Rearrangements of Pinane Derivatives. Part 9.[1] 8,8-Dimethyltricyclo-[5.1.1.$0^{2,5}$]nonan-2β-ol, a Tricyclic Pinane Derivative

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Acetolysis of the toluene-*p*-sulphonate ester of 2-(2-hydroxyethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (nopol) (**1**; R = OH) gave a good yield of the acetate of the previously unknown tricyclic pinane derivative 8,8-dimethyltricyclo[5.1.1.$0^{2,5}$]nonan-2β-ol (**4a**). This molecule has a bridgehead hydroxy group, and so is remarkably stable to acids, despite being highly strained from having two cyclobutane rings. However, the hydroxy group is adjacent to the new cyclobutane ring, so that (**4a**) is readily oxidised to the acetate of the hydroxytetrahydrofuran, 2β-hydroxy-8,8-dimethyl-10-oxatricyclo-[5.1.1.$1^{2,5}$]decane (**5**; R = OAc). Hydrolysis of the acetate group, followed by oxidation of the alcohol (**5**; R = OH), yields 8,8-dimethylbicyclo[5.1.1]nonane-2,5-dione (**6**).

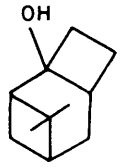
The base-catalysed dehydration of 2-(2-hydroxyethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (nopol) (**1**; R = OH) yields a mixture of the dienes (**2**) and (**3**), but the reaction does not yield any tricyclic pinane derivatives.[2] The Clarke–Eschweiler cyclisation has been demonstrated[3] to take place with 2-(2-aminoethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (nopylamine) (**1**; R = NH_2), but does not yield a system with a pinane skeleton; rearrangement gives products based on the fenchyl and terpinyl systems. The only reported tricyclic pinane derivative is 10,10-dimethyltricyclo[7.1.1.$0^{2,7}$]undec-2(7)-en-6-one, prepared from β-pinene during the synthesis of β-selinene.[4] In this case, a second six-membered ring was added to the pinane skeleton. This suggested that a pinane with two cyclobutane rings may well exist, but could be highly labile, and thus isolable only under mild conditions. We attempted to prepare it by the solvolysis of the toluene-*p*-sulphonate of nopol.

Results and Discussion

The toluene-*p*-sulphonate of nopol (**1**; R = OH) was prepared by conventional methods.[5] It readily underwent solvolysis in methanol, acetic acid, or aqueous ethanol. In 9:1 (v/v) ethanol–water at 62.5 °C the reaction was first-order, with k_1 = 2.64 × 10^{-5} s^{-1}. A product study showed 46% of an unidentified alcohol and 31% of unrearranged diene (**2**), together with seven minor products. The main one of these was subsequently identified as 1-ethyl-4-isopropylbenzene (**8**) (6%); the others (each less than 5%) were not investigated further. In the presence of 0.68M-NaOH, the initial reaction rate increased to 9.0 × 10^{-5} s^{-1} and the plot showed deviation from linearity. Consistent with this representing a rate increase in a concurrent bimolecular reaction, the diene yield rose to 60%. In less nucleophilic conditions (acetic acid containing sodium acetate in excess over the ester) a single product, obtained in 91% yield, was found to be the acetate of the unidentified alcohol. The reaction yielded 3% of (**2**), plus a component subsequently identified as 1-ethyl-4-isopropylbenzene (**8**). This reaction of (**1**; R = OTs) in acetic acid containing sodium acetate was used as the source of the unknown alcohol throughout the rest of this work.

The unknown acetate was purified by distillation under reduced pressure through a spinning-band column. The ^{13}C n.m.r. spectrum showed it to be a saturated tertiary acetate; this suggests the presence of an unrearranged pinane skeleton plus an extra ring, since any ring expansion would give a secondary acetate, and any ring opening an unsaturated acetate. Reduction of the acetate with lithium aluminium hydride gave the alcohol, a white crystalline solid. The proton n.m.r. spectrum of the alcohol was too complex for full assignment; the addition of a europium shift reagent caused loss in resolution.

Unimolecular solvolysis of a primary alkyl toluene-*p*-sulphonate usually involves an intramolecular electronic interaction. In the case of (**1**; R = OTs) the most probable interaction is with the electrons of the double bond; the probable saturated products of such an interaction are the alcohol (**4**) and a spiro[cyclopropanepinane], but the latter is inconsistent with the n.m.r. data.



