Cascade rearrangement of spiroepoxymethyl radicals into 2-oxocycloalkyl radicals: evaluation of a two-carbon cycloalkanone ring expansion

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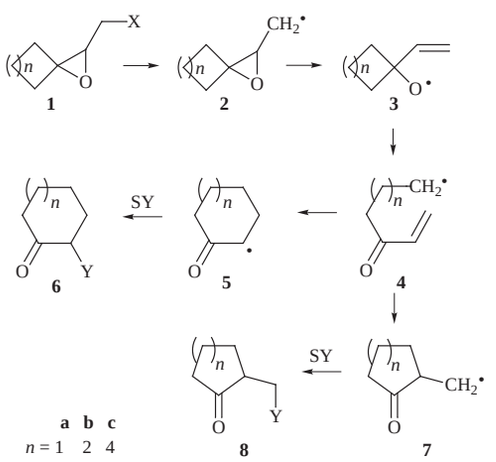
Series of 2-bromomethyl- and 2-hydroxymethyl-1-oxaspiro[2.*n*]alkanes were prepared from cycloalkanones by initial Wadsworth–Horner–Emmons methodology to afford ester-substituted methylenecycloalkanes. The latter were selectively reduced to hydroxymethylmethylenecycloalkanes which were epoxidised with peroxyacetic acid. Homolytic reactions were studied by EPR spectroscopy which enabled transient 3-oxoalk-1-enyl radicals, and their cyclisation products, 2-oxocycloalkyl and 2-oxocycloalkylmethyl radicals, to be characterised. This evidence, together with end product analyses of organotin hydride reductions of the 2-bromomethyl-1-oxaspiro[2.*n*]alkanes, established that the initial spiroepoxymethyl radicals rearranged by a three-stage cascade of two consecutive β-scissions followed by a cyclisation. Cyclisations of the 3-oxoalk-1-enyl radicals took place mainly in the *endo*-mode to afford 2-oxocycloalkyl radicals, except for the 5-oxohept-6-enyl radical for which *exo*-cyclisation to generate the 2-oxocyclohexylmethyl radical was preferred. Kinetic data for the *exo*- and *endo*-cyclisations of the 4-oxohex-5-enyl radical were obtained from tributyltin hydride mediated reactions of 2-bromomethyl-1-oxaspiro[2.3]hexane.

Introduction

The most useful free radical cascade rearrangements are those which involve carbon–carbon bond formation, and thus multiple cyclisation sequences leading to the assembly of polycyclic compounds have received the most attention.[1–3] In contrast, multiple β-scissions usually lead to degradation of the original molecular architecture, as illustrated by the comprehensive disassembly of the 3D-cage of cubylmethyl radicals by a cascade of three β-scissions producing a biscyclobutenyl structure.[4,5] A fair range of unimolecular cascades combining these two rearrangement steps, *i.e.* β-scissions with cyclisations, has been studied. For example, β-scissions of suitably unsaturated epoxymethyl radicals followed by cyclisations led to the production of vinyltetrahydrofurans.[6,7] Several of the penultimate vinyltetrahydrofuranylmethyl radicals underwent a second cyclisation to afford 7-oxabicyclo[2.2.1]heptane derivatives. Intramolecular additions of alkyl radicals to carbonyl bonds, followed by β-scission of the resulting alkoxyl radicals have been exploited as a means of ring expansion by one, and by three or more C-atoms, but not by two C-atoms.[8] The rapid β-scission of appropriately unsaturated cyclopropylmethyl radicals, followed by cyclisation, has been utilised for the production of a fledgling range of spirocyclic and polycyclic structures. Noteworthy examples employed functionalised alkynylbicyclo[4.1.0]heptanes, and the corresponding bicycloheptan-2-ones, as precursors.[9–11] To date, however, unimolecular cascades embodying two β-scissions and a cyclisation are rare and select phenomena.

Certain β-scissions, notably those of alkoxyl radicals which yield ketones, do not require excessive ring strain as the driving force.[12] In principle, therefore, this fragmentation could be combined with several unimolecular radical steps to achieve potentially valuable molecular reorganisation. An intriguing cascade sequence incorporating three of these homolytic steps is outlined in Scheme 1. Simple epoxymethyl radicals related to radical **2** are known to undergo very rapid β-scissions[13,14] of their carbon–oxygen bonds[7,15] and hence 1-vinylcycloalkoxyl radicals **3** should form with great ease. Intermediate **3** is expected to undergo a second β-scission, at moderate temperature, to selectively afford the more stabilised 3-oxoalkenyl



Scheme 1 SY = initial radical source (Y = H or halogen).

radical **4**, in preference to scission of the vinyl–carbon bond. Radical **4** has a choice of either ring closure in the *exo*-mode with production of a 2-oxocycloalkanylmethyl radical **7** or in the *endo*-mode to yield the 2-oxocycloalkyl radical **5** as a reorganised product of elegant simplicity. The presence of the 3-oxo group in **4** might predispose this radical to *endo*-cyclisation as a result of its electron-withdrawing character inducing a favourable polar effect in the transition state and because the *endo*-radical **5** is stabilised by resonance delocalisation of the unpaired electron onto oxygen. This mode of the cascade is potentially of synthetic value because the overall transformation amounts to a rare two-carbon ring expansion process.

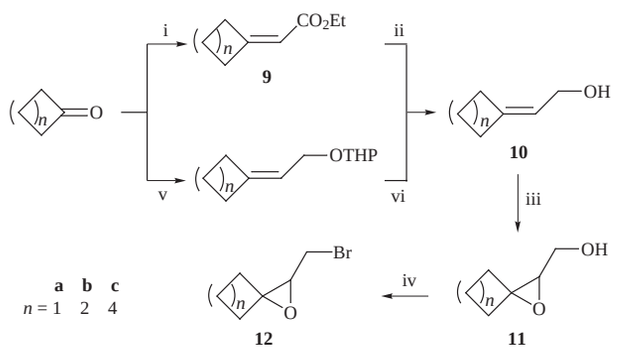
A cascade closely related to this was first reported by Kim and Lee who examined the addition of organotin and phenylthiyl radicals to 2-vinylspiroepoxides. They observed mainly one-carbon ring expansion on starting with 1-oxa-2-vinylspiro[2.3]hexane derivatives and analogous spiro[2.4]heptane derivatives, presumably as a result of final *exo*-cyclisation.[16] Galatsis and co-workers[17] briefly reported a product study of the organotin hydride induced rearrangement of iodomethylspiroepoxides analogous to **1**. Moderate to low yields of the

two-carbon ring-expanded products (**6**, Y = H) were isolated for several medium ring sizes, but for the cyclopentane ring (**1**, $n = 2$) the *exo*-product (**8**, Y = H) predominated in a low yielding reaction carried out in refluxing benzene. In this paper we report our systematic study of this cascade in which we have probed the regioselectivity and kinetics of the cyclisation steps as a function of ring size and of reaction temperature and have characterised several intermediates by EPR spectroscopy.

Results and discussion

Synthesis of spiroepoxyalkyl precursors 1

Spiroepoxymethyl bromides (**12**) and alcohols (**11**) were chosen as the radical precursors and two flexible synthetic routes were examined (Scheme 2). Cycloalkanones were converted to



Scheme 2 i, $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, reflux 5 h; ii, $LiAlH_3(OEt)$, Et_2O, 17 h; iii, AcO_2H, AcOH, DCE, reflux 4 h; iv, $MeSO_2Cl$, Et_3N, DCM, then LiBr, Me_2CO, reflux 1 h; v, $Ph_3P^+CH_2CH_2OTHP$, BuLi, Et_2O, reflux 12 h; vi, EtOH, PPTS.

unsaturated esters **9** using Wadsworth–Horner–Emmons conditions. Selective reductions to the unsaturated alcohols **10** were troublesome due to co-production, during use of $LiAlH_4$, Red-Al or DIBAL-H, of some of the saturated analogue. However, for the unsaturated esters **9b**,**c** with larger ring sizes, selective reduction to **10b**,**c** was achieved cleanly with lithium aluminium ethoxide hydride.[18] For **9a** however, the best results were obtained by reduction using DIBAL-H and subsequent chromatographic purification of **10a**. An alternative strategy avoiding this reduction was examined. Normal Wittig chemistry was used to convert cyclopentanone to the THP-protected allylic alcohol (Scheme 2) by use of the triphenylphosphonium salt of THP-protected 2-bromoethanol. Deprotection with PPTS afforded the same allylic alcohol **10b** but the overall yield was inferior to that of the first route. Epoxidations were carried out efficiently with peroxyacetic acid and the resulting epoxyalcohols **11** were converted to the spiro-bromides **12** by reaction of the corresponding mesylates with lithium bromide.

