Rhodium Carbenoid Mediated Cyclisations. Part 7.[1] Synthesis and Coupling Reactions of 2-Substituted 3-Oxooxepanes

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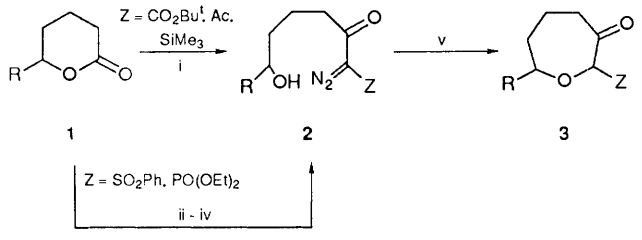
A range of 2-substituted oxepanes **3** has been prepared from δ-lactones *via* rhodium(II) acetate catalysed cyclisation of the intermediate diazo alcohols **2**. The phenylsulphonyloxepane **3e** and the oxepane phosphonate **3f** are versatile substrates for further elaboration, and are readily converted into substituted oxepanes **12–14**.

The introduction of substituents into the 2-position (anomeric position) of cyclic ethers is an important synthetic goal, and in recent years many solutions to this problem in 5- and 6-membered rings have been advanced.[2] In continuation of our work on the synthesis and reactions of 7-membered ring ethers,[3] we have investigated the preparation of 3-oxooxepanes containing functional groups at the 2-position, that are suitable for further elaboration, and we now report our results in full.[4]

Results and Discussion

The route to 2-functionalised oxepanes is based on our previously reported novel 2-step ring expansion of δ-lactones.[3b] In its original form, the reaction sequence involved the ring opening of the lactone **1** with ethyl lithiodiazoacetate, followed by rhodium(II) acetate catalysed cyclisation of the resulting diazo alcohol **2** (Z = CO_2Et) to give, by formal OH insertion, 3-oxooxepane 2-esters **3** (Z = CO_2Et) (Scheme 1). Although



Scheme 1 *Reagents:* i, Z(Li)C=N_2, THF, low temp.; ii, ZCH_2Li, THF, −78 °C; then LDA (1 equiv.); Me_3SiCl (2 equiv.); iii, MsN_3, Et_3N; iv, 0.5 M HCl, THF; v, cat. $Rh_2(OAc)_4$, benzene, reflux

ethyl lithiodiazoacetate is the most frequently used and the most readily accessible diazo anion, a small range of other diazo compounds have been successfully metallated.[5] Therefore, we attempted the ring opening of δ-lactones **1** with a range of diazo anions. The organolithiums derived by deprotonation of t-butyl diazoacetate,[6] diazoacetone[7] and trimethylsilyldiazomethane[8] using butyllithium or lithium diisopropylamide (LDA) reacted readily with δ-valerolactone and undecanoic acid δ-lactone to give the diazo alcohols **2a–d** (Table 1 and Scheme 1), although in the latter case the trimethylsilyl group was lost on work-up. Use of triethylsilyldiazomethane[9] also gave the diazo alcohol **2d**, the bulkier silyl group still being lost on work-up.

We were also interested in the preparation, and OH insertion reactions of α-diazo β-keto sulphones, and phosphonates.[10] However, attempted deprotonation of phenylsulphonyldiazomethane[11] using either LDA or butyllithium at −90 °C resulted only in decomposition of the substrate. Diethyl diazomethylphosphonate,[12] however, was readily lithiated, and although the lithium species is known to react with aldehydes and ketones,[5,13] we were unable to isolate any products from its reaction with δ-valerolactone. Therefore, an alternative approach to diazo sulphones and phosphonates was used (Scheme 1). The δ-lactone was ring opened using the anions derived from methyl phenyl sulphone or diethyl methylphosphonate, and the diazo group was introduced subsequently by diazo transfer, originally using toluene-4-sulphonyl azide,[4] although methanesulphonyl azide[14] was found to be a superior reagent for these transformations, giving cleaner reactions and higher yields. However, the ring opening of lactones with anions such as diethyl lithiomethylphosphonate is not straightforward, since the product β-keto compounds are more acidic than the substrates from which they are derived. Therefore, a modification developed by Dietrich and Hoffmann[15] was used. In this one-pot procedure, the δ-lactone was added to the anion (formed using butyllithium as base), followed by the addition of one equivalent of LDA, and quenching with an excess of trimethylsilyl chloride. The resulting trimethylsilyl enol ether was readily hydrolysed on work-up, and the crude product was immediately treated under diazo transfer conditions, before final acidic cleavage of the trimethylsilyl ether. Using this method the overall yields of the diazo alcohols **2e**, **2f** and **2g** were 40, 56 and 62%, respectively.

Table 1 Preparation and cyclisation of diazo alcohols **2**

2/3	R	Z	Yield 2 (%)	Yield 3 (%)
a	H	CO_2Bu^t	87	48–56
b	C_6H_{13}	CO_2Bu^t	67	64
c	H	Ac	26	62
d	C_6H_{13}	$Me_3Si(H)$	32	56
e	C_6H_{13}	SO_2Ph	40	73
f	C_6H_{13}	$PO(OEt)_2$	56	54
g	H	$PO(OIt)_2$	62	52

When heated in boiling benzene in the presence of a catalytic amount of rhodium(II) acetate, the diazo alcohols **2** underwent rhodium carbenoid mediated cyclisation by a formal intramolecular OH insertion, and gave the 3-oxooxepanes **3** in good yield (Table 1). Like the corresponding methyl and ethyl esters,[3a,3b] the t-butyl esters **3a** and **3b** existed as a mixture of keto and enol forms in solution, whereas the 2-acetyloxepane **3c** was completely enolised. On the other hand, the sulphone **3e** and the phosphonates **3f** and **3g** existed exclusively in the keto form as evidenced by their ^1H NMR spectra, and NOE spectroscopy established the stereochemistry of the sulphone **3e**. Thus pre-irradiation of the singlet at δ 4.67 (2-H) resulted in enhancement of the multiplet at δ 3.18 (7-H).

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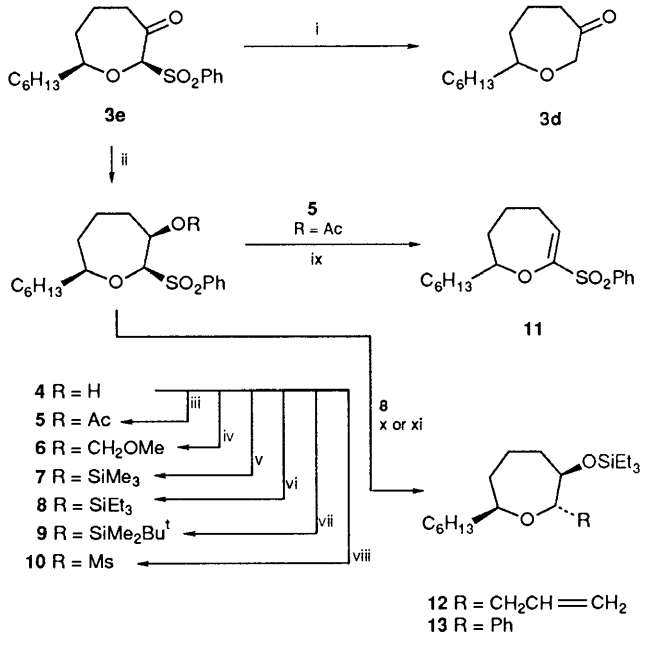
The phenylsulphonyloxepane **3e** and the oxepane phosphonate **3f** are ideal substrates for further elaboration. Thus treatment of the phenylsulphonyloxepane **3e** with sodium amalgam in methanol containing sodium dihydrogen phosphate led to very slow desulphonylation, though the product appeared to have ring opened, and was not the expected oxepane **3d**. However, the β-keto sulphone **3e** was readily desulphonylated using tributyltin hydride[16] and gave 7-hexyloxepan-3-one **3d** in 73% yield. The ketone group in **3e** was stereoselectively reduced using sodium borohydride and cerium(III) chloride to give the crystalline all-*cis*-alcohol **4** in excellent yield. In the absence of cerium(III) chloride the yield was lower, although the diastereoselectivity was the same. High diastereoselectivity in the sodium borohydride reduction of acyclic β-keto sulphones has been noted previously.[17] The stereochemistry of the alcohol **4** was confirmed by NOE spectroscopy in which pre-irradiation of the singlet at δ 4.36 (2-H) caused an enhancement of the multiplet at δ 3.37 (7-H) and the triplet at δ 4.75 (3-H). Pre-irradiation of the latter signal also caused a strong enhancement of the singlet at δ 4.36.* The alcohol **4** was converted into a number of derivatives **5**–**10** by conventional means (Scheme 2). Of these derivatives, the acetate