(**4**)

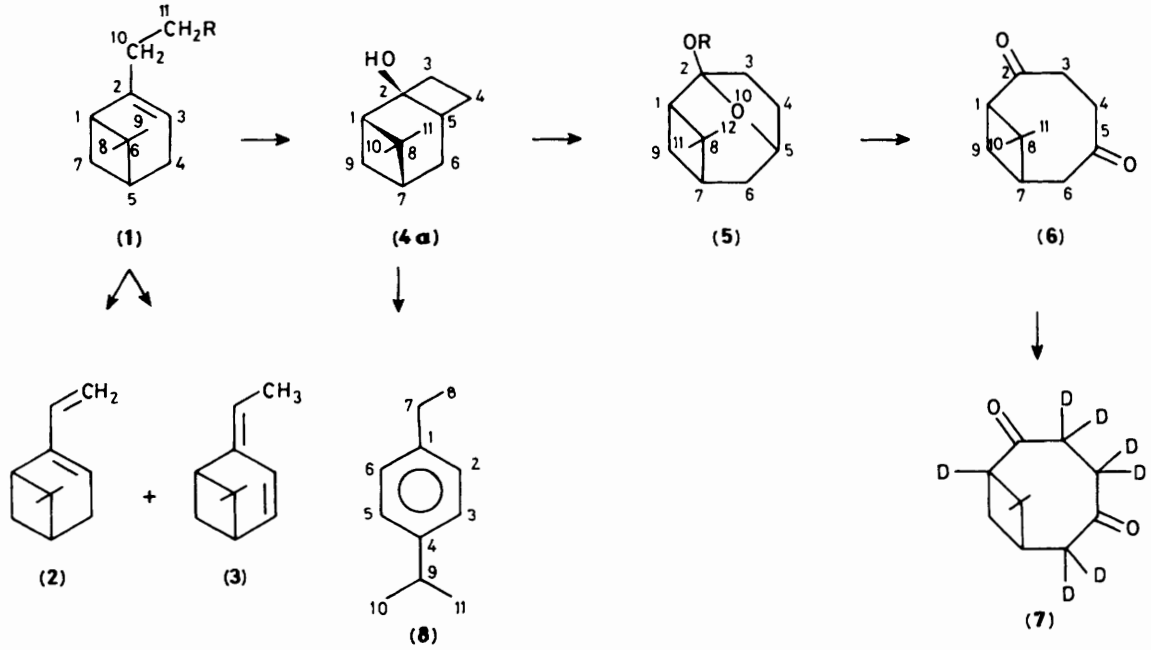
On this basis, we tentatively suggested structure (**4**). The sole stereochemical question, that of hydroxy group orientation, was readily answered from the lanthanide shift data. Both ^1H and ^{13}C spectra showed that one of the *gem*-methyl groups was strongly affected and the other much less so, suggesting that the OH was close to one of the *gem*-methyl groups, as would be expected if it was on the same side of the molecule. This suggests that the ring has the α-orientation, the molecule being 8,8-dimethyltricyclo[5.1.1.$0^{2,5}$]nonan-2β-ol (**4a**).

The structure (**4a**) cannot be unequivocally proved by spectroscopy, so to establish the presence of a cyclobutanol unit we oxidised the molecule with lead tetra-acetate. This reaction is known to cleave cyclobutanols,[6] usually giving hydroxytetrahydrofurans.[7] The product was a mixture of two acetates: the acetate of the starting material, and a new acetate. Isolation of the new acetate, followed by saponification, gave an alcohol, the ^{13}C n.m.r. spectrum of which had peaks at 98.3 p.p.m. (singlet) and 87.3 p.p.m. (doublet); the ^1H n.m.r. had a double doublet at δ_H 3.62. These data are consistent with an H–C–O–C–OH unit, which would be expected of the oxidation product of (**4a**), and hence we consider this alcohol to be 2β-hydroxy-8,8-dimethyl-10-oxatricyclo[5.1.1.$1^{2,5}$]decane (**5**; R = OH). In confirmation, we oxidised (**5**; R = OH) by the method of Jones[8] to yield a diketone, with carbonyl i.r. absorption at 1 700 and 1 730 cm^{-1}, and ^{13}C n.m.r. peaks at δ 211.1 and 225.1 p.p.m. We suggest that this diketone is 8,8-dimethylbicyclo[5.1.1]nonane-2,5-dione (**6**). As expected for

Table 1. ^{13}C N.m.r. chemical shifts (p.p.m. from Me_4Si in $CDCl_3$)

