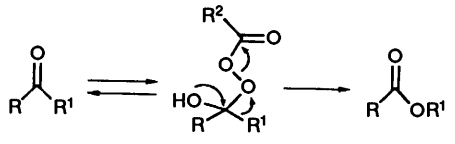
A Study of the Regioselectivity of Oxygen Insertion in the Baeyer–Villiger Oxidation of Bicyclo[2.2.1]heptan-2-ones

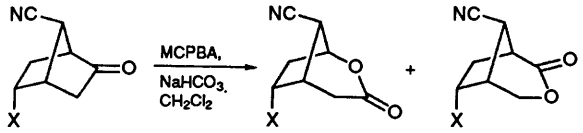
Peter Hamley,[a] Andrew B. Holmes,*[a] David R. Marshall[b] and John W. M. MacKinnon[b]
[a] *University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK*
[b] *Glaxo Group Research, Ware, SG12 0DP, UK*

Synthesis and Baeyer–Villiger oxidation of the series of bicyclic ketones **3** and **6** is described. The ratio of methine to methylene carbon migration in the oxidation was found to vary depending on the 5-*endo* and 7-*anti* substituents of the ketones. Possible reasons for the observed regioselectivity are discussed.

The Baeyer–Villiger oxidation of bicyclic ketones[1] is an important and well-established reaction and has been much used in synthesis, since the resulting lactones can be ring-opened with a nucleophile to afford the corresponding monocyclic compounds with predefined stereochemistry. The mechanism is thought to be a two step process, in which the peracid attacks the carbonyl group of the ketone to form a tetrahedral intermediate (known as the 'Criegee intermediate'),[2,3] the breakdown of which has been found to be the rate determining step in most studies.[4,5] The regiochemistry of oxygen insertion can usually be predicted by assuming that the carbon atom best able to support a positive charge will migrate preferentially.[6] However, a number of anomalous examples of regioselectivity continue to appear in the literature concerning bicyclic ketones,[1] leading to the conclusion that other factors must also be at work in these systems.

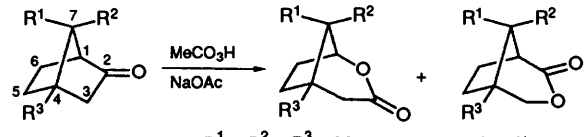


The bicyclo[2.2.1]heptan-2-one system has been most commonly studied, as the Baeyer–Villiger oxidation of these ketones has often been used in natural product synthesis.[1,7] It would be expected that the more substituted bridgehead carbon atom would migrate preferentially, and this is indeed the case with unsubstituted bicyclo[2.2.1]heptan-2-one.[1] However, Roberts *et al.*[8] have found that ketones **1** with an electron-withdrawing cyano group at the 7-*anti*-position give predominantly methylene migration, presumably because the methine carbon (C-1) is now less able to support a positive charge.



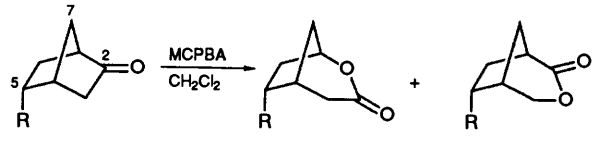
1 X = Br 25 : 75
X = OMe 0 : 100

In addition to electronic effects, steric effects have been shown to be important; for example, *exo* attack of peracid, *i.e.* from the less sterically encumbered face, is preferred in these systems. However, ketones **2** with 7-*syn* (R^2) substitution, in which *endo* peracid attack is assumed to predominate, give predominantly methylene migration.[9] These results have been rationalised by assuming that any methylene migration occurring after *endo* attack must proceed through a chair-like transition state, whereas the alternative methine migrations requires a higher centre boat-like pathway. This energy difference overrides the electronic preference for tertiary centre migration. Where there is no 7-*syn* substituent, *exo* attack leads to migration through a chair-like intermediate to afford the electronically preferred methine migrated product.[10]



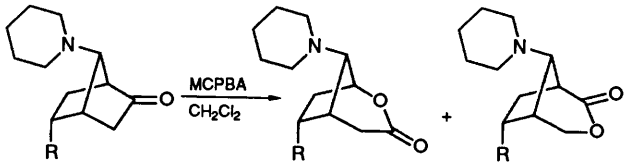
2 $R^1 = R^2 = R^3 = Me$ 0 : 100 (94%)
$R^1 = R^3 = H$, $R^2 = Br$ 30 : 70 (75%)
$R^1 = R^3 = H$, $R^2 = Cl$ 50 : 50 (77%)

It has been noted that 5- and 7-substituents may influence the regioselectivity of Baeyer–Villiger oxidations of bicyclo-[2.2.1]heptan-2-ones.[8] We decided to undertake a systematic comparative study of the oxidation of the two series **3** and **6** in



3 **a**; R = H
b; R = Et
c; R = $OCOCCl_3$
d; R = OAc
e; R = OMe
f; R = OBn

4 **5**



6 **a**; R = H
b; R = $OCOCCl_3$
c; R = $OCOCH_2Cl$
d; R = OAc
e; R = OMe
f; R = $OCOC_6H_4C_6H_5$-*p*
g; R = $OCH_2C_6H_4C_6H_5$-*p*
h; R = OBn

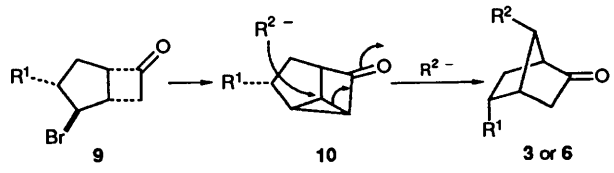
7 **8**

order to assess the relative importance of substituents at these positions. A major objective was to obtain high yields, thus reducing any uncertainty in the ratios due to hydrolysis, since the methylene-migrated lactone has been shown to undergo

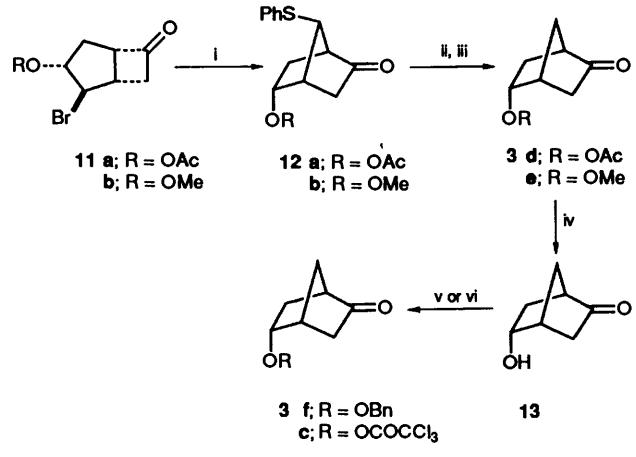
rapid hydrolysis relative to its regioisomer.[1,11] One of the major uncertainties in the previously published literature[1] results from a failure to account for all the reaction product. Standard conditions of peracid, temperature, concentration and solvent, have been used throughout in this work, as a comparison of the literature data is made difficult by the use of a wide variety of peracids and conditions.

Results

Synthesis of Bicyclo[2.2.1]*heptan-2-ones.*—For the synthesis of both series of ketones, we chose to use some methodology originally introduced by Roberts and his co-workers.[12] Thus bicycloheptanone **9**, when treated with base, undergoes intramolecular enolate alkylation to form the tricyclic intermediate **10**, which can either be isolated or treated *in situ* with a nucleophile, selectively cleaving the bond shown to form ketones with the 7-*anti*, 5-*endo* substitution pattern.



Synthesis of the C-7 unsubstituted series[12] **3c–f** was accomplished by treating **11a** with potassium *tert*-butoxide in tetrahydrofuran (THF) followed by thiophenol, which gave the 7-phenylthio ketone **12a** in 65% yield (Scheme 1). Sodium borohydride has recently been used for the homoconjugate reduction of a compound related to **10**, but this over-reduces the ketone.[7j] Desulphurisation of **12** with Raney nickel also reduced the ketone functionality to a mixture of alcohols which was subjected to a Swern oxidation[13] to give the required compound **3d** in 88% overall yield. The same procedure furnished the 5-*endo* methoxy compound **3e**. The acetoxy group of **3d** was removed by methanolysis, and the resulting alcohol **13** was converted into both the benzyl ether (OBn) **3f** and the trichloroacetoxy ester **3c**.



Scheme 1 *Reagents:* i, KOBu^t, then PhSH (R = OAc, 65%; R = OMe, 63%); ii, Raney Ni, iii, R = OAc; Swern oxidation[13] (88% from **12a**); R = OMe; CrO_3, H_2SO_4 (72% from **12b**); iv, R = OAc: K_2CO_3, methanol (96%); v, NaOH, BnBr, $BnEt_3N^+Cl^-$ (**3f** 87%); vi, Cl_3CCOCl, pyridine (**3c** 86%)

The 5-*endo* ethyl-substituted ketone **3b** was prepared by a three step sequence (Scheme 2). Wittig reaction of 5-*endo* benzyloxy ether **3f** with ethyltriphenylphosphonium bromide and sodium hydride in dimethyl sulphoxide gave an 85% yield of the alkene **14** as a 1:1 mixture of isomers. Hydrogenation of the mixture with palladium on carbon afforded the alcohol **15** quantitatively by reduction from the less hindered face. Jones oxidation[14] afforded the required ketone **3b**, the structure of which was determined unambiguously by ^{1}H NMR nuclear Overhauser enhancement (NOE) studies on the derived lactone **16**. These enhancements are shown in Fig. 1. No NOE was observed between the ethyl group and the hydrogens of the one carbon bridge.

