Silicon-mediated Annulation. Part 1. A Synthesis of Tetrahydropyran-4-ones, Oxepan-4-ones, and Oxocan-4-ones *via* Intramolecular Directed Aldol Reactions†

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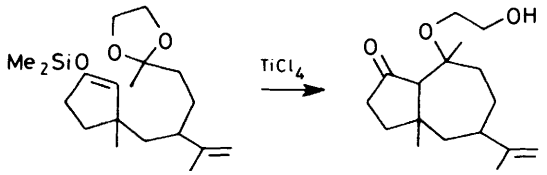
A Lewis acid-catalysed intramolecular directed aldol condensation of enol silanes and acetals was used to prepare tetrahydropyran-4-ones, oxepan-4-ones, and oxocan-4-ones. The course of the cyclisations was influenced by the Lewis acid and the stereochemistry of the starting material.

The intramolecular variant of the Mukaiyama directed aldol condensation[1] is a valuable annulation method which has received compartively scant attention. In the simplest case there are four basic reaction types (Table) leading to monocyclic products which we have classified on the premise that the reaction proceeds in two stages. The first stage involves Lewis acid-catalysed cleavage of an acetal to a trigonal oxonium ion. The second stage involves intramolecular capture of the oxonium ion by a trigonal enol silane. By a modification of the familiar Baldwin nomenclature[2] we can define each ring closure in the Table by a numerical prefix denoting the size of the ring, and the terms *endo* and *exo* which define the relation of the electrophilic (e) oxonium ion and nucleophilic (n) enol silane in relation to the ring being created. Thus the first reported[3] intramolecular Mukaiyama reaction leading to intermediate (**2**) is a 7-*exo*$_e$*exo*$_n$ cyclisation.



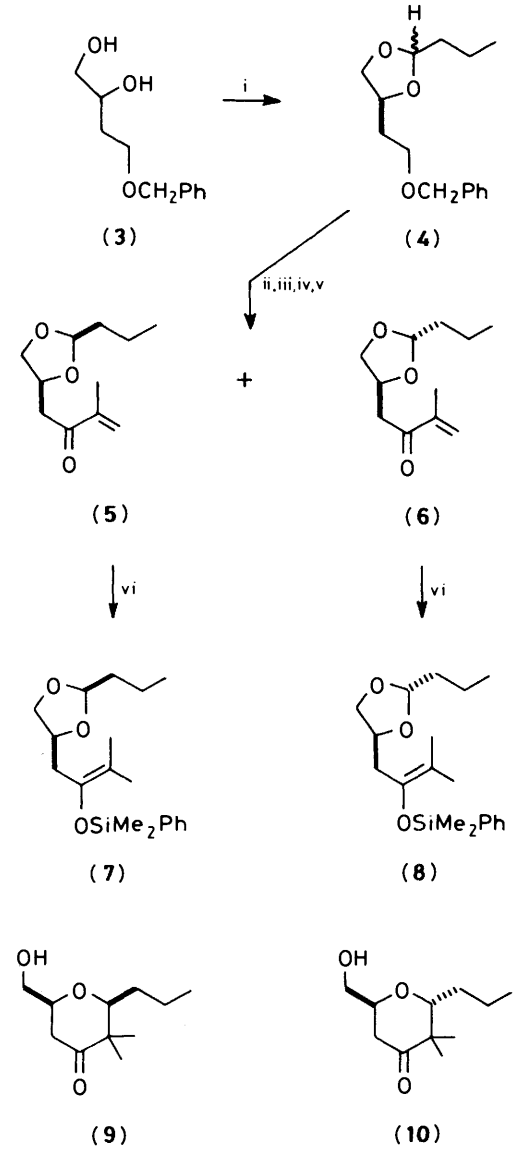
(**1**) (**2**)

In this paper, we show that the intramolecular Mukaiyama reaction can be used to effect 6-, 7-, and 8-*endo*$_e$*endo*$_n$ cyclisations to tetrahydropyran-4-ones, oxepan-4-ones, and oxocan-4-ones respectively.[4]

In an attempt to control the stereoselectivity of the intramolecular Mukaiyama reaction which served as a key step in our synthesis of pederol dibenzoate,[5] we examined the cyclisation of model dioxolanes (**7**) and (**8**) which were prepared as shown in Scheme 1. The inseparable equilibrium mixture of dioxolanes (**4**)[6] (*cis*:*trans* = 3:1) was converted into a mixture of (**5**) and (**6**) which were separated by column chromatography with difficulty. Hydrosilylation[7] gave the desired enol silanes (**7**) and (**8**) in high yield. This has proved to be the method of choice for the regiospecific synthesis of enol silanes from base-sensitive precursors.

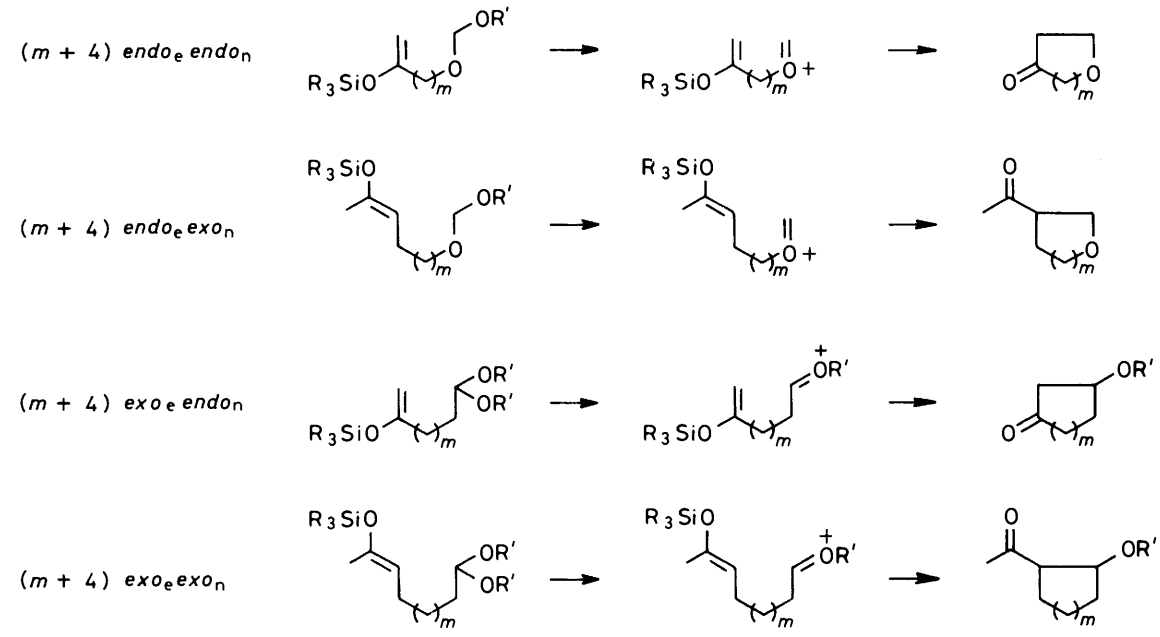
Treatment of *cis*-dioxolane (**7**) with 1—2 equivalents of $TiCl_4$ in CH_2Cl_2 at −78 °C rapidly gave the *cis*-tetrahydropyran-4-one (**9**) exclusively in 65% yield, whereas similar reactions of the *trans*-dioxolane (**8**) gave a 1:1 mixture of (**9**) and (**10**) in 72% yield. However, treatment of either (**7**) or (**8**) with trimethylsilyl

† All compounds reported are racemic.



Scheme 1. *Reagents:* i, n-butanal, H^+, 91%; ii, Na–NH_3(l); iii, $Me_2\overset{+}{S}Cl$, Cl^-–CH_2Cl_2, then Et_3N, −60 → 0 °C, 81% for two steps; iv, CH_2=CH(Me)MgBr; v, $PyHCrO_3Cl$, 50% for two steps; vi, $PhMe_2SiH$, [$Rh(PPh_3)_3Cl$], 55 °C, 90%.

Table. Classification of intramolecular Mukaiyama directed aldol reactions

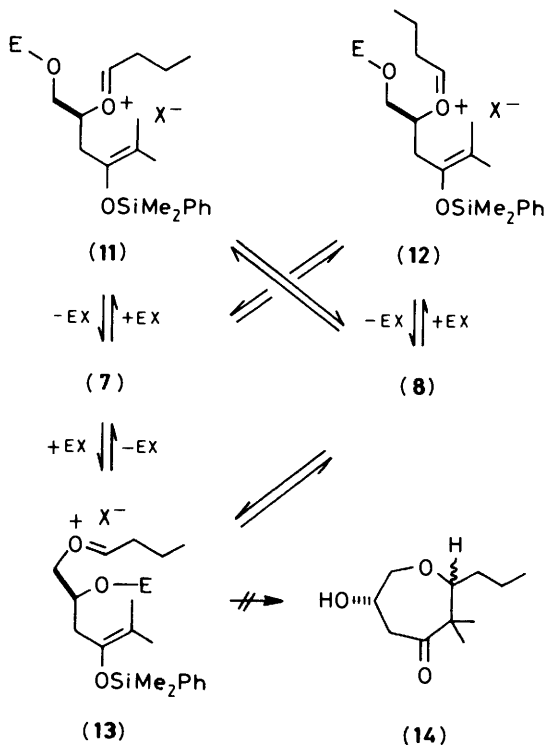


trifluoromethanesulphonate–CH_2Cl_2 at −78 °C or $(Pr^iO)_2$-$TiCl_2$–CH_2Cl_2 at −40 °C gave only the *cis*-tetrahydropyran-4-one (**9**) in *ca.* 42% yield. No cyclisation products were obtained with $SiCl_4$, $ZnCl_2$, or $EtAlCl_2$ in CH_2Cl_2 under a variety of conditions. Thus the stereochemistry of the reaction depended on the stereochemistry of the precursors (**7**) and (**8**) only when $TiCl_4$ was used as catalyst.

