Preparation and Some Reactions of Tricyclo[3.3.0.0^{1,4}]octan-2-ones and Tricyclo[3.2.0.0^{1,4}]heptan-2-ones

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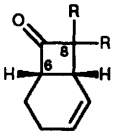
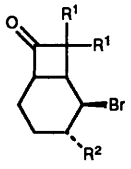
Bicyclo[4.2.0]oct-2-en-7-ones (**1**)–(**4**) provide the corresponding 2-bromo derivatives (**5**)–(**15**) through a range of highly stereoselective reactions. From chosen compounds in the latter series, the tricyclo[3.3.0.0]octanones (**16**)–(**22**) were prepared. The tricycles (**16**) and (**18**) provided the bicyclo[3.3.0]octenones (**23**) and (**24**) respectively on treatment with acid or base. The reaction of the ketone (**19**) with nucleophiles (such as azide, fluoride, or iodide ion) gave the appropriate product (**27**), (**29**), or (**30**) derived by a regiospecific homo-conjugate addition process. Cyanide ion converted the diphenyltricycloalkanone (**22**) into the cyano ketone (**32**) in like manner but this strained ketone (**22**) reacted in a different way with methoxide ion to give the methyl esters (**33**) and (**34**). Treatment of the tricycloalkanones (**19**) and (**22**) with bromine gave the 1,4-dibromobicyclo[3.3.0]octan-2-ones (**38**) and (**39**). The structure of the compound (**20**) was confirmed by *X*-ray crystallography. Dehydrobromination of the 2-bromobicycloheptan-6-ones (**43**), (**45**)–(**47**), (**49**), and (**50**) gave the series of tricyclo[3.2.0.0^{1,4}]heptanones (**51**)–(**56**). While the dimethyltricycloheptanone (**55**) reacted with methoxide ion and toluene-α-thiolate ion to give the ketones (**57**) and (**58**) as the major products, the analogous diphenyl compounds (**52**)–(**54**), and (**56**) reacted with various nucleophiles to regenerate the bicyclo[3.2.0]heptan-6-one ring system. The reaction of compound (**54**) with methoxide ion was exceptional; the esters (**66**), (**68**), and (**69**) were formed in the ratio 13:5:4. Bromine added to the tricyclo[3.2.0.0.^{1,4}]heptanone (**53**) to give the dibromo ketones (**71**) and (**74**) in the ratio 2:3. The tricycloalkanone (**54**) behaved in a similar manner. The lactone (**79**) was prepared and a crystal structure was obtained by *X*-ray analysis allowing the crystal structures of compounds (**20**), (**52**), and (**79**) to be compared. The bicycloheptenone (**2**) was partially resolved using *Clostridium* spp.

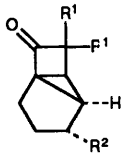
The bicyclo[4.2.0]oct-2-en-7-ones (**1**)–(**4**) are readily available.[1] Compounds (**2**)–(**4**) undergo addition across the alkene unit with exquisite stereoselectivity to give the polysubstituted bicyclo-octanones (**5**)–(**13**). The bromohydrins (**5**) and (**12**) were converted into the silylated derivatives (**14**) and (**15**) by the standard method. Treatment of compound (**6**) with potassium t-butoxide was expected to give a tricyclo[4.2.0.0^{2,8}]octan-7-one[2] but instead the tricyclo[3.3.0.0.^{1,4}]octan-2-one (**16**) was obtained in good yield. Similarly the bromo compounds (**8**) and (**14**) furnished the tricyclic ketones (**17**) and (**18**) respectively on treatment with a non-nucleophilic base. The elimination reaction is reminiscent of a process described by Carpino some years ago.[3]

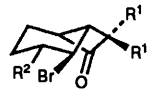


(1) R = Cl
(2) R = H
(3) R = Me
(4) R = Ph



	R^1	R^2		R^1	R^2
(5)	H,	OH	(6)	H,	OAc
(7)	H,	OMe	(8)	H,	Br
(9)	Me,	OH	(10)	Me,	OAc
(11)	Me,	Br	(12)	Ph,	OH
(13)	Ph,	OAc	(14)	H,	$OSiMe_2Bu^t$
(15)	Ph,	$OSiMe_2Bu^t$			





(A)

	R^1	R^2
(16)	H,	OAc
(17)	H,	Br
(18)	H,	$OSiMe_2Bu^t$
(19)	Me,	OAc
(20)	Me,	Br
(21)	Ph,	OAc
(22)	Ph,	$OSiMe_2Bu^t$

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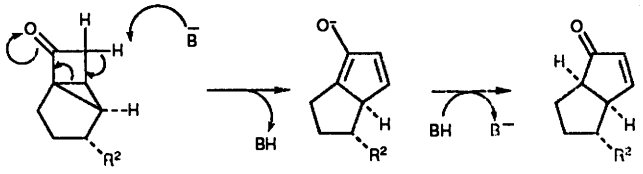
Table 1.

Starting material	Nucleophile or reagent	Product	% Yield
(17)	KCN	(25)	23
(18)	$PhCH_2S^-$	(26)	61
(19)	I^-	(27)	49
(19)	$(CO_2Et)_2CH^-$	(28)	70
(19)	$Et_3N{\cdot}3HF$	(29)	80
(19)	N_3^-	(30)	63
(19)	Me_2CuLi	(31)	82
(22)	Et_2AlCN	(32)	67

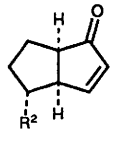
The preferential reaction *via* the bridgehead enolate anion has been reationalised by consideration of the shape of the bicyclic molecule, with the six-membered ring preferentially taking up a quasi-chair conformation (**A**).[4] The formation of the tricyclic compounds (**16**)–(**18**) is believed to be due to stereochemical control and not to a difference in acidity of the active methine and methylene protons. Indeed deuterium labelling studies on the bicyclic ketone (**2**) showed that the proton 6-H was *not* more labile than the protons 8-H in a basic medium. Thus a solution of compound (**2**) in dichloromethane was treated with sodium deuterioxide in D_2O and a phase transfer catalyst was added. After the mixture had been stirred for 14 h at room temperature, the ratio of 6-deuterio-, 8*endo*-deuterio-, and 8*exo*-deuterio-bicyclo[4.2.0]octen-7-one was 5:4:5 respectively.

Similarly, 3,3-disubstituted tricyclo[3.3.0.0^{1,4}]octan-2-ones (**19**)–(**22**) were prepared by treatment of the corresponding bromo compounds with potassium t-butoxide. The structure of the tricyclic compound (**20**) was confirmed by *X*-ray crystallography.[4]

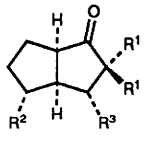
The tricyclo[3.3.0.0.^{1,4}]alkan-2-ones (**16**) and (**18**), lacking substituents at C-3, are labile to acid (*e.g.* silica gel) and base (*e.g. N*-benzyltrimethylammonium hydroxide or DBU) to form the bicyclo[3.3.0]oct-3-en-2-ones (**23**)–(**24**) by the mechanism outlined (for the base treatment) in Scheme 1. The more heavily substituted tricyclo-octanones (**19**)–(**22**) are much more stable and, for example, can be chromatographed over silica without difficulty.



Scheme 1.



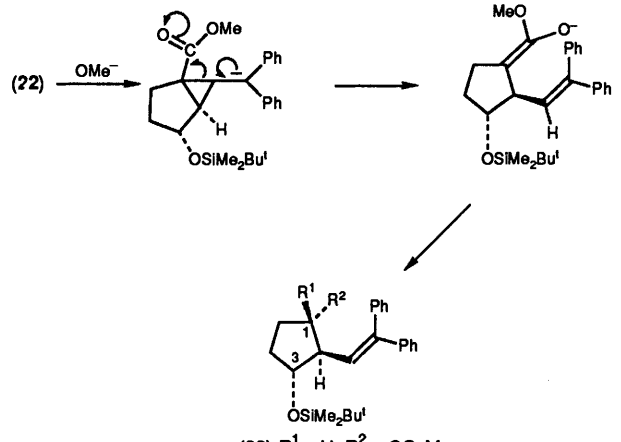
(**23**) R^2 = AcO
(**24**) R^2 = $OSiMe_2Bu^t$



	R^1	R^2	R^3
(**25**)	H	Br	CN
(**26**)	H	$OSiMe_2Bu^t$	SCH_2Ph
(**27**)	Me	OAc	I
(**28**)	Me	OAc	$CH(CO_2Et)_2$
(**29**)	Me	OAc	F
(**30**)	Me	OH	N_3
(**31**)	Me	OH	Me
(**32**)	Ph	$OSiMe_2Bu^t$	CN

The potential usefulness of the tricyclo-octanones (**16**)–(**20**) lies in the stereospecific reactions undergone by these strained compounds with a wide variety of nucleophiles. The tricyclo-octanones contain a cyclopropyl ketone entity which is susceptible to homo-Michael addition reactions with iodide, cyanide, azide, and thiolate ions and is also attacked with equally high selectivity by malonate and cuprate anions. A selection of the results obtained is depicted in Table 1. In general, nucleophilic opening of the 3-unsubstituted tricyclo[3.3.0.0.^{1,4}]octan-2-ones was unpredictable and low yields were obtained, but for reactions involving the 3,3-dimethyl derivatives good to excellent yields of products were the norm. The corresponding 3,3-diphenyl derivatives were much less reactive with bulky anions, probably owing to the steric hindrance provided by the *exo*-phenyl group towards the incoming nucleophile. Only the reaction of compound (**22**) with diethylaluminium cyanide gave a well-characterised product (**32**) in good yield. (We believe that this is the first time that diethylaluminium cyanide has been used in a conjugate addition reaction *not* involving an αβ-unsaturated carbonyl compound as the electrophile.)

Interestingly, reaction of the compound (**22**) with methoxide ion proceeds in a different way. Attack by the oxy anion takes place at the carbonyl carbon atom (Scheme 2) with formation of

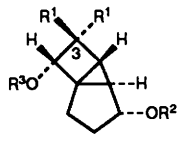


(**33**) R^1 = H, R^2 = CO_2Me
(**34**) R^1 = CO_2Me, R^2 = H

Scheme 2.

a transient carbanion; breakdown of the cyclopropyl ring affords the esters (**33**) and (**34**) (ratio 83:17). The two esters were separated by chromatography and identified by NOE difference experiments. Thus, for the major isomer, saturation of the signal due to the vinylic proton led to a 9% enhancement in the signals due to 1-H and 3-H. Cyclobutanone ring-opening reactions similar to the one postulated above have precedent in the literature.[5]

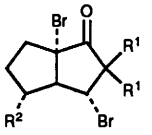
A second series of reactions giving products resulting from nucleophilic attack at the carbonyl carbon atom involved lithium aluminium hydride reductions. Thus, treatment of the tricycle (**18**) with this hydride gave an alcohol (**35**) which was fully characterised by conversion into the acetate (**36**). Similar reduction of the acetate (**19**) gave, after acetylation, the diester (**37**). The configuration of the hydroxy group in compound (**35**) was elucidated by NMR spectroscopy using the shift reagent [Eu(fod)$_3$]. The signal due to the proton 3*endo*-H was shifted more than the signal due to the proton 3*exo*-H (1.35 ppm *versus* 0.75 ppm) on addition of the shift reagent, indicating that the reducing agent had approached the ketone from the more exposed *exo*-face.



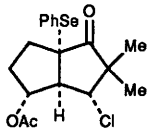
(35) $R^1 = R^3 = H$, $R^2 = SiMe_2Bu^t$
(36) $R^1 = H$, $R^2 = SiMe_2Bu^t$, $R^3 = Ac$
(37) $R^1 = Me$, $R^2 = R^3 = Ac$

Several features of the above reactions merit comment (leaving aside the reactions involving methoxide ion). First, nucleophilic attack on the tricycloalkanones (**16**)–(**22**) is regiospecific, leading to fracture of the C(1)–C(4) bond. The cyclopentanone moiety of the bicyclo[3.3.0]octan-2-ones (**25**)–(**32**) represents a heavily substituted C-5 cyclic synthon. Secondly, the stereochemistry of the substituent R^2 relative to the bridge changes during the transition from the bicyclo[4.2.0]octan-7-ones to the bicyclo[3.3.0]octan-2-ones. Thus, in compounds (**5**)–(**15**) the substituent R^2 is in the *endo*-configuration. The intramolecular S_N2 reaction involving loss of HBr and formation of compounds (**16**)–(**22**) takes place with only a little movement in the relative positions of the atom or group R^2 and the adjacent tertiary hydrogen atom. On cleavage of the C(1)–C(4) bond and formation of the *cis*-ring junction the substituent R^2 assumes an *exo*-configuration in the new bicyclic ring system. Thirdly, and somewhat surprisingly, tricyclo-[3.3.0.$0^{1,4}$]octan-2-ones can be regenerated from some of the bicyclo[3.3.0]octan-2-ones. Thus treatment of the iodide (**27**) with potassium t-butoxide produced the tricyclic compound (**19**) in quantitative yield.

The tricycloalkanones (**19**) and (**22**) were also subjected to attack by electrophilic reagents. The tricycloalkanone (**19**) in carbon tetrachloride reacted with bromine at 0 °C to give a crystalline compound, after work-up, in 78% yield. The ^{13}C and ^1H NMR spectra of the compound were strikingly similar to the corresponding spectra obtained for the iodo compound (**27**). The structure of the dibromo compound was tentatively assigned as (**38**) and this was confirmed by single crystal *X*-ray analysis (Figure 1). The diphenyltricycloalkanone (**22**) behaved in a similar manner and furnished the polysubstituted bicyclo-octanone (**39**). More information was obtained on



(38) R^1 = Me, R^2 = OAc
(39) R^1 = Ph, R^2 = $OSiMe_2Bu^t$



(40)

the *mechanism* of the attack by electrophiles on the tricyclo[3.3.0.0]alkanones by the reaction of benzeneselenenyl chloride with the tricyclic ketone (**19**). A single product was obtained from this reaction in 86% yield; ^{13}C NMR spectroscopy revealed that C-1 was coupled to ^{77}Se by 78 Hz thus locating the site of attachment of the SePh unit.[6] Irradiation of the signals in the ^1H NMR spectrum due to the aromatic protons led to a small (2%) enhancement in the signal due to 5-H suggesting a *cis* fused ring junction and the coupling constant J_{45} = 9.5 Hz was almost exactly the same as the equivalent coupling constant found in compounds (**38**) and (**39**) ($J_{4,5}$ = 10 ± 0.5 Hz). The compound was therefore assigned structure (**40**).