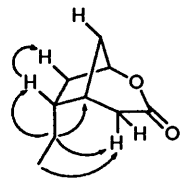
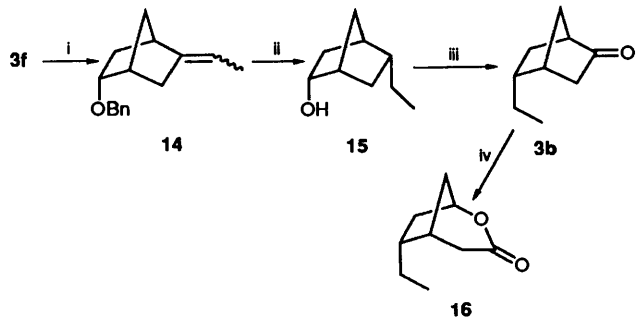
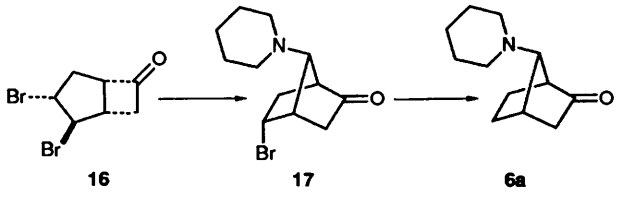


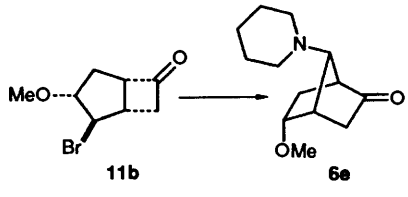
Fig. 1 NOE for lactone **5b**



Scheme 2 *Reagents:* i, $[EtPPh_3]^+Br^-$, NaH, DMSO (85%); ii, H_2/Pd (100%); iii, CrO_3, H_2SO_4 (82%); iv, MCPBA (97%)

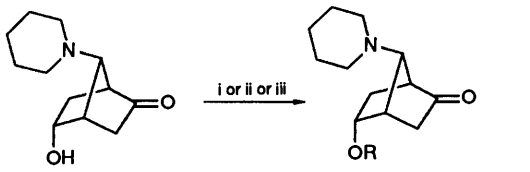


The piperidine series was synthesised in a similar manner to that described above. Simply treating the dibromobicycloheptanone **16**[12] with piperidine gave the 7-*anti* piperidino ketone **17** (85%). The bromine atom could be removed with tributyltin hydride in 99% yield to afford ketone **6a**, unsubstituted at the 5-*endo* position. The corresponding 5-*endo*



methoxy ketone **6e** was prepared from **11b**[12] with piperidine in a similar manner (72%). Other ketones **6b**, **6c** and **6h** in this series, were prepared from the 5-*endo* hydroxy ketone **18** which, together with compounds **6f** and **6g** were generously supplied by Glaxo Group Research (Scheme 3).

Baeyer–Villiger Oxidations.—Oxidation with trifluoroperacetic acid gave generally low yields. However, 3-chloroperoxybenzoic acid (MCPBA) in dry dichloromethane generally gave good yields of crude product lactones (see Table 1). A standard reaction and aqueous work-up procedure was adopted. The ratios of lactones were determined by GC analysis wherever possible, and always by ^{1}H NMR integration of relevant signals (see Experimental section).

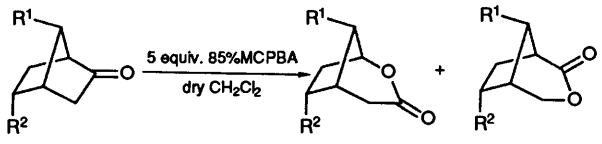


18

6 **b**; R = $OCOCCl_3$
c; R = $OCOCH_2Cl$
h; R = OBn

Scheme 3 *Reagents:* i, Cl_3CCOCl, pyridine (**6b** 47%); ii, $ClCH_2COCl$, pyridine (**6c** 68%); iii, NaOH, BnBr, $BnEt_3N^+Cl^-$ (**6h** 74%)

Table 1 Baeyer–Villiger oxidations of bicyclic ketones **3** and **6** with MCPBA[a]



Compound	R^1	R^2	Ratio[c] (4:5)	Yield[b] (%)
3a	H	H	93:7[d]	97
3b	H	Et	95:5	97
3c	H	$OCOCCl_3$	88:12	100
3d	H	OAc	85:15	87
3e	H	OMe	84:16	100
3f	H	OBn	75:25[d]	99
			Ratio (7:8)	
6a	$N(C_5H_{10})$	H	89:11	65[e]
6b	$N(C_5H_{10})$	$OCOCCl_3$	83:17	55[e]
6c	$N(C_5H_{10})$	$OCOCH_2Cl$	80:20	82[e]
6d	$N(C_5H_{10})$	OAc	74:26	92[e]
6e	$N(C_5H_{10})$	OMe	67:33	95[e]
6f	$N(C_5H_{10})$	$OCOC_6H_4C_6H_5$-*p*	68:32[d]	100
6g	$N(C_5H_{10})$	$OCH_2C_6H_4C_6H_5$-*p*	60:40[d]	97
6h	$N(C_5H_{10})$	OBn	58:42[d]	98

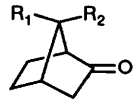
[a] All reactions were carried out at 20 °C in dry dichloromethane at 0.05 mol dm^{-3} concentration. [b] Reaction time 18–22 h. Yields quoted are for crude lactones. [c] All ratios were determined by capillary GC with exceptions [d] which were determined by ^1H NMR. [e] Yield is corrected for residual 3-chlorobenzoic acid.

The piperidinyl group in the series **6** was almost immediately oxidised to the *N*-oxide, as evidenced by the rapid formation of a more polar intermediate which could be converted into starting material by the addition of sodium hydrogen sulphite. This polar intermediate subsequently undergoes Baeyer–Villiger oxidation to form a crude product which upon reductive work-up affords a mixture of lactones (see Table 1).

Discussion

There is a striking difference in selectivity for the preference for methine migration. We can summarise the trends that give some insight into the reaction: (a) The series of ketones with piperidine at the 7-*anti* position gives appreciably greater amounts of methylene migration; however, there is a wide variation within this series which must therefore be due to the nature of the 5-*endo* group. There seems to be an increasing preference for methylene migration, enhanced in the 7-piperidino series, for 5-*endo*-substituents which are capable of hydrogen bonding. (b) It is interesting to note that the introduction of the more remote 5-*endo* oxygen substituents promotes more methylene migration than the introduction of the electronegative *N*-oxide substituent at a position (C-7) adjacent to the methine migrating centre (*cf.* the entry for compound **3a** against those for **6a** and **3e**). (c) Oxidation of the 5-*endo* ethyl ketone **3b** gives a large amount of methine migration, comparable to bicycloheptan-2-one **3a** itself. In comparison, the methoxy substituted ketone **3e** is less selective for methine migration. This suggests that the ethyl group (which should have a similar steric demand to that of a methoxy group) has no effect on the regioselectivity, and that the 5-*endo* directing effect must be a function of the oxygen atom of this latter group. (d) The combination of the effects of each of the two substituents in the same molecule produces a greater preference for methylene migration than might have been predicted from a simple additive treatment of the perturbation caused by individual substituents. Thus, the estimated combined effect of the preference for methylene migration of **3e** and **6a** (compared with the unsubstituted molecule **3a**) is much *less* than the observed preference for methylene migration for **6e**. (e) The *endo* nature of the 5-substituent has a profound effect. Thus the significant proportion of methylene migration noted in the entry for compound **3f** is to be compared with the exclusive methine migration noted for the corresponding 5-*exo*-isomer.[7j]

These observations can be rationalised by assuming that the 5-*endo* oxygen group directs a certain amount of peracid to the *endo* face of the ketone, presumably by some type of hydrogen bonding effect, resulting in more methylene migration *via* a chair transition state. We are assuming in this analysis that *endo* attack of peracid on the ketone always produces methylene migration. The postulated hydrogen bond would be stronger for more basic oxygen atoms which is consistent with our results, notably in the piperidine series **6**. A similar directing effect has been shown to operate in the epoxidation of allylic alcohols with MCPBA,[15] and with allyl esters and carbamates,[16,17] though generally not in the case of allylic ethers with one exception.[18] A related observation in the Baeyer–Villiger oxidation of an acyclic keto ester has recently been disclosed by Bird.[19] The concept of a directing effect similarly explains the preference for methine migration in the series of compounds **19**; the directed attack of peracid by the substituent R^2 (whether it be ester,**19a** [7a] alcohol **19b** [7i] or acid **19c** [7l]) to the apparently more hindered *exo* face of the carbonyl group leads to methine migration.



19 **a**; R^1 = Me, R^2 = CO_2Me
b; R^1 = H, R^2 = CH_2OH
c; R^1 = H, R^2 = CO_2H

For migration involving *exo* attack (see Fig. 2), *i.e. via* TS1 or TS2, we suggest that TS1 is considerably lower in energy than TS2, and thus *exo* attack usually leads to methine migration *via* TS1. This is clearly favoured in the unsubstituted series **3** because there it involves both a low energy chair-like transition state and migration of the more substituted methine carbon. In the piperidine *N*-oxide series **6** the 7-*anti*-electron withdrawing group is antiperiplanar to this migrating bond and so methine migration is less pronounced, thus perhaps allowing an alternative pathway, leading to methylene migration.