Very little is known about the mechanism and stereochemistry of the intramolecular Mukaiyama reaction.[8] Some indication of the complexity of the problem at hand is given in Scheme 2. Electrophilic cleavage of dioxolanes (**7**) and (**8**) could occur with stereoelectronic control to give the corresponding (*E*)- and (*Z*)-oxonium ions (**11**) and (**12**) respectively,* which may cyclise directly to products or equilibrate *via* re-closure to the isomeric dioxolanes. Added to the uncertainty of geometry of the intermediate oxonium ions is the problem of relative rates of cyclisation and equilibration. Taken together these uncertainties preclude meaningful speculation on the role of the Lewis acid catalyst or the acetal geometry in the course of the reaction.

The absence of oxepanone (**14**) from the cyclisation products is not conclusive evidence for regiospecific acetal cleavage since a compartively slow 7-*endo*$_e$*endo*$_n$ cyclisation of the oxonium ion (**13**) to give (**14**) may not compete favourably with the corresponding 6-*endo*$_e$*endo*$_n$ cyclisations of (**7**) and (**8**) derived from (**13**) by equilibration. Alternatively, irreversible formation of (**13**) followed by intermolecular reaction leading to polymeric products—which account for 30% of the mass—could explain the absence of (**14**). In order to show that 7-*endo*$_e$*endo*$_n$ cyclisations are feasible by a directed aldol reaction, the diastereoisomeric dioxepanes (**20**) were prepared as shown in Scheme 3 and their cyclisation examined.

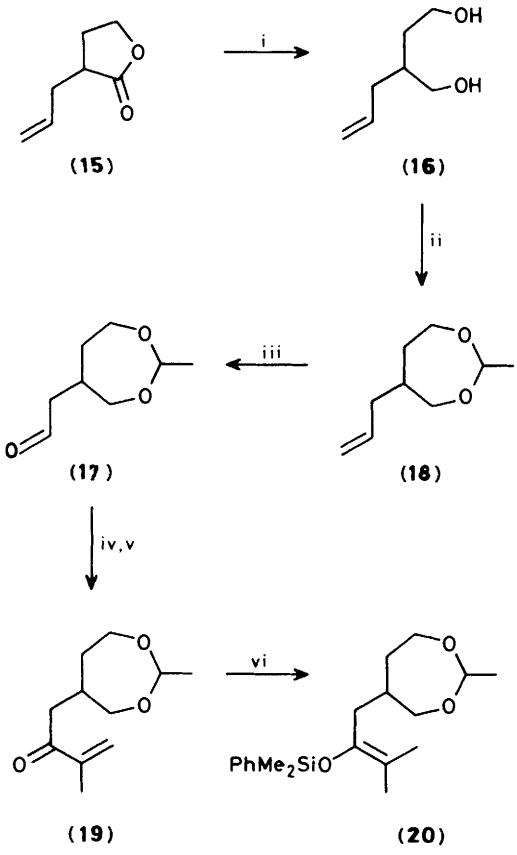
The inseparable 1:1 mixture of dioxepanes (**20**) reacted with

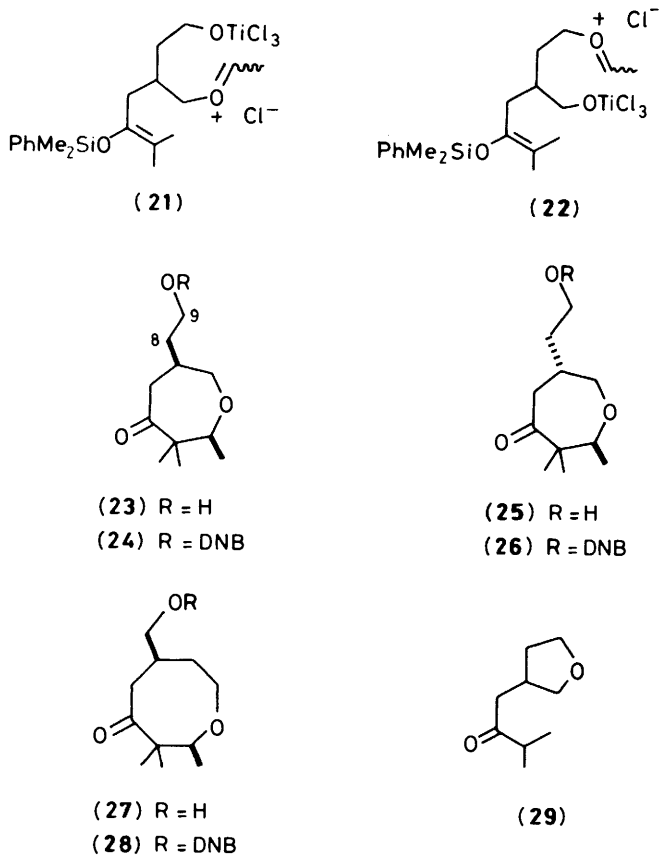


Scheme 2.

2 equivalents of $TiCl_4$ in CH_2Cl_2 at −78 °C to give the oxepanones (**23**) and (**25**) and the oxocanone (**27**) in 88% combined yield. High pressure liquid chromatography (h.p.l.c.) analysis of the crude 3,5-dinitrobenzoate (DNB) derivatives showed (**24**), (**26**), and (**28**) to be present in the ratio 7:6:4 respectively. The crystalline dinitrobenzoates were easily separable by column chromatography and their structures

* Nucleophilic attack on dioxolanes catalysed by less oxyphilic Lewis acids such as $SnCl_4$ may not proceed *via* oxonium ions; rather an S_N2-like attack on a polarised CO bond may take place.[9]





Scheme 3. *Reagents:* i, $LiAlH_4$, 75%; ii, MeCHO, H^+, 98%; iii, O_3–MeOH, then Me_2S, 69%; iv, CH_2=C(Me)MgBr, 95%; v, $PyHCrO_3Cl$–alumina, 66%; vi, $PhMe_2SiH$, $[Rh(PPh_3)_3Cl]$, 55 °C, 91%.

deduced by ^1H and ^{13}C n.m.r. spectroscopy. The relative stereochemistry and conformation of (**24**) and (**26**) were consistent with structures (**30**) and (**31**) respectively based on coupling constants and nuclear Overhauser experiments. However, the conformational analysis of oxocanone (**28**) was complicated by apparently contradictory nuclear Overhauser interactions 3-Me′ ⟷ 5-H′ and 8-H ⟷ 2-H indicating a crown or chair–chair conformation (**32**) and weaker interactions 2-H ⟷ 5-H and 7-H ⟷ 2-H indicating chair–boat conformation (**33**). Taken together, the nuclear Overhauser data suggest an equilibrium (**32**) ⇌ (**33**) in which (**32**) is predominant. The proposed equilibrium is consistent with the expected relative stabilities of (**32**) and (**33**) calculated from known A-values for cyclo-octanones.[10]

Treatment of dioxepanes (**20**) with 2 equivalents of $SnCl_4$ in CH_2Cl_2 at −78 °C gave 15% each of (**23**) and (**25**), 20% of the tetrahydrofuran (**29**) but less than 2% of the oxocanone (**27**). Thus 7-*endo*$_e$*endo*$_n$ cyclisations are feasible by intramolecular Mukaiyama reactions and once again the course of the reaction depended on the Lewis acid catalyst.

In the cyclic acetals (**7**), (**8**), and (**20**) discussed thus far, a clear preference for cyclisation to the smaller of two alternative rings was noted. That the oxocanone (**27**) was formed as a single diastereoisomer by a direct ring closure was significant and worthy of further pursuit. Therefore, the 1,3-dioxanes (**40**) and (**41**) were prepared as shown in Scheme 4 and their cyclisation examined. As before two alternative modes of acetal cleavage are possible; however, reaction of (**40**) and (**41**) with $TiCl_4$ gave—aside from polymer—only the 8-*endo*$_e$*endo*$_n$ product (**42**) as a single diastereoisomer in 34 and 9% yield respectively. None of the 10-*endo*$_e$*endo*$_n$ product (**44**) was detected.