The mechanism of the electrophilic reactions on the tricycloalkanones (**19**) and (**22**) probably involves attack by the

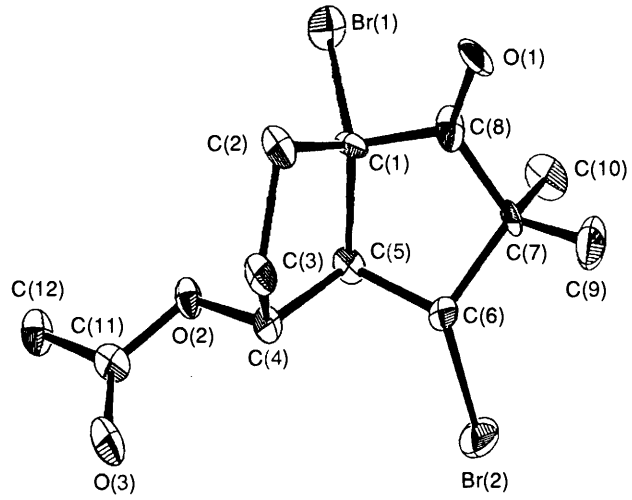


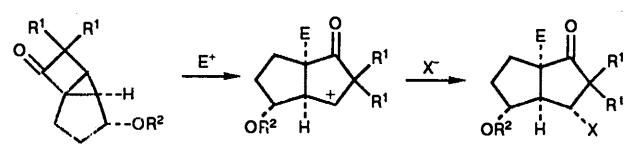
Figure 1. Crystal data for compound (**38**). $C_{12}H_{16}O_3Br_2$, M = 457.5, Monoclinic, a = 11.886(3), b = 7.776(1), c = 15.420(4) Å, β = 102.50(2), U = 1 391.15 Å^3, space group $P2_1/n$, Z = 4, D_c = 1.68 g cm^{-3}, μ(Mo-K_α) = 56.9 cm^{-1}, F(000) = 760. Data were measured at room temperature on a Hilger and Watts Y290 four-circle diffractometer in the range $2 < \theta < 24°$. 3 650 Reflections were collected of which 1 493 were unique with $I \geqslant 3\sigma I$. Data were corrected for Lorentz and polarization effects and also for absorption. The structure was solved by conventional Patterson methods. All atoms were allowed to vibrate anisotropically in the final stages of convergence. Hydrogens were included at calculated positions. Final residuals after 10 cycles of full-matrix least squares were $R = R_w$ = 0.0820 for unit weights. The total number of parameters varied was 154. Max. final shift/esd was 0.002, and the max. and min. residual densities were 0.52 and −0.63 eÅ^{-3}. Final fractional atomic co-ordinates are given in Table 4. Tables of bond distances, bond angles, temperature factors and hydrogen atom positions are available on request from the Cambridge Crystallographic Data Centre (see Instructions for Authors (1990), *J. Chem. Soc., Perkin Trans. 1*, 1990, Issue 1).

Table 2. Selected *X*-ray data on tricyclic compounds (**20**), (**52**), and (**79**).

	Compound		
Bond angles (°)	(**20**)	(**52**)	(**79**)
C(2)–C(1)–C(7/8)	138.5	149.2	135.2
C(5)–C(1)–C(4)	56.1	55.4	58.0
Bond lengths (Å)			
C(5)–C(4)	1.479	1.433	1.487
C(5)–C(1)	1.568	1.563	1.563
C(4)–C(1)	1.579	1.519	1.503

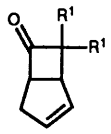
electrophile at the 'edge' of the cyclopropane ring[7] leading to the more stable of the two possible carbenium ions (Scheme 3); attack by the attendant halide ion then takes place from the more exposed *exo*-face of the molecule.

Following the successful preparation of tricyclo-[3.3.0.$0^{1,4}$]octan-2-ones we turned our attention to the synthesis of the more highly strained tricyclo[3.2.0.0.^{1,4}]heptan-2-ones. The bicycloheptanones (**41**) and (**42**) are easily prepared

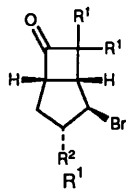


Scheme 3.

on a large scale,[8] and for both compounds the double bond can be functionalised in a highly stereoselective manner by known methods[9] to give the bicycloheptanones (**43**)–(**48**). The bromohydrins (**44**) and (**48**) were converted into the silylated derivatives (**49**) and (**50**).



(**41**) R^1 = Me
(**42**) R^1 = Ph



	R^1	R^2
(**43**)	Me	Br
(**44**)	Me	OH
(**45**)	Ph	Br
(**46**)	Ph	OAc
(**47**)	Ph	OMe
(**48**)	Ph	OH
(**49**)	Me	$OSiMe_2Bu^t$
(**50**)	Ph	$OSiMe_2Bu^t$

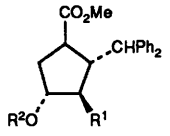
Dehydrobromination of compounds (**43**), (**45**)–(**47**), (**49**), and (**50**) gave a series of tricyclo[3.2.0.0.^{1,4}]heptanones (**51**)–(**56**). A crystal structure of compound (**52**) was obtained.[10]

The 3,3-dimethyltricycloheptanone (**55**) reacted with methoxide ion in a non-regioselective manner (as expected from other results involving the tricycloheptane as a reactive intermediate[11]) to give the bicycloheptan-2-one (**57**) and the bicycloheptan-6-one (**59**) in the ratio 9.5:1 (93% yield). Reaction of the strained tricyclic ketone (**55**) with toluene-α-thiolate anion gave the sulphide (**58**) as the major product and a small amount of a second component, which we tentatively suggest to be the isomer (**60**).

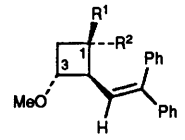
The diphenyltricycloheptanones (**52**)–(**54**) and (**56**) behaved in quite a different manner towards nucleophiles. Reaction of the bromo compound (**52**) with toluene-α-thiolate gave the bicyclo[3.2.0]heptan-6-one (**61**) as the only identifiable product (30%). The tricycle (**53**) produced the 2-fluorobicycloheptanone (**62**) (64%) on reaction with triethylamine tris-hydrofluoride. Iron dust and ammonium chloride converted the tricycloalkanone (**56**) into the chloro compound (**63**) (93%), while benzylamine added to the ketone (**54**) to furnish the bicyclic compound (**64**) in quantitative yield.

Obviously the two phenyl groups in compounds (**52**)–(**54**) and (**56**) restrict access of the nucleophile to C-4. In the above cases (unlike the 3,3-diphenyltricyclo[4.2.0.0^{1,4}]octan-2-ones) the C(1)–C(5) bond is sufficiently reactive and/or the approach to C-5 sufficiently unhindered to allow reaction at this alternative site to give the observed products (**61**)–(**64**).

Reaction of the tricyclic compound (**54**) with methoxide ion leads to a three-component mixture of products. Separation of the mixture by chromatography gave the ester (**66**) as the major product (38%). The compound is a single diastereoisomer: coupling constant data (see Experimental section) suggests that the methoxy carbonyl group is in the α-configuration but since such data are not always reliable this must remain a moot point. The least polar of the three compounds was the cyclobutanone derivative (**68**) (15%) and the other component was the diastereoisomer (**69**) (12%). Compounds (**68**) and (**69**) could be distinguished by NOE experiments. Irradiation of compound (**69**) at the frequency at which 3-H resonates produced a 16% enhancement in the signal assigned to 1-H.

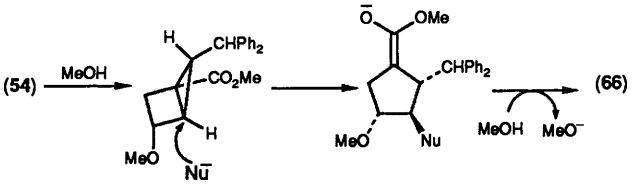


(**66**) R^1 = OMe, R^2 = Me
(**67**) R^1 = N_3, R^2 = H



(**68**) R^1 = CO_2Me, R^2 = H
(**69**) R^1 = H, R^2 = CO_2Me

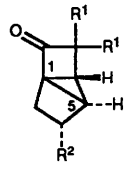
Presumably the mechanism of formation of the cyclobutane derivatives (**68**) and (**69**) is similar to that described in Scheme 2 for the homologous series. The production of the ester (**66**) may occur by nucleophilic attack of methoxide ion on the intermediate bicyclo[2.1.0]pentane (Scheme 4).



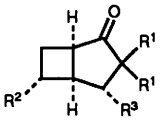
Scheme 4.

Credence was added to this idea by having a good nucleophile, azide ion, present during the reaction of the tricyclic compound (**53**) with methoxide ion in methanol. With this added ingredient, the reaction afforded only the azide (**67**) (49%) after 40 min at 0 °C. The intermediate formation of 2-azido-3-acetoxy (or hydroxy)-7,7-diphenylbicyclo[3.2.0]heptan-6-one is considered less likely since the cyclobutanone ring would not be cleaved under the mild conditions of the latter reaction.

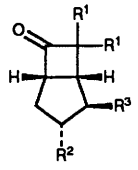
Lithium aluminium hydride reduction of the tricyclic compound (**53**) gave the diol (**70**) (44%) while lithium aluminium tri-t-butoxyhydride reduction of the same compound gave the ketone (**65**) (89%). For this series of compounds hydride ion preferentially attacks the tricyclic system at C-5.



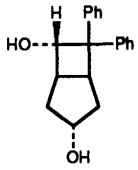
	R^1	R^2
(**51**)	Me	Br
(**52**)	Ph	Br
(**53**)	Ph	OAc
(**54**)	Ph	OMe
(**55**)	Me	$OSiMe_2Bu^t$
(**56**)	Ph	$OSiMe_2Bu^t$



(**57**) R^1 = Me, R^2 = $OSiMe_2Bu^t$, R^3 = OMe ..... (**59**)
(**58**) R^1 = Me, R^2 = $OSiMe_2Bu^t$, R^3 = SCH_2Ph ... (**60**)

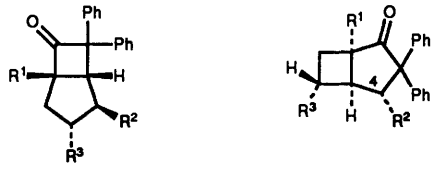


(**61**) R^1 = Ph, R^2 = Br, R^3 = SCH_2Ph
(**62**) R^1 = Ph, R^2 = OAc, R^3 = F
(**63**) R^1 = Ph, R^2 = $OSiMe_2Bu^t$, R^3 = Cl
(**64**) R^1 = Ph, R^2 = OMe, R^3 = $NHCH_2Ph$
(**65**) R^1 = Ph, R^2 = OAc, R^3 = H



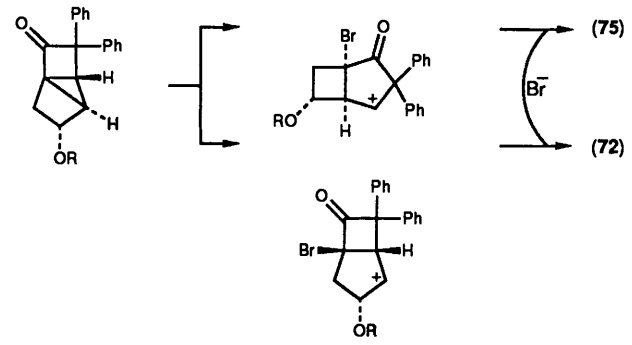
(70)

Reaction of the tricyclo[3.2.0.0^{1,4}]heptanone (**53**) with bromine gave the 2,5-dibromobicyclo[3.2.0]heptan-6-one (**71**) (39%) and the 1,4-dibromobicyclo[3.2.0]heptan-2-one (**74**) (56%). The latter compound showed the signal due to 4-H at an anomalously lowfield position in the NMR spectrum (δ 5.83). However an *X*-ray study confirmed the structure of the major component[10] and indicated that the proton 4-H falls into the deshielding region created by the phenyl group occupying the *endo*-configuration at C-3. This effect is not seen in the homologous series [*e.g.* compound (**39**)] presumably owing to the fact that the less rigid bicyclo[3.3.0]octanone system allows the phenyl group to occupy a less crowded space at a greater distance from 4-H. The reaction of the tricyclic ketone (**54**) with



(**71**) $R^1 = R^2 = Br$, $R^3 = OAc$ .... (**74**)
(**72**) $R^1 = R^2 = Br$, $R^3 = OMe$ .... (**75**)
(**73**) $R^1 = PhSe$, $R^2 = Cl$, $R^3 = OAc$ .... (**76**)
(**77**) $R^1 = PhSe$, $R^2 = Cl$, $R^3 = OMe$

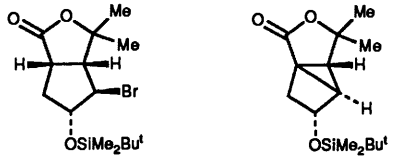
bromine gave the two products (**72**) and (**75**) in the ratio 1:7 (77%). The relatively small amount of the bicyclo[3.2.0]heptan-6-one reflects less stabilization of the incipient carbenium ion at C-2 by the methoxy group compared to the effect of the acetoxy group (Scheme 5). In accord with this suggestion, the tricycloalkanone (**53**) reacted with benzeneselenenyl chloride to



Scheme 5.

give a mixture of the ketones (**73**) and (**76**) in the ratio (2:9) (69% yield) while the tricycloalkanone (**54**) gave only the ketone (**77**) (89% yield) when treated with the same reagent.

Finally, the ketone (**49**) was oxidised to the lactone (**78**) using *m*-chloroperoxybenzoic acid. Treatment of the lactone with potassium t-butoxide gave the tricyclic compound (**79**). The



(**78**) (**79**)

latter compound did not react with nucleophiles (*e.g.* thiolate ion) under the conditions required to transform the corresponding tricyclo[3.3.0.0]octan-2-ones and the tricyclo[3.2.0.0]heptan-2-ones described above.

X-Ray crystallographic analysis of the lactone (**79**) (see Figure 2) allowed a comparison of the structures of compounds (**20**), (**52**), and (**79**). Some of the data are described in Table 2.

There are some discernible trends in the data for these three compounds, for which we expect an increase in inherent strain in the order (**79**) < (**20**) < (**52**). First, the bond angle C(2)–C(1)–C(7/8) increases in line with the strain in the compound giving a maximum value of 149.2° for the tricyclo-

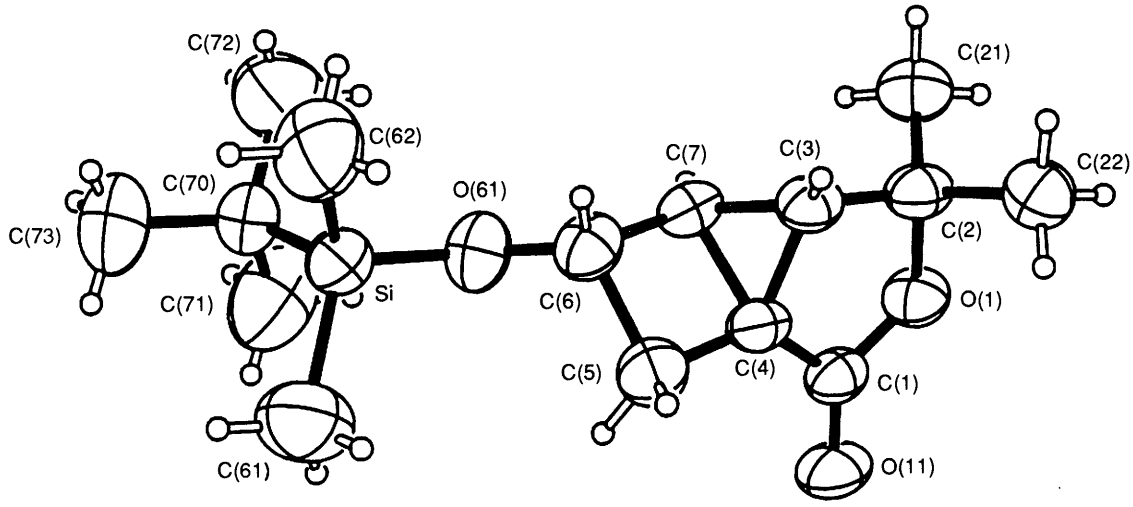


Figure 2. Crystal data for compound (**79**). $C_{15}H_{26}O_3Si$, M = 282.5, Triclinic, space group $P\bar{1}$, Z = 2, a = 6.891(2), b = 8.152(2), c = 15.887(9) Å, α = 76.76(4), β = 87.02(4), γ = 87.06(2)°, U = 1 475.0(9) Å^3, $F(000)$ = 324. The structure was solved by direct methods from data collected at 295 K to 2θ = 98° on a Nicolet R3m/V diffractometer with monochromatised Cu-K_α X-radiation. For the 1 629 observed reflections [$I > 3.0\ \sigma(I)$], and with anisotropic thermal parameters for all non-hydrogen atoms, R = 0.050, R_w = 0.065, goodness-of-fit = 1.68. Atomic co-ordinates are given in Table 5. Tables of bond lengths, bond angles, thermal parameters and hydrogen atom co-ordinates are available from the Cambridge Crystallographic Data Centre (see Instructions for Authors (1990), *J. Chem. Soc., Perkin Trans 1*, 1990, Issue 1).

