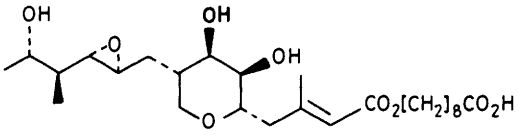
Formal Total Synthesis of (±)-Pseudomonic Acids from Dihydropyran

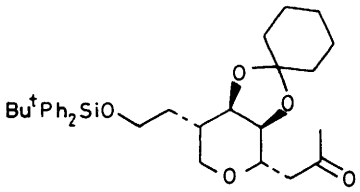
Richard F. W. Jackson, Ralph A. Raphael,* John H. A. Stibbard, and Raymond C. Tidbury
University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW

A new, convenient, and stereoselective route to a central intermediate in pseudomonic acid synthesis *via* the *cis*-fused γ-lactone, 2,7-dioxabicyclo[4.3.0]non-4-en-8-one (**3**), is described. The required relative stereochemistry of the 2- and 5-side chains is established by a palladium(0)-mediated allylic substitution of the γ-lactone(3) by di-t-butyl sodiomalonate.

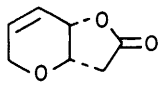
The antibiotic activity of the pseudomonic acids[1] [*e.g.* acid A; (**1**)] has prompted considerable interest in the synthesis of this group of bacterial metabolites.[2] We now describe a new, convenient, and stereoselective route to compound (**2**), a central intermediate in the Kozikowski,[2a] Snider,[2b] and Fleet[2c] syntheses of the pseudomonic acids. The key intermediate in our work was the *cis*-fused γ-lactone (**3**), which was prepared by the following route.



(1)

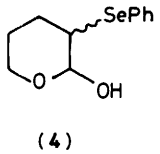


(2)

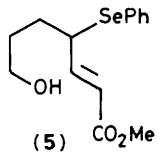


(3)

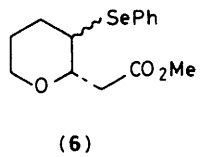
The reaction of benzeneselenenyl chloride with dihydropyran, followed by hydrolysis of the adduct with aqueous triethylamine gave the phenylselenolactol (**4**) (76.5%). This compound was converted into the open chain hydroxy ester (**5**) (89%) using methoxycarbonyl(methylene)triphenylphosphorane in acetonitrile. Cyclisation to the pyran (**6**) using methanolic sodium methoxide and oxidation to the selenoxide using ozone,[3] followed by thermal elimination of benzeneseleninic acid, gave the pyranylacetic ester (**7**) (75%). The ester (**7**) was hydrolysed to the pyranylacetic acid (**8**) (95%) using aqueous methanolic potassium hydroxide. Conversion of the pyranylacetic acid (**8**) into the required lactone (**3**) was achieved by two routes. Phenylselenolactonisation of the pyranylacetic acid (**8**) using phenylselenyl hexafluorophosphate in dichloromethane[4] gave the selenolactone (**9**) (77%). When benzeneselenenyl chloride was used very poor yields of the selenolactone were obtained, together with the addition product of benzeneselenenyl chloride to the double bond. Subsequent oxidation of the selenolactone (**8**) to the selenoxide using hydrogen peroxide and elimination of benzeneseleninic acid gave the required lactone (**3**) (93%) as a homogeneous crystalline compound, m.p. 71—72 °C. As a much more convenient alternative, the pyranylacetic acid was treated with sodium hydrogen carbonate—iodine—potassium iodide to give the iodolactone (**10**) (90%) which, on treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene in tetrahydrofuran, gave the lactone (**3**) (85%), identical with the lactone prepared by the alternative method. Iodolactonisation is known to give *cis*-fused bicyclic systems,[5] but in order to confirm the relative stereochemistry an *X*-ray crystal structure determination was performed on the iodolactone (**10**), which did indeed confirm the structure.† Since elimination of hydrogen iodide from the iodolactone (**3**) would not be expected to alter the *cis*-fusion, we are confident that our assignment of the stereochemistry of the lactone (**3**) is sound.



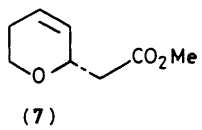
(4)



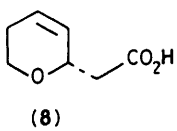
(5)



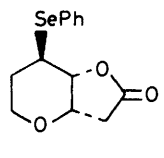
(6)



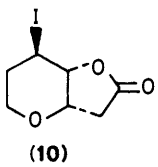
(7)



(8)



(9)

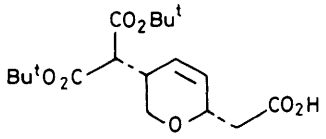


(10)

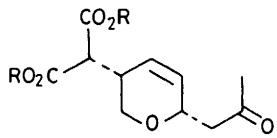
Reaction of the lactone (**3**) with di-t-butyl sodiomalonate in tetrahydrofuran in the presence of bis(dibenzylidenacetonato)-palladium(0) and bis(1,2-diphenylphosphino)ethane[6] led to allylic displacement of the internal carboxylate leaving group with double inversion[7] to give the pyranylacetic acid (**11**) with the stereochemistry indicated. Confirmation of the stereochemistry is provided by coupling constants of the vinylic protons in the ^{1}H n.m.r. spectrum. One vinylic proton, besides being strongly coupled to the adjacent vinylic proton, is also strongly coupled to a vicinal pseudoequatorial proton (*J* 5.5 Hz). The other vinylic proton is only weakly coupled to a vicinal pseudoaxial proton (*J* 1 Hz). If the 2- and 5-substituents were *trans*, the allylic protons would both be pseudoaxial, and the coupling constants of the vinylic hydrogens would be similar.[2b]

The pyranylacetic acid (**11**) was converted into the methyl ketone (**12**) (59%) by reaction with oxalyl chloride to give the acid chloride, which was then treated with lithium dimethylcuprate. Two other products with structures (**13**) (12%) and

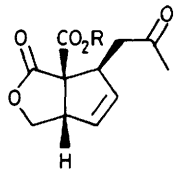
† We thank Dr. P. Raithby for this *X*-ray structure determination



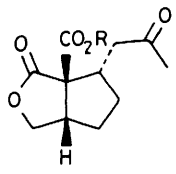
(11)



