Palladium-catalysed Synthesis of *endo*- and *exo*-Brevicomin and Related Di- and Tri-oxabicyclo[*x*.2.1] Systems.[1]

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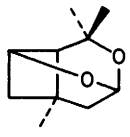
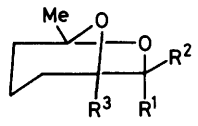
Ethyl nona-3,8-dienoate prepared from the palladium-catalysed reaction of butadiene with carbon monoxide and ethanol was found to consist of a 79:21 mixture of *trans*- and *cis*- isomers. This ester was used to prepare *threo*- and *erythro*-3,4-dihydroxynon-8-ene which were cyclised by a Wacker-type catalyst ($PdCl_2$–$CuCl_2$–O_2) to *exo*- and *endo*-brevicomin. Analogous cyclisations were effected on several other ene-diols derived from octa-1,6-diene, octa-1,7-diene, allyl glycidyl ether and two substituted diallyl ethers. The mechanism of the key cyclisation step is discussed.

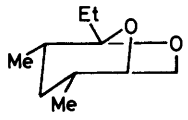
Bicyclic ketals occur as structural units in a range of natural products such as sugars,[2] alkaloids,[3] terpenes,[4] and pheromones.[5] Pheromones encompass ketals of a diverse nature, including spiro-[6] and bridged ring-ketals and more complicated skeletons such as that found in lineatin (**1**).[7] Dioxabicyclo[3.2.1]alkanes have attracted particular interest since this skeleton occurs in important constitutents of bark beetle pheromone systems such as *endo*- (**2a**) and *exo*-brevicomin (**2b**),[8] frontalin (**2c**),[9] and the Dutch elm beetle pheromone multistriatin (**3**).[10]



(**1**)



(**2**) **a**; R^1=Et, R^2=H_a, R^3=H_b
b; R^1=H_a, R^3=H_b, R^2=Et
c; R^1=R^2=H, R^3=Me

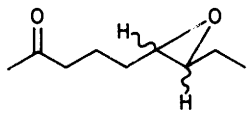


(**3**)

These pheromonal ketals are potential agents for surveying and controlling insect populations and, as such, have attracted considerable synthetic interest. Numerous syntheses of brevicomin have appeared[11] which employ either the epoxy ketone (**4**) or the corresponding keto diol (**5**) as the key intermediate. Our synthesis employs a palladium-catalysed cyclisation of the ene-diol (**6**) as the key step.

Lloyd and Luberoff[12] showed that terminal olefins can be oxidised to methyl ketones by a catalytic amount of palladium chloride in alcoholic solvents (**7**)→(**8**)→(**9**) and under suitable conditions it was possible to isolate the intermediate ketal. It occurred to us that an intramolecular version of this reaction, utilising (**6**) could provide a possible route to brevicomin with the stereochemistry of the diol controlling the stereochemistry of the product.

Butadiene was selected as the starting material for the synthesis of (**6**) since it is known to undergo palladium(II)-catalysed linear dimerisation and in the presence of appropriate co-reactants a series of C_8 (**10**; X = H, OCOR, OR, NR_2)[13–16] or



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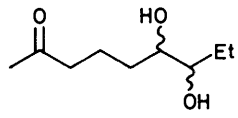

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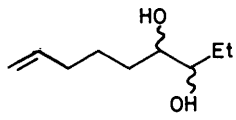
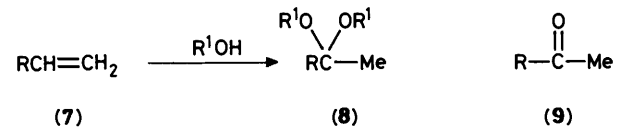
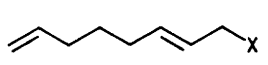


(**6**)

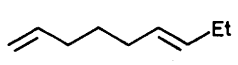


(**7**) (**8**) (**9**)

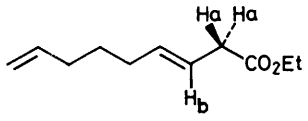
C_{10} dienes [*e.g.* (**10**; X = CH $(CO_2Et)_2$ *etc.*] are formed.[17] Our initial target was the C_9 diene (**11**) and two routes were explored to this compound. Firstly the dimerisation of butadiene in the presence of ethanol and carbon monoxide (50 atm) using palladium acetate–triphenylphosphine (1:4) as catalyst, is known to give ethyl nonadienoate (**12**).[18] The reported syntheses of (**12**) do not specifically discuss the stereochemistry of the internal double bond although it is depicted as *trans* in both cases.[18] Capillary g.l.c. analyses (100 m DC 550 WCOT column, 150 °C) of crude reaction mixtures of ethyl nonadienoate show it to consist of a mixture of *trans*- (**12**) and *cis*- (**13**) isomers in the ratio 79:21. The i.r. spectrum of distilled ethyl nonadienoate contains a strong band at 969 cm^{-1} (*trans* CH=CH) and a very weak band at 702 cm^{-1} (*cis* CH=CH). The



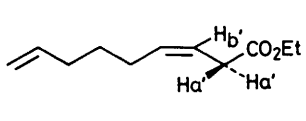
(**10**)



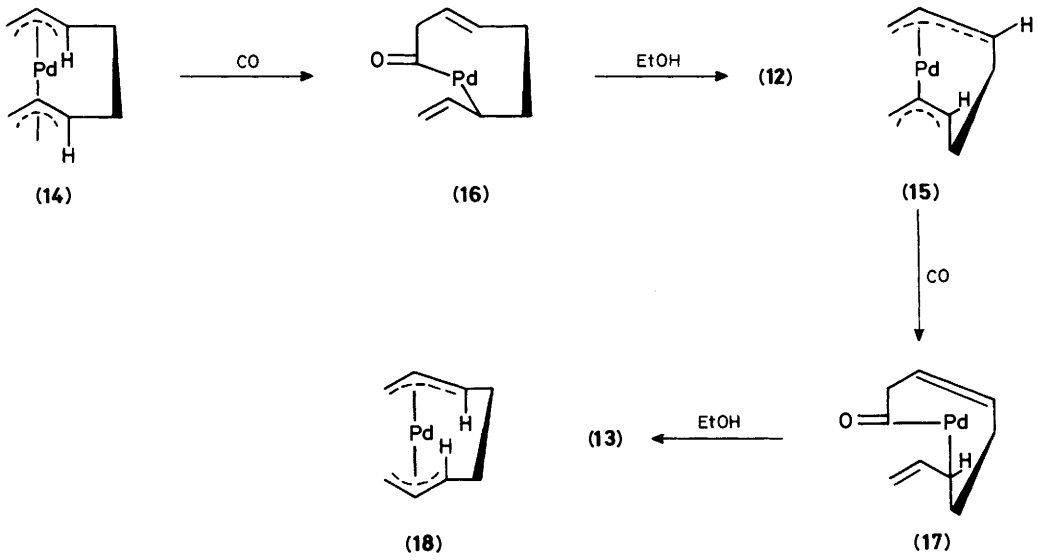
(**11**)



(**12**)



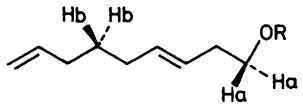
(**13**)



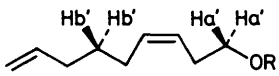
250 MHz ^{1}H n.m.r. spectrum of distilled nonadienoate exhibits two doublets (ratio 81:19), assigned to the allylic protons H_a and $H_{a'}$ of the *trans*- (**12**) and *cis*- (**13**) isomers respectively at δ 3.02 (J_{ab} 4.8 Hz) and δ 3.08 ($J_{a'b'}$ 5.2 Hz).

Since a stereochemically pure diene would be preferable for the projected brevicomin synthesis we examined the source of the *cis*-compound. The *cis*-nonadienoate could arise directly from the dimerisation reaction or in a subsequent palladium-catalysed *trans–cis* isomerisation of an initial *trans*-product. The latter process would involve co-ordination to the internal double bond of (**12**) which is less favourable than co-ordination to the terminal double bond. Indeed slow distillation of the crude nonadienoate does result in extensive terminal double-bond migration presumably catalysed[19] by soluble palladium salts remaining in the crude nonadienoate. However, no terminal double-bond migration is observed during the butadiene dimerisation–carbonylation reaction (85 °C, 20 h) which suggests that co-ordination of (**12**) to palladium does not occur in the presence of an excess of butadiene. Thus it would appear that (**13**) arises directly from the dimerisation–carbonylation reaction. This is readily accommodated by proposing that both *syn*- (**14**) and *anti*- (**15**)-palladium bis-π-allyl complexes are formed during the reaction and that the *syn*-complex (**14**) leads, *via* (**16**), to the *trans*-nonadienoate (**12**) whilst the *anti*-complex (**15**) leads, *via* (**17**), to the *cis*-nonadienoate (**13**). Due to the constraining influence of the saturated two-carbon chain in the postulated *cis*-bis-π-allyl palladium complex (**14**), the corresponding *trans*-complex (**18**) appears, from inspection of Dreiding models, to be unfavourable.

Reduction of ethyl nona-3,8-dienoate [(**12**):(**13**), 79:21)] gave (96%) a mixture of alcohols (**19a**) and (**20a**). The 400 MHz n.m.r. spectrum ($CDCl_3$) of the mixture in the presence of $Eu(fod)_3$ resolved the signals due to the pairs of methylene protons $H_a/H_{a'}$ and $H_b/H_{b'}$ and allowed calculation of the *trans* (**19a**)- to *cis* (**20a**)-ratio (80:20).* The mixture of alcohols (**19a**), (**20a**) was converted into the corresponding mixture of tosylates (88%) [(**19b**):(**20b**), 80:20, n.m.r.] followed by reduction with lithium aluminium hydride to give a mixture (74%) of *trans*-nona-1,6-diene (**11**) and the corresponding *cis*- (**21**) isomer (ratio 80:20).

