Cyclisation of 5-Bromomethyl-cycloheptene and -cyclo-octene: a New Route to Bicyclo[3.2.1]octanes and Bicyclo[4.2.1]nonanes

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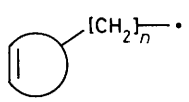
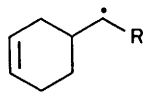
Reduction of 5-(bromomethyl)cycloheptene with tributyltin hydride gave bicyclo[3.2.1]octane; similar reduction of 5-(bromomethyl)cyclo-octene gave bicyclo[4.2.1]nonane together with some bicyclo[3.3.1]nonane. The cyclohept-4-enylmethyl radical intermediate exists as a rapidly equilibrating mixture of conformers, including the axial boat form from which cyclisation occurs. The rates of the two main cyclisation reactions are *ca.* 10^5 s^{-1} at 25 °C. Condensation of the dimethylamine enamine of 4-methylcyclohexanone with acrylaldehyde and subsequent treatment with methyl iodide and base gave 6-methyloctahydro-1-benzopyran-2-one.

The number of useful syntheses of bi- and poly-cyclic structures which involve free radical cyclisation is steadily growing.[1–7] In a transannular cyclisation of a radical of type (**1**) the side chain must normally be at least two carbon atoms long ($n \geqslant 1$) for significant bicyclisation to occur.[2,8,9] Exceptions to this rule, *i.e.*



(**1**)

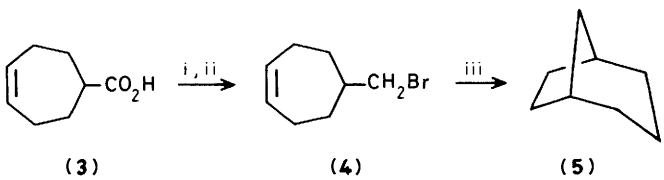


(**2**)

bicyclisation with a one-carbon side chain, can, however, be found when the ring conformation is favourable. In particular, if the C_1 side chain ($CR_2^{\bullet}$ group) occupies an axial or quasi-axial site then the radical centre may be able to approach from above the plane of the double bond. This is the stereoelectronically preferred orientation from which cyclisation is favoured. In the cyclohex-3-enylmethyl case (**2**) the side chain can occupy the quasi-axial site in the half-chair conformation, but bicyclisation was not observed in the parent radical (**2**; R = H)[10] or in derivatives.[8] Models indicated that transannular cyclisation might occur more readily for seven- and eight-membered rings, and this proved to be the case.[11] This paper describes our studies of the bicyclisation of cycloheptenylmethyl and cyclo-octenylmethyl radicals and a study of the conformational preferences of the former.

Results and Discussion

Synthesis of Bicyclo[3.2.1]octane and Bicyclo[4.2.1]nonane.—Cyclohept-4-enylmethyl bromide (**4**) was obtained by reduction of cyclohept-4-enecarboxylic acid[12] (**3**) and conversion of the alcohol into the bromide *via* the mesyl ester (Scheme 1).



(**3**) (**4**) (**5**)

Scheme 1. *Reagents:* i, $LiAlH_4$; ii, $MeSO_2Cl$, Et_3N then LiBr; iii, Bu_3SnH

Reduction of compound (**4**) under radical conditions gave bicyclo[3.2.1]octane (**5**) together with some 5-methyl-cycloheptene. The proportion of (**5**) depended strongly on the temperature and concentration of tributyltin hydride; yields of 60—70% were achieved with equimolar amounts of (**5**) and Bu_3SnH (see Table 1). A yield of 75% was obtained by slow addition of the hydride at 165 °C.

Table 1. Reduction of cyclohept-4-enylmethyl bromide (**4**)[a] with tributyltin hydride in t-butylbenzene

Temp (°C)	[Bu_3SnH] (mol dm^{-3})	(**5**)	5-Methyl-cycloheptene	$k_c(5)/k_H$ (mol l^{-1})
0	0.576	5	95	0.026
21	0.576	7	93	0.040
43[b]	0.646	14	86	0.086
48[c]	0.244	34	66	0.087
50[d]	0.814	12	88	0.094
55	0.576	13	87	0.080
64[e]	0.457	20	80	0.091
73	0.576	17	83	0.106
73	0.576	18	82	0.114
94	0.576	22	78	0.146
113	0.576	33	67	0.247
144[f]	0.576	38	62	0.315
148[a]	0.34	72	28	
177[f]	0.576	51	49	0.533
193[c,g]	0.34	78	22	

[a] [(**4**)] 0.129M. [b] [(**4**)] 0.243M. [c] [(**4**)] 0.275M. [d] [(**4**)] 0.229M. [e] [(**4**)] 0.258M. [f] In hexadecane as solvent. [g] ([**4**]) 0.34M.