Scheme 2 *Reagents:* i, Bu_3SnH, AIBN, toluene, reflux; ii, $NaBH_4$, $CeCl_3$, MeOH; iii, Ac_2O, pyridine, DMAP; iv, $MeOCH_2Cl$, Pr^i_2NEt, CH_2Cl_2; v, Me_3SiCl, Et_3N, DMAP, CH_2Cl_2; vi, $Et_3SiOSO_2CF_3$, 2,6-dimethylpyridine, CH_2Cl_2; vii, $Bu^tMe_2SiOSO_2CF_3$, 2,6-dimethylpyridine, CH_2Cl_2; viii, MsCl, pyridine, DMAP; ix, NaOH, dioxane; x, $Bu_3SnCH_2CH{=}CH_2$, $Bu_3SnOSO_2CF_3$, benzene; xi, PhMgBr, $ZnBr_2$, THF

5 underwent the expected elimination reaction on treatment with base to give the vinyl sulphone **11** in high yield. Attempts to carry out Julia reactions with aldehydes on the β-keto sulphone **3e** were unsuccessful, presumably because the derived anion is too stable. We also attempted to couple the vinyl sulphone **11** with Grignard reagents in the presence of iron(III) or nickel(II) acetylacetonate,[18] again without success.

Although the β-keto sulphone **3e** could not be utilised directly in coupling reactions, the phenylsulphonyl group in the all-*cis* protected alcohol **8** could be displaced by carbon nucleophiles

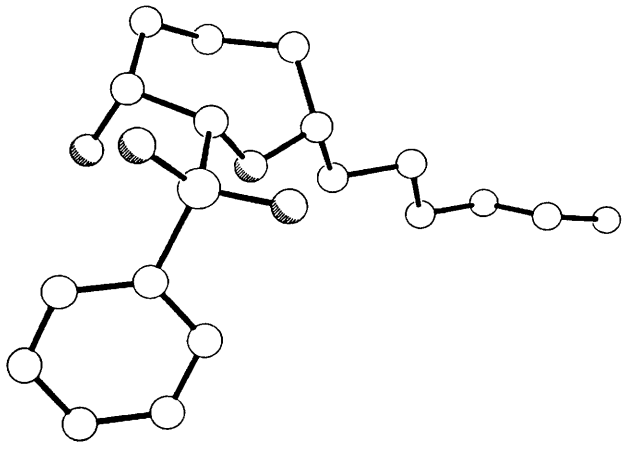
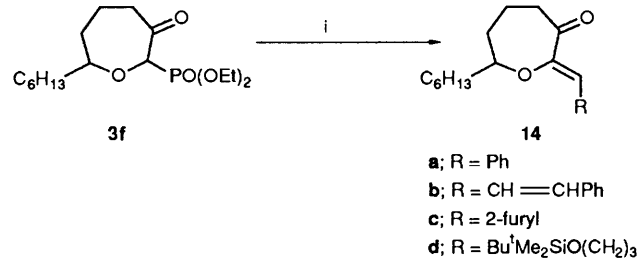


Fig. 1 X-Ray crystal structure of 7-hexyl-2-phenylsulphonyloxepan-3-ol **4**

under conditions similar to those reported for 6-membered ring ethers. Thus radical alkylation of **8** with allyl(tributyl)tin in the presence of tributyltin triflate[2c] gave the trisubstituted oxepane **12** (76%) (Scheme 2). Similarly, reaction with phenylmagnesium bromide in the presence of zinc bromide[2b] gave the oxepane **13** (70%). The stereochemistry of the 2,3,7-trisubstituted oxepane **12** is assigned on the basis of its NMR spectrum and on literature precedent.[2c] Similarly, the major (*ca.* 3:1) oxepane **13** has its 2- and 7-substituents *trans* to one another.

On the other hand, the phosphonate **3f** could be used directly, and underwent smooth Wadsworth–Emmons reaction with a range of aldehydes to give the oxepanes **14** in good yield (Scheme 3). The reaction gives largely (>90%) one geometrical



Scheme 3 *Reagents:* i, NaH, THF; RCHO

isomer, which on the basis of the chemical shift of the vinyl proton in the ^1H NMR is assigned as the *Z*-alkene. Thus the use of oxepan-2-ylphosphonates constitutes a versatile route to 2-alkenylated 7-membered ring ethers which complements that based on phosphine oxides developed by Ley and co-workers for 5- and 6-rings.[2d] However, the extra stability imparted to the enol ethers by the ring carbonyl group makes them easier to handle and characterise.

Experimental

For general points, see refs. 3*a* and 3*b*. In addition, all *J* values are in Hz.

Preparation of Diazo Alcohols

t-Butyl 2-Diazo-7-hydroxy-3-oxoheptanoate **2a**.—t-Butyl diazoacetate (0.750 g, 5.25 mmol) was added dropwise to a solution of LDA (5.25 mmol) in THF (30 ml) at −90 °C. After 15 min at −90 °C, δ-valerolactone (5.00 mmol, 0.501 g) was added dropwise over 5 min. After 15 min at −90 °C, the solution was warmed to −77 °C for 4.5 h. Acetic acid (0.3 ml) was added, and the mixture allowed to warm to 0 °C before the addition of water and extraction into dichloromethane. The

* The stereochemistry was further confirmed by X-ray crystallography (Fig. 1). Details can be obtained from Dr. D. J. Williams, Department of Chemistry, Imperial College.

crude product was purified by chromatography to give the *title compound* **2a** (1.06 g, 87%) as a pale yellow oil (Found: C, 54.6; H, 7.7; N, 11.4. $C_{11}H_{18}N_2O_4$ requires C, 54.5; H, 7.5; N, 11.6%); ν_{max}(film)/cm^{-1} 3421, 2133, 1713, 1655, 1315 and 1135; δ_H(250 MHz; $CDCl_3$) 1.52 (9 H, s, Bu^t), 1.50–1.80 (4 H, m), 1.90 (1 H, s, OH), 2.84 (2 H, t, *J* 7.1, CH_2CO) and 3.64 (2 H, t, *J* 6.4, CH_2O); *m/z* (FAB; glycerol) 243 (MH^+), 225, 187, 169, 141, 99 and 57.

t-Butyl 2-Diazo-7-hydroxy-3-oxotridecanoate **2b**.—To a solution of t-butyl diazoacetate (2.6 g, 18 mmol) and undecanoic acid δ-lactone (3.17 ml, 3.04 g, 16 mmol) in THF (80 ml) at −78 °C under nitrogen was added *via* a catheter a cooled solution of LDA [prepared from diisopropylamine (2.57 ml, 1.85 g, 18 mmol) and butyllithium (1.6 mol dm^{-3}; 11.41 ml, 0.018 mol)] in THF (60 ml). The reaction mixture was stirred at −78 °C for 4 h, after which acetic acid (2.06 ml, 2.16 g, 36 mmol) was added and the solution allowed to warm to room temperature. The mixture was diluted with water (20 ml) and extracted with dichloromethane (3 × 50 ml) and the combined organic extracts were washed with water (50 ml) and brine (50 ml), dried (Na_2SO_4) and evaporated. The residue purified by column chromatography on silica (light petroleum–ether) gave the *title compound* **2b** (3.5 g, 67%) as a yellow oil (Found: C, 62.6; H, 9.5; N, 8.3. $C_{17}H_{30}N_2O_4$ requires C, 62.55; H, 9.3; N, 8.6%); ν_{max}(film)/cm^{-1} 3410, 2930, 2131, 1714, 1655, 1371 and 1091; δ_H(270 MHz; $CDCl_3$) 0.85 [3 H, ~t, *J* 10, *Me*$(CH_2)_5$], 1.24–1.50 and 1.60–1.95 (15 H, 2 m), 1.54 (9 H, s, Bu^tO_2C) 2.72–2.95 (2 H, m, 4-CH_2) and 3.54–3.65 (1 H, m, 7-CH); *m/z* 298 (M^+ − N_2), 242, 224, 197 and 99.