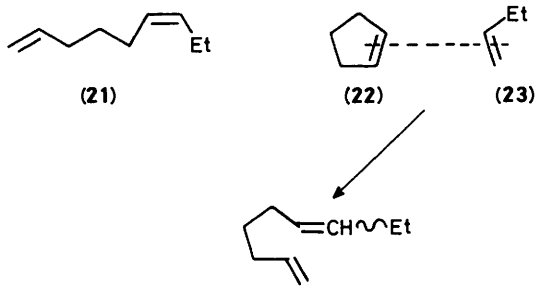


(**19**) **a**; R = H
b; R = Ts



(**20**) **a**; R = H
b; R = Ts

A second route, involving olefin metathesis, to the *trans*- (**11**) and *cis*- (**21**) nona-1,6-dienes was explored. Thus metathesis of cyclopentene (**22**) and but-1-ene (**23**) could lead to (**11**) and/or (**21**).



(**21**) (**22**) (**23**)

α,ω-Diolefins have been synthesised by the reaction of cyclic olefins with acyclic olefins using both heterogeneous[20] and homogeneous[21] catalysts. Use of MoO_3 (Table) and $Mo(CO)_6$ supported on alumina failed to produce any nona-1,6-diene. Indeed, no cyclopentene-derived products were detected, only products of self-dismutation and isomerisation of (**23**) (Table). Use of the WCl_6–EtOH–$EtAlCl_2$ 'homogeneous' metathesis catalyst system did, however, lead to nona-1,6-diene. This 'homogeneous' system shows little activity towards the metathesis of terminal olefins[22] but is extremely active in the metathesis of internal olefins and with mixtures of terminal and internal olefins leads to selective formation of crossed metathesis products.[23] Using a tungsten:mixed olefin ratio of 1:500, and 1:2 ratio of (**22**) and (**23**) under strictly anhydrous conditions it was possible to obtain nona-1,6-diene as the sole

* Capillary g.l.c. (100 m QF-1 or Carbowax 20M) was less satisfactory due to incomplete peak resolution. The *trans*:*cis* ratio calculated from g.l.c. was 84:16.

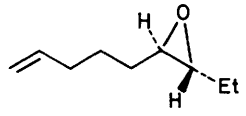
Table. Metathesis of a 1:1.8 mixture of (**22**) and (**23**) using MoO_3–Al_2O_3 as catalyst.*

Time (min)	Temp. (°C)	Product ratio† (22)	(23)	C_2H_4	C_3H_6	But-2-ene‡	Pentenes	Hexenes
120	100	10	9	0.48	0.35	0.64 (*t*), 0.64 (*c*)	0	0
35	150	10	6.25	0.69	0.69	0.76 (*t*), 0.60 (*c*)	0.66	0.58
95	150	10	4.35	0.64	1.98	0.96 (*t*), 0.84 (*c*)	2.04	1.20
140	150	10	3.18	0.39	2.44	0.89 (*t*), 1.10 (*c*)	2.30	1.70

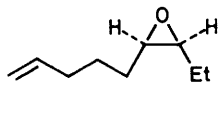
* A 1:1 mixture of (**22**) and (**23**) gave similar results.
† Determined by g.l.c. using a 4 m 5% SGR column and measured with respect to (**22**).
‡ *t* = *trans*, *c* = *cis*.

product after a short reaction time (15—30 min) and at low conversion (10%). The unchanged (**22**) and (**23**) could be recovered by distillation. When the reaction was carried out for 1 h the nona-1,6-diene underwent extensive isomerisation to at least two internal dienes. The non-1,6-diene prepared by the metathesis route consisted of a *ca.* 3:2 mixture of trans- (**11**) and *cis*- (**21**) isomers (the ratio varied slightly from experiment to experiment). The low conversion of (**22**) and (**23**) to nona-1,6-diene, the stringent reaction conditions and the unfavourable *cis*:*trans* nona-1,6-diene ratio led us to abandon this approach and concentrate on the *ca.* 80:20 mixture of (**11**) and (**21**) resulting from the butadiene route.

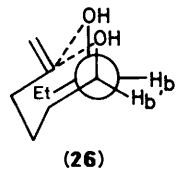
Epoxidation of a *ca.* 80:20 mixture of (**11**) and (**21**) with *m*-chloroperbenzoic acid in methylene chloride occurred cleanly at the more substituted double bond and gave the corresponding mixture of epoxides (**24**) and (**25**). Ring opening with sulphuric acid in aqueous THF afforded a solid diol which on recrystallisation gave the *erythro*-diol (**26**), m.p. 76 °C. The *cis*-diene (**21**), which would give rise to the *threo*-diol (**27**), was removed in the hydrolysis–crystallisation sequence. Reaction of the *erythro*-diol (**26**) with palladium chloride–cupric chloride in



(**24**)

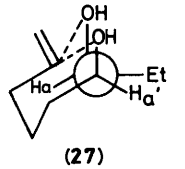


(**25**)



(**26**)

Pd^{II}/Cu^{II}, O_2 → (**2a**)

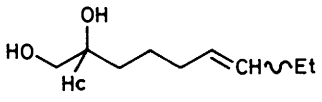


(**27**)

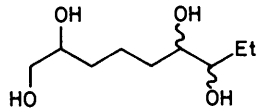
Pd^{II}/Cu^{II}, O_2 → (**2b**)

anhydrous dimethoxyethane at 65 °C gave *endo*-brevicomin (**2a**) (45%) which was identified by spectral comparisons with published data (see Figure 4).

exo-Brevicomin (**2b**) is the more important isomer from the pheromone point of view and the synthesis of this isomer by an analogous route requires the *threo*-diol (**27**). There are two potential routes to the *threo*-diol involving either *cis*-hydroxylation of the *trans*-diene (**11**) or *trans*-hydroxylation (epoxidation, H_3O^+ opening) of the *cis*-diene (**21**). Various methods for the *cis*-hydroxylation of (**11**) were explored and the catalytic osmium tetraoxide–*N*-methylmorpholine *N*-oxide method[24,25] proved most suitable. Using this method the *ca.* 80:20 mixture of *trans*- (**11**) and *cis*- (**21**) nonadienes was converted (63%) into a 1:4.6:7.0 mixture of 1,2-diol (**28**), 3,4-diol (**6**), and 1,2,6,7-tetraol (**29**) after 6.3 h at room temperature. Lowering the



(**28**)



(**29**)

temperature to 0 °C resulted in a shift in the product distribution towards the 3,4-diol giving a 1:4.1:1 mixture of (**28**), (**6**) and (**29**) (67% conversion after 29 h). The variation of product with time was monitored by g.l.c. (Figure 1) to maximise the yield of the desired 3,4-diol (**6**).

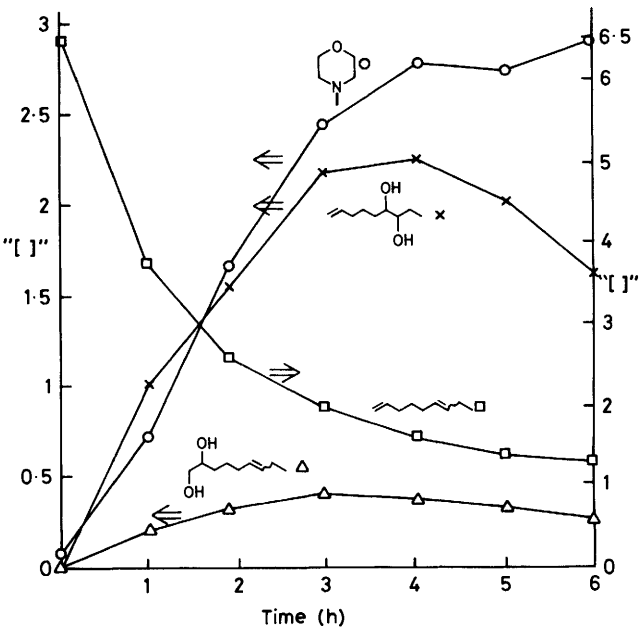


Figure 1. OsO_4 hydroxylation of octa-1,6-diene at ambient temperature "[ ]" = g.l.c. peak area/internal standard area. Internal standard hexamethylbenzene. G.l.c. conditions: 1.5 m 5% SGR, 100—220 °C at 8 °C/min

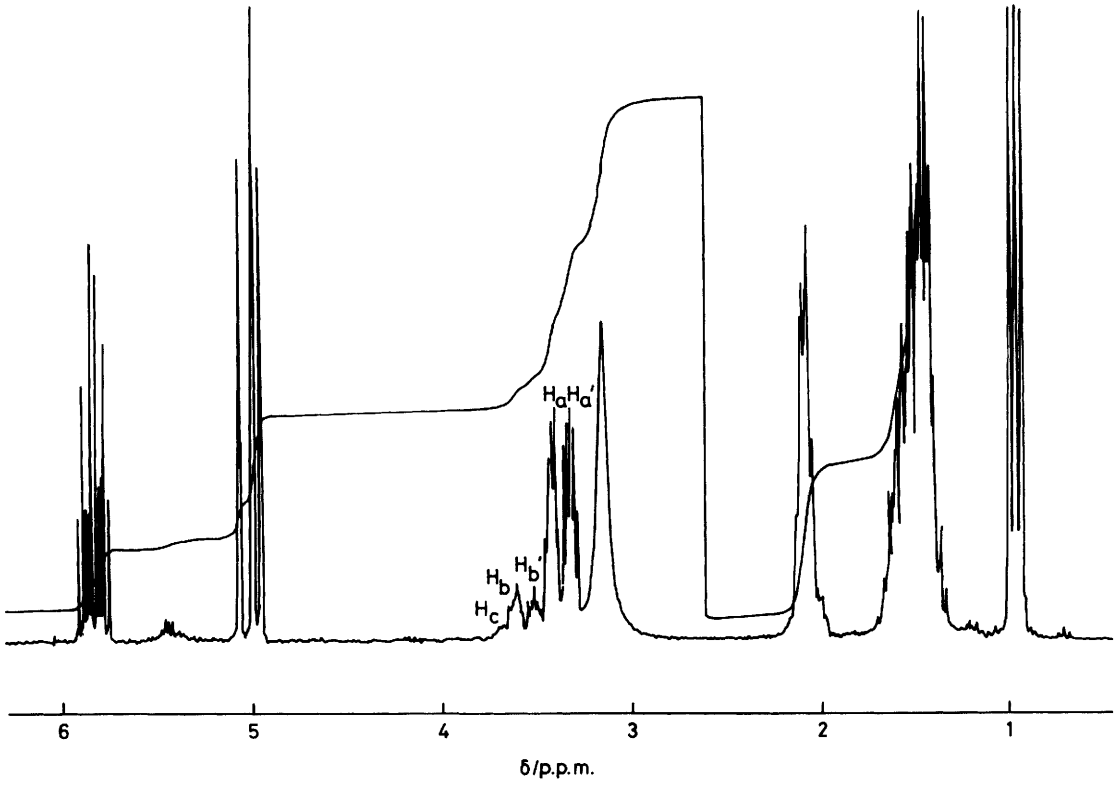


Figure 2. 250 MHz N.m.r. spectrum ($CDCl_3$) of a *ca.* 80:15:5 mixture of (**27**), (**26**), and (**28**)