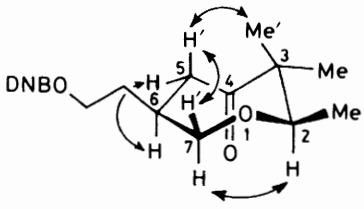
Structures (**42**) and (**44**) were readily differentiated by 400 MHz ^1H n.m.r. spectroscopy of the 3,5-dinitrobenzoate (**43**). The conformation (**45**) was deduced from the 10 Hz coupling between pseudoaxial protons 2-H and 3-H and the close spatial relation between 2-H, 5-H, and 7-H revealed by nuclear Overhauser experiments. The absence of a nuclear Overhauser interaction between 2-H and 8-H was taken as evidence in favour of *trans*-stereochemistry.

In the final two 8-*endo*$_e$*endo*$_n$ cyclisations examined, the regiochemical ambiguity which attended the acetal cleavages cited above was avoided by exploiting the known regioselective cleavage of (2-methoxyethoxy)methyl (MEM) ethers induced by $TiCl_4$.[11] Thus treatment of acetals (**48**) (Scheme 5) and (**54**) (Scheme 6) with $TiCl_4$ at −78 °C gave the oxocanones (**49**) (43%) and (**55**) (25%).

The rapid formation of eight-membered rings by directed aldol reaction *without the need for high dilution conditions* is unprecedented and noteworthy since eight- and nine-membered rings are usually the most difficult to construct by any method of ring closure.[12] Among the factors responsible for facilitating the annulations reported herein may be the steric constraints imposed on intermediates in which the enol silane and acetal oxygen atoms are both co-ordinated to the titanium catalyst. The scope of this template effect will be examined further.

Experimental

Thin layer chromatography (t.l.c.) was carried out using Kieselgel 60 F_{254} precoated sheets (0.2 mm thick) and compounds were visualised with 10% ceric ammonium nitrate in 2M-sulphuric acid. Column chromatography was carried out on Kieselgel 60 (0.04—0.063 mm) and column dimensions



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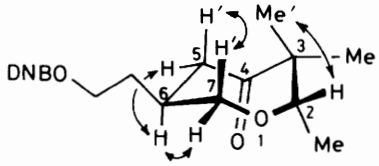

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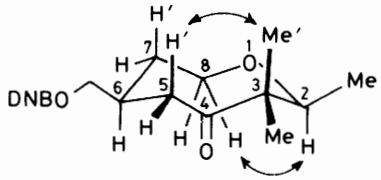

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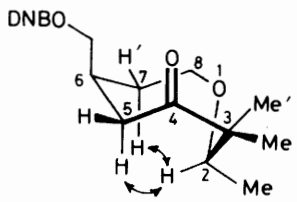

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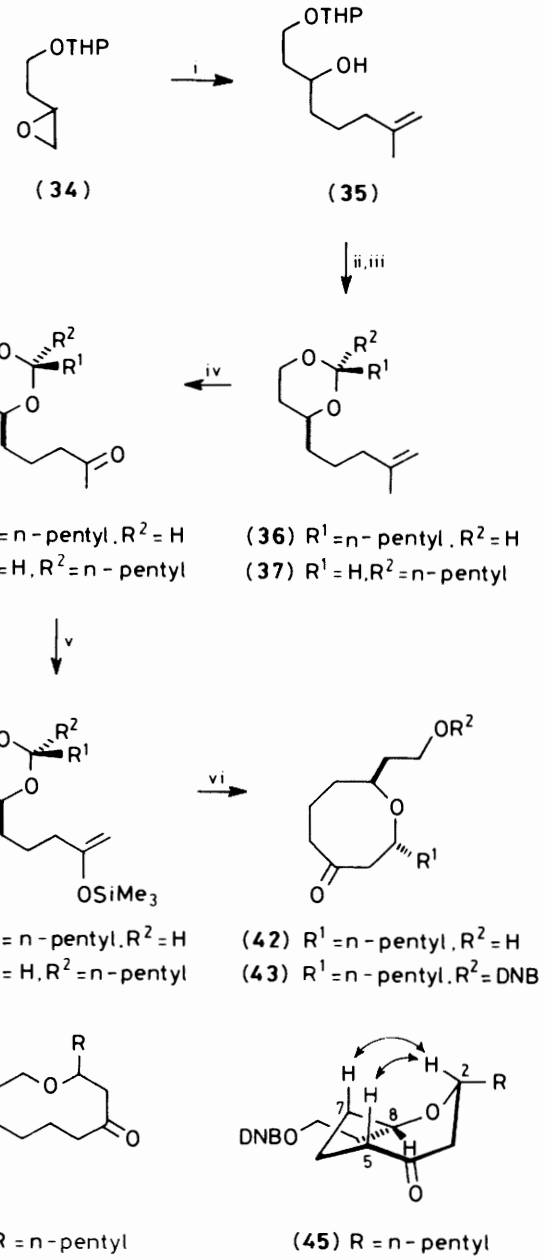


(34) (35) (36) R^1 = n-pentyl, R^2 = H; (37) R^1 = H, R^2 = n-pentyl; (38) R^1 = n-pentyl, R^2 = H; (39) R^1 = H, R^2 = n-pentyl; (40) R^1 = n-pentyl, R^2 = H; (41) R^1 = H, R^2 = n-pentyl; (42) R^1 = n-pentyl, R^2 = H; (43) R^1 = n-pentyl, R^2 = DNB; (44) R = n-pentyl; (45) R = n-pentyl

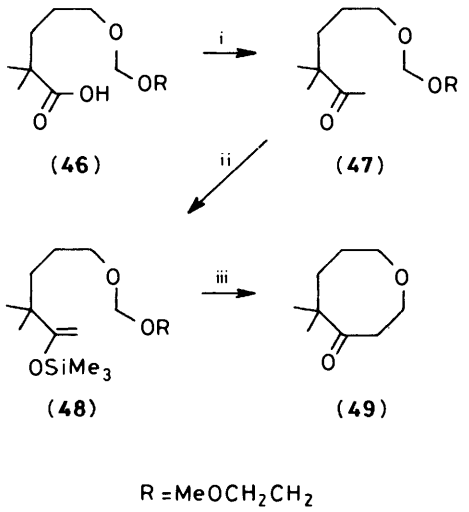
Scheme 4. *Reagents:* i, CH_2=C(Me)CH_2CH_2MgCl, CuI–THF, −30 °C, 96%; ii, H^+, MeOH; iii, n-hexanal, H^+, 77, 6, %; iv, O_3–MeOH, then Me_2S, 90%; v, Pr^i_2NLi–THF, −78 °C, then Me_3SiCl; vi, 1.2 equiv $TiCl_4$–CH_2Cl_2, −78 °C, 34% from (**38**), 9% from (**39**).

(length × diameter) and eluant are specified in parenthesis. H.p.l.c. analyses were performed with a Varian Si-10 column.

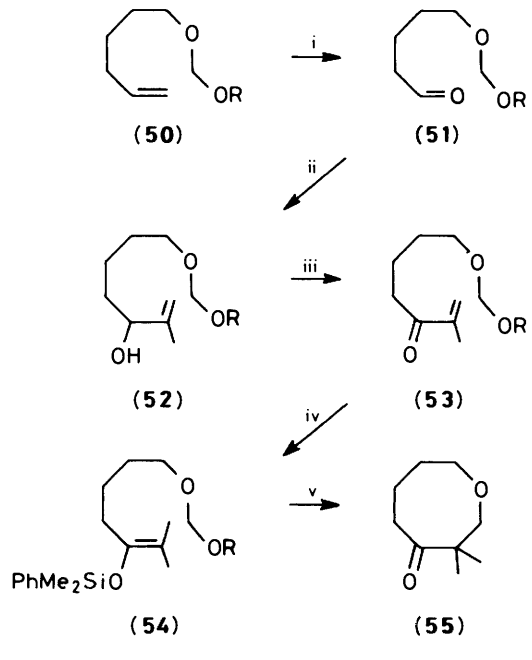
All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under a static atmosphere of dry nitrogen. Organic extracts were dried over $MgSO_4$ and evaporated at aspirator pressure using a Büchi rotary evaporator. All distillations were performed with a Büchi Kugelrohr apparatus.

Light petroleum refers to the fraction of b.p. 60—80 °C. Diethyl ether (referred to as ether) and tetrahydrofuran were distilled from Na wire; CH_2Cl_2 from P_2O_5; dimethyl sulphoxide, pyridine, triethylamine, and di-isopropylamine from CaH_2. Methanol and ethanol were distilled from $Mg(OMe)_2$ and $Mg(OEt)_2$ respectively. $TiCl_4$ and $SnCl_4$ were freshly distilled under a stream of dry nitrogen and were dispensed as solutions in dry dichloromethane *via* a syringe. Molecular sieves (3Å) were activated at 210 °C and stored at 125 °C prior to use. Dowex-60W-8X was activated by washing with water and methanol. Cuprous iodide was purified by Soxhlet extraction (18 h) with dry tetrahydrofuran and cupric chloride was dried over P_2O_5.