Entry to the bicyclo[3.2.1]octane series has previously been obtained by ring expansion of a suitable norbornene derivative, *e.g.* by treatment of trinorbornene with dichlorocarbene and subsequent reduction and hydrolysis to give bicyclo[3.2.1]octan-3-one[13] or by conversion of 5-hydroxymethyltrinorbornene into bicyclo[3.2.1]octan-2-one.[14] The main bottleneck in the present synthesis was the low yield of acid (**3**) obtained by the Stork method.[12] However, an improved synthesis of compound (**3**) has recently been described,[15] and this makes the route of Scheme 1 an attractive alternative.

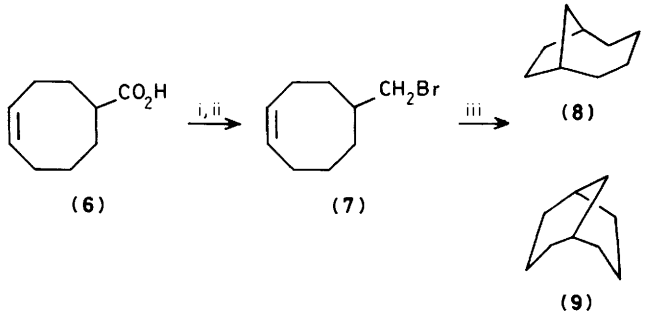
Cyclo-oct-4-enylmethyl bromide (**7**) was obtained from acid (**6**) as shown in Scheme 2. Reduction of compound (**7**) with tributyltin hydride gave bicyclo[4.2.1]nonane (**8**) in yields of up to 70%, together with minor amounts of bicyclo[3.3.1]nonane (**9**) and 5-methylcyclo-octene (see Table 2). Other routes to the bicyclo[4.2.1]nonane system are comparatively tedious and include: treatment of bicyclo[3.2.1]octene derivatives with dichlorocarbene with ring expansion, reduction, and hydrolysis to the 2-ketone,[16] cyclisation of *cis*-4-(3-cyanocyclopentyl)-butyronitrile,[17] and cyclisation of 5-(tosyloxymethyl)cyclo-octanone.[18]

The main drawback to the synthesis of Scheme 2 was again the poor yield of acid (**6**) obtainable by the literature method.[12]

Table 2. Reduction of cyclo-oct-4-enylmethyl bromide (7)[a] with tributyltin hydride in hexadecane

Temp (°C)	$[Bu_3SnH]$ (mol dm^{-3})	(8)	(9)	5-Methylcyclooctene	$k_c(8)/k_H$ (mol l^{-1})	$k_c(9)/k_H$ (mol l^{-1})
7[b]	0.255	20	3	77	0.031	0.005
41	0.255	50	7	43	0.130	0.030
95	0.255	64	9	27	0.249	0.064
98[c]	0.668	38	6	56	0.289	0.050
102[d]	0.472	51	7	42		0.051
104[e]	0.842	31	5	64	0.298	0.048
136	0.255	58	9	33	0.242	0.056
152	0.255	72	11	17	0.326	0.129
190	0.255	70	13	17	0.431	0.156

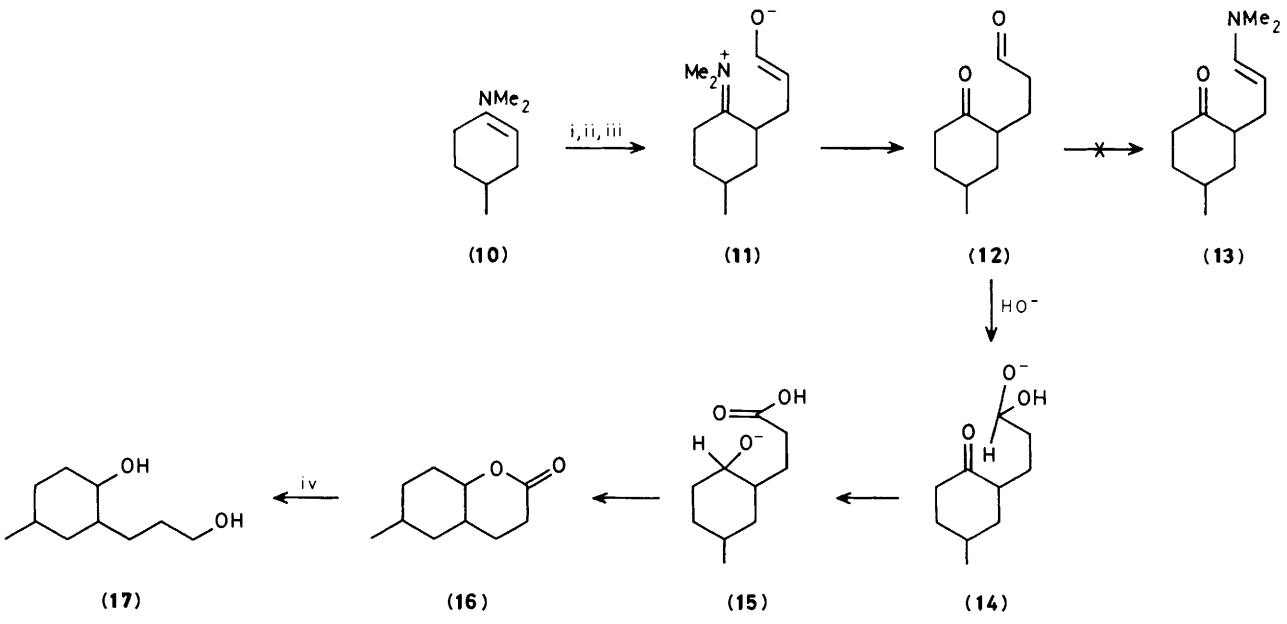
[a] [(7)] 0.255M. [b] In cyclopentane as solvent. [c] [(7)] 0.225M. [d] [(7)] 0.239M. [e] [(7)] 0.212M.