The tetraol (**29**) was too involatile to be analysed by g.l.c. but Figure 1 clearly shows the expected faster hydroxylation of the internal double bond compared to the terminal double bond and the fall in concentration of the 3,4-diol (**6**) after *ca.* 4 h, due to its transformation into the tetraol (**29**). The tetraol (**29**) is water soluble and was removed by partitioning the crude hydroxylation mixture between water and ether. The remaining mixture of diols comprised *threo*- and *erythro*- (**6**) and (**28**) in the ratio 82:18. Selective tritylation[26] of this mixture with trityl chloride improved the ratio of (**6**):(**28**) to 95:5. The *threo*:*erythro* ratio (**27**):(**26**) of the 3,4-diol fraction was found to be 84:16 by g.l.c. analysis of the $SiMe_3$ ethers (1.5 m 5% SGR, 100—220 °C at 2 °C/min.). The marginally more favourable *threo*:*erythro* ratio may reflect a marginally slower *cis*-hydroxylation of the *cis*-nona-1,6-diene (**21**) due to the more crowded transition state compared to the *trans*-nonadiene hydroxylation reaction. This effect was noted by Huisgen in 1,3-dipolar cycloaddition reactions.[27] The 250 MHz n.m.r. spectrum (Figure 2) of the 95:5 mixture of (**6**) and (**28**) shows four complex multiplets assigned to the protons next to oxygen in the *threo*- (**27**) ($H_{aa'}$) and *erythro*- (**26**) ($H_{bb'}$)-diols together with the poorly resolved signal for H_c of the 1,2-diol (**28**).

The 95:5 diol mixture (**6**):(**28**) was catalytically cyclised at ambient temperature by the $PdCl_2$–$CuCl_2$ catalyst system in dry dimethoxyethane. Dry air was continuously bubbled through the solution. On a small scale (40 mg of mixed diols) the reaction was complete in 2 h (g.l.c. monitoring) and gave an 84:16 mixture of *exo*- (**2b**)- and *endo*- (**2a**)-brevicomin in 76% yield. On a larger scale (400 mg), a lag phase was observed and the reaction took 17 h to go to completion when the yield of brevicomin isomers was 62%. The pure *exo*-isomer (**2b**) was isolated by preparative g.l.c. (4.6 m × 7 mm i.d., 10% SGR, 90—220 °C at 10 °C/min). The 400 MHz n.m.r. spectra of *endo*- (**2a**) and *exo*- (**2b**)-brevicomin are shown in Figures 3 and 4.

The cyclisation of the diols (**26**) and (**27**) to (**2a**) and (**2b**),

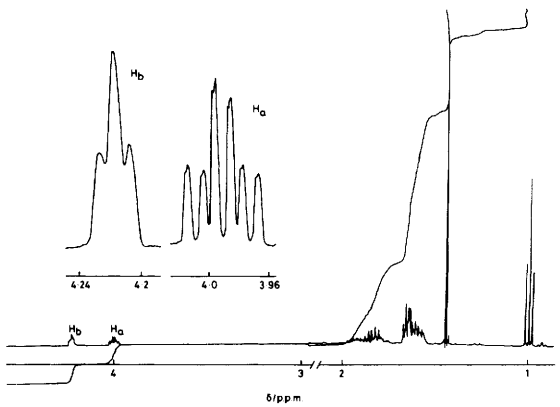


Figure 3. 400 MHz N.m.r. spectrum ($CDCl_3$) of *endo*-brevicomin (**2a**)

respectively, is an example of an intramolecular Wacker-type reaction. Reactions of this type involve nucleophilic attack on a palladium–alkene π-complex. Nucleophilic attack of this type can proceed *cis* (Scheme 1, path A) or *trans* (Scheme 1, path B) with respect to co-ordinated palladium. *cis*-Addition occurs *via* an intermediate metal-bound nucleophile and is preferred when the nucleophile is $aryl^-$, Me^-, or H^-. *trans*-Addition occurs by attack of an external nucleophile and is favoured by hetero-nucleophiles and soft carbon nucleophiles.[28] Recent work has established the latter path (Scheme 1, path B) for the Wacker process.[28] In a study of ethylene ketal formation from mercuriated olefins catalysed by a Wacker-type catalyst it was shown that a 1,2-H shift was involved, *i.e.* (**30**)→(**31**).[29] This suggests a pinacol type rearrangement occurs with palladium as the leaving group.

In the context of the cyclisations generating *endo*- and *exo*-

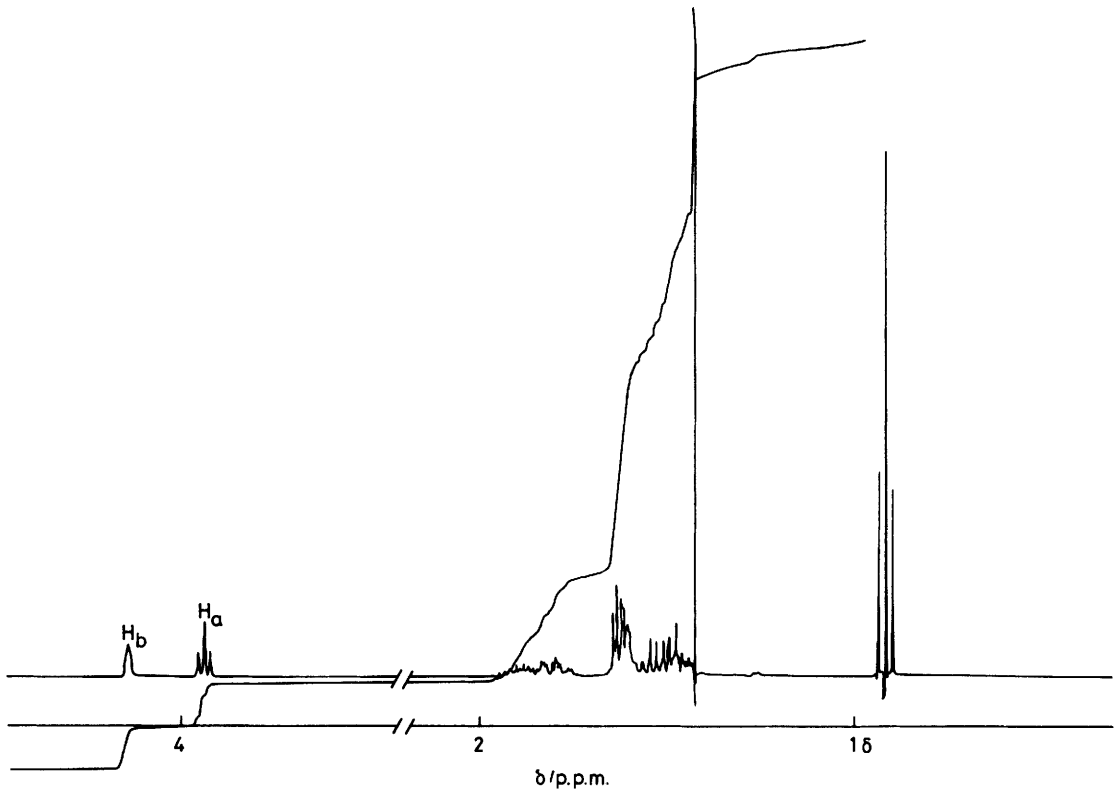
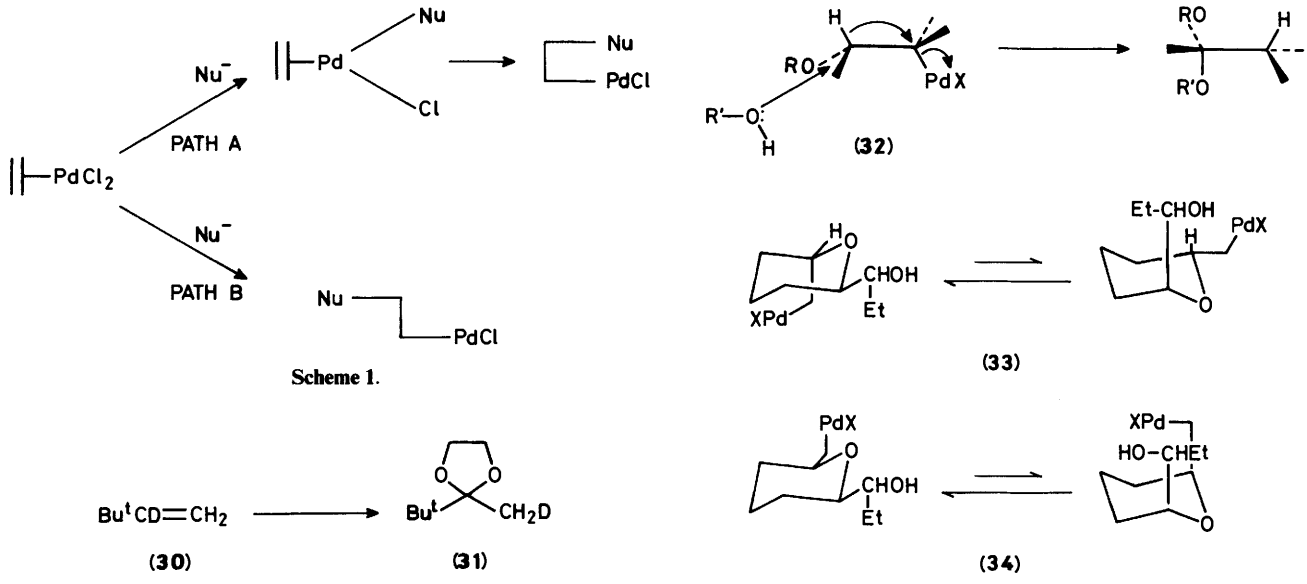
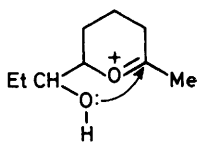


Figure 4. 400 MHz N.m.r. spectrum ($CDCl_3$) of *exo*-brevicomin (**2b**)

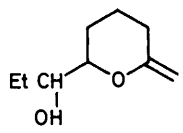


brevicomin a concerted rearrangement is not feasible. The geometrical requirements for such a process are illustrated in (**32**). Thus the initial intramolecular attack by OH leads to the pyran (**33**) or (**34**).