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	Acetate	
(**4a**)	44.8	85.8	41.2*	49.5*	60.1	27.7	38.2	48.8	38.8	23.5	21.3			
Acetate of (**4a**)	44.5	9.21	38.0	48.6	58.7	28.1	37.5	48.6	37.0	23.3	21.2		169.8	21.7
(**5**; R = OH)	45.2†	98.3	35.4*	24.9*	87.3	44.3*	35.6†	44.4	37.8*		26.5	23.1		
(**5**; R = OAc)	42.3†	103.5	32.3*	21.4*	85.2	38.8*	32.9†	41.6	33.7*		23.6	20.2	168.0	21.8
(**6**)	44.5	225.1	29.4	27.2	211.1	40.1*	41.4	49.1	46.7*	26.2	18.8			
(**8**)	141.2	127.6	126.1	145.8	126.1	127.6	28.5	15.6	33.7	24.1	24.1			
3α-Ethylnopinone	57.6	214.2	43.7	25.4*	40.9	42.5	22.5*	26.3	21.8	28.6	11.8			

Assignments marked * or † could be interchanged.



this structure, exchange with D_2O–MeOD in the presence of base leads to the incorporation of seven deuterium atoms, which ^{13}C n.m.r. showed to be located on four carbon atoms [see (**7**)].

During this work, we noted that, contrary to our expectations, the alcohol 8,8-dimethyltricyclo[5.1.1.$0^{2,5}$]nonan-2β-ol (**4a**) was stable and displayed no tendency towards skeletal rearrangements during our reactions. The material is, in fact, very resistant to the action of acids; refluxing the acetate of (**4a**) in 1M-sulphuric acid in acetic acid for a week produced a small amount (*ca.* 10%) of 1-ethyl-4-isopropylbenzene (**8**), but left the bulk of the starting material unchanged. This is in marked contrast to the structurally similar bicyclic pinane,[9] pinan-2β-ol, which rearranges at 25 °C in aqueous dioxane (4:1 v/v) containing 0.025M-acid with $k_1 = 6.40 \times 10^{-5}$ s^{-1}. However, ionisation of the latter is facilitated by shift of the C(1)–C(7) bond electrons as the cyclobutane ring expands. Our tricyclic pinane has a rigid structure in which none of the bonds can shift until ionisation of the hydroxy group is complete. The hydroxy group thus displays the resistance to separation which is well documented for bridgehead alcohols.[10]

The solvolysis reaction forming (**4a**) proceeds stereospecifically. However, repulsion between the *gem*-dimethyl group and the leaving toluene-*p*-sulphonate, and between the *gem*-dimethyl group and the forming cyclobutane ring, ensures that (**4a**) is at all times energetically favoured over its isomer having the new cyclobutane ring on the β face of the molecule.

Attempts to synthesize (**4a**) by the alternative route of u.v. irradiation of 3α-ethylnopinone were unsuccessful; the ketone polymerised.

Experimental

6,6-*Dimethyl*-2-(p-*tolylsulphonylethyl*)*bicyclo*[3.1.1]*hept*-2-*ene* (**1**; R = OTs).—A commercial sample of 2-(2-hydroxyethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (nopol) was converted into its toluene-*p*-sulphonate ester by reaction with toluene-*p*-sulphonyl chloride in dry pyridine.[5] It had m.p. 48—49 °C (from pentane) (lit.,[2] 49—50 °C).

Acetolysis of the Toluene-p-*sulphonate* (**1**; R = OTs).—Initial experiments were carried out in a sealed tube, but for the bulk preparation of (**4a**) the following procedure was used. The tosylate (60 g) and sodium acetate (19 g) were refluxed in acetic acid (800 ml) for *ca.* 100 h; solvolysis was then complete. To decompose the diene, and any minor impurities, concentrated sulphuric acid (100 ml) was added slowly, and the solution refluxed for a further 10 h. The cooled solution was poured into water and extracted with ether. The extract was washed with sodium hydrogen carbonate solution and water, and then dried ($MgSO_4$). Removal of the solvent left a black oil, which was distilled through a spinning-band column to give two fractions, one boiling at 75—77 °C (12 Torr), identified from its ^{13}C n.m.r. spectrum as 1-ethyl-4-isopropylbenzene, and one at 114—

Table 2. Effect of lanthanide shift reagent on the ^{1}H n.m.r. spectra of the *gem*-dimethyl group of 8,8-dimethyltricyclo[5.1.1.0^{2,5}]nonan-2β-ol (**4a**)