(12) R = Bu^t
(15) R = H

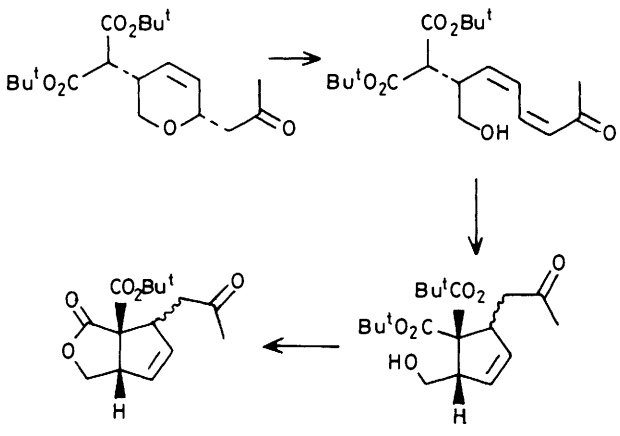


(13) R = Bu^t
(13a) R = H



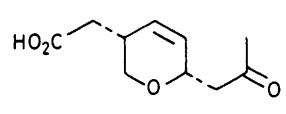
(14) R = Bu^t
(14a) R = H

(14) (6%) were also isolated from the reaction. A plausible mechanism for the formation of compounds (13) and (14) is shown in the Scheme. As further confirmation of the structures

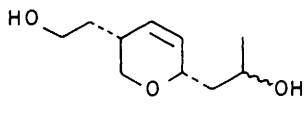


Scheme

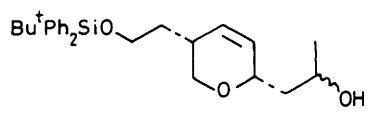
of compounds (13) and (14), each was separately hydrolysed to give the crystalline carboxylic acids (13a) and (14a). The methyl ketone (12) was treated with formic acid to give the diacid (15) (80%) which was then decarboxylated by heating in toluene to give the monoacid (16). Reduction of the monoacid (16) with lithium aluminium hydride gave the diol (17) [95% from the diacid (15)]. The conversion of the diol (17) into compound (2)



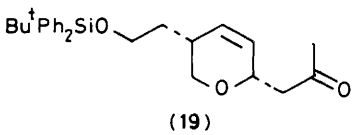
(16)



(17)



(18)



(19)

was achieved by means similar to those employed by Snider,[2b] although the experimental conditions were determined independently. The primary alcohol of the diol (17) was selectively silylated using t-butyldiphenylsilyl chloride[8] to give the siloxy alcohol (18) (70%) which was then oxidised to the siloxy ketone (19) (87%) using pyridinium chlorochromate. Hydroxylation of the double bond was achieved using *N*-methylmorpholine *N*-oxide and a catalytic amount of osmium tetraoxide.[9] Hydroxylation was shown to have occurred from the face opposite to the 2- and 5-side chains by conversion of the diol into the cyclohexylidene acetal (2) (75% overall), which was identical by spectral and chromatographic comparison with an authentic sample kindly supplied by Professor Snider.

Experimental

M.p.s were determined on a Kofler hot-stage. Spectrometric measurements were determined on the following instruments in the indicated solvents: i.r. Perkin-Elmer 297 ($CHCl_3$); ^1H n.m.r. ($CDCl_3$) Varian EM390A (internal standard tetramethylsilane) and Bruker WM250 (internal deuterium lock); ^{13}C n.m.r. ($CDCl_3$) Bruker WM250; mass spectrometry MS30 or MS902. Thin layer chromatography (t.l.c.) and preparative t.l.c. were performed on plates coated with Merck Kieselgel 60 F_{254} silica. Column chromatography was performed with Merck Kieselgel 60 silica. Flash column chromatography[10] was performed with Merck Kieselgel 60, 230—400 mesh silica. Dry THF refers to tetrahydrofuran dried by distillation from potassium benzophenone ketyl in a recycling still. Dry ether refers to diethyl ether dried by distillation from sodium benzophenone ketyl in a recycling still. Dichloromethane was distilled from phosphorus pentaoxide. Triethylamine was distilled from calcium hydride. DBU refers to 1,5-diazabicyclo[5.4.0]undec-5-ene. Light petroleum refers to that fraction with a b.p. in the range 60—80 °C.

3-*Phenylselenotetrahydropyran*-2-*ol* (4).—A solution of benzeneselenenyl chloride (10.11 g, 52.8 mmol) in dry THF (50 ml) was added dropwise over 45 min to a solution of dihydropyran (4.0 g, 48 mmol) in dry THF (20 ml). A solution of triethylamine (10.0 ml, 71.7 mmol) and water (1.5 ml, 88.9 mmol) in THF (16 ml) was then added dropwise over 30 min. Faster addition of this solution led to lower yield of the product. The reaction mixture was stirred for a further 1.25 h and, after removal of the precipitated triethylamine hydrochloride by filtration, solvent was removed under reduced pressure. The residue was purified by flash column chromatography [6 in × 2 in silica column; eluant 1:19 ether–light petroleum (1 l), 1:9 ether–light petroleum (500 ml), 1:4 ether–light petroleum (500 ml), 3:7 ether–light petroleum (500 ml), and 1:1 ether–light petroleum (800 ml)] to yield the *selenolactol* (4) (9.37 g, 76.5%) as a mixture of diastereoisomers; $\nu_{max.}$ 3 600—2 700 (OH), 1 595, 1 575, 1 340, and 1 120 cm^{-1}; δ(250 MHz) 1.5—1.86 and 2.0—2.35 (4 H, m, 4-H_2 and 5-H_2), 2.86 (d, *J* 4.7 Hz, 3-H *trans*), 3.35—3.42 (m), 3.51—3.61 (m), and 3.97—4.06 (m), (total 3 H, 6-H_2 and 3-H *cis* and *trans*), 4.80 (dd, *J* 6.7 and 4.7 Hz) and 4.89 (dd, *J* 8.2 and 2.3 Hz), (total 1 H, 2-H *cis* and *trans*), 7.2—7.31 (3 H, m, PhSe), and 7.5—7.6 (2 H, m, PhSe); *m/z* 258 (M^+, Se^{80}), 240 ($M^+ - H_2O$), 184, and 157.

Methyl 7-*Hydroxy*-4-*phenylselenohept*-2-*enoate* (5).—The mixture of diastereoisomeric selenolactols (4) (9.37 g, 36.5 mmol) was dissolved in acetonitrile (150 ml) and methoxycarbonylmethylene(triphenyl)phosphorane (25 g, 75 mmol) was added. The suspension was stirred for 40 h, when a further quantity of phosphorane (5 g, 15 mmol) was added. After being stirred for a further 47 h, the mixture was filtered and the filtrate evaporated under reduced pressure. The residue was purified by flash column chromatography (8 in × 2 in silica column) using

3:1 ether–light petroleum as eluant to yield the *hydroxy ester* (**5**) (10.21 g, 89%) as an oil (Found: C, 53.65; H, 5.85. $C_{14}H_{18}O_3Se$ requires C, 53.65; H, 5.75%); $\nu_{max.}$ 3 600—2 850 (OH), 1 710 (unsaturated ester), and 1 650 cm^{-1} (C=C); δ(250 MHz) 1.51 (1 H, br s, OH), 1.64—1.87 (4 H, m, 5-H_2 and 6-H_2), 3.68 (3 H, s, CO_2Me), 3.62—3.74 (3 H, m, 4-H and 7-H), 5.29 (1 H, dd, *J* 15.6 and 0.6 Hz, 2-H), 6.89 (1 H, dd, *J* 10 and 15.6 Hz, 3-H), 7.23—7.31 (3 H, m, PhSe), and 7.46—7.50 (2 H, m, PhSe); *m/z* 314 (M^+ ^{80}Se), 283 (M^+ − OMe), and 157.