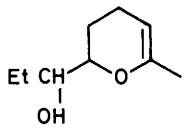
The *trans*-pyran (**33**) is geometrically incapable of the process depicted by (**32**) whilst the *cis*-pyran (**34**) would experience severe steric interactions in the transition state which would require the diaxial conformation. The oxonium ion intermediate (**35**) produced by loss of palladium and a 1,2-hydride shift appears a reasonable alternative. However, such an intermediate would not account for the report that cyclohexene gives cyclohexanone in high yield, *via* the diethyl ketal, when treated with palladium chloride in ethanol.[12] If only *trans*-ethoxypalladiation occurs then a concerted loss of palladium and 1,2-hydride shift (H and Pd *trans*-co-planar) is not possible. Thus it seems likely that the 1,2-hydride shift is favoured in the absence of geometrical or steric constraints but that loss of hydridopalladium chloride by *cis*-elimination of hydride and and $PdCl^{30}$ may be an energetically favoured alternative process. When the 3,4-diol cyclisation was conducted at room temperature and monitored by g.l.c. the formation and decay of several species (possibly intermediates) was evident. The dihydropyrans (**36**) and (**37**) are possible intermediates resulting from elimination of hydridopalladium chloride.



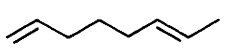
(35)



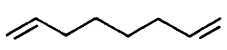
(36)



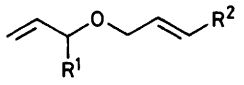
(37)



(38)



(39)



(40)

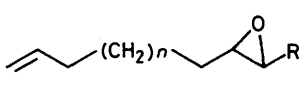
a; $R^1 = H, R^2 = Me$

b; $R^1 = R^2 = Me$

The intramolecular Wacker-type cyclisation was further exemplified by carrying out a similar epoxide→diol→cyclic ketal sequence with the dienes (**38**)—(**40**). We were unable to repeat the reported palladium acetate-catalysed synthesis of (**38**)[13] from butadiene in dimethylformamide (DMF) containing formic acid. We found that anhydrous cupric acetate was required as a co-catalyst before appreciable amounts of octa-1,6-diene were formed. Epoxidation of (**38**) with peracetic acid gave (**41a**) (51%), which on acid-catalysed opening gave the diol (**42**) (90%). Cyclisation of (**42**) at 65 °C in dry dimethoxyethane by the $PdCl_2$–$CuCl_2$ catalyst system gave the ketal (**43**) (49%). A similar series of reactions with the commercially available (**39**) gave, *via* (**41b**), the diol (**44**) which was cyclised to (**45**) (30%) by the Wacker-type catalyst (40 h, 65 °C).

Allyl glycidyl ether (**46a**) was converted into the diol (**47a**) which underwent extensive decomposition on distillation giving only a low yield (14%) of pure diol. Cyclisation ($PdCl_2$–$CuCl_2$–O_2, 65 °C/24 h) gave the ketal (**48a**) (21%). The epoxides (**46b**) and (**46c**) were prepared from (**40a**) and (**40b**) respectively and were found, by g.l.c., to consist of a 5:1 mixture of *trans*- and *cis*-isomers. Conversion of (**46b**) to (**47b**) followed by catalytic cyclisation gave (**48b**) (20%) as a *ca.* 5:1 mixture of *endo*- and *exo*-isomers (g.l.c.), whilst cyclisation of (**47c**) gave a mixture of isomers of (**48c**) (19%). Finally, the oxa-analogue (**49**) of *exo*-brevicomin was prepared as outlined in Scheme 2. The final catalytic cyclisation step occurred in 40% yield.

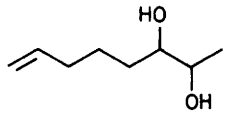
No attempt was made to optimise the catalytic cyclisation step in the current work but it appears that low temperature (0 °C) and longer reaction times are more favourable.



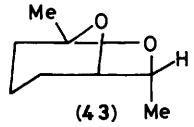
(41)

a; $n = 1$, R = Me

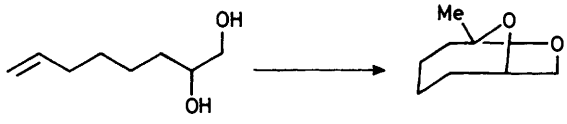
b; $n = 2$, R = H



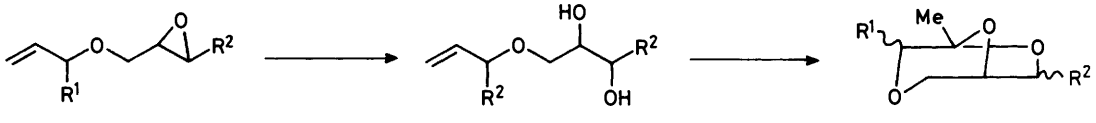
(42)



(43)



(44) (45)

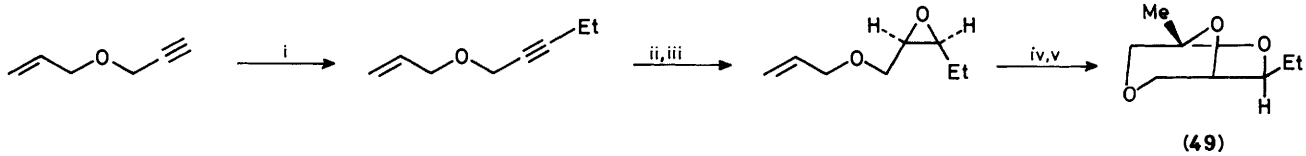


(46) (47) (48)

a; R = R^1 = H

b; R^1 = H, R^2 = Me

c; $R^1 = R^2$ = Me



(49)

Scheme 2. *Reagents* i. $NaNH_2$–liquid NH_3, EtBr; ii, 10% Pd–$BaSO_4$–H_2; iii, *m*-$ClC_6H_5CO_3H$; iv, H_2SO_4–aq THF; v, $PdCl_2$–$CuCl_2$–O_2

Experimental

N.m.r. spectra were determined for solutions in deuteriochloroform, except where otherwise stated, with Jeol-PMX60 (60 MHz), Bruker WP90 (90 MHz), and Bruker WP250 (250 MHz) instruments. Mass spectra were obtained by direct insertion into the ion source of an AEI MS902 instrument at 70 eV. Mass spectra/g.l.c. were recorded using a Pye Unicam 104 gas chromatograph coupled to an AEI MS30 mass spectrometer. I.r. data were determined for films, except where otherwise stated, on a Perkin-Elmer 457 i.r. spectrophotometer. M.p.s were recorded with a Kofler hot-stage apparatus and are uncorrected. Analytical g.l.c. was performed on a Perkin-Elmer F11 or Pye 104 instruments. Preparative gas chromatography was performed on a Perkin-Elmer F21 or Aerograph A-700 autoprep. Ether refers to diethyl ether.

Ethyl trans- (**12**) *and* cis- (**13**)-*Nona*-3,8-*dienoate*.—These compounds were prepared by the general method of Tsuji *et al.*[18] with a few modifications. A typical experiment was as follows.

Palladium acetate (900 mg, 4×10^{-3} mol), triphenylphosphine (4.22 g, 1.6×10^{-2} mol), and dry ethanol (73.6 g, 1.6 mol) were charged into a 500 ml rotary stirred autoclave. The vessel was flushed with nitrogen, sealed, and cooled in a CO_2–acetone bath at −78 °C. Butadiene (145 ml) which had been passed through molecular sieves (type 5A) was condensed in a trap and then distilled into the vessel. The autoclave was allowed to warm to ambient temperature, pressurised with carbon monoxide (45 atm), and then heated to 110 °C when the pressure rose to 67 atm. After being stirred (500 rev. min^{-1}) at this temperature for 20 h the pressure fell to 20 atm. The vessel was cooled to ambient temperature overnight, vented, and the contents removed. The autoclave was washed with a few portions of ethanol and the organic layers were combined. Removal of low-boiling material under reduced pressure and distillation of the residue gave the *ester* (78.12 g, 51% based on charged butadiene), b.p. 86—90 °C/5 mmHg (lit.,[18] 108—112 °C/18 mmHg). Both the n.m.r. and i.r. spectra agreed with the published spectra. Capillary g.l.c. using a DCC 550 WCOT, 100 × 0.25 mm column at 150 °C showed that the product comprised a 79:21 mixture of (**12**) and (**13**).

trans- (**19a**) *and* cis- (**20a**)-*Nona*-3,8-*dien*-1-*ol*.—Lithium aluminium hydride (9.10 g, 0.24 mol) was added to sodium-dried ether (600 ml) contained in a flask (3 l) fitted with a nitrogen inlet, dropping funnel, double-surface condenser, and mechanical stirrer. The stirrer was started and a solution of ethyl nona-3,8-dienoate (72.59 g, 0.40 mol) in anhydrous ether (200 ml) was added dropwise at such a rate as to allow the solvent to reflux gently. The mixture was stirred for a further 30 min after the addition was complete and more dry ether (200 ml) was added. Ethyl acetate (40 ml) was added dropwise, to destroy the excess of hydride, followed by the cautious addition of water (20 ml). The residual white solid was filtered off and washed with dry ether. The washings and filtrate were combined, dried (Na_2SO_4), and the solvent removed under reduced pressure to leave the pure alcohol (54.98 g, 98%), b.p. 52—54 °C/0.5 mmHg (Found: C, 77.25; H, 11.75. $C_9H_{16}O$ requires C, 77.09; H, 11.50%); $\nu_{max.}$ 3 300 and 1 640 cm^{-1}; *m/z* 122 ($M^+ - H_2O$, 12%), 109 (14), 106 (17), 98 (34), 97 (14), 96 (30), 95 (14), 94 (31), 93 (27), 83 (9), 82 (10), 81 (87), 80 (32), 79 (39), 70 (9), 69 (17), 68 (66), and 67 (100); δ_H 1.70 (1 H, s, OH), 1.52 (2 H, m, CH_2), 2.12 (6 H, m, C=C–CH_2), 3.60 (2 H, t, CH_2OH), 5.50 (2 H, m, CH=CH), and 4.75—5.15 and 5.35—6.15 (3 H, ABX, m, CH_2=CH).