Wt. Eu(fod)$_3$ (mg)	δ_{Me}	
0	0.98	1.22
15	1.24	1.84
30	1.52	2.52
45	1.88	3.42
60	2.12	3.98

116 °C (12 Torr). The latter component, a colourless oil (12 g) was 8,8-*dimethyltricyclo*[5.1.1.0^{2,5}]*nonan*-2β-*yl acetate* [(**4a**) acetate], pure by g.l.c. (Carbowax 20M); for ^{13}C n.m.r. see Table 1; *m/z* 208, 166, 148, and 133; $\nu_{max.}$ 2 900s, 2 840s, 1 730s, 1 455s, 1 375s, 1 360s, 1 320m, 1 310s, 1 295s, 1 260s, 1 225s, 1 205s, 1 140s, 1 115w, 1 090w, 1 075s, 1 050s, 1 025s, 1 010s, 965m, 940w, 920m, 910m, 895w, 880m, 845w, 820w, and 725w cm^{-1}.

8,8-*Dimethyltricyclo*[5.1.1.0^{2,5}]*nonan*-2β-*ol* (**4a**).—Reduction of the acetate of (**4a**) with lithium aluminium hydride in ether gave 8,8-*dimethyltricyclo*[5.1.1.0^{2,5}]*nonan*-2β-*ol* (**4a**) as a white crystalline solid, m.p. 75—77 °C (from ether) (Found: C, 79.6; H, 10.7. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%), >99% pure by g.l.c. (Carbowax 20M); *m/z* 166, 151, 133, 125, and 109; $\nu_{max.}$ 3 260s, 2 920s, 2 850s, 1 380s, 1 375s, 1 310s, 1 300m, 1 245m, 1 225m, 1 215m, 1 200m, 1 150w, 1 085m, 1 060s, 1 035m, 1 010m, 975w, 945w, 925w, 910w, and 850w cm^{-1}; for ^{13}C n.m.r. see Table 1; δ_H (220 MHz; $CDCl_3$; Me_3Si) 0.93 (3 H, s, Me), 1.18 (3 H, s, Me), 1.36 (2 H, m), 1.57 (3 H, m), 1.83 (3 H, m), and 2.16 (4 H, br m). The effect of lanthanide shift reagent on the positions of the ^{1}H methyl peaks is shown in Table 2.

Oxidation of 8,8-*Dimethylbicyclo*[5.1.1.0^{2,5}]*nonan*-2β-*ol* (**4a**) *with Lead Tetra-acetate*.—A mixture of lead tetra-acetate (30.0 g) and calcium carbonate (20.0 g) was heated in benzene (400 ml). A solution of (**4a**) (5 g) in benzene (300 ml) was added, and the mixture was refluxed for 24 h. Water and ether were added to the cooled suspension, which was filtered, and the ether layer was separated. The aqueous phase was extracted twice with ether, and the combined extracts were washed with sodium hydrogen carbonate solution, then water, and dried ($MgSO_4$). Removal of the solvent left a pale yellow oil (6.9 g) contaminated with small amounts of (**4a**) and its acetate. Chromatography on a Florisil column (pentane–ether) gave 8,8-*dimethyl*-10-*oxatricyclo*[5.1.1.1^{2,5}]*decan*-2β-*yl acetate* (**5**; R = OAc), 98% pure by g.l.c.; $\nu_{max.}$ 2 920s, 2 880m, 1 735s, 1 460m, 1 450m, 1 390m, 1 370s, 1 350m, 1 330m, 1 280s, 1 265s, 1 245s, 1 230s, 1 210s, 1 195s, 1 190s, 1 140m, 1 155s, 1 130m, 1 095s, 1 065s, 1 040s, 1 030s, 1 000s, 970s, 930s, 920m, 915w, 860m, 845m, 745w, and 705w cm^{-1}; *m/z* 224, 182, 141, and 122; for ^{13}C n.m.r. see Table 1; δ_H (220 MHz; $CDCl_3$; Me_4Si) 0.89 (3 H, s, Me), 1.25 (3 H, s, Me), 1.49 (1 H, d), 1.65 (1 H, m), 1.81 (2 H, m), 2.08 (3 H, s, Me), 2.17 (4 H, m), 2.45 (2 H, m), and 3.69 (1 H, d).