Methyl 3-*Phenylselenotetrahydropyran*-2-*ylacetate* (**6**).—The hydroxy ester (**5**) (10.21 g, 28.6 mmol) was dissolved in a solution of sodium methoxide in methanol, prepared by dissolving sodium (0.5 g) in distilled methanol (200 ml), and left for 24 h at room temperature. Methanol was then removed under reduced pressure and the residue dissolved in ether (200 ml). The ethereal solution was washed with a saturated aqueous solution of sodium hydrogen sulphate (50 ml) and brine (50 ml), before being dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave the crude *phenylselenopyranylacetic ester* (**6**) as a mixture of diastereoisomers. This could be purified by flash column chromatography [8 in × 2 in silica column; eluant 1:6 ether–light petroleum (1 l) and 1:3 ether–light petroleum (1l)], but was usually used in the next step without purification (Found: C, 53.85; H, 5.9. $C_{14}H_{18}O_3Se$ requires C, 53.65; H, 5.75%); $\nu_{max.}$ 1 735 cm^{-1} (ester); δ(250 MHz) 1.43—1.77 (2 H, m, 4-H_2), 2.01—2.27 (2 H, m, 5-H_2), 2.43 (dd, *J* 15.3 and 9.4 Hz, $H_bCH_aCO_2Me$ *cis*), 2.67 (dd, *J* 16.2 and 5.8 Hz, $H_bCH_aCO_2Me$ *trans*), 2.81 (dd, *J* 16.2 and 7.5 Hz, $H_aCH_bCO_2Me$ *trans*), and 3.13 (dd, *J* 15.3 and 2.8 Hz, $H_aCH_bCO_2Me$ *cis*) (total 2 H), 2.98 (dt, *J* 3.6 and 10.4 Hz, 3-H *trans*), 3.61 (s, CO_2Me *trans*), 3.68 (s, CO_2Me *cis*), 3.31—3.81 (m) and 3.88—4.03 (m) (total 7 H, 2-H, 3-H, 6-H_2, and CO_2Me), 7.19—7.32 (3 H, m, PhSe), and 7.48—7.57 (2 H, m, PhSe); *m/z* 314 (M^+ ^{80}Se), 283 (M^+ − OMe), 260, 241, and 157.

Methyl 5,6-*Dihydro*-2H-*pyran*-2-*ylacetate* (**7**).—Ozonised oxygen was passed into a solution of the crude phenylselenopyranylacetic ester (**6**) [from 10.21 g of the hydroxy ester (**5**)] in dichloromethane cooled to −78 °C, until a blue colouration appeared. The excess of ozone was removed in a stream of nitrogen (30 min), before the solution was allowed to reach room temperature. Solvent was removed under reduced pressure and the residue was dissolved in carbon tetrachloride (150 ml). Calcium carbonate (3 g) was added and the suspension heated at reflux for 20 min under an atmosphere of nitrogen. After filtration and evaporation of the solvent under reduced pressure, the residue was purified by flash column chromatography (6 in × 2 in silica column; eluant 1:19 ether–light petroleum (1 l) 1:9 ether–light petroleum (500 ml), 1:4 ether–light petroleum, (500 ml), and 1:3 ether–light petroleum (500 ml)] to yield the *ester* (**7**) [3.82 g, 75% from the hydroxy ester (**5**)] as an oil, together with diphenyl diselenide. A sample was Kugelrohr distilled in an attempt to obtain analytically pure material, but the carbon analysis was low (Found: C, 60.9; H, 7.65. $C_8H_{12}O_3$ requires C, 61.55; H, 7.7%); $\nu_{max.}$ 1 735 (ester) and 1 660 cm^{-1} (C=C); δ(250 MHz) 1.94 (1 H, d m, *J* 16.5 Hz, 5-H_b), 2.19—2.35 (1 H, m, 5-H_a), 2.45 (1 H, dd, *J* 5.4 and 15.6 Hz, $H_bCH_aCO_2Me$), 2.57 (1 H, dd, *J* 9.3 and 15.6 Hz, $H_aCH_bCO_2Me$), 3.70 (3 H, s, CO_2Me), 3.62—3.72 (1 H, m, 6-H_{ax}), 3.94 (1 H, ddd, *J* 11.3, 5.5, and 3.1 Hz, 6-H_{eq}), 4.53 (1 H, m, 2-H), 5.63 (1 H, dq, *J* 10.3 and 2 Hz, 3-H), and 5.89 (1 H, dm, *J* 10.3 Hz, 4-H); *m/z* 156 (M^+, 15%), 96 (38), and 83 (100) (Found: M^+, 156.0775. $C_8H_{12}O_3$ requires *M*, 156.0786).

5,6-*Dihydro*-2H-*pyran*-2-*ylacetic Acid* (**8**).—The methyl ester (**7**) (3.82 g, 24.5 mmol) was dissolved in distilled methanol (100 ml) and a solution of potassium hydroxide (3.16 g) in water (100 ml) was added. The solution was allowed to stand at room temperature for 20 h and then titrated with dilute hydrochloric acid (1 M) until pink to Methyl Orange indicator. Methanol was removed under reduced pressure and the residue extracted with ethyl acetate (2 × 100 ml). The organic extracts were dried ($MgSO_4$) and solvent evaporated under reduced pressure to yield the *pyranylacetic acid* (**8**) (3.30 g, 95%) as a crystalline solid, m.p. 71—72 °C (Found: C, 58.95; H, 6.85. $C_7H_{10}O_3$ requires C, 59.15; H, 7.1%); $\nu_{max.}$ 3 550—2 400 (OH), 1 720 (C=O), and 1 660 cm^{-1} (C=C); δ(250 MHz) 1.98 (1 H, dm, *J* 16.6 Hz, 5-H_a), 2.21—2.42 (1 H, m, 5-H_b), 2.56 (1 H, dd, *J* 15.6 and 5.7 Hz, $H_bCH_aCO_2H$), 2.59 (1 H, dd, *J* 15.6 and 7.5 Hz, $H_aCH_bCO_2H$), 3.72 (1 H, ddd, *J* 11.3, 9.5 and 4.0 Hz, 6-H_{ax}), 4.00 (1 H, ddd, *J* 11.3, 5.6 and 2.8 Hz, 6-H_{eq}), 4.53 (1 H, m, 2-H), 5.64 (1 H, dq, *J* 10.3 and 2 Hz, 3-H), 5.88—5.97 (1 H, dm, *J* 10.3 Hz, 4-H), and 10.3 (1 H, br s, CO_2H); *m/z* 143 (M^+, 11%), 124 (13), and 96 (65).