trans- (**19b**) *and* cis- (**20b**)-*Nona*-3,8-*dien*-1-*yl Tosylate*.—Nona-3,8-dien-1-ol (28.07 g, 0.20 mol) was dissolved in dry pyridine (450 ml) and the solution cooled in an ice-bath. Freshly crystallised (ether) toluene *p*-sulphonyl chloride (45.75 g, 0.25 mol) was added in small portions with stirring to the cold (5 °C) solution. After the addition was complete the solution was kept below 0 °C for 36 h. The resultant pale-yellow liquid and white solid were added to ice–water and extracted with ether. The organic layers were washed with water, 15% hydrochloric acid, and water, and then dried (Na_2SO_4). Removal of the ether under reduced pressure at room temperature left a pale yellow oil (52 g, 88.4%), which gave a satisfactory elemental analysis (Found: C, 65.4; H, 7.65; S, 10.8. $C_{16}H_{22}O_3S$ requires C, 65.30; H, 7.54; S, 10.90%); $\nu_{max.}$ 1 740 and 1 645 cm^{-1}; δ_H 1.42 (2 H, m, CH_2), 1.8—2.4 (6 H, m, C=CCH_2), 2.45 (3 H, s, ArMe), 4.04 (2 H, t, CH_2O), 4.75—6.1 (5 H, m, olefinic-H), and 7.22—7.45 and 7.70—7.85 (4 H, m, ArH).

trans- (**11**) *and* cis- (**21**)-*Nona*-1,6-*diene*.—A solution of nona-3,8-dien-1-yl tosylate (21.85 g, 0.074 mol) in dry ether (100 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (4.24 g, 0.11 mol) in dry ether (150 ml). After the addition was complete the mixture was stirred at ambient temperature for 1 h and the excess lithium aluminium hydride destroyed by careful addition of dilute sulphuric acid. Ethyl acetate could not be used for this purpose because it was found to form an azeotrope with the product. The precipitate was removed by filtration and washed with ether. The washings and filtrate were combined, dried (Na_2SO_4), and the solvent removed by distillation at atmospheric pressure. Distillation of the residual liquid gave nona-1,6-diene (6.8 g, 74.0%), b.p. 137—140 °C/760 mmHg (Found: C, 87.05; H, 12.7. C_9H_{16} requires C, 87.00; H, 13.00%); $\nu_{max.}$ 1 634 cm^{-1}; *m/z* 124 (M^+, 6%), 95 (33), 82 (100), 81 (40), 69 (20), 68 (30), and 67 (73); δ_H 0.96 (3 H, t, Me), 1.44 (2 H, m), 1.95—2.17 (6 H, m, C=CCH_2), 5.03 (2 × d, *J* 10.5 and 17.6 Hz, 2 H, CH_2=CH), 5.32—5.58 (m, 2H, CH=CH), 5.87 (1 H, m, CH_2=C*H*).

Metathesis of Cyclopentene and But-1-ene

(a) *Heterogeneous Catalysis.—Preparation of* MoO_3–Al_2O_3. Laporte Alumina type A (4 g, 30#) was dried at 500 °C for 24 h. This pre-activated alumina was added to a hot solution (70 °C) of ammonium molybdate (0.5 g, 2.5×10^{-3} mol) in distilled water (25 ml). The paste was taken to dryness on a steam-bath and then transferred to a porcelain dish and heated to 500 °C for 12 h. At this temperature the ammonium molybdate decomposes to give MoO_3. The catalyst so prepared was stored *in vacuo* in a desiccator.

Attempted metathesis with MoO_3–Al_2O_3. The reaction was performed in a static reactor[31] which was charged with a 1:1.18 mixture of cyclopentene and but-1-ene together with the MoO_3–Al_2O_3 catalyst. The reaction vessel was heated to the desired temperature (Table) and the reaction mixture periodically sampled and analysed by means of a Pye 104 g.l.c. to which the apparatus was connected. The products were identified by co-injection with authentic olefins and the results are collected in the Table.

(b) *Homogeneous Catalysis.*—WCl_6–$EtAlCl_2$-*catalysed metathesis of cyclopentene and but*-1-*ene*. A 2-necked flask (250 ml) fitted with a stirring bar, septum cap and dry-cold condenser was purged with dry nitrogen. Dry hexane (40 ml) was syringed into the flask. Tungsten hexachloride (0.4 g, 1.01×10^{-3} mol) was weighed under nitrogen and quickly transferred to the flask with rapid stirring. Ethanol was slowly added to the solution dropwise (16 × 0.05 ml) by means of a syringe to give a deep burgundy red solution (evolution of HCl). Stirring was continued for 5 min before the addition of cyclopentene (40 ml, 0.45 mol). Dry but-1-ene (56 g, 1 mol) previously condensed, was distilled into the reaction flask by means of the solid CO_2-cooled condenser. Finally, $EtAlCl_2$ (25% solution in toluene; 2 ml,

2.4×10^{-3} mol) was added by syringe. The resulting deep brown solution was stirred rapidly at ambient temperature under nitrogen. After 30 min ethanol (1 ml) was added to destroy the catalyst and the hexane, unchanged but-1-ene, and cyclopentene were removed by distillation to leave an oil (4.0 g). Fractional distillation afforded nona-1,6-diene (1.2 g), b.p. 38 °C/14 mmHg. G.l.c. analysis using a 2 m, 2.5% SGR column at 60 °C showed the presence of one component, identified as nona-1,6-diene by its spectral characteristics, and by comparison with the material prepared above from ethyl nona-3,8-dienoate. Separation of *cis*- and *trans*-nona-1,6-diene was achieved using a 100 m polypropylene glycol capillary column at 80 °C and nitrogen carrier gas at 10 lb/in^2. The ratio of *trans*:*cis* was measured at 3:2. No separation of *trans*- and *cis*-isomers was achieved on either 100 m SGR or Apeizon L capillary columns.

Longer reaction times led to extensive double-bond isomerisation as shown by combined gas chromatography–mass spectrometry monitoring using a 2 m 5% SGR column at 30 °C.

3,4-*Epoxynon*-8-*ene* (**24**) *and* (**25**).—A solution of 85% *m*-chloroperbenzoic acid (5.3 g, 0.025 mol) in methylene chloride (70 ml) was added dropwise with stirring to a solution of nona-1,6-diene (3.0 g, 0.024 mol) in methylene chloride (40 ml) which was cooled in an ice–water bath. The mixture was stirred at ambient temperature for 14 h after which the white solid was filtered off and washed with methylene chloride. The washings and filtrate were combined, washed with water and aqueous 5% sodium carbonate, and dried (Na_2SO_4). The solvent was removed at atmospheric pressure and the residue distilled under reduced pressure to give the epoxide (2.6 g, 76%), b.p. 65—67 °C/11 mmHg (Found: C, 77.05; H, 11.5. $C_9H_{16}O$ requires C, 77.10; H, 11.50%); $\nu_{max.}$ 1 640 cm^{-1}; *m*/*z* 111 (*M* − Et, 14%), 82 (17), 81 (12), 68 (9), and 67 (100); δ_H 1.0 (3 H, t, Me), 1.55 (2 H, m, CH_2Me), 2.1 (2 H, m, C=CCH_2), 2.75 (2 H, m, 2 × CH–O), and 4.8—5.2 and 5.5—6.15 (3 H, ABX, CH_2=C*H*).

erythro-3,4-*Dihydroxynon*-8-*ene* (**26**).—3,4-Epoxynon-8-ene (2.58 g, 0.018 mol) was dissolved in THF (15 ml) and a solution of concentrated sulphuric acid (150 mg) in water (6 ml) added. The mixture was stirred at ambient temperature for 14 h and then poured into water and extracted with ether. The ethereal solution was washed with water and dried (Na_2SO_4), and the solvent removed under reduced pressure at room temperature to give the diol (**27**) as a white solid (2.09 g, 73.6%). Crystallisation from light petroleum (b.p. 40—60 °C) containing a little ethanol gave an analytical sample, m.p. 76 °C (Found: 68.4; H, 11.45. $C_9H_{18}O_2$ requires C, 68.30; H, 11.45%); $\nu_{max.}$(KBr disc) 3 320 and 1 640 cm^{-1}; *m*/*z* 100 (M^+ −58, 24%), 99 (28), 98 (7), 83 (9), 82 (41), and 81 (100); δ_H 1.0 (3 H, t, Me), 1.5 (6 H, m, 3 × CH_2), 2.05 (2 H, m, C=CCH_2), 2.7 (2 H, br s, 2 × OH), 3.55 (2 H, m, 2 × C*H*OH), and 4.85—5.25 and 5.6—6.25 (3 H, ABX, CH_2=C*H*).

endo-*Brevicomin* (**2a**).—A mixture of palladium chloride (0.13 g, 7.0×10^{-4} mol) and anhydrous cupric chloride (0.45 g, 3.3×10^{-3} mol) in dry dimethoxyethane (40 ml) was stirred and heated at 65 °C. Air was bubbled through the mixture whilst a solution of *erythro*-3,4-dihydroxynona-8-ene (2.2 g, 0.014 mol) in dry dimethoxyethane (10 ml) was added dropwise over *ca.* 10 min. After the addition was complete, the mixture was stirred at this temperature for 24 h and then cooled to room temperature. Ether was added and the mixture filtered (sintefed glass funnel) and then passed through a short column of neutral alumina. After removal of solvent, the residue was distilled to give the product (**2a**) (0.97 g, 45%) as a colourless liquid, b.p. 70—72 °C/12 mmHg (Found: C, 69.25; H, 10.4. Calc. for $C_9H_{16}O_2$: C, 69.20; H, 10.35%); $\nu_{max.}$ 2 960, 2 940, 2 880, 1 465, 1 360, 1 350, 1 200, 1 100, 965, 870, and 850 cm^{-1}; *m*/*z* 156 (*M*, 1%) 127 (1), 114 (9), 99 (17), 74 (14), 56 (50), and 43 (75); δ_H the 400 MHz spectrum is reproduced as Figure 4.