The observed relative increase in preference for methylene migration in molecules containing a 5-*endo*-substituent is rationalised by intramolecular *endo* delivery of peracid and a rearrangement *via* TS3. The preference is apparently stronger in the cases where there is also a 7-*anti* piperidine *N*-oxide group. For migration resulting from *endo* attack, *i.e. via* species TS3 or TS4 (see Fig. 2), we suggest that in the piperidine *N*-oxide series TS3 is considerably lower in energy than TS4 and thus all of the *endo* attack leads to methylene migration *via* TS3. Transition state TS3 is chair-like, but it involves the usually less preferred

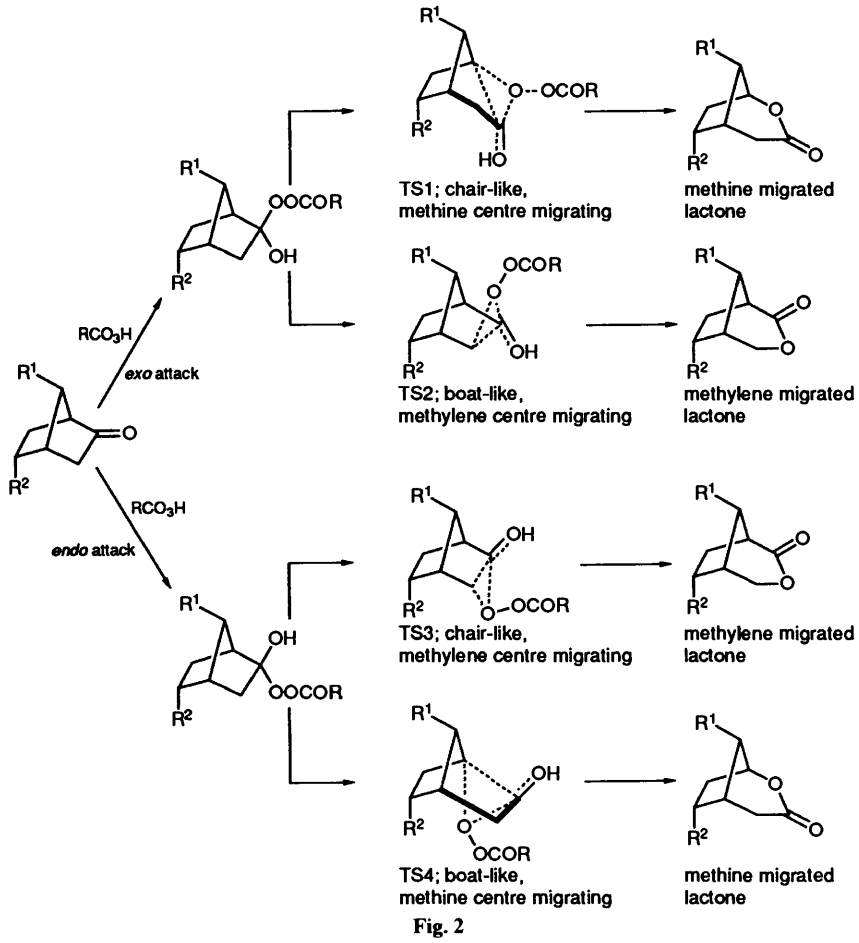


Fig. 2

methylene migration. The species TS4 is a higher energy boat-like structure, and although this might normally be offset by the usually preferred methine migration, it is counterbalanced in series **6** by the electron-withdrawing 7-*anti* group, which would lower the migratory aptitude of the methine carbon. In the unsubstituted series **3** (R^2 = H in Fig. 2) the transition states TS3 and TS4 are closer together in energy because TS3 is a low energy chair-like species, but has a less favourable methylene migration, whereas TS4 has the migratory preference of the more substituted methine carbon competing against the higher energy boat-like transition state.

Torsional effects resulting in an energy difference which favours one of the two regioisomeric lactones have been suggested to be important in Baeyer–Villiger oxidations of steroidal ketones.[20] However, as mentioned before, the 5-*endo*-ethyl substituent of compound **3b** does not have a significant effect on the regioselectivity of migration.

We have considered explanations for the variations in the facial selectivity of attack of the peracid on the bicyclic ketones **3** and **6** based on a Cieplak[21] orbital argument for rigid bicyclic systems.[22] The electron-withdrawing piperidine *N*-oxide group would reduce the σ-donor ability of the C(1)–C(7) bond, thus suppressing *endo*-attack. However this is not borne out by the trends exhibited in Table 1. It is possible that the predominant interaction is the long range one[22a–c] between the σ_{C-O} bond of the electronegative 5-*endo*-substituent and the developing *exo* σ^*_{C-OCOR} which would disfavour *exo* attack of peracid.

We have established, then, the likely existence of an *endo* directing effect in the attack of MCPBA on a 5-*endo*-substituted bicyclo[2.2.1]heptane-2-one. Whether this is due to intramolecular delivery or to stereoelectronic effects remains unclear. We have also attempted to explain how the 5-*endo* and 7-*anti* substituents work in tandem. Although the general explanation is by no means fully proven by our results, it is nevertheless obvious that very subtle steric and electronic factors contribute to the regioselectivities observed in the Baeyer–Villiger oxidation of bicyclic ketones. Knowledge of regioselectivity in these reactions will continue to grow, and be made use of in synthetic applications. Work towards this latter goal is ongoing in our group.

Experimental

^{1}H NMR spectra were recorded on Bruker WP-80 SY (80 MHz), Bruker WM-250 (250 MHz) or Bruker WM-400 (400 MHz) instruments. Chemical shifts are quoted on the δ scale relative to TMS (δ = 0) using $CHCl_3$ as an internal standard. ^{13}C NMR spectra were recorded on a Bruker WM-400 (100 MHz) spectrometer with proton decoupling. *J* Values are given in Hz. IR spectra were recorded as a solution in CCl_4 on a Perkin-Elmer 1310 spectrophotometer. Mass spectra were determined using an A.E.I. MS 30 instrument, or by the SERC Mass Spectrometry Service at Swansea. Gas chromatography was performed on a Carlo Erber Strumentazione 10 using a silica BP5 column (25 m × 0.32 mm i.d.). M.p.s were recorded on a Köfler hot-stage apparatus. Microanalyses were performed by the staff of the University Chemical Laboratory, Cambridge. Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). The yields of the products of the Baeyer–Villiger oxidations described in Table 1 refer to crude material which was analysed by ^{1}H NMR and capillary gas chromatography. In each case the analyses indicated that the only compounds present were the isomeric lactones in the ratios reported in Table 1. These were identified by comparison of the spectra with those of the fully characterised compounds **4b**, **4e**, **7e**, **7g** and **8g**.

Dry THF was distilled from potassium and benzophenone in a recycling still. Dry ether was distilled from sodium and benzophenone. Other dry solvents were purified by standard techniques. MCPBA was purified by washing as a solution in ether with an aqueous pH 7.5 buffer, and assayed by titration (sodium thiosulphate–iodine–starch).

Brine refers to a solution of saturated aqueous sodium chloride. Reactions were routinely performed under argon.

5-endo-*Acetoxy*-7-anti-*phenylthiobicyclo*[2.2.1]*heptan*-2-*one* **12a**.—Potassium *tert*-butoxide (1.74 g, 15.5 mmol) was added to a stirred solution of 3-*endo*-acetoxy-2-*exo*-bromobicyclo[3.2.0]heptan-6-one (3.83 g, 15.5 mmol) in THF (40 cm^3) at room temperature. The solution was stirred for 15 min. Thiophenol (0.53 cm^3, 1 equiv.) was added dropwise and the solution stirred for a further 30 min, poured into saturated aqueous sodium hydrogen carbonate (300 cm^3) and extracted with dichloromethane (3 × 30 cm^3). The organic extracts were washed with brine (40 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was flash columned over silica eluting with ether–hexane (2:5) to afford the *title compound* as a white crystalline solid **12a** (2.79 g, 65%), m.p. 81–82 °C (Found: C, 65.0; H, 5.8. $C_{15}H_{16}O_3S$ requires C, 65.2; H, 5.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3050–2850m, 1750s (CO) and 1740s (OAc); δ_H(250 MHz; $CDCl_3$) 5.55 (1 H, m, 5-H), 3.64 (1 H, 7-H, *J* 2.7), 2.94 (2 H, m, 4-H, 3*endo*-H), 2.87 (1 H, m, 6*exo*-H), 2.64 (1 H, m, 1-H), 2.14 (1 H, dd, 3*exo*-H, *J* 4.5 and 18.4), 2.04 (3 H, s, OAc) and 1.47 (1 H, m, 6*endo*-H, *J* 2.7); δ_C(100 MHz; $CDCl_3$) 212.45 (CO), 170.61 (CO, acetoxy), 133.66, 131.79, 129.29, 127.71 (aromatics), 72.58 (C-5), 55.05 (C-7), 54.28 (C-4), 43.29 (C-1), 39.68 (C-6), 30.62 (C-3) and 20.98 (CH_3, acetoxy); *m*/*z* 276 (M^+, 45%), 217 (10) and 125 (100) (Found: M^+, 276.0827. $C_{15}H_{16}O_3S$ requires *M*, 276.0820).

5-endo-*Methoxy*-7-anti-*phenylthiobicyclo*[2.2.1]*heptan*-2-*one* **12b**.—This was prepared by the same procedure as for compound **12a** to afford the *title compound* as a colourless volatile oil **12b** (365 mg, 63%); $\nu_{max}(CCl_4)/cm^{-1}$ 3060–2880m, 2820w (OMe) and 1750s (CO); δ_H(250 MHz; $CDCl_3$) 4.31 (1 H, m, 5-H), 3.62 (1 H, d, 7-H, *J* 1.3), 3.29 (3 H, s, OMe), 2.88 (1 H, m, 4-H), 2.75–2.63 (3 H, m, 1-H, 3*endo*-H, 6*exo*-H), 2.05 (1 H, dd, 3*exo*-H, *J* 18.3 and 4.6) and 1.43 (1 H, dm, 6*endo*-H, *J* 13); δ_C(100 MHz; $CDCl_3$) 213.24 (CO), 134.33, 131.18, 129.24, 127.38 (aromatics), 78.60 (C-5), 57.06 (OMe), 55.06 (C-7), 54.44 (C-4), 42.89 (C-1), 38.99 (C-6) and 30.30 (C-3); *m*/*z* 248 (M^+, 80%), 139 (90) and 107 (80) (Found: M^+, 248.0805. $C_{14}H_{16}O_2S$ requires *M*, 248.0791).