3-Diazo-8-hydroxyoctane-2,4-dione **2c**.—A solution of LDA (2.38 mmol) in THF (5 ml) was added dropwise to a solution of diazoacetone (200 mg, 2.38 mmol) and δ-valerolactone (238 mg, 2.38 mmol) in THF (10 ml) at −92 °C. The solution was stirred at −90 °C for 0.5 h followed by 4.5 h at −75 °C, before the addition of acetic acid (0.15 ml). Aqueous work-up and purification of the residue by chromatography gave the *title compound* **2c** (114 mg, 26%) as a yellow oil (Found: M^+, 184.0844. $C_8H_{12}N_2O_3$ requires M, 184.0848); ν_{max}(film)/cm^{-1} 3419, 2130, 1662, 1367 and 1299; δ_H(250 MHz; $CDCl_3$) 1.43–1.56 (2 H, m), 1.56–1.70 (2 H, m), 2.33 (3 H, s, COMe), 2.66 (2 H, t, *J* 6.9, CH_2CO), 2.66 (1 H, br, OH) and 3.53 (2 H, t, *J* 5.8, CH_2O); *m/z* 184 (M^+), 166, 156, 138, 126, 100, 85, 55 and 43.

1-Diazo-6-hydroxydodecan-2-one **2d**.—Butyllithium (1.9 ml, 3.00 mmol) was added dropwise to a standardised solution of trimethylsilyldiazomethane in ether (1.50 ml, 3.0 mmol), diluted with THF (15 ml) at −65 °C. The solution was stirred for 20 min before the dropwise addition of undecanoic acid δ-lactone (498 mg, 2.70 mmol). After 3 h at −70 °C, acetic acid (0.17 ml, 3.0 mmol) was added. The reaction mixture was warmed to 0 °C, diluted with water and rapidly extracted with ether. The crude product was purified by chromatography on neutral alumina, to give the *title compound* **2d** (198 mg, 32%) as a low melting yellow solid, m.p. 30–33 °C (Found: M^+, 198.1625. $C_{12}H_{22}N_2O_2 - N_2$ requires M, 198.1620); ν_{max}(film)/cm^{-1} 3319, 3083, 2105, 1634, 1377, 1130 and 1087; δ_H(250 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 7, CH_3), 1.15–1.60 (12 H, m), 1.62–1.85 (3 H, m), 2.36 (2 H, ~t, *J* 7, CH_2CO), 3.58 (1 H, m, CHO) and 5.26 (1 H, br, CHN); *m/z* 198 (M^+ − N_2), 185, 167, 156, 141, 113, 84 and 55.

1-Diazo-6-hydroxy-1-phenylsulphonyldodecan-2-one **2e**.—To a solution of methyl phenyl sulphone (3.0 g, 19 mmol) in THF (25 ml) at −78 °C under nitrogen was added dropwise over 5 min butyllithium (1.6 mol dm^{-3}; 12 ml, 19 mmol). After the resulting yellow anion solution had been stirred for 30 min, undecanoic acid δ-lactone (3.6 ml, 3.5 g, 19 mmol) in THF (5 ml) was added. The solution was stirred for 1 h at −78 °C and then allowed to warm to 0 °C; it was then maintained at this temperature for a further 2 h before being recooled to −78 °C LDA [prepared from diisopropylamine (2.65 ml, 1.9 g, 19 mmol) and butyllithium (1.6 mol dm^{-3}; 12 ml, 19 mmol)] in THF (25 ml) was added *via* a catheter and stirred for a further 30 min. Chlorotrimethylsilane (4.79 ml, 4.1 g, 38 mmol) was added and the solution allowed to come to room temperature overnight, whereupon saturated aqueous ammonium chloride (50 ml) was added. The mixture was extracted with ether (2 × 100 ml) and the ethereal solution was washed with brine (100 ml), dried (Na_2SO_4) and evaporated to give the crude β-keto sulphone intermediate. This was immediately subjected to diazo transfer using methanesulphonyl azide (2.39 g, 20 mmol) and triethylamine (7.9 ml, 5.7 g, 57 mmol) in ethanol (40 ml). After 60 h at room temperature, the residue taken up in ether (300 ml), and the solution washed with water (2 × 100 ml) and brine (100 ml), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica (light petroleum–ether) to give *1-diazo-1-phenylsulphonyl-6-trimethylsiloxydodecan-2-one* (4.18 g, 49%) as a yellow oil, ν_{max} (film)/cm^{-1} 2112, 1668, 1448, 1344, 1250, 1178, 1157, 1086, 841 and 724; δ_H(60 MHz; $CDCl_3$) 0.08 (9 H, s), 0.50–1.65 (17 H, m), 2.38 (2 H, t, *J* 6, CH_2CO), 3.10–3.50 (1 H, m, CHO) and 7.03–7.98 (5 H, m, ArH); *m/z* 423 (M^+ − Me), 397, 395, 379, 351, 327, 297, 281, 273, 187 and 73.

This oil was dissolved in THF (40 ml) and hydrochloric acid (0.5 mol dm^{-3}; 20 ml) was added slowly. The mixture was stirred for 5 min, after which standard work-up as above and recrystallisation (light petroleum–ether) gave the *title compound* **2e** (2.8 g, 81%) as colourless needle crystals, m.p. 77–78 °C (Found: C, 59.0; H, 7.1; N, 7.7. $C_{18}H_{26}N_2O_4S$ requires C, 59.0; H, 7.2; N, 7.7%); ν_{max}(melt)/cm^{-1} 3436, 2114, 1667, 1448, 1337, 1155 and 725; δ_H(250 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.7, *Me*), 1.16–1.57 (13 H, m), 1.57–1.83 (2 H, m), 2.60 (2 H, t, *J* 7.1, CH_2CO), 3.43–3.57 (1 H, m, CHOH), 7.54–7.73 (3 H, m, ArH) and 7.98 (2 H, ~dd, *J* 6.7, 1, ArH); *m/z* 320 (M^+ − N_2), 281, 274, 253, 211, 197, 125, 99 and 77.

Diethyl (1-Diazo-6-hydroxy-3-oxododecyl)phosphonate **2f**.—To a solution of diethyl methyl phosphonate (6.0 g, 39.4 mmol) in THF at −78 °C under nitrogen was added butyllithium (1.6 mol dm^{-3}; 24.6 ml, 39.4 mmol) and the solution stirred for 30 min. Undecanoic acid δ-lactone (3.40 ml, 3.29 g, 17.8 mmol) in THF (5 ml) was added over 5 min and the solution allowed to warm to 0 °C. Stirring was continued for 2 h after which the solution was recooled to −78 °C and a solution of LDA [prepared from diisopropylamine (2.76 ml, 1.99 g, 19.7 mmol) and butyllithium (1.6 mol dm^{-3}; 12.6 ml, 19.7 mmol)] in THF (20 ml) was added *via* a catheter. After a further 30 min at −78 °C, chlorotrimethylsilane (7.47 ml, 6.38 g, 59.1 mmol) was added, and the solution allowed to warm to room temperature overnight. Saturated aqueous ammonium chloride (50 ml) was added, and the solution extracted with ether (2 × 200 ml). The ethereal extracts were washed with brine (100 ml), dried (Na_2SO_4), and evaporated to give crude *diethyl (2-oxo-6-trimethylsiloxydodecyl)phosphonate*, (ν_{max} 1719 cm^{-1}), which was dissolved in dichloromethane (13 ml) and triethylamine (13 ml). Methanesulphonyl azide (2.38 g, 19.7 mmol) was added and the mixture stirred at room temperature for 48 h, whereupon it was diluted with dichloromethane (100 ml), washed with water (2 × 50 ml) and brine (50 ml), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica (ether) to give *diethyl (1-diazo-2-oxo-6-trimethylsiloxydodecyl)-phosphonate* (4.42 g, 57%) as a yellow oil; ν_{max}(film)/cm^{-1} 2121, 1661, 1370, 1250, 1022, 973 and 841; δ_H(250 MHz; $CDCl_3$) 0.08 (9 H, s), 0.85 (3 H, t, *J* 6.7, Me), 1.04–1.80 (20 H, m), 2.53 (2 H,

t, *J* 7.1, CH_2CO), 3.58 (1 H, quin, *J* 5.5, CHO) and 3.96–4.27 (4 H, m, $POCH_2$); *m/z* 419 (M^+ − Me), 408, 393, 318, 269, 179 and 73.