threo-3,4-*Dihydroxynon*-8-*ene* (**27**).—A solution of osmium tetraoxide (112.4 mg, 1.1 mol%) in t-butyl alcohol (3.4 ml) was mixed with *N*-methylmorpholine *N*-oxide (5.98 g, 35.5 mmol), water (10 ml), and acetone (18 ml). The mixture was stirred under nitrogen and nona-1,6-diene (4.99 g, 40.2 mmol) was added. Stirring was continued and samples were taken periodically and analysed by g.l.c. using tetramethylbenzene as internal standard. The reaction was terminated as soon as possible after the maximum concentration of diol was obtained (*ca.* 4—4.5 h, see Figure 1), by addition of a solution of sodium metabisulphite (1.04 g) in water (30 ml). The mixture was concentrated under reduced pressure to remove the organic solvents and then extracted with ether (4 × 25 ml). The combined ether extracts were dried ($MgSO_4$) and the ether evaporated. The residual oil was distilled to afford the *product* (1.97 g), b.p. 64 °C/0.1 mmHg as an 82:18 mixture of *threo*- (**27**) and *erythro*- (**26**) diols (g.l.c.). When the reaction was repeated at 0 °C for 29 h an improved yield (45%) of diol was obtained.

Selective Tritylation of the Mixed 1,2- *and* 3,4-*Dihydroxynona*-1-*enes*.—A solution of the above diol mixture (1.61 g, 10.19 mmol) in dry pyridine (49 ml), containing freshly prepared trityl chloride (2.66 g, 9.54 mmol) was stirred at ambient temperature under nitrogen for 11 h. G.l.c. analysis (2.5% SGR) showed that the concentration of 3,4-diol remained constant during the reaction. Pyridine was removed on a rotary evaporator at *ca.* 60 °C leaving an oily orange solid. To this was added brine (20 ml) and ether (20 ml). This mixture was shaken, filtered, and separated. The aqueous layer was extracted with ether (5 × 25 ml). The combined ether extracts were dried (Na_2SO_4) and the ether evaporated. The residue was treated with light petroleum (b.p. 40—60 °C) (25 ml) and insoluble material (triphenylmethanol, m.p. 163—164 °C) was filtered off. The filtrate was concentrated on a rotary evaporator and the residual orange liquid distilled to afford a 95:5 mixture (0.94 g, 69%) of 3,4-dihydroxynon-8-enes (**26**) and (**27**) and 1,2-dihydroxynon-6-ene (**28**) in a ratio of 95:5 (g.l.c., see below), *i.e.* most of the 1,2-diol (**28**) was removed. This mixture was used as starting material in the brevicomin cyclization reaction (Found: C, 68.2; H, 11.2. $C_9H_{18}O_2$ requires C, 68.30; H, 11.45%); *m*/*z* 158 (M^+, 3%) 140 (*M* − H_2O, 1), 100 (17), 99 (18), and 81 (100); δ_H see Figure 3.

Derivatisation of the Diol Mixture for G.l.c.—The post-tritylated mixture of diols (42 mg) (above) was dissolved in dry pyridine (1 ml) and trimethylsilyl chloride (15 μl) and hexamethyldisilazane (20 μl) added. After 3 h more trimethylsilyl chloride (30 μl) and hexamethyldisilazane (45 μl) were added. After the mixture had been kept for a further 30 min the pyridine was evaporated, saturated brine (2 ml) and ether (2 ml) were added, and the ether layer separated, dried ($MgSO_4$), and analysed by g.l.c. (see Figure 2).

exo-*Brevicomin* (**2b**). Dry air was bubbled through a stirred solution of palladium chloride (76.6 mg, 17 mol %) and cupric chloride (127.8 mg, 0.95 mmol) in dry dimethoxyethane (10 ml). To this was added a solution of 3,4-dihydroxynon-8-ene [0.4 g, 2.56 mmol; *threo*- (**27**): *erythro*- (**26**) = 84:16] in dimethoxyethane (1 ml). The colour of the reaction immediately changed from brown to green. After 17 h, dry ether (7 ml) and activated (500 °C, 12 h) neutral alumina (3 g) were added and the mixture stirred for 30 min. It was then filtered and the ether evaporated from the filtrate on a rotary evaporator at room temperature to leave a colourless oil (236 mg, 62%) which comprised a mixture of *exo*- (**2b**) and *endo*- (**2a**)-brevicomin (86:14) as determined by g.l.c. (1.5 m × 4 mm i.d., 5% SGR column, temperature

programmed 100—220 °C at 8 °C/min.). The pure *exo*-isomer (**2b**) was isolated by preparative g.l.c. (4.6 m × 7 mm i.d., 10% SGR column, 90—220 °C at 10 °C/min) (Found: C, 68.9; H, 10.5. Calc. for $C_9H_{16}O_2$: C, 69.20; H, 10.35%); $\nu_{max.}$ 2 922, 1 455, 1 378, 1 232, 1 181, 1 169, 1 102, 1 026, 1 001, 983, 922, 875, and 850 cm^{-1} *m/z* 156 (M^+, 9%), 127 (6), 114 (51), 99 (7), 98 (24), 86 (20), 85 (50), 68 (21), 57 (10), and 43 (100); δ_H the 400 MHz n.m.r. spectrum is reproduced in Figure 5.

Octa-1,6-Diene (**38**).—Using the method of Gardner and Wright[13] no reaction with butadiene was obtained. An improved procedure was developed.

Formic acid (24.2 g, 0.53 mol) and dimethylformamide (36.7 g, 0.50 mol) were mixed in a rotary stirred autoclave (500 ml). Palladium acetate (41 mg, 1.8×10^{-4} mol) and cupric acetate (393 mg, 2.16×10^{-3} mol) were added and the vessel cooled under nitrogen in a solid CO_2–acetone bath. Butadiene (70 g, 1.33 mol) was added and the autoclave assembled quickly. A pressure of 20 atm. (N_2) was applied and the mixture stirred at 50 °C for 20 h. After the mixture had cooled to ambient temperature the vessel was vented and the residual pale yellow solution extracted with light petroleum (b.p. 40—60 °C). The petroleum extract was washed with water, dried (Na_2SO_4), and the solvent removed. Distillation of the residue gave octa-1,6-diene (14.5 g, 25.5% based on formic acid), b.p. 121—122 °C/760 mmHg; $\nu_{max.}$ 1 640, 990, 960, and 910 cm^{-1}; δ_H 1.45 (2 H, m, CH_2), 1.65 (3 H, m, Me), 1.97 (4 H, m, C=CCH_2), 4.85—5.2 and 5.6—6.1 (3 H, ABX, CH_2=CH), and 5.45 (2 H, m, CH=CH).

Pressurising the autoclave at 15 atm (air) did not alter the yield.

2,3-*Epoxyoct-7-ene* (**41a**).—Octa-1,6-diene (39.0 g, 0.355 mol) in methylene chloride (400 ml) containing anhydrous sodium carbonate (80 g, 0.75 mol) was stirred and cooled to 0 °C. Peracetic acid (103.0 g of 22% as determined by titration, 0.309 mol) to which a small amount of potassium acetate had been added, was added dropwise over 0.75 h and the mixture stirred at ambient temperature for a further 24 h, when the solution gave a negative peroxide test with starch–iodide paper. The solution was filtered, the solid washed with methylene chloride, and the combined methylene chloride extracts distilled at atmospheric pressure. The residual oil was then distilled under reduced pressure to give the pure *epoxide* (**41a**) (20.1 g, 51.6%), b.p. 66—70 °C/30 mmHg (Found: C, 76.05; H, 11.35. $C_8H_{14}O$ requires C, 76.20; H, 11.20%); $\nu_{max.}$ 1 645, 995, and 915 cm^{-1}; *m/z* 110 ($M-16$, 11%) 99 (19), 93 (12), 83 (9), 82 (33), 81 (35), 79 (19), 71 (13), 69 (10), 68 (35), and 67 (100); δ_H 1.25 (3 H, d, Me), 1.55 [4 H, m, $(CH_2)_2$], 2.12 (2 H, m, C=CCH_2), 2.72 (2 H, m, 2 × CHO), and 4.8—5.2 and 5.5—6.15 (3 H, ABX, CH_2=CH).