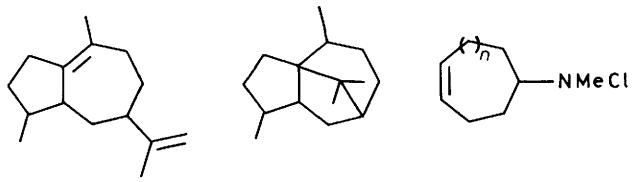
Scheme 2. *Reagents:* i, $LiAlH_4$; ii, $MeSO_2Cl$, Et_3N then LiBr; iii, Bu_3SnH

In an attempt to improve this end of the process, the Newcomb procedure for the preparation of acid (**3**)[15] was tried with 2- and 4-methylcyclohexanone. For the former ketone no enamine was obtained after prolonged (three months) reaction with dimethylamine at ambient temperature. The enamine (**10**) from the latter ketone was treated with acrylaldehyde, and the product then treated with methyl iodide followed by base.[15] A single product, *trans*-6-methyloctahydro-1-benzopyran-2-one (**16**) was obtained (Scheme 3). The *trans* ring junction was confirmed by the δ-value of 3-H (δ 3.8), which is similar to that of other *trans*-octahydrocoumarins.[19,20] Further support for the structure of compound (**16**) came from its reduction to diol (**17**). Compound (**16**) is a novel product from the reaction of an enamine with an α,β-unsaturated carbonyl compound. It is likely that enamine (**10**) condenses with acrylaldehyde to give the dicarbonyl compound (**12**) *via* intermediate (**11**). Dicarbonyl compounds have been obtained from a number of similar reactions.[21,22] Apparently the aldehyde enamine (**13**), which is required for the next stage in the production of acid (**6**), fails to form. The dicarbonyl compound (**12**) then undergoes a hydride transfer, probably when the NaOH is added in the final stage, to give the coumarin (**16**) possibly *via intermediates* (**14**) and (**15**) (Scheme 3). Thus, enamine (**10**) does not provide a straightforward route to the cyclo-oct-4-enyl series.

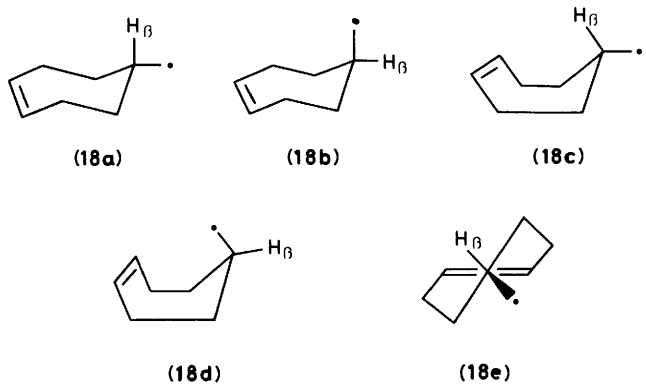
The cyclisations (**4**) to (**5**) and (**7**) to (**8**) and (**9**) occur *via* cycloheptenylmethyl (**18**) and cyclo-octenylmethyl (**19**) radicals respectively. The most stable conformation of (**18**) is expected to be the chair form with the $CH_2^{\bullet}$ group equatorial (**18a**) (see later). In this conformation the $CH_2^{\bullet}$ group is too far removed from the double bond for intramolecular addition and thus the high yield of bicycloalkane (**5**) [and (**8**)] was somewhat surprising. The only previous example of a bicyclisation of a cycloheptenylmethyl-type radical known to us comes from the photolysis of α-bulnesene (**20**) with dimethyl disulphide. This reaction gave a complex mixture of products containing, after desulphurisation, a small amount of the cyclised material (**21**).[23] However, the *N*-chloroamines (**22**; $n = 1$) and (**22**; $n = 2$) gave low yields of the corresponding 8-azabicyclo-octane and 9-azabicyclononane in reactions which probably involved cycloalkenylaminyl radicals.[24] Transannular cyclisation of cyclo-octenyloxyl radicals has also been observed recently.[25]