EPR spectroscopic study of the cascade

EPR spectra of the transient radicals generated by bromine abstraction in the temperature range 150–200 K were examined by photolysis of a cyclopropane solution containing the 4-membered spiroepoxide (**12a**) triethylsilane and di-*tert*-butyl peroxide directly in the microwave cavity of an EPR spectrometer [reactions (1)–(3)]. At higher temperatures a *tert*-butylbenzene solution was used in which hexamethylditin replaced the silane and peroxide.

$$t\text{-BuOOBu-}t + h\nu \longrightarrow 2t\text{-BuO}^{\bullet} \quad (1)$$

$$t\text{-BuO}^{\bullet} + Et_3SiH \longrightarrow Et_3Si^{\bullet} + t\text{-BuOH} \quad (2)$$

$$Et_3Si^{\bullet} + \mathbf{12} \longrightarrow \mathbf{2} + Et_3SiBr \quad (3)$$

Table 1 EPR data for radicals generated from 2-bromomethyl-1-oxaspiro[2.*n*]alkanes[a]

Radical	*T*/K	H(α)	H(β)	H(other)	T_{mid}/K[b]
4a	155	22.3 (2H)	29.2 (2H)	0.55 ($2H_\gamma$)	205
15aH	150	22.8 (2H)	30.0 (2H)	0.5 ($2H_\gamma$)	>260
15aD	150	22.8 (2H)	30.2 (2H)	0.52 ($2H_\gamma$)	>260
4b					<200
15bH	240	22.4 (2H)	28.4 (2H)	0.70 ($2H_\gamma$)	250
15bD	235	22.2 (2H)	28.8 (2H)	0.75 (2H)	
4c	200	22.6 (2H)	29.0 (2H)		270
5a	235	18.0 (1H)	34.2 (2H)[c]		
7b	210	22.6 (2H)	30.4 (1H)		
5c	290	18.0 (1H)	21.0 (2H)		
17bH[d]	240	17.4 (1H)	17.4 (1H)	1.5 (OH)	
17bD[d]	280	17.4 (1H)	17.4 (1H)		

[a] Hfs in G (10 G = 1 mT), all *g*-factors 2.003 ± 0.001 except as noted below. [b] Temperature at which the cyclised and uncyclised radical are equal in concentration. [c] Lines broadened due to ring inversion: hfs of the 2 non-equivalent H(β) were *ca.* 24 and 43 G at 210 K. [d] *g*-factor = 2.0031.

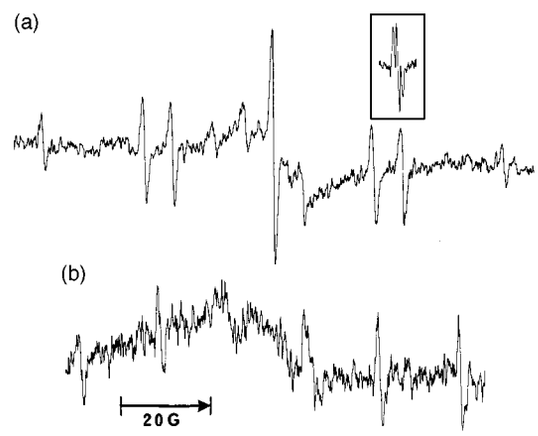
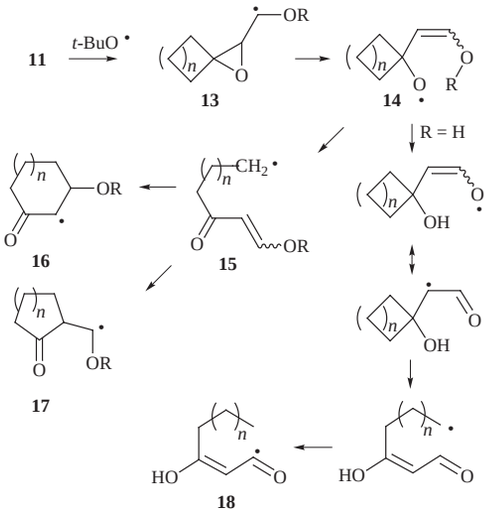


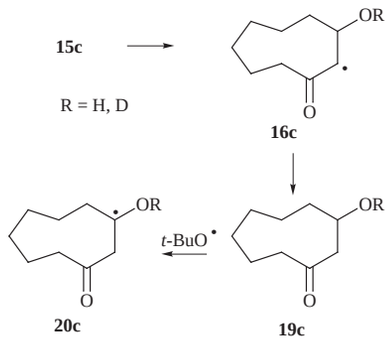
Fig. 1 9.4 GHz EPR spectra of radicals derived from 2-bromomethyl-1-oxaspiro[2.3]hexane **12a** in cyclopropane solution. Upper spectrum shows the 4-oxohex-5-enyl radical **4a** at 190 K with one line displayed under higher resolution in the inset. Lower spectrum shows the 2-oxocyclohexyl radical **5a** at 235 K; note the broadening on the two inner lines.

In the temperature range 150 to 190 K a nine line spectrum (Fig. 1a) was observed with EPR parameters (Table 1) which enabled this to be reliably attributed to the primary radical **4a**. As expected therefore, the β-scissions of both **2a** and **3a** were very rapid even at 150 K. At higher temperatures (>210 K) the spectrum of **4a** was replaced by a new one containing a total of six lines, the inner two being strongly broadened (Fig. 1b). The EPR parameters were identical to those recorded in the literature[19,20] for radical **5a**. This spectroscopic observation of two of the intermediates corroborates the cascade sequence and shows that cyclisation in the *endo*-mode dominates at these low temperatures. The intermediate from *exo*-cyclisation, *i.e.* **7a** was not detected up to *ca.* 240 K, above which the spectra became too weak for analysis.

Hydroxy- and deuteroxy-substituted spiroepoxymethyl radicals **13aH** and **13aD** were generated by hydrogen abstraction, with photochemically generated *tert*-butoxyl radicals, from alcohol **11a** and the corresponding deuterium-substituted compound (Scheme 3). In both cases good spectra due to the primary ring-opened radicals **15aH** and **15aD** were observed (Table 1) but cyclised radicals could not be identified with certainty at temperatures up to 260 K. Thus, *endo*-cyclisation was slower, as would be expected for a hex-5-enyl type radical containing a substituent at the attacked centre. The spectra at lower temperatures ($T < 190$ K) showed the presence of an additional radical with a doublet hyperfine splitting (hfs) [a(1H) = 19.9 G, $g = 2.001$] which disappeared at higher temperatures. The



Scheme 3



Scheme 4

g-factor identifies this as an acyl radical and the doublet hfs suggests an unsaturated species of the general type >C=CH–C$^{\bullet}$=O, similar to MeCH=CH–C$^{\bullet}$=O [g = 2.0005, a(H_β) = 19.5 G] and analogous species observed by Davies and co-workers.[21] A likely structure for this additional radical is **18a** formed *via* a 1,5-hydrogen migration in radical **14a** followed by β-scission of the second ring and a second hydrogen transfer as outlined in Scheme 3.