2,3-*Dihydroxyoct-7-ene* (**42**).—2,3-Epoxyoct-7-ene (12.0 g, 0.095 mol) was dissolved in THF (45 ml) and a solution of concentrated sulphuric acid (450 mg) in water (18 ml) added. The two-phase system was stirred at ambient temperature for 36 h during which it became homogeneous. Ether was then added to the reaction mixture and the two layers separated. The aqueous layer was extracted a number of times with ether and the organic layers combined, dried (Na_2SO_4), and concentrated under reduced pressure at room temperature. The residue was distilled to give the *diol* (**42**) (12.29 g, 89.6%) as a colourless liquid, b.p. 80—82 °C/0.7 mmHg (Found: C, 66.4; H, 11.2. $C_8H_{16}O_2$ requires C, 66.65; H, 11.20%); $\nu_{max.}$ 3 360br, 1 645, 995, and 912 cm^{-1}; *m/z* 100 ($M-44$, 7%), 99 (18), 82 (21), and 81 (100); δ_H 1.05 (3 H, d, Me), 1.4 [4 H, m, $(CH_2)_2$], 2.05 (2 H, m, C=CCH_2), 3.6 (2 H, br s, 2 × OH), 3.4—3.8 (2 H, m, 2 × CHOH), and 4.75—5.15 and 5.45—6.1 (3 H, ABX, CH_2=CH).

endo-5,7-*Dimethyl-6,8-dioxabicyclo*[3.2.1]*octane* (**43**).—A mixture of palladium chloride (178.9 mg, 1.01×10^{-3} mol), anhydrous cupric chloride (654 mg, 4.86×10^{-3} mol), and dry dimethoxyethane (40 ml) was stirred and heated at 65 °C, while air was bubbled through the solution. 2,3-Dihydroxyoct-7-ene (2.84 g, 1.97×10^{-2} mol) dissolved in dry dimethoxyethane (10 ml) was added over a period of 10 min and heating continued for a further 6 h. The mixture was then cooled to room temperature and diethyl ether (*ca.* 150 ml) added to precipitate the metal salts. The fine suspension was filtered off and the filtrate passed through a short column (110 mm × 25 mm) of neutral alumina (Hopkins and Williams 100—250 mesh), and eluted with ether to remove any soluble metal derivatives. The solvent was removed by distillation at atmospheric pressure and the residue distilled to give the *product* (1.38 g, 49.3%), b.p. 68—70 °C/24 mmHg (Found: C, 67.45; H, 10.1. $C_8H_{14}O_2$ requires C, 67.55; H, 9.90%); $\nu_{max.}$ 2 980, 2 930, 2 870, 1 710, 1 470, 1 430, 1 376, 1 340, 1 303, 1 268, 1 236, 1 190, 1 170, 1 120, 1 098, 1 068, 1 044, 1 025, 964, 918, 904, 868, 855, 835, and 790 cm^{-1}; *m/z* 142 (M^+, 7%), 99 (9), 98 (16), 82 (8), 72 (19), 71 (16), 67 (8), 58 (5), 57 (9), 55 (14), 54 (10), 43 (100), and 41 (14); δ_H 1.33 (3 H, d, Me), 1.40 (3 H, s, bridgehead Me), 1.7 [6 H, m, $(CH_2)_3$], and 4.10—4.35 (2 H, m, OCHMe and OCH).

1,2-*Epoxyoct-7-ene* (**41b**).—A solution of *m*-chloroperbenzoic acid (36.46 g of 85%, 0.18 mol) in methylene chloride (460 ml) was added dropwise to a stirred solution of octa-1,7-diene (39.54 g, 0.36 mol) in methylene chloride (320 ml). The resultant mixture was stirred at ambient temperature for 24 h, filtered, and the precipitate washed with methylene chloride. The organic layers were combined and the solvent removed by distillation at atmospheric pressure. Distillation of the residue gave the *product* (**41b**) (14.76 g, 65.1%), b.p. 76—78 °C/29 mmHg (Found: C, 76.2; H, 11.05. $C_8H_{14}O$ requires C, 76.20; H, 11.20%); $\nu_{max.}$ 1 645, 995, and 910 cm^{-1}; *m/z* 97 (M^+-29, 7%) 95 (25), 93 (32), 84 (6), 83 (25), 82 (12), 81 (24), 80 (20), 79 (31), 71 (20), 70 (12), 69 (14), 68 (62), 67 (86), 66 (7), 59 (5), 58 (13), 57 (22), 56 (10), 55 (77), 54 (100), 53 (24), 43 (24), 42 (18), 41 (81), and 39 (53); δ_H 1.42 [6 H, m, $(CH_2)_3$], 2.07, (2 H, m, C=CCH_2), 2.47 and 2.82 (3 H, 2 × m, OCH and OCH_2) and 4.75—5.16 and 5.5—6.15 (3 H, ABX, CH_2=CH).

1,2-*Dihydroxyoct-7-ene* (**44**).—1,2-Epoxyoct-7-ene (6 g, 4.76×10^{-2} mol) was dissolved in THF (20 ml) and concentrated sulphuric acid (200 mg) in water (8 ml) was added. The mixture was stirred at room temperature for 15 h after which ether was added and the two layers separated. The aqueous phase was washed with ether and the organic layers combined, washed with brine, dried (Na_2SO_4), and the solvent removed. The n.m.r. spectrum of the residue (5.78 g, 85.5%), showed it to be pure diol. A small amount was distilled, b.p. 98—100 °C/0.5 mmHg (Found: C, 66.5; H, 11.05. $C_8H_{16}O_2$ requires C, 66.65; H, 11.20%); $\nu_{max.}$ 3 360br, 1 640, 990, and 910 cm^{-1}; δ_H 1.37 [6 H, m, $(CH_2)_3$], 2.04 (2 H, m, C=CCH_2), 3.10 (2 H, s, 2 × OH), 3.57 (3 H, m, CH_2OH and CHOH), and 4.77—5.15 and 5.47—6.15 (3 H, ABX, CH_2=CH).

6-*Methyl-7,9-dioxabicyclo*[4.2.1]*nonane* (**45**).—This was prepared from dihydroxyoct-7-ene in a manner analogous to that described above for (**43**). The *product* (31%) was obtained as a colourless oil, b.p. 54—56 °C/14 mmHg (Found: C, 67.35; H, 10.1. $C_8H_{14}O_2$ requires C, 67.55; 9.95%); $\nu_{max.}$ 2 995, 2 940, 2 880, 1 780, 1 740, 1 470, 1 455, 1 440, 1 375, 1 280, 1 240, 1 205, 1 180, 1 150, 1 120, 1 070, 1 060, 1 035, 1 025, 1 000, 970, 945, 925, 900, 850, 835, 805, 780, 750, 630, and 600 cm^{-1}; *m/z* 142 (M^+, 9%) 100 (13), 85 (11), 83 (6), 82 (14), 81 (5), 72 (18), 71 (7), 67 (27), 58 (29), 57 (25), 55 (13), 54 (22), 43 (100), and 41 (16); δ_H 1.37 (3 H, s, Me), 1.65 [8 H, m, $(CH_2)_4$], 3.8 (2 H, m, CH_2O), and 4.5 (1 H, m, CHO).

Allyl 2,3-*Dihydroxypropyl Ether* (**47a**).—A solution of sulphuric acid (900 mg) in water (15 ml) was added dropwise to a stirred ice-cold solution of allyl glycidyl ether (6.0 g) in tetrahydrofuran (22.5 ml). After the addition was complete the solution was stirred at room temperature for 24 h and then poured into water (25 ml) and extracted several times with ether. The ethereal extracts were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure to leave a pale yellow oil (3.32 g). Distillation gave a colourless oil (1 g, 14.4%), b.p. 70 °C/0.1 mmHg (the product decomposed during distillation) (Found: 54.3; H, 8.95. $C_6H_{12}O_3$ requires C, 54.55; H, 9.15%); $\nu_{max.}$ 3 340 and 1 650 cm^{-1}; δ_H 3.26 (2 H, br s, 2 × OH), 3.6 (5 H, m, 2 × CH_2O and CHO), 4.0 (2 H, m, CH_2O), 5.17 (2 H, m, CH_2=CH), and 5.58—6.2 (1 H, m, CH_2=C*H*).

5-*Methyl*-3,6,8-*trioxabicyclo*[3.2.1]*octane* (**48a**).—A mixture of palladium chloride (215 mg, 1.2 mmol), anhydrous cupric chloride (790 mg, 5.9 mmol), and dry dimethoxyethane (40 ml) was stirred and heated at 65 °C. Air was bubbled through the mixture and a solution of allyl 2,3-dihydroxypropyl ether (3.32 g, 27 mmol) in dry dimethoxyethane (10 ml) was added dropwise over *ca.* 10 min. The mixture was stirred at 65 °C for 24 h and then cooled to room temperature and ether added to precipitate palladium salts. Work-up in the usual way followed by distillation gave the *product* as a colourless liquid (800 mg, 21%), b.p. 80—82 °C/33 mmHg (Found: C, 55.1; H, 7.5. $C_6H_{10}O_3$ requires C, 55.35; H, 7.75%); δ_H 1.35 (3 H, s, Me), 3.5 (2 H, s, CH_2O), 3.6—3.72 (2 H, 2 × d, CH_2O), 3.88 (1 H, m, bridgehead H), and 4.25 (2 H, m, CH_2O).

Allyl 2,3-*Epoxybutyl Ether* (**46b**).—A solution of *m*-chloroperbenzoic acid (6.9 g, 40 mmol) in methylene chloride (100 ml) was added dropwise with stirring to an ice-cold mixture of allyl crotyl ether (4.41 g, 39 mmol) and anhydrous sodium carbonate (3.32 g, 33.2 mmol) in methylene chloride. After the addition was complete the reaction mixture was stirred at room temperature for 2 d when it gave a negative starch–iodine test. The precipitated solid was filtered off and washed with methylene chloride. The combined filtrates were washed with 10% aqueous sodium sulphite, 5% aqueous sodium carbonate, and water, dried (Na_2SO_4), and the solvent removed under reduced pressure. The pale yellow residue was distilled to give the *product* as a colourless liquid (2.3 g, 46%), b.p. 68—70 °C/25 mmHg. G.l.c. (Carbowax 20M, 80 °C) showed the *product* was a mixture of *cis*- and *trans*-isomers (ratio 1:5) (Found: C, 65.55; H, 9.6. $C_7H_{12}O_2$ requires C, 65.60; H, 9.44%); $\nu_{max.}$ 1 650 cm^{-1}; δ_H 1.30 (3 H, d, Me), 2.87 (2 H, m, 2 × CHO), 3.35 (2 H, m, CH_2), 4.0 (2 H, m, CH_2), 5.03—5.46 and 5.52—6.27 (3 H, ABX, CH_2=CH).

Allyl 2,3-*Dihydroxybutyl Ether* (**47b**).—Allyl 2,3-epoxybutyl ether (5 g) in tetrahydrofuran (15 ml) was hydrolysed with a solution of sulphuric acid (900 mg) in water (16 ml) in the usual manner. Work-up gave the *dihydroxy product* as a yellow oil (3 g, 52.6%) which decomposed on attempted distillation. It was therefore used directly for the cyclisation reaction; $\nu_{max.}$ 3 340 and 1 650 cm^{-1}; δ_H 1.2 (3 H, d, Me), 3.25 (2 H, br s, 2 × OH), 6.55 (4 H, m, CH_2O and CHO), 4.0 (2 H, m, CH_2), and 5.0—5.4 and 5.51—6.2 (3 H, ABX, CH_2=CH).