5β-*Phenylseleno*-1α,6α-2,7-*dioxabicyclo*[4.3.0]*nonan*-8-*one* (**9**).—Silver hexafluorophosphate (0.76 g, 3 mmol) was weighed under an argon atmosphere into a flame-dried flask and then dissolved in dry dichloromethane (20 ml). Benzeneselenenyl chloride (0.57 g, 3 mmol) in dry dichloromethane (20 ml) was added and the mixture was stirred for 30 min at room temperature. The precipitate of silver chloride was allowed to settle and the mixture was cooled to −78 °C. The supernatant liquid was added *via* a cannula to a solution of the pyranylacetic acid (**8**) (0.3 g, 2.1 mmol) in dry dichloromethane (20 ml), also cooled to −78 °C, under an argon atmosphere. The reaction mixture was kept at −78 °C for 1 h and then left at room temperature for 14 h, before being washed with saturated aqueous sodium hydrogen carbonate and then dried (Na_2SO_4). Solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (adsorbent 50 g) using 1:1 diethyl ether–light petroleum as eluant to yield the *phenylselenolactone* (**9**) (0.48 g, 77%). A sample was recrystallised from diethyl ether–dichloromethane, m.p. 117—118 °C (Found: C, 52.3; H, 4.7; Se, 26.55. $C_{13}H_{14}O_3Se$ requires C, 52.55; H, 4.75; Se, 26.55%); $\nu_{max.}$ 1 785 cm^{-1} (lactone); δ(250 MHz) 1.80 (1 H, dm, *J* 14.8 Hz, 4-H_b), 2.34—2.45 (1 H, m, 4-H_a), 2.53 (1 H, dt, *J* 17.2 and 0.7 Hz, 9-H_b), 2.62 (1 H, dd, *J* 17.2 and 3.8 Hz, 9-H_a), 3.71 (1 H, dd, *J* 11.9 and 1.8 Hz, 3-H_{eq}), 3.78 (1 H, ddm, *J* 11.9 and 4.9 Hz, 3-H_{ax}), 3.92 (1 H, m, 5-H), 4.28 (1 H, br s, 1-H), 4.54 (1 H, m, 6-H), 7.26—7.35 (3 H, m, aryl), and 7.52—7.57 (2 H, m, aryl); *m/z* 298 (M^+, Se^{80}), 157, and 99.

2,7-*Dioxabicyclo*[4.3.0]*non*-4-*en*-8-*one* (**3**).—A solution of the phenylselenolactone (**9**) (0.98 g, 3.3 mmol) in THF was cooled to 0 °C and treated with chilled hydrogen peroxide (30%; 4 ml, *ca.* 40 mmol). The solution was allowed to stand for 48 h at room temperature. It was then diluted with water (20 ml) and extracted with dichloromethane (50 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 × 25 ml), and the combined washings were back-extracted with dichloromethane (30 ml). The combined organic extracts were dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (adsorbent 50 g) using diethyl ether as eluant to yield the *lactone* (**3**) (0.43 g, 93%) as a crystalline solid. A sample was recrystallised from diethyl ether–light petroleum and had m.p. 71—72 °C (Found: C, 59.95; H, 5.7. $C_7H_8O_3$ requires C, 60.0; H, 5.75%); $\nu_{max.}$ 1 790, 1 775 (lactone), and 1 660 cm^{-1} (C=C); δ_H(250 MHz) 2.64 (1 H, d, *J* 17.9 Hz, 9-H_b), 2.83 (1 H, dd, *J* 17.9 and 5.4 Hz, 9-H_a), 4.11 (1 H, dq, *J* 17.0 and 2.0 Hz, 3-H_{ax}), 4.20 (1 H, dddd, *J* 17.0, 3.9, 1.7, and 0.5 Hz, 3-H_{eq}), 4.26 (1 H, dd, *J* 5.4 and 3.3 Hz, 1-H), 4.55 (1 H, m, 6-H), 6.09 (1 H, dm, *J* 10.3 Hz, 5-H), and 6.26 (1 H, dddd, *J* 10.3, 3.9, 2.0 and 0.9 Hz, 4-H); δ_C(62.5 MHz) 37.5 (dd, C-9), 63.8 (t, C-3), 71.9 (d, C-1), 73.1 (d, C-

6), 120.2 (d) and 134.1 (d) (C-5 and C-4), 175.2 p.p.m. (s, C-8); *m/z* 140 (M^+, 60%), 96 (51), and 84 (100).

5β-*Iodo*-1α,6α-2,7-*dioxabicyclo*[4.3.0]*nonan*-8-*one* (**10**).—The pyranylacetic acid (**8**) (3.74 g, 26.3 mmol) was dissolved in THF (100 ml) and a solution of sodium hydrogen carbonate (2.37 g, 28.2 mmol) in water (70 ml) was added. The solution was stirred for 15 min and then a solution of iodine (18.16 g, 71.5 mmol) and potassium iodide (37.2 g, 224 mmol) in water (250 ml) was added. The solution was stirred for 22 h in the dark at room temperature and then extracted with dichloromethane (2 × 300 ml). The organic extracts were washed with saturated aqueous sodium thiosulphate (100 ml) and brine (100 ml), before being dried ($MgSO_4$). Solvent was removed under reduced pressure to yield the *iodolactone* (**10**) (6.37 g, 90%) as a pale yellow crystalline solid. A sample was recrystallised from ethyl acetate, m.p. 133—135 °C (Found: C, 31.1; H, 3.2. $C_7H_9IO_3$ requires C, 31.35; H, 3.35%); $\nu_{max.}$ 1 800 cm^{-1} (lactone); δ(250 MHz) 1.84 (1 H, br d, *J* 15.5 Hz, 4-H_a), 2.10—2.30 (1 H, m, 4-H_b), 2.55 (1 H, d, *J* 17.3 Hz, 9-H_b), 2.65 (1 H, dd, *J* 17.3 and 2.7 Hz, 9-H_a), 3.8—3.9 (2 H, m, 3-H_2), 4.52 (1 H, br s, 1-H), 4.62 (1 H, m, 6-H), and 4.76 (1 H, m, 5-H); *m/z* 268 (M^+, 25%), 197 (5), 141 (M^+ − I, 68), and 99 (100).