Table 3. Biotransformation of bicyclo[4.2.0]oct-2-en-7-one using whole cell systems.

Micro-organism	Yield (%) Ketone	Alcohol	Configuration of alcohol	Optical purity[c] (% e.e.)
C. pasteurianum	0	5	1(*S*),6(*R*),7(*S*)	⩾96
C. tyrobutyricum (La 1)[a]	36	48	1(*R*),6(*S*),7(*R*)	77
C. tyrobutyricum (La 1)[b]	24	28	1(*R*),6(*S*),7(*R*)	43
C. kluyveri	30	40	1(*S*),6(*R*),7(*S*)	57

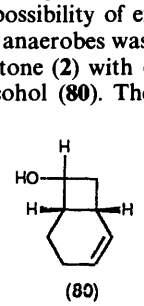
[a] Micro-organism grown on glucose. [b] Micro-organism grown on crotonate. [c] Determined by polarimetry.

alkanone (**52**). Compounds with more distorted tetravalent carbon atoms have been reported in the literature[12] but the value of 149.2° may represent the largest bond angle around a tetra-co-ordinate carbon centre recorded by *X*-ray analysis of a compound at room temperature. The C(4)–C(5) bond length decreases in the series (**79**) > (**20**) > (**52**) and the bond angle C(5)–C(1)–C(4) also decreases in the same order. For all three compounds the carbon atom C(1) occupies a position very close to the plane containing three of its bonding partners, namely C(2), C(4), and C(7/8).

In conclusion, the tricyclo[3.3.0.0^{1,4}]octan-3-ones (**19**)–(**22**) and the tricyclo[3.3.0.0^{1,4}]heptan-2-ones (**51**)–(**56**) have been prepared and have been found to be surprisingly stable. The compounds can be stored under an inert atmosphere at 0 °C for an indefinite period. Reactions of the tricycloalkanones with a variety of nucleophilic and electrophilic reagents take place readily, often with high regio- and stereo-selectivity. Most nucleophiles attack the cyclopropyl ring that forms the heart of the tricyclic molecules. On the other hand, oxyanions, perhaps because of their harder nature, attack the carbonyl carbon atom preferentially. In view of this, it may be possible to design a suitable tricyclo[3.2.0.0^{1,4}]alkanone to act as a protease inhibitor, with the reactive bicyclo[2.1.0]alkane carboxylic ester being unmasked after initial attack by a serine residue in the active site of the enzyme.

Studies Concerning the Resolution of Bicyclo[4.2.0]*octanone* (**2**) *using* Clostridia.—In view of the usefulness of bicyclo[3.2.0]heptanones and bicyclo[4.2.0]heptanones as starting materials in organic synthesis as illustrated above, it was of interest to us to investigate a new method for the provision of optically active materials in the latter series of compounds. Thus bicyclo[3.2.0]hept-2-en-6-one and the 7,7-dimethyl derivative (**41**) can be resolved using fungi or dehydrogenase enzymes,[13] while 6-acetoxybicyclo[3.2.0]hept-2-ene and 7-acetoxybicyclo-[4.2.0]oct-2-enol are hydrolysed in enantioselective fashion by certain lipases.[14] The possibility of effecting the resolution of bicycloalkanones using anaerobes was investigated.

Incubation of the ketone (**2**) with *Clostridium* spp gave the corresponding *endo*-alcohol (**80**). The yields, optical purities,



(80)

and absolute configuration of the products obtained are listed in Table 3. *Clostridium pasteurianum* gave a low yield of the dextrorotatory enantiomer in an optically pure state. *C. kluyveri* gave a better yield of the same compound but the optical purity was poor. *C. tyrobutyricum* provided the laevorotatory alcohol in 77% e.e. when the organism was grown on glucose. The same enantiomer was produced preferentially when the organism was grown on crotonate[15] but the enantiomeric excess was disappointing. Thus *Clostridium* spp can be included in the number of micro-organisms that have been shown to effect the enantioselective reduction of bicycloalkanones.

Experimental

General.—Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium–benzophenone ketyl immediately prior to use. Methanol (MeOH) was distilled from magnesium methoxide. Unless indicated otherwise, LP (40–60) refers to the light petroleum fraction of b.p. from 40–60 °C and LP (60–80) that fraction of b.p. 60–80 °C; both were distilled from phosphorus pentoxide (P_2O_5) and stored over sodium. Dimethylformamide (DMF) was stirred over anhydrous copper(II) sulphate for 24 h, and then distilled from calcium hydride. This was then stored over 4 Å molecular sieves under argon, and used when required. All reactions involving organometallic reagents or other moisture-sensitive reactants were executed under an atmosphere of dry nitrogen or argon. M.p.s were carried out on an 'Electrothermal' device, and are uncorrected. IR spectra were recorded on a Perkin-Elmer 881 grating infrared spectrophotometer as either solutions in chloroform, neat, or as mulls in Nujol, as indicated. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM250 spectrometer. Spectra are quoted for solutions in $CDCl_3$, with Me_4Si as internal standard, unless otherwise indicated. High resolution mass spectra were run at the SERC Mass Spectrometry Centre, Swansea, using a VG ZAB-E High Resolution instrument. Elemental analyses were conducted both by C.H.N. Analysis Ltd., Leicester, and by The Chemical Analysis Department, Glaxo Group Research, Ware. Single-crystal X-ray analyses were obtained from three different sources: Glaxo Group Research, Greenford; Chemistry Department, Imperial College, London; Chemistry Department, Bath University.

2exo-*Bromo*-3endo-*hydroxybicyclo*[4.2.0]*octan*-7-*one* (**5**).—To a stirred solution of bicyclo[4.2.0]oct-2-en-7-one (**2**) (0.89 g) in acetone (15 ml) and water (5 ml) was added, 1,3-dibromo-5,5-dimethylhydantoin (DDH) (2.58 g) portionwise. After addition was complete, stirring was continued for 1 h and then 10% aqueous sodium metabisulphite was added until the yellow colour disappeared. The solvent was removed under reduced pressure and the residue was extracted with dichloromethane (4 × 20 ml). The combined extracts were dried and evaporated to give an oil which was chromatographed over silica using 50–90% ether in LP (40–60) as eluant to give the *title compound* (**5**) (0.89 g), ν_{max} 3 298 and 1 765 cm^{-1}; $\delta(CD_2Cl_2)$ 3.70–3.62 (2 H, m, 2-H and 3-H), 3.42 (1 H, m, 6-H), 3.34 (1 H, m, 8*exo*-H), 3.01 (1 H, m, 1-H), 2.65 (1 H, m, 8*endo*-H), 2.57 (1 H, br s, OH), 2.10 (1 H, m, 5*endo*-H), 1.99 (1 H, m, 4*exo*-H), 1.61 (1 H, m, 5*exo*-H), and 1.34 (1 H, m, 4*endo*-H) (Found: M^+, 219.0026. $C_8H_{12}{}^{79}BrO_2$ requires M + H 219.0020).

3endo-*Acetoxy*-2exo-*bromobicyclo*[4.2.0]*octan*-7-*one* (**6**).—To a stirred solution of bicyclo[4.2.0]oct-2-en-7-one (**2**) (0.51 g) in acetic acid (6 ml) and dichloromethane (2 ml) was added DDH (1.07 g) portionwise. After the addition was complete, stirring was continued for 45 min at room temp. 10% Aqueous sodium metabisulphite was added until a colourless solution was obtained. Water (10 ml) was added and the solution was extracted with dichloromethane (4 × 20 ml). The organic

extracts were combined, washed with water (10 ml), and 2M aqueous sodium carbonate (2 × 10 ml). The organic phase was dried and evaporated to give an oil which was chromatographed over silica using 25% ether in LP (40–60) as eluant to give the *title compound* (**6**) (0.58 g), ν_{max}(Nujol) 1 786 and 1 743 cm^{-1}; $\delta(CDCl_3)$ 4.97 (1 H, dm, *J* 10.2 Hz, 3-H), 3.73 (1 H, dd, *J* 10.2 and 9.2 Hz, 2-H), 3.45 (1 H, tm, 6-H), 3.38 (1 H, ddd, *J* 16.5, 8.6, and 2.4 Hz, 8*exo*-H), 3.05 (1 H, m, 1-H), 2.72 (1 H, ddd, *J* 16.5, 2.6, and 1.6 Hz, 8*endo*-H), 2.13 (1 H, m, 5*endo*-H), 2.10 (3 H, s, Me), 2.00 (1 H, m, 4*exo*-H), 1.71 (1 H, m, 5*exo*-H), and 1.48 (1 H, m, 4*endo*-H) (Found: M^+, 263.0084. $C_{10}H_{14}{}^{81}BrO_3$ requires *M*, 263.0106).

2exo-*Bromo*-3endo-*methoxybicyclo*[4.2.0]*octan*-7-*one* (**7**).—Bicyclo[4.2.0]oct-2-en-7-one (**2**) (1.0 g) was dissolved in methanol (10 ml) and DDH (2.58 g) was added portionwise with stirring at room temp. After 2 h 10% aqueous sodium metabisulphite was added until the yellow colour was discharged. The methanol was removed under reduced pressure and the residue was extracted with dichloromethane (3 × 20 ml). The combined organic fractions were dried and evaporated to give a residue which was chromatographed over silica to give the title compound (0.84 g), m.p. 61–63 °C; ν_{max} 1 778 and 1 117 cm^{-1}; $\delta(CDCl_3)$ 3.77 (1 H, t, *J* 8.6 Hz, 2-H), 3.41 (3 H, s, Me), 3.45–3.25 (3 H, m, 3-H, 6-H and 8*exo*-H), 2.99 (1 H, m, 1-H), 2.77 (1 H, dt, *J* 16 and 1.5 Hz, 8*endo*-H), 2.10—1.98 (2 H, m, 4*exo*-H and 5*endo*-H), 1.61 (1 H, m, 5*exo*-H), and 1.39 (1 H, m, 4*endo*-H).

2exo,3endo-*Dibromobicyclo*[4.2.0]*octan*-7-*one* (**8**).—A solution of bromine (0.5 ml) in carbon tetrachloride (4 ml) was added dropwise to a suspension of sodium hydrogencarbonate (1.7 g), the ketone (**2**) (1.0 g), and carbon tetrachloride (14 ml) under nitrogen at 0 °C. Stirring was continued at 0 °C for 2 h before the reaction was cooled to −14 °C for 18 h. The mixture was filtered, and the residue washed with carbon tetrachloride (5 ml). The solvent was evaporated to give an oil which was chromatographed over silica to give the *title compound* (**8**) (1.16 g), m.p. 67–69 °C (ether); ν_{max}(Nujol) 1 763 cm^{-1}; $\delta(CDCl_3)$ 4.25 (1 H, dm, *J* 9 Hz, 3-H), 4.03 (1 H, dd, *J* 9.3 and 7.8 Hz, 2-H), 3.45 (1 H, m, 6-H), 3.35 (1 H, ddd, *J* 16.5, 8.7, and 2.9 Hz, 8*exo*-H), 3.10 (1 H, m, 1-H), 2.94 (1 H, ddd, *J* 16.5, 3.5, and 1.6 Hz, 8*endo*-H), 2.40 (1 H, m, 4*exo*-H), 2.12 (1 H, m, 5*endo*-H), 1.95 (1 H, m, 4*endo*-H), and 1.69 (1 H, m, 5*exo*-H (Found: C, 34.2; H, 3.6; Br, 56.8. $C_8H_{10}Br_2O$ requires C, 34.1; H, 3.6; Br, 56.7%).

3endo-*Acetoxy*-2exo-*bromo*-8,8-*dimethylbicyclo*[4.2.0]*octan*-7-*one* (**10**).—To the ketone (**3**) (2.01 g) in glacial acetic acid (20 ml) and dichloromethane (6 ml) was added DDH (3.51 g) portionwise with stirring. After reaction (1 h), work-up and chromatography as described for compound (**6**) gave the *acetoxy ketone* (**10**) (3.23 g), m.p. 112–113 °C; $\delta(CDCl_3)$ 4.90 (1 H, td, *J* 10.3, 4.2 Hz, 3-H), 3.79 (1 H, t, *J* 10.3 Hz, 2-H), 3.66 (1 H, ddd, *J* 10.3, 8.3, and 2.9 Hz, 6-H), 2.81 (1 H, t, *J* 10.3 Hz, 1-H), 2.07 (3 H, s, Ac), 2.14–1.89 (2 H, m, 4*exo*-H and 5*endo*-H), 1.67 (1 H, m, 5*exo*-H), 1.35 (1 H, m, 4*endo*-H), and 1.41 and 1.23 (6 H, 2 × s, CMe_2) (Found: $M + NH_4^+$, 306.0706. $C_{12}H_{17}{}^{79}BrO_3$ requires $M + NH_4$, 306.0705).

2exo,3endo-*Dibromo*-8,8-*dimethylbicyclo*[4.2.0]*octan*-7-*one* (**11**).—To a stirred suspension of sodium hydrogen carbonate (0.76 g) in the ketone (**3**) (1.02 g) and carbon tetrachloride (6 ml) at 0 °C was added a solution of bromine (1.07 g) in carbon tetrachloride (3 ml) dropwise under an atmosphere of nitrogen. On completion of the addition the reaction mixture was treated as described for compound (**8**) to give the dibromo compound (**11**) (0.90 g), m.p. 72–74 °C; $\delta(CDCl_3)$ 4.05 (1 H, td, *J* 10.6 and 3.9 Hz, 3-H), 3.88 (1 H, dd, *J* 10.6 and 9.4 Hz, 2-H), 3.69 (1 H, ddd, *J* 10.7, 8.4, and 2.5 Hz, 6-H), 2.88 (1 H, dd, *J* 10.7 and 9.4 Hz, 1-H), 2.37 (1 H, ddd, *J* 17.8, 9.5, and 2.5 Hz, 5*endo*-H), 2.09 (1 H, ddd, *J* 14.2, 6.9, and 3.9 Hz, 4*exo*-H), 1.85 (1 H, m, 5*exo*-H), 1.62 (1 H, m, 4*endo*-H), and 1.41 and 1.23 (6 H, 2 × s, CMe_2) (Found: $[M + NH_4]^+$ 327.9736. $C_{10}H_{14}{}^{79}Br^{81}BrO$ requires $M + NH_4$ 327.9735).

3endo-*Acetoxy*-2exo-*bromo*-8,8-*diphenylbicyclo*[4.2.0]*octan*-7-*one* (**13**).—DDH (0.92 g) was added portionwise to a stirred solution of the ketone (**4**) (0.97 g) in glacial acetic acid (7 ml), and dichloromethane (7 ml) at room temp. under an atmosphere of nitrogen. After 45 min the reaction was treated as described for compound (**6**) to give the title compound (1.01 g), m.p. 135–137 °C; $\delta(CDCl_3)$ 7.52–7.23 (10 H, m, ArH), 5.01 (1 H, td, *J* 10.8 and 3.8 Hz, 3-H), 4.06 (1 H, dd, *J* 10.8 and 8.8 Hz, 2-H), 3.63 (1 H, dd, *J* 10.7 and 8.8 Hz, 1-H), 3.51 (1 H, m, 6-H), 2.26 (1 H, m, 5*endo*-H), 2.02 (3 H, s, $COCH_3$), 2.00 (1 H, m, 4*exo*-H), 1.70 (1 H, m, 5*exo*-H), and 1.40 (1 H, m, 4*endo*-H) (Found: $M + NH_4^+$ 430.1023. $C_{22}H_{21}{}^{79}BrO_3$ requires $M + NH_4$ 430.1018).