The EPR spectra obtained on bromine atom abstraction from the next higher spiroepoxymethyl bromide **12b** were too weak and broad at T < 200 K for definite observation of the uncyclised radical **4b**. Above this temperature a well-marked spectrum of a triplet of doublets was obtained due to radical **7b**, the product of *exo*-cyclisation (Table 1). The magnitude of a(H_β) decreased as the temperature was increased and hence, in the preferred conformation of radical **7b**, the SOMO eclipses the C–H_β bond. A spectral study of hydrogen abstraction from spiroepoxymethanol **11b** revealed the primary radical **15bH** at 240 K accompanied by a second species with a spectrum consisting of a triplet of doublets (Table 1). The EPR parameters of the latter radical are consistent with it being radical **17bH** from *exo*-cyclisation, and this was corroborated by observation of the deuterium isotopomer **17bD** with similar EPR parameters. The lower T_{mid} values for **4b** and **15bH** indicate that cyclisation occurs significantly faster than for the shorter chain **4a** and **15aH**. Interestingly, however, the preferred cyclisation mode changes from *endo* for **4a** and **15aH** to *exo* for the next higher analogues.

The uncyclised radical **4c** was readily detected at temperatures below 250 K on bromine abstraction from the 7-membered ring spiroepoxymethyl bromide **12c**. By 290 K this had been completely replaced by a new spectrum (Table 1) which we attribute to the *endo*-cyclised radical **5c**, none of the product of *exo*-cyclisation could be detected in this temperature range. Only a single weak spectrum was obtained during hydrogen abstraction from the 7-membered ring alcohol **11c** and this consisted of a pentet of doublets [a(4H) = 19.8, a(1H) = 1.8 G at 240 K]. Hydrogen abstraction from the deuteroxy analogue **11cD** gave rise to a spectrum consisting of only a pentet [a(4H) = 19.8 G at 290 K] which demonstrated that the small doublet hfs was due to an OH group attached to the radical centre. The observed hfs are very similar to those of the 1-hydroxycycloheptyl radical [a(4H) = 19.0, a(1H) = 1.0 at 200 K][22] and hence our spectrum is almost certainly that of the 1-hydroxy-3-oxocyclononyl radical **20c**. It is probable that this is formed by hydrogen abstraction from the product 3-hydroxycyclononanone **19c** as shown in Scheme 4, and this is indirect evidence that *endo*-cyclisation predominates in this system.

The EPR spectra provide good evidence in support of the 3-stage cascade and imply that the final cyclisation is the slow rate-controlling step in each case and is predominantly *endo*, at temperatures below 298 K, except for the 5-membered ring spiroepoxide **1b** (5-oxohept-6-enyl radical **4b**). The mid point of each cyclisation under EPR conditions is denoted by the temperature (T_{mid}) at which the concentrations of the uncyclised and cyclised radicals are equal, and these are listed in Table 1. These T_{mid} values are related to the rate constants for cyclisation of the 3-oxoalk-1-enyl radicals[23] and hence these decrease in the following order for the temperature range 200 to 270 K: **4b**(*exo*) > **4a**(*endo*) > **15bH**(*exo*) > **4c**(*endo*). The fastest rate is therefore *exo*-cyclisation of the 5-oxohept-6-enyl radical, which exceeds that of *endo*-cyclisation of the 4-oxohex-5-enyl radical. The slower rates for longer chain radicals, and for the hydroxy substituted radicals, are in accord with expectation.

Reaction of spiroepoxymethyl bromides with organotin hydrides

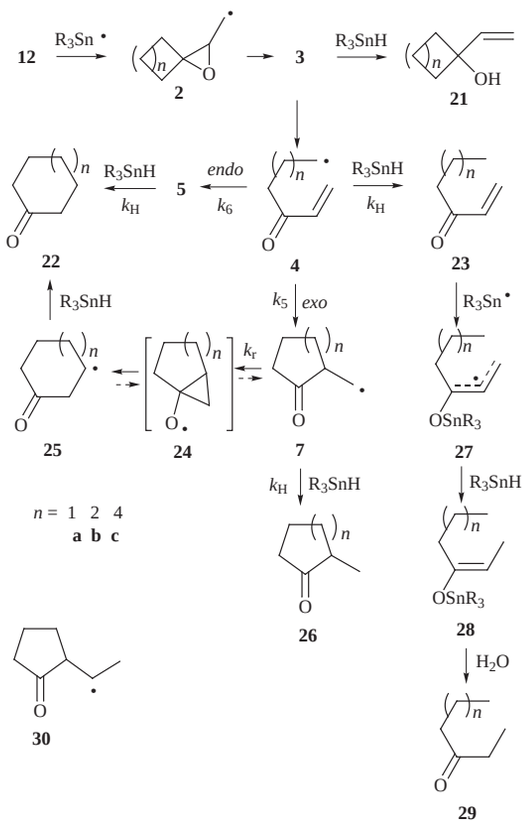
The photo-initiated reaction of each spiro-bromide **12** with triphenyltin hydride and/or with tributyltin hydride in benzene furnished a mixture of four main products: a cycloalkanone **22**, a 2-methylcycloalkanone **26**, an alk-1-en-3-one **23** and an alkan-3-one **29** (Scheme 5). The proportions of these products depended on temperature and organotin hydride concentration. The 1-vinylcycloalkanols **21** were not detected under any reaction conditions or for any of the ring sizes, except for traces of **21c** identified in a low temperature (22 °C) reaction of the 7-membered ring spiroepoxy bromide **12c**. It can be concluded that β-scission of all the alkoxyl radicals **3a**–**c** must be fast in comparison with hydrogen abstraction from the organotin hydrides. The alkan-3-ones were only produced in substantial quantities when a large excess of organotin hydride was used. It is probable that they were formed from the initially produced alk-1-en-3-ones **23** by addition of a stannyl radical to the carbonyl group to generate resonance stabilised allyl type radicals **27** which then abstracted hydrogen to afford stannyl ethers **28**. The latter would hydrolyse and tautomerise to ketones **29**, the overall reaction being reduction of the double bond (Scheme 5). Production of open chain ketones **23** and **29** was reduced to a very low level when gradual addition of the organotin hydride was employed.

The product yields under various reaction conditions are listed in Table 2 which shows that for the 4-membered ring substrate **12a** *endo*-cyclisation yielding cyclohexanone **22a** predominated over *exo*-cyclisation yielding 2-methylcyclopentanone **26a** at 80 °C. The predominance of **22a** at lower temperatures is in gratifying agreement with the EPR results which showed radical **5a** (the precursor of **22a**) to be the main cyclised intermediate at low temperatures. Reductions were also carried out at 120 and 180 °C in *tert*-butylbenzene and hexadecane as solvent, respectively, and the **[22a]**/**[26a]** ratio decreased from 3.2 at 80 °C to *ca*. 0.9 at both higher temper-

Table 2 Product yields from reduction of 2-bromomethyl-1-oxaspiro[2.*n*]alkanes **12** with organotin hydrides[a,b]

Substrate	Tin hydride	Temp/°C	**22**	**26**	**23**	**29**
12a	Bu_3SnH	80	45	14	28	14
12a	Ph_3SnH[c]	80	58	22	17	—
12b	Bu_3SnH[c]	82	25	50	5	trace
12b	Bu_3SnH[d]	150	63	13	3	trace
12c	Bu_3SnH	75	8	44	13	13
12c	Ph_3SnH	20	[20]		[11]	
12c	Ph_3SnH	75	[36]			

[a] Photolytic initiation in benzene solution with 1 equiv. of organotin hydride. [b] Yields in mol% as determined by GC, except those in parenthesis which are isolated yields. [c] Yields determined by ^1H NMR. [d] Tin hydride added in small portions.