Melting points were determined with a Reichert hot stage microscope and are uncorrected. Chemical shifts are reported as δ_H values relative to Me_4Si as an internal standard. ^{1}H N.m.r. spectra were recorded in $CDCl_3$ with a Perkin-Elmer R32 spectrometer operating at 90 MHz or with a Bruker WH400 spectrometer operating at 400 MHz. All coupling constants (J) are given in Hz. ^{13}C N.m.r. spectra were recorded in $CDCl_3$ with a Jeol FX90Q spectrometer operating at 22.5 MHz. Inverted signals obtained with an INEPT pulse sequence are indicated by an asterisk. I.r. spectra were recorded as thin films unless otherwise stated. Peak intensities are specified as s (strong), m (medium), or w (weak). Accurate mass determinations were made on distilled compounds which were estimated to be >95% pure by ^{1}H or ^{13}C n.m.r. and t.l.c.



Scheme 5. *Reagents:* i, MeLi–Et_2O, 86%; ii, Pr^i_2NLi–THF, −78 °C, then Me_3SiCl; iii, 1.2 equiv. $TiCl_4$–CH_2Cl_2, −78 °C, 43% from (**47**).



Scheme 6. *Reagents:* i, O_3–CH_2Cl_2, then Zn–HOAc, 98%; iii, CH_2=C(Me)MgBr, 92%; iii, pyHCrO$_3$Cl, 3Å molecular sieves, 61%; iv, $PhMe_2SiH$, [$Rh(PPh_3)_3Cl$], 55 °C, 95%; v, 2 equiv. $TiCl_4$–CH_2Cl_2, −78 °C, 25%.

cis, trans-4-(2-*Benzyloxyethyl*)-2-*propyl*-1,3-*dioxolane* (**4**).—The diol (**3**)[5] (3.26 g, 16.5 mmol), n-butanal (2.3 g, 33 mmol), and toluene-*p*-sulphonic acid (0.1 g) were refluxed in benzene with azeotropic removal of water. The benzene solution was washed with 1M-Na_2CO_3, dried, and evaporated. The residue was chromatographed on Kieselgel (10 × 4 cm, 5% EtOAc in light petroleum) to give after distillation (**4**) (3.78 g, 91%), b.p. 180 °C (bath)/0.5 mmHg; $\nu_{max.}$ 2 960s, 2 870s, 1 455m, 1 365m, 1 110s, 1 020m, 735s, and 700s cm^{-1}; δ_C 138.5, 128.4, 127.6, 104.5 (C-2, *cis*), 103.8 (C-2, *trans*), 74.3 (C-4, *cis*), 73.6 (C-4, *trans*), 73.1, 70.7 (C-5, *trans*), 69.8 (C-5, *cis*), 67.1, 36.3, 34.0, 17.4, and 14.8 (Found: M^+, 250.156 91. $C_{15}H_{22}O_3$ requires *M*, 250.156 885).

cis-4-(3-*Methyl*-2-*oxobut*-3-*enyl*)-2-*propyl*-1,3-*dioxolane* (**5**) *and the* trans *Isomer* (**6**).—Reductive removal of the benzyl group from (**4**) (3.78 g, 15.2 mmol) in a mixture of NH_3 (50 cm^3) and Et_2O (10 cm^3) at −78 °C with Na metal in the usual way gave cis, trans-4-(2-*hydroxyethyl*)-2-*propyl*-1,3-*dioxolane* as a colourless oil; b.p. 90 °C (bath)/0.55 mmHg; $\nu_{max.}$ 3 410s and 1 050s cm^{-1}; δ_C 104.6 (C-2, *cis*), 103.8 (C-2, *trans*), 74.6 (C-4, *cis*) 73.9 (C-4, *trans*), 69.7 (C-5, *cis*), 70.5 (C-5, *trans*), 36.2 (2 signals), 17.3, and 14.0. Swern oxidation[13] of the mixture of alcohols (0.80 g, 5.0 mmol) then gave cis, trans-4-*formylmethyl*-2-*propyl*-1,3-*dioxolane* (0.64 g, 81%) as a labile colourless oil; b.p. 80 °C (bath)/0.02 mmHg; $\nu_{max.}$ 1 725s and 1 140s cm^{-1}; δ_C 199.9, 104.9 (C-2, *cis*), 104.2 (C-2, *trans*), 71.0 (C-4, *cis*), 70.5 (C-4, *trans*), 69.5 (C-5, *cis*), 70.3 (C-5, *trans*), 48.1 (*cis*), 47.3 (*trans*), 36.0, 17.2, and 13.8; *m/z* 157 (M^+ − 1, 0.3%), 131 (6), 115 (11), 85 (11), 71 (21), 69 (100), 57 (15), and 43 (39).

Reaction of the aldehyde (1.31 g, 8.2 mmol) with the Grignard reagent prepared from Mg (394 mg, 16.4 mol) and 2-bromopropene (2.1 cm^3, 12.3 mmol) in THF (25 cm^3) gave 1.64 g of a crude mixture of diastereoisomeric allylic alcohols after aqueous work-up. The crude mixture in CH_2Cl_2 was oxidised with pyridinium chlorochromate as described[14] to give a 3:1 mixture of enones (**5**) and (**6**) (0.82 g, 50% for 2 steps) after distillation; b.p. 130 °C (bath)/0.2 mmHg. A sample of the mixture (0.80 g) was separated by column chromatography on Kieselgel (20 × 3.8 cm, 5% EtOAc in light petroleum) to give pure (**6**) (162 mg), pure (**5**) (428 mg), and mixed fractions (103 mg). The enone (**5**) gave $\nu_{max.}$ 1 675s, 1 630s, 965m, and 935m cm^{-1}; δ_H 0.94 (3 H, distorted t), 1.6 (4 H, m), 1.87 (3 H, s), 2.71 (1 H, dd, *J* 17, *J'* 8), 3.31 (1 H, dd, *J* 17, *J'* 5), 5.38 (1 H, dd, *J* 8, *J'* 5), 4.08 (1 H, dd, *J* 8, *J'* 8), 4.30 (1 H, dddd, *J* 8, *J'* 5, *J''* 5, *J'''* 8), 4.86 (1 H, t, *J* 4), 5.8 and 6.0 (1 H, each, br s); δ_C 199.4, 144.5, 125.5, 104.3, 72.6, 70.0, 42.3, 36.1, 17.3, 17.2, and 14.0 (Found: M^+, 198.1249. $C_{11}H_{18}O_3$ requires *M*, 198.125 586). The enone (**6**) gave $\nu_{max.}$ 1 675s, 1 642s, 970m, and 940 cm^{-1}; δ_H 0.94 (3 H, distorted t), 1.6 (4 H, m), 1.88 (3 H, d, *J* 1), 2.80 (1 H, dd, *J* 16, *J'* 8), 3.32 (1 H, dd, *J* 16, *J'* 5), 3.46 (1 H, dd, *J* 8, *J'* 5), 4.28 (1 H, dd, *J* 8, *J'* 7), 4.50 (1 H, dddd, *J* 7, *J'* 5, *J''* 5, *J'''* 8), 4.96 (H, t, *J* 4), and 5.96 and 5.78 (1 H each, br s); δ_C 199.4, 144.5, 125.5, 103.9, 72.2, 70.8, 41.4, 36.1, 17.3, 17.2, and 140 (Found: M^+, 198.1247. $C_{11}H_{18}O_3$ requires *M*, 198.125 586).

Hydrosilylation of (**5**) *and* (**6**).—A neat mixture of (**5**) (209 mg, 1.05 mmol), $PhMe_2SiH$ (0.12 cm^3, 1.10 mmol), and [$Rh(PPh_3)_3Cl$] (2 mg) was heated at 55 °C under N_2 for 1 h whereupon the enol silane (**7**) (357 mg, 0.92 mmol) was distilled directly from the reaction mixture; b.p. 120 °C (bath)/0.02 mmHg; $\nu_{max.}$ 1 680m, 1 430s, 1 250s, 1 165s, 1 115s, 960s, 825s, 790s, 735s, and 700s cm^{-1}; δ_H 1.6 and 1.56 (3 H each, s), and 0.4 (6 H, s). An identical procedure was used to prepare (**8**) from (**6**). The enol silanes (**7**) and (**8**) were used immediately in the next step.