2exo-*Bromo*-3endo-*t-butyldimethylsilyloxybicyclo*[4.2.0]-*octan*-7-*one* (**14**).—To a stirred solution of t-butyldimethylsilyl chloride (1.23 g) and imidazole (1.12 g) in dry dimethylformamide (DMF) (6 ml) was added a solution of the bromohydrin (**5**) (1.50 g) in dry DMF (5 ml). After 24 h the mixture was diluted with water (10 ml) and extracted with ether (4 × 10 ml). The organic extracts were washed with water (2 × 10 ml), dried, and evaporated to leave a residue which was chromatographed over silica using 40% ether in LP (40–60) as eluant to give the title compound (2.04 g), m.p. 34–36 °C; $\delta(CDCl_3)$ 3.80 (1 H, td, *J* 8.2 and 3.5 Hz, 3-H), 3.72 (1 H, t, *J* 8.2 Hz, 2-H), 3.32 (1 H, m, 6-H), 3.25 (1 H, ddd, *J* 16.2, 8.8, and 3.0 Hz, 8*exo*-H), 2.96 (1 H, m, 1-H), 2.83 (1 H, ddd, *J* 16.2, 3.7, and 1.8 Hz, 8*endo*-H), 2.06 (1 H, m, 5*endo*-H), 1.91 (1 H, m, 4*exo*-H), 1.62 (1 H, m, 5*exo*-H), 1.42 (1 H, m, 4*endo*-H), 0.88 (9 H, s, Bu^t), and 0.12 and 0.07 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 334.0789. $C_{14}H_{25}{}^{81}BrO_2Si$ requires *M*, 334.0786).

2exo-*Bromo*-3endo-*t-butyldimethylsilyloxy*-8,8-*diphenylbicyclo*[4.2.0]*octan*-7-*one* (**15**).—To the ketone (**4**) (0.97 g) in acetone (15 ml) and water (5 ml) was added DDH (1.15 g) portionwise with stirring. After 1 h, 10% aqueous sodium metabisulphite was added until the yellow colour was discharged. The acetone was removed under reduced pressure and the residue was extracted with dichloromethane (4 × 20 ml). The combined organic fractions were dried and evaporated to give a residue which was chromatographed over silica using 50–90% ether in LP (40–60) as eluant to give the bromohydrin (**12**) (0.79 g), m.p. 150–152 °C and 2*endo*-bromo-3*exo*-hydroxy-8,8-diphenylbicyclo[4.2.0]octan-7-one (0.22 g). The bromohydrin (**12**) (0.72 g) in dry DMF (4 ml) was added dropwise to a stirred solution of t-butyldimethylsilyl chloride (0.36 g) and imidazole (0.35 g) in dry DMF (2 ml) under an atmosphere of argon. After 22 h the reaction was worked up as described for compound (**14**) to give the required product (**15**), m.p. 119–121 °C, ν_{max}($CHCl_3$) 1 775 cm^{-1} (Found: M^+, 486.1410. $C_{26}H_{33}{}^{81}BrO_2Si$ requires *M*, 486.1412).

General Procedure for the Preparation of Tricyclo[3.3.0.$0^{1,4}$]-*octan*-2-*ones* (**16**)–(**22**).—To a stirred suspension of potassium t-butoxide in dry ether at −78 °C was added the 2-bromobicyclo-octan-7-one in dry ether dropwise under an atmosphere of argon. The mixture warmed to 0 °C over 1 h. After 30 min the solution was filtered through Celite and the solvent evaporated to give the tricyclic compound.

6-*Acetoxytricyclo*[3.3.0.0^{1,4}]*octan*-2-*one* (**16**).—The ketone (**6**) (0.12 g) in ether (3.5 ml) was dehydrobrominated using potassium t-butoxide (0.07 g) in ether (5.5 ml) to give the *title compound* (0.05 g); δ(CDCl$_3$) 5.13 (1 H, d, *J* 5.0 Hz, 6-H), 2.72 (1 H, dd, *J* 15 and 3.5 Hz, 3*endo*-H), 2.58 (1 H, br s, 4-H), 2.30–2.12 (3 H, m, 5-H, 3*exo*-H and 8*exo*-H), 2.04 (3 H, s, OCOCH$_3$), 2.04 (1 H, m, 8*endo*-H), 1.85 (1 H, m, 7-H), and 1.46 (1 H, m, 7-H); δ$_c$(CDCl$_3$) 190.90, 170.39, 73.67, 61.50, 46.34, 44.48, 29.16, 23.07, 21.11, and 20.73.

6-*Acetoxy*-3,3-*dimethyltricyclo*[3.3.0.0^{1,4}]*octan*-2-*one* (**19**).—The ketone (**10**) (0.52 g) in ether (13 ml) was dehydrobrominated using potassium t-butoxide (0.25 g) in ether (22 ml) to give the *title compound* (**19**) (0.36 g) as an oil; ν$_{max}$ 1 750 br and 1 245 cm^{-1}; δ(CDCl$_3$) 5.08 (1 H, d, *J* 7.0 Hz, 6-H), 2.48 (1 H, m, 4-H), 2.29 (1 H, m, 5-H), 2.17 (1 H, m, 8*exo*-H), 2.02 (3 H, s, OCOCH$_3$), 1.94 (1 H, m, 8*endo*-H), 1.80 (1 H, m, 7*exo*-H), 1.39 (1 H, m, 7*endo*-H), 1.19 (3 H, s, Me), and 0.91 (3 H, s, Me).

6-*Bromo*-3,3-*dimethyltricyclo*[3.3.0.0^{1,4}]*octan*-2-*one* (**20**).—The ketone (**11**) (0.25 g) in ether (6 ml) was dehydrobrominated using potassium t-butoxide (0.11 g) in ether (10 ml) to give the *title compound* (**20**) (0.15 g) as colourless cubes, m.p. 81–82 °C; δ(CDCl$_3$) 4.39 (1 H, d, *J* 5 Hz, 6-H), 2.86 (1 H, m, 4-H), 2.44–2.31 (2 H, m, 5-H and 8*exo*-H), 2.12 (1 H, ddd, *J* 16.0, 7.0, and 0.5 Hz, 7*exo*-H), 1.99 (1 H, dd, *J* 13.0, 6.6 Hz, 8*endo*-H), and 1.70 (1 H, m, 7*endo*-H) (Found: *M*$^+$, 149.0961. C$_{10}$H$_{13}$BrO requires *M* − Br, 149.0966).

6-*Acetoxy*-3,3-*diphenyltricyclo*[3.3.0.0^{1,4}]*octan*-2-*one* (**21**).—The ketone (**13**) (0.89 g) in ether (15 ml) was dehydrobrominated using potassium t-butoxide (0.36 g) in ether (30 ml) to give the *title compound* (**21**) (0.45 g) as an oil; δ(CDCl$_3$) 7.4–7.2 (10 H, m, ArH), 5.22 (1 H, d, *J* 4.9 Hz, 6-H), 3.22 (1 H, m, 4-H), 2.29 (1 H, br s, 5-H), 2.30 (1 H, m, 8*exo*-H), 2.10 (1 H, dd, *J* 12.8, 7.0 Hz, 8*endo*-H), 1.92 (3 H, s, OAc), 1.87 (1 H, m, 7*exo*-H), and 1.52 (1 H, m, 7*endo*-H).

6-*t-Butyldimethylsilyloxy*-3,3-*diphenyltricyclo*[3.3.0.0^{1,4}]-*octan*-2-*one* (**22**).—The ketone (**15**) (0.74 g) in ether (11 ml) was dehydrobrominated using potassium t-butoxide (0.22 g) in ether (19 ml) to give the *title compound* (**22**) (0.47 g) as an oil; δ(CDCl$_3$) 7.41–7.26 (10 H, m, ArH), 4.34 (1 H, d, *J* 4.6 Hz, 6-H), 3.13 (1 H, d, 4-H), 2.40 (1 H, m, 8*exo*-H), 2.25 (1 H, br s, 5-H), 2.12 (1 H, m, 8*endo*-H), 1.81 (1 H, m, 7*exo*-H), 1.46 (1 H, m, 7*endo*-H), 0.91 (9 H, s, Bu^t), and 0.10 and 0.05 (6 H, 2 × s, SiMe$_2$).

6-*Acetoxybicyclo*[3.3.0]*oct*-3-*en*-2-*one* (**23**).—To a stirred solution of the tricyclic ketone (**16**) (0.048 g) in dichloromethane (2 ml) was added a few drops of diazobicycloundecene. After 2 h saturated aqueous ammonium chloride was added; the organic phase was separated and the aqueous phase washed with dichloromethane (3 × 5 ml). The combined organic extracts were dried, and evaporated to give an oil which was chromatographed over silica [eluant 50% ether/LP (40–60)] to give the *title compound* (0.034 g) ν$_{max}$ 1 737 and 1 586 cm^{-1}; δ(CDCl$_3$) 7.70 (1 H, dd, *J* 5.7, 2.9 Hz, 4-H), 6.20 (1 H, dd, *J* 5.7, 2.0 Hz, 3-H), 5.06 (1 H, d, *J* 4.3 Hz, 6-H), 3.37 (1 H, m, 5-H, 2.83 (1 H, ddd, *J* 9.8, 5.8, and 1.8 Hz, 1-H), 2.12 (1 H, m, 8*exo*-H), 2.05 (3 H, s, OAc), 1.95 (1 H, m, 8*endo*-H), 1.79 (1 H, m, 7*exo*-H), and 1.54 (1 H, m, 7*endo*-H) (Found: *M*$^+$, 181.0856. Calc. for C$_{10}$H$_{12}$O$_3$, *M* + H, 181.0865).

6-*t-Butyldimethylsilyloxybicyclo*[3.3.0]*oct*-3-*en*-2-*one* (**24**).—To the ketone (**18**) (0.31 g) was added *N*-benzyltrimethylammonium hydroxide (1 ml) in methanol (20 ml). After 2 h, the reaction mixture was concentrated under reduced pressure and the residue was chromatographed over silica [eluant 10% ether in LP (40–60)] to give the *title compound* (0.19 g) as an oil, ν$_{max}$(neat) 1 714 cm^{-1}; δ(CDCl$_3$) 7.50 (1 H, dd, *J* 5.6, 2.8 Hz, 4-H), 6.03 (1 H, dd, *J* 5.6, 2.1 Hz, 3-H), 4.06 (1 H, dd, *J* 3.8, 0.8 Hz, 6-H), 3.12 (1 H, m, 5-H), 2.71 (1 H, ddd, *J* 9.8, 5.7, and 1.4 Hz, 1-H), 2.08 (1 H, tdd, *J* 13.0, 9.8, and 6.6 Hz, 8*exo*-H), 1.75 (1 H, dddd, *J* 13, 7, 1.4, and 1.0 Hz, 8*endo*-H), 1.50 (1 H, ddd, *J* 13, 6.6, and 0.8 Hz, 7*exo*-H), 1.29 (1 H, tdd, *J* 13, 7, and 3.8 Hz, 7*endo*-H), 0.90 (9 H, s, Bu^t), and 0.05 (6 H, 2s, SiMe$_2$) (Found: *M*$^+$, 270.1891. C$_{14}$H$_{24}$O$_2$Si requires *M* + NH$_4$, 270.1889).

6exo-*Bromo*-4exo-*cyanobicyclo*[3.3.0]*octan*-2-*one* (**25**).—To a solution of the ketone (**17**) (0.44 g) in methanol (5 ml) at 0 °C was added potassium cyanide (0.28 g). After 1 h, chloroform (15 ml) and water (15 ml) were added. The two layers were separated and the aqueous phase was extracted with chloroform (3 × 10 ml). The combined organic fractions were dried and evaporated and the residue was chromatographed over silica using 40% ether in LP (40–60) as eluant to give the *title compound* (**25**) (0.08 g), m.p. 89–91 °C; δ(CDCl$_3$) 4.15 (1 H, m, 6-H), 3.39 (1 H, m), 3.07 (1 H, m), 2.84–2.66 (3 H, m), 2.35 (1 H, m), 2.15–2.05 (2 H, m), and 1.90 (1 H, m).

4exo-*Benzylthio*-6exo-*t-butyldimethylsilyloxybicyclo*[3.3.0]-*octan*-2-*one* (**26**).—Toluene-α-thiol (0.1 g) and piperidine (1 drop) were added to the ketone (**18**) (0.19 g) in dry THF (5 ml) at room temp. with stirring under an atmosphere of argon. After 3 days the solvent was evaporated and the residue chromatographed over silica to give the *title compound* (**26**) (0.18 g) as an oil; ν$_{max}$ 1 742 cm^{-1}; δ(CDCl$_3$) 7.4–7.2 (5 H, m, ArH), 3.96 (1 H, td, *J* 4.3 and 2.8 Hz, 6-H), 3.77 (m, 2 H, SCH$_2$), 2.88 (1 H, tdm, *J* 10 and 1.7 Hz, 1-H), 2.75 (1 H, ddd, *J* 7.8, 7.5, and 6.5 Hz, 4-H), 2.60–2.48 (2 H, m, 3*exo*-H and 5-H), 2.33 (1 H, ddd, *J* 17.7, 7.8, and 1.7 Hz, 3*endo*-H), 2.10 (1 H, dm, *J* 10 Hz, 8-H), 1.74 (1 H, m, 8-H), 1.64–1.48 (2 H, m, 2 × 7-H), 0.87 (9 H, s, Bu^t), and 0.2–0.0 (6 H, 2 × s, SiMe$_2$) (Found: *M*$^+$, 394.2238. C$_{21}$H$_{32}$O$_2$SSi requires *M* + NH$_4$ 394.2237).

6exo-*Acetoxy*-4exo-*iodo*-3,3-*dimethylbicyclo*[3.3.0]*octan*-2-*one* (**27**).—To a solution of sodium iodide (0.5 g) in acetone (3 ml) at room temp. under an atmosphere of argon was added dropwise a solution of the ketone (**19**) (0.21 g) in dry ether (3 ml). After 2 min the solvent was evaporated, water (10 ml) was added, and the mixture was extracted with dichloromethane (4 × 6 ml). The combined organic fractions were dried and evaporated to give a residue which was purified by chromatography over silica using 20% ether in LP (40–60) as eluant to give the *title compound* (0.17 g), m.p. 102–104 °C; δ(CDCl$_3$) 5.07 (1 H, d, *J* 3.7 Hz, 6-H), 3.43 (1 H, d, *J* 9.7 Hz, 4-H), 3.14–3.06 (2 H, m, 1-H and 5-H), 1.98 (3 H, s, Ac), 2.02–1.52 (4 H, m, 2 × 7-H and 2 × 8-H), and 1.04 and 0.92 (6 H, 2 × s, CMe$_2$) (Found: *M*$^+$, 354.0571. C$_{12}$H$_{17}$IO$_3$ requires *M* + NH$_4$, 354.0567).

6exo-*Acetoxy*-4exo-[*bis*(1,1-*ethoxycarbonyl*)*methyl*]3,3-*dimethylbicyclo*[3.3.0]*octan*-2-*one* (**28**).—To a stirred slurry of sodium hydride (60% dispersion in oil; 0.045 g) in dry THF (1 ml) at 0 °C under an atmosphere of argon was added diethyl malonate (0.20 g) in anhydrous THF (5 ml). After 10 min, a solution of the ketone (**19**) (0.12 g) in dry ether (3 ml) was added over 2 min. After 1 h saturated aqueous ammonium chloride (10 ml) was added and the solution was extracted with ether (5 × 10 ml). The combined ethereal fractions were dried and evaporated: the residue was chromatographed over silica using 30% ether in LP (40–60) to give the *title compound* (**28**) (0.14 g), m.p. 66–68 °C; δ(CDCl$_3$) 5.02 (1 H, d, *J* 3.3 Hz, 6-H), 4.17–4.05 (4 H, m, 2 × CO$_2$CH$_2$), 3.46 [1 H, d, *J* 9.1 Hz, CH(CO$_2$Et)$_2$], 2.98 (1 H, m, 1-H), 2.66 (1 H, t, *J* 9.1 Hz, 5-H), 2.06 (1 H, t, *J* 9.1

Hz, 4-H), 1.89 (3 H, s, Ac), 1.93–1.83 (2 H, m, 2 × 8-H), 1.68 (1 H, m, 7*exo*-H), 1.50 (1 H, m, 7*endo*-H), 1.18 (6 H, t, *J* 7.1 Hz, 2 × $CO_2CH_2CH_3$), and 0.89 (6 H, s, CMe_2) (Found: C, 62.0; H, 7.6. $C_{19}H_{28}O_7$ requires C, 61.9; H, 7.7%).