To a solution of this diazo compound in THF (50 ml) was added hydrochloric acid (0.5 mol dm^{-3}; 20 ml). After being stirred for 5 min at room temperature, the solution was diluted with water (200 ml) and extracted with dichloromethane (2 × 100 ml) and the organic extracts were washed with brine (100 ml), dried (Na_2SO_4) and evaporated. The residue was purified by passage through a short silica gel column (ether) to give the *title compound* **2f** (3.62 g, 98%) as a clear oil (Found: M^+, 334.1907. $C_{16}H_{31}N_2O_5P - N_2$ requires M, 334.1909); ν_{max}(film)/cm^{-1} 3487, 2121, 1658, 1369, 1262, 1018 and 975; δ_H(250 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.7 Me), 1.19–1.57 (18 H, m), 1.76 (2 H, quin, *J* 7.2), 1.95 (1 H, br, OH), 2.46–2.72 (2 H, m, CH_2CO), 3.57 (1 H, m, C*H*OH) and 4.01–4.31 (4 H, m, CH_2O); *m/z* 334 ($M^+ - N_2$), 318, 316, 277, 220, 194, 179 and 65.

Diethyl (1-*Diazo*-6-*hydroxy*-2-*oxohexyl*)*phosphonate* **2g**.—To a solution of diethyl methylphosphonate (6 g, 39.4 mmol) in THF (40 ml) at −78 °C under nitrogen was added dropwise over 10 min butyllithium (1.6 mol dm^{-3}; 24.6 ml, 39.4 mmol). The mixture was stirred for 30 min after which valerolactone (1.83 ml, 1.97 g, 19.7 mmol) in THF (4 ml) was added and the solution allowed to come to 0 °C. After being stirred for a further 3 h, the solution was recooled to −78 °C and a solution of LDA [prepared as above, 19.7 ml in THF (20 ml)] was added *via* a catheter. After 30 min, chlorotrimethylsilane (7.47 ml, 6.38 g, 59.1 mmol) was added, and the solution allowed to warm to room temperature overnight. Work-up as previously gave crude diethyl (2-oxo-6-trimethylsiloxyhexyl)phosphonate which was dissolved in dichloromethane (13 ml) and triethylamine (13 ml). Methanesulphonyl azide (2.38 g, 19.7 ml) was added and the mixture stirred at room temperature for 48 h. It was then diluted with dichloromethane (100 ml), washed with water (2 × 50 ml) and brine (50 ml), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica (ether) to give diethyl (1-diazo-2-oxo-6-trimethylsiloxyhexyl)phosphonate (5.14 g, 75%) as a yellow oil. This oil was immediately dissolved in THF (60 ml), and hydrochloric acid (0.5 mol dm^{-3}; 25 ml) was added. After being stirred at room temperature for 5 min, the mixture was diluted with water (300 ml) and extracted with dichloromethane (2 × 200 ml), and the organic extracts were washed with brine (100 ml), dried (Na_2SO_4) and evaporated. The residue was purified by passage through a short silica gel column (ether) to give the *title compound* **2g** (2.4 g, 83%) as a viscous yellow oil (Found: C, 43.1; H, 6.9; N, 10.1. $C_{10}H_{19}N_2O_5P$ requires C, 43.2; H, 6.9; N, 10.1%); ν_{max}(film)/cm^{-1} 3412, 2938, 2122, 1657, 1020 and 799; δ_H(270 MHz; $CDCl_3$) 1.35 [6 H, t, *J* 10, $(OCH_2CH_3)_2$], 1.50–1.62 and 1.68–1.80 (4 H, 2 m, 4-CH_2 and 5-CH_2), 1.97 (1 H, br s, OH), 2.60 (2 H, t, *J* 10, 6-CH_2), 3.58–3.67 (2 H, m, 3-CH_2) and 4.12–4.28 (4 H, m, $(OCH_2CH_3)_2$); *m/z* (C.I., NH_3) 2.96 ($M^+ + NH_4$), 268 (M^+ − N, $+NH_4$), 251, 235 and 189.

Preparation of 2-*Substituted* 3-*Oxooxepanes by Rhodium(II) Acetate Catalysed Cyclisation of Diazo Alcohols*

t-Butyl 3-*Oxooxepane*-2-*carboxylate* **3a**.—A solution of the diazo alcohol **2a** (979 mg, 4.04 mmol) in benzene (9 ml) was added dropwise to a suspension of dirhodium tetraacetate (8.1 mg, 0.45 mol %) in benzene **(CAUTION)** (51 ml) at reflux over 13 min. After 3 min at reflux the reaction mixture was cooled, filtered, evaporated and the residue distilled to give the *title compound* **3a** (420 mg, 48%) as a clear oil, b.p. 90–95 °C at 0.03 mmHg (Found: C, 61.5; H, 8.6. $C_{11}H_{18}O_4$ requires C, 61.7; H, 8.5%); ν_{max}(film)/cm^{-1} 3475, 1746, 1718, 1652, 1621, 1370, 1326, 1275, 1248 and 1153; δ_H(250 MHz; $CDCl_3$) 1.42 (9 H, s, Bu^t, keto), 1.48 (9 H, s, Bu^t, enol), 1.50–1.98 (4 H, m, keto/enol), 2.40–2.54 (2 + 1 H, m, CH_2CO enol and HC*H*CO keto), 2.85 (1 H, dt, *J* 11.7, 2.5, HC*H*CO, keto), 3.42 (1 H, ddd, *J* 12.0, 9.7, 2.4, CHO, keto), 3.71 (2 H, t, *J* 5.1, CH_2O, enol), 4.22 (1 H, ddt, *J* 13.0, 3.8, 1.4, CHO, keto), 4.31 (1 H, s, CHCO, keto) and 10.97 (1 H, s, OH); *ca.* 10% enol form; δ_C(62.9 MHz; $CDCl_3$) 22.6 (enol), 23.5, 27.7, 28.2 (enol), 30.7, 31.80 (enol), 33.1 (enol), 41.5, 72.3, 72.9 (enol), 81.6 (enol), 82.4, 86.8, 165.4 and 208.1; *m/z* 214 (M^+), 158, 140, 113, 101 and 57.

t-Butyl 7-*Hexyl*-3-*oxooxepane*-2-*carboxylate* **3b**.—To a solution of dirhodium tetraacetate (38 mg, 0.086 mmol) in dry benzene (260 ml) under nitrogen at reflux was added dropwise over 10 min the diazo alcohol **2b** (3.5 g, 0.01 mol) in dry benzene **(CAUTION)** (100 ml). Heating was continued for a further 5 min, after which the solution allowed to cool. It was then filtered through Celite, the Celite washed with benzene (50 ml) and the combined organic filtrates were evaporated. The residue was passed through a short silica gel column (light petroleum–ether) and further purified by Kugelrohr distillation to give the *title compound* **3b** (1.9 g, 64%), b.p. 120 °C at 0.2 mmHg (Found: C, 68.4; H, 10.2. $C_{17}H_{30}O_4$ requires C, 68.4; H, 10.1%); ν_{max}(film)/cm^{-1} 2932, 1743, 1720, 1651, 1622, 1369, 1326, 1248, 1157 and 844; δ_H(270 MHz; $CDCl_3$) 0.80–0.90 [3 H, m, *Me*$(CH_2)_5$, keto and enol], 1.44 and 1.50 (9 H, 2s, Bu^t, keto, axial and equatorial), 1.55 (9 H, s, Bu^t, enol), 1.22–2.01 (14 H, m), 2.19–2.32 (1 H, dd, 16, 5, 4-C*H*H, enol), 2.36–2.49 (1 H, dd, *J* 13, 5, 4-C*H*H, keto), 2.59–2.80 (1 H, m, 4-C*H*H, keto), 2.87–3.01 (1 H, dt, *J* 16, 2.5, 4-C*H*H, enol), 3.17–3.30 (1 H, m, 7-CH), 4.29 and 4.58 (1 H, 2s, 2-CH, keto, axial and equatorial) and 11.15 (1 H, s, OH, enol), *ca.* 50% enol form; *m/z* 298 (M^+), 242, 197, 167, 149, 99 and 57.