$TiCl_4$-*Mediated Cyclisation of Enol Silanes* (**7**) *and* (**8**).—To a rapidly stirred solution of $TiCl_4$ in CH_2Cl_2 (0.53M; 3.3 cm^3) at −78 °C was added dropwise the enol silane (**7**) (353 mg, 0.89 mmol) in CH_2Cl_2 (5 cm^3). After 45 min at −78 °C, the cooling bath was removed and saturated brine (10 cm^3) added with rapid stirring. The organic layer was washed with $NaHCO_3$, dried, evaporated, and the residue chromatographed on Kieselgel (5 × 2.75 cm, 25% EtOAc in light petroleum) to give (**9**) (113 mg, 0.56 mmol, 65%) after distillation, b.p. 60 °C (bath)/0.05 mmHg; $\nu_{max.}$ 3 410m, 1 710s, 1 468m, and 1 080s cm^{-1}; δ_H 0.94 (3 H, distorted t), 0.96 (3 H, s), 1.08 (3 H, s), 1.45 (4 H, m), 2.19 (1 H, dd, *J* 13, *J'* 3), 2.45 (1 H, s, OH), 2.73 (1 H, dd, *J*

13, *J'* 11), 3.28 (1 H, m), 3.66 (2 H, m), and 3.74 (1 H, m); δ_C 211.9, 84.1, 77.6, 65.3, 49.4, 40.2, 31.3, 20.0, 19.2, 18.9, and 14.0; *m/z* 200 (M^+, 2%), 169 (4), 128 (65), 97 (14), 84 (14), 70 (100), 57 (27), 55 (33), and 43 (71). The tetrahydropyranone (**9**) formed a crystalline 3,5-dinitrobenzoate derivative, m.p. 114—115 °C (CH_2Cl_2–hexane) (Found: C, 54.7; H, 5.55; N, 7.25. $C_{18}H_{22}N_2O_8$ requires C, 54.8; H, 5.58; N, 7.11%).

Similar treatment of the enol silane (**8**) (227 mg, 0.58 mmol) gave a 1:1 mixture of the tetrahydropyranones (**9**) and (**10**) (76 mg, 0.38 mmol, 68%) after chromatographic purification and distillation. A pure sample of (**10**) gave $\nu_{max.}$ 1 710s, 1 465m, and 1 080s cm^{-1}; δ_H 0.98 (3 H, distorted t), 1.00 (3 H, s), 1.26 (3 H, s), 1.42 (4 H, m), 2.24 (1 H, dd, *J* 13, *J'* 5), 2.27 (1 H, s, OH), 2.72 (1 H, dd, *J* 13, *J'* 10), 3.68 (2 H, m), and 4.0 (1 H, ddt, *J* 10, *J'* 5, *J''* 5); δ_C 212.0, 82.9, 71.3, 65.0, 49.6, 39.2, 30.1, 24.6, 19.4, 18.8, and 13.8; *m/z* 200 (M^+, 5%), 169 (6), 128 (98), 113 (13), 95 (16), 84 (21), 70 (100), 55 (22), and 43 (24). The 3,5-dinitrobenzoate derivative of (**10**) gave m.p. 135—136.5 °C (CH_2Cl_2–hexane) (Found: C, 54.75; H, 5.6; N, 7.25. $C_{18}H_{22}N_2O_8$ requires C, 54.8; H, 5.58; N, 7.11%).

The relative composition of the mixture (**9**) and (**10**) was best determined by h.p.l.c. analysis (8% EtOAc in hexane) of the 3,5-dinitrobenzoates which were easily separable by column chromatography.

3-*Hydroxymethylhex*-5-*en*-1-*ol* (**16**).—Lithium aluminium hydride (456 mg, 12 mmol) in THF (19 cm^3) was stirred under N_2 whilst 2-allylbutyrolactone (**15**)[15] (1 g, 8 mmol) in THF (3 cm^3) was added at a rate sufficient to maintain reflux. After refluxing for 1 h, the reaction mixture was cooled in ice and 15% aqueous NaOH was added dropwise until the precipitation of finely divided aluminate salts was complete. The heterogeneous mixture was diluted with ether (50 cm^3), and filtered, concentrated, and distilled to give the diol (**16**) (0.761 g, 5.85 mmol, 75%) as a colourless oil; b.p. 155 °C (bath)/15 mmHg; $\nu_{max.}$ 3 320s, 1 680m, and 890s cm^{-1}; δ_H 5.75 (1 H, ddt, *J* 16, *J'* 9, *J''* 7), 5.10 (1 H, dd, *J* 1, *J'* 9), 5.06 (1 H, dd, *J* 1, *J'* 16), 4.05 (2 H, s, OH), 3.6 (4 H, m), 2.10 (2 H, m), and 1.65 (3 H, m); *m/z* 28 (100%), 112 (0.2), 79 (45), 67 (27), 57 (18), and 41 (40) (Found: M^+, 130.096 15. $C_7H_{14}O_2$ requires *M*, 130.099 373).

cis, trans-5-*Allyl*-2-*methyl*-1,3-*dioxepane* (**17**).—3-Hydroxymethylhex-5-en-1-ol (**16**) (1.184 g, 7.6 mmol) was dissolved in CH_2Cl_2 (13 cm^3) with toluene-*p*-sulphonic acid (10 mg), acetaldehyde (4 cm^3, 44 mmol), and molecular sieves (3Å, 5 g). The reaction was stirred at room temperature overnight and then filtered through Celite, neutralised with saturated $NaHCO_3$ (5 cm^3), dried, and concentrated to give, after distillation, the dioxepane (**17**) (1.2 g, 7.6 mmol, 98%) as a colourless oil, b.p. 105 °C (bath)/15 mmHg; $\nu_{max.}$ 2 985s, 2 940s, 1 640m, and 890s cm^{-1}; δ_H 5.80 (1 H, ddt, *J* 16, *J'* 9, *J''* 7), 5.10 (1 H, dd, *J* 9, *J'* 1), 5.02 (1 H, dd, *J* 16, *J'* 1), 4.92 (1 H, q, *J* 5), 3.78 (2 H, m), 3.62 (1 H, dd, *J* 12, *J'* 7), 3.38 (1 H, dd, *J* 12, *J'* 8), 2.02 (2 H, m), 1.80 (3 H, m), and 1.28 (3 H, 2 × d, *J* 5); *m/z* 67 (100%), 141 (13), 112 (9), 95 (32), 84 (33), 54 (76), and 43 (25) (Found: M^+, 156.114 74. $C_9H_{16}O_2$ requires *M*, 156.114 023).

cis, trans-5-*Formylmethyl*-2-*methyl*-1,3-*dioxepane* (**18**).—The dioxepane (**17**) (1.195 g, 7.59 mmol) in dry MeOH (18 cm^3) was ozonolysed at −78 °C in the usual way. Dimethyl sulphide (2 cm^3) was added and the solution stirred at ambient temperature for 1 h. After concentration the residue was chromatographed (5 × 4.75 cm, 50% ether in light petroleum) to give, after distillation, the aldehyde (**18**) (0.835 g, 5.28 mmol, 69%) as a colourless oil, b.p. 105 °C (bath)/15 mmHg; $\nu_{max.}$ 1 725s and 1 090s cm^{-1}; δ_H 9.78 (1 H, s), 4.92 (1 H, q, *J* 6), 3.7 (4 H, m), 2.45 (2 H, m), 2.40 (1 H, m), 1.90 (2 H, m), and 1.27 (3 H, 2 × d) (Found: M^+, 158.096 11. $C_8H_{14}O_3$ requires *M*, 158.094 288).

cis, trans-2-*Methyl*-5-(2-*oxo*-3-*methylbut*-3-*enyl*)-1,3-*dioxepane* (**19**).—To the Grignard reagent prepared from 2-bromopropene (1 cm^3, 11.3 mmol) in THF (15 cm^3) was added dropwise at 0 °C the aldehyde (**18**) (0.89 g, 5.64 mmol) in THF (4 cm^3) and the mixture was stirred at 0 °C for 20 min. The mixture was poured into saturated aqueous NH_4Cl (15 cm^3) and extracted with ether. The combined extracts were dried and concentrated and the residue distilled to give the allylic alcohol (1.071 g, 5.25 mmol, 95%) as a colourless oil, b.p. 150 °C (bath)/0.3 mmHg which was used directly in the next step.

The allylic alcohol (255 mg, 1.25 mmol) in CH_2Cl_2 (5 cm^3) was added to a rapidly stirred suspension of pyridinium chlorochromate adsorbed on alumina[16] (12.4 g, 10 mmol) in CH_2Cl_2 (5 cm^3) and stirred at room temperature for 6 h. Ether (50 cm^3) was added and the mixture filtered. Concentration and distillation gave 164 mg (0.83 mmol, 66%) of the enone (**19**) as a colourless oil, b.p. 140 °C (bath)/0.07 mmHg; $\nu_{max.}$ 1 670s, 1 630w, and 1 090s cm^{-1}; δ_H 5.95 (1 H, d, *J* 1), 5.76 (1 H, d, *J* 1), 4.87 and 4.90 (1 H, 2 × q, *J* 6), 3.80 (3 H, m), 3.40 (1 H, dd, *J* 11, *J'* 8), 2.69 (1 H, dd, *J* 7, *J'* 4), 1.40 (1 H, m), 1.88 (3 H, s), 1.78 (2 H, m), and 1.27 (3 H, 2 × d, *J* 6) (Found: M^+, 198.125 49. $C_{11}H_{18}O_3$ requires *M*, 198.125 586).

cis, trans-5-(2-*Dimethylphenylsilyloxy*-3-*methylbut*-3-*enyl*)-2-*methyl*-1,3-*dioxepane* (**20**).—The enone (**19**) (140 mg, 2 mmol) was stirred at 55 °C under N_2 with [$Rh(PPh_3)_3Cl$] (5 mg) and dimethylphenylsilane (0.24 cm^3, 2 mmol) for 1 h. Distillation afforded the enol silane (**20**) (612 mg, 1.83 mmol, 91%) as a colourless oil; b.p. 150 °C (bath)/0.44 mmHg; $\nu_{max.}$ 1 675w, 1 590w, 1 250s, 1 170s, 1 140s, and 835s cm^{-1}; δ_H 7.60 (2 H, m), 7.40 (3 H, m), 4.90 (1 H, 2 × q, *J* 6), 3.45—3.95 (4 H, m), 3.50 (2 H, m), 2.96 (3 H, m), 1.06 (6 H, s), 1.25 (3 H, 2 × d, *J* 6), and 0.41 (6 H, s). The enol silane (**20**) was used immediately in the next step.