Scheme 5

atures. Clearly, the relative amounts of the products are governed by a fine balance between stereoelectronic effects and thermodynamic factors.

Rearrangement of radical **7a** by intramolecular addition to the neighbouring carbonyl group *via* bicycloalkanoxyl radical **24a** to 3-oxocyclohexyl radical **25a** could be envisaged. Hydrogen abstraction by radical **25a** would then produce additional cyclohexanone. If this ring expansion took place it would be expected to increase in importance at higher temperatures. Literature precedent[8] indicates that β-scission of the inter-ring bond of bicycloalkanoxyl radicals of type **24** only occurs rapidly if the ring-enlarged radical **25** is stabilised by an adjacent electron-delocalising substituent (Ph, CO_2R). In a recent paper Chatgilialoglu *et al.*[24] reported the direct generation of radical **30** which is closely related to **7**. From a careful study of the five- and six-membered ring products they established that the rate constant for rearrangement of **30** to the corresponding six-membered ring radical was given by $\log(k_r/s^{-1}) = 10.51 - (39.3\ kJ\ mol^{-1})/2.3RT$ and that the reverse ring contraction was at least an order of magnitude slower. It follows that at the lower end of our temperature range this ring expansion will be negligible ($k_r/s^{-1} = 4.2 \times 10^3$ at 298 K) but that at the upper end of the range it will make a significant contribution.

Table 3 Kinetic data for 3-oxohex-5-enyl radical cyclisation[a]

	T/K			
	278	323	393	458
[29a]/[22a]	11.2	10.1	9.09	4.93
[29a]/[26a]	11.7	9.43	7.04	5.38
$k_6/10^5\ s^{-1}$	0.88	2.4	7.9	29.0
$k_5/10^5\ s^{-1}$	0.76	2.7	10.4	27.9

[a] Reactions with **[12a]** = 0.176 mol dm^{-3}, $[Bu_3SnH]$ = 0.685 mol dm^{-3} with photolytic initiation in benzene, *tert*-butylbenzene and hexadecane as solvents. Rate constants obtained from eqns. (1) and (2) as described in the text.

By way of contrast, the 5-membered ring substrate **12b** yielded 2-methylcyclohexanone **26b** as the major product derived from predominant *exo*-cyclisation (Table 2). This was also in good agreement with the EPR spectroscopic finding of radical **7b** as the major cyclised intermediate at lower temperatures, and with the major product reported by Galatsis[17] from the analogous spiro-iodide. Reduction of **12b** at 150 °C indicated that the **[22b]/[26b]** ratio increased from 0.50 at 80 °C to 0.85 at the higher temperature. This trend is as expected from the greater thermodynamic stability of the *endo*-radical **5b**.

Treatment of the 7-membered ring spiroepoxymethyl bromide **12c** with organotin hydrides afforded the products of both *endo*- **22c** and *exo*-cyclisation **26c** in proportions which varied with temperature (Table 2). Of these two, only cyclononanone could be isolated from larger scale reactions employing triphenyltin hydride. The chromatograms disclosed the presence of trace amounts of 1-vinylcycloheptanol **21c** in this case. This is understandable because the low ring strain in the 7-membered ring alkoxyl radical **3c** is expected to diminish its β-scission rate in comparison with radicals **3a**,**b** and hence a small proportion is trapped as alcohol **21c** by hydrogen abstraction from the organotin hydride. Tin hydride reactions of **12c** at higher temperatures (>100 °C) showed a lot of by-products including heptane which can be attributed to degradative conversion of the substrate.

Kinetics of cyclisation of the 3-oxohex-5-enyl radical 4a

The EPR spectroscopic evidence and the product analyses demonstrated beyond any reasonable doubt that the slowest, rate-determining step of the cascade is the final cyclisation. A kinetic appraisal of the *endo*- and *exo*-cyclisations of the 3-oxohex-5-enyl radical **4a** was made by measuring the proportions of the products, at a series of temperatures, from reactions of **12a** with a fourfold excess of tributyltin hydride (Table 3). Under these conditions, the unsaturated ketone **23a** was wholly replaced by hexan-3-one **29a** probably arising as shown in Scheme 5. Analysis of the reaction scheme shown in Scheme 5, assuming negligible ring contraction of radical **25a**, leads to relationships (4) and (5). Assuming that the conversion of **23a**

$$[\mathbf{29a}]_f/[\mathbf{26a}]_f = (k_H[Bu_3SnH] + k_r)/k_5 \quad (4)$$

$$[\mathbf{29a}]_f/[\mathbf{22a}]_f = k_H[Bu_3SnH]/\{k_6 + k_5k_r/(k_H[Bu_3SnH] + k_r)\} \quad (5)$$

to **29a** was quantitative, that the rate constants for hydrogen abstraction from tributyltin hydride (k_H) by radicals **7a** and **5a**, **25a** are equal to the literature values for primary and secondary alkyl radicals,[25,26] and that k_r was the same as that reported for radical **30**, the Arrhenius data in eqns. (6) and (7) for

$$\log(k_6/s^{-1}) = 8.7 \pm 1.5 - (20.0 \pm 4.0\ kJ\ mol^{-1}/2.3RT) \quad (6)$$

$$\log(k_5/s^{-1}) = 8.8 \pm 1.5 - (21.0 \pm 4.0 \text{ kJ mol}^{-1}/2.3RT) \quad (7)$$

endo- (k_6) and *exo*-cyclisation (k_5) were derived from the product ratios.

Neglect of the ring expansion reaction channel (k_r) simplifies the kinetic equations but has only a minor effect on the cyclisation parameters, and changes the activation energies by ≤1 kJ mol^{-1} and the pre-exponential factors by ≤0.2 log units. The rate constant for *exo*-cyclisation of radical **4a** (Table 3) is very similar to that for *exo*-cyclisation of the hex-5-enyl radical (2.5×10^5 s^{-1} at 25 °C).[25,26] However, the rate constant for *endo*-cyclisation of the 3-oxohex-5-enyl radical is very much greater than that of *endo*-cyclisation of hex-5-enyl (4×10^3 s^{-1} at 25 °C). The major effect of 3-oxo-substitution on the cyclisation is to substantially favour the *endo*-mode and this is logically accounted for in that the 2-oxo substituent is expected to thermodynamically stabilise the product 2-oxocyclohexyl radical.

Conclusions

Spectroscopic examination of the intermediate radicals, and end product analysis, paint a consistent picture in which spiroepoxymethyl radicals with a range of ring sizes undergo a rapid one-pot cascade of two β-scissions and one cyclisation. This cascade entails changes in hybridisation at five of the original atoms and yet the molecules traverse this complex reaction coordinate with apparent ease. The carbonyl substituent in the intermediate oxoalkenyl radical **4** enhances *endo*-mode cyclisation and this predominates, except for the 5-oxohept-6-enyl radical **4b** at low temperatures. The final cyclisation is not sufficiently regioselective for the cascade to be of general use as a 2-carbon ring-expansion method. However, if an alkyl substituent were incorporated at C-2 of the 1-oxaspiro[2.*n*]alkyl moiety this should hinder *exo*-cyclisation and hence augment the *endo*-cyclisation product. Spiroepoxides of type **1** are easily made by several alternative methods[17,27] and therefore this provides some scope for incorporating the cascade into selected syntheses.