Scheme 3. *Reagents:* i, CH_2=CHCHO; ii, MeCN then MeI; iii, NaOH; iv, $LiAlH_4$



(20) (21) (22)



(18a) (18b) (18c) (18d) (18e)

Conformations of Cyclohept-4-enylmethyl Radicals.—The transannular cyclisations of radicals (**18**) and (**19**) were unexpectedly efficient in view of the unfavourable nature of conformation (**18a**) and the expected quasi-equatorial conformation of radical (**19**). The conformations of radicals (**18**) and (**19**) were therefore examined by e.s.r. spectroscopy.[26] Radicals (**18**) and (**19**) were generated by abstraction of bromine from bromides (**4**) and (**7**), respectively, with photochemically generated trimethyltin and, at low temperatures, triethylsilyl radicals. The spectrum of radical (**18**) (Figure) showed the presence of at least two and probably three different conformers. The major component had $a(2\ H_\alpha)$ 2.23 and $a(H_\beta)$ 3.62 mT at 140 K and the magnitude of the β-hydrogen hyperfine splitting (hfs) shows[26] that this conformation has the $CH_2^\bullet$ group in the equatorial position. Under high resolution (inset, Figure) this radical shows additional fine structure which suggests that it is actually a mixture of two overlapping equatorial conformations. The minor radical had $a(2\ H_\alpha)$ 2.23 and $a(H_\beta)$ 4.56 mT at 140 K. The much larger β-hydrogen hfs indicates[26] that the $CH_2^\bullet$ group is axial or quasi-axial in this conformer.

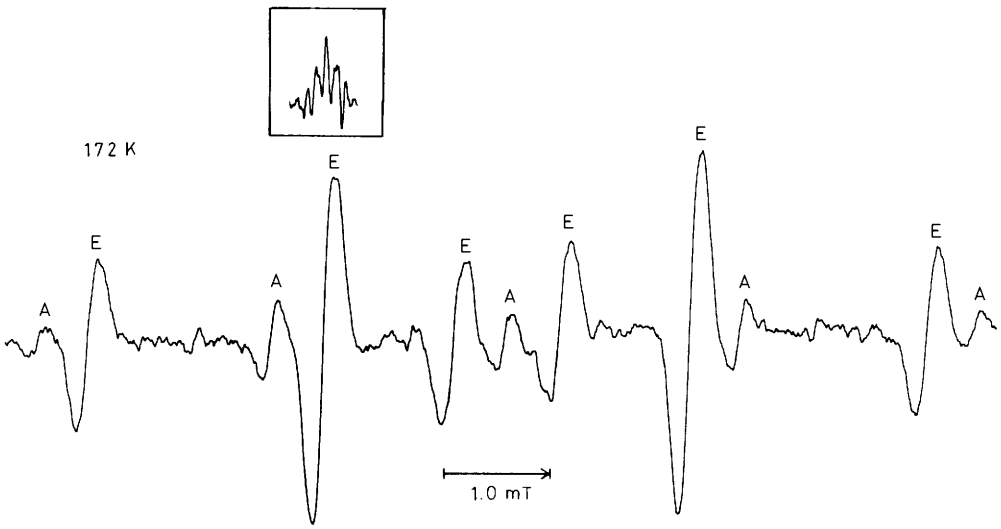


Figure. E.p.r. spectrum (9.4 GHz) of cyclohept-4-enylmethyl radicals (**18**) at 172 K in cyclopropane solvent. Quasi-equatorial radicals marked E, quasi-axial radicals marked A. Inset shows the quasi-equatorial multiplet under higher resolution with second-derivative presentation

By analogy with cycloheptene[27,28] there are at least five possible conformations of the cyclohept-4-enylmethyl radical (**18a—e**). It is probable that the major component (79% at 270 K) (Figure) is a mixture of the chair (**18a**) and boat (**18c**) equatorial forms. The minor component (21% at 270 K) could be either or both of the axial conformers (**18b**) and (**18d**). The characteristic β-hydrogen hfs of twist-boat conformations such as (**18e**) are not known. This form could be present at below the limit of detection, or it might contribute to either the major or minor species. The e.s.r. spectra confirm that conformations other than (**18a**) are populated at ambient temperature. The equilibria between them are fast[29,30] so the radical has access to the axial boat conformation (**18d**) in which the $CH_2^\bullet$ group is almost ideally placed for cyclisation.