2,7-*Dioxabicyclo*[4.3.0]*non*-4-*en*-8-*one* (**3**).—The iodolactone (**10**) (6.37 g, 23.8 mmol) was dissolved in dry THF (150 ml) and DBU (4.81 g, 31.61 mmol) was added. The reaction mixture was stirred for 27 h at room temperature and then solvent was removed under reduced pressure. The residue was partitioned between water (50 ml) and ethyl acetate (100 ml) and after separation of the organic layer, the aqueous layer was extracted with more ethyl acetate (100 ml). The organic extracts were washed with 1M hydrochloric acid (50 ml), saturated aqueous sodium hydrogen carbonate (50 ml), and brine (50 ml), before being dried ($MgSO_4$). Solvent was removed under reduced pressure and the residue purified by flash column chromatography [6 in × 2 in silica column; eluant ether (1 l)] to yield the lactone (**3**) [2.82 g, 76.5% from the pyranylacetic acid (**8**)], identical with that prepared previously.

5,6-*Dihydro*-5α-[*bis*(*t-butoxycarbonyl*)*methyl*]-2H-*pyran*-2α-*ylacetic Acid* (**11**).—Di-t-butyl malonate (3.24 g, 15 mmol) was added to a suspension of sodium hydride (50% suspension in mineral oil; 0.72 g) in dry THF (40 ml). After being stirred for 15 min, the pale yellow solution of di-t-butyl sodiomalonate was added to a solution of the lactone (**3**) (0.7 g, 5 mmol), bis(dibenzylideneacetonato)palladium(0) (70 mg), and bis(1,2-diphenylphosphino)ethane (50 mg) in dry THF (70 ml). The solution was stirred for 1 h and then poured into water (100 ml) and extracted with ether (2 × 75 ml). The organic extracts were washed with water (50 ml) and the combined aqueous extracts acidified with a solution of oxalic acid dihydrate (1.26 g, 10 mmol) in water (30 ml). The acidified aqueous phase was extracted with ether (4 × 75 ml) and these organic extracts were washed with brine (50 ml) and dried ($MgSO_4$). Solvent was evaporated under reduced pressure to give the *pyranylacetic acid* (**11**) (1.72 g, 97%) as an oil; $\nu_{max.}$ 3 550—2 500 (OH), 1 740 (ester), and 1 720 cm^{-1} (acid); δ(250 MHz) 1.44 (9 H, s, Bu^t), 1.45 (9 H, s, Bu^t), 2.52 (1 H, dd, *J* 15 and 5.5 Hz, $H_bCH_aCO_2H$), 2.60 (1 H, dd, *J* 15 and 7.5 Hz, $H_aCH_bCO_2H$), 2.65—2.73 (1 H, m, 5-H), 3.32 [1 H, d, *J* 10 Hz, $CH(CO_2Bu^t)_2$, 3.78 (1 H, dd, *J* 12 and 3.5 Hz, 6-H_b), 3.90 (1 H, d, *J* 12 Hz, 6-H_a), 4.51 (1 H, m, 2-H), 5.74 (1 H, d, *J* 10 Hz, 3-H), 5.87 (1 H, dd, *J* 10 and 5.5 Hz, 4-H), and 9.4 (1 H, br s, OH); *m/z* 300 (M^+ − C_4H_8), 283 (M^+ − C_4H_8–OH), 244, 237, 185, and 140.

5,6-*Dihydro*-5α-[*bis*(*t-butoxycarbonyl*)*methyl*]-2H-*pyran*-2α-*ylpropan*-2-*one* (**12**).—The pyranylacetic acid (**11**) (1.72 g, 4.8 mmol) was dissolved in dry benzene (20 ml) and oxalyl chloride (1.46 g, 11.5 mmol) was added to it. The reaction mixture was stirred for 50 min and then solvent and excess of oxalyl chloride were removed under reduced pressure. The residue was dissolved in dry ether (15 ml) and added to a solution of lithium dimethylcuprate, prepared from methyllithium (1.4M solution in ether; 25 ml, 35 mmol) and dry copper(I) iodide (4.17 g, 21.9 mmol) in dry ether (25 ml) at 0 °C, cooled to −70 °C. The mixture was mechanically stirred for 15 min at −70 °C and then quenched by addition of distilled methanol (3 ml) and solid sodium hydrogen sulphate (5 g). The mixture was then allowed to warm to room temperature with continuous stirring and then filtered through silica gel (1.5 in × 3 in; eluant, ether). Solvent was removed under reduced pressure and the residue purified by flash column chromatography [6 in × 1 in silica column; eluant 3:7 ethyl acetate–light petroleum (b.p. 60—80 °C)] to yield the *methyl ketone* (12) (1.05 g, 59%), R_F 0.31, 1α, 5α-3-*oxa*-5β-*t-butoxycarbonyl*-6β-(2-*oxopropyl*)-*bicyclo*[3.3.0]*oct*-7-*en*-4-*one* (**13**) (0.17 g, 12%), R_F 0.20, and 1α, 5α-3-*oxa*-5β-*t-butoxycarbonyl*-6α-(2-*oxopropyl*)*bicyclo*-[3.3.0]*oct*-7-*en*-4-*one* (**14**) (0.08 g, 6%), R_F 0.14. The methyl ketone (**12**) had the following physical characteristics (Found: C, 64.6; H, 8.55. $C_{19}H_{30}O_6$ requires C, 64.4; H, 8.5%); $\nu_{max.}$ 1 740 (ester), 1 720 (ketone), and 1 600 cm^{-1} (w, C=C); δ(250 MHz) 1.44 (9 H, s, Bu^t), 1.45 (9 H, s, Bu^t), 2.18 (3 H, s, COMe), 2.50 (1 H, dd, *J* 5.2 and 15.4 Hz, H_bCH_aCOMe), 2.65 (1 H, m, 5-H), 2.71 (1 H, dd, *J* 8 and 15.4 Hz, H_aCH_bCOMe), 3.31 (1 H, d, *J* 10 Hz, $CH(CO_2Bu^t)_2$), 3.77 (1 H, dd, *J* 3.4 and 12 Hz, 6-H_a), 3.83 (1 H, d, *J* 12 Hz, 6-H_b), 4.55 (1 H, m, 2-H), 5.72 (1 H, d, *J* 10 Hz, 3-H), and 5.85 (1 H, dd, *J* 10 and 5.5 Hz, 4-H); *m/z* 298 (M^+ − C_4H_8), 281 (M^+ − C_4H_8 − OH), 242, 241, 235, and 138.

