One-Pot Oxapropellane Skeleton Formation Based on Conjugate Addition

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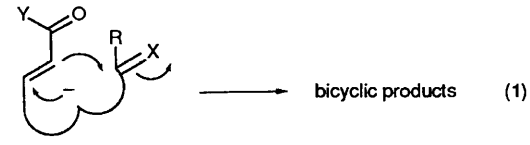
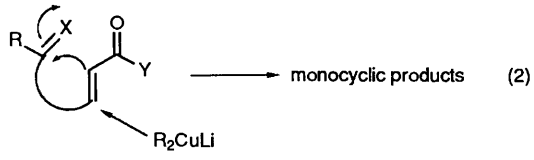
Reactions of five- and/or six-membered-ring ketones **1**–**5** possessing an ω-halogenoalkyl group and α',β'-unsaturated ester function at the α-position with diorganocuprates afforded the oxapropellane compounds **20**–**24** in a one-pot, three-step procedure *via* 1,4-addition followed by intramolecular aldol condensation and *O*-alkylation. Similar reaction of α,α'-disubstituted cyclopentanone **6** afforded bicyclic products **28** and **29**.

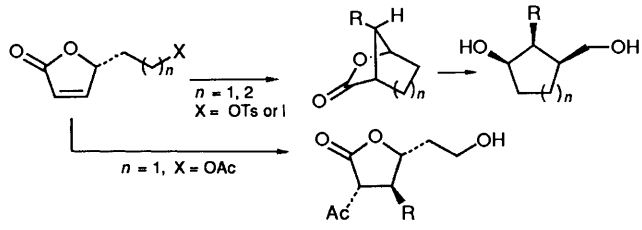
Conjugate addition of diorganocuprates is one of the valuable tools of organic synthesis. Some applications of conjugate addition for ring construction have been reported, and which may be classified into two groups. One is the double cyclization by intramolecular conjugated addition of a carbanion generated by base, and *C*-trapping of the resulting enolate with an intramolecular electrophile [eqn. (1)]. As examples of this type of reaction, there are the double-Michael reaction,[1] 1,4-addition–aldol condensation,[2] and 1,4-addition–substitution.[3] In these cases, bicyclic compounds are obtained from acyclic substrates. The other group consists of monocyclizations by *C*-trapping of the enolate generated by the conjugated addition of a diorganocuprate [eqn. (2)]. As examples of this type, there are 1,4-addition–aldol condensation[4] and 1,4-addition–substitution with halide and epoxide.[5] In these cases, monocyclic compounds are obtained from acyclic substrates. The ynenone system is also applicable to this type of reaction.[5] These reactions have been found to be effective for stereoselective construction of cyclic compounds, especially polycyclic compounds.



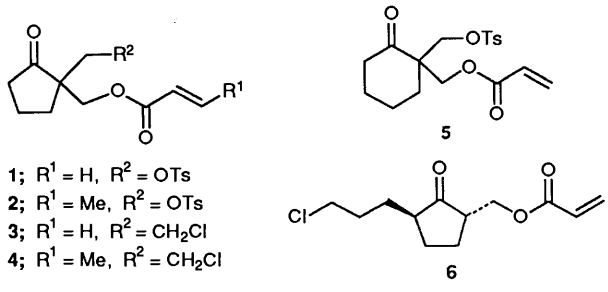


Previously, we had reported the diastereoselective synthesis of 1,2,3-trisubstituted cyclopentanes and cyclohexanes *via* bicyclic lactones, which could be obtained by stereoselective 1,4-addition of a diorganocuprate to an α,β-unsaturated lactone and subsequent intramolecular *C*-alkylation of the resulting enolate (Scheme 1).[6] The acetate also afforded the 2-acetyl derivative *via* intramolecular acylation (Scheme 1). These findings prompted us to investigate the selectivity of *C*-trapping reactions of enolates generated by conjugate addition of a diorganocuprate to the substrates **1**–**6**, which have intramolecular electrophiles such as ketone and halide (or tosyl ester).[7]

Preparation of Substrates.—Substrates **1**–**4** and **6** were synthesized according to the route depicted in Scheme 2. Alkylation of β-keto ester **7** with electrophiles such as benzyl chloromethyl ether, 1-bromo-2-chloroethane and 1-bromo-3-chloropropane afforded products **8a**, **b**, **c** respectively, in 56–66% yield. Compounds **8a**, **b** were converted into the methanols **10a**, **b** *via* a sequence of acetalization (to **9a**, **b**), $LiAlH_4$ reduction of ester function, and deacetalization. Compound **10a** further elaborated to substrates **1** and **2** by toluene-*p*-sulphonylation, debenzylation and acylation. Substrates **3** and **4** were obtained from compound **10b** by acylation.



Scheme 1 *Reagent:* R_2CuLi



Substrate **6** was also synthesized *via* deethoxycarbonylation of compound **8c**, followed by regioselective ethoxycarbonylation at C-5, and subsequent functional-group interconversions as shown in Scheme 2. In the final step, 2,5-*cis* and -*trans* isomers were obtained as a mixture, and the 2,5-*trans*-isomer **6** was purified by recrystallization. Its stereochemistry was confirmed by X-ray analysis.† Substrate **5** was prepared from β-hydroxy ester **16** according to a conventional route as shown in Scheme 3.

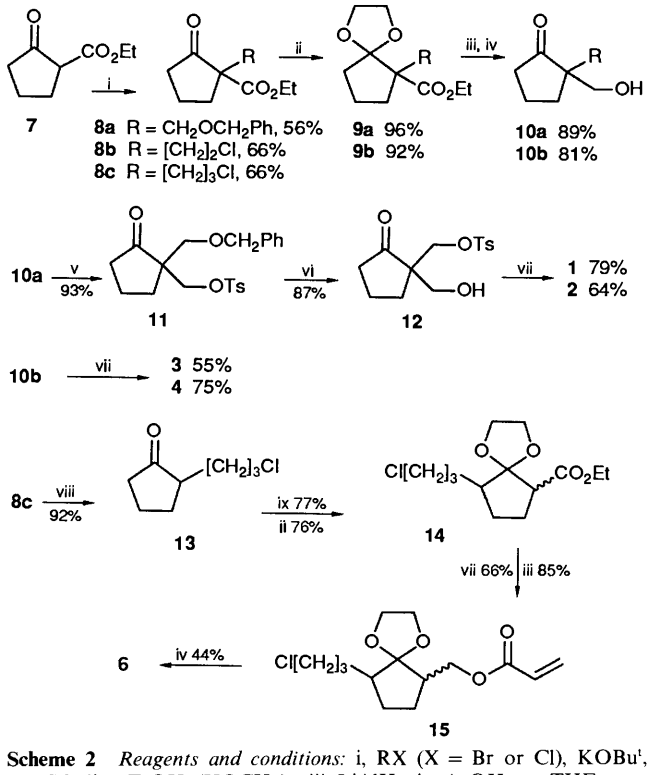
Results and Discussion

Substrates **1**–**6** were subjected to 1,4-addition with diorganocuprate, prepared from CuBr–Me_2S and MeLi (or PhLi). The results are summarized in Table 1. In a typical example, the reaction of compound **1** with Ph_2CuLi in entry 2 proceeded at −30 °C to afford oxapropellane compound **20b** as a diastereoisomeric mixture at the C-2 position in the ratio 7:1. In

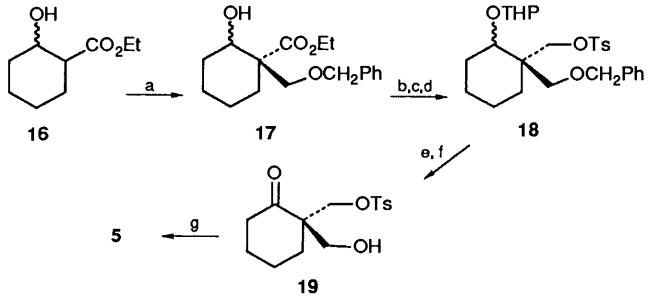
† Full details of the X-ray structure analysis of compound **6** are given in C. Fang, K. Suganuma, H. Suemune, N. Marubayashi and K. Sakai, *Chem. Pharm. Bull.* manuscript in preparation.