$TiCl_4$-*Mediated Cyclisation of* (**20**).—The enol silane (**20**) (1.207 g, 3.61 mmol) in CH_2Cl_2 (15 cm^3) was added dropwise to a solution of $TiCl_4$ (7.2 mmol) in CH_2Cl_2 (45 cm^3) at −78 °C. After being stirred for 1 h at −78 °C the mixture was allowed to warm to room temperature and poured into a saturated aqueous $NaHCO_3$–salt solution (1:1; 20 cm^3). This was extracted with CH_2Cl_2 and combined extracts were dried and concentrated. Chromatography of the residue (4.75 × 5 cm, 50% ether in light petroleum) gave 583 mg (2.92 mmol, 88%) of a mixture of oxepanones (**23**) and (**25**) and oxocanone (**27**) the relative composition of which was determined by h.p.l.c. analysis (15% EtOAc in hexane) of the corresponding 3,5-dinitrobenzoates [(**28**) (R_t 9.5 min):(**24**) (R_t 14 min):(**26**) (R_t 19 min) = 4:7:6].

The 3,5-dinitrobenzoates were separated by column chromatography (15 × 2.75 cm, 30% $CHCl_3$ in light petroleum) to give in order of elution; cis-6-(3,5-*dinitrobenzoyloxymethyl*)-2,3,3-*trimethyloxocan*-4-*one* (**28**); m.p. 117.6—119.1 °C ($CHCl_3$–light petroleum); $\nu_{max.}$(CCl_4) 1 750s, 1 710s, and 1 645 cm^{-1}; δ_H (400 MHz) 9.24 (1 H, t, *J* 2.5), 9.17 (2 H, d, *J* 2.5), 4.41 (1 H, A portion of an ABX system, 9-H), 4.405 (1 H, B portion of an ABX system, 9-H), 2.632 (1 H, m, 6-H), 2.270 (1 H, dd, *J* 12, *J'* 3, 5-H), 3.125 (1 H, dd, *J* 12, *J'* 10, 5-H), 1.848 (1 H, dddd, *J* 4, *J'* 15, *J''* 7, *J'''* 3, 7-H), 1.575 (1 H, dddd, *J* 9, *J'* 15, *J''* 3, *J'''* 8, 7-H), 4.115 (1 H, ddd, *J* 7, *J'* 3, *J''* 12, 8-H'), 3.30 (1 H, ddd, *J* 3, *J'* 8, *J'* 12, 8-H), 3.528 (1 H, q, *J* 7, 2-H), 1.158 (3 H, d, *J* 7, *Me*CH), 1.273 and 0.982 (3 H each, s); δ_C 217.5, 162.5, 148.7, 133.0, 129.4, 122.4, 83.8, 69.9*, 69.7*, 52.0, 39.4*, 36.8, 31.3, 21.6, 17.0, and 15.0 (Found: C, 54.5; H, 5.6. $C_{18}H_{22}N_2O_8$ requires C, 54.8; H, 5.6%); cis-6-[2-(3,5-*dinitrobenzoyloxy*)*ethyl*]-2,3,3-*trimethyloxepan*-4-*one* (**24**), m.p. 126.9—128.1 °C ($CHCl_3$–light petroleum); $\nu_{max.}$(CCl_4) 1 750s, 1 710s, and 1 645m cm^{-1}; δ_H (400 MHz) 9.26 (1 H, t, *J* 2.5), 9.18 (2 H, d, *J* 2.5), 4.56 (2 H, dd, *J* 7, *J' ca.* 7, 9-H),

1.79 (1 H, dddd, *J* 7, *J' ca.* 7, *J''* 14, *J'''* 7, 8-H), 1.89 (1 H, dddd, *J* 7, *J' ca.* 7, *J''* 16, *J'''* 6.5, 8-H'), 2.05 (1 H, m), 4.02 (1 H, ddd, *J* 1.5, *J'* 13, *J''* 1.5, 7-H), 3.79 (1 H, dd, *J* 3.5, *J'* 13, 7-H'), 2.52 (1 H, ddd, *J* 6, *J'* 1.5, *J''* 12, 5-H), 3.18 (1 H, dd, *J* 3, *J'* 12, 5-H'), 3.78 (1 H, q, *J* 7, 2-H), 1.18 (3 H, d, *J* 7, *Me*CH), 1.16 and 0.98 (3 H each, s); δ_C 214.7, 162.5, 148.7, 134.0, 129.5, 122.5, 83.3, 76.7*, 64.7*, 53.0, 42.5*, 35.2, 30.0, 23.7, 16.6, and 16.3 (Found: C, 55.0; H, 5.8. $C_{18}H_{22}N_2O_8$ requires C, 54.8; H, 5.6%); and trans-6-[2-(3,5-*dinitrobenzoyloxy*)*ethyl*]-2,3,3-*trimethyloxepan*-4-*one* (**26**); m.p. 117.9—118.6 °C (Et_2O–light petroleum); $\nu_{max.}$(CCl_4) 1 750s, 1 710s, and 1 640 cm^{-1}; δ_H (400 MHz) 9.26 (1 H, t, *J* 2.5), 9.17 (2 H, d, *J* 2.5), 4.48 (2 H, m, 9-H), 1.78 (2 H, m, 8-H), 2.10 (1 H, m, 6-H), 4.13 (1 H, ddd, *J* 5, *J'* 12, *J''* 1.5, 7-H), 3.38 (1 H, dd, *J* 12, *J'* 12, 7-H'), 2.46 (1 H, ddd, *J* 2, *J'* 15, *J''* 11, 5-H), 3.00 (1 H, dd, *J* 12, *J'* 11, 5-H'), and 3.81 (1 H, q, *J* 6, 2-H), 1.15 (3 H, d, *J* 6, *Me*CH), 1.08 and 0.99 (3 H each, s); δ_C 213.0 (C-4), 162.4 (C-10), 148.7, 133.7, 129.4, 122.5, 83.0, 77.7*, 64.4*, 52.9, 44.1*, 38.0, 30.8*, 23.1, 16.3, and 16.1 (Found: C, 55.0; H, 5.58. $C_{18}H_{22}N_2O_8$ requires C, 54.8; H, 5.6%).

Tin(IV) *Chloride-Mediated Cyclisation of* (**20**).—Reaction of the enol silane (**20**) (266 mg, 0.80 mmol) with $SnCl_4$ (1.55 mmol) in CH_2Cl_2 (3 cm^3) at −78 °C as described above for $TiCl_4$ gave 57 mg (0.29 mmol, 35%) of a mixture of (**23**), (**25**), and (**27**) (9:9:1 by h.p.l.c. analysis of the corresponding 3,5-dinitrobenzoates) and 25 mg (0.16 mmol, 25%) of 3-(3-methyl-2-oxobutyl)oxolane (**29**), b.p. 100 °C (bath)/0.33 mmHg; $\nu_{max.}$ 1 710s and 1 050s cm^{-1}; δ_H 3.80 (3 H, m), 3.35 (1 H, m), 2.50 (2 H, m), 2.10 (1 H, septet, *J* 7), 1.50 (3 H, m), and 1.10 (6 H, d, *J* 7); *m/z* 156 (M^+, 21%), 70 (100), 137 (10), 113 (15), 95 (6), 87 (15), 55 (37), 43 (62) (Found: M^+, 156.114 69. $C_9H_{16}O_2$ requires *M*, 156.115 023).