5,7-*Dimethyl*-3,6,8-*trioxabicyclo*[3.2.1]*octane* (**48b**).—The method was essentially the same as that for the preparation of 5-methyl-3,6,8-trioxabicyclo[3.2.1]octane (**48a**) using palladium chloride (200 mg, 11 mmol), anhydrous cupric chloride (700 mg, 52 mmol), allyl 2,3-dihydroxybutyl ether (3 g, 20 mmol), and dry dimethoxyethane (50 ml). The product was a colourless liquid (0.6 g; 20%), b.p. 70—72 °C/15 mmHg (Found: C, 58.25; H, 8.5. $C_7H_{12}O_3$ requires C, 58.30; H, 8.40%); *m/z* 144 (M^+, 2%) 114 (15), and 43 (100); δ_H 1.33 (3 H, s, Me), 1.54 (3 H, d, CH*Me*), 3.48 (2 H, s, CH_2O), 3.80 (2 H, d, CHCH_2O), and 3.9—4.6 (2 H, m, bridgehead H and C*H*Me). G.l.c. analysis (Carbowax 20M, 80 °C) showed the *product* was a 1:5 mixture of *exo*- and *endo*-isomers.

2,3-*Epoxybutyl* 1-*Methylallyl Ether* (**46c**).—But-2-enyl 1-methylallyl ether (12.6 g, 1.0×10^2 mol) in methylene chloride (100 ml) was epoxidised with *m*-chloroperbenzoic acid (17.25 g, 1.0×10^{-2} mol) in the usual way. Work-up gave the *product* as a colourless liquid (11.75 g, 82.8%), b.p. 75 °C/12 mmHg (Found: C, 68.0; H, 10.0. $C_8H_{14}O_2$ requires C, 67.57; H, 9.92%); $\nu_{max.}$ 1 650 cm^{-1}; *m/z* 132 (*M*, % not observed), 127 (6), 112 (3), 82 (10), 71 (65), and 55 (100); δ_H 1.2 (3 H, d, Me), 1.3 (3 H, d, Me), 2.82 (2 H, m, 2 × CHO), 3.8 (3 H, m, CH_2 and CH), and 5.2—5.92 (3 H, ABX, CH_2=CH). G.l.c. analysis (Carbowax 20M, 80 °C) showed the product was a mixture of *cis*- and *trans*-isomers (ratio 1:5).

2,3-*Dihydroxybutyl* 1-*Methylallyl Ether* (**47c**).—2,3-Epoxybutyl 1-methylallyl ether (5 g) in tetrahydrofuran (15 ml) was hydrolysed with a solution of sulphuric acid (900 mg) in water (16 ml) by the usual method. Work-up gave the product as a pale yellow oil (3 g, 56.8%); $\nu_{max.}$ 3 450 and 1 650 cm^{-1}; δ_H 1.15 and 1.23 (2 × d, 2 × 3 H, 2 × Me), 3.25 (2 H, br s, 2 × OH), 3.8 (5 H, m, 2 × CH_2O and CHO) and 5.35—5.92 (3 H, ABX, CH_2=CH). The diol decomposed on attempted distillation and was, therefore, used directly in the next stage with purification.

4,5,7-*Trimethyl*-3,6,8-*trioxabicyclo*[3.2.1]*octane* (**48c**).—The method was essentially the same as that for the preparation of (**48b**). Palladium chloride (180 mg, 10 mmol) anhydrous cupric chloride (700 mg, 52 mmol) and 2,3-dihydroxybutyl 1-methylallyl ether (3 g, 1.88×10^{-2} mole) in anhydrous dimethoxyethane (50 ml), gave on work-up the *product* as a colourless oil (600 mg, 19%), b.p. 70—72 °C/14.5 mmHg (Found: C, 60.85; H, 9.15. $C_8H_{14}O_3$ requires C, 60.75; H, 8.90%); *m/z* 158 (M^+, 5%) 131 (5), 114 (25), 98 (10), 72 (28), 55 (25), and 43 (100); δ_H 1.16, 1.33, and 1.44 (3 × d, 3 × 3 H, 3 × Me), 3.6 (2 H, m, CH_2O), and 3.88—4.3 (3 H, m, bridgehead H and 2 × methine H).

Allyl Pent-2-*ynyl Ether*.—Small pieces of sodium (23 g, 1 g-atom) were slowly added to liquid ammonia giving a blue solution. The mixture was stirred at room temperature for 2 h, then allyl prop-2-ynyl ether (81 g, 0.84 mol) was added dropwise and the mixture stirred for a further 4 h. Ethyl bromide (138 g, 1.1 mol) was then added dropwise with stirring over 1 h and the mixture stirred for a further 50 h. The ammonia was then allowed to evaporate and solid ammonium chloride was added followed by water (50 ml). The mixture was extracted with ether and the combined ether extracts were dried (Na_2SO_4), evaporated, and the residue distilled to give the *product* as a colourless oil (70.2 g, 67%), b.p. 123—124 °C/25 mmHg (Found: C, 77.1; H, 10.0. $C_8H_{12}O$ requires C, 77.35; H, 9.75%); $\nu_{max.}$ 2 280, 2 230, and 1 650 cm^{-1}; *m/z* 124 (M^+, 2%), 123 (4), 109 (5), 95 (28), 79 (40), 67 (82), and 41 (100); δ_H 1.15 (3 H, t, CH_2*Me*), 2.15 (2 H, q, CH_2Me), 4.0 (4 H, m, 2 × CH_2O), and 5.1—5.4 and 5.7—6.1 (3 H, ABX, CH_2=C*H*).

Allyl Pent-cis-2-*enyl Ether*.—The reaction flask of a low-pressure hydrogenation apparatus was charged with allyl pent-2-ynyl ether (24.8 g, 0.2 mol), 10% palladium on $BaSO_4$ catalyst (1 g), quinoline (10 ml), and light petroleum (b.p. 60—80 °C; 150 ml). The apparatus was evacuated and hydrogen was admitted to a pressure of 1 atm. The mixture was stirred, causing rapid absorption of hydrogen (4.5 l). The solution was then filtered and the solvent removed. The residue was distilled to give the

product as a colourless oil (21.75 g, 86%), b.p. 145—147 °C/760 mmHg (Found: C, 76.0; H, 11.25. $C_8H_{14}O$ requires C, 76.15; H, 11.20%); $\nu_{max.}$ 3 090, 3 020, and 1 650 cm^{-1} *m/z* 126 (M^+, 1%), 111 (3), 97 (17), 84 (14), 69 (25), 55 (19), and 41 (100); δ_H 0.9 (3 H, t, CH_2Me), 2.0 (2 H, m, CH_2Me), 3.9 (4 H, m, 2 × CH_2), 5.2 (2 H, m, CH_2=CH), 5.5 (2 H, m, CH=CH), and 6.1 (1 H, m, CH_2=CH).

Allyl cis-2,3-*Epoxypentyl Ether*.—Allyl pent-*cis*-2-enyl ether (15 g, 0.12 mol) was epoxidised by *m*-chloroperbenzoic acid (28.45 g of 85%, 0.14 mol) and sodium carbonate (14.84 g, 0.14 mol) in methylene chloride (450 ml). Work-up by distillation gave the product as a colourless oil (12.8 g, 89%), b.p. 64—67 °C/14 mmHg (Found: C, 67.30; H, 10.0. $C_8H_{14}O_2$ requires C, 67.55; H, 9.90%); $\nu_{max.}$ 1 650, 1 260, 900, and 805 cm^{-1}; *m/z* 142 (M^+, 1%), 139 (5), 97 (6), 71 (9), 57 (60), and 41 (100); δ_H 0.95 (3 H, t, CH_2Me), 1.5 (2 H, m, CH_2Me), 3.05 (2 H, m, 2 × CHO), 3.5 (2 H, m, CH_2), 4.05 (2 H, m, CH_2), and 5.1—5.3 and 6.1 (3 H, ABX, CH_2=CH).

Allyl threo-2,3-*Dihydroxypentyl Ether*.—Allyl 2,3-epoxypentyl ether (5 g) in tetrahydrofuran (25 ml) was treated with dilute sulphuric acid [concentrated H_2SO_4 (0.7 g) in water (20 ml)] to give the product as a pale yellow oil (4.3 g, 76.4%) which decomposed on attempted distillation; $\nu_{max.}$ 3 420 and 1 650 cm^{-1}; δ_H 1.0 (3 H, t, CH_2Me), 1.6 (2 H, m, CH_2Me), 2.7 (2 H, br s, 2 × OH), 3.5—3.8 (4 H, m, CH_2O and 2 × CHO), 3.98 (2 H, m, CH_2), and 5.05—5.45 and 5.69—6.30 (3 H, ABX, CH_2=CH).The diol was used for the next stage without further purification.

exo-7-*Ethyl*-5-*methyl*-3,6,8-*trioxabicyclo*[3.2.1]*octane* (**49**).—The method was essentially the same as that for the preparation of (**48c**) using palladium chloride (350 mg, 19 mmol), anhydrous cupric chloride (600 mg, 48.6 mmol), and allyl 2,3-dihydroxypentyl ether (5 g, 3.12 × 10^{-2} mol) in dry dimethoxyethane (50 ml). The *product* was a colourless oil (2.0 g, 40%), b.p. 80—82 °C/20 mmHg (Found: C, 60.6; H, 8.8. $C_8H_{14}O_3$ requires C, 60.75; H, 8.90%); *m/z* 158 (M^+, 18%), 99 (6), 86 (25), 71 (18), 68 (34), and 43 (100); δ_H 0.94 (3 H, t, CH_2Me), 1.30 (2 H, m, CH_2Me), 1.37 (3 H, s, Me), 3.4 (2 H, s, CH_2O), 3.65 and 3.78 (2 × d, 2 × 2 H, 2 × CH_2O), 4.1 (1 H, s, bridgehead H), and 4.32 (1 H, t, EtCHO); δ_C 9.26 (CH_2Me), 19.95 (CH_2Me), 28.21 (C-*Me*), 68.37, 72.46 (C-2, C-4), 78.10 (C-1), 80.26 (C-7), and 105.4 (C-5).

Acknowledgements

We thank D.E.N.I. and Queen's University for support.

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Received 2nd September 1983; *Paper* 3/1527