Table 1

Entry	Substrate	Reagent	Reaction Time (*t*/h)	Oxapropellane yields (%) [ratio of 2α-H(I) to 2β-H(II)]	Yields of 1,4-addition products
1	**1**	Me_2CuLi	0.5	20a, 47 (6:1)	0
2	**1**	Ph_2CuLi	0.5	20b, 55 (7:1)	0
3	**2**	Me_2CuLi	0.5	21a, 31 (2.5:1)	21
4	**2**	Ph_2CuLi	0.5	21b, 69 (3:2:1:1)	0
5	**2**	Bu_2CuLi	0.5	21c, 30	15
6	**3**	Me_2CuLi	0.5	22a, 50 (7:1)	0
7	**3**	Ph_2CuLi	0.5	22b, 32 (4:1)	6
8	**4**	Me_2CuLi	1.0	23a, 39 (1:1)	30
9	**4**	Ph_2CuLi	1.0	23b, 75 (3:2:1:1)	8
10	**5**	Me_2CuLi	1.0	24a, 61 (2:1)	0
11	**5**	Ph_2CuLi	1.0	24b, 49 (2:1)	2



Scheme 2 *Reagents and conditions:* i, RX (X = Br or Cl), $KOBu^t$, DMSO; ii, *p*-TsOH, $(HOCH_2)_2$; iii, $LiAlH_4$; iv, AcOH, aq. THF; v, *p*-TsCl, Py; vi, 10% Pd–C, H_2; vii, acrylic acid, $(NCO_2Et)_2$, PPh_3 or $(MeCH{=}CHCO)_2O$, Py; viii, HCl; ix, LDA, $NCCO_2Et$



Scheme 3 *Reagents and conditions:* (i) LDA, $BnOCH_2Cl$, 84%; ii, DHP, *p*-TsOH, 80%; iii, $LiAlH_4$, 90%; iv, *p*-TsCl, Py, 91%; v, Jones oxid., 80%; vi, H_2, 10% Pd-C, MeOH, 93%; vii, $(NCOOEt)_2$, PPh_3, $CH_2{=}CHCOOH$, 85%

the ^{13}C NMR spectrum of the major product **20b-I**, the carbonyl function at δ_C 218.7 in substrate **2** disappeared, and a new quaternary carbon was observed at δ_C 94.4, in addition to the original quaternary carbon at δ_C 53.5. In the 270 MHz ^1H NMR spectrum, the disappearance of the vinyl protons and tosyl function, and the appearance of aromatic protons, supported the 1,4-addition of phenyl function and replacement of the tosyl group. The above spectroscopic data supported the proposed oxapropellane structure and excluded the possibility of spirolactone **25** which might be produced *via* 1,4-addition followed by intramolecular substitution.

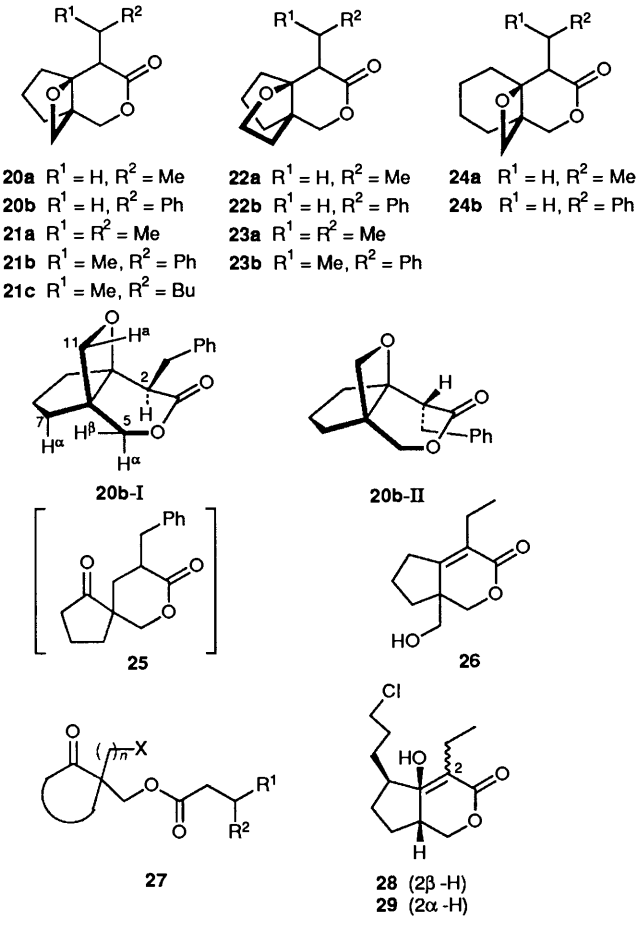
An analytical sample of the minor product **20b-II** was obtained in a small amount from careful column chromatography and recrystallization. The stereochemistry at C-2 for each product was determined on the basis of two-dimensional $^1H,^1H$-COSY and NOESY spectra. In the major product **20b-I** (2-H^α), NOEs between 2-H^α and 5-H^α, and between 5-H^β and 11-H^a were observed. The 11-H^a was assigned to the signals at δ 4.52 (dd, J_{gem} 6.93, ^4J 1.32 Hz) from its coupling constants, especially from W-type long-range coupling constant with 7-H^α. These spectroscopic data suggest that the six-membered lactone ring is in boat form, and 2β-CH_2Ph occupies the equatorial orientation. In the minor product **20-II** (2β-H), NOEs between one of benzylic protons and 5-H^α, and between 5-H^β and 11-H^a were observed, which suggests the 2α-CH_2Ph function occupies the axial orientation in the boat form.

Chemical evidence for the oxapropellane skeleton was obtained as follows. Diastereoisomerically mixed product **20a** in entry 1 was readily converted into the α,β-unsaturated lactone **26** as the sole product in 87% yield by treatment with 2% methanolic KOH for 10 min at room temperature. This finding supports the presence of an oxetane ring at the β-position of the lactone carbonyl.