t-Butyl 3-(*t-Butyldimethylsiloxy*)-7-*hexyl*-4,5,6,7-*tetrahydro*-*oxepine*-2-*carboxylate*.—To a solution of the oxepane **3b** (200 mg, 0.67 mmol) in dry dichloromethane (10 ml) was added triethylamine (0.23 ml, 169 mg, 1.67 mmol), t-butyldimethylsilyl trifluoromethanesulphonate (0.35 ml, 408 mg, 1.54 mmol), and the reaction mixture stirred under nitrogen at room temperature for 1 h. The solution was diluted with dichloromethane (20 ml), washed with saturated aqueous sodium hydrogen carbonate (10 ml) and brine (10 ml), dried (Na_2SO_4) and evaporated. The residue was purified by rapid column chromatography on silica (light petroleum–ether) to give the *title compound* (254 mg, 92%) as a colourless oil (Found: C, 66.9; H, 11.05. $C_{23}H_{44}SiO_4$ requires C, 66.9; H, 10.75%); ν_{max}(film)/cm^{-1} 2930, 2859, 1698, 1610, 1472, 1240, 839 and 789; δ_H(270 MHz; $CDCl_3$) 0.14 and 0.15 (6 H, 2s, Si*Me*$_2$Bu^t), 0.89 [3 H, ~t, *J* 10, *Me*$(CH_2)_5$], 0.96 and 0.98 (18 H, 2s, SiMe$_2$*Bu*^{t} and CO_2*Bu*^{t}), 1.21–1.92 (14 H, m), 2.09–2.18 (1 H, dd, *J* 14, 8, 4-C*H*H), 2.73–2.86 (1 H, ~dt, *J* 14, 2.5, 4-C*H*H) and 3.30–3.42 (1 H, m, 7-CH); *m/z* 413 (M^+ + H), 257, 189, 147, 73 and 28.

2-*Acetyloxepan*-3-*one* [*Enol Form*] **3c**.—A solution of the diazo alcohol **2c** (87.9 mg, 0.477 mmol) in benzene (7 ml) was added dropwise to a suspension of dirhodium tetraacetate (3 mg) in benzene **(CAUTION)** (15 ml) at reflux over 5 min. After 2 min at reflux the suspension was cooled, filtered and evaporated, and the residue purified by chromatography to give the *title compound* **3c** (46.4 mg, 62%) as a clear oil, b.p. 130 °C at 0.25 mmHg (Found: M^+, 156.0783. $C_8H_{12}O_3$ requires M, 156.0786); ν_{max}(film)/cm^{-1} 2700, 1736w, 1711w, 1596, 1435, 1300 and 873; δ_H(250 MHz; $CDCl_3$) 1.70 (2 H, quin, *J* 5.5, CH_2CH_2CO), 1.87 (2 H, quin, *J* 5.4, CH_2CH_2O), 2.10 (3 H, s, COMe), 2.59 (2 H, *ca.* t, *J* 6.2, CH_2CO), 3.81 (2 H, t, *J* 7.1, CH_2O) and 13.97 (1 H, s, OH); *m/z* 156 (M^+), 155, 129, 101, 83, 55 and 43.

7-Hexyloxepan-3-one **3d**.—A solution of the diazo alcohol **2d** (99 mg, 0.44 mmol) in benzene (5 ml) was added dropwise to a suspension of dirhodium tetraacetate (3 mg) in benzene **(CAUTION)** (20 ml) at reflux over 3 min. After 1 min at reflux, the reaction mixture was cooled, filtered and evaporated, and the residue purified by chromatography on Florisil to give the *title compound* **3d** (49 mg, 56%) as a clear oil, b.p. 150 °C at 0.2 mmHg (Found: C, 72.9; H, 11.4. $C_{12}H_{22}O_2$ requires C, 72.7; H, 11.2%); ν_{max}(film)/cm^{-1} 1714, 1456, 1332, 1127 and 1110; δ_H(250 MHz; $CDCl_3$) 0.83 (3 H, t, *J* 6.7, CH_3), 1.13–1.70 (12 H, m), 1.77–2.00 (2 H, m), 2.43 (1 H, ~dd, *J* 12.5, 5.8, CH_2CO), 2.86 (1 H, dt, *J* 12.2, 2.5, CH_2CO), 3.17 (1 H, ~t, *J* 8.9, CH_2CHO), 3.88 (1 H, d, *J* 18.3 Hz, OCH_2CO) and 4.23 (1 H, d, *J* 18.3, OCH_2CO); *m/z* 198 (M^+), 166, 124, 113, 98, 84, 55 and 41.

7-Hexyl-2-phenylsulphonyloxepan-3-one **3e**.—A solution of the diazo alcohol **2e** (270 mg, 0.794 mmol) in benzene (7 ml) was added to a suspension of dirhodium tetraacetate (4 mg) in benzene **(CAUTION)** (30 ml) at reflux over 7 min. After 5 min at reflux, the suspension was cooled, filtered and evaporated and the residue subjected to chromatography to give the *title compound* **3e** (182 mg, 73%) as white needles, m.p. 60–62 °C (ether–hexane) (Found: M^+, 338.1558. $C_{18}H_{26}O_4S$ requires *M*, 338.1552); ν_{max}(melt)/cm^{-1} 1722, 1449, 1131, 1083, 758, 721 and 688; δ_H(250 MHz; $CDCl_3$) 0.83 (3 H, t, *J* 6.7, Me), 0.90–1.85 (12 H, m), 1.85–2.04 (2 H, m), 2.49 (1 H, dd, *J* 11.1, 5.4, CH_2CO), 2.86 (1 H, ddd, *J* 13.4, 8.9, 2.2, CH_2CO), 3.12–3.25 (1 H, m, CH_2CHO), 4.67 (1 H, s, CHS), 7.48–7.62 (2 H, m, ArH), 7.62–7.71 (1 H, m, ArH) and 7.93 (2 H, ~dd, *J* 6.7; 1, ArH); *m/z* 338 (M^+), 197, 143, 125, 95, 69, 55 and 41.

Diethyl 7-Hexyl-3-oxooxepan-2-ylphosphonate **3f**.—A solution of the diazo alcohol **2f** (140 mg, 0.39 mmol) in benzene (7 ml) was added to a suspension of dirhodium tetraacetate (4 mg) in benzene **(CAUTION)** (15 ml) at reflux over 5 min. After 20 min at reflux, the reaction mixture was cooled, filtered and evaporated and the residue purified by chromatography to give the *title compound* **3f** (70 mg, 54%) as a clear oil, b.p. 160–165 °C at 0.25 mmHg (Found: C, 57.6; H, 9.6. $C_{16}H_{31}O_5P$ requires C, 57.5; H, 9.4%); ν_{max}(film)/cm^{-1} 3473, 1715, 1632, 1259, 1118, 1055 and 1025; δ_H(250 MHz; $CDCl_3$) 0.85 (3 H, t, *J* 6.7, *Me*), 1.18–1.84 (18 H, m), 1.89–2.04 (2 H, m), 2.44 (1 H, dd, *J* 15.0, 6.2, HC*H*CO), 3.02–3.20 (2 H, m, HC*H*CO and CH_2CHO) and 4.09–4.28 (5 H, m, CH_2CH_3 and CHP); *m/z* 334 (M^+), 167, 139, 111, 84 and 41.