6exo-*Acetoxy*-4exo-*fluoro*-3,3-*dimethylbicyclo*[3.3.0]*octan*-2-*one* (**29**).—To a solution of the ketone (**19**) (0.12 g) in dry dichloromethane (3 ml) at 0 °C under an atmosphere of argon was added triethylamine trishydrofluoride (0.2 ml). After 5 min, the reaction mixture was allowed to warm to room temp. and after 24 h saturated aqueous ammonium chloride (8 ml) was added. The mixture was extracted with dichloromethane (3 × 5 ml). The combined organic extracts were dried and evaporated to give an oil which was chromatographed over silica using 20% ether in LP (40–60) as eluant to give the *title compound* (**29**) (0.10 g), m.p. 42–44 °C; ν_{max} 1 740 and 1 728 cm^{-1}; $\delta(CDCl_3)$ 5.19 (1 H, m, 6-H), 4.34 (1 H, dd, *J* 53.3 and 6.4 Hz, 4-H), 3.19 (1 H, td, *J* 10.5 and 3.4 Hz, 1-H), 2.87 (1 H, ddd, *J* 25.5, 10.5, and 6.4 Hz, 5-H), 2.00–1.74 (3 H, m, 7*exo*-H, and 2 × 8-H), 1.50 (1 H, m, 7*endo*-H), and 1.04 (6 H, s, CMe_2) (Found: M^+, 246.1516. $C_{12}H_{17}FO_3$ requires $M + NH_4$, 246.1506).

4exo-*Azido*-6exo-*hydroxy*-3,3-*dimethylbicyclo*[3.3.0]*octan*-2-*one* (**30**).—To a stirred suspension of sodium azide (0.37 g) in methanol (3 ml) at 0 °C under an atmosphere of argon was added a solution of the ketone (**19**) (0.15 g) in cold (0 °C) methanol (3 ml) dropwise. After 18 h at 0 °C the solvent was evaporated and the residue taken up in water (10 ml) and dichloromethane (10 ml). The aqueous layer was separated and washed with dichloromethane (4 × 10 ml). The combined organic extracts were dried and evaporated to give a residue which was purified by chromatography over silica using 50–90% ether in LP (40–60) to give the title compound (**30**) (0.10 g) as an oil; ν_{max} 3 420, 2 100, and 1 740 cm^{-1}; $\delta(CDCl_3)$ 4.33 (1 H, d, *J* 3.5 Hz, 6-H), 3.14 (1 H, ddd, *J* 13.1, 10.4, and 2.6 Hz, 1-H), 3.02 (1 H, d, *J* 9.6 Hz, 4-H), 2.64 (1 H, t, *J* 9.6 Hz, 5-H), 2.45 (1 H, br s, OH), 2.09 (1 H, m, 8*exo*-H), 1.86 (1 H, m, 8*endo*-H), 1.74 (1 H, m, 7*exo*-H), 1.51 (1 H, m, 7*endo*-H), and 1.05 and 1.01 (6 H, 2 × s, CMe_2).

6exo-*Hydroxy*-3,3,4exo-*trimethylbicyclo*[3.3.0]*octan*-2-*one* (**31**).—To a stirred slurry of copper(I) iodide (1.12 g) in anhydrous ether (20 ml) at 0 °C under an atmosphere of argon was added methyl-lithium (1.4M solution in ether; 8.3 ml). After 5 min, a solution of the ketone (**19**) (0.12 g) in ether (3 ml) was added dropwise. After 20 min, saturated aqueous ammonium chloride (10 ml) was added. The mixture was stirred vigorously for 45 min and then extracted with ether (4 × 15 ml). The combined ethereal extracts were dried and evaporated to give an oil which was purified by chromatography over silica using 50% ether in LP (40–60) as eluant to give the *title compound* (**31**) (0.08 g) as an oil; ν_{max} 3 613, 3 451, and 1 732 cm^{-1}; $\delta(CDCl_3)$ 4.10 (1 H, d, *J* 3.4 Hz, 6-H), 2.95 (1 H, m, 1-H), 2.42 (1 H, br s, OH), 2.21 (1 H, m, 5-H), 2.04 (1 H, m, 8*exo*-H), 1.82 (1 H, m, 8*endo*-H), 1.61 (1 H, m, 7*exo*-H), 1.47 (1 H, m, 7*endo*-H), 1.03 (1 H, m, 4-H), 1.02 (3 H, d, *J* 1.7 Hz, $CHCH_3$), and 0.87 and 0.82 (6 H, 2 × s, CMe_2) (Found: M^+, 182.1299. $C_{11}H_{18}O_2$ requires *M*, 182.1307).

6exo-*t-Butyldimethylsilyloxy*-4exo-*cyano*-3,3-*diphenylbicyclo*[3.3.0]*octan*-2-*one* (**32**).—To a stirred solution of the ketone (**22**) (0.14 g) in dry toluene (2 ml) under an atmosphere of argon was added diethylaluminium cyanide (1.0M solution in toluene; 1.7 ml). After 75 min, 2M aqueous sodium hydroxide (10 ml) and ice were added. The solution was extracted with dichloromethane (3 × 15 ml) and the combined organic extracts were dried and evaporated. The residue was purified by chromatography over silica using 13% ether in LP (40–60) as eluant to give the *title compound* (**32**) (0.10 g) as an oil; ν_{max} 2 240 and 1 748 cm^{-1}; $\delta(CDCl_3)$ 7.5–7.2 (10 H, m, ArH), 4.40 (1 H, dm, *J* 3.8 Hz, 6-H), 3.22 (1 H, td, *J* 8.0 and 2.3 Hz, 1-H), 3.05–2.95 (2 H, m, 4-H and 5-H), 2.27 (1 H, m, 8*exo*-H), 2.05 (1 H, m, 8*endo*-H), 1.81 (1 H, m, 7*exo*-H), 1.66 (1 H, m, 7*endo*-H), 0.91 (9 H, s, Bu^t), and 0.15 and 0.13 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 431.2272. $C_{27}H_{33}NO_2Si$ requires *M*, 431.2280).

Reaction of 6-*t-Butyldimethylsilyloxy*-3,3-*diphenyltricyclo*-[3.3.0.$0^{1,4}$]*octan*-2-*one with Methoxide Ion*.—To a stirred suspension of sodium carbonate (0.16 g) in dry methanol (2 ml) at 0 °C under an atmosphere of argon was added the ketone (**22**) (0.11 g) in dry ether (3 ml). After 10 min, the reaction was warmed to room temp. Potassium t-butoxide (0.10 g) was added and stirring was continued overnight. Saturated aqueous ammonium chloride (10 ml) was added and the solution was extracted with dichloromethane (5 × 10 ml). The combined organic extracts were dried and evaporated under reduced pressure and the residue was chromatographed over silica using 5% ether in LP (40–60) to provide the *ester* (**34**) (0.02 g) as an oil; ν_{max} 1 728 cm^{-1}; $\delta(CDCl_3)$ 7.37–7.18 (10 H, m, ArH), 5.82 (1 H, d, *J* 10.8 Hz, =CH), 4.22 (1 H, dm, *J* 4.8 Hz, 3-H), 3.65 (3 H, s, OMe), 3.10 (1 H, m, 1-H), 2.94 (1 H, ddd, *J* 10.8, 8.3, and 4.8 Hz, 2-H), 2.15–1.53 (4 H, m, 2 × 4-H and 2 × 5-H), 0.84 (9 H, s, Bu^t), 0.01 and −0.02 (6 H, 2 × s, $SiMe_2$) (Found M^+, 454.2774. $C_{27}H_{36}O_3Si$ requires $M + NH_4$, 454.2778). The more polar isomer (**33**) (0.095 g) was obtained as an oil; ν_{max} 1 735 cm^{-1}; $\delta(CDCl_3)$ 7.36–7.24 (10 H, m, ArH), 5.85 (1 H, d, *J* 10.5 Hz, =CH), 4.05 (1 H, dm, *J* 7.3 Hz, 3-H), 3.58 (3 H, s, OMe), 3.00 (1 H, ddd, *J* 10.5, 9.4, and 7.3 Hz, 2-H), 2.63 (1 H, dm, *J* 9.4 Hz, 1-H), 2.13–1.64 (4 H, m, 2 × 4-H and 2 × 5-H), 0.90 (9 H, s, Bu^t), and 0.07 and 0.05 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 437.2513. $C_{27}H_{36}O_3Si$ requires M + H, 437.2512).

6-*t-Butyldimethylsilyloxy*-2-*hydroxytricyclo*[3.3.0.$0^{1,4}$]-*octane* (**35**) *and* 2-*Acetoxy*-6-*t-butyldimethylsilyloxytricyclo*-[3.3.0.$0^{1,4}$]*octane* (**36**).—To a stirred suspension of lithium aluminium hydride (0.02 g) in dry ether (1 ml) under an atmosphere of argon at −78 °C was added a solution of the ketone (**18**) (0.09 g) in ether (2 ml) dropwise. After 1 h the reaction mixture was poured into ice–water (15 ml) and the resultant mixture was extracted with ether (4 × 5 ml). The combined ethereal extracts were dried and evaporated to give a residue which was chromatographed over silica using 10% ether in petroleum to give the *alcohol* (**35**) (0.05 g); $\delta(CDCl_3)$ 4.18 (1 H, tdm, *J* 3.2 and 1.7 Hz, 2-H), 4.03 (1 H, d, *J* 4.7 Hz, 6-H), 1.77–1.62 (2 H, m, 2 × 3-H), 1.57 (1 H, dd, *J* 4.0 and 3.2 Hz, 4-H), 1.54 (1 H, dd, *J* 13.7 and 7.0 Hz, 7-H), 1.35 (1 H, s, 5-H), 1.13 (1 H, dtd, *J* 13.7, 7.0, and 4.7 Hz, 7-H), 0.89 (9 H, s, Bu^t), and 0.07 and 0.05 (6 H, 2 × s, $SiMe_2$). The alcohol (**35**) (0.05 g) in dry dichloromethane (1 ml) was added to a stirred solution of dimethylaminopyridine (4 mg), acetic anhydride (0.03 g), and pyridine (0.03 g) in dry dichloromethane (0.5 ml) at 0 °C under an atmosphere of argon. The reaction was stirred at room temp. for 24 h before ether (10 ml) and 0.5M hydrochloric acid (10 ml) was added. The aqueous phase was separated and extracted with ether (4 × 5 ml). The combined organic fractions were dried and evaporated to afford a residue which was chromatographed over silica using 20% ether in LP (40–60) to give the ester (**36**) (0.034 g) as an oil; $\nu_{max}(CHCl_3)$ 1 727 cm^{-1}; $\delta(CDCl_3)$ 4.88 (1 H, td, *J* 3.2 and 1.7 Hz, 2-H), 4.04 (1 H, d, *J* 4.6 Hz, 6-H), 2.09 (3 H, s, OAc), 2.03–1.70 (4 H, m, 2 × 3-H and 2 × 8-H), 1.61 (1 H, m, 4-H), 1.53 (1 H, dd, *J* 13.7 and 7.7 Hz, 7*exo*-H), 1.45 (1 H, s, 5-H), 1.12 (1 H, m, 7*endo*-H), 0.89 (9 H, s, Bu^t), and 0.08 and 0.06 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 297.1892. $C_{16}H_{28}O_3Si$ requires M + H, 297.1886).

2,6-*Diacetoxy*-3,3-*dimethyltricyclo*[3.3.0.0^{1,4}]*octane* (**37**).—To a stirred suspension of lithium aluminium hydride (2.87 ml, 5 equiv.) in THF at −78 °C under an atmosphere of argon was added the ketone (**19**) (0.125 g) in ether (4 ml) dropwise. After 45 min, the reaction was warmed to 4 °C and stirred for 18 h. Saturated aqueous ammonium chloride (10 ml) was added and the mixture was extracted with dichloromethane (6 × 10 ml). The combined organic extracts were dried and evaporated to give a solid which was recrystallized from ethyl acetate to give 2,6-dihydroxy-3,3-dimethyltricyclo[3.3.0.0^{1,4}]octane (0.08 g), m.p. 139–141 °C (Found: M^+, 186.1487. $C_{10}H_{16}O_2$ requires M + NH_4, 186.1494). The diol (0.06 g) in dichloromethane (1 ml) was added to acetic anhydride (0.04 g), pyridine (0.04 g), and dimethylaminopyridine (4 mg) in dichloromethane (0.5 ml) at room temp. under an atmosphere of argon. After 30 h, saturated aqueous ammonium chloride was added and the solution was extracted with dichloromethane (4 × 10 ml). The combined organic extracts were dried and evaporated to give a residue which was chromatographed over silica using 20% ether in LP (40–60) as eluant to give the *diester* (**37**) (0.07 g) as an oil; ν_{max} 1 740, 1 370, and 1 238 cm^{-1}; δ($CDCl_3$) 4.90 (1 H, d, *J* 5.0 Hz, 6-H), 4.45 (1 H, d, *J* 2.3 Hz, 2-H), 2.06 and 2.01 (6 H, 2 × s, 2 × OAc), 1.91–1.75 (2 H, m, 2 × 8-H), 1.67 (1 H, m, 7*exo*-H), 1.30 (1 H, d, *J* 2.3 Hz, 4-H), 1.22 (1 H, m, 7*endo*-H), and 1.03 and 0.86 (6 H, 2 × s, CMe_2) (Found: M^+, 270.1704. $C_{14}H_{20}O_4$ requires M + NH_4 270.1705).

6exo-*Acetoxy*-1,4exo-*dibromo*-3,3-*dimethylbicyclo*[3.3.0]*octan*-2-*one* (**38**).—To a solution of the ketone (**19**) (0.08 g) in carbon tetrachloride (2 ml) at 0 °C under an atmosphere of argon was added bromine (0.31 g) dropwise. On completion of the addition the solvent was removed and the residue was chromatographed over silica using 15% ether in LP (40–60) as eluant to give the *ketone* (**38**) (0.11 g), m.p. 97–99 °C; ν_{max} 1 755 and 1 237 cm^{-1}; δ($CDCl_3$) 5.20 (1 H, ddd, *J* 4.9, 3.2, and 0.9 Hz, 6-H), 3.46 (1 H, d, *J* 10.5 Hz, 4-H), 3.31 (1 H, dd, *J* 10.5 and 0.9 Hz, 5-H), 2.47–2.26 (2 H, m, 2 × 8-H), 2.08 (3 H, s, OAc), 2.11–1.90 (2 H, m, 2 × 7-H), and 1.36 and 1.09 (6 H, 2 × s, CMe_2) (Found: C, 39.0; H, 4.3; Br, 43.3. $C_{12}H_{16}Br_2O_3$ requires C, 39.2; H, 4.4; Br, 43.4%).