Experimental

^{1}H NMR spectra were recorded at 200 or 300 MHz and ^{13}C NMR spectra at 75 MHz, in $CDCl_3$ solution with tetramethylsilane ($\delta_H = \delta_C = 0$) as reference. Coupling constants are expressed in Hz. Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 40–60 °C. EI mass spectra were obtained with 70 eV electron impact ionisation and CI spectra were obtained with isobutane as target gas on a VG autospec spectrometer. GC-MS analyses were run on a Finnigan Incos 50 quadrupole instrument coupled to a Hewlett Packard HP 5890 chromatograph fitted with a 25 m HP 17 capillary column (50% phenyl methyl silicone). For the calculation of yields from GC data, the detector response was calibrated with known amounts of authentic materials (or close analogues) and *n*-dodecane, or *n*-heptane was added as a standard. EPR spectra were obtained with Bruker ER 200D and Bruker EMX 10/12 spectrometers operating at 9.1 GHz with 100 kHz modulation. Samples of the substrate (*ca.* 40 mg) in di-*tert*-butyl peroxide (500 μl) or in *tert*-butylbenzene (0.5 cm^3) (occasionally cyclopropane) were degassed by bubbling nitrogen for 20 min and photolysed in the resonant cavity by light from a 500 W super pressure mercury arc lamp. EPR spectra were simulated with programs provided by Heinzer[28] and Whitwood.[29] The deuteriated alcohols **11D** were obtained from the protio-analogues by shaking with D_2O; one drop of D_2O was included in the EPR tube to ensure complete exchange was maintained during photolysis in the resonant cavity.

α-(Ethoxycarbonyl)methylenecyclobutane 9a

To a suspension of sodium hydride (6.28 g, 0.157 mol) in dry THF (300 cm^3) under nitrogen, was added dropwise over a 45 min period a solution of triethyl phosphonoacetate (32.03 g, 0.143 mol) in dry THF (15 cm^3). The rate of addition was regulated such that the temperature of the stirred mixture did not rise above 30 °C. After this addition was complete, the reaction mixture was stirred until hydrogen liberation had stopped. Cyclobutanone (10.0 g, 0.143 mol), diluted with THF (15 cm^3) was added to the flask while maintaining the temperature of the reaction mixture around 30 °C. Immediately after the addition of the ketone, a sample of the solution was analysed by TLC and the progress of the reaction was subsequently monitored every 30 min. After 2 h the reaction was arrested by pouring the contents of the flask slowly into a slurry of ice and water. Once the ice had melted the aqueous layer was separated and extracted with ether (3×50 cm^3). The ethereal extracts were combined, dried over anhydrous sodium sulfate and the solvents were removed under reduced pressure. The product **9a** was obtained as a colourless liquid by distillation using a Vigreux column (16.48 g, 82%), bp 48–50 °C/1.0 mmHg; δ_H (300 MHz, $CDCl_3$) 1.25 (3H, t, J = 7.4, CH_3), 2.08 (2H, q, J = 8.0), 2.83 (2H, t, J = 8.0), 3.12 (2H, t, J = 8.0), 4.13 (2H, q, J = 7.4), 5.57 (1H, m, CH); δ_C 12.5 (CH_2), 15.7 (CH_3), 31.2 (CH_2), 37.1 (CH_2), 57.2 (CH_2), 59.6 (CH), 80.1 (C), 172.5 (CO); *m*/*z* 140 (M$^+$, 46%), 112 (80), 95 (100), 84 (23), 67 (86), 55 (31), 41 (74) (Found: M$^+$, 140.0843. $C_8H_{12}O_2$ requires 140.0837).

α-(Hydroxymethyl)methylenecyclobutane 10a

DIBAL-H (45.58 g, 0.321 mol) was added to α-(ethoxycarbonyl)methylenecyclobutane **9a** (15.0 g, 0.107 mol) in dry THF (120 cm^3) under nitrogen, in small aliquots at hourly intervals, and the progress of the reaction was monitored by TLC. After the last addition of the reducing agent, the reaction mixture was stirred for a another 60 min. Finally, the excess reagent was decomposed by the slow addition of methanol–THF (40 cm^3/80 cm^3 resp.) to the reaction mixture. This hydrolysis was fully completed by the dropwise addition of water (25 cm^3), with cooling. The precipitated aluminium salts were filtered off and washed with methanol (3×50 cm^3). After drying the methanolic solution over anhydrous sodium sulfate, it was concentrated at the rotary evaporator and the remaining solvents were removed from it by distillation at atmospheric pressure. The residue was distilled using a Vigreux column to afford alcohol **10a** as a colourless liquid (5.4 g, 36%), bp 39–48 °C/0.9 mmHg. The product was purified by column chromatography on silica eluting with EtOAc–petroleum ether (2:8, v/v resp.); δ_H (300 MHz) 1.99 (2H, q, J = 7.8, CH_2), 2.10 (1H, br s, OH), 2.70 (4H, t, J = 7.8, 2 × CH_2), 4.01 (2H, d, CH_2OH), 5.32 (1H, m, CH); δ_C 17.2 (CH_2), 29.3 (CH_2), 31.1 (CH_2), 59.3 (CH_2), 119.3 (CH), 145.1 (C); *m*/*z* 98 (M$^+$, 10%), 83 (24), 79 (43), 70 (100), 69 (45), 67 (20), 55 (35), 53 (24), 41 (72) (Found: M$^+$, 98.0734. $C_6H_{10}O$ requires 98.0732).

2-Hydroxymethyl-1-oxaspiro[2.3]hexane 11a

To anhydrous sodium carbonate (0.98 g, 0.01 mol) in anhydrous dichloroethane (100 cm^3) was added the alcohol **10a** (1.20 g, 0.012 mol). Peroxyacetic acid (1.07 g, 0.014 mol) was introduced dropwise over a period of 15 min. The resulting mixture was stirred for 1.5 h after which period it was refluxed. TLC analysis performed on the reaction mixture after 5.5 h of heating indicated the complete absence of the starting material. After cooling, the crude material was concentrated under reduced pressure followed by the removal of residual acetic acid under high vacuum to afford **11a** as a pale yellow viscous liquid (1.18 g, 86%); δ_H (300 MHz) 1.85 (2H, m, CH_2), 2.32 (2H, m, CH_2), 2.50 (2H, m, CH_2), 2.86 (1H, br s, OH), 3.07 (1H, dd, J = 6.1, 3.7, CH), 3.53 (1H, dd, J = 12.2, 6.1, CH_2), 3.82 (1H, dd, J = 12.2, 3.7, CH_2); δ_C 13.2 (CH_2), 28.8 (CH_2), 31.2 (CH_2), 61.0 (CH), 62.1 (CH_2), 63.9 (C) (Found M$^+$ + 1, 115.0764. $C_6H_{11}O_2$ requires 115.0759).

2-Bromomethyl-1-oxaspiro[2.3]hexane 12a

2-Hydroxymethyl-1-oxaspiro[2.3]hexane (1.01 g, 8.86 mmol), was added to triethylamine (1.09 g, 11.0 mmol) in dry dichloromethane (30 cm^3) under nitrogen, cooled by an ice-salt bath. Methanesulfonyl chloride (0.93 g, 8.14 mmol) was added slowly to the reaction mixture which was stirred for a further 30 min. Following the addition of water (25 cm^3), the dichloromethane layer was separated and washed successively with 2 M hydrochloric acid (35 cm^3), 5% brine (20 cm^3) and saturated sodium bicarbonate solution (35 cm^3). The mesylate was obtained from the dried solution (anhydrous Na_2SO_4) by evaporation of the solvent.

To the mesylate in dry acetone (25 cm^3) was added dried lithium bromide (1.81 g, 20.80 mmol) and the solution was refluxed until all the lithium mesylate had precipitated out of the solution as a white solid. The latter was filtered off and the acetone was evaporated at room temperature. The residue was treated with water (15 cm^3) and this aqueous mixture was extracted with pentane (3 × 15 cm^3). The pentane was evaporated, residual solvent being removed under high vacuum. The 2-bromomethyl-1-oxaspirohexane was purified by high vacuum distillation, at room temperature, using a specially designed micro-distillation apparatus which yielded a colourless liquid (1.09, 76%); δ_H (300 MHz) 1.90 (2H, m, CH_2), 2.32 (2H, m, CH_2), 2.44 (1H, t, CH_2), 2.55 (1H, t, CH_2), 3.05 (1H, dd, J = 10.0, 7.5), 3.17 (1H, dd, J = 7.5, 5.4), 3.45 (1H, dd, J = 10.0, 5.4); δ_C 12.9 (CH_2), 28.0 (CH_2), 30.7 (CH_2), 31.0 (CH_2), 59.2 (CH), 65.7 (C); *m/z* 176 (M^+ + 1, 11%), 137 (5), 113 (12), 112 (17), 111 (10), 99 (32), 97 (100) (Found M^+ + 1, 176.9921. $C_6H_{10}O^{79}Br$ requires 176.9915).