Diethyl 3-Oxooxepan-2-ylphosphonate **3g**.—To a solution of dirhodium tetraacetate (14 mg, 31 μmol) in dry benzene **(CAUTION)** (120 ml) at reflux under nitrogen was added dropwise over 5 min a solution of the diazo alcohol **2g** (870 mg, 3.1 mmol) in dry benzene (50 ml). When addition was complete, heating was continued for a further 20 min. The solution was then cooled, filtered through Celite, the Celite washed with further benzene (50 ml), and the combined benzene washings were evaporated. The residue was purified by column chromatography on silica (ether) to give the *title compound* **3g** (401 mg, 52%) as a colourless oil (Found: C, 48.1; H, 7.6. $C_{10}H_{19}O_5P$ requires C, 48.0; H, 7.7%); ν_{max}(film)/cm^{-1} 2938, 1714, 1259, 1024 and 961; δ_H(270 MHz; $CDCl_3$) 1.28–1.38 (6 H, m, $(OCH_2CH_3)_2$), 1.40–2.05 (6 H, m), 3.04–3.14 (1 H, ddd, *J* 16, 13.5, 5, 4-CHH), 3.25–3.36 (1 H, ~ddd, *J* 16, 13.5, 3), 4.15–4.27 [4 H, m $(OCH_2CH_3)_2$] and 4.35–4.44 (1 H, m, 2-CH); *m/z* 250 (M^+), 167, 138, 111, 55 and 29.

Reactions of 7-Hexyl-2-phenylsulphonyloxepan-3-one **3e**

7-Hexyloxepan-3-one **3d**.—A solution of the sulphone **3e** (200 mg, 0.59 mmol) and tributyltin hydride (0.635 ml, 687 mg, 2.36 mmol) in toluene (6 ml) under nitrogen was heated to reflux. AIBN (192 mg, 1.17 mmol) was added in four equal portions at intervals of 4–5 min. When addition was complete, heating was continued for a further 20 min. On cooling, the toluene was evaporated at reduced pressure, and the column chromatograph column chromatography on silica (hexane–ether) to give 7-hexyloxepan-3-one **3d** (85 mg, 73%) as a colourless oil, the spectroscopic properties of which corresponded with those already reported.

7-Hexyl-2-phenylsulphonyloxepan-3-ol **4**.—To a solution of the β-keto sulphone **3e** (400 mg, 1.18 mmol) in methanol (3 ml) at room temperature was added cerium trichloride heptahydrate (448 mg, 1.20 mmol), followed by sodium borohydride (45 mg, 1.20 mmol). After being stirred for 5 min. the suspension was acidified to pH 2 using 0.5M hydrochloric acid, diluted with water (10 ml) and extracted with ether (2 × 50 ml). The ethereal extracts were dried (Na_2SO_4) and evaporated, and the resulting solid residue was recrystallised from hexane–ether to give the *title compound* **4** (392 mg, 97%) as colourless needles, m.p. 82–83 °C (Found: C, 63.7; H, 8.45. $C_{18}H_{28}O_4S$ requires C, 63.5; H, 8.3%); ν_{max}($CHCl_3$)/cm^{-1} 3310, 2959, 1600, 1459, 1219 and 1041; δ_H(250 MHz; $CDCl_3$) 0.89 [3 H, t, *J* 10, *Me*$(CH_2)_5$], 1.06–1.35 (8 H, m), 1.39–2.04 (8 H, m), 2.70 (1 H, br s, OH), 3.37–3.48 (1 H, m, 7-CH), 4.36 (1 H, s, 2-CH), 4.75 (1 H, ~t, *J* 4, 3-CH), 7.50–7.70 and 7.94–8.00 (5 H, 2m, ArH); *m/z* 341 (M^+ + H), 276, 246, 227, 199, 163, 143, 95 and 55.

3-Acetoxy-7-hexyl-2-phenylsulphonyloxepane **5**.—To a solution of the alcohol **4** (195 mg, 0.57 mmol) in pyridine (2 ml) at room temperature under nitrogen was added acetic anhydride (81 μl, 88 mg, 0.86 mmol) and 4-(dimethylamino)pyridine. After being stirred for 12 h, the reaction mixture was diluted with ether (20 ml), washed with water (20 ml), saturated aqueous copper sulphate (20 ml), water (20 ml) and brine (20 ml), dried ($MgSO_4$) and evaporated. The resulting solid residue was recrystallised from ether–light petroleum (b.p. 60–80 °C) to give the *title compound* **5** (196 mg, 89%) as a colourless solid, m.p. 96–98 °C (Found: C, 62.6; H, 8.0. $C_{20}H_{30}O_5S$ requires C, 62.8; H, 7.9%); ν_{max}($CHCl_3$)/cm^{-1} 2932, 2861, 1739, 1596, 1238, 914 and 866; δ_H(270 MHz; $CDCl_3$) 0.88 [3 H, t, *J* 10, *Me*$(CH_2)_5$], 1.10–1.50 and 1.52–2.05 (16 H, 2m), 1.88 (3 H, s, $OCOCH_3$), 3.32–3.40 (1 H, m, 7-CH), 4.49 (1 H, d, *J* 2, 2-CH), 5.66–5.75 (1 H, dt, *J* 6, 2, 3-CH) and 7.50–7.68 and 7.89–7.99 (5 H, 2m, ArH); *m/z* 322 (M^+ − AcOH), 279, 241, 198, 181, 163, 97 and 43.

7-Hexyl-2-phenylsulphonyl-4,5,6,7-tetrahydrooxepine **11**.—To a solution of the acetoxy sulphone **5** (96.5 mg, 0.25 mmol) in dry dioxane (15 ml) under nitrogen was added powdered sodium hydroxide (40 mg, 1 mmol). The mixture was stirred at room temperature for 16 h after which it was diluted with water (20 ml) and extracted with ether (2 × 30 ml). The ethereal extracts were dried ($MgSO_4$) and evaporated, and the residue was purified by column chromatography on silica (light petroleum–ether) to give the *title compound* **11** (75 mg, 92%) as a colourless oil (Found: C, 67.3; H, 8.4. $C_{18}H_{26}O_3S$ requires C, 67.0; H, 8.1%); ν_{max}(film)/cm^{-1} 2927, 1650, 1586, 1324, 1159, 1062 and 755; δ_H(270 MHz; $CDCl_3$) 0.88 [3 H, t, *J* 10, *Me*$(CH_2)_5$], 1.10–2.96 (14 H, m), 2.17–2.44 (2 H, m, 4-CH_2), 3.44–3.54 (1 H, m, 7-CH), 6.51–6.61 (1 H, dd, *J* 14, 6, 3-CH), 7.50–7.65 and 7.89–7.95 (5 H, 2m, ArH); *m/z* 322 (M^+), 197, 181, 143, 125, 83, 69 and 55.

7-Hexyl-3-(methoxymethoxy)-2-phenylsulphonyloxepane **6**.—To a solution of the alcohol **4** (14.9 mg, 0.44 mmol) in dry dichloromethane (2.5 ml) under nitrogen was added chloro-

methyl methyl ether (1 ml, 106 mg, 1.3 mmol) and diisopropylethylamine (0.46 ml, 340 mg, 2.6 mmol). The solution was stirred at room temperature for 12 h after which the dichloromethane was evaporated and ether (20 ml) was added. The ether solution was washed with water (2 × 20 ml) and brine (20 ml), dried ($MgSO_4$) and evaporated and the residue purified by column chromatography on silica (light petroleum–ether) to give the *title compound* **6** (110 mg, 65%) as a colourless solid, m.p. 53–55 °C (ether–light petroleum) (Found: C, 62.8; H, 8.5. $C_{20}H_{32}O_5S$ requires C, 62.5; H, 8.4%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2931, 1586, 1448, 1153, 1040 and 689; δ_H(270 MHz; $CDCl_3$) 0.90 [3 H, t, *J* 10, $Me(CH_2)_5$], 1.10–2.00 (16 H, m), 3.17–3.27 (1 H, m, 7-CH), 3.40 (3 H, s, OCH_3), 4.42 (1 H, d, *J* 2, 2-CH), 4.58–4.67 (1 H, m, 3-CH), 4.64 and 4.83 (2 H, 2 dd, *J* 25, 8, OCH_2OCH_3) and 7.50–7.67 and 7.94–8.00 (5 H, 2m, ArH); *m/z* 353 ($M^+ - CH_3O$), 323, 273, 257, 169 and 45.