The lactone (**13**) had the following physical characteristics: $\nu_{max.}$ 1 770 (lactone), 1 735 (ester), and 1 720 cm^{-1} (ketone); δ(250 MHz), 1.46 (9 H, s, Bu^t), 2.17 (3 H, s, COMe), 2.57 (1 H, dd, *J* 9.5 and 18.4 Hz, H_bCH_aCOMe), 3.17 (1 H, dd, *J* 5.3 and 18.4 Hz, H_aCH_bCOMe), 3.74 (1 H, m, 6-H) and 3.88 (1 H, m, 1-H) (these assignments may be interchangeable), 4.17 (1 H, dd, *J* 1.3 and 9 Hz, 2-H_a), 4.40 (1 H, dd, *J* 7 and 9 Hz, 2-H_b), 5.52 (1 H, m, 8-H), and 5.72 (1 H, m, 7-H); *m/z* 224 (M^+ − C_4H_8), 207 (M^+ − C_4H_8 − OH), and 178.

The lactone (**14**) had the following physical characteristics: $\nu_{max.}$ 1 770 (lactone), 1 735 (ester), and 1 720 cm^{-1} (ketone); δ(250 MHz) 1.45 (9 H, s, Bu^t), 2.11 (3 H, s, COMe), 2.59 (1 H, dd, *J* 8 and 17.5 Hz, H_bCH_aCOMe), 2.88 (1 H, dd, *J* 5 and 17.5 Hz, H_aCH_bCOMe), 3.64 (1 H, m, 6-H), and 3.89 (1 H, dm, *J* 6 Hz, 1-H) (these assignments may be interchangeable), 4.22 (1 H, d, *J* 9 Hz, 2-H_a), 4.44 (1 H, dd, *J* 6 and 9 Hz, 2-H_b), 5.59 (1 H, m, 8-H), and 5.79 (1 H, m, 7-H); *m/z* 224 (M^+ − C_4H_8), 207 (M^+ − C_4H_8 − OH), and 178.

Hydrolysis of the Lactone (**13**).—The lactone (**13**) (0.53 g, 1.9 mmol) was dissolved in trifluoroacetic acid (7.5 ml) and heated at reflux for 2 h. Solvent was removed under reduced pressure and the residue heated at 120 °C for 1 h at 0.05 mmHg. On cooling, the product crystallised and was recrystallised from ethyl acetate–light petroleum (b.p. 60—80 °C) to give 5β-*carboxy*-6β-(2-*oxopropyl*-1α,5α-3-*oxabicyclo*[3.3.0]*oct*-7-*en*-4-*one* (**13a**) (0.345 g, 81%), m.p. 129—131 °C (Found: C, 59.25; H, 5.45. $C_{11}H_{12}O_5$ requires C, 58.95; H, 5.35%); $\nu_{max.}$ 3 600—2 400 (OH), 1 770 (lactone), and 1 720 cm^{-1} (ketone); δ(250 MHz) 2.24 (3 H, s, COMe), 2.73 (1 H, dd, *J* 6.7 and 19 Hz, H_bCH_aCOMe), 3.02 (1 H, dd, *J* 8.3 and 1.9 Hz, H_aCH_bCOMe), 3.91 (1 H, br t, *J* 7 Hz, 6-H), 4.04 (1 H, br d, *J* 7 Hz, 1-H), 4.19 (1 H, dd, *J* 1.5 and 9 Hz, 2-H_a), 4.50 (1 H, dd, *J* 7.5 and 9 Hz, 2-H_b), 4.3—4.8 (1 H, br s, OH), and 5.64 (2 H, s, 7-H and 8-H); *m/z* 224 (M^+, 7%), 206 (M^+ − H_2O, 18), 178 (M^+ − H_2O − CO, 32), 91 (98), and 77 (100).

The lactone (**14**) was subjected to the same reaction

conditions and yielded 5β-*carboxy*-6α-(2-*oxopropyl*)-1α,5α-3-*oxabicyclo*[3.3.0]*oct*-7-*en*-4-*one* (**14a**), m.p. 133—143 °C (Found: C, 58.9; H, 5.55. $C_{11}H_{12}O_5$ requires C, 58.95; H, 5.35%); $\nu_{max.}$ 3 600—2 400 (OH), 1 770 (lactone), and 1 720 cm^{-1} (ketone); δ(250 MHz) 2.14 (3 H, s, COMe), 2.34 (1 H, br s, OH), 2.59 (1 H, dd, *J* 8 and 17.5 Hz, H_bCH_aCOMe), 2.88 (1 H, dd, *J* 5 and 17.5 Hz, H_aCH_bCOMe), 3.72 (1 H, m, 6-H), 4.02 (1 H, m, 1-H), 4.28 (1 H, d, *J* 9 Hz, 2-H_a), 4.52 (1 H, dd, *J* 6.5 and 9.5 Hz, 2-H_b), 5.64 (1 H, m, 8-H), and 5.83 (1 H, m, 7-H); *m/z* 224 (M^+, 1.4%), 206 ($M^+ - H_2O$, 5), 178 ($M^+ - H_2O - CO$, 20), 91 (95), and 77 (100).

5,6-*Dihydro*-2α-(2-*oxopropyl*)*pyran*-5α-*ylmalonic Acid* (**15**).—The methyl ketone (**12**) (930 mg, 2.62 mmol) was dissolved in formic acid (15 ml) and the solution was stirred at room temperature for 100 min. Formic acid was removed under reduced pressure and the residue solidified after pumping at 0.2 mmHg. The product was dissolved in ethyl acetate (30 ml) and light petroleum (b.p. 60—80 °C) was added to precipitate the pure *diacid* (**15**) (505 mg, 80%), m.p. 138—140 °C (Found C, 54.55; H, 5.9. $C_{11}H_{14}O_6$ requires C, 54.55; H, 5.8%); $\nu_{max.}$(Nujol mull) 3 300—2 700 (br, acid OH) and 1 720 cm^{-1} (ketone and acid); δ(90 MHz, trifluoroacetic acid); 2.13 (3 H, s, COMe), 2.65—2.9 (3 H, m, CH_2COMe and 5-H), 3.65 [1 H, d, *J* 9 Hz, $CH(CO_2H)_2$], 3.8—4.2 (2 H, m, 6-H), 4.55 (1 H, m, 2-H), 5.65 (1 H, d, *J* 10 Hz, 3-H), and 5.82 (1 H, dd, *J* 10 and 5.5 Hz, 4-H); *m/z* 185 ($M^+ - CH_2COMe$, 3%), 180 ($M^+ - Me - CO_2H$, 9), and 138 [$M^+ - CH_2(CO_2H)_2$, 100].