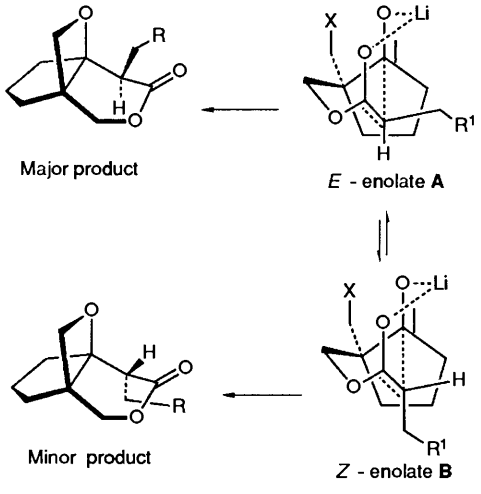
The diastereoselectivity of oxapropellane formation in entries 1–11 was determined in a similar manner to entry 2. In the case of reaction with Bu_2CuLi (entry 5), diastereoisomers could not be distinguished by ^1H or ^{13}C NMR spectroscopy. In entries 4 and 9, a mixture of four possible diastereoisomers was obtained, but the stereochemistry of each was not clarified. Furthermore, a small amount of 1,4-addition product **27** was obtained in entries 3, 5, 7, 8, 9 and 11.

In the case of another type of substrate, compound **6**, 1,4-addition and subsequent intramolecular aldol condensation proceeded to afford bicyclic lactones **28** (48%) and **29** (50%), and no tricyclic product was obtained. The 2-ethyl group might hinder the formation of an ether ring.

The reaction mechanisms for the construction of the oxapropellane skeleton were considered as follows (Scheme 4). Taking into account the approach of the lithium enolate to the carbonyl function, two possible intermediates, **A** (*E*-enolate) and **B** (*Z*-enolate), were assumed. Both of them might be stabilized by chelation with the lithium cation. The CH_2R group in **A** possesses the equatorial orientation, and that in **B** is



in the axial orientation. Therefore, species **A** might be more favourable than **B**. The above assumption agrees with the results that 2-substituents of major diastereoisomers have the *cis*-configuration of the oxetane ring, and that stereoselectivity in the case with acrylate as substrate (entries 1, 2, 6 and 7) was higher than in the case of crotonate (entries 3, 4, 8 and 9).



Scheme 4

Experimental

IR spectra were measured with a JASCO A-202 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-PS-100 or a JNM-GM-270 spectrometer. *J*-Values are given in Hz. Mass spectra were taken on a JEOL JMS-D-300 spectrometer. X-ray diffractions were measured on an Enraf-Nonius CAD 4F-11 apparatus. For column chromatography, silica gel (Merck, Kieselgel 60, 70–230 mesh) was used. All organic solvent extracts were washed with brine and dried over anhydrous sodium sulphate.

Synthesis of Substrates.—*2-Substituted 2-(ethoxycarbonyl)-cyclopentanones* (*ethyl 1-substituted-2-oxocyclopentanecarboxylates*) **8a**, **b**, **c**. To a solution of keto ester **7** (5.0 g, 32.0 mmol) in dimethyl sulphoxide (DMSO) (40 cm^3)–hexamethylphosphoric triamide (HMPA) (3 cm^3) at 0 °C was added KOBu^t (4.3 g, 38.0 mmol) portionwise. After the mixture had been stirred for 0.5 h, an electrophile [benzyl chloromethyl ether, 1-bromo-2-chloroethane, or 1-bromo-3-chloropropane (48.0 mmol)] was added dropwise. The mixture was stirred at room temperature for 24 h, and then was quenched with aq. NH_4Cl, and the usual work-up afforded a crude product, which was purified by silica gel column chromatography.

Compound **8a** was obtained as an oil (56%); ν_{max}(film)/cm^{-1} 1745, 1720, 1450 and 1360; δ_H($CDCl_3$) 1.22 (3 H, t, *J* 7.1, OCH_2*Me*), 3.62 and 3.85 (each 1 H, d, *J* 8.0, together 2-CH_2), 4.12 (2 H, q, *J* 7.1, OCH_2Me), 4.26 (2 H, s, CH_2Ph), and 7.24 (5 H, s, Ph); FD *m*/*z* 276 (M^+, 100) and 107 (15%) (Found: M^+, 276.135 84. $C_{16}H_{20}O_4$ requires M, 276.13614). *Compound* **8b** was obtained as an oil (66%); ν_{max}(film)/cm^{-1} 1745, 1715 and 1225; δ_H($CDCl_3$) 1.22 (3 H, t, *J* 7.1, OCH_2*Me*), 2.21–2.61 (4 H, m, CH_2CO and 2-CH_2), 3.61 (2 H, m, CH_2Cl) and 4.18 (2 H, q, *J* 7.1, OCH_2Me); δ_C($CDCl_3$) 14.0 (q), 19.7 (t), 33.5 (t), 36.7 (t), 37.6 (t), 40.3 (t), 59.3 (s), 61.7 (t), 170.5 (s) and 213.7 (s); *m*/*z* 218 (M^+, 1.0), 182 (29), 156 (61) and 95 (100%) (Found: M^+, 218.071 75. $C_{10}H_{15}ClO_3$ requires M, 218.070 96).

Compound **8c** was obtained as an oil (66%); ν_{max}(film)/cm^{-1} 1750, 1715 and 1230; δ_H($CDCl_3$) 1.26 (3 H, t, *J* 7.1, OCH_2*Me*), 3.53 (2 H, t, *J* 6.0, CH_2Cl) and 4.17 (2 H, q, *J* 7.1, OCH_2Me); *m*/*z* 232 (M^+, 1.0), 204 (80), 187 (36), 156 (65) and 95 (100%) (Found: M^+, 232.086 12. $C_{11}H_{17}ClO_3$ requires M, 232.086 61).

2-Substituted 2-ethoxycarbonyl-1,1-ethylenedioxycyclopentanes (*ethyl 1-substituted-2,2-ethylenedioxycyclopentanecarboxylates*) **9a**, **b**. A mixed solution of compounds **8a**, **b** (40.0 mmol), ethylene glycol (2.79 g, 80 mmol), and *p*-TsOH (432 mg, 4.0 mmol) in benzene (110 cm^3) was refluxed in a Dean–Stark apparatus for 4.5 h. After the usual work-up, the crude product was purified by column chromatography on silica gel.

Compound **9a** was obtained as an oil (90%); ν_{max}(film)/cm^{-1} 1725, 1450, 1360 and 1240; δ_H($CDCl_3$) 1.24 (3 H, t, *J* 7.1, OCH_2*Me*), 3.45 and 3.48 (each 1 H, d, *J* 8.8, 2-CH_2), 3.79–3.99 (4 H, m, OCH_2CH_2O), 4.16 (2 H, q, *J* 7.1, OCH_2Me), 4.51 (2 H, s, CH_2Ph) and 7.29 (5 H, s, Ph); *m*/*z* 320 (M^+, 100), 229 (10) and 107 (12%).

Compound **9b** was obtained as an oil (92%); ν_{max}(film)/cm^{-1} 1720, 1445, 1250 and 1170; δ_H($CDCl_3$) 1.27 (3 H, t, *J* 7.1, OCH_2*Me*), 2.41 (2 H, m, 2-CH_2), 3.45 (2 H, m, CH_2Cl), 3.84–3.98 (4 H, m, OCH_2CH_2O) and 4.16 (2 H, q, *J* 7.1, OCH_2Me); *m*/*z* 262 (M^+, 3), 227 (53), 154 (21) and 99 (100%).