1,4exo-*Dibromo*-6exo-*t-butyldimethylsilyloxy*-3,3-*diphenylbicyclo*[3.3.0]*octan*-2-*one* (**39**).—To a stirred solution of the ketone (**22**) (0.11 g) in dry ether (3 ml) at 0 °C under an atmosphere of argon was added a solution of bromine (0.05 g) in carbon tetrachloride (1.0 ml). After 1 h, the solvent was evaporated and the residue was chromatographed over silica using LP (40–60)→20% ether in LP (40–60) as eluant to give the *ketone* (**39**) (0.14 g), m.p. 151–153 °C; ν_{max} 1 751 and 1 255 cm^{-1}; δ 7.45–7.30 (10 H, m, ArH), 4.55 (1 H, t, *J* 4.3 Hz, 6-H), 4.25 (1 H, d, *J* 11.3 Hz, 4-H), 3.48 (1 H, d, *J* 11.3 Hz, 5-H), 2.62–2.31 (2 H, m, 2 × 8-H), 2.14–2.06 (2 H, m, 2 × 7-H), 0.96 (9 H, s, Bu^t), and 0.19 and 0.16 (6 H, 2 × s, $SiMe_2$) (Found: C, 55.5; H, 5.85; Br, 28.5. $C_{26}H_{32}Br_2O_2Si$ requires C, 55.3; H, 5.7; Br, 28.3%).

6exo-*Acetoxy*-4exo-*chloro*-3,3-*dimethyl*-1-*phenylselenylbicyclo*[3.3.0]*octan*-2-*one* (**40**).—To a solution of the ketone (**19**) (0.12 g) in dichloromethane (3 ml) at 0 °C under an atmosphere of argon was added a solution of benzeneselenenyl chloride (0.23 g) in dichloromethane (3 ml). After 30 min, the reaction was warmed to room temp. After a further 40 min dilute aqueous hydrochloric acid was added with vigorous stirring. After 30 min, the mixture was extracted with dichloromethane (4 × 7 ml) and the combined organic extracts were dried and evaporated to give a residue which was chromatographed over silica using 5%→50% ether in LP (40–60) to give the *ketone* (**40**) (0.20 g) as an oil; ν_{max} 1 729 and 1 201 cm^{-1}; δ($CDCl_3$) 7.60–7.25 (5 H, m, ArH), 5.18 (1 H, m, 6-H), 3.46 (1 H, d, *J* 9.5 Hz, 4-H), 2.80 (1 H, d, *J* 9.5 Hz, 5-H), 2.01 (3 H, s, OAc), 2.17–1.76 (4 H, m, 2 × 7-H and 2 × 8-H), and 1.08 and 1.02 (6 H, 2 × s, CMe_2) (Found: M^+, 400.0312. $C_{18}H_{21}{}^{37}ClO_3{}^{78}Se$ requires M, 400.0323.

2exo-*Bromo*-3endo-*methoxy*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one* (**47**).—To a solution of the ketone (**42**) (4.0 g) in dry methanol (20 ml) and toluene (10 ml) was added 1,3-dibromo-5,5-dimethylhydantoin (4.56 g) portionwise under an atmosphere of nitrogen. After 2 h 10% aqueous sodium metabisulphite was added until the yellow colour was discharged. The mixture was evaporated to low volume and extracted with dichloromethane. The combined organic extracts were dried and evaporated and the residue was chromatographed over silica using 5% ether in LP (40–60) as eluant to give the title compound (**47**) (5.18 g), m.p. 98–99 °C; ν_{max} 1 777 and 1 089 cm^{-1}; δ($CDCl_3$) 7.50–7.15 (10 H, m, ArH), 4.51 (1 H, d, *J* 1.0 Hz, 3-H), 4.17 (1 H, d, *J* 8.1 Hz, 1-H), 4.00 (1 H, br s, 2-H), 3.88 (1 H, td, *J* 8.1 and 1.8 Hz, 5-H), 2.62 (3 H, s, OMe), and 2.47–2.27 (2 H, m, 2 × 4-H) (Found: C, 64.6; H, 5.25; Br 21.8. $C_{20}H_{19}BrO_2$ requires C, 64.7; H, 5.2; Br 21.5%).

2exo-*Bromo*-3endo-*t-butyldimethylsilyloxy*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one* (**50**).—To a stirred solution of t-butylchlorodimethylsilane (0.76 g) and imidazole (0.70 g) in dry dimethylformamide (3 ml) under an atmosphere of argon at room temp. was added a solution of the bromohydrin (**48**) (1.50 g) in dry dimethylformamide (4.5 ml). After 24 h, water (6 ml) was added and the solution was extracted with ether (4 × 10 ml). The combined organic extracts were dried and evaporated to give a residue which was chromatographed over silica to give the silyl ether (**50**) (1.94 g), m.p. 104–105 °C; ν_{max} 1 778 cm^{-1}; δ 7.55–7.15 (10 H, m, ArH), 4.42 (1 H, m, 3-H), 4.13 (1 H, t, *J* 3.2 Hz, 2-H), 4.04 (1 H, dd, *J* 8.8 and 3.2 Hz, H-1), 3.82 (1 H, ddd, *J* 9.0, 8.8, and 3.5 Hz, 5-H), 2.33 (1 H, ddd, *J* 13.7, 9.0, and 5.2 Hz, 4*exo*-H), 2.04 (1 H, dt, *J* 13.7 and 3.5 Hz, 4*endo*-H), 0.73 (9 H, s, Bu^t), and −0.01 and −0.07 (6 H, 2 × s, $SiMe_2$).

General Procedure for the Preparation of Tricyclo[3.2.0.0^{1,4}]*heptan*-2-*ones*.—The procedure used for the preparation of tricyclo[3.3.0.0^{1,4}]octan-2-ones (*vide supra*) was adopted.

6-*Bromo*-3,3-*dimethyltricyclo*[3.2.0.0^{1,4}]*heptan*-2-*one* (**51**). The ketone (**43**) (0.45 g) in ether (10 ml) was dehydrobrominated using potassium t-butoxide (0.22 g) in ether (17 ml). Chromatography of the crude product over silica using 10% ether in LP (40–60) as eluant gave the title compound (0.076 g) as an oil; ν_{max} 1 744 cm^{-1}; δ($CDCl_3$) 3.74 (1 H, ddd, *J* 5.3, 4.1, and 1.5 Hz, 6-H), 3.45 (1 H, br s, 5-H), 2.84 (1 H, dd, *J* 12.8 and 4.1 Hz, 7-H), 2.71 (1 H, br s, 4-H), 2.61 (1 H, dd, *J* 12.8 and 5.3 Hz, 7-H), and 1.20 and 0.86 (6 H, 2 × s, CMe_2).

6-*Bromo*-3,3-*diphenyltricyclo*[3.2.0.0^{1,4}]*heptan*-2-*one* (**52**).—The ketone (**45**) (0.76 g) in ether (13 ml) was dehydrobrominated using potassium t-butoxide (0.24 g) in ether (22 ml) to give a crude product which was chromatographed over silica using 10% ether in LP (40–60) as eluant to give the *title compound* (**52**) (0.27 g), m.p. 124–126 °C; ν_{max} 1 755 cm^{-1}; δ($CDCl_3$) 7.40–7.22 (10 H, m, ArH), 3.86 (1 H, ddd, *J* 5.3, 4.1, and 1.7 Hz, 6-H), 3.58 (1 H, t, *J* 0.7 Hz, 4-H), 3.19 (1 H, dddd, *J* 1.7, 0.7, 0.6, and 0.5 Hz, 5-H), 2.99 (1 H, dddd, *J* 13.0, 4.1, 0.7, and 0.6 Hz, 7-H), and 2.77 (1 H, ddd, *J* 13.0, 5.3, and 0.5 Hz, 7-H) (Found: C, 67.2; H, 4.6; Br 23.6. $C_{19}H_{15}BrO$ requires C, 67.3; H, 4.5; Br, 23.55%).

6-*Acetoxy*-3,3-*diphenyltricyclo*[3.2.0.0^{1,4}]*heptan*-2-*one* (**53**).—The ketone (**46**) (0.36 g) in ether (7.0 ml) was dehydrobrominated using potassium t-butoxide (0.13 g) in ether (12 ml) to give a crude product which was chromatographed

over silica using 15% ether in LP (40–60) as eluant to give the title compound (**53**), m.p. 100–103 °C; ν_{max} 1 752 cm^{-1}; δ($CDCl_3$) 7.5–7.2 (10 H, m, ArH), 4.63 (1 H, ddd, *J* 4.6, 3.5, and 0.9 Hz, 6-H), 3.65 (1 H, br d, *J* 0.9 Hz, 4-H), 2.97 (1 H, t, *J* 0.9 Hz, 5-H), 2.58 (1 H, dd, *J* 12.5 and 3.5 Hz, 7-H), 2.48 (1 H, dd, *J* 12.5 and 4.6 Hz, 7-H), and 2.01 (3 H, s, OAc) (Found: M^+, 318.1259. $C_{21}H_{18}O_3$ requires *M*, 318.1256).

6-*Methoxy*-3,3-*diphenyltricyclo*[3.2.0.0^{1,4}]*heptan*-2-*one* (**54**).—The ketone (**47**) (1.01 g) in ether (20 ml) was dehydrobrominated using potassium t-butoxide (0.41 g) in ether (34 ml). The crude product was chromatographed over silica using 10% ether in LP (40–60) as eluant to give the *title ketone* (**54**) (0.31 g), m.p. 113–115 °C; δ($CDCl_3$) 7.45–7.25 (10 H, m, ArH), 3.59–3.54 (2 H, m, 4-H and 6-H), 3.25 (3 H, s, OMe), 2.96 (1 H, br s, 5-H), 2.45 (1 H, dd, *J* 12.0 and 3.4 Hz, 7-H), and 2.33 (1 H, dd, *J* 12.0 and 4.5 Hz, 7-H) (Found: M^+, 291.1389. $C_{20}H_{18}O_2$ requires *M* + H, 291.1386).

6-*t*-*Butyldimethylsilyloxy*-3,3-*dimethyltricyclo*[3.2.0.0^{1,4}]-*heptan*-2-*one* (**55**).—The ketone (**49**) (0.51 g) in ether (11 ml) was dehydrobrominated using potassium t-butoxide (0.26 g) in ether (18 ml). The crude product was chromatographed over silica using 5% ether in LP (40–60) as eluant to give the *title compound* (0.26 g) as an oil; ν_{max}($CHCl_3$) 1 737 cm^{-1}; δ 3.78 (1 H, ddd, *J* 4.6, 3.3, and 1.1 Hz, 6-H), 3.18 (1 H, br s, 5-H), 2.67 (1 H, br s, 4-H), 2.29 (1 H, dd, *J* 11.6 and 3.3 Hz, 7-H), 2.18 (1 H, dd, *J* 11.6 and 4.6 Hz, 7-H), 1.18 (6 H, s, CMe_2), 0.87 (9 H, s, Bu^t), and 0.04 and 0.02 (6 H, 2 × s, $SiMe_2$).

6-*t*-*Butyldimethylsilyloxy*-3,3-*diphenyltricyclo*[3.2.0.0^{1,4}]-*heptan*-2-*one* (**56**).—The ketone (**50**) (0.60 g) in ether (10 ml) was dehydrobrominated using potassium t-butoxide (0.19 g) in ether (16 ml). The crude product was chromatographed using ether in LP (40–60) as eluant to give the *title compound* (**56**) (0.40 g); ν_{max} 1 747 cm^{-1}; δ($CDCl_3$) 7.60–7.20 (10 H, m, ArH), 3.98 (1 H, m, 6-H), 3.57 (1 H, br s, 4-H), 2.97 (1 H, br s, 5-H), 2.50–2.37 (2 H, m, 2 × 7-H), 0.93 (9 H, s, Bu^t), and 0.10 (6 H, s, $SiMe_2$).

Reaction of the Tricyclic Ketone (**55**) *with Methoxide Ion*.—To a solution of potassium t-butoxide (0.06 g) in dry methanol (1 ml) at 0 °C under an atmosphere of argon was added the ketone (**55**) (0.095 g) in ether (2.5 ml) with stirring. The mixture was warmed to room temp. After 2.5 h saturated aqueous ammonium chloride was added. The solution was extracted with ethyl acetate and the combined organic fractions were dried and evaporated. The crude product was chromatographed over silica using 10% ether in LP (40–60) as eluant to give in the first fractions 6exo-*t*-*butyldimethylsilyloxy*-4exo-*methoxy*-3,3-*dimethylbicyclo*[3.2.0]*heptan*-2-*one* (**57**) (0.090 g) as an oil, ν_{max} 1 737 cm^{-1}; δ($CDCl_3$) 4.02 (1 H, m, 6-H), 3.46 (1 H, d, *J* 3.7 Hz, 4-H), 3.36 (3 H, s, OMe), 3.12 (1 H, m, 1-H), 2.65 (1 H, m, 5-H), 2.35–2.11 (2 H, m, 2 × 7-H), 1.15 and 0.94 (6 H, 2 × s, CMe_2), 0.86 (9 H, s, Bu^t), and 0.03 and 0.01 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 299.2043. $C_{16}H_{30}O_3Si$ requires *M* + H, 299.2042). From later fractions was isolated 3-endo-*t*-*butyldimethylsilyloxy*-2exo-*methoxy*-7,7-*dimethylbicyclo*[3.2.0]*heptan*-6-*one* (**59**) (0.009 g) as an oil; ν_{max} 1 769 cm^{-1}; δ($CDCl_3$) 4.27 (1 H, m, 3-H), 3.70 (1 H, td, *J* 8.0 and 3.3 Hz, 5-H), 3.62 (1 H, br s, 2-H), 3.36 (3 H, s, OMe), 2.41 (1 H, d, *J* 8 Hz, 1-H), 1.99–1.93 (2 H, m, 2 × 4-H), 1.30 and 1.18 (6 H, 2 × s, CMe_2), 0.88 (9 H, s, Bu^t), and 0.09 and 0.06 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 299.2043. $C_{16}H_{30}O_3Si$ requires *M* + H, 299.2042).

Reaction of the Tricyclic Ketone (**55**) *with Toluene-α-thiol*.—To a stirred solution of the ketone (**55**) (0.06 g) in dry tetrahydrofuran (3 ml) at −78 °C under an atmosphere of argon was added toluene-α-thiol (0.1 ml) and piperidine (3 drops). After 80 min, the mixture was warmed to room temp. and after a further 75 min the solvent was removed under reduced pressure and the residue was chromatographed over silica using 2% ether in LP (40–60) as eluant. From the first fractions was isolated 4exo-*benzylthio*-6exo-*t*-*butyldimethylsilyloxy*-3,3-*dimethylbicyclo*[3.2.0]*heptan*-2-*one* (**58**) (0.02 g) as an oil; ν_{max} 1 729 cm^{-1}; δ($CDCl_3$) 7.45–7.25 (5 H, m, ArH), 3.84–3.72 (2 H, m, SCH_2Ph), 3.78 (1 H, m, 6-H), 3.20 (1 H, ddd, *J* 13.0, 8.0, and 6.0 Hz, 1-H), 2.74 (1 H, d, *J* 7.2 Hz, 4-H), 2.59 (1 H, dddd, *J* 8.0, 7.2, 2.1, and 0.9 Hz, 5-H), 2.34–2.11 (2 H, m, 2 × 7-H), 1.11 and 1.00 (6 H, 2 × s, CMe_2), 0.90 (9 H, s, Bu^t), and 0.07 and 0.05 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 391.2134. $C_{22}H_{34}O_2SSi$ requires *M* + H, 391.2127). From later fractions was isolated a second compound tentatively assigned as 2-benzylthio-3-t-butyldimethylsilyloxy-7,7-dimethylbicyclo[3.2.0]heptan-6-one (**60**) (0.007 g) as an oil; ν_{max} 1 770 cm^{-1}; δ($CDCl_3$) 7.35–7.25 (5 H, m, ArH), 4.27 (1 H, m, 3-H), 3.87–3.75 (2 H, m, SCH_2Ph), 3.72 (1 H, m, 5-H), 3.05 (1 H, br s, 2-H), 2.37 (1 H, dd, *J* 8.1 and 1.8 Hz, 1-H), 2.12 (1 H, ddd, *J* 13.5, 9.0, and 4.5 Hz, 4*exo*-H), 1.97 (1 H, dm, *J* 13.5 Hz, 4*endo*-H), 1.23 and 1.04 (6 H, 2 × s, CMe_2), 0.85 (9 H, s, Bu^t), and 0.04 and 0.03 (6 H, 2 × s, $SiMe_2$).