5,6-*Dihydro*-2α-(2-*oxopropyl*)*pyran*-5α-*acetic Acid* (**16**).—The diacid (**15**) (121 mg, 0.5 mmol) was suspended in toluene (5 ml) and heated at reflux for 19 h, at which time the mixture had become homogeneous. Toluene was removed under reduced pressure to yield a yellow oil (104 mg, theoretical yield 99 mg) which solidified with time at 4 °C. This proved to be the monoacid (**16**) in a slightly impure form. A sample was recrystallised from diethyl ether–pentane at −30 °C to give the pure *monoacid* (**16**), m.p. 46—48 °C (Found: C, 60.45; H, 6.8. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.05%); $\nu_{max.}$ 3 400—2 700 (acid hydroxy) and 1 720 cm^{-1} (ketone and acid); δ(250 MHz) 2.19 (3 H, s, COMe), 2.4—2.8 (5 H, m, CH_2COMe, CH_2CO_2H, and 5-H), 3.76 (2 H, d, *J* 2.4 Hz, 6-H_2), 4.54 (1 H, m, 2-H), 5.67 (1 H, d, *J* 10.2 Hz, 3-H), 5.86 (1 H, dm, *J* 10.2 Hz, 4-H), and 10.0 (1 H, br s, CO_2H); *m/z* 198 (M^+, 2%), 183 (M^+ − Me, 3), 180 ($M^+ - H_2O$, 4), 141 ($M^+ - CH_2COMe$, 17), and 138 ($M^+ - CH_3CO_2H$, 100).

5,6-*Dihydro*-5α-(2-*hydroxyethyl*)-2H-*pyran*-2α-*ylpropan*-2-*ol* (**17**).—The crude monoacid (**16**) (104 mg) was dissolved in dry THF (10 ml) and lithium aluminium hydride (160 mg, 4.22 mmol) was added in three portions. The reaction mixture was stirred for 3 h at room temperature and the excess of lithium aluminium hydride was destroyed by addition of ethyl acetate (1 ml). Water (5 drops), sodium hydroxide (10% aqueous solution; 5 drops), and more water (15 drops) were added sequentially, and the precipitated aluminium salts were filtered off. The solvent was evaporated under reduced pressure and the residue was then filtered through a silica column (adsorbent 2 g) using ethyl acetate as the eluant. Removal of the solvent under reduced pressure gave the diol (**17**) [88 mg, 95% from the diacid (**15**)] as a mixture of diastereoisomers, $\nu_{max.}$ 3 550 cm^{-1} (OH); δ(250 MHz) 1.18 [d, *J* 6.2 Hz, CH(OH)*Me*] and 1.19 [d, *J* 6.3 Hz, CH(OH)*Me*] (total 3 H, diastereoisomers), 1.5—1.8 [4 H, m, CH_2CH_2OH and $CH_2CH(OH)$], 2.23 (1 H, m, 5-H), 3.6—3.8 (6 H, m, 6-H_2, CH_2CH_2OH and 2 × OH), 4.05 [1 H, sext, *J* 6 Hz, CH(OH)Me], 4.28 and 4.33 (total 1 H, m, 2-H, diastereoisomers), 5.64 (1 H, dd, *J* 10.5 and 1.4 Hz, 3-H), and 5.79 (1 H, ddm, *J* 10.5 and 5 Hz, 4-H); *m/z* 168 ($M^+ - H_2O$, 12%), 153 (22), 142 (28), 127 (65), 97 (96), and 79 (100) (Found: M^+, 168.1158. $C_{10}H_{16}O_2$ requires *M*, 168.1150.

5α-{2-[*Diphenyl*(*t-butyl*)*siloxy*]*ethyl*}-5,6-*dihydro*-2H-*pyran*-2α-*ylpropan*-2-*ol* (**18**).—The diol (**17**) (100 mg, 0.54 mmol) was dissolved in dry dichloromethane (5 ml). Dry triethylamine (0.08 ml, 0.57 mmol) and diphenyl(t-butyl)silyl chloride (0.15 ml, 0.58 mmol) were added, followed by 4-dimethylaminopyridine (5 mg). The solution was stirred for 20 h at room temperature and then the reaction mixture was washed with water (5 ml) and saturated aqueous ammonium chloride (5 ml), before being dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue purified by p.l.c. using 1:3 ethyl acetate–light petroleum (b.p. 60—80 °C) as eluant to yield the siloxy alcohol (**18**) (160 mg, 70%) as a mixture of diastereoisomers; $\nu_{max.}$ 3 450 cm^{-1} (OH); δ(250 MHz) 1.03 (9 H, s, Bu^t), 1.16 [d, *J* 6 Hz, CH(OH)*Me*] and 1.19 [d, *J* 6 Hz, CH(OH)*Me*] (total 3 H, diastereoisomers), 1.5—1.8 [4 H, m, CH_2CH_2OSi and $CH_2CH(OH)Me$], 2.25 (1 H, m, 5-H), 3.6—3.8 (5 H, m, 6-H_2, CH_2CH_2OSi, and OH), 4.04 [1 H, sext, *J* 6 Hz, CH(OH)Me], 4.28 and 4.39 (total 1 H, m, 2-H, diastereoisomers), 5.53 (1 H, d, *J* 10.5 Hz, 3-H), 5.8 (1 H, dm, *J* 10.5 Hz, 4-H), 7.3—7.5 (6 H, m, aryl), and 7.6—7.7 (4 H, m, aryl); *m/z* 323 ($M^+ - Bu^t - CH_3CHO$, 5%), and 199 (100).

5α-{2-[*Diphenyl*(*t-butyl*)*siloxy*]*ethyl*}-5,6-*dihydro*-2H-*pyran*-2α-*ylpropan*-2-*one* (**19**).—The siloxy alcohol (**18**) (160 mg, 0.38 mmol) was dissolved in dry dichloromethane (5 ml) and added to a stirred suspension of pyridinium chlorochromate (0.30 g, 1.39 mmol) in dichloromethane (2 ml). The mixture was stirred for 3 h and more pyridinium chlorochromate (0.29 g, 1.34 mmol) was added. The mixture was stirred for a further 1 h and then diluted with ether (10 ml). The reaction mixture was filtered through Florisil (1.5 in × 1.5 in) and solvent was removed under reduced pressure. The residue was purified by p.l.c. using 1:3 ethyl acetate–light petroleum as eluant to yield the siloxy ketone (**19**) (139 mg, 87%); $\nu_{max.}$ 1 710 cm^{-1} (CO); δ(250 MHz) 1.03 (9 H, s, Bu^t), 1.67 (2 H, q, *J* 6.5 Hz, CH_2CH_2OSi), 2.16 (3 H, s, COMe), 2.26 (1 H, m, 5-H), 2.47 (1 H, dd, *J* 5 and 16 Hz, H_bCH_aCOMe), 2.67 (1 H, dd, *J* 8 and 16 Hz, H_aCH_bCOMe), 3.55—3.8 (4 H, m, 6-H_2 and CH_2CH_2OSi), 4.52 (1 H, m, 2-H), 5.58 (1 H, d, *J* 10 Hz, 3-H), 5.81 (1 H, m, 4-H), 7.3—7.45 (6 H, m, Ph), and 7.6—7.7 (4 H, m, Ph); *m/z* 365 ($M^+ - Bu^t$, 100%), 335 (75), and 307 (36) (Found: $M^+ - Bu^t$, 365.1568. $C_{22}H_{25}O_3Si$ requires $M - Bu^t$, 365.1572).