2-(3-*Hydroxy*-7-*methyloct*-7-*enyloxy*)*tetrahydropyran* (**35**).—The Grignard reagent prepared from 4-chloro-2-methylbut-1-ene[17] (3.135 g, 30 mmol) and Mg (884 mg, 36 mol) in THF (20 cm^3) was added dropwise to a suspension of CuI (266 mg, 1.4 mmol) in THF (5 cm^3) at −60 °C with rapid stirring. After 20 min at −30 °C, the oxirane (**34**) (2.45 g, 14.2 mmol) in THF (12 cm^3) was added dropwise over 5 min. After 1 h at −30 °C and 1 h at 0 °C the mixture was poured into saturated aqueous NH_4Cl. The organic layer was separated and the aqueous layer extracted with Et_2O (2 × 50 cm^3). The combined extracts were washed with brine, dried, and evaporated. The residue was distilled to give (**35**) (3.31 g, 13.7 mmol, 96%) as a colourless oil, b.p. 125 °C (bath)/0.25 mmHg; $\nu_{max.}$ 3 440s, 3 060m, 2 930s, 2 860s, 1 640m, and 1 070s cm^{-1}; δ_H 4.68 (2 H, s), 4.64 (1 H, m), 4.14 (5 H, m), 2.96 (1 H, s, OH), 2.08 (2 H, m), 1.72 (3 H, s), and 1.45—1.92 (12 H, m); *m/z* 242 (M^+, 0.05%), 85 (100), 140 (6), 123 (5), 101 (13), 68 (20), 55 (29), and 43 (16) (Found: M^+, 242.187 29. $C_{14}H_{26}O_3$ requires *M*, 242.188 183).

cis, trans-4-(4-*Methylpent*-5-*enyl*)-2-*pentyl*-1,3-*dioxane* (**36**), (**37**).—A solution of the THP ether (**35**) (4.8 g, 19.9 mmol) in methanol (25 cm^3) was stirred at room temperature with 4.4 g of Dowex-50W-8X (H^+) ion exchange resin for 1 h. The mixture was filtered and concentrated to give 7-methyloct-7-ene-1,3-diol, $\nu_{max.}$ 3 350s, 1 640m, and 1 060s cm^{-1}; δ_H 4.68 (2 H, s), 3.87 (2 H, t, *J* 7), 3.70 (1 H, m), 2.54 (2 H, s, OH), 2.06 (2 H, m), 1.72 (3 H, s), and 1.30—1.88 (6 H, m). The crude diol was stirred in CH_2Cl_2 (40 cm^3) with Dowex-50W-8X (800 mg), anhydrous sodium sulphate (10 g) and n-hexanal (2.64 cm^3, 21 mmol) for 14 h after which it was filtered through Celite and concentrated. Chromatography (5 × 6 cm, 2—20% ether in light petroleum) gave, after distillation the *cis*-dioxane (**36**) (3.66 g, 15.2 mmol, 77%) as a colourless oil, b.p. 100 °C (bath)/0.25 mmHg; $\nu_{max.}$ 1 640m, 1 135s, and 890s cm^{-1}; δ_H 4.68 (2 H, s), 4.49 (1 H, t, *J* 5), 4.10 (1 H, ddd, *J* 10, *J'* 5, *J''* 2), 3.71 (1 H, ddd, *J* 10, *J'* 10, *J''* 4), 3.70 (1 H, m), 2.05 (2 H, m), 1.71 (3 H, s), 1.10—1.80 (14 H, m), and 0.89 (3 H, m); δ_C 145.6, 109.9, 102.3, 76.5, 66.6*, 37.6*, 36.1*, 35.6*, 31.7*, 31.6*, 23.9*, 23.0*, 22.6*, 22.3, and 14.0; *m/z* 240 (M^+, 2%), 123 (100), 169 (13), 107 (16), 95 (27), 81 (71), 67 (46), 55 (54), and 43 (31) (Found: M^+, 240.208 87. $C_{15}H_{28}O_2$ requires *M*, 240.208 919), and the *trans*-dioxane (**37**) (300 mg, 1.25 mmol, 6%), $\nu_{max.}$ 1 650m, 1 130s, and 890s cm^{-1}; δ_H 4.77 (1 H, t, *J* 5), 4.71 (2 H, s), 4.0 (1 H, m), 3.93 (2 H, dd, *J* 8, *J'* 4), 2.10 (2 H, m), 1.73 (3 H, s), 1.10—1.90 (14 H, m), and 0.89 (3 H, m); δ_C 145.5, 110.1, 95.1, 71.2, 62.1, 37.6*, 34.8*, 31.8*, 30.2*, 28.8*, 23.9*, 23.7*, 22.6*, 22.3, and 14.0 (Found: M^+, 240.208 89. $C_{15}H_{28}O_2$ requires *M*, 240.208 919).

cis-4-(4-*Oxopentyl*)-2-*pentyl*-1,3-*dioxane* (**38**).—The alkene (**36**) (3.59 g, 14.9 mmol) in MeOH (50 cm^3) was ozonolysed in the usual way to give after reductive work-up with an excess of Me_2S, chromatography (4 × 4 cm, 5% ether in light petroleum), and distillation, the ketone (**38**) (3.24 g, 13.5 mmol, 90%) as a colourless oil, b.p. 120 °C (bath)/0.2 mmHg; $\nu_{max.}$ 1 710s and 1 140s cm^{-1}; δ_H 4.48 (1 H, t, *J* 5), 4.10 (1 H, ddd, *J* 10, *J'* 4, *J''* 2), 3.715 (1 H, ddd, *J* 10, *J'* 10, *J''* 3.5), 3.59 (1 H, m), 2.5 (2 H, m), 2.14 (3 H, s), 1.4—1.95 (14 H, m), and 0.89 (3 H, m); δ_C 208.5, 102.2, 76.4, 66.5*, 43.5*, 35.4*, 35.2*, 31.7*, 31.5*, 29.8, 23.8*, 22.6*, 19.6*, and 14.0; *m/z* 242 (M^+, 0.2%), 43 (100), 171 (32), 143 (13), 125 (39), 99 (16), 85 (14), 71 (21), and 55 (21) (Found: M^+, 242.183 73. $C_{14}H_{26}O_3$ requires *M*, 242.188 183).

trans-4-(4-*Oxopentyl*)-2-*pentyl*-1,3-*dioxane* (**39**).—Ozonolysis of the *trans*-alkene (**37**) (577 mg, 2.44 mmol) in MeOH (15 cm^3) as above gave the *trans*-ketone (**39**) (535 mg, 2.20 mmol, 91%), δ_H 4.77 (1 H, t, *J* 5), 3.91 (2 H, dd, *J* 9, *J'* 3), 3.95 (1 H, m), 2.51 (2 H, t, *J* 6), 2.145 (3 H, s), 1.20—1.95 (14 H, m), and 0.89 (3 H, m); δ_C 208.3, 95.1, 70.9, 62.03*, 43.2*, 34.6*, 31.1*, 30.1*, 29.8, 28.7*, 23.8*, 22.6*, 20.0*, and 14.0 (Found: M^+, 242.183 71. $C_{14}H_{26}O_3$ requires *M*, 242.188 183).

cis-2-*Pentyl*-4-(4-*trimethylsilyloxypent*-5-*enyl*)-1,3-*dioxane* (**40**).—To a rapidly stirred solution of Pr^i_2NH (0.7 cm^3, 5 mmol) in THF (3 cm^3) was added dropwise at 0 °C n-butyllithium in hexane (1.4M 3.5 cm^3; 4.9 mmol). After 5 min, the mixture was cooled to −78 °C and the ketone (**38**) (674 mg, 2.8 mmol) in THF (5 cm^3) was added dropwise. After 30 min at −78 °C, Me_3SiCl (0.85 cm^3, 5.6 mmol) was added in one portion and the mixture was stirred at −78 °C for 1 h. After warming to room temperature the solvent was removed under reduced pressure and pentane (15 cm^3) added to the residue. The mixture was filtered through Celite and evaporated. The crude enol silane (**40**) was used immediately in the next step without further purification. The crude product showed $\nu_{max.}$ 1 620m and 1 250s cm^{-1}; δ_H 3.88 and 3.82 (1 H each, br s, $=CH_2$) characteristic of a terminal enol silane.

trans-8-(2-*Hydroxyethyl*)-2-*pentyloxocan*-4-*one* (**42**).—To a rapidly stirred solution of $TiCl_4$ (637 mg, 0.37 cm^3, 3.36 mmol) in CH_2Cl_2 (15 cm^3) was added dropwise the crude enol silane (**40**) in CH_2Cl_2 (3 cm^3). Work-up and chromatographic purification as described above gave (**42**) (230 mg, 0.95 mmol, 34% overall for 2 steps) as a colourless oil, b.p. 135 °C/0.35 mmHg; $\nu_{max.}$ 3 440s, 1 685s, and 1 065s cm^{-1}; δ_H 3.72 (2 H, t, *J* 7), 3.26—3.88 (2 H, m), 2.83 (1 H, dd, *J* 11, *J'* 9), 2.1—2.65 (3 H, m), 2.53 (1 H, s, OH), 1.67 (2 H, dt, *J* 2.5, *J'* 6.5), 1.1—2.0 (12 H, m), and 0.90 (3 H, distorted t); δ_C 215.5, 80.6, 76.1, 60.8*, 48.9*, 44.1*, 39.3*, 37.1*, 34.7*, 31.7*, 25.6*, 22.6*, 20.7*, and 14.0; *m/z* 242 (M^+, 0.5%), 43 (100), 142 (14), 127 (10), 109 (10), 97 (25), 81 (32), 71 (51), and 55 (67) (Found: M^+, 242.187 97. $C_{14}H_{26}O_3$ requires *M*, 242.188 183).