2exo-*Benzylthio*-3endo-*bromo*-7,7-*diphenylbicyclo*[3.2.0]-*heptan*-6-*one* (**61**).—To a solution of the ketone (**52**) (0.17 g) in dry THF (4 ml) at room temp. was added toluene-α-thiol (0.06 g) and piperidine (2 drops). After 1 h, the solvent was evaporated and the crude residue was chromatographed over silica using LP (40–60)→40% ether in LP (40–60) as eluant to give the title compound (**61**) (0.07 g) as a colourless oil; ν_{max} 1 775 cm^{-1}; δ($CDCl_3$) 7.60–7.20 (15 H, m, ArH), 4.25 (1 H, dt, *J* 7.5 and 7 Hz, 3-H), 3.75 (1 H, ddd, *J* 9.6, 9.5, and 4.9 Hz, 5-H), 3.89 and 3.52 (2 H, 2 × d, *J* 12.5 Hz, SCH_2Ph), 3.53 (1 H, dd, *J* 9.5 and 6.3 Hz, 1-H), 3.15 (1 H, dd, *J* 7.0 and 6.3 Hz, 2-H), 2.67 (1 H, ddd, *J* 14.3, 9.6, and 7.0 Hz, 4*exo*-H), and 2.44 (1 H, ddd, *J* 14.3, 7.5, and 4.9 Hz, 4*endo*-H) (Found: M^+, 480.1004. $C_{26}H_{23}{}^{79}BrOS$ requires *M* + NH_4, 480.0997).

3endo-*Acetoxy*-2exo-*fluoro*-7,7-*diphenylbicyclo*[3.2.0]-*heptan*-6-*one* (**62**).—To a stirred solution of the ketone (**53**) (0.08 g) in dichloromethane (1 ml) under nitrogen at room temp. was added triethylamine trishydrofluoride (0.5 ml). The reaction mixture was heated at 50 °C for 24 h, cooled to room temp. and diluted with water (10 ml). The solution was extracted with dichloromethane (4 × 5 ml) and the combined organic extracts were dried and evaporated. The residue was chromatographed over silica using 10% ether in LP (40–60) as eluant to give the *ketone* (**62**) (0.05 g), m.p. 145–146 °C; ν_{max}($CHCl_3$) 1 780 and 1 738 cm^{-1}; δ($CDCl_3$) 5.24 (1 H, dm, *J* 11.8 Hz, 3-H), 5.11 (1 H, ddd, *J* 47.0, 1.8, and 1.0 Hz, 2-H), 3.98–3.83 (2 H, m, 1-H and 5-H), 2.31–2.25 (2 H, m, 2 × 4-H), and 1.71 (3 H, s, OAc) (Found: C, 74.5; H, 5.9. $C_{21}H_{19}FO_3$ requires C, 74.5; H, 5.7%).

3endo-*t*-*Butyldimethylsilyloxy*-2exo-*chloro*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one* (**63**).—To a suspension of iron dust (0.05 g) and ammonium chloride (0.24 g) in water (1 ml) and methanol (9 ml) at room temp. was added a solution of the ketone (**56**) (0.10 g) in ether (3 ml). After 3 h, water (2 ml) was added and the solution was extracted with ether (6 × 10 ml). The combined ethereal extracts were dried and evaporated under reduced pressure to give a residue which was chromatographed over silica using LP (40–60) as eluant to give the ketone (**63**) (0.10 g), m.p. 111–113 °C; ν_{max} 1 776 cm^{-1}; δ($CDCl_3$) 7.55–7.15 (10 H, m, ArH), 4.31 (1 H, q, *J* 4.0 Hz, 3-H), 4.10 (1 H, t, *J* 4.0 Hz, 2-H), 3.86 (1 H, m, 1-H), 3.82 (1 H, td, *J* 8.7 and 3.0 Hz, 5-H), 2.27 (1 H, m, 4*exo*-H), 2.04 (1 H, ddd, *J* 13.0,

4.0, and 3.0 Hz, 4*endo*-H), 0.75 (9 H, s, Bu^t), and 0.01 and −0.05 (6 H, 2 × s, $SiMe_2$) (Found: C, 69.9; H, 7.4. $C_{25}H_{31}ClO_2Si$ requires C, 70.3; H, 7.3%).

2exo-*Benzylamino*-3endo-*methoxy*-7,7-*diphenylbicyclo*-[3.2.0]*heptan*-6-*one* (**64**).—To a stirred solution of the ketone (**54**) (0.08 g) in dry dichloromethane (3 ml) under an atmosphere of argon at room temperature was added a solution of benzylamine (0.04 g) in dichloromethane (0.5 ml). After 72 h, the solvent was evaporated and the residue was chromatographed over silica using 40% ether in LP (40–60) as eluant to give the *bicyclic ketone* (**64**) (0.105 g) as an oil; ν_{max} 3 339br and 1 772 cm^{-1}; δ($CDCl_3$) 7.50–7.15 (15 H, m, ArH), 3.85 (2 H, m, CH_2Ph), 3.76 (1 H, ddd, *J* 8.7, 8.4, and 2.6 Hz, 5-H), 3.70 (1 H, dddd, *J* 4.7, 2.6, 2.2, and 2.1 Hz, 3-H), 3.52 (1 H, dd, *J* 8.4 and 2.1 Hz, 1-H), 3.32 (1 H, dd, *J* 2.2 and 2.1 Hz, 2-H), 2.79 (3 H, s, OMe), 2.26 (1 H, dt, *J* 14.0 and 2.6 Hz, 4*endo*-H), 2.14 (1 H, ddd, *J* 14.0, 8.7, and 4.7 Hz, 4*exo*-H), and 1.48 (1 H, br s, NH) (Found: M^+, 398.2109. $C_{27}H_{27}NO_2$ requires *M* + H, 398.2120).

3endo-*Acetoxy*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one*-(**65**).—To a stirred suspension of lithium tri-t-butoxyaluminuim hydride (0.23 g) in dry THF (3 ml) at −78 °C under an atmosphere of argon was added a solution of the ketone (**53**) (0.12 g) in dry ether (3 ml). The reaction mixture was allowed to warm to room temp. After 18 h, saturated aqueous ammonium chloride (10 ml) was added and the solution was extracted with ether (5 × 10 ml). The combined organic extracts were dried and evaporated to give a residue which was chromatographed over silica to furnish the ketone (**65**) (0.11 g), m.p. 101–102 °C; ν_{max}(Nujol) 1 771 and 1 737 cm^{-1}; δ($CDCl_3$) 7.50–7.05 (10 H, m, ArH), 5.18 (1 H, m, 3-H), 3.82–3.75 (2 H, m, 1-H and 5-H), 2.36–1.92 (4 H, m, 2 × 2-H and 2 × 4-H), and 1.72 (3 H, s, OAc) (Found: M^+, 338.1746. $C_{21}H_{24}NO_3$ requires *M*, 338.1756).

Reaction of 6-*Methoxy*-3,3-*diphenyltricyclo*[3.2.0.0^{1,4}]*heptan*-2-*one* (**54**) *with Methoxide Ion*.—To a stirred solution of potassium t-butoxide (0.16 g) in dry methanol (2 ml) at 0 °C was added a solution of the ketone (**54**) (0.08 g) in dry dichloromethane (2 ml). After 2 h, the reaction mixture was warmed to room temp. and after a further 18 h dilute aqueous hydrochloric acid was added. The solution was extracted with dichloromethane (5 × 10 ml). The combined extracts were dried and evaporated to give a residue which was chromatographed over silica using LP (40–60)→40% ether in LP (40–60) as eluant to give, in the first fractions, *methyl* 3-*methoxy*-2-(2,2-*diphenylvinyl*)*cyclobutane*-1-*carboxylate* (**68**) (0.013 g); ν_{max} ($CHCl_3$) 1 725 cm^{-1}; δ($CDCl_3$) 7.45–7.20 (10 H, m, ArH), 6.08 (1 H, d, *J* 9.9 Hz, =CH), 4.18 (1 H, ddd, *J* 7.9, 7.8, and 7.5 Hz, 3-H), 3.71 (3 H, s, CO_2Me), 3.25 (3 H, s, OMe), 3.23 (1 H, ddd, *J* 9.9, 9.8, and 7.5 Hz, 2-H), 3.02 (1 H, dddd, *J* 9.8, 8.8, 2.6, and 0.8 Hz, 1-H), 2.52 (1 H, dddd, *J* 11.6, 7.8, 2.6, and 0.7 Hz, 4-H), and 1.91 (1 H, ddd, *J* 11.6, 8.8, and 7.9 Hz, 4-H) (Found: M^+, 323.1658. $C_{21}H_{22}O_3$ requires *M* + H, 323.1647). From later fractions was isolated the isomeric ester (**69**) (0.01 g) as an oil; ν_{max}($CHCl_3$) 1 726 cm^{-1}; δ($CDCl_3$) 7.50–7.15 (10 H, m, ArH), 6.09 (1 H, d, *J* 10.1 Hz, =CH), 3.70 (1 H, dt, *J* 8.4 and 8.0 Hz, 3-H), 3.64 (3 H, s, CO_2Me), 3.22 (3 H, s, OMe), 3.15 (1 H, dt, *J* 10.1 and 8.0 Hz, 2-H), 2.60–2.33 (2 H, m, 1-H and 4-H), and 2.04 (1 H, td, *J* 10.3 and 8.4 Hz, 4-H) (Found: M^+, 323.1644. $C_{21}H_{22}O_3$ requires *M* + H, 323.1647). The final fractions contained methyl 3,4-dimethoxy-2-diphenylmethylcyclopentanecarboxylate (**66**) (0.035 g), m.p. 99-100 °C; ν_{max}($CHCl_3$) 1 727 cm^{-1}; δ($CDCl_3$) 7.45–7.10 (10 H, m, ArH), 4.26 (1 H, d, *J* 12.2 Hz, $CHPh_2$), 3.63 (1 H, ddd, *J* 7.5, 5.8, and 2.7 Hz, 4-H), 3.47 (1 H, dd, *J* 4.5 and 2.7 Hz, 3-H), 3.27 (3 H, s, CO_2Me), 3.21 (1 H, ddd, *J* 12.2, 7.5, and 4.5 Hz, 2-H), 3.02 (1 H, m, 1-H), 3.04 and 2.97 (6 H, 2 × s, 2 × OMe), and 2.33–2.06 (2 H, m, 2 × 5-H) (Found: M^+, 355.1914. $C_{22}H_{26}O_4$ requires *M* + H, 355.1910).

Methyl 3-*Azido*-4-*hydroxy*-2-*diphenylmethylcyclopentane*-*carboxylate* (**67**).—To a stirred suspension of sodium azide (0.39 g) in dry methanol (3 ml) at 0 °C under an atmosphere of argon was added a solution of the ketone (**53**) (0.12 g) in dry ether (3 ml). After 40 min, the solvent was evaporated and the residue was taken into water and dichloromethane. The aqueous phase was separated and washed with dichloromethane. The combined organic extracts were dried and evaporated and the residue was chromatographed over silica to give the *ester* (**67**) (0.07 g), m.p. 106–107 °C; ν_{max}($CHCl_3$) 3 406, 2 109, and 1 708 cm^{-1}; δ($C_6D_5CD_3$) 7.20–6.85 (10 H, m, ArH), 4.09 (1 H, d, *J* 11.8 Hz, $CHPh_2$), 3.88 (1 H, br s, 4-H), 3.72 (1 H, dd, *J* 6.1 and 3.7 Hz, 3-H), 3.40 (1 H, br s, OH), 2.85 (3 H, s, CO_2Me), 2.86–2.72 (2 H, m, 1-H and 2-H), 1.85 (1 H, ddd, *J* 14.3, 8.2, and 6.5 Hz, 5-H), and 1.70 (1 H, ddd, *J* 14.3, 3.8, and 3.7 Hz, 5-H) (Found: M^+, 352.1666. $C_{20}H_{21}N_3O_3$ requires *M*, 352.1661).

7,7-*Diphenylbicyclo*[3.2.0]*heptane*-3endo,6endo-*diol* (**70**).—To a stirred suspension of lithium aluminium hydride (0.14 g) in dry ether (2 ml) and dry THF (4 ml) at −78 °C under an atmosphere of argon was added a solution of the tricyclic ketone (**53**) (0.25 g) in dry ether (6 ml) dropwise. After 45 min, the reaction mixture was warmed to 0 °C and after a further 20 min saturated aqueous ammonium chloride was added. The solution was extracted with ethyl acetate (6 × 8 ml) and the combined organic fractions were dried and evaporated to give a residue which was chromatographed over silica to give the *diol* (**70**) (0.10 g), m.p. 79–85 °C; δ($CDCl_3$) 7.50–7.10 (10 H, m, ArH), 4.88 (1 H, d, *J* 6.7, 6-H), 4.28 (1 H, m, 3-H), 3.39 (1 H, m, 1-H), 2.55 (1 H, dm, *J* 6.7, 5-H), 2.21–1.25 and (6 H, m, 2 × OH, 2 × 2-H, and 2 × 4-H) (Found: M^+, 298.1806. $C_{19}H_{20}O_2$ requires $M + NH_4$, 298.1807).

Reaction of the Tricyclic Ketone (**53**) *with Bromine*.—To a solution of the ketone (**53**) (0.11 g) in dry ether (3 ml) at 0 °C under an atmosphere of argon was added a solution of bromine (0.05 g) in carbon tetrachloride (4 ml) dropwise. After 10 min, the reaction was warmed to 20 °C and the solvent was evaporated under reduced pressure. The residue was chromatographed over silica using 10% ether in LP (40–60) as eluant to give, in the first fractions, 3endo-*acetoxy*-2exo,5-*dibromo*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one* (**71**) (0.06 g) as an oil; ν_{max} 1 787 and 1 746 cm^{-1}; δ($CDCl_3$) 7.55–7.10 (10 H, m, ArH), 5.31 (1 H, dddd, *J* 5.2, 2.0, 1.5, and 1.4 Hz, 3-H), 4.51 (1 H, ddd, *J* 1.5, 1.4, and 1.0 Hz, 2-H), 4.37 (1 H, t, *J* 1.5 Hz, 1-H), 2.92 (1 H, dd, *J* 15.0 and 5.2 Hz, 4*exo*-H), 2.65 (1 H, ddd, *J* 15.0, 2.0, and 1.0 Hz, 4*endo*-H), and 1.61 (3 H, s, OAc) (Found: M^+, 493.9971. $C_{21}H_{18}{}^{79}Br_2O_3$ requires $M + NH_4$, 493.9966). From later fractions was isolated 6exo-*acetoxy*-1,4-exo-*dibromo*-3,3-*diphenylbicyclo*[3.2.0]*heptan*-2-*one* (**74**) (0.08 g), m.p. 176–178 °C; ν_{max}($CHCl_3$) 1 750 cm^{-1}; δ($CDCl_3$) 7.70–7.15 (10 H, m, ArH), 5.84 (1 H, d, *J* 1.8 Hz, 4-H), 4.54 (1 H, td, *J* 6.4 and 4.2 Hz, 6-H), 3.72 (1 H, dd, *J* 4.2 and 1.8 Hz, 5-H), 2.72–2.69 (2 H, m, 2 × 7-H), and 2.08 (3 H, s, OAc) (Found: C, 52.3; H, 3.8; Br 32.9. $C_{21}H_{18}Br_2O_3$ requires C, 52.75; H, 3.8; Br 33.4%).