When the sample was warmed above *ca.* 230 K the spectra of conformers (**18**) weakened and were eventually replaced by a new spectrum at *ca.* 340 K. This rather weak spectrum analysed quite well for $a(1\ H)$ 2.20, $a(2\ H)$ 2.50, $a(1\ H)$ 5.00 mT and can probably be attributed to the bicyclo[3.2.1]octan-2-yl radical (**23**) formed by cyclisation.

(23)

The e.s.r. signals from radical (**19**) showed a single spectrum with $a(2\ H_\alpha)$ 2.20, $a(H_\beta)$ 3.87 mT at 140 K. The lines of this spectrum remained broad under high-resolution conditions, *i.e.* it was not possible to determine by this technique if more than one conformation contributes. At higher temperatures the spectrum of (**19**) weakened and disappeared, but the cyclised radical was not detectable.

Kinetics of the Cyclisations of Radicals (**18**) *and* (**19**).—The rates of the cyclisations were determined by quantitative analysis of the products of the tin hydride reductions of

Table 3. Kinetic data for transannular cyclisation of cyclohept-4-enylmethyl and cyclo-oct-4-enylmethyl radicals

Cyclisation	10^{-5} $k_c(s^{-1})$ (298 K)	E(kJ mol^{-1})	Log (A/s^{-1})
Hex-5-enyl[a]	2.5	28.6	10.4
(**18**) ⟶ (**5**)	1.0	32.9	10.9
(**19**) ⟶ (**8**)	1.5	29.3	10.3
(**19**) ⟶ (**9**)	0.3	33.3	10.3

[a] Data from ref. 33.

bromides (**4**) and (**7**). Photochemical reductions of (**4**) were carried out in the temperature range 0—170 °C in t-butylbenzene or hexadecane as solvent and the product analysis is shown in Table 1. The ratio of the cyclisation rate constant, k_c, to the rate constant for hydrogen abstraction by radicals (**18**) and (**23**) from Bu_3SnH, k_H, was evaluated at each temperature from the data in Table 1 by the usual method.[31,32] For the reduction of (**7**) both cyclised products (**8**) and (**9**) were analysed, together with the unrearranged 5-methylcyclo-octene (Table 2). The k_c/k_H ratios for *both* cyclisations were then determined at each temperature as described above. The k_H value of Ingold and co-workers[33] was used to derive absolute cyclisation rate constants. The k_c values and Arrhenius parameters are compared with those of the archetypal hex-5-enyl radical in Table 3. The rate constants and Arrhenius parameters for cyclisation of (**18**) to (**5**) and (**19**) to (**8**) are very similar to, but slightly less than, those of hex-5-enyl.[33] The rate of cyclisation of (**19**) to the symmetrical product (**9**) is about an order of magnitude slower at 298 K and this is expected because this is a 1,6-cyclisation which is normally[2] less favoured than a 1,5-cyclisation. The somewhat slower k_c values for (**18**) and (**19**) in comparison with the hex-5-enyl radical are probably a consequence of the fact that several different conformations are populated, but cyclisation can only occur from (**18d**), and from an analogous quasi-axial conformation of (**19**). The direct rate of cyclisation of (**18d**) is not experimentally accessible, but the data in Table 3 suggest that it would be faster than that of hex-5-enyl. Cyclisation rates of $> 10^2$ s^{-1} are indicative of reactions with synthetic potential. The cyclisation rates of radicals (**18**) and (**19**) very comfortably exceed this (Table 3), which is a further indication of the synthetic potential of these reactions.

Experimental

Silica for column chromatography was Sorbsil M60. Light petroleum refers to the fraction boiling in the range 40—60 °C. Ether refers to diethyl ether. ^{1}H N.m.r. spectra were determined on Bruker WP80 and AM300 instruments. ^{13}C N.m.r. spectra were determined on AM300 and Varian CFT20 instruments. Mass spectra were obtained on an AEI MS902 spectrometer. E.s.r. spectra were run on a Bruker ER 200 D instrument; samples were made up in Spectrosil tubes, degassed by bubbling N_2 for 15 min, and photolysed in the cavity with light from a 500 W super-pressure Hg arc.