α-(Ethoxycarbonyl)methylenecyclopentane 9b

Sodium (2.76 g, 0.12 mol) was added, in small amounts, to absolute ethanol (80 cm^3). Once the metal had dissolved, triethyl phosphonoacetate (21.50 g, 0.096 mol) was added to the cooled solution of the ethoxide. The resulting mixture was stirred at 0 °C for 2 h and cyclopentanone (10.08 g, 0.12 mol) was added to it at such a rate so as to maintain the temperature of the reaction mixture below 10 °C. The ice-bath was removed and the contents of the flask were stirred for an additional 14 h. Dilution with brine (200 cm^3) was followed by extraction of the product with hexane (6 × 50 cm^3). The combined extracts were dried over anhydrous magnesium sulfate and concentrated at the rotary evaporator. Distillation, using a Vigreux column, gave the unsaturated ester **9b** as a colourless liquid (11.03 g, 75%); (bp 38 °C/0.7 mmHg); δ_H (300 MHz) 1.28 (3H, t, CH_3), 1.72 (4H, m, 2 × CH_2), 2.44 (2H, t, CH_2), 2.78 (2H, t, CH_2), 4.14 (2H, q, CH_2), 5.80 (1H, m, CH); δ_C 14.4 (CH_3), 26.6 (CH_2), 27.7 (CH_2), 32.5 (CH_2), 36.6 (CH_2), 59.4 (CH_2), 111.8 (CH), 127.8 (C), 168.8 (CO), GC-MS t_R = 11.17 min. *m/z* 154 (M^+, 41%), 125 (11), 108 (36), 81 (100), 80 (85), 79 (99), 67 (27), 53 (21), 41 (20), 29 (24) (Found M^+ + 1, 155.1069. $C_9H_{15}O_2$ requires 155.1072).

α-(Hydroxymethyl)methylenecyclopentane 10b

Preweighed lithium aluminium hydride (5.29 g, 0.135 mol) was quickly added, under nitrogen gas, to stirred ether under nitrogen in a three-necked flask equipped with a dropping funnel. A separate flask was charged with dry ether (250 cm^3) under an atmosphere of nitrogen gas and α-(ethoxycarbonyl)methylenecyclopentane (10.0 g, 0.065 mol) was added to it. Ethanol (4.99 g, 0.108 mol), diluted with dry ether (10 cm^3), was placed in the dropping funnel containing the hydride suspension. The ethanol was added dropwise to the contents of the flask. After allowing the resulting lithium aluminium ethoxide hydride to stir for 30 min, aliquots (10.0 cm^3, 2.70 mmol) of it were added, hourly, to the flask containing the ester. The progress of the reaction was monitored by TLC which, after 17 h, showed the reaction to be complete. The reagent (170.0 cm^3, 0.046 mol) had been consumed in achieving a complete reaction which was terminated by decomposing the excess reducing agent initially with wet diethyl ether (2 × 50 cm^3) and subsequently with water (50 cm^3) and with periodic cooling of the reaction vessel. The precipitated aluminium salts were filtered, washed with water (3 × 50 cm^3) and then with ether (3 × 50 cm^3). The aqueous layer was separated and extracted with ether (3 × 50 cm^3). These ethereal extracts were combined with the organic layer obtained previously and the resulting solution was dried over anhydrous sodium sulfate. α-(Hydroxymethyl)methylenecyclopentane was obtained as a colourless, viscous liquid after evaporation of the solvent (7.87 g, 95%); δ_H (300 MHz) 1.65 (4H, m, 2 × CH_2), 1.90 (1H, br s, OH), 2.28 (4H, dt, J = 2.3, 1.2, 2 × CH_2), 4.12 (2H, dq, J = 7.0, 1.2, CH_2), 5.49 (1H, tt, J = 7.0, 2.3, CH); δ_C 26.0 (CH_2), 26.3 (CH_2), 28.6 (CH_2), 33.7 (CH_2), 60.9 (CH_2), 119.1 (CH), 147.6 (C); *m/z* 112 (M^+, 32%), 94 (48), 83 (58), 79 (100), 67 (61), 55 (46), 41 (52) (Found M^+, 112.0883. $C_7H_{12}O$ requires 112.0888).

Reduction of **9b** with sodium bis(1-methoxyethoxy)-aluminium hydride (Red-Al) yielded a 50 : 50 mixture of **10b** and the saturated analogue (75%). Use of diisobutylaluminium hydride (DIBAL-H) yielded an 85 : 15 mixture of **10b** and the saturated analogue (73%).

2-(Hydroxyethyl)triphenylphosphonium bromide

2-Bromoethanol (18.80 g, 0.15 mol) and triphenylphosphine (26.60 g, 0.10 mol) in dry ether (30 cm^3) were refluxed for 6 h. The precipitated phosphonium salt was filtered and the crude solid was purified by dissolving it in chloroform and then reprecipitating it by dropwise addition of ether. Filtration afforded the phosphonium salt as a white solid that was dried under high vacuum (22.90 g, 60%); δ_H 3.70 (2H, dt, CH_2), 3.97 (2H, dt, CH_2), 4.70 (1H, br s, OH), 7.53–7.80 (15H, m, 3 × Ph).

THP protection of the phosphonium salt

2-(Hydroxyethyl)triphenylphosphonium bromide (4.40 g, 0.01 mol) was added to dry dichloromethane (85 cm^3), dihydropyran (1.26 g, 0.015 mol), and the catalyst pyridinium toluene-*p*-sulfonate (0.31 g, 1.22 mmol). This mixture was stirred at room temperature for 4 h and then diluted with dry ether (90 cm^3). The catalyst was decomposed by use of half-saturated brine (15 cm^3) and the organic layer was evaporated to afford a viscous oily liquid which, when washed with dry ether (5 × 15 cm^3), and dried overnight under high vacuum, gave the THP-protected phosphonium salt as a white solid (4.70 g, 99%); δ_H 1.20–1.40 (4H, m, 2 × CH_2), 3.32 (2H, dt, CH_2), 3.42 (2H, t, CH_2), 3.80 (2H, t, CH_2), 4.02 (2H, dt, CH_2), 4.22 (1H, m, CH), 7.54–7.81 (15H, m, 3 × Ph).

α-(Tetrahydropyranyloxymethyl)methylenecyclopentane

n-Butyllithium (12.5 cm^3) was added to the THP-protected phosphonium salt of 2-bromoethanol (7.10 g, 0.015 mol) in dry ether (50 cm^3) under nitrogen over a 10 min period. The resulting suspension was stirred for 4 h. Cyclopentanone (1.26 g, 0.015 mol) was added and, after stirring for 1 h, refluxing was continued for a further 12 h. The precipitated triphenylphosphine oxide was removed by filtration. The residue was washed with dry ether (3 × 50 cm^3) and these washings were combined with the filtrate from the earlier stage. The resulting solution was treated with portions of water (25 cm^3) until the latter was neutral. After removal of the solvent, the product was obtained as a colourless liquid by distillation at 95–105 °C/1.3 mmHg using a Kugelrohr (1.10 g, 37%); δ_H 0.89 (2H, m, CH_2), 1.28 (2H, m, CH_2), 1.69 (4H, m, 2 × CH_2), 1.94 (2H, q, CH_2), 2.30 (4H, m, 2 × CH_2), 2.55 (2H, m, CH_2), 2.78 (2H, m, CH_2), 3.64 (1H, t, CH), 5.38 (1H, m, CH).