Reaction of the Tricyclic Ketone (**54**) *with Bromine*.—To a stirred solution of the ketone (**54**) (0.08 g) in dichloromethane (2 ml) was added bromine (0.04 g) in dichloromethane (1 ml) under an atmosphere of argon at 0 °C. After 18 h at room temp., the solvent was removed under reduced pressure and the residue was chromatographed over silica using 5% ether in LP (40–60) as eluant. From the first fractions was isolated 2exo,5-*dibromo*-3-endo-*methoxy*-7,7-*diphenylbicyclo*[3.2.0]*heptan*-6-*one* (**72**) (0.01 g) as an oil; ν_{max}($CHCl_3$) 1 786 cm^{-1}; δ($CDCl_3$) 7.55–7.10

(10 H, m, ArH), 4.51 (1 H, br s, 2-H), 4.34 (1 H, br s, 1-H), 3.97 (1 H, m, 3-H), 2.80 (1 H, dd, *J* 14.4 and 4.5 Hz, 4*exo*-H), 2.65 (1 H, d, *J* 14.4 Hz, 4*endo*-H), 2.57 (3 H, s, OMe) (Found: M^+, 466.0025. $C_{20}H_{18}{}^{79}Br_2O_2$ requires $M + NH_4$, 466.0018). From later fractions was obtained 1,4exo-*dibromo*-6exo-*methoxy*-3,3-*diphenylbicyclo*[3.2.0]*heptan*-2-*one* (**75**) (0.08 g), m.p. 136–138 °C; ν_{max}($CHCl_3$) 1 750 cm^{-1}; δ($CDCl_3$) 7.45–7.25 (10 H, m, ArH), 5.34 (1 H, d, *J* 3.7 Hz, 4-H), 3.70 (1 H, m, 6-H), 3.53 (1 H, m, 5-H), 3.25 (3 H, s, OMe), 2.80 (1 H, ddd, *J* 14.5, 6.4, and 1.5 Hz, 7-H), and 2.57 (1 H, ddd, *J* 14.5, 4.4, and 1.9 Hz, 7-H) (Found: M^+, 466.0016. $C_{20}H_{18}{}^{79}Br_2O_2$ requires $M + NH_4$, 466.0018).

Reaction of the Tricyclic Ketone (**53**) *with Benzeneselenenyl Chloride*.—To a stirred solution of the ketone (**53**) (0.09 g) in dichloromethane (2 ml) under an atmosphere of argon at 0 °C was added a solution of benzeneselenenyl chloride (0.07 g) in dichloromethane (2 ml). After 5 min, the reaction mixture was warmed to room temp. and 3 h later 1M HCl was added. The mixture was stirred vigorously for 30 min and then diluted with dichloromethane. The aqueous phase was separated and extracted with dichloromethane (3 × 6 ml). The combined organic fractions were dried and evaporated and the residue was chromatographed over silica using 20% ether in LP (40–60) as eluant to give in the first fractions 3endo-*acetoxy*-2exo-*chloro*-7,7-*diphenyl*-5-*phenylselenobicyclo*[3.2.0]*heptan*-6-*one* (**73**) (0.02 g); ν_{max}($CHCl_3$) 1 771 and 1 741 cm^{-1}; δ($CDCl_3$) 7.80–7.15 (15 H, m, ArH), 5.15 (1 H, m, 3-H), 4.41 (1 H, br s, 2-H), 3.80 (1 H, br s, 1-H), 2.58 (1 H, dd, *J* 15.0 and 5.2 Hz, 4*exo*-H), 2.38 (1 H, dd, *J* 15.0 and 2.7 Hz, 4*endo*-H), and 1.63 (3 H, s, OAc) (Found: M^+, 528.0858. $C_{27}H_{23}{}^{35}ClO_3{}^{80}Se$ requires $M + NH_4$, 528.0845). From later fractions was isolated 6exo-*acetoxy*-4exo-*chloro*-3,3-*diphenyl*-1-*phenylselenobicyclo*[3.2.0]*heptan*-2-*one* (**76**) (0.07 g) as a foam; ν_{max}($CHCl_3$) 1 736 cm^{-1}; δ($CDCl_3$) 7.85–7.15 (15 H, m, ArH), 5.73 (1 H, d, *J* 1.6 Hz, 4-H), 4.48 (1 H, ddd, *J* 7.3, 6.1, and 4.4 Hz, 6-H), 3.18 (1 H, ddd, *J* 4.4, 1.6, and 1.2 Hz, 5-H), 2.54–2.33 (2 H, m, 2 × 7-H), and 1.91 (3 H, s, OAc) (Found: M^+, 510.0499. $C_{27}H_{23}{}^{35}ClO_3{}^{80}Se$ requires *M*, 510.0501).

4exo-*Chloro*-6exo-*methoxy*-3,3-*diphenyl*-1-*phenylselenobicyclo*[3.2.0]*heptan*-2-*one* (**77**).—To a stirred solution of the ketone (**54**) (0.077 g) in dichloromethane (2 ml) under an atmosphere of argon at 0 °C was added a solution of benzeneselenenyl chloride (0.14 g) in dichloromethane (2 ml). The reaction mixture was allowed to warm to room temp. After 18 h, dilute aqueous hydrochloric acid was added and the mixture was stirred vigorously. The mixture was extracted with dichloromethane (4 × 7 ml) and the combined organic extracts were dried and evaporated under reduced pressure. The residue was chromatographed over silica using 10% ether in LP (40–60) as eluant to give the *title compound* (**77**) (0.11 g) as an oil; ν_{max} 1 736 cm^{-1}; δ($CDCl_3$) 7.85–7.25 (15 H, m, ArH), 5.31 (1 H, d, *J* 3.2 Hz, 4-H), 3.53 (1 H, ddd, *J* 6.9, 5.2, and 3.7 Hz, 6-H), 3.26 (1 H, dddd, *J* 3.7, 3.2, 1.2, and 1.1 Hz, 5-H), 2.54 (1 H, ddd, *J* 13.6, 6.9, and 1.2 Hz, 7*endo*-H), and 2.29 (1 H, ddd, *J* 13.6, 5.2, and 1.1 Hz, 7*exo*-H) (Found: M^+, 482.0556. $C_{26}H_{23}{}^{35}Cl^{80}SeO_2$ requires *M*, 482.0552).

6exo-*Bromo*-7endo-*t*-*butyldimethylsilyloxy*-4,4-*dimethyl*-3-*oxabicyclo*[3.3.0]*octan*-2-*one* (**78**).—To a solution of the ketone (**49**) (0.10 g) in dry dichloromethane (2 ml) was added sodium hydrogen carbonate (0.09 g) and *m*-chloroperoxybenzoic acid (0.11 g). The reaction mixture was stirred under an atmosphere of argon for 30 h and then diluted with water and dichloromethane. The two phases were separated and the organic phase was washed with saturated aqueous sodium sulphite (4 × 5 ml) and saturated aqueous sodium hydrogen carbonate (3 × 5 ml). The aqueous layers were back extracted with dichloromethane (2 × 5 ml). The combined organic layers were dried and evaporated under reduced pressure. The residue was chromatographed over silica using 10% ether in LP (40–60) as eluant to give the *title compound* (**78**) (0.09 g), m.p. 58–60 °C; ν_{max} 1 770 cm^{-1}; δ($CDCl_3$) 4.27 (1 H, m, 7-H), 4.08 (1 H, t, *J* 4.3 Hz, 6-H), 3.26 (1 H, td, *J* 9.5 and 2.8 Hz, 1-H), 2.98 (1 H, dd, *J* 9.5 and 4.3 Hz, 5-H), 2.46 (1 H, ddd, *J* 13.6, 9.5, and 5.0 Hz, 8*exo*-H), 2.10 (1 H, dt, *J* 13.6 and 2.8 Hz, 8*endo*-H), 1.52 and 1.43 (6 H, 2 × s, CMe_2), 0.87 (9 H, s, Bu^t), and 0.09 and 0.07 (6 H, 2 × s, $SiMe_2$) (Found: C, 49.0; H, 7.4. $C_{15}H_{27}BrO_3Si$ requires C, 49.6; H, 7.5%).

7-*t*-*Butyldimethylsilyloxy*-4,4-*dimethyl*-3-*oxatricyclo*-[4.2.0.$0^{1,5}$]*octan*-2-*one* (**79**).—To a solution of di-isopropylamine (0.29 g) in dry tetrahydrofuran (1.5 ml) under an atmosphere of argon at 0 °C was added a solution of butyllithium (2.5M in hexanes; 0.32 ml). After 5 min, a solution of the lactone (**78**) (0.21 g) in dry THF (2 ml) was added dropwise. After the mixture had been stirred for 45 min, saturated aqueous ammonium chloride was added. The mixture was extracted with dichloromethane (5 × 10 ml) and the combined organic extracts were dried and evaporated. The residue was chromatographed over silica to give the *title compound* (0.1 g), m.p. 58–61 °C; ν_{max}($CHCl_3$) 1 766 cm^{-1}; 3.73 (1 H, ddd, *J* 4.3, 3.0, and

Table 4. Fractional atomic co-ordinates for compound (**38**).

Atom	*x*	*y*	*z*
Br(1)	0.173 24(2)	0.115 00(3)	0.151 54(1)
Br(2)	0.574 66(2)	0.455 63(3)	0.261 59(1)
O(1)	0.396 75(15)	−0.131 03(18)	0.132 37(11)
O(2)	0.253 48(10)	0.517 91(14)	0.037 82(7)
O(3)	0.310 67(13)	0.695 86(18)	−0.059 51(8)
C(1)	0.312 14(15)	0.153 54(22)	0.110 33(11)
C(2)	0.286 90(18)	0.152 81(22)	0.008 15(11)
C(3)	0.365 37(16)	0.300 69(23)	−0.016 30(11)
C(4)	0.363 19(15)	0.429 22(21)	0.051 30(11)
C(5)	0.372 53(14)	0.331 30(21)	0.138 23(11)
C(6)	0.497 95(14)	0.276 78(22)	0.179 95(10)
C(7)	0.493 92(16)	0.103 00(23)	0.222 01(11)
C(8)	0.398 84(17)	0.019 86(24)	0.152 45(12)
C(9)	0.607 71(17)	0.005 21(30)	0.230 08(15)
C(10)	0.452 92(18)	0.106 69(27)	0.309 25(11)
C(11)	0.235 92(16)	0.651 46(22)	−0.017 65(11)
C(12)	0.124 93(16)	0.733 28(24)	−0.026 57(12)

Table 5. Atomic co-ordinates (× 10^4) for compound (**79**).

Atom	*x*	*y*	*z*
Si	2 060(1)	9 701(1)	8 322(1)
C(1)	5 326(3)	12 876(3)	4 856(1)
O(1)	4 640(2)	12 707(2)	4 101(1)
C(2)	2 477(3)	12 758(3)	4 132(2)
C(3)	1 889(3)	12 678(3)	5 066(1)
C(4)	3 748(3)	12 741(2)	5 510(1)
C(5)	3 558(4)	12 904(3)	6 434(2)
C(6)	2 107(4)	11 447(3)	6 632(2)
C(7)	2 475(3)	11 154(3)	5 730(1)
O(11)	7 037(2)	13 078(2)	4 920(1)
C(21)	1 893(4)	11 284(3)	3 781(2)
C(22)	1 840(4)	14 442(3)	3 562(2)
O(61)	2 648(3)	10 033(2)	7 282(1)
C(61)	3 531(6)	11 005(6)	8 845(2)
C(62)	−561(5)	10 310(5)	8 465(2)
C(70)	2 566(4)	7 391(4)	8 740(2)
C(71)	4 699(6)	6 939(5)	8 574(3)
C(72)	1 324(7)	6 392(4)	8 285(3)
C(73)	2 133(7)	6 860(5)	9 715(2)

0.5 Hz, 7-H), 2.39 (1 H, br s, 6-H), 2.32 (1 H, dd, *J* 11.4 and 3.0 Hz, 8-H), 2.23 (1 H, d, *J* 1.5 Hz, 5-H), 2.12 (1 H, ddd, *J* 11.4, 4.3, and 0.7 Hz, 8-H), 1.47 and 1.25 (6 H, 2 × s, CMe_2), 0.85 (9 H, s, Bu^t) and 0.01 and 0.00 (6 H, 2 × s, $SiMe_2$) (Found: M^+, 283.1727. $C_{15}H_{26}O_3Si$ requires M + H, 283.1730).

Microbiological Studies.—Growth of organisms. The micro-organisms used were *Clostridium pasteurianum* ATCC 6013, *Clostridium tyrobutyricum* DSM 1460 (Strain Lal), and *Clostridium kluyveri* NCIB 10680. *C. pasteurianum* and *C. tyrobutyricum* were maintained on agar solidified plates of Reinforced Clostridial Medium (RCM, LabM, Salford, U.K.) whilst *C. kluyveri* was maintained on agar solidified ethanol–acetate medium.

C. pasteurianum was grown in a minimal medium containing glucose (4%, w/v) as carbon source, this medium has previously been described;[16] *C. tyrobutyricum* was grown in the same medium supplemented with yeast extract (0.5%, w/v) with glucose or crotonic acid (1%, w/v) as major carbon and energy source. *C. kluyveri* was grown in an ethanol–acetate medium essentially as described[17] except that potassium carbonate, biotin, and *p*-aminobenzoic acid were omitted and the phosphate concentration increased to 65 mM.

C. pasteurianum and *C. tyrobutyricum* cultures were seeded with a 5% inoculum of RCM-grown cells and were incubated for 20 h in 1-l batches contained in 2-l conical flasks. The cultures were incubated without shaking at 37 °C in an anaerobic cabinet in which the gas phase consisted of 90% N_2, 5% H_2, 5% CO_2. *C. pasteurianum* cultures yielded 1.7 g dry weight of cells l^{-1} whilst *C. tyrobutyricum* yielded 0.57 g dry weight of cells l^{-1}.

Ethanol–acetate medium was seeded with a 5% inoculum of ethanol–acetate grown *C. kluyveri*. The 10-l culture, contained in a glass carboy fitted with a rubber bung and gassing manifold to allow the culture to be covered by a blanket of anaerobic gas (90% N_2, 5% H_2, 5% CO_2), was incubated without shaking at 37 °C for 48 h. Such cultures yielded 0.13 g dry weight of cells l^{-1}.

Reduction Procedure. Cultures were harvested by centrifugation to yield 1.3 g dry weight of *C. kluyveri* and 1.7 g dry weight of *C. tyrobutyricum*. The cells were resuspended in 500 ml of anaerobic potassium phosphate buffer (0.1M, pH 7.0) containing 1.6 mM magnesium sulphate. 100-ml Volumes of the cell suspensions were transferred to five separate 160-ml serum bottles and sealed with rubber stoppers, the gas phase was exchanged for hydrogen by repeated evacuation and flushing through a hypodermic needle inserted through the rubber stopper. After addition of bicyclo[4.2.0]oct-2-en-7-one the bottles were pressurised with hydrogen to 2 bar and incubated at 37 °C on a horizontal shaker with a displacement of 12 cm operating at 70 oscillations min^{-1}. Bioreduction with *C. pasteurianum* was performed similarly except that 1.2 g dry weight of cells was resuspended in 200 ml of buffer.

Following incubation for 24 h the cells were removed by centrifugation and the supernatants extracted 3 times with an equal volume of diethyl ether. The ether extracts were dried with anhydrous sodium sulphate and the ether removed by rotary evaporation at 30 °C. The alcohol and residual ketone were separated by chromatography and the specific optical activity of the alcohol was calculated.

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