Cyclohept-4-enylmethyl Bromide (**4**).—A solution of cyclohept-4-enecarboxylic acid (**3**)[12] (4.9 g, 35 mmol) in dry ether (20 ml) was added to ice-cold $LiAlH_4$ (1.5 g, 39 mmol) in dry ether (80 ml) and the suspension was subsequently refluxed for 3.5 h. The suspension was cooled, water was added, and the ether layer was decanted. 2M-H_2SO_4 (100 ml) was added to the aqueous phase, which was then extracted with ether. The combined ether layers were washed with water (2 × 100 ml), dried over Na_2SO_4, and distilled to give cyclohept-4-enylmethanol (4.3 g, 97%) as an oil, b.p. 120 °C/2 Torr; δ_H(80 MHz) 0.9—1.5 (2 H, m), 1.5—2.5 (7 H, m), 2.7 (1 H, br s), 3.45 (2 H, d, J 7 Hz), and 5.77 (2 H, br s).

A solution of the alcohol (1.6 g, 13 mmol) and Et_3N (1.3 g, 13 mmol) in dry CH_2Cl_2 (75 ml) was cooled in an ice–salt-bath under N_2 and methanesulphonyl chloride (1.73 g, 15 mmol) was added dropwise. The solution was stirred for 0.5 h, water (100 ml) was added, and the separated CH_2Cl_2 layer was washed successively with 2M-HCl, 5% brine, and saturated aq. $NaHCO_3$, then dried over Na_2SO_4, and the solvent was removed at room temperature on a rotary evaporator. The mesyl ester showed the expected i.r. bands at 1 290 and 1 110 cm^{-1}.

The crude mesyl derivative was added to LiBr (4 g, 46 mmol) in dry acetone (50 ml) and the solution was refluxed for 11 h, then filtered, the acetone was distilled off, and water (20 ml) was added. The mixture was extracted with ether (2 × 50 ml), the extract was dried (Na_2SO_4), and the solvent was removed. The resulting oil was chromatographed on silica (light petroleum) and then distilled to give the *title compound* (**4**) (1.6 g, 67%) as an oil, b.p. 150 °C/15 Torr; δ_H 1.0—2.5 (9 H, m), 3.35 (2 H, d, J 6 Hz), and 5.8 (2 H, m); δ_C 26.5 (2 C), 31.7 (2 C), 40.7 (1 C), 44.3 (1 C), and 131.9 (2 C); m/z 188.0199 (M^+, $C_8H_{13}{}^{79}Br$ requires M, 188.0201), 109 (100%), 95 (44), 81 (32), 79 (24), 67 (100), 56 (40), and 55 (36).

Reduction of Cyclohept-4-enylmethyl Bromide (**4**) *with Tributyltin Hydride.*—Bromide (**4**) (1.5 g, 8 mmol) and Bu_3SnH (2.1 g, 8 mmol) were placed in a quartz tube, degassed by bubbling N_2 for 15 min, and then photolysed with light from a 250 W medium-pressure Hg arc for 2 h at 80 °C. The products were distilled out on a vacuum line (0.75 g). G.l.c. analysis showed two components, together with a trace of unchanged bromide (**4**). The mixture was separated by preparative g.l.c. on a 3 m × 1 cm column packed with 10% MS 200/50 on Chromosorb WAW at 110 °C. The first eluted component (80%), 5-methylcycloheptene, was a clear liquid, δ_H(80 MHz) 0.95 (3 H, d, J 7 Hz), 1.0—2.1 (9 H, m), and 5.75 (2 H, m); δ_C 243 (q), 28.0 (t), 36.2 (t), 38.2 (d), and 133.1 (d); m/z 110 (M^+, 40%), 95 (60), 82 (90), 81 (70), 68 (60), 67 (100), 54 (90), and 41 (70). The second component, bicyclo[3.2.1]octane (**5**), was obtained as a white solid, m.p. (sealed tube, sublimed) 137—141 °C (lit.,[34] 139—141 °C); δ_H 1.2—1.7 (12 H, m) and 2.10 (2 H, br s). The ^{13}C n.m.r. spectrum was essentially identical with that given in the literature.[35]

Cyclo-oct-4-enylmethyl Bromide (**7**).—A solution of cyclo-oct-4-enecarboxylic acid (**6**)[12] (1.0 g, 6.5 mmol) in dry ether (10 ml) was added slowly to ice-cold $LiAlH_4$ (0.2 g, 5.2 mmol) in dry ether (20 ml). The suspension was refluxed for 5 h, cooled, water was added, and the ether layer was decanted. Dil. H_2SO_4 (20 ml) was added to the aqueous phase, which was then extracted with ether (2 × 30 ml). The ether layers were combined, washed with water, and dried over Na_2SO_4. The ether was evaporated off and the residue was distilled on a Büchi Kugelrohr to give the alcohol as an oil (0.73 g, 80%), b.p. 126 °C/0.5 Torr; δ_H(80 MHz) 1.0—1.9 (8 H, m), 2.0—2.4 (4 H, m), 3.4 (2 H, d, J 5 Hz), and 5.5—5.9 (2 H, m).