5-endo-*Acetoxybicyclo*[2.2.1]*heptan*-2-*one* **3d**.—An excess of Raney nickel in ethanol (25 cm^3) was washed in with ethanol (5 cm^3) to a stirred solution of 5-*endo*-acetoxy-7-*anti*-phenylthiobicyclo[2.2.1]heptan-2-one **12a** (2.50 g, 9.05 mmol). The reaction was refluxed for 90 min, filtered, washed with water and extracted with dichloromethane (5 × 20 cm^3). The combined organic extracts were washed with brine (30 cm^3), dried (Na_2SO_4) and evaporated to afford a crude mixture of epimeric alcohols as a colourless oil (1.458 g, 95%). This mixture was oxidised as follows. Dimethyl sulphoxide (11.2 mmol, 0.78 cm^3) was added dropwise to a stirred solution of oxalyl chloride (5.59 mmol, 0.50 cm^3) in dichloromethane (15 cm^3) at −70 °C. After being stirred for 20 min the crude alcohol mixture (475 mg, 2.79 mmol) was added dropwise, the temperature being kept below −65 °C. The solution was stirred for a further 45 min after which triethylamine (27.9 mmol, 3.9 cm^3) was added dropwise and stirring continued for 10 min; the solution was then warmed to room temperature over 30 min. Evaporation afforded a brown oil which was separated by flash-column chromatography, eluting with ether–hexane (1:1), to furnish the *title compound* **3d** as a pale yellow oil (438 mg, 93%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2800m, 1750s (CO) and 1730s(OAc); δ_H(250 MHz; $CDCl_3$) 5.14 (1 H, dt, 5-H), 2.87 (1 H, m, 4-H), 2.54 (1 H, d, 1-H, *J* 5.0), 2.40–2.26 (2 H, m, 3*endo*-H, 6*exo*-H), 2.00 (3 H, s, OAc), 1.98 (1 H, dd, 3*exo*-H, *J* 17.9 and 4.7) 1.77 (1 H, d, 7*syn*-H, *J* 11), 1.68 (1 H, dm, 7*anti*-H, *J* 11) and 1.35 (1 H, ddd, 6*endo*-H, *J* 14.2, 3.3 and 3.3); δ_C(100 MHz; $CDCl_3$) 216.12 (CO), 170.84 (OAc), 73.08 (C-5), 49.82 (C-4), 39.07 (C-1), 38.07 (C-6), 35.98 (C-7), 32.98 (C-3) and 20.96 (CH_3, acetoxy); *m*/*z* 168 (M^+, 30%), 126 (70, M − CH_2CO) and 108 (43, M − CH_3CO_2H) (Found: M^+, 168.0776. $C_9H_{12}O_3$ requires *M*, 168.0786).

5-endo-*Methoxybicyclo*[2.2.1]*heptan*-2-*one* **3e**.—An excess of Raney nickel was added to a stirred solution of 5-*endo*-methoxy-7-*anti*-phenylthiobicyclo[2.2.1]heptan-2-one **12b** (128 mg, 0.516 mmol) in ethanol (5 cm^3). The reaction mixture was heated at 50 °C for 30 min and then at reflux for 30 min; it was then filtered, washed with water and extracted with dichloromethane (6 × 20 cm^3). The combined organic extracts were washed with brine (30 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to afford a yellow oil which was subjected to column chromatography [flash, eluting with ether–hexane (2:1)] to afford starting material (R_f 0.5) **12b** (4.8 mg, 4%), the *title compound* **3e** as a colourless, volatile oil (R_f 0.25) (25.0 mg, 35%), and an epimeric mixture of alcohols as a colourless oil (R_f 0.15) (31.8 mg, 43%). In addition, the alcohol mixture could be transformed into the title compound by the following procedure. To a stirred solution of the alcohol mixture (60.0 mg, 0.422 mmol) in acetone (3 cm^3) at 5 °C was added fresh Jones reagent [3] dropwise over 15 min until the green solution changed to orange. Propan-2-ol was added to destroy excess of Jones reagent, and the two layers were separated. The aqueous layer was further extracted with dichloromethane (3 × 10 cm^3) and the organic extracts were combined, washed with saturated aqueous sodium hydrogen carbonate (20 cm^3) and brine (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure. The crude ketone was chromatographed on a flash column [eluting with ether–hexane (1:1)] to produce the *title compound* **3e** as a colourless, volatile oil (51.0 mg, 86%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2860m, 2820w (OMe) and 1750s (CO); δ_H(400 MHz; $CDCl_3$) 3.96 (1 H, m, 5-H), 3.28 (3 H, s, OMe), 2.82 (1 H, sbr, 4-H), 2.52 (1 H, d, 1-H, *J* 5.2), 2.41 (1 H, dd, 3*endo*-H, *J* 18.0 and 4.1), 2.17 (1 H, ddd, 6*exo*-H, *J* 13.8, 9 and 5), 1.93 (1 H, dd, 3*exo*-H, *J* 18.0 and 4.8), 1.77 (1 H, d, 7*syn*-H, *J* 16), 1.65 (1 H, d, 7*anti*-H, *J* 16) and 1.33 (1 H, ddd, 6*endo*-H, *J* 13.8, 3.3 and 3.3); δ_C(100 MHz; $CDCl_3$) 216.94 (CO), 79.50 (C-5), 56.73 (OMe), 49.92 (C-4), 38.17 (C-1), 37.20 (C-6), 35.81 (C-7) and 32.77 (C-3); *m*/*z* 140 (M^+, 20%), 108 (56, M − MeOH) and 67 (100) (Found: M^+, 140.0831. $C_8H_{12}O_2$ requires *M*, 140.0831).

5-endo-*Hydroxybicyclo*[2.2.1]*heptan*-2-*one* **13**.—A solution of 5-*endo*-acetoxybicyclo[2.2.1]heptan-2-one **3d** (66.4 mg, 0.395 mmol) and potassium carbonate (14 mg, 25 mol%) in dry methanol (3 cm^3) was stirred at room temperature for 20 h after which the methanol was evaporated and the residue chromatographed [flash, eluting with ether–hexane (2:1)] to produce the *title compound* **13** as a white crystalline powder (47.9 mg, 96%), m.p. 158–159 °C (Found: C, 66.45; H, 8.1. $C_7H_{10}O_2$ requires C, 66.64; H, 7.99%); $\nu_{max}(CCl_4)/cm^{-1}$ 3630m (OH, not H-bonded), 3000–2850m and 1745s (CO); δ_H(250 MHz; $CDCl_3$) 4.48 (1 H, m, 5-H), 2.67 (1 H, dd, 4-H, *J* 4.2 and 5.9), 2.62–2.51 (2 H, m, 1-H, 3*endo*-H), 2.24 (1 H, ddd, 6*exo*-H, *J* 14, 9 and 5), 2.04 (1 H, sbr, OH), 1.95 (1 H, dd, 3*exo*-H, *J* 18.2 and 4.2), 1.75 (1 H, dm, 7*syn*-H, *J* 14), 1.67 (1 H, dm, 7*anti*-H, *J* 14) and 1.25 (1 H, ddd, 6*endo*-H, *J* 13.8, 3.1 and 3.1); δ_C(100 MHz; $CDCl_3$) 217.45 (CO), 70.61 (C-5), 50.68 (C-4), 41.13 (C-1), 37.15 (C-6), 36.29 (C-7) and 35.35 (C-3); *m*/*z* 126 (M^+, 28%), 108 (14, M − OH) and 77 (100) (Found: M^+, 126.0673. $C_7H_{10}O_2$ requires *M*, 126.0681).

5-endo-*Benzyloxybicyclo*[2.2.1]*heptan-2-one* **3f**.—A solution of 5-*endo*-hydroxybicyclo[2.2.1]heptan-2-one **13** (37.2 mg, 0.295 mmol), benzyltriethylammonium chloride (10 mol%; 6.7 mg) and benzyl bromide (76 mg, 0.05 cm^3, 1.5 equiv.) in dichloromethane (4 cm^3) was stirred vigorously at reflux with 47% w/v aqueous sodium hydroxide (1 cm^3) for 20 h. The organic layer was separated and the aqueous layer further extracted with dichloromethane (2 × 20 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated to give a colourless oil which was subjected to column chromatography over silica eluting with ether–hexane (2:3) to afford the *title compound* **3f** as white crystals (55.3 mg, 87%), m.p. 85–86 °C (Found: C, 77.4; H, 7.4. $C_{14}H_{16}O_2$ requires C, 77.7; H, 7.5%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2850m and 1745s (CO); δ_H(250 MHz; $CDCl_3$) 7.37–7.25 (5 H, m, phenyl), 4.50 (1 H, d, CH_2Ph, *J* 11.9), 4.44 (1 H, d, CH_2Ph, *J* 11.9), 4.16 (1 H, m, 5-H), 2.84 (1 H, brs, 4-H), 2.54 (2 H, m, 1-H, 3*endo*-H), 2.19 (1 H, ddd, 6*exo*-H, *J* 13.7, 9.4 and 5.2), 1.96 (1 H, dd, 3*exo*-H, *J* 18.0 and 4.6), 1.77 (1 H, m, dm 7*syn*-H, *J* 11), 1.64 (1 H, dm, 7*anti*-H, *J* 11) and 1.44 (1 H, ddd, 6*endo*-H, *J* 13.8, 3.2 and 3.2); δ_C(100 MHz; $CDCl_3$) 216.95 (CO), 138.06, 128.41, 127.67, 127.55 (aromatics), 77.56 (C-5), 71.16 (benzyl), 50.00 (C-4), 38.61 (C-1), 37.49 (C-6), 35.86 (C-7) and 32.95 (C-3); *m/z* 126 (M^+, 28%), 108 (14, M − OH) and 77 (100) (Found: M^+, 216.1160. $C_{14}H_{16}O_2$ requires *M*, 216.1150).