2-Substituted 2-(hydroxymethyl)cyclopentanone **10a**, **b**. $LiAlH_4$ reduction of compounds **9a**, **b** and subsequent deacetalization [AcOH–tetrahydrofuran (THF)–water, 3:1:1) afforded compounds **10a**, **b** in 89 and 81% yield, respectively.

Compound **10a** was an oil; ν_{max}(film)/cm^{-1} 3430, 1730, 1580, 1450 and 1360; δ_H($CDCl_3$) 3.56 (2 H, br s, CH_2OH), 3.60 (2 H, s, CH_2OBn), 4.49 (2 H, s, CH_2Ph) and 7.31 (5 H, s, Ph); *m*/*z* 234 (M^+, 0.5), 216 (2.5), 185 (4), 126 (16) and 91 (100%) (Found: M^+, 234.124 79. $C_{14}H_{18}O_3$ requires M, 234.125 58).

Compound **10b** was obtained as an oil; ν_{max}(film)/cm^{-1} 3400, 1720, 1440 and 1265; δ_H($CDCl_3$) 2.34 (1 H, s, OH), 2.35 (2 H, m, CH_2CO), 3.57 (2 H, m, CH_2Cl) and 3.59 (2 H, s, CH_2OH);

m/z 158 ($M^+ - 18$, 1.3), 144 (14) and 140 (100%) [Found: ($M^+ - H_2O$), 158.050 21. $C_8H_{11}ClO$ requires *m/z* 158.049 83].

2-*Benzyloxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclopentanone* **11**. Toluene-*p*-sulphonyl chloride (2.73 g, 14.4 mmol) was added portionwise to a solution of compound **10a** (2.25 g, 9.6 mmol) in pyridine (14 cm^3) at 0 °C. The mixture was stirred for 10 h at room temperature. Usual work-up and purification by silica gel column chromatography afforded compound **11** (3.5 g, 93%) as an oil; ν_{max}(film)/cm^{-1} 1735, 1595, 1495, 1355 and 1170; δ_H($CDCl_3$) 2.44 (3 H, s, ArMe), 3.28 and 3.37 (each 1 H, d, *J* 11.1, together 2-CH_2OBn), 3.94 and 4.03 (each 1 H, d, *J* 10.8, together 2-CH_2OTs), 4.40 (2 H, s, CH_2Ph), 7.29 (5 H, s, Ph) and 7.32 and 7.74 (each 2 H, d, *J* 8.4, ArH); *m/z* 388 (M^+, 0.5), 370 (18), 216 (16) and 185 (100%).

2-*Hydroxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclopentanone* **12**. Compound **11** (3.5 g, 9.0 mmol) in MeOH (85 cm^3) was hydrogenated in the presence of 10% Pd–C (1.75 g) under H_2. Usual work-up afforded an oily residue, which was purified by silica gel column chromatography. *Compound* **12** (2.32 g, 87%) was obtained as an oil; ν_{max}(film)/cm^{-1} 3460, 1740, 1500, 1480, 1365 and 1100; δ_H($CDCl_3$) 2.46 (3 H, s, ArMe), 3.55 (2 H, s, 2-CH_2OH), 4.03 and 4.07 (each 1 H, d, *J* 10.8, together 2-CH_2OTs), 7.35 and 7.76 (each 2 H, d, *J* 8.3, ArH); *m/z* 299 ($M^+ + 1$, 0.5), 280 (5), 268 (2), 172 (50) and 126 (100%) [Found: ($M^+ + H$), 299.096 52. $C_{14}H_{19}O_5S$ requires *m/z* 299.095 31].

2-*Acryloyloxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclopentanone* **1**. A mixture of compound **12** (820 mg, 2.75 mmol) and PPh_3 (795 mg, 3.0 mmol) in Et_2O (3 cm^3) was added to a solution of acrylic acid (217 mg, 3.0 mmol) and diethyl azodicarboxylate (527 mg, 3.0 mmol) in Et_2O (12 cm^3) at 0 °C. After being stirred for 15 h at room temperature, the mixture was diluted with diethyl ether (25 cm^3) and the resulting precipitate was filtered off. The filtrate was concentrated under reduced pressure and the residue was subjected to silica gel column chromatography to afford *compound* **1** (764 mg, 79%) as an oil; ν_{max}(film)/cm^{-1} 1730, 1630, 1595, 1460, 1360 and 1180; δ_H($CDCl_3$) 2.46 (3 H, s, Ar*Me*), 4.02 and 4.03 (each 1 H, d, *J* 10.3, together 2-CH_2OCO), 4.08 and 4.10 (each 1 H, d, *J* 11.5, together 2-CH_2OTs), 5.85 (1 H, dd, *J* 10.0, 2.7, vinylic H), 6.08 (1 H, dd, *J* 16.6, 10.0, vinylic H), 6.36 (1 H, dd, *J* 16.6, 2.7, vinylic H) and 7.35 and 7.75 (each 2 H, d, *J* 8.6, ArH); *m/z* 352 (M^+, 6), 280 (20), 108 (30) and 55 (100%) (Found: M^+, 352.099 12. $C_{17}H_{20}O_6S$ requires M, 352.098 04).

2-*Crotonoyloxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclopentanone* **2**. Acylation of compound **12** in the usual manner [crotonic anhydride–pyridine–4-(dimethylamino)pyridine] afforded *compound* **2** (64%) as an oil. ν_{max}(film)/cm^{-1} 1740, 1720, 1655, 1600, 1380 and 1175; δ_H($CDCl_3$) 1.83 (3 H, dd, *J* 6.9, 1.7, Me), 2.46 (3 H, s, Ar*Me*), 4.01 and 4.02 (each 1 H, d, *J* 10.4 together 2-CH_2OCO), 4.04 and 4.05 (each 1 H, d, *J* 11.5, together 2-CH_2OTs), 5.75 (1 H, dq, *J* 16.6, 1.7, vinylic H), 6.39 (1 H, dq, *J* 16.6, 6.9, vinylic H) and 7.36 and 7.76 (each 2 H, d, *J* 8.4, ArH); *m/z* 366 (M^+, 8), 280 (19), 195 (64) and 155 (100%) (Found: M^+, 366.112 85. $C_{18}H_{22}O_6S$ requires M, 366.113 69).

2-*Acryloyloxymethyl*-2-(2-*chloroethyl*)*cyclopentanone* **3** *and* 2-(2-*chloroethyl*)-2-(*crotonoyloxymethyl*)*cyclopentanone* **4**. Compounds **3** and **4** were prepared from substrate **10b** in a similar manner to that described for the preparation of compounds **1** and **2**. *Compound* **3** was obtained as an oil (55%); ν_{max}(film)/cm^{-1} 1728, 1630, 1407, 1265 and 1190; δ_H($CDCl_3$) 3.56 (2 H, m, CH_2Cl), 4.16 (2 H, s, 2-CH_2OCO), 5.83 (1 H, dd, *J* 10.0, 2.2, vinylic H), 6.05 (1 H, dd, *J* 17.0, 10.0, vinylic H) and 6.38 (1 H, dd, *J* 17.0, 2.2, vinylic H); δ_C($CDCl_3$) 18.9 (t, 31.5 (t), 36.4 (t), 38.0 (t), 39.9 (t), 51.3 (s), 66.2 (t), 127.8 (d), 131.4 (t), 165.6 (s) and 218.7 (s); *m/z* 230 (M^+, 2), 194 (5), 158 (10) and 55 (100%) (Found: M^+, 230 072 31. $C_{11}H_{15}ClO_3$ requires M 230.070 96).