3β,4β-*Cyclohexylidenedioxy*-5α-{2-[*diphenyl*(*t-butyl*)*siloxy*]-*ethyl*}*tetrahydro*-2H-*pyran*-2α-*ylpropan*-2-*one* (**2**).—The siloxy ketone (**19**) (150 mg, 0.35 mmol) was dissolved in a mixture of THF (2 ml), t-butyl alcohol (1.5 ml), and water (0.3 ml). *N*-Methylmorpholine *N*-oxide (110 mg, 0.81 mmol) was added followed by osmium tetraoxide (10 drops of a solution containing 0.1 g in 10 ml of water). The reaction mixture was refluxed for 27 h and then cooled. Saturated aqueous sodium sulphite (25 drops) was added followed by Florisil (1 g). The reaction mixture was filtered through Celite, which was then washed with acetone. The filtrate and washings were combined and the solvent evaporated under reduced pressure. The residue was partitioned between ethyl acetate (20 ml) and dilute sulphuric acid (1M; 1 ml), and after separation and re-extraction of the aqueous phase with more ethyl acetate (10 ml), the combined organic extracts were washed with brine (5 ml) and dried ($MgSO_4$). Solvent was evaporated under reduced pressure to give the dihydroxy ketone.

The dihydroxy ketone was dissolved in dry benzene (6 ml) and cyclohexanone (0.7 ml) was added, followed by anhydrous copper sulphate (160 mg) and toluene-*p*-sulphonic acid (3 crystals). The reaction mixture was stirred at room temperature

for 50 min and then benzene and excess of cyclohexanone were removed under reduced pressure. The residue was dissolved in diethyl ether and filtered through Celite. Solvent was removed under reduced pressure and the residue purified by p.l.c. using 1:3 ethyl acetate–light petroleum as eluant to give the cyclohexylidene acetal (**2**) [144 mg, 75% from the siloxy ketone (**19**)]; $\nu_{max.}$ 1 720 cm^{-1} (CO); δ(250 MHz) 1.03 (9 H, s, Bu^t), 1.3—1.8 (12 H, m), 2.17 (3 H, s, COMe), 2.25 (1 H, m), 2.52 (1 H, dd, *J* 7.5 and 15 Hz, H_bCH_aCOMe), 2.69 (1 H, dd, *J* 2 and 15 Hz, H_aCH_bCOMe), 3.5—3.8 (6 H, m, 3-H, 4-H, 6-H_2, and CH_2CH_2OSi), 4.12 (1 H, m, 2-H), 7.35—7.45 (6 H, m, Ph), and 7.6—7.65 (4 H, m, Ph); *m/z* 536 (M^+, 12%), 479 ($M^+ - Bu^t$, 22), 381 (75), 363 (20), 351 (28), 323 (70), and 200 (100) (Found: M^+, 536.2990. $C_{32}H_{44}O_5Si$ requires *M*, 536.2958).

Acknowledgements

We thank the S.E.R.C. and Roche Products Ltd. for support, and both Professor B. B. Snider and Dr. G. W. J. Fleet for their generous provision of spectra and samples.

References

1 J. P. Clayton, J. P. O'Hanlon, and N. H. Rogers, *Tetrahedron Lett.*, 1980, 881; J. P. Clayton, R. S. Oliver, N. H. Rogers, and T. J King, *J. Chem. Soc., Perkin Trans 1*, 1979, 838 and references therein; J. P. O'Hanlon, N. H. Rogers, and John W. Tyler, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2655.

2 (*a*) A. P. Kozikowski, R. J. Schmiesing, and K. L. Sorgi, *J. Am. Chem. Soc.*, 1980 **102**, 6577; *Tetrahedron Lett.*, 1981, 2059; (*b*) B. B. Snider, D. J. Rodini, M. Karras, T. C. Kirk, E. A. Deutsch, R. Cordova, and R. T. Price, *Tetrahedron*, 1981, **37**, 3927; B. B. Snider, D. J. Rodini, T. C. Kirk, and R. Cordova, *J. Am. Chem. Soc.*, 1982, **104**, 555; B. B. Snider and G. B. Phillips, *J. Am. Chem. Soc.*, 1982, **104**, 1113; B. B. Snider, G. B. Phillips, and R. Cordova, *J. Org. Chem.*, 1983, **48**, 3003; (*c*) G. W. J. Fleet and C. R. C. Spensley, *Tetrahedron Lett.*, 1982, 109; G. W. J. Fleet and M. J. Gough *Tetrahedron Lett.*, 1982, 4509; G. W. J. Fleet and T. K. M. Shing, *Tetrahedron Lett.*, 1983, 3657; G. W. J. Fleet, M. J. Gough, and T. K. M. Shing *Tetrahedron Lett.*, 1983, 3661 (Chiral Synthesis); (*d*) J.-M. Beau, S. Aburaki, J.-R. Pougny, and P. Sinaÿ, *J. Am. Chem. Soc.*, 1983, **105**, 621; (*e*) D. P. Curran, *Tetrahedron Lett.*, 1982, 4309; (*f*) B. Schonenberger, W. Summermatter, and C. Ganter, *Helv. Chim. Acta*, 1982, **65**, 2333.

3 H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434.

4 W. P. Jackson, S. V. Ley, and A. J. Whittle, *J. Chem. Soc., Chem. Commun.*, 1980, 1173.

5 M. D. Doyle and D. I. Davies, *Chem. Soc. Rev.*, 1979, 171.

6 J. C. Fiaud and J. L. Malleron, *Tetrahedron Lett.*, 1980, 4437.

7 B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, 1980, **102**, 4730.

8 S. K. Chaudhary and O. Hernandez, *Tetrahedron Lett.*, 1979, 99.

9 V. VanRheenen, R. C. Kelly, and D. Y. Cha, *Tetrahedron Lett.*, 1976, 1973.

10 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

Received 8*th February* 1984; *Paper* 4/220