proton), 5.47 (1 H, d, *J* 5 Hz, C-7 proton), 1.34 (3 H, s, 5-Me), and 0.95 (3 H, s, 1-Me); *m/e* 215 (M^+). A gas chromatogram (column C) of (18) indicated 97% homogeneity.

5β-*Formyl*-1β-5α-*dimethyl*-3αH-cis-*tricyclo*[6.3.1.$0^{3,8}$]-*dodec*-6-*ene* (19).—A solution of (18) (1.3 g) in hexane (50 ml) was cooled to −70 °C and a solution (12 ml, 1M) of di-isobutylaluminium hydride in hexane was added. After stirring the mixture at −70 °C for 30 min and at ambient temperature for 5 h, ethyl formate (1 ml) was added and stirring was continued for 1 h. The mixture was poured into saturated ammonium chloride solution and, after 20 min, aqueous sulphuric acid was added. The usual work-up with ether followed by evaporative distillation (100 °C at 0.1 mmHg) yielded the aldehyde (19) (1.2 g, 90%) (Found: C, 82.5; H, 10.1. $C_{15}H_{22}O$ requires C, 82.5; H, 10.0%); $\nu_{max.}$ 2 720 (aldehyde C–H stretch), 1 710, 1 640w, and 1 460

cm^{-1}; δ(CCl_4) 9.3 (1 H, s, CHO), 6.27 (1 H, d, *J* 5 Hz, C-6 proton), 5.53 (1 H, d, *J* 5 Hz, C-7 proton), 1.38 (3 H, s, 5-Me), and 0.95 (3 H, s, 1-Me); *m/e* 218 (M^+).

(±)-*Pseudoclovene-B* (1).—The aldehyde (19) (700 mg) was mixed with hydrazine (10 ml, 99%) and diethylene glycol (30 ml) and heated to 130 °C (inner temperature) under a slow stream of nitrogen for 80 min. The reaction cooled, potassium hydroxide (4 g) was added, and the reaction was finally heated to 210 °C for 2 h. The usual work-up with pentane, after diluting with water, and evaporative distillation (112 °C at 10 mmHg) yielded the desired hydrocarbon (1) (600 mg, 92%) (Found: C, 88.1; H, 11.7. $C_{15}H_{24}$ requires C, 88.2; H, 11.8%); $\nu_{max.}$ 3 010, 1 640w, 1 375, 1 360, and 750 cm^{-1}; δ(CCl_4) 5.34 (2 H, s, C-6 and C-7 protons), 0.97 (6 H, s, 5-Me_2), and 0.92 (3 H, s); *m/e* 204 (M^+); gas chromatogram [column B, 95 °C, R_t 12.8 min, 30 lb in^{-2} (He)] indicated >99% homogeneity; it was found to be identical on co-injection with an authentic sample of (1).

A small portion of the hydrocarbon (1) (100 mg) was treated with bromine (0.1 ml) in carbon tetrachloride (2 ml) and stirred in the cold for 2 h. The reaction mixture was diluted with water, and the usual work-up with hexane gave a solid which was crystallised from hexane–benzene to give the dibromide, m.p. 123 °C.

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