Compound **4** was obtained as an oil (75%) ν_{max}(film)/cm^{-1} 1720, 1650, 1440, 1260 and 1175; δ_H($CDCl_3$) 1.89 (3 H, dd, *J* 6.8, 1.7, Me), 3.56 (2 H, m, CH_2Cl), 4.12 (2 H, s, 2-CH_2OCO), 5.82 (1 H, dq, *J* 15.6, 1.7, vinylic H) and 6.97 (1 H, dq, *J* 15.6, 6.8, vinylic H); δ_C($CDCl_3$) 18.1 (q), 19.0 (t), 31.5 (t), 36.4 (t), 40.0 (t), 51.3 (t), 51.4 (s), 65.9 (t), 122.0 (d), 145.7 (d), 166.0 (s) and 218.9 (s); *m/z* 244 (M^+, 3), 208 (15) and 158 (100%) (Found: M^+, 244.086 12. $C_{12}H_{17}ClO_3$ requires M, 244.086 61).

2-(3-*Chloropropyl*)*cyclopentanone* **13**. A suspension of compound **8c** (4.97 g, 21.4 mmol) in 23% HCl (30 cm^3) was refluxed for 1.5 h. After the usual work-up, the crude product was purified by silica gel column chromatography to afford title compound **13** (3.15 g, 92%) as an oil; ν_{max}(film)/cm^{-1} 1735, 1450, 1400 and 1270; δ_H($CDCl_3$) 2.11–2.34 (3 H, m, 2-H and 5-H) and 3.54 (2 H, t, *J* 6.4, CH_2Cl); *m/z* 160 (M^+, 4), 124 (8), 97 (18) and 84 (100%).

1-(3-*Chloropropyl*)-3-(*ethoxycarbonyl*)-2,2-*ethylenedioxycyclopentane* [*ethyl* 3-(3-*chloropropyl*)-2,2-*ethylenedioxycyclopentanecarboxylate*] **14**. A solution of compound **13** (3.15 g, 19.6 mmol) in THF (15 cm^3) was added dropwise to a stirred solution of lithium diisopropylamide (LDA) (1.5 mol dm^{-3} in hexane; 15.7 cm^3, 21.4 mmol) in THF (70 cm^3) at −78 °C. After the mixture had been stirred for 1.5 h, a solution of ethyl cyanoformate (2.15 ml, 21.5 mmol) in HMPA (2.5 cm^3) was added. The reaction mixture was stirred for an additional 1.5 h at −78 °C. The reaction was quenched with aq. NH_4Cl, and the crude product was extracted with Et_2O. Purification by silica gel column chromatography afforded 2-(3-chloropropyl)-5-(ethoxycarbonyl)cyclopentanone in 77% yield as a mixture of 2,5-*cis* and -*trans* isomers, which was converted into compound **14** (76%), by the usual acetalization, as an oil; ν_{max}(film)/cm^{-1} 1725, 1440, 1365, 1190 and 1080; δ_H($CDCl_3$) 1.27 (3 H, t, *J* 7.1, OCH_2*Me*), 2.87 (1 H, m, 3-H), 3.53 (2 H, t, *J* 6.6, CH_2Cl), 3.95 (4 H, m, OCH_2CH_2O) and 4.16 (2 H, q, *J* 7.1, OCH_2Me); *m/z* 276 (M^+, 6), 213 (20), 175 (55) and 99 (100%).

1-*Acryloyloxymethyl*-3-(3-*chloropropyl*)-2,2-*ethylenedioxycyclopentane* **15**. *Compound* **15** was obtained from ester **14** by $LiAlH_4$ reduction (85% yield) and subsequent acylation (66% yield) as an oil; ν_{max}(film)/cm^{-1} 1720, 1630, 1615, 1455 and 1275; δ_H($CDCl_3$) 2.29 (1 H, m, 1-H), 3.53 (2 H, t, *J* 6.4, CH_2Cl), 3.92 (4 H, m, OCH_2CH_2O), 4.03 (1 H, dd, *J* 11.2, 6.8, 1-CH), 4.24 (1 H, dd, *J* 11.2, 6.5, 1-CH), 5.81 (1 H, dd, *J* 9.8, 2.7, vinylic H), 6.10 (1 H, dd, *J* 16.9, 9.8, vinylic H) and 6.42 (1 H, dd, *J* 16.9, 2.7, vinylic H); *m/z* 288 (M^+, 13), 225 (35), 217 (59) and 175 (100%) (Found: M^+, 288.112 18. $C_{14}H_{21}ClO_4$ requires M^+, 288.112 82).

trans-2-*Acryloyloxymethyl*-5-(3-*chloropropyl*)*cyclopentanone* **6**. Deacetalization of compound **15** afforded a mixture of the 2,5-*cis* and -*trans* isomers as solids (70% yield), whose recrystallization from Et_2O–hexane afforded the pure 2,5-trans-*isomer* **6** (44% from **15**) as prisms, m.p. 54–55 °C; ν_{max}(film)/cm^{-1} 1725, 1630, 1405, 1270 and 1190; δ_H($CDCl_3$) 3.55 (2 H, m, CH_2Cl), 4.32 (1 H, dd, *J* 11.2, 5.6, 2-CH), 4.44 (1 H, dd, *J* 11.2, 4.0, 2-CH), 5.83 (1 H, dd, *J* 10.4, 1.6, vinylic H), 6.09 (1 H, dd, *J* 17.3, 10.4, vinylic H) and 6.39 (1 H, dd, *J* 17.3, 1.6, vinylic H); δ_C($CDCl_3$) 24.8 (t), 27.3 (t), 27.6 (t), 30.4 (t), 44.7 (t), 48.5 (d), 49.0 (d), 63.0 (t), 128.1 (d), 131.0 (t), 166.0 (s) and 217.9 (s); *m/z* 244 (M^+, 3), 209 (62), 189 (21) and 173 (100%) (Found: M^+, 244.087 95. $C_{12}H_{17}ClO_3$ requires M, 244.086 61).

2-*Benzyloxymethyl*-2-*ethoxycarbonylcyclohexanol* (*ethyl* 1-*benzyloxymethyl*-2-*hydroxycyclohexanecarboxylate*) **17**. A solution of hydroxy ester **16** (1.61 g, 9.36 mmol) in THF (10 cm^3) was added dropwise to a stirred solution of LDA (16 mmol) in THF (25 cm^3) at −78 °C under Ar. After the mixture had been stirred for 30 min, a solution of benzyl chloromethyl ether (1.82 cm^3, 13.1 mmol) in HMPA (3 cm^3) was added dropwise, and the mixture was stirred for an additional 2.5 h at the same temperature. The reaction was quenched with aq.

NH_4Cl (20 cm^3), and usual work-up afforded compound **17** (2.29 g, 84%) as an oil; ν_{max}(film)/cm^{-1} 3480, 1715, 1455, 1365 and 1095; δ_H($CDCl_3$) 1.23 (3 H, t, *J* 7.2, OCH_2Me), 3.69 (2 H, s, 2-H, s, 2-CH_2), 4.21 (2 H, q, *J* 7.2, OCH_2Me), 4.23 (1 H, m, 1-H), 4.53 (2 H, s, CH_2Ph) and 7.51 (5 H, m, Ph); *m/z* 292 (M^+, 0.4), 274 (5), 245 (15), 108 (43) and 91 (100%).