5-endo-*Trichloroacetoxybicyclo*[2.2.1]*heptan-2-one* **3c**.—Trichloroacetyl chloride (2 equiv., 93 mg, 0.06 cm^3) was added to a solution of 5-*endo*-hydroxybicyclo[2.2.1]heptan-2-one **13** (32.2 mg, 0.255 mmol) and pyridine (2 equiv., 0.04 cm^3). The solution and white precipitate were stirred for 3 h, poured into saturated aqueous sodium hydrogen carbonate and extracted with dichloromethane (3 × 20 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated and the residue was purified by flash chromatography eluting with ether–hexane (1:2) to afford white crystals of the *title compound* **3c** (59.7 mg, 86%), m.p. 120–122 °C (Found: C, 40.0; H, 3.3. $C_9H_9Cl_3O_3$ requires C, 39.8; H, 3.3%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000s, 2920m and 1770s (CO); δ_H(250 MHz; $CDCl_3$) 5.27 (1 H, m, 5-H), 3.07 (1 H, m, 4-H), 2.66 (1 H, d, 1-H, *J* 5.0), 2.52–2.40 (2 H, m, 3*endo*-H,6*exo*-H), 2.10 (1 H, dd, 3*exo*-H, *J* 4.5 and 18.4), 1.88 (dm, 1 H, 7*syn*-H, *J* 12), 1.79 (1 H, dm, 7*anti*-H, *J* 12) and 1.57 (ddd, 1 H, 6*endo*-H, *J* 3.3, 3.3 and 14.5); δ_C(100 MHz; $CDCl_3$) 214.47 (CO), 161.67 (trichloroacetoxy), 89.57, 76.30, 49.57, 39.21, 37.77, 36.03 and 32.38; *m/z* 270 (M^+, 65%), 226 (10), 109 (75) and 66 (100) (Found: M^+, 269.9616. $C_9H_9O_3Cl_3$ requires *M*, 269.9617).

5-endo-*Benzyloxy*-2-*ethylidenebicyclo*[2.2.1]*heptane* **14**.—Sodium hydride (60% in oil; 88 mg, 2.19 mmol) was washed with dry pentane, dried *in vacuo* and the process repeated. Dry DMSO (5 cm^3) was added, the solution heated to 70 °C for 1 h, allowed to cool to room temperature and a portion (2.23 cm^3, 0.978 mmol) added to a solution of ethyltriphenylphosphonium bromide (363 mg, 0.978 mmol) in DMSO (0.5 cm^3). The bright red solution was stirred for 10 min and 5-*endo*- benzyloxybicyclo[2.2.1]heptan-2-one **3f** (212 mg, 0.978 mmol) in DMSO (2 cm^3) was added dropwise. After a further 2 h the reaction was quenched with water (15 cm^3) and extracted with dichloromethane (3 × 15 cm^3). The combined extracts were washed with brine (20 cm^3), dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography eluting with 3% ether in hexane to afford the *title compound* **14** as a colourless oil (GC trace indicated 45:55 ratio of double bond isomers) (190 mg, 85%); $\nu_{max}(CCl_4)/cm^{-1}$ 3030m (CH olefin), 2960m and 2860m; δ_H (250 MHz; $CDCl_3$) 7.35–7.22 (5 H, m, phenyl), 5.26 [1 H, m, CH_3CH=C (one isomer)], 5.08 [1 H, dd, CH_3CH=C (one isomer), *J* 7, 13], 4.50 [1 H, d, CH_2Ph (one isomer), *J* 12], 4.49 [1 H, d, CH_2Ph (one isomer), *J* 12], 4.41 [1 H, d, CH_2Ph (one isomer), *J* 12], 4.39 [1 H, d, CH_2Ph (one isomer), *J* 12], 4.00 (1 H, m, 4-H), 2.88 [1 H, d, (one isomer), *J* 5], 2.64–2.43 (3 H, m), 2.08–1.98 (2 H, m), 1.61 [3 H, ddd, CH_3, *J* 6.7, 1.9 and 1.9 (one isomer)], 1.53 [3 H, ddd, CH_3, *J* 1.5, 1.5 and 6.7 (one isomer)], 1.39 (2 H, m) and 1.2 (1 H, m); δ_C(100 MHz; $CDCl_3$) (downfield region); δ 145.77, 144.64 (*C*=CHCH$_3$, two isomers), 138.74, 128.30, 127.67, 127.62 and 127.40 (aromatic) and 111.63 and 110.72 (C=*C*HCH$_3$, two isomers); *m/z* 228 (M^+, 5%), 211 (4), 184 (6), 137 (42) and 91 (100) (Found: M^+, 228.1514. $C_{16}H_{20}O$ requires *M*, 228.1514).

5-endo-*Ethylbicyclo*[2.2.1]*heptan-2-ol* **15**.—A solution of 5-*endo*-2-ethylidene-benzyloxybicyclo[2.2.1]heptan-2-one **14** (69.2 mg, 0.303 mmol) and palladium (10% on carbon; 10 mol%, 30 mg) in ethyl acetate (3 cm^3) was stirred under a hydrogen atmosphere for 18 h, filtered through Celite and evaporated to give the crude title compound **15** as a colourless oil (42.4 mg, 100%). GC analysis showed only one peak; $\nu_{max}(CCl_4)/cm^{-1}$ 3600s (free OH), 3500–3400m (H-bonded OH) and 3000–2850s; δ_H(250 MHz; $CDCl_3$) 4.20 (1 H, m, 5-H), 2.1 (2 H, m, 4-H, 6*exo*-H), 2.1 (10 H, m) and 0.86 (3 H, t, CH_3, *J* 7.3 and 7.3); *m/z* (CI) 158 (M + NH_4^+).

5-endo-*Ethylbicyclo*[2.2.1]*heptan-2-one* **3b**.—Jones reagent was added dropwise over 15 min to a solution of 5-*endo*-ethylbicyclo[2.2.1]heptan-2-ol **15** (42.4 mg, 0.302 mmol) in acetone (1 cm^3) at 5 °C until the green solution changed to orange. Propan-2-ol was added to destroy excess oxidising agent after which the solution was diluted with water (5 cm^3) and extracted with dichloromethane (3 × 10 cm^3). The combined organic extracts were washed with brine (10 cm^3), dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography eluting with ether–hexane (1:3) to afford the *title compound* **3b** as a colourless oil (34.2 mg, 82%) (Found: C, 78.0; H, 10.35. $C_9H_{14}O$ requires C, 78.2; H, 10.2%); GC analysis showed only one peak; $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2870s and1740s (CO); δ_H(250 MHz; $CDCl_3$) 2.53 (2 H, m, 1-H, 4-H), 2.17–1.82 (4 H, m, 3*endo*-H, 3*exo*-H, 5-H, 6*exo*-H), 1.77 (1 H, dm, 7*syn*-H, *J* 11), 1.66 (1 H, m, 7*anti*-H, *J* 11), 1.33 [2 H, m, CH_2-(ethyl)], 1.00 (1 H, dm, 6*endo*-H, *J* 11) and 0.89 (3 H, t, CH_3, *J* 7 and 7); δ_C(100 MHz; $CDCl_3$) 216.35 (CO), 50.70, 40.27, 39.05, 36.75, 36.29, 31.76, 25.34 and 12.72; *m/z* 138 (M^+, 4%), 94 (25), 84 (55) and 49 (100) (Found: M^+, 138.1045. $C_9H_{14}O$ requires *M*, 138.1045).

5-endo-*Bromo*-7-anti-*piperidinobicyclo*[2.2.1]*heptan-2-one* **17**.—Piperidine (5.16 cm^3, 4.44 g, 2 equiv.) was added dropwise to a solution of 3-*exo*-bromo-3-*endo*-bromobicyclo-[3.2.0]heptan-6-one **16** (7.00 g, 24.7 mmol) in dichloromethane (30 cm^3) at 0 °C, and the mixture stirred at room temperature for 20 h. The solution was washed with water (80 cm^3) and ammonium chloride (2.0 mol dm^{-3}; 2 × 80 cm^3) and extracted into hydrochloric acid (5 mol dm^{-3}; 2 × 40 cm^3). The combined acid extracts were treated with 47% w/w aqueous sodium hydroxide with cooling until the pH rose to *ca.* 10. The white emulsion was extracted into dichloromethane (3 × 40 cm^3), and the combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as an orange oil. This was flash chromatographed using hexane–ether (1:1) as solvent to yield a white–yellow solid which was further purified by recrystallisation from cold light petroleum (b.p. 60–80 °C) to afford *compound* **17** as off-white crystals (5.70 g, 85%), m.p. 63–64 °C (Found: C, 53.0; H, 6.7; N, 5.2. $C_{12}H_{18}BrNO$ requires C, 53.0; H, 6.7; N, 5.2%); $\nu_{max}(CCl_4)/cm^{-1}$ 2920, 2790, 1750 and 650; δ_H(250 MHz; $CDCl_3$) 4.67 (1 H, m, 5-H), 2.87–2.74 (3 H, m, 3*endo*-H, 4-H, 6*exo*-H), 2.63 (1 H, d, 1-H, *J* 4.9), 2.55 (1 H, s, 7-H), 2.40–2.12 (5 H, m, 3*exo*-H, piperidino), 1.69 (1 H, ddd, 6*endo*-H, *J* 1.0, 4.1 and 14.0) and 1.58–1.39 (6 H, m, piperidino); δ_C(100 MHz; $CDCl_3$) 213.24 (CO), 71.79 (C-7), 53.29, 51.79, 49.13, 43.84, 41.83, 33.82, 25.79 and 24.16.

7-anti-*Piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6a**.—Tributyltin hydride (1 equiv.; 1.37 mmol, 0.37 cm^3) was added to a solution of 5-*endo*-bromo-7-*anti*-piperidinobicyclo[2.2.1]heptan-2-one **17** (73 mg, 1.37 mmo) and AIBN (azoisobutyronitrile) (10 mg) in dry benzene (15 cm^3) and the mixture was refluxed for 1 h. The mixture was evaporated under reduced pressure and carefully chromatographed in light petroleum (60–80 °C)–ether (4:1) to afford the *title compound* **6a** as a yellowish oil (262 mg, 99%) (Found: C, 74.4; H, 9.85; N, 7.4. $C_{12}H_{19}NO$ requires C, 74.6; H, 9.9; N, 7.25%); $\nu_{max}(CCl_4)/cm^{-1}$ 2920s, 2840s, 2795s, 2700m and 1740s (CO); δ_H(250 MHz; $CDCl_3$) 2.60 (1 H, d, *J* 4.3), 2.56 (1 H, m), 2.38–2.21 (4 H, m), 2.13–1.12 (5 H, m) and 1.56–1.23 (8 H, m); δ_C(100 MHz; $CDCl_3$) 216.8 (CO), 71.69, 53.06, 51.95, 45.42, 36.75, 26.01, 24.77, 24.47 and 21.72 (Found: M^+, 193.470. $C_{12}H_{19}NO$ requires *M*, 193.467).