2β-*Hydroxy*-8,8-*dimethyl*-10-*oxatricyclo*[5.1.1.1^{2,5}]*decane* (**5**; R = OH).—Saponification of (**5**; R = OAc) with aqueous 10% sodium hydroxide, followed by extraction with ether, drying ($MgSO_4$), and solvent removal gave 2β-*hydroxy*-8,8-*dimethyl*-10-*oxatricyclo*[5.1.1.1^{2,5}]*decane* as a colourless oil, 99% pure by g.l.c. (Carbowax 20M); $\nu_{max.}$ 3 370 cm^{-1}; *m/z* 182, 141, and 122; for ^{13}C n.m.r. see Table 1; δ_H (220 MHz; $CDCl_3$, standard Me_4Si) 0.82 (3 H, s, Me), 1.18 (3 H, s, Me), 1.38 (1 H, d), 1.51 (1 H, m), 1.62 (1 H, m), 1.73 (2 H, m), 1.89 (2 H, m), 2.09 (2 H, m), 2.34 (1 H, s), and 3.62 (1 H, m). The product was further characterised by conversion into its 3,5-dinitrobenzoate ester with the acyl chloride in dry pyridine. Recrystallisation from ether–pentane gave 8,8-*dimethyl*-10-*oxatricyclo*-[5.1.1.1^{2,5}]*decan*-2β-*yl* 3,5-*dinitrobenzoate*, m.p. 135—138 °C (after sublimation) (Found: C, 57.2; H, 5.4; N, 7.6. $C_{18}H_{20}N_2O_7$ requires C, 57.4; H, 5.3; N, 7.5%); *m/z* 376, 195, 181, 164, 149, 136, 111, and 109; δ_H (220 MHz; $CDCl_3$; Me_4Si) 0.92 (3 H, s, Me), 1.20 (1 H, m), 1.33 (3 H, s, Me), 1.56 (1 H, d), 1.92 (2 H, m), 2.22 (2 H, m), 2.32 (2 H, m), 2.55 (2 H, m), 3.83 (1 H, d), 9.11 (2 H, m), and 9.19 (1 H, m).

Oxidation of 2-*Hydroxy*-8,8-*dimethyltricyclo*[5.1.1.1^{2,5}]-*decan*-10-*one*.—The alcohol (**5**; R = OH) (2.6 g) was oxidised by the method of Jones[8] to give 8,8-*dimethylbicyclo*[5.1.1]-*nonane*-2,5-*dione* (**6**) (1.2 g) as a colourless oil, which polymerised on attempted distillation; $\nu_{max.}$ 1 730 and 1 700 cm^{-1}; *m/z* 180 and 159; for ^{13}C n.m.r. see Table 1; δ_H (220 MHz; $CDCl_3$; Me_4Si) 1.22 (6 H, s, 2-Me), 1.89 (4 H, m), 2.49 (2 H, m), and 2.61 (4 H, m).

Deuteriation of 8,8-*Dimethylbicyclo*[5.1.1]*nonane*-2,5-*dione* (**6**).—The diketone (0.7 g) was added to a solution of sodium methoxide (2 g) in D_2O (2 ml) and CH_3OD (10 ml). The mixture, sealed in an ampoule, was heated to 60 °C for 7 days, then poured into water and extracted with ether; the ether solution was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate and water, then dried ($MgSO_4$). The pale yellow oil (now only 70% pure) was purified by chromatography on a Florisil column (pentane–ether). The mass spectrum showed extra peaks introduced by deuteriation (molecular ion peaks are given as % of the molecular ion at *m/z* 180 in the unlabelled material): 180 (0%), 181 (1), 182 (5), 183 (19), 184 (31), 185 (27), 186 (13), and 187 (4).

3α-*Ethylnopinone*.—Nopinone (2 g) (from the ozonolysis of β-pinene[11]) was treated with lithium di-isopropylamide in tetrahydrofuran at −78 °C for 1 h. Ethyl iodide (2.4 g) was added, and the solution stirred for 6 h at −78 °C. The mixture was then poured into ether; the ethereal solution was washed, dried, and evaporated to leave a yellow oil. 3α-Ethylnopinone and traces of nopinone were separated on a Florisil column with light petroleum (b.p. 40—60 °C)–diethyl ether, giving 3α-ethylnopinone (1.6 g); $\nu_{max.}$ 1 705 cm^{-1}; for ^{13}C n.m.r. see Table 1.

Irradiation of 3α-*Ethylnopinone*.—3α-Ethylnopinone (1.0 g) dissolved in pentane (1 l) was irradiated in a quartz vessel with twelve 15 W mercury vapour lamps for 24 h. Evaporation left only a yellow gum.

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