1-*Benzyloxymethyl*-2-[(*tetrahydropyran*-2-*yl*)*oxy*]-1-(p-*tolylsulphonyloxymethyl*)*cyclohexane* **18**. Compound **18** was obtained by a conventional 3-step sequence of reactions from ester **17** (protection of OH function as THP ether, $LiAlH_4$ reduction of ester function, and toluene-*p*-sulphonylation of 2-hydroxymethyl function). The title product was obtained as an oil; ν_{max}(film)/cm^{-1} 1600, 1500, 1450, 1360 and 1190; δ_H($CDCl_3$) 2.40 (3 H, s, Ar*Me*), 3.55 (1 H, m, 2-H), 3.25 and 3.57 (each 1 H, d, *J* 9, together 2-CH_2OBn), 4.22 and 4.38 (each 1 H, d, *J* 9.2, together 2-CH_2OTs), 4.41 (2 H, s, CH_2Ph), 4.94 (1 H, m, OCHO), 7.26 (5 H, m, Ph) and 7.30 and 7.77 (each 2 H, d, *J* 8.3, ArH); *m/z* (FD) 489 (M^+ + 1, 100), 488 (M^+, 55) and 369 (15%).

2-*Hydroxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclohexanone* **19**. Jones oxidation of compound **18** and subsequent hydrogenolysis of the benzyl ether function afforded *ketone* **19** (74% from **18**) as an oil; ν_{max}(film)/cm^{-1} 3500, 1705, 1595, 1490 and 1175; δ_H($CDCl_3$) 2.38 (1 H, br, OH), 2.46 (3 H, s, Ar*Me*), 3.77 (2 H, m, 2-CH_2OH), 4.04 and 4.37 (each 1 H, d, *J* 10.0, together 2-CH_2OTs) and 7.36 and 7.79 (each 2 H, d, *J* 8.3, ArH); *m/z* 313 (M^+ + 1, 3), 294 (5), 282 (30) and 157 (100%) [Found: (M^+ + H), 313.112 07. $C_{15}H_{21}O_5S$ requires M + H, 313.110 96].

2-*Acryloyloxymethyl*-2-(p-*tolylsulphonyloxymethyl*)*cyclohexanone* **5**. Acylation of compound **19**, afforded the ester **5** (80% yield) as an oil by a similar manner to that described for the preparation of ester **1** from the alcohol **12**. Compound **5** showed ν_{max}(film)/cm^{-1} 1730, 1710, 1630, 1490, 1360 and 1170; δ_H($CDCl_3$) 2.43 (3 H, s, Ar*Me*), 4.06 and 4.33 (each 1 H, d, *J* 10.0, together 2-CH_2OTs), 4.12 and 4.58 (each 1 H, d, *J* 11.7, together 2-CH_2OCO), 5.78 (1 H, dd, *J* 10.4, 1.6, vinylic H), 5.91 (1 H, dd, *J* 17.0, 10.4, vinylic H), 6.26 (1 H, dd, *J* 17.0, 1.6, vinylic H) and 7.33 and 7.77 (each 2 H, d, *J* 8.4, ArH); δ_C($CDCl_3$) 20.7 (t), 21.7 (q), 27.0 (t), 32.5 (t), 39.0 (t), 52.0 (s), 63.6 (t), 70.4 (t), 127.5 (d), 131.5 (t), 128.0, 129.9, 132.9 and 145.0 (arom. C), 165.3 (s) and 209.5 (s); *m/z* 366 (M^+, 5), 294 (3), 194 (61) and 139 (100%) (Found: M^+, 366.114 53 $C_{18}H_{22}O_6S$ requires M, 366.113 69).

General Procedure for the Reaction of Substrates **1–6** *with Diorganocuprates*.—An alkyllithium (4.30 mmol) in diethyl ether was added dropwise in a stirred suspension of CuBr–Me_2S (2.15 mmol) in diethyl ether (10 cm^3) at −30 °C under Ar. A solution of substrate (0.43 mmol) in diethyl ether (2 cm^3) was added dropwise at the same temperature, and the mixture was stirred for 1 h, quenched with saturated aq. NH_4Cl (30 cm^3), and extracted with diethyl ether. The extract was washed successively with 5% aq. $NaHCO_3$ and brine, dried over sodium sulphate, and evaporated under reduced pressure to leave an oily residue, which was subjected to flash column chromatography on silica gel. The following products were obtained.

5-*Ethyl*-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]*undecan*-4-*one* **20a** 47% yield, 71% diastereoisomeric excess (de), as an oil; ν_{max}(film)/cm^{-1} 1740, 1460, 1385, 1210 and 1104; δ_H($CDCl_3$) for the major (minor) isomer 1.09 (1.06) (3 H, t, *J* 7.9, Me), 2.31 (3.09) [1 H, dd, *J* 7.9, 1.5 (7.9, 3.6), 5-H], 4.13 and 4.33 (4.26 and 4.62) [each 1 H, d, *J* 12.0 (11.7), 2-H], 4.27 (4.31) [1 H, d, *J* 6.6 (6.8), 10-H] and 4.63 (4.56) [1 H, dd, *J* 6.6 (6.8), 1.3 (1.3), 10-H]; δ_C($CDCl_3$) 13.0 (12.5) (q), 17.6 (18.6) (t), 26.0 (24.5) (t), 31.8 (32.7) (t), 37.6 (34.4) (t), 47.4 (46.3) (s), 49.9 (51.2) (d), 69.2 (70.8) (t), 73.3 (74.9) (t), 97.0 (95.7) (s) and 172.7 (172.5) (s); *m/z* 196 (M^+, 12), 181 (30), and 127 (100%) (Found: M^+, 196.108 12. $C_{11}H_{16}O_3$ requires M, 196.109 93).

(1R*,5R*,6S*)-5-*Benzyl*-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]-*undecan*-4-*one*. 55% Yield as a mixture of **20b-I** and **20b-II**. Isomer **20b-I** was an oil; ν_{max}(film)/cm^{-1} 1745, 1605, 1385, 1210, 1175 and 1050; δ_H($CDCl_3$) 2.81 (1 H, dd, *J* 14.1, 4.8, C*H*Ph), 3.15 (1 H, dd, *J* 14.1, 8.3, C*H*Ph), 3.51 (1 H, dd, *J* 8.3, 4.8, 5-H),* 4.28 (1 H, d, *J* 11.7, 2-H),* 4.30 (1 H, d, *J* 6.9, 10-H),* 4.52 (1 H, dd, *J* 6.9, 1.3, 10-H)* and 4.60 (1 H, d, *J* 11.7, 2-H);* δ_C($CDCl_3$) 24.5 (t), 30.7 (t), 32.8 (t), 34.8 (t), 46.4 (s), 52.1 (d), 70.8 (t), 74.9 (t), 95.4 (s), 126.5 (d), 128.4 (d × 2), 129.2 (d × 2), 139.2 (s) and 172.0 (s); *m/z* 258 (M^+, 35), 228 (10), 181 (18) and 91 (100%) (Found: M^+, 258.127 13. $C_{16}H_{18}O_3$ requires M, 258.125 58).