5-endo-*Methoxy*-7-anti-*piperidinobicyclo*[2.1.1]*heptan*-2-*one* **6e**.—Piperidine (5.16 cm^3, 4.44 g, 2 equiv.) was added dropwisely to an ice-cooled solution of 2-*exo*-bromo-3-*endo*-methoxybicyclo[3.2.0]heptan-6-one (27.0 g, 123 mmol) in dichloromethane (135 cm^3) at 0 °C. The mixture was stirred at room temperature for 20 h. An identical work-up procedure to that given above for compound **17** gave the crude product which was filtered through silica eluting with ether, evaporated and recrystallised from cold light petroleum (b.p. 60–80 °C) to afford *compound* **6e** as beige crystals (18.52 g, 72%), m.p. 47–48 °C (Found: C, 69.6; H, 9.5; N, 6.4. $C_{13}H_{21}NO_2$ requires C, 69.9; H, 9.5; N, 6.3%); $\nu_{max}(CCl_4)/cm^{-1}$ 2900s, 2850m, 2780m, 2740m and 1740s (CO); δ_H(250 MHz; $CDCl_3$) 4.15 (1 H, m, 5-H), 3.28 (3 H, s, OMe), 2.85 (1 H, m, 4-H), 2.75–2.2 (8 H, m), 1.95 (1 H, dd, 3*exo*-H, *J* 4 and 18), 1.7–1.35 (6 H, m, piperidino) and 1.32 (1 H, dm, 6*endo*-H, *J* 14); δ_C(100 MHz; $CDCl_3$) 215.45 (CO), 78.64, 72.55, 56.79, 53.30, 51.93, 39.71, 38.01, 30.27, 25.86 and 34.32.

5-endo-*Trichloroacetoxy*-7-anti-*piperidinobicyclo*-[2.2.1]-*heptan*-2-*one* **6b**.—Trichloroacetyl chloride (7.62 mmol, 0.85 cm^3) was added dropwise (fumes) to an ice-cooled solution of 5-*endo*-hydroxy-7-*anti*-piperidinobicyclo[2.2.1]heptan-2-one **18** (798 mg, 3.81 mmol) and pyridine (2 equiv. 0.62 cm^3) in dichloromethane (2 cm^3). The solution was stirred for 30 min at room temperature, poured into water and extracted with dichloromethane (2 × 20 cm^3). The combined extracts were washed with brine (20 cm^3), dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography eluting with dichloromethane–hexane (1:1) to give the *title compound* as a white crystalline solid (631 mg, 47%), m.p. 103–104 °C (Found: C, 47.3; H, 5.0; N, 4.0. $C_{14}H_{18}Cl_3NO_3$ requires C, 47.4; H, 5.1; N, 3.95%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2700s, 1750s (CO) and 1755–1750s (CO, $OCOCCl_3$); δ_H(250 MHz; $CDCl_3$) 5.53 (1 H, m, 5-H), 3.11 (1 H, dd, 4-H, *J* 4.3 and 4.3), 2.82–2.71 (2 H, m, 6*exo*-H, 7-H), 2.61 (1 H, d, 1-H, *J* 3.9), 2.55–2.21 (5 H, m, 3*endo*-H, piperidino), 2.10 (1 H, dd, 3*exo*-H, *J* 4.5 and 19) and 1.7–1.4 (7 H, m, 6*endo*-H, piperidino); δ_C(100 MHz; $CDCl_3$) 213.27 (CO), 161.69 ($OCOCCl_3$), 78.80, 72.44, 53.05, 51.97, 40.47, 38.23, 29.80, 25.82 and 24.23; *m*/*z* 192 (M^+ − 161, 100%), 134 (3), 119 (18), 105 (5), 84 (18) and 49 (55) [Found: $(M + H)^+$, 354.0431. $C_{14}H_{19}Cl_3NO_3$ requires *M*, 354.0431].

5-endo-*Chloroacetoxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6c**.—Piperidine (2 equiv., 0.87 mmol, 0.07 cm^3) was added to a stirred solution of 5-*endo*-hydroxy-7-*anti*-piperidinobicyclo-[2.2.1]heptan-2-one **18** (91.2 mg, 0.436 mmol) in dry ether (2 cm^3), followed by chloroacetyl chloride (2 equiv., 0.87 mmol, 0.07 cm^3) dropwise. The resulting white suspension was stirred for 3 h, dissolved in water (30 cm^3), extracted with dichloromethane (3 × 20 cm^3), and the extracts were washed with brine (20 cm^3), dried (Na_2SO_4) and evaporated to give a brown residue which was flash chromatographed with ether–hexane (1:3) to afford the title compound **6c** as a pale yellow solid (84.0 mg, 68%) (Found: C, 58.8; H, 7.1; N, 5.0. $C_{14}H_{20}ClNO_3$ requires C, 58.8; H, 7.05; N, 4.9%); $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2750s, 1750s (CO) and 1735s ($OCOCH_2Cl$); δ_H(250 MHz; $CDCl_3$) 5.44 (1 H, m, 5-H), 4.02 (2 H, s, OCH_2Cl), 2.99 (1 H, dd, 4-H, *J* 4, 4), 2.73–2.66 (2 H, m, 1-H, 6*exo*-H), 2.56 (1 H, s, 7-H), 2.50 (1 H, d, 3*endo*-H, *J* 18), 2.38–2.25 (4 H, m, piperidino), 2.05 (1 H, dd, 3*exo*-H, *J* 4.3 and 18.6) and 1.6–1.38 (7 H, m, 6*endo*-H, piperidino); δ_C(100 MHz; $CDCl_3$) 214.06 (CO), 167.12 ($OCOCH_2Cl$), 75.23, 72.44, 53.17, 51.97, 40.60, 40.42, 38.45, 30.28, 25.82 and 24.27; *m*/*z* 285 (M^+, 10%), 192 (100), 164 (5), 138 (12) and 124 (40) [Found: $(M + H)^+$, 286.1210. $C_{14}H_{21}ClNO_3$ requires *M*, 286.1210].

5-endo-*Benzyloxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6f**.—A solution of 5-*endo*-hydroxy-7-*anti*-piperidinobicyclo-[2.2.1]heptan-2-one **18** (2.00 g, 9.56 mmol), benzyltriethylammonium chloride (10 mol%; 218 mg) and benzyl bromide (1.5 equiv.; 14.3 mmol, 2.45 g, 1.70 cm^3) in dichloromethane (40 cm^3) and 47% w/w aqueous sodium hydroxide (10 cm^3) was refluxed for 18 h, poured into water (20 cm^3), and extracted with dichloromethane (3 × 20 cm^3). The combined extracts were washed with brine (20 cm^3), dried (Na_2SO_4), evaporated and the residue purified by flash chromatography eluting with dichloromethane to furnish the *title compound* **6f** as a white solid (2.119 g, 74%), m.p. 52–53 °C (Found: C, 76.2; H, 8.4; N, 4.5. $C_{19}H_{25}NO_2$ requires C, 76.2; H, 8.4; N, 4.7%); $\nu_{max}(CCl_4)/cm^{-1}$ 2920s, 2830, 2780 and 2740 (m, CN) and 1745s (CO); δ_H(250 MHz; $CDCl_3$) 7.36–7.25 (5 H, m, phenyl), 4.45 (2 H, s, OCH_2Ph), 4.39 (1 H, m, 5-H), 2.87 (1 H, dd, 4-H, *J* 4.2 and 4.2), 2.66 (1 H, d, 3*endo*-H, *J* 18.4), 2.65 (1 H, d, 1-H, *J* 5.4), 2.56–2.45 (2 H, m, 6*exo*-H, 7-H), 2.36–2.20 (4 H, m, piperidino), 1.95 (1 H, dd, 3*exo*-H, *J* 4.6 and 18.3) and 1.61–1.38 (7 H, m, 6*endo*-H, piperidino); *m*/*z* 299 (M^+, 12%), 210 (25) and 192 (100) (Found: M^+, 299.1876. $C_{19}H_{25}NO_2$ requires *M*, 299.1885).

Baeyer–Villiger Oxidations with MCPBA.—Method A. To a stirred solution of ketone in dry dichloromethane (concentration 0.05 mmol cm^{-3}) at room temperature was added a solution of freshly purified MCPBA (83%; 5 equiv.) in dry dichloromethane. The solution was stirred for 17–20 h, washed with 10% aqueous sodium metabisulphite, separated and the aqueous layer extracted with dichloromethane (3 portions). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate, separated and the aqueous layer extracted with dichloromethane (3 portions). The combined extracts were washed with brine which was back-extracted with a portion of dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to afford the lactone mixture.

Method B. The reaction was performed using the conditions as for Method A above. After reaction, the solution was further stirred vigorously with 10% aqueous sodium metabisulphite for up to 1 h (monitoring for complete disappearance of polar *N*-oxide by TLC). The organic layer was separated and the aqueous layer extracted with dichloromethane (3 portions). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate and work-up continued as for Method A.