A solution of the alcohol (1.30 g, 9.4 mmol) and Et_3N (1.4 ml) in dry CH_2Cl_2 (50 ml) was cooled and stirred in an ice-bath under N_2. $MeSO_2Cl$ (1.25 g) was added during 10 min. The solution was stirred and gradually warmed to room temperature during 30 min, water (80 ml) was added, and the CH_2Cl_2 layer was washed successively with 2M-HCl, brine, and saturated aq. $NaHCO_3$, then dried over Na_2SO_4, and the solvent was evaporated off at room temperature.

The crude mesyl ester was added to LiBr (2.9 g) in refluxing dry acetone (40 ml). Reflux was continued for 16 h. The solution was filtered, the acetone was evaporated off, and water (20 ml)

was added. The mixture was extracted with ether (2 × 50 ml), the extract was dried (Na_2SO_4), and the solvent was evaporated off. The resulting oil was chromatographed on silica (light petroleum) and then distilled on a Büchi Kugelrohr to give the title bromide (**7**) as an oil (1 g, 53%), b.p. 87 °C/1 Torr; δ_H 1.1—2.0 (7 H, m), 2.0—2.3 (4 H, m), 3.3 (2 H, dd, J_1 4.5, J_2 1.5 Hz), and 5.5—5.8 (2 H, m), δ_C 24.6 (1 C), 25.9 (1 C), 27.7 (1 C), 32.1 (1 C), 34.0 (1 C), 39.8 (1 C), 43.1 (1 C), 129.9 (1 C), and 130.3 (1 C); *m/z* 204 (8%), 202 (8), 176 (8), 174 (8), 123 (80), 95 (96), 81 (100), and 79 (100).

Reduction of Cyclo-oct-4-enylmethyl Bromide (**7**) *with Tributyltin Hydride.*—Bromide (**7**) (0.5 g, 2.5 mmol) and Bu_3SnH (0.74 g, 2.5 mmol) were placed in a quartz tube, degassed by bubbling N_2 for 15 min, then photolysed with light from a 250 W medium-pressure Hg arc for 2.5 h at 135 °C. The products were distilled out on a vacuum line (0.24 g, 78 mol %). G.l.c. analysis showed three components. The mixture was separated by preparative g.l.c. on a 6 m × 1 cm Carbowax 20 M column at 70 °C. The first eluted component was 5-methylcyclooctene (62 rel. %), δ_H(300 MHz) 0.9 (3 H, d, *J* 1.7 Hz), 1.1—1.2 (1 H, m), 1.4 (3 H, br s), 1.5—1.7 (3 H, m), 2.0—2.3 (4 H, m), and 5.6—5.7 (2 H, m); δ_C(75 MHz) 25.2, 25.4, 26.0, 27.8, 32.4, 34.9, 37.7, 129.8, and 130.3; *m/z* 124 (M^+, 11%), 109 (16), 96 (100), 81 (74), 67 (75), and 54 (63). The second eluted component was bicyclo[3.3.1]nonane (6 rel. %), δ_H(300 MHz) 1.5 (6 H, br s), 1.6—1.7 (7 H, m), and 1.8—2.0 (3 H, m); δ_C [36] (75 MHz) (23.2 (C-3), 28.6 (C-1), 32.3 (C-2), and 35.7 (C-9); *m/z* 124 (M^+, 85%), 82 (51), and 81 (100%). The third eluted component was bicyclo[4.2.1]nonane (32 rel. %), δ_H(300 MHz) 1.3—1.6 (12 H, m), 1.8—1.9 (2 H, m), and 2.3 (2 H, br s); δ_C [36] (75 MHz) 25.5 (C-3), 32.9 (C-7), 35.4 (C-9), 35.7 (C-2), and 37.2 (C-1); *m/z* 124 (M^+, 29%), 96 (75), 81 (52), and 67 (100).

1-*Dimethylamino*-4-*methylcyclohexene* (**10**).—Me_2NH·HCl (40 g) was dissolved in the minimum amount of water and the solution was added dropwise to NaOH (40 g). The Me_2NH liberated was collected over solid CO_2–acetone and dissolved in dry ether (250 ml). $CaCl_2$ (30 g) was added, followed by 4-methylcyclohexanone (12.6 g, 113 mmol). The mixture was kept at ambient temperature for 80 h, and was then filtered, the solvent was evaporated off, and the residue was distilled under reduced pressure to give the enamine (**10**) (12.8 g, 83%), b.p. 66 °C at 15 Torr (lit.[15] 85—86 °C at 98 Torr); δ_H(60 MHz) 1.0 (3 H, d, *J* 4 Hz), 1.0—2.5 (7 H, m), 2.6 (6 H, s), and 4.6 (1 H, br s).