7-*Hexyl*-2-*phenylsulphonyl*-3-(*trimethylsiloxy*)*oxepane* **7**.—To a solution of the alcohol **4** (72 mg, 0.21 mmol) in dry dichloromethane (1.5 ml) under nitrogen was added sequentially trimethylsilyl chloride (42 μl, 34 mg, 0.34 mmol), triethylamine (47 μl, 34 mg, 0.34 mmol) and 4-(dimethylamino)pyridine (1 crystal). After being stirred for 1 h at room temperature, the reaction mixture was diluted with dichloromethane (25 ml), washed with water (20 ml) and brine (20 ml), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica (light petroleum–ether) to give the *title compound* **7** (80 mg, 70%) as a colourless oil (Found: C, 61.2; H, 8.5. $C_{21}H_{36}O_4SSi$ requires C, 61.1; H, 8.8%); ν_{max}(film)/cm^{-1} 2931, 1601, 1308, 1251, 844 and 689; δ_H(270 MHz; $CDCl_3$) 0.15 (9 H, s, $SiMe_3$), 0.84 [3 H, t, *J* 10, $Me(CH_2)_5$], 1.07–1.38 and 1.42–2.00 (16 H, 2m), 3.10–3.20 (1 H, m, 7-CH), 4.36 (1 H, d, *J* 2, 2-CH), 4.70–4.78 (1 H, dt, *J* 6, 2, 3-CH), 7.45–7.63 and 7.90–8.00 (5 H, 2m, ArH); *m/z* 412 (M^+), 397, 271, 199, 163, 129 and 73.

7-*Hexyl*-2-*phenylsulphonyl*-3-(*triethylsiloxy*)*oxepane* **8**.—To a solution of the alcohol **4** (300 mg, 0.88 mmol) in dry dichloromethane (15 ml) under nitrogen was added 2,6-dimethylpyridine (0.154 ml, 142 mg, 1.32 mmol) and triethylsilyl trifluoromethanesulphonate (0.279 ml, 326 mg, 1.24 mmol). After being stirred at room temperature for 30 min, the reaction mixture was diluted with dichloromethane (30 ml), washed with saturated aqueous sodium hydrogen carbonate (20 ml), water (20 ml) and brine (20 ml), dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography on silica (light petroleum–ether) to give the *title compound* **8** (240 mg, 61%) as a low-melting colourless solid, m.p. 31–34 °C (Found: C, 63.3; H, 9.4. $C_{24}H_{42}O_4SSi$ requires C, 63.4; H, 9.3%); ν_{max}(melt)/cm^{-1} 2931, 1599, 1308, 1251, 1084 and 688; δ_H(270 MHz; $CDCl_3$) 0.5 [6 H, q, *J* 8, $OSi(CH_2CH_3)_3$], 0.83 [3 H, t, *J* 10, $Me(CH_2)_5$], 0.95 (9 H, t, *J* 8, $OSi(CH_2CH_3)$), 1.04–1.35 and 1.40–1.95 (16 H, 2m), 3.00–3.11 (1 H, 7-CH), 4.33 (1 H, d *J* 2, 2-CH), 4.74–4.83 (1 H, m, 3-CH) and 7.46–7.65 and 7.91–8.00 (5 H, 2m, ArH); *m/z* 425 ($M^+ - C_2H_5$), 375, 283, 227, 163, 95, 55 and 41.

3-(*t-Butyldimethylsiloxy*)-7-*hexyl*-2-*phenylsulphonyloxepane* **9**.—A solution of the alcohol **4** (150 mg, 0.44 mmol) in dry dichloromethane (0.5 ml) was added to a solution of 2,6-(0.102 ml, 95 mg, 0.88 mmol) and t-butyldimethylsilyl trifluoromethanesulphonate (0.152 ml, 174 mg, 0.66 mmol) in dry dichloromethane (0.5 ml) under nitrogen. After being stirred at room temperature for 24 h, work-up as above gave the *title compound* **9** (55 mg, 27%) as a colourless solid, m.p. 51–53 °C (Found: M^+, 313.2566. $C_{24}H_{42}O_4SSi - C_6H_5O_2S$ requires M, 313.2563); ν_{max}(melt)/cm^{-1} 2929, 1463, 1254, 1084, 837 and 688; δ_H(270 MHz; $CDCl_3$) 0.10 and 0.19 (6 H, 2s, $SiMe_2Bu^t$), 0.84 [3 H, t, *J* 10, $Me(CH_2)_5$], 0.93 (9 H, s, Bu^t), 0.94–1.88 (16 H, m), 2.93–3.05 (1 H, m, 7-CH), 4.30 (1 H, d, *J* 2, 2-CH), 4.75–5.83 (1 H, m, 3-CH), 7.45–7.55 and 7.92–8.00 (5 H, 2m, ArH); *m/z* 455 (M^+), 397, 313, 297, 283, 255, 199 and 73.

7-*Hexyl*-3-(*methylsulphonyloxy*)-2-*phenylsulphonyloxepane* **10**.—To a solution of the alcohol **4** (67 mg, 0.197 mmol) in pyridine (0.5 ml) was added methanesulphonyl chloride (23 μl, 34 mg, 0.29 mmol) and a crystal of 4-(dimethylamino)pyridine. The solution was stirred under nitrogen at room temperature for 24 h after which it was diluted with water (20 ml) and the aqueous layer extracted with dichloromethane (2 × 20 ml). The organic extracts were washed with saturated aqueous copper sulphate (20 ml) and brine (20 ml), dried (Na_2SO_4) and evaporated. The solid residue recrystallised from ether–hexane to give the *title compound* **10** (86 mg, 96%) as a colourless solid, m.p. 140–142 °C (Found: C, 54.3; H, 7.3. $C_{19}H_{30}O_6S_2$ requires C, 54.5; H, 7.2%); $\nu_{max}(CCl_4)/cm^{-1}$ 2950, 1583, 1470, 1160 and 720; δ_H(270 MHz; $CDCl_3$) 0.88 [3 H, t, *J* 10, $Me(CH_2)_5$], 1.04–1.35 (10 H, m), 1.45–1.75 (4 H, m), 1.85–2.06 (2 H, m), 3.10–3.15 (1 H, m, 7-CH), 3.15 (3 H, s, CH_3SO_2O), 4.42 (1 H, d, *J* 2, 2-CH), 5.57–5.64 (1 H, m, 3-CH), 7.55–7.74 and 7.95–8.00 (5 H, 2m, ArH); *m/z* 277 ($M^+ - PhSO_2H$), 245, 181, 163, 125 and 97.

7-*Hexyl*-2-(*prop*-1-*enyl*)-3-*triethylsiloxyoxepane* **12**.—To a solution of the oxepane **8** (118 mg, 0.26 mmol) and allyltributyl)tin (161 μl, 172 mg, 0.52 mmol) in benzene **(CAUTION)** (3 ml) at 60 °C under nitrogen was added a solution of tributyltin trifluoromethanesulphonate (34 mg, 78 μmol) in benzene (0.5 ml). The solution was heated to reflux for 24 h, after which it was cooled and the benzene removed at reduced pressure. The residue was purified by column chromatography on silica (light petroleum–ether 30:1) to give the *title compound* **12** (70 mg, 76%) as a colourless oil (Found: M^+, 354.2987. $C_{21}H_{42}O_2Si$ requires M, 354.2954); ν_{max}(film)/cm^{-1} 2931, 1642, 1459, 1084 and 813; δ_H(270 MHz; $CDCl_3$) 0.54–0.65 [6 H, q, *J* 10, $Si(CH_2CH_3)_3$], 0.88 [3 H, m, $Me(CH_2)_5$], 0.95 [9 H, t, *J* 10, $Si(CH_2CH_3)_3$], 1.18–1.56 and 1.60–2.17 (18 H, 2m), 3.39–3.45 and 3.47–3.58 (3 H, m, 2-CH, 3-CH and 7-CH), 5.00–5.14 (2 H, m, $CH{=}CH_2$) and 5.80–5.96 (1 H, m, CH_2CHCH_2); *m/z* 354 (M^+), 325, 313, 255, 227, 154, 103 and 87.