The 3,5-dinitrobenzoate (gum) (**43**) gave $\nu_{max.}$ 1 730s, 1 685s, and 1 630 cm^{-1}; δ_H (400 MHz), 9.221 (1 H, t, *J* 2.5), 9.112 (2 H, d,

J 2.5), 4.532 (2 H, dd, *J* 6.5, *J'* 7.5), 3.636 (1 H, dddd, *J* 9, *J'* 4.5, *J''* 4.5, *J'''* 3), 3.404 (1 H, dddd, *J* 7.5, *J'* 7, *J''* 7, *J'''* 4), 2.861 (1 H, dd, *J* 10, *J'* 11.5), 2.572 (1 H, m), 2.326 (2 H, m), 1.925 (2 H, m), 1.67—1.885 (2 H, m), 1.63 (2 H, m), 1.493 (2 H, m), 1.272 (6 H, m), and 0.882 (3 H, m).

11,11-*Dimethyl*-2,5,7-*trioxatridecan*-12-*one* (**47**).—To a stirred solution of (**46**) (2.34 g, 10 mmol) in Et_2O (35 cm^3) was added dropwise at 0 °C MeLi in Et_2O (1.7 M; 14 cm^3, 23.8 mmol). After the addition was complete the mixture was refluxed for 24 h and then poured into iced NH_4Cl solution (200 cm^3). The organic layer was washed with aqueous $NaHCO_3$, dried, evaporated and the residue distilled to give (**47**) (1.99 g, 8.6 mmol, 86%) as a colourless oil, b.p. 110 °C (bath)/0.1 mmHg; $\nu_{max.}$ 1 705s, 1 475s, and 1 070s cm^{-1}; δ_H 4.67 (2 H, s), 3.4—3.8 (6 H, m), 3.35 (3 H, s), 2.10 (3 H, s), and 1.1—1.8 (4 H, m) (Found: M^+, 232.167 17. $C_{12}H_{24}O_4$ requires M, 232.167 448).

11,11-*Dimethyl*-2-(*trimethylsilyloxy*)-2,5,7-*trioxatridec*-12-*ene* (**48**).—The ketone (**47**) (179 mg, 0.88 mmol) was converted into the enol silane (**48**) using Pr^i_2NLi and Me_3SiCl as described above. The crude enol silane gave $\nu_{max.}$ 1 650w, 1 245s, 1 070s, and 840s cm^{-1}; δ_H 4.69 (2 H, s), 4.05 and 3.98 (1 H each, d, *J* 1), 3.4—3.75 (6 H, m), 3.37 (3 H, s), 1.2—1.9 (4 H, m), and 1.1 and 0.98 (3 H each, s). The crude enol silane was used immediately in the next step.

5,5-*Dimethyloxocan*-4-*one* (**49**).—Treatment of the enol silane (**48**) (prepared above) with $TiCl_4$ (1.2 equiv) in CH_2Cl_2 (10 cm^3) in the usual manner, gave the oxocan-4-one (**49**) (60 mg, 0.384 mmol, 43%) after chromatography (6 × 1 cm, 40% $CHCl_3$ in light petroleum) and distillation as a colourless oil, b.p. 132 °C (bath)/15 mmHg; $\nu_{max.}$ 1 690s and 1 080m cm^{-1}; δ_H 3.9 (2 H, m), 3.31 (2 H, dd, *J* 9, *J'* 6), 2.6 (2 H, m), 2.04—1.82 (2 H, m), 1.41—1.72 (2 H, m), and 1.01 (6 H, s); δ_C 219.4, 72.1*, 68.7*, 46.7*, 40.0, 34.3*, 26.1*, and 24.0; *m/z* 156 (M^+, 7%), 85 (100), 128 (25), 99 (5), 69 (32), 56 (43), and 43 (17) (Found: M^+, 156.114 77. $C_9H_{16}O_2$ requires *M*, 156.115 023).

2,5,7-*Trioxadodecan*-12-*al* (**51**).—The MEM ether of hex-6-en-1-ol (**50**) (350 mg, 1.86 mmol) in CH_2Cl_2 (15 cm^3) was ozonolysed in the usual manner. The ozonide was reduced in acetic acid (10 cm^3) with an excess of zinc powder until no ozonide was detectable by starch-iodide. Aqueous NaOH (4M; 10 cm^3) was added and the aqueous phase extracted with CH_2Cl_2. The organic extract was dried and concentrated and distillation gave 349 mg (1.84 mmol, 98%) of the aldehyde (**51**) as a colourless oil, b.p. 110 °C (bath)/0.4 mmHg; $\nu_{max.}$ 1 715s and 1 040s cm^{-1}; δ_H 9.78 (1 H, t, *J* 1), 4.70 (2 H, s), 3.45—3.85 (6 H, m), 3.4 (3 H, s), 2.50 (2 H, m), and 1.5—1.9 (4 H, m).

13-*Methyl*-2,5,7-*trioxatetradec*-13-*en*-12-*ol* (**52**).—To the Grignard reagent prepared from 2-bromopropene (0.45 cm^3, 5.1 mmol) and Mg (161 mg, 6.3 mol) in THF (8 cm^3) was added dropwise at 0 °C the aldehyde (**51**) (480 mg, 2.53 mmol) in THF (4 cm^3). Standard extractive work up with aqueous NH_4Cl gave (**52**) (518 mg, 2.33 mmol, 92%) after distillation, b.p. 140 °C (bath)/0.4 mmHg; $\nu_{max.}$ 3 440s, 1 640w, and 1 040s; δ_H 4.92 and 4.81 (1 H each, d, *J* 1), 4.69 (2 H, s), 4.14 (1 H, t with fine splitting, *J* 6), 3.4—3.8 (7 H, m), 3.37 (3 H, s), 1.71 (3 H, s), and 1.3—1.8 (6 H, m) (Found: M^+, 232.167 21. $C_{12}H_{24}O_4$ requires *M*, 232.167 448).

13-*Methyl*-2,5,7-*trioxatetradec*-13-*en*-12-*one* (**53**).—Oxidation of (**53**) (947 mg, 4.4 mmol) with pyridinium chlorochromate (2 g) and finely ground 3Å molecular sieves[18] (2 g) in CH_2Cl_2 (30 cm^3) gave (**53**) (625 mg, 2.71 mmol, 61%) after chromatography (6 × 2.8 cm, 30% Et_2O in light petroleum) and distillation, b.p. 120 °C/0.4 mmHg; $\nu_{max.}$ 1 670s, 1 620w, and 1 040s cm^{-1}; δ_H 5.95 and 5.75 (1 H each, d, *J* 1), 4.70 (2 H, s), 3.3—3.8 (6 H, m), 3.39 (3 H, s), 2.73 (2 H, t, *J* 7), 1.89 (3 H, s), and 1.4—2.0 (4 H, m) (Found: M^+, 230.151 168. $C_{12}H_{22}O_4$ requires *M*, 230.151 799).

12-[(*Dimethylphenylsilyl*)*oxy*]-2-*methyl*-2,5,7-*trioxatetradec*-12-*ene* (**54**).—The enone (**53**) (150 mg, 0.652 mmol), dimethylphenylsilane (102 mg, 0.71 mmol) and $[Rh(PPh_3)_3Cl]$ (10 mg) were stirred together at 50 °C under N_2 for 1 h. The enol silane (**54**) (229 mg, 0.62 mmol, 95%) was distilled from the reaction mixture as a colourless oil, b.p. 180 °C (bath)/0.8 mmHg; $\nu_{max.}$(film) 1 670m, 1 250s, 1 040s, and 850s cm^{-1}; δ_H 7.26—7.82 (5 H, m), 4.71 (2 H, s), 3.36—3.92 (6 H, m), 3.44 (3 H, s), 1.91—2.30 (2 H, m), 1.65 (3 H, s), 1.63 (3 H, s), 1.26—1.88 (4 H, m), and 0.46 (6 H, s). The enol silane was used immediately in the next step.

3,3-*Dimethyloxocan*-4-*one* (**55**).—Treatment of the enol silane (**54**) with 2 equiv. of $TiCl_4$ in CH_2Cl_2 (30 cm^3) in the usual manner gave, after chromatography (6 × 2.8 cm, 20—50% ether in light petroleum) and distillation the oxocanone (**55**) (52 mg, 0.33 mmol, 25%) as a colourless oil, b.p. 120 °C (bath)/15 mmHg; $\nu_{max.}$ 1 690s and 1 095s cm^{-1}; δ_H 3.64 (2 H, t, with fine splitting, *J* 6), 3.55 (2 H, s), 2.64 (2 H, t with fine splitting, *J* 7.5), 1.43—1.91 (4 H, m), and 1.11 (6 H, s); δ_C 215.1, 76.6*, 71.0*, 49.2*, 37.0, 27.2*, 25.2*, and 21.3; *m/z* 156 (M^+, 0.9%), 101 (100), 126 (13), 83 (57), 70 (37), 55 (96), and 43 (48) (Found: M^+, 156.115 34. $C_9H_{16}O_2$ requires *M*, 156.115 023).

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