Baeyer–Villiger oxidation of bicyclo[2.2.1]*heptan*-2-*one* **3a**. The title compound (62.4 mg, 0.566 mmol, recrystallised from pentane) was treated with MCPBA (589 mg) and dichloromethane (11.8 cm^3 total volume) using Method A, to afford a volatile pale yellow oil (69.2 mg, 97%); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone, prominent signals) 4.82 (1 H, brs, 1-H); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone,

prominent signals) 4.29 (1 H, dd, 4*endo*-H, *J* 10.6 and 3.2), 4.08 (1 H, d, 4*exo*-H, *J* 10.6) and 2.88 (1 H, dd, 1-H, *J* 4.6 and 4.6). The ratio of lactone isomers based on integration of 1-H signal (methine-migrated lactone) to 4*endo*-H and 4*exo*-H (methylene-migrated lactone) was 93:7 respectively (the lactones could not be separated by GC).

Baeyer–Villiger oxidation of 5-endo-*ethylbicyclo*[2.2.1]-*heptan*-2-*one* **3b**. The title compound (22.8 mg, 0.165 mmol) was treated with MCPBA (168 mg) and dichloromethane (3.3 cm^3 total volume) using Method A, to afford a pale yellow oil (24.7 mg, 97%). Ratio of lactone isomers was 95:5 by GC analysis. A pure sample of the methine-migrated lactone **4b** was purified by chromatography to give a colourless oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3000–2850m and 1745s (CO); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 4.77 (1 H, m, 1-H), 2.64 (1 H, dd, 4*endo*-H, *J* 2 and 19), 2.53 (1 H, dd, 4*exo*-H, *J* 1 and 19), 2.40 (1 H, m, 5-H), 2.22 (1 H, ddd, 7*exo*-H, *J* 5.0, 11.2 and 14.9), 2.05 (1 H, dm, 8*syn*-H, *J* 13), 2.0 (1 H, m, 6-H), 1.73 (1 H, dm, 8*anti*-H, *J* 13) and 1.6 (1 H, m, 7*endo*-H); *m/z* (CI) 155 ($M + H^+$, 100%), 98 (5) and 95 (3) [Found: $(M + H)^+$ 155.1072. $C_9H_{15}O_2$ requires $(M + H)^+$ 155.1072].

Baeyer–Villiger oxidation of 5-endo-*trichloroacetoxybicyclo*-[2.2.1]*heptan*-2-*one* **3c**. The title compound (29.1 mg, 0.107 mmol) was treated with MCPBA (111 mg) and dichloromethane (2.1 cm^3 total volume) using Method A, to afford a pale yellow oil (30.9 mg, 100%); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 5.37 (1 H, m, 6-H), 4.83 (1 H, s, 1-H), 2.95–2.91 (2 H, m, 4*endo*-H, 5-H), 2.69 (1 H, dd, 4*exo*-H, *J* 5.4 and 19), 2.59 (1 H, ddd, 7*exo*-H, *J* 5, 10.5 and 16), 2.20–2.11 (2 H, m, 8*syn*-H, 7*endo*-H) and 1.86 (1 H dm, 8*anti*-H, *J* 11); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.55 (1 H, d, 4*endo*-H, *J* 11) and 4.28 (1 H, dd, 4*exo*-H, *J* 3.6 and 11). Ratio of lactone isomers was 83:17 by GC analysis.

Baeyer–Villiger oxidation of 5-endo-*acetoxybicyclo*[2.2.1]-*heptan*-2-*one* **3d**. The title compound (33.4 mg, 0.200 mmol) was treated with MCPBA (208 mg) and dichloromethane (4.0 cm^3 total volume) using Method A, to afford a colourless oil (31.7 mg, 87%); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone, prominent signals) 5.5 (1 H, m, 6-H), 4.74 (1 H, brs, 1-H) and 2.06 (3 H, s, OAc); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 5.5 (1 H, m, 6-H), 4.44 (1 H, d, 4*endo*-H, *J* 11.4), 4.20 (1 H, dd, 4*exo*-H, *J* 11.4 and 3.4). Ratio of lactone isomers based on integration of 1-H signal (methine-migrated lactone) to 4*endo*-H and 4*exo*-H (methylene-migrated lactone) was 86:14 respectively (the lactones could not be separated by GC).

Baeyer-Villiger oxidation of 5-endo-*methoxybicyclo*[2.2.1]-*heptan*-2-*one* **3e**. The title compound (19.6 mg, 0.140 mmol) was treated with MCPBA (145 mg) and dichloromethane (2.8 cm^3 total volume) using Method A, to afford a pale yellow oil (21.9 mg, 100%); δ_H(400 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.56 (1 H, d, 4*endo*-H, *J* 11), 4.16 (1 H, dd, 4*exo*-H, *J* 11), 3.8 (1 H, m, 6-H), 3.33 (3 H, s, OMe), 2.81 (1 H, m, 1-H). Ratio of lactone isomers was 84:16 by GC analysis. A pure sample of the methine-migrated lactone **4e** was obtained as a colourless oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2930s, 2860m, 2820m and 1740s (CO); δ_H(250 MHz; $CDCl_3$) 4.70 (1 H, m, 1-H), 3.91 (1 H, m, 6-H), 3.30 (3 H, s, OMe), 2.91 (1 H, ddd, 4*endo*-H, *J* 18.4, 1.9 and 1.3), 2.61 (1 H, dd, 5-H, *J* 10.2 and 5.0), 2.51 (1 H, ddd, 4*exo*-H, *J* 18.4, 5.6 and 1.1), 2.29 (1 H, ddd, 7*exo*-H, *J* 14.8, 10.8 and 5.2), 2.03 (1 H, dd, 8*syn*-H, *J* 13.1 and 3.5), 1.89 (1 H, ddd, 7*endo*-H, *J* 15.6, 4.1 and 4.1) and 1.69 (1 H, br m, 8*anti*-H); δ_C(100 MHz; $CDCl_3$) 170.43 (CO), 81.15, 78.81, 57.45, 38.80, 34.49, 33.80 and 32.19; *m/z* (CI) 157 ($M + H^+$, 100%) and 98 (5) [Found: $(M + H)^+$ 157.0865. $C_8H_{13}O$ requires $(M + H)^+$, 157.0865].

Baeyer–Villiger oxidation of 5-endo-*benzyloxybicyclo*[2.2.1]-*heptan*-2-*one* **3f**. The title compound (22.6 mg, 0.109 mmol) was treated with MCPBA (113 mg) and dichloromethane (2.2 cm^3 total volume) using Method A, to afford a colourless oil (24.0 mg, 99%); δ_H(400 MHz; $CDCl_3$) 7.36–7.25 (5 H, m, phenyl), 4.72 (1 H, m, 1-H), 4.49 (2 H, s, benzyl), 4.12 (1 H, m, 6-H), 3.04 (1 H, dd, 4*endo*-H, *J* 18.5 and 1.2), 2.61 (1 H, m, 5-H), 2.54 (1 H, m, 4*exo*-H), 2.30 (1 H, ddd, 7*exo*-H, *J* 15, 10 and 5), 2.01 (2 H, m, 7*endo*-H, 8*syn*-H) and 1.68 (1 H, dm, 8*anti*-H, *J* 12); δ_H(400 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.18 (1 H, dd, 4*exo*-H, *J* 10.5 and 4) and 2.84 (1 H, m, 1-H), 2.2 (1 H, m, 6-H). Ratio of lactone isomers based on integration of 1-H and 4*endo*-H signals (methine-migrated lactone) to 1-H (methylene-migrated lactone) was 75:25 respectively (the lactones could not be separated by GC).

Baeyer–Villger oxidation of 7-anti-*piperidinobicyclo*[2.2.1]-*heptan*-2-*one* **6a**. The title compound (36.9 mg, 0.191 mmol) was treated with MCPBA (194 mg) and dichloromethane (3.8 cm^3 total volume) using Method B, to afford a brown oil (37.8 mg, 65% correcting for residual 3-chlorobenzoic acid by NMR); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 4.80 (1 H, brs, 1-H), 2–1 (19 H, m). Ratio of lactone isomers was 89:11 by GC analysis.

Baeyer–Villiger oxidation of 7-anti-*piperidino*-5-endo-*trichloroacetoxybicyclo*[2.2.1]*heptan*-2-*one* **6b**. The title compound (59.6 mg, 0.168 mmol) was treated with MCPBA (171 mg) and dichloromethane (3.4 cm^3 total volume) using Method B, to afford a brownish oil (40.2 mg, 55% corrected for residual 3-chlorobenzoic acid by NMR); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 5.49 (1 H, m, 5-H), 4.79 (1 H, d, 1-H, *J* 4.0), 3.07–2.7 (4 H, m, 4*endo*-H, 5-H, 7*exo*-H, 8-H), 2.65 (1 H, dd, 4*exo*-H, *J* 5.5 and 19), 2.5–2.3 (4 H, m, piperidino), 2.08 (1 H, dm, 7*endo*-H, *J* 18) and 1.7–1.4 (6 H, m, piperidinyl); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.54 (1 H, dd, 4*endo*-H, *J* 1.1 and 11.6), 4.20 (1 H, dd, 4*exo*-H, *J*, 3.4 and 11.5) and 1.90 (1 H, dm, 7*endo*-H, *J* 13). Ratio of lactone isomers was 83:17 by GC analysis.

Baeyer–Villiger of 5-endo-*chloroacetoxy*-7-anti-*piperidino-bicyclo*[2.2.1]*heptan*-2-*one* **6c**. The title compound (29.5 mg, 0.103 mmol) was treated with MCPBA (105 mg) and dichloromethane (2.1 cm^3 total volume) using Method B, to afford a pale yellow oil (29.8 mg, 82% correcting for residual 3-chlorobenzoic acid by NMR); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 5.38 (1 H, m, 6-H), 4.72 (1 H, d, 1-H, *J* 4), 4.07 (2 H, s, $OCOCH_2Cl$), 2.93–2.72 (4 H, m, 4*endo*-H, 5-H, 8-H and 7*exo*-H), 2.59 (1 H, dd, 4*exo*-H, *J* 6 and 18), 2.48–2.35 (4 H, m, piperidinyl), 1.91 (1 H, ddd, 7*endo*-H, *J* 1.7, 3.9 and 15.9) and 1.56–1.33 (6 H, m, piperidino); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.45 (1 H, d, 4*endo*-H, *J* 12), 4.15 (1 H, dd, 4*exo*-H, *J* 3.4 and 11.5), 4.08 (2 H, s, $OCOCH_2Cl$), 3.10 (1 H, d, 1-H, *J* 7) and 1.77 (1 H, m, 7*endo*-H, *J* 16). Ratio of lactone isomers was 80:20 by GC analysis.