Deprotection of α-(tetrahydropyranyloxymethyl)methylenecyclopentane

α-(Tetrahydropyranyloxymethyl)methylenecyclopentane (0.40 g, 2.04 mmol) was added to ethanol (20 cm^3) and pyridinium toluene-*p*-sulfonate (0.05 g, 0.21 mmol). After 3 h the catalyst was decomposed with half-saturated brine (10 cm^3) and the product was extracted with dry ether (3 × 20 cm^3). These ethereal extracts were combined and dried over anhydrous sodium sulfate. After removing the solvent, the residue was distilled using a Vigreux column and α-(hydroxymethyl)methylenecyclopentane **10b** was collected as a colourless, viscous liquid (0.12 g, 52%) (bp 80–85 °C/1.7 mmHg) (spectrum as above).

2-Hydroxymethyl-1-oxaspiro[4.2]heptane 11b

α-(Hydroxymethyl)methylenecyclopentane **10b** (0.21 g, 0.019 mol) in dichloromethane (35 cm^3) was stirred and *m*-chloroperoxybenzoic acid (4.31 g, 0.025 mol) dissolved in dichloromethane (50 cm^3) was added to it slowly over 15 min. The reaction was allowed to proceed for a further 30 min and the excess peroxy acid was decomposed by addition of sodium sulfite solution (10%) until a starch–iodide paper gave a negative result. The organic layer was separated and washed with 5% sodium bicarbonate solution to extract the by-product *m*-chlorobenzoic acid. This was followed by washing it with water (50 cm^3) and finally with saturated sodium chloride solution (50 cm^3). The separated dichloromethane layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. High-vacuum removal of the solvent gave **11b** as a *ca*. 2:1 mixture with *m*-chlorobenzoic acid (1.57 g). The latter was difficult to remove without decomposing **11b** and hence the preferred method employed peroxyacetic acid.

Alcohol **10b** (6.50 g, 0.058 mol) was introduced into a suspension of anhydrous sodium carbonate (13.36 g, 0.126 mol) in anhydrous dichloroethane (300 cm^3) under nitrogen. Peroxyacetic acid (12.61 g, 0.063 mol), diluted with dichloroethane (10 cm^3), was added dropwise into the reaction mixture over a period of 1 h. After stirring the contents of the reaction flask for a further 1 h, it was heated to reflux for 1 h, when TLC showed reaction had gone to completion, and a gelatinous white precipitate had appeared. The mixture was allowed to cool to room temperature and the white solid was removed by filtration and washed with dichloroethane (3 × 50 cm^3). The filtrate was initially concentrated at the rotary evaporator and then the residual solvent was removed from it under high vacuum. The product 2-hydroxymethyl-1-oxaspiro[4.2]heptane was obtained as a colourless, oily liquid (6.75 g, 91%); δ_H 1.62 (4H, m, 2 × CH_2) 1.82 (4H, m, 2 × CH_2), 1.92 (2H, m, CH_2), 2.91 (1H, br s, OH), 3.21 (1H, dd, CH), 3.60 (1H, dd, CH_2), 3.83 (1H, dd, CH); δ_C 25.4 (CH_2), 25.8 (CH_2), 29.8 (CH_2), 34.4 (CH_2), 62.2 (CH), 63.0 (CH_2), 70.1 (C); *m*/*z* 128 (M^+, 4%), 111 (20), 97 (39), 85 (100), 83 (26), 67 (98), 57(22), 55 (40), 43 (24), 41 (56) (Found M^+, 128.0840. $C_7H_{12}O_2$ requires 128.0837).

2-Bromomethyl-1-oxaspiro[2.4]heptane 12b

To the epoxy alcohol **11b** (6.50 g, 0.05 mol) and triethylamine (6.36 g, 0.06 mol) in dry dichloromethane (175 cm^3) under nitrogen at −5 °C, was added methanesulfonyl chloride (5.38 g, 0.047 mol), drop by drop and the solution was stirred for 30 min. The reaction was terminated by addition of water (145 cm^3) and the organic layer was separated and washed successively with 2 M hydrochloric acid (200 cm^3), 5% brine (100 cm^3) and saturated sodium bicarbonate (200 cm^3). The resulting solution was dried over anhydrous sodium sulfate and concentrated at room temperature.

Lithium bromide (10.44 g, 0.120 mol), dried under high vacuum with gentle periodic heating for 1 h, was quickly added to continuously stirred acetone (125 cm^3) under nitrogen and the mesylate, diluted with dry acetone (10 cm^3), was gradually added to the reaction mixture over 15 min. The contents of the reaction vessel were stirred until no further precipitate appeared. The white solid was filtered off and the filtrate was concentrated using a rotary evaporator operated at room temperature. The residue was treated with water (90 cm^3) and the aqueous mixture was extracted with pentane (3 × 50 cm^3) which was completely evaporated leaving a very pale yellow oily material. The latter was purified by distillation using a Kugelrohr (30 °C/0.10 mmHg) over several hours to yield a pale yellow oily product **12b** (2.75 g, 31%); δ_H 1.70 (4H, q, 2 × CH_2), 1.95 (4H, q, 2 × CH_2), 3.26 (1H, dd, CH), 3.33 (1H, dd, CH_2), 3.58 (1H, dd, CH_2); δ_C 25.0 (2 × CH_2), 28.5 (CH_2), 31.1 (CH_2), 33.4 (CH_2), 60.0 (CH), 71.6 (C); *m*/*z* 192, 190 (M^+ 1%), 97 (24), 83 (39), 67 (30), 55 (100), 53 (25), 41 (89), 39 (63), 29 (37) 28 (27), 27 (99) (Found M^+ + 1, 191.0081. $C_7H_{12}O^{79}Br$ requires 191.0073).

α-(Ethoxycarbonyl)methylenecycloheptane 9c

This was prepared from cycloheptanone by the same method as for **9a** as a colourless liquid (91%) (bp 42–46 °C/0.02 mmHg); δ_H 1.25 (3H, t, *J* = 7.1, CH_3), 1.54 (4H, m, 2 × CH_2), 1.68 (4H, m, 2 × CH_2), 2.38 (2H, dd, *J* = 1.2, 6.0, CH_2), 2.86 (2H, dd, *J* = 1.2, 6.0, CH_2), 4.14 (2H, q, *J* = 7.1, CH_2), 5.67 (1H, m, *J* = 1.2, CH); δ_C 14.4 (CH_3), 26.6 (CH_2), 28.0 (CH_2), 29.0 (CH_2), 29.8 (CH), 32.1 (CH_2), 39.0 (CH_2), 59.3 (CH_2), 115.6 (CH), 166.7 (CO) (Found M^+ + 1, 183.1392. $C_{11}H_{19}O_2$ requires 183.1385).

α-(Hydroxymethyl)methylenecycloheptane 10c

The same methodology as for **10a** was applied to selectively reduce the unsaturated ester **9c** yielding **10c** as a viscous, colourless liquid (82%); δ_H 1.56 (8H, m, 4 × CH_2), 2.26 (4H, m, 2 × CH_2), 4.14 (2H, d, CH_2), 5.40 (1H, t, CH); δ_C 28.0 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 30.4 (CH_2), 30.6 (CH_2), 38.4 (CH_2), 59.8 (CH_2), 124.5 (CH), 146.3 (C); *m*/*z* 140 (M^+, 14%), 122 (86), 107 (31), 96 (60), 83 (54), 81 (100), 70 (64), 67 (92), 57 (56), 55 (82), 41 (92) (Found M^+, 140.1206. $C_9H_{16}O$ requires 140.1201).