(1R*,5S*,6S*)-5-*Benzyl*-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]-*undecan*-4-*one* **20b-II**. An oil; δ_H($CDCl_3$) 2.73 (1 H, dd, *J* 8.3, 6.4, 5-H),* 2.75 (1 H, dd, *J* 14.1, 6.4, C*H*Ph), 3.48 (1 H, dd, *J* 14.1, 8.3, C*H*Ph), 4.12 (1 H, d, *J* 12.0, 2-H),* 4.28 (1 H, d, *J* 6.9, 10-H),* 4.34 (1 H, d, *J* 12.0, 2-H)* and 4.66 (1 H, dd, *J* 6.9, 1.3, 10-H); δ_C($CDCl_3$) 25.9 (t), 30.1 (t), 31.7 (t), 38.0 (t), 47.4 (s), 50.8 (d), 69.1 (t), 73.3 (t), 96.5 (s), 126.3 (d), 129.1 (d × 2), 130.0 (d × 2), 140.2 (s) and 172.0 (s) (Found: M^+, 258.126 99).

5-*Isopropyl*-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]*undecan*-4-*one* **21a**. 31% Yield, 43% de; an oil; ν_{max}(film)/cm^{-1} 1740, 1455, 1175 and 1085; δ_H($CDCl_3$) 2.91 (1 H, m, 5-H)* and 4.00–4.70 (4 H, m, 2- and 10-H_2);* δ_C($CDCl_3$) 14.2 (14.1) (q), 18.8 (18.7) (*q*), 24.5 (22.7) (t), 29.7 (29.4) (d), 32.3 (31.9) (t), 34.6 (32.8) (t), 47.5 (49.0) (s), 56.5 (53.0) (d), 70.4 (70.6) (t), 74.7 (74.6) (t), 95.9 (s) and 172.0 (s); *m/z* 210 (M^+, 5), 195 (69), 138 (48) and 69 (100%) (Found: M^+, 210.125 10. $C_{12}H_{18}O_3$ requires M, 210.125 58).

5-(1-*Phenylethyl*)-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]*undecan*-4-*one* **21b**. 69% Yield, diastereoisomeric preparations 3:2:2:1 from GC-MS was an oil; ν_{max}(film)/cm^{-1} 1750, 1610, 1500, 1455 and 1180; δ_H($CDCl_3$) for the major isomer 1.28 (3 H, d, *J* 7.1, Me), 2.67–3.64 (2 H, m, 5-H and 5-CH),* 4.11–4.70 (4 H, m, 2- and 10-H_2* and 7.26–7.34 (5 H, m, Ph); δ_C($CDCl_3$) 21.3 (q), 24.5 (t), 32.3 (t), 34.5 (t), 37.8 (d), 47.7 (s), 55.7 (d), 70.3 (t), 74.8 (t), 95.8 (s), 127.3 (d), 128.3 (d × 2), 128.4 (d × 2), 145.9 (s) and 171.2 (s); *m/z* 272 (M^+, 16), 195 (9), 167 (22) and 105 (100%) (Found: M^+, 272.143 98. $C_{17}H_{20}O_3$ requires M, 272.141 23).

5-(1-*Methylpentyl*-3,11-*dioxatricyclo*[4.3.2.$0^{1,6}$]*undecan*-4-*one* **21c**. 30% Yield, an oil; ν_{max}(film)/cm^{-1} 1740, 1465, 1370 and 1100; δ_H($CDCl_3$) 2.70 (1 H, m, 5-H), 3.84–4.58 (4 H, m, 2- and 10-H_2); *m/z* 252 (M^+, 2), 195 (15) and 138 (100%) (Found: M^+, 252.170 98. $C_{15}H_{24}O_3$ requires M, 252.172 53).

5-*Ethyl*-3,7-*dioxatricyclo*[4.3.3.$0^{1,6}$]*dodecan*-4-*one* **22a**. 50% Yield, 75% de; an oil; ν_{max}(film)/cm^{-1} 1740, 1450, 1380, 1270 and 1195; δ_H($CDCl_3$) 1.07 (1.09) (3 H, t, *J* 7.4, Me), 2.47 (2.13) [1 H, dd, *J* 9.2, 3.3 (7.6, 1.7), 5-H],* 3.66 and 4.00 (3.66–3.83) [each 1 H (2 H), m, 8-H) and 4.10 and 4.23 (3.97 and 4.26) (each 1 H, d, *J* 11.5, 2-H);* δ_C($CDCl_3$) 13.3 (13.8) (q), 18.5 (18.8) (t), 22.1 (24.7) (t), 35.8 (t), 36.4 (t), 38.0 (38.7) (t), 48:2 (50.0) (d), 54.5 (s), 66.0 (66.2) (t), 70.7 (71.6) (t), 94.4 (95.0) (s) and 173.4 (s); *m/z* 210 (M^+, 49), 195 (100) and 123 (89%) (Found: M^+, 210.126 51. $C_{12}H_{18}O_3$ requires M, 210.125 58).

5-*Benzyl*-3,7-*dioxatricyclo*[4.3.3.$0^{1,6}$]*dodecan*-4-*one* **22b**. 32% Yield, 60% de; an oil; ν_{max}(film)/cm^{-1} 1740, 1490, 1450, 1380 and 1060; δ_H($CDCl_3$) 2.87 (2.59) [1 H, dd, *J* 9.4, 2.1 (8.1, 3.8), 5-H],* 2.97 (2.94) [1 H, dd, *J* 13.9, 2.1 (13.9, 3.8), C*H*Ph], 3.20 (3.43) [1 H, dd, *J* 13.9, 9.4 (13.9, 8.1), Hz, C*H*Ph], 3.68 and 4.02 (3.72–3.85) [1 H each, (2 H), m, 8-H], 4.04 and 4.21 (3.98 and 4.26) (each 1 H, d, *J* 11.7, 2-H) and 7.15–7.36 (5 H, m, Ph); δ_C($CDCl_3$) 22.1 (24.7) (t), 31.0 (31.5) (t), 35.8 (t), 36.5 (t), 38.1 (39.0) (t), 49.3 (50.7) (d), 53.6 (s), 66.0 (66.5) (t), 70.0 (71.6) (t),

* 5-H ≡ 2-H in Results and Discussion section, and in non-systematic numbering scheme given in structural presentation. 2-H ≡ 5-H. 10-H ≡ 11-H.

94.4 (95.0) (s) 126.1 (d), 128.3 (d × 2), 129.3 (d × 2), 140.8 (s) and 172.9 (s); *m/z* 272 (M^+, 49), 181 (13) and 124 (100%) (Found: M^+, 272.140 05. $C_{17}H_{20}O_3$ requires M, 272.141 23).