7-*Hexyl*-2-*phenyl*-3-(*triethylsiloxy*)*oxepane* **13**.—To a solution of zinc bromide (1.0 mol dm^{-3} in THF; 204 μl, 0.24 mmol) in tetrahydrofuran (0.8 ml) at room temperature under nitrogen was added phenylmagnesium bromide (2.0 mol dm^{-3} in THF; 170 μl, 34 mmol). After the mixture had been stirred for 30 min a solution of the oxepane **8** (76 mg, 0.17 mmol) in tetrahydrofuran (0.8 ml) was added and the solution stirred overnight. It was then diluted with water (5 ml) and extracted with ether (2 × 20 ml). The ethereal extracts were washed with brine (20 ml), dried (Na_2SO_4) and evaporated and the residue purified by column chromatography on silica (light petroleum–ether) to give the *title compound* **13** (46 mg, 70%) as a colourless oil (Found: M^+, 361.2562. $C_{24}H_{42}O_2Si - C_2H_5$ requires M, 361.2563); ν_{max}(film)/cm^{-1} 2930, 1604, 1452, 1239, 1097 and 739; δ_H(270 MHz; $CDCl_3$) 0.20–0.35 [6 H, m, $Si(CH_2CH_3)_3$], 0.74 [9 H, t, *J* 10, $Si(CH_2CH_3)_3$, 0.90–0.95 [3 H, m, $Me(CH_2)_5$], 1.05–1.35 and 1.40–2.00 (16 H, 2m), 3.65–3.75 (2 H, m, 3-CH and 7-CH), 4.28 (1 H, d, *J* 10, 2-CH, *trans*-isomer), 4.50 (1 H, d, *J* 2.7, 2-CH, *cis*-isomer), 7.15–7.35 (5 H, m, ArH), *ca.* 3:1 *trans*:*cis*; *m/z* 390 (M^+), 375, 361, 255, 152, 103 and 75.

Reactions of Diethyl 7-*Hexyl*-3-*oxooxepan*-2-*ylphosphonate* **3f**

2-*Benzylidene*-7-*hexyloxepan*-3-*one* **14a**.—To a solution of the phosphonate **3f** (83 mg, 0.27 mmol) in tetrahydrofuran (3 ml) at 0 °C under nitrogen was added sodium hydride (60% as a

dispersion in oil; 15 mg, 0.30 mmol) and the solution stirred for 30 min. Benzaldehyde (30 μl, 32 mg, 0.30 mmol) was added, and the reaction mixture allowed to come to room temperature. It was then stirred overnight, diluted with water and extracted into ether. The ether extracts were washed with brine, dried (Na_2SO_4), concentrated and the residue chromatographed to give the *title compound* **14a** (50 mg, 73%) as a yellow oil (Found: C, 79.8; H, 8.85. $C_{19}H_{26}O_2$ requires C, 79.7; H, 9.15%); ν_{max}(film)/cm^{-1} 2930, 1692, 1613, 1327, 1180, 694 and 525; δ_H(270 MHz; $CDCl_3$) 0.85 [3 H, t, *J* 8 Hz, *Me*$(CH_2)_5$], 1.13–1.42 and 1.60–2.09 (14 H, 2m), 2.55–2.66 (1 H, ddd, *J* 14, 10, 8.5, 4-C*H*H), 2.81–2.92 (1 H, ddd, *J* 14, 8, 2.5), 3.63–3.77 (1 H, m, 7-CH), 6.60 (1 H, s, C=C*H*Ph) and 7.24–7.39 and 7.73–7.82 (5 H, 2m, ArH); *m/z* 286 (M^+), 162, 118, 91, 55, 51 and 28.

7-*Hexyl*-2-(3-*phenylpropenylidene*)*oxepan*-3-*one* **14b**.—To a solution of the phosphonate **3f** (53 mg, 0.173 mmol) in tetrahydrofuran (3 ml) at 0 °C under nitrogen was added sodium hydride (100%; 5 mg, 0.208 mmol). The mixture was stirred for 30 min after which cinnamaldehyde (24 μl, 25 mg, 0.190 mmol) was added and the solution allowed to warm to room temperature. The mixture was stirred for a further 6 h after which work-up and purification as above gave the *title compound* **14b** (33 mg, 66%) as a pale yellow solid, m.p. 70–81 °C (hexane–ether) (Found: M^+, 312.2089. $C_{21}H_{28}O_2$ requires M, 312.2089); ν_{max}($CHCl_3$)/cm^{-1} 2934, 1678, 1610, 1600, 1582, 1327 and 1152; δ_H(270 MHz; $CDCl_3$) 0.88–0.99 [3 H, m, *Me*$(CH_2)_5$, 1.28–1.51 and 1.56–2.03 (14 H, 2m), 2.59–2.68 (1 H, ddd, *J* 14, 8, 1.5, 4-C*H*H), 2.83–2.95 (1 H, dt, *J* 14, 3.5, 4-C*H*H), 3.62–3.70 (1 H, m, 7-CH), 6.78 (1 H, d, *J* 16, CH·*CH*=CHPh), 6.90 (1 H, d, *J* 19, C*H*·CH=CHPh) and 7.28–7.55 (6 H, m, CH·CH=C*H*Ph and ArH); *m/z* 312 (M^+), 206, 144, 115, 55 and 41.

2-*Furylidene*-7-*hexyloxepan*-3-*one* **14c**.—To a solution of the phosphonate **3f** (56 mg, 0.283 mmol) in tetrahydroduran (3 ml) at 0 °C under nitrogen was added sodium hydride (100%; 6.5 mg, 0.274 mol). The mixture was stirred for 30 min after which 2-furfuraldehyde (30 μl, 35 mg, 0.366 mmol) was added and the solution allowed to come to room temperature. The mixture was stirred overnight after which work-up and purification as above gave the *title compound* **14c** (39 mg, 77%) as a pale yellow oil (Found: M^+, 276.1725. $C_{17}H_{24}O_3$ requires M, 276.1725); ν_{max}(film)/cm^{-1} 1687, 1610, 1328, 1283, 1012 and 740; δ_H(270 MHz; $CDCl_3$) 0.87 [3 H, t, *J* 10 Hz, *Me*$(CH_2)_5$], 1.17–1.46 (8 H, m), 1.53–2.08 (6 H, m), 2.52–2.62 (1 H, ddd, *J* 14, 8, 1.5, 4-C*H*H), 2.75–2.89 (1 H, ~dt, *J* 14, 3.5, 4-C*H*H), 3.68–3.79 (1 H, m, 7-CH), 6.44–6.47 (1 H, m, ArH), 6.65 (1 H, s, C=C*H*-), 6.89 (1 H, d, *J* 2, ArH) and 7.45 (1 H, d, *J* 1, ArH); *m/z* 276 (M^+), 258, 201, 152, 108, 81, 55 and 41.

2-(4-*t*-*Butyldimethylsiloxybutylidene*)-7-*hexyloxepan*-3-*one* **14d**.—To a solution of the phosphonate **3f** (39 mg, 0.127 mmol) in tetrahydrofuran (2 ml) at 0 °C under nitrogen was added sodium hydride (100%; 4.6 mg, 0.19 mmol). The mixture was stirred for 30 min after which 4-(t-butyldimethylsiloxy)butanal (51 mg, 0.254 mmol) was added, and the solution allowed to come to room temperature. The mixture was stirred overnight after which work-up and purification as above gave the *title compound* **14d** (36 mg, 80%) as a colourless oil (Found: M^+, 382.2903. $C_{22}H_{42}O_3Si$ requires M, 382.2903); ν_{max}(film)/cm^{-1} 2930, 1697, 1630, 1471, 1327, 1256, 1103 and 837; δ_H(270 MHz; $CDCl_3$) 0.05 (6 H, s, SiBu^t*Me*$_2$), 0.87 (s, 9 H, Si*Bu*^{t}Me$_2$), 0.85–0.90 (3 H, m, *Me*$(CH_2)_5$), 1.20–1.35 (8 H, m), 1.44–1.99 (8 H, m), 2.21–2.34 (2 H, dq, *J* 11, 6, C=CHCH_2CH$_2$), 2.35–2.45 1 H, m, 4-C*H*H), 2.72–2.83 (1 H, dt, *J* 14, 3.5, 4-C*H*H), 3.37–3.48 (1 H, m, 7-CH), 3.62 (2 H, t, *J* 14, CH_2CH_2OSi) and 6.00 (1 H, t, *J* 13 Hz, C=CH); *m/z* 382 (M^+), 325, 281, 197, 157 and 75.

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