2-Hydroxymethyl-1-oxaspiro[2.6]nonane 11c

This preparation was accomplished in the same manner as described for **11a** to give the spiroepoxy alcohol **11c** as a colourless oily liquid (87%); δ_H 1.55 (8H, m), 1.70 (4H, m), 2.70 (1H, br s, OH), 2.97 (1H, dd, CH), 3.65 (1H, dd), 3.83 (1H, dd); δ_C 25.0 (CH_2), 25.3 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 32.1 (CH_2), 38.1 (CH_2), 61.9 (CH_2), 65.4 (C), 65.5 (CH); *m*/*z* 157 (M^+ + 1, 8%), 139 (20), 121 (26), 113 (100), 95 (62), 81 (37), 67 (46), 55 (46), 43 (38), 41 (46) (Found M^+ + 1, 157.1231. $C_9H_{16}O_2$ requires 157.1229).

2-Bromomethyl-1-oxaspiro[2.6]nonane 12c

This spiroepoxymethyl bromide was prepared by the same method as that described for **12a** which gave **12c** as a colourless liquid (87%); δ_H 1.59 (8H, m), 1.74 (4H, m), 3.06 (1H, dd, *J* = 6.0, 7.6), 3.26 (1H, dd, *J* = 7.6, 10.4), 3.52 (1H, dd, *J* = 6.0, 10.4); δ_C 24.3 (CH_2), 24.7 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 29.9 (CH_2), 30.9 (CH_2), 37.0 (CH_2), 63.1 (CH), 66.6 (C); *m*/*z* 220, 218 (M^+, 6%), 125 (100), 121 (33), 107 (17), 95 (37), 81 (74), 67 (29), 55 (41), 41 (26) (Found M^+, 218.0300. $C_9H_{15}O^{79}Br$ requires 218.0306).

Reaction of 2-bromomethyl-1-oxaspiro[2.3]hexane 12a with tributyltin hydride

Tributyltin hydride (128.0 mg, 0.44 mmol) was weighed into an NMR tube and dissolved in benzene (500.0 μl). A single portion of the spiro-bromide **12a** (20.0 mg, 0.11 mmol) was added to the diluted organotin reagent *via* a microsyringe. After introducing heptane (10.0 μl), the contents of the tube were

thoroughly mixed and photolysed with light from a 250 W Hg lamp in a continuously stirred water-bath maintained at 5 °C for 4 h. The experiment was repeated at 50 °C, 120 °C and 185 °C. In view of the high volatility of benzene at higher temperatures, *tert*-butylbenzene and hexadecane were used as solvents. The reaction times were appropriately adjusted. GC-MS peak no. 138, t_R 2.52 min, heptane standard; peak no. 172, t_R 3.15 min, hexan-3-one **29a**, peak no. 215, t_R 3.92 min, 2-methylcyclopentanone **26a**; peak no. 275, t_R 5.03 min, cyclohexanone **22a**. Product identities were confirmed by matching t_R and MS data with that of authentic materials.

Reaction of 2-bromomethyl-1-oxaspiro[2.4]heptane 12b with tributyltin hydride

2-Bromomethyl-1-oxaspiro[2.4]heptane **12b** (50.0 mg, 0.26 mmol) was placed into an NMR tube. After dilution with benzene (500 µl), an aliquot of tributyltin hydride (10.51 mg, 36.13 µmol) was introduced into the tube which was photolysed for 8 h at 30 °C with the addition of the above mentioned amount of the organotin reagent every 30 min until a total of 16 such portions had been added to the reaction mixture. This experiment was repeated at 80 °C, 150 °C and 180 °C. *tert*-Butylbenzene was used as a solvent at higher temperatures and the duration of the reactions was appropriately adjusted. Products at 30 °C were identified by GC-MS which indicated the presence of a minor amount of unreacted starting material: peak no. 246, t_R 4.51 min, heptan-3-one **29b**, (7%), peak no. 310, t_R 5.62 min, hept-1-en-3-one **23b**, (12%), *m*/*z* 112 (M^+, 14%), 71 (36), 69 (50), 68 (21), 43 (100), 41 (86), 39 (39), 27 (25), peak no. 340, t_R 6.22 min, 2-methylcyclohexanone **26b**, (34%), *m*/*z* 112 (M^+, 18%), 84 (11), 69 (24), 68 (48), 56 (37), 55 (59), 42 (40), 41 (100), 39 (55), 29 (20), 28 (29), 27 (69); peak no. 417, t_R 7.62 min, cycloheptanone **22b** (34%). In the reaction at 180 °C, the only compounds obtained were: the open-chain enone **23b**, the α-methylated cycloalkanone **26b** and the cycloalkanone **22b**.

Reaction of 2-bromomethyl-1-oxaspiro[2.6]nonane 12c with tributyltin hydride

2-Bromomethyl-1-oxaspiro[2.6]nonane **12c** (44.09 mg, 0.21 mmol) diluted with benzene (500 µl) was placed in an NMR tube. Tributyltin hydride (66.06 mg, 0.23 mmol) in benzene (200 µl) was divided up into eight equal portions which were added to the photolysing solution at 75 °C every 30 min. The reaction was terminated after 4 h. The experiment was repeated at 150 °C using *tert*-butylbenzene as a solvent. GC-MS peak no. 532, t_R 9.80 min, nonan-3-one **29c**; peak no. 585, t_R 10.80 min, 2-methylcyclooctanone **26c**, *m*/*z* 111 (96%), 97 (76), 83 (35), 67 (33), 55 (80), 41 (100), 27 (78); peak no. 559, t_R 10.90 min, non-1-en-3-one **23c**, *m*/*z* 111 (17%), 97 (15), 83 (57), 70 (38), 55 (75), 41 (62), 27 (62); peak no. 591, t_R 11.1 min, 1-vinylcyclononanol **21c** *m*/*z* 140 (2%), 138 (7), 109 (17), 94 (19), 81 (22), 79 (30), 70 (33), 67 (96), 56 (38), 55 (64), 43 (39), 41 (100), 39 (78); peak no. 744, t_R 12.10 min, cyclononanone **22c.** In addition several unidentified products were observed. The reactions at 150 °C and 180 °C showed little of the above products but indicated the presence of cycloheptane and a range of unidentified materials.

Triphenyltin hydride initiated reactions

A mixture of bromide **12a** (31.0 mg, 0.18 mmol), perdeuteriobenzene (600 µl) and triphenyltin hydride (9.26 mg, 26.38 µmol) was heated to 80 °C and aliquots (9.26 mg) of the organotin reagent were added every 30 min to the reacting solution for 4 h. The contents of the tube were cooled and dichloromethane (9.26 mg, 5 µl) was added as a standard. A ^{1}H NMR spectrum of the resulting solution showed the composition of the reaction mixture to be hex-1-en-3-one **23a** (17%), cyclohexanone **22a** (58%) 2-methylcyclopentanone **26a** (22%).

Reduction of bromide **12b** with Ph_3SnH was carried out in a similar way. Signals from the ^{1}H NMR spectrum could not be analysed with certainty owing to severe overlapping of the peaks. GC-MS analysis showed the same four products as in the tributyltin hydride reductions.

A small scale reduction of **12c** with Ph_3SnH using a similar method at 20 °C showed the same products as in the tributyltin hydride reaction. The reaction was scaled up using **12c** (0.43 g, 1.96 mmol), benzene (100 cm^3) and the organotin reagent (1.38 g, 3.92 mmol). This mixture was photolysed at 75 °C and progress was monitored by TLC which showed complete consumption of starting material after 10 h of photolysis. The solvent was completely evaporated, following the removal of solid residues by filtration. The residual solution was separated by column chromatography using silica gel (mesh size 40–63 µm). The column was eluted with petroleum ether–EtOAc (initially 40 : 60) of increasing polarity and this yielded cyclononanone **22c** (0.10 g, 36%). Similarly, cyclononanone (20%) and 3-oxonon-1-ene **23c** (11%) were isolated from a reaction carried out at 20 °C.

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