Baeyer–Villiger oxidation of 5-endo-*acetoxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6d**. The title compound (48.1 mg, 0.191 mmol) was treated with MCPBA (194 mg) and dichloromethane (3.8 cm^3 total volume) using Method B above, to afford a yellow oil (55.1 mg, 92% correcting for residual 3-chlorobenzoic acid by NMR); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 5.28 (1 H, m, 6-H), 4.71 (1 H, d, 1-H, *J* 4.4), 2.9–2.3 (9 H, m), 2.06 (3 H, s, OAc), 1.91 (1 H, dm, 7*endo*-H, *J* 16.4), 1.6–1.4 (6 H, m, piperidino); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.44 (1 H, d, 4*endo*-H, *J* 10.9), 4.14 (1 H, dd, 4*exo*-H, *J* 10.9 and 4.4), 3.06 (1 H, d, 1-H, *J* 8), 2.07 (3 H, s, OAc) and 1.72 (1 H, dd, 7*endo*-H, *J* 15.3). Ratio of lactone isomers was 74:26 by GC analysis.

Baeyer–Villiger oxidation of 5-endo-*methoxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6e**. The title compound (71.9 mg, 0.322 mmol) was treated with MCPBA (327 mg) and dichloromethane (6.4 cm^3 total volume) using Method B above, to

afford a brown oil (79.0 mg, 92% correcting for residual 3-chlorobenzoic acid by NMR); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.59 (1 H, d, 4*endo*-H, *J* 10.1), 3.30 (3 H, s, OMe). Ratio of lactone isomers was 67:33 by GC analysis. A pure sample of the methine-migrated lactone was obtained as a pale yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2940s and 1750s (CO); δ_H(250 MHz; $CDCl_3$) 4.66 (1 H, dm, 1-H, *J* 4.2), 4.05 (1 H, m, 6-H), 2.98 (1 H, dd, 4*endo*-H, *J* 1.6 and 18.7), 2.74 (1 H, m, 5-H), 2.69 (1 H, s, 8-H), 2.58–2.31 (6 H, m, 4*exo*-H, 7*exo*-H, piperidino), 1.82 (1 H, dm, 7*endo*-H, *J* 15.3) and 1.56–1.41 (6 H, m, piperidino); δ_C(100 MHz; $CDCl_3$) 170.50, 80.29, 80.00, 70.68, 57.42, 51.54, 36.83, 36.68, 31.86, 31.59, 25.91 and 24.25; *m/z* (CI) 240 (M + H^+, 100%) [Found: (M + H)$^+$, 240.1600. $C_{13}H_{22}NO_3$ requires *M*, 240.1600).

Baeyer–Villiger oxidation of 5-endo-*biphenyl*-4-*yloxycarbonyl*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6f**. The title compound (225.6 mg, 0.559 mmol) was treated with MCPBA (581 mg) and dichloromethane (11.2 cm^3 total volume) using Method B above, to afford a pale yellow foam (236.3 mg, 100%); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone, prominent signals) 8.1–7.3 (9 H, m, phenyl), 5.6 (1 H, m, 6-H), 4.80 (1 H, brd, 1-H, *J* 4.1) and 2.12 (1 H, dm, 7*endo*-H, *J* 15.3); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 8.1–7.3 (9 H, m, phenyl), 5.6 (1 H, m, 6-H), 4.55 (1 H, d, 4*endo*-H, *J* 11.3), 4.21 (1 H, dd, 4*exo*-H, *J* 11.3 and 3.3) and 1.94 (1 H, dd, 7*endo*-H, *J* 14.5). Ratio of lactone isomers based on integration of 1-H signal (methine-migrated lactone) to 4*endo*-H and 4*exo*-H (methylene-migrated lactone) was 68:32 respectively.

Baeyer–Villiger oxidation of (+)-5-endo-*biphenyl*-4-*ylmethoxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6g**. The title compound (148.3 mg, 0.395 mmol) was treated with MCPBA (411 mg) and dichloromethane (7.9 cm^3 total volume) using Method B above, to afford an orange foam (149.2 mg, 97%). Ratio of lactone isomers based on integration of 4*endo*-H signal (methine-migrated lactone) to 1-H (methylene-migrated lactone), and also 7*endo*-H signal to 7*endo*-H, was 60:40 respectively. Pure samples of both lactones were obtained. *Methine-migrated lactone* **7g**: m.p. 127.5–128.5 °C (Found: C, 76.6; H, 7.35; N, 3.7. $C_{25}H_{29}NO_3$ requires C, 76.7; H, 7.5; N, 3.5%); $[\alpha]_D^{25}$ −28.08 10^{-1} deg cm^2 g^{-1} (*c* 2.19, $CHCl_3$); $\nu_{max}(CCl_4)/cm^{-1}$ 2940s, 2850m, 2800m, 2760m and 1750s (CO); δ_H(250 MHz; $CDCl_3$) 7.61–7.31 (9 H, aromatic), 4.70 (1 H, d, 1-H, *J* 4.5), 4.55 (1 H, d, benzyl, *J* 11.8), 4.48 (1 H, d, benzyl, *J* 11.8), 4.33 (1 H, m, 6-H), 3.14 (1 H, dd, 4*endo*-H, *J* 1.3 and 18.6), 2.78 (1 H, dd, 5-H, *J* 5.3 and 5.3), 2.73 (1 H, s, 8-H), 2.65–2.53 (6 H, m, 4*exo*-H, 7*exo*-H, piperidino), 1.96 (1 H, m, 7*endo*-H, *J* 15.2) and 1.53–1.43 (6 H, m, piperidino); δ_C(100 MHz; $CDCl_3$) 170.50 (CO), 140.81, 140.66, 137.03, 127.78, 127.91, 127.31, 127.18, 127.08, 80.00, 78.69, 71.71, 70.71, 51.56, 37.17, 37.06, 31.91, 25.92 and 24.27; *m/z* (CI) 392 (M + H^+, 100%) and 226 (15) (Found: M + H^+, 392.2226. $C_{25}H_{30}NO_3$ requires *M* + H^+, 392.2226). *Methylene-migrated lactone* **8g**: m.p. 125.5–126.5 °C (Found: C, 76.45; H, 7.3; N, 3.5. $C_{25}H_{29}NO_3$ requires C, 76.7; H, 7.5; N, 3.6%); $[\alpha]_D^{25}$ −2.88 10^{-1} deg cm^2 g^{-1} (*c* 2.15, $CHCl_3$); $\nu_{max}(CCl_4)/cm^{-1}$ 2940s, 2855m, 2800m, 2775m and 1750s (CO); δ_H(250 MHz; $CDCl_3$), 7.61–7.31 (9 H, aromatic), 4.74 (1 H, d, 4*endo*-H, *J* 10.8), 4.59 (1 H, d, benzyl, *J* 11.8), 4.50 (1 H, d, benzyl, *J* 11.8), 4.35 (1 H, m, 6-H), 4.10 (1 H, dd, 4*exo*-H, *J* 3.6 and 10.8), 3.06 (1 H, d, 1-H, *J* 7.2), 2.74 (1 H, brs, 5-H), 2.70 (1 H, s, 8-H), 2.51 (1 H, ddd, 7*exo*-H, *J* 14.0, 7.7 and 8.9), 2.35 (4 H, m, piperidino), 1.77 (1 H, dd, 7*endo*-H, *J* 14.0 and 3.2) and 1.59–1.42 (6 H, m, piperidino); δ_C(100 MHz; $CDCl_3$) 174.33 (CO), 140.80, 140.65, 137.15, 128.78, 127.87, 127.32, 127.16, 127.08, 77.24, 71.88, 67.70, 62.10, 51.07, 43.86, 40.08, 33.26, 25.93 and 24.37; *m/z* (CI) 392 (M + H^+, 100%), 224 (10), 167 (3), 124 (5) and 86 (5) [Found: (M + H)$^+$ 392.2226. $C_{25}H_{30}NO_3$ requires (*M* + H)$^+$, 392.2226].

Baeyer–Villiger oxidation of 5-endo-*benzyloxy*-7-anti-*piperidinobicyclo*[2.2.1]*heptan*-2-*one* **6h**. The title compound (18.1 mg, 0.0605 mmol) was treated with MCPBA (63 mg) and dichloromethane (1.2 cm^3 total volume), using Method B above, to afford a colourless oil (18.9 mg, 98%); δ_H(250 MHz; $CDCl_3$) (methine-migrated lactone) 7.45–7.2 (5 H, m, phenyl), 4.69 (1 H, br s, 1-H), 4.61 (1 H, d, benzyl, *J* 11.8), 4.45 (1 H, d, benzyl, *J* 11.8), 4.3 (1 H, m, 6-H), 3.12 (1 H, dd, 4*endo*-H, *J* 18.7 and 1.5), 2.85–2.4 (8 H, m), 1.92 (1 H, dm, 7*endo*-H, *J* 15.3) and 1.6–1.4 (6 H, m, piperidino); δ_H(250 MHz; $CDCl_3$) (methylene-migrated lactone, prominent signals) 4.73 (1 H, m, 4*endo*-H), 4.61 (1 H, d, benzyl, *J* 11.8), 4.43 (1 H, d, benzyl, *J* 11.8), 4.08 (1 H, dd, 4*exo*-H, *J* 10.8 and 3.6), 3.05 (1 H, m, 1-H) and 1.73 (1 H, dd, 7*endo*-H, *J* 14.1 and 3.4). Ratio of lactone isomers based on integration of 7*endo*-H signal (methine-migrated lactone) to 7*endo*-H (methylene-migrated lactone) was 58:42 respectively.

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