5-*Isopropyl*-3,7-*dioxatricyclo*[4.3.3.0^{1,6}]*dodecan*-4-*one* **23a**. 39% Yield, 0% de; an oil; ν_{max}(film)/cm^{-1} 1740, 1470, 1450, 1380 and 1120; δ_H($CDCl_3$) 1.27 and 1.11 (1.17 and 1.11) each 3 H, d, *J* 6.7, together Me), 2.39 (2.20) [1 H, d, *J* 8.4 (4.5), 5-H],* 3.67 and 3.96 (3.75–3.84) [each 1 H (2 H), m, 8-H] and 4.10 and 4.19 (4.24 and 3.99) (each 1 H, d, *J* 11.6, 2-H);* δ_C($CDCl_3$)† 20.3, 21.8, 22.3 and 24.9 (q), 22.7 and 22.8 (t), 26.4 and 26.9 (d), 35.8 and 36.0 (t), 36.5 and 37.5 (t), 38.0 and 40.0 (t), 52.1 and 53.1 (d), 54.8 and 55.3 (s), 65.8 and 66.8 (t), 69.5 and 71.9 (t), 94.6 and 95.5 (s) and 172.4 and 173.1 (s); *m/z* 224 (M^+, 17), 209 (100) and 123 (67%) (Found: M^+, 224.141 95. $C_{13}H_{20}O_3$ requires M, 224.141 23).

5-(1-*Phenylethyl*)-3,7-*dioxatricyclo*[4.3.3.0^{1,6}]*dodecan*-4-*one* **23b**. 75% Yield. Diastereoisomeric proportions 3:2:1:1 from ^{1}H NMR; an oil; ν_{max}(film)/cm^{-1} 1745, 1605, 1495, 1450 and 1110; δ_H($CDCl_3$) for the major isomer 1.51 (3 H, d, *J* 6.8, Me), 2.77 (1 H, d, *J* 7.8, 5-H),* 3.30–4.28 (5 H, m, 2- and 8-H_2 and C*H*Ph) and 7.14–7.38 (5 H, m, Ph); *m/z* 286 (M^+, 16), 271 (24) and 140 (100%) (Found: M^+, 286.154 81. $C_{18}H_{22}O_3$ requires M, 286.156 88).

5-*Ethyl*-3,12-*dioxatricyclo*[4.4.2.0^{1,6}]*dodecan*-4-*one* **24a**. 61% Yield, 33% de; an oil; ν_{max}(film)/cm^{-1} 1740, 1460, 1385, 1210, 1170 and 1105; δ_H($CDCl_3$) 1.06 (3 H, t, *J* 7.4, Me), 2.32 (2.76) [1 H, dd, *J* 7.6, 2.8 (9.7, 6.3), 5-H], 4.04 (2 H, s, 2-H_2) (4.16 and 4.33) (each 1 H, d, *J* 11.9, 2-H) and 4.46 and 4.56 (4.41 and 4.53) [each 1 H, d, *J* 6.6 (6.4), 11-H]; δ_C($CDCl_3$) 12.5 (q), 18.3 (16.6) (t), 18.4 (17.0) (t), 18.6 (17.2) (t), 23.8 (25.5) (t), 30.3 (30.7) (t), 39.6 (38.7) (s), 49.4 (54.0) (d), 69.6 (71.9) (t), 73.4 (72.4) (t), 87.2 (86.0) (s) and 172.9 (172.5) (s); *m/z* 210 (M^+, 30), 195 (100) and 180 (11%) (Found: M^+, 210.127 03. $C_{12}H_{18}O_3$ requires M, 210.125 58).

5-*Benzyl*-3,12-*dioxatricyclo*[4.4.2.0^{1,6}]*dodecan*-4-*one* **24b**. 49% Yield, 33% de; an oil; ν_{max}(film)/cm^{-1} 1745, 1600, 1495, 1450, 1385, 1210 and 1160; δ_H($CDCl_3$) 2.80–3.00 (2.69–2.76) (2 H, m, 5-H and C*H*Ph), 3.41 (3.30) [1 H, dd, *J* 7.3, 7.1 (9.2, 5.0), C*H*Ph], 4.03 (2 H, s, 2-H_2) (4.11 and 4.48) (each 1 H, d, *J* 11.7, together 2-H_2), 4.46 and 4.60 (4.43 and 4.54) (each 1 H, d, *J* 6.6, 11-H) and 7.26–7.30 (5 H, m, Ph); δ_C($CDCl_3$) 17.0 (17.4) (t), 17.7 (18.2) (t), 24.2 (25.9) (t), 28.9 (30.0) (t), 30.8 (t), 39.5 (39.1) (s), 51.2 (54.0) (d), 69.3 (72.6) (t), 73.3 (72.9) (t), 87.2 (86.2) (s), 126.1 (126.7) (d), 128.4 (d × 2), 128.9 (d × 2), 141.0 (138.6) (s) and 172.7 (172.1) (s); *m/z* 272 (M^+, 12), 242 (23), 151 (12) and 91 (100%) (Found: M^+, 272.141 56. $C_{17}H_{20}O_3$ requires M, 272.14 23).

5-*Ethyl*-1-*hydroxymethyl*-3-*oxabicyclo*[4.3.0]*non*-5-*en*-4-*one* **26**. An oil; ν_{max}(film)/cm^{-1} 3430, 1700, 1460, 1395, 1295, 1120 and 1035; δ_H($CDCl_3$) 1.02 (3 H, t, *J* 7.4, Me), 2.80 (1 H, br, OH), 3.42 and 3.61 (each 1 H, d, *J* 11.0, together CH_2OH) and 3.92 and 4.58 (each 1 H, d, *J* 10.7, 2-H); δ_C($CDCl_3$) 13.1 (q), 21.4 (t), 22.5 (t), 28.8 (t), 30.8 (t), 47.9 (s), 60.9 (t), 71.9 (t), 126.2 (s), 161.9 (s) and 165.5 (s); *m/z* 196 (M^+, 40), 166 (100) and 165 (29%) (Found: M^+, 196.110 74. $C_{11}H_{16}O_3$ requires M, 196.109 93).

7β-(3-*Chloropropyl*)-5α(β)-*ethyl*-6β-*hydroxy*-3-*oxa*-(1$_\beta$H)-*bicyclo*[4.3.0]*nonan*-4-*one* **28** (**29**). Less polar diastereoisomer **28**; obtained as prisms; m.p. 99–100 °C (from Et_2O–hexane); ν_{max}(KBr)/cm^{-1} 3400, 1720, 1460, 1380 and 1040; δ_H($CDCl_3$) 1.09 (3 H, t, *J* 7.3, Me), 2.34 (1 H, dd, *J* 10.1, 2.7, 5-H),* 3.57 (2 H, t, *J* 6.4, CH_2Cl), 3.92 (1 H, dd, *J* 11.7, 10.2, 2-H) * and 4.44 (1 H, dd, *J* 11.7, 6.6, 2-H); *m/z* 260 (M^+, 10), 173 (100) and 137 (53%) (Found: M^+ 260.118 37. $C_{13}H_{21}ClO_3$ requires M, 260.117 91).

More polar diastereoisomer **29**; obtained as prisms; m.p. 113–113.5 °C (from Et_2O–hexane); ν_{max}(KBr)/cm^{-1} 3480, 1720, 1460, 1275 and 1040; δ_H($CDCl_3$) 1.06 (3 H, t, *J* 7.3, Me), 2.56 (1 H, dd, *J* 10.4, 2.6, 5-H),* 3.55 (2 H, t, *J* 7.2, CH_2Cl), 4.13 (1 H, dd, *J* 11.9, 1.3, 2-H * and 4.48 (1 H, dd, *J* 11.9, 3.3, 2-H);* *m/z* 258 (M^+, 8), 173 (100) and 137 (45%) (Found: M^+, 260.115 76. $C_{13}H_{21}ClO_3$ requires M, 260.117 91).

† Unattributable to either diastereoisomer.

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