Reaction of Enamine (**10**) *with Acrylaldehyde, followed by Methyl Iodide and Base.*[15]—Enamine (**10**) (11.7 g, 84 mmol) was cooled to 0 °C under dry N_2. Freshly distilled acrylaldehyde (5.6 ml) was added dropwise during 1 h. The mixture was warmed to room temperature and stirred for 16 h. Anhydrous acetonitrile (20 ml) was purged with N_2 and added to the yellow oil. The solution was cooled to 0 °C, MeI (5.3 ml) was added dropwise, the mixture was warmed to room temperature and stirred for 2 h, 20% aq. NaOH (80 ml) was added, and the mixture was refluxed for 16 h. The solution was cooled and the aqueous layer was removed, extracted with CH_2Cl_2 (50 ml), acidified, and extracted with ether (2 × 100 ml); the ether extract was dried over Na_2SO_4 and evaporated. Recrystallisation of the crude product from light petroleum gave white needles (1.2 g, 9%) identified as 6-methyloctahydrocoumarin (**16**) m.p. 83—85 °C; δ_H(300 MHz) 1.0 (3 H, d, *J* 1.6 Hz), 1.2—2.1 (10 H, m), 2.5—2.8 (2 H, m), and 3.8 (1 H, dt, J_t 2.4, J_d 0.8 Hz); δ_C(75 MHz) 17.9 (CH_3), 26.7 (CH_2), 26.7 (CH_2), 26.8 (CH), 29.4 (CH_2), 30.0 (CH_2), 32.8 (CH), 36.8 (CH_2), 84.0 (CH), and 171.6 (C=O); *m/z* 168 (M^+, 6%), 124 (5), 111 (12), 96 (33), 81 (100), 67 (36), and 55 (58); ν 1 740 cm^{-1} (C=O) (Found: C, 71.2; H, 9.7. Calc. for $C_{10}H_{16}O_2$: C, 71.4; H, 9.59%).

Reduction of Lactone (**16**) *with Lithium Alumininum Hydride.*—A solution of 6-methyloctahydrocoumarin (**16**) (1.30 g, 7.7 mmol) in dry ether (20 ml) was added to ice-cold $LiAlH_4$ (0.30 g, 7.9 mmol) in dry ether (20 ml). The solution was refluxed for 3.5 h then stirred at ambient temperature for 16 h. Water was added carefully and the ether layer was decanted. Dil. H_2SO_4 (50 ml) was added to the aqueous phase which was then extracted with ether (2 × 50 ml). The ether layers were combined, dried over Na_2SO_4, the solvent evaporated off, and the residue was distilled on a Büchi Kugelrohr to give a thick oil (1.17 g, 88%), identified as 2-(3-hydroxypropyl)-4-methylcyclohexanol (**17**), δ_H(300 MHz) 0.9 (3 H, d, *J* 1.6 Hz), 1.2—1.3 (2 H, m), 1.4—1.8 (10 H, m), 2.1 (2 H, br s), 3.4 (1 H, q, *J* 0.8 Hz), and 3.6 (2 H, t, *J* 1.2 Hz); δ_C(75 MHz) 19.9, 26.7, 27.9, 29.4, 29.6, 30.0, 35.0, 39.4, 62.9, and 73.2; *m/z* 172 (M^+, 1%), 154 (3), 136 (10), 115 (20), 103 (18), 97 (49), 95 (62), 81 (49), 67 (34), 61 (27), and 55 (100); ν 3 330br cm^{-1} (OH).

Kinetics of Tributyltin Hydride Reductions.—The solvent, t-butylbenzene or hexadecane (0.5 ml), was placed in a Pyrex tube, heated to the desired temperature, and degassed by bubbling nitrogen for *ca.* 15 min. To this was added the bromide (20 μl), Bu_3SnH (see Tables 1 and 2), and octane (20 μl) as internal standard. The solution was photolysed for 1 h with light from a 250 W medium-pressure Hg arc and then analysed by g.l.c. on a PYE UNICAM PU 4800 chromatograph. The values of k_c/k_H were obtained at each temperature from the initial Bu_3SnH concentration and the final product concentrations (Tables 1 and 2) using an integrated rate equation.[31,32] The best values of k_c/k_H were located with an iterative computer program based on NAG routine CO5AXF.

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