Preparation of a Chiral Lactone from Laevoglucosan; a Key Intermediate for Synthesis of the Spiroacetal Moieties of the Avermectins and Milbemycins

Raymond Baker,* R. Hugh O. Boyes, D. Mark P. Broom, Mary J. O'Mahony, and Christopher J. Swain
Department of Chemistry, The University, Southampton SO9 5NH.

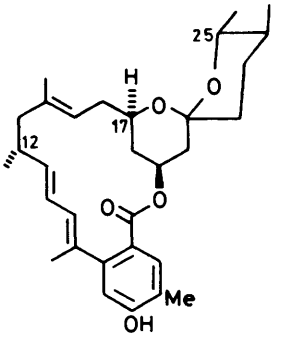
A synthesis of two diprotected (4*S*,6*S*)-4-hydroxy-6-hydroxymethyltetrahydropyran-2-ones has been developed from laevoglucosan. Reaction of these lactones with a substituted chiral lithium acetylide followed by hydrogenation and acid-catalysed cyclisation led to formation of the spiroacetal moiety of milbemycin β_1 and β_3. The acetylene was prepared by resolution of racemic material obtained from reaction of lithium acetylide and *cis*-butene epoxide. Alternatively a stereocontrolled synthesis was developed from (*S*)-methyl-3-hydroxy-2-methylpropionate which involved 'chelation controlled' addition of lithium dimethylcuprate to the corresponding tetrahydropyranyloxy aldehyde.

The milbemycins comprise a group of naturally occurring insecticides isolated from cultures of Streptomyces B-41-146, the simplest of them being milbemycin β_3 (**1**).[1] They show activity against mites, aphids, and the larval forms of many insects with little or no phytotoxicity. Interest in these compounds has increased since the isolation and identification of a structurally related series of macrolides, the avermectins [(**2**) is avermectin B_{2b}].[2] The avermectins are effective against helminths and arthropods at very low concentrations. This activity is believed to be due to interference with invertebrate neurotransmission.[3] The combination of high invertebrate toxicity and low mammalian toxicity gives these compounds enormous potential as broad spectrum antiparasitic agents.[4]

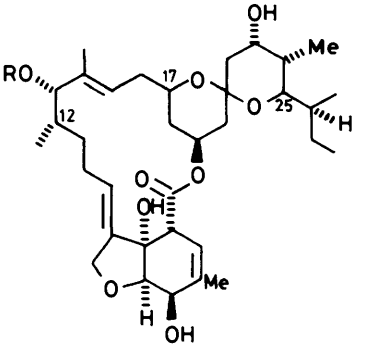
A feature common to all the avermectins and milbemycins is the spiroacetal moiety, three carbons of which form part of the 16-membered macrolide ring. Synthesis of the spiroacetal portion could form the basis of a total synthesis of any of these macrolides. Spiroacetals occur as important structural features in a variety of natural products; insect pheromones,[5] antibiotics,[6] and avian toxins[7] and have thus stimulated considerable synthetic endeavour. In addition many reports concerned with the synthesis of the spiroacetal portion of milbemycin β_3 have appeared in the literature[8–12] together with a few concerned with the synthesis of the more complex spiroacetals of the avermectin/milbemycin families.[13,14]

The most frequently employed methodology for the synthesis of spiroacetals is the addition of a nucleophile to a lactone followed by cyclisation. The efficacy of this approach is demonstrated by the variety of nucleophiles that have been employed. Acetylenes,[15] Grignard reagents,[8] the dianion of a β-diketone,[12] and α-lithio-sulphinyl carbanions[9] have all been used. Cyclisation to form the spirocentre is normally achieved *via* an intramolecular acetalisation onto the lactol.[15] Other methodologies have been used to generate a masked carbonyl that is deprotected in the spirocyclisation step. Dithianes,[16] dihydroisoxazoles,[17] and vinyl sulphides[18] have all been used in this context.

An alternative approach involves the reaction of sulphone-stabilised[19] or phosphine oxide-stabilised[20] 2-lithiotetrahydropyrans with a variety of electrophiles followed by cyclisation to form the spiroacetal. An extension of this strategy is the use of 2-lithiodihydropyrans.[21] A variety of cyclisations onto carbon–carbon multiple bonds have been employed, ranging from organoselenium-mediated electrophilic cyclisation[22] to intramolecular conjugate additions,[23] and double cyclisations onto acetylenes.[24] The hetero-Diels–Alder reaction has been used to generate a substituted dihydro-γ-pyrone,

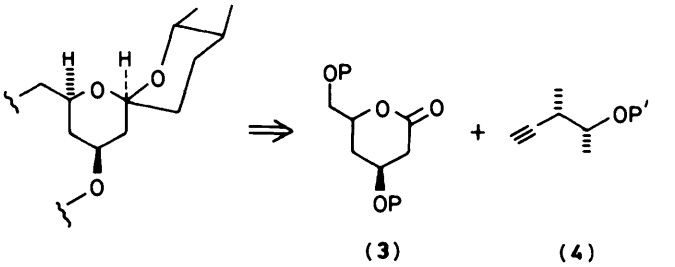


(**1**)



(**2**)

R = α-L-oleandrosyl-α-L-oleandrosyloxy



(**3**) (**4**)

subsequent cyclisation affording the spiroacetal.[25] A different approach to the cyclisation is the use of an oxy-radical, generated either chemically[26] or photochemically.[27]

From the outset it was our intention to develop a route that could be generally applied to all the milbemycins and avermectins, as well as to potentially important unnatural analogues. In this and the following paper we describe a synthetic strategy culminating in a total synthesis of (+)-milbemycin β_3.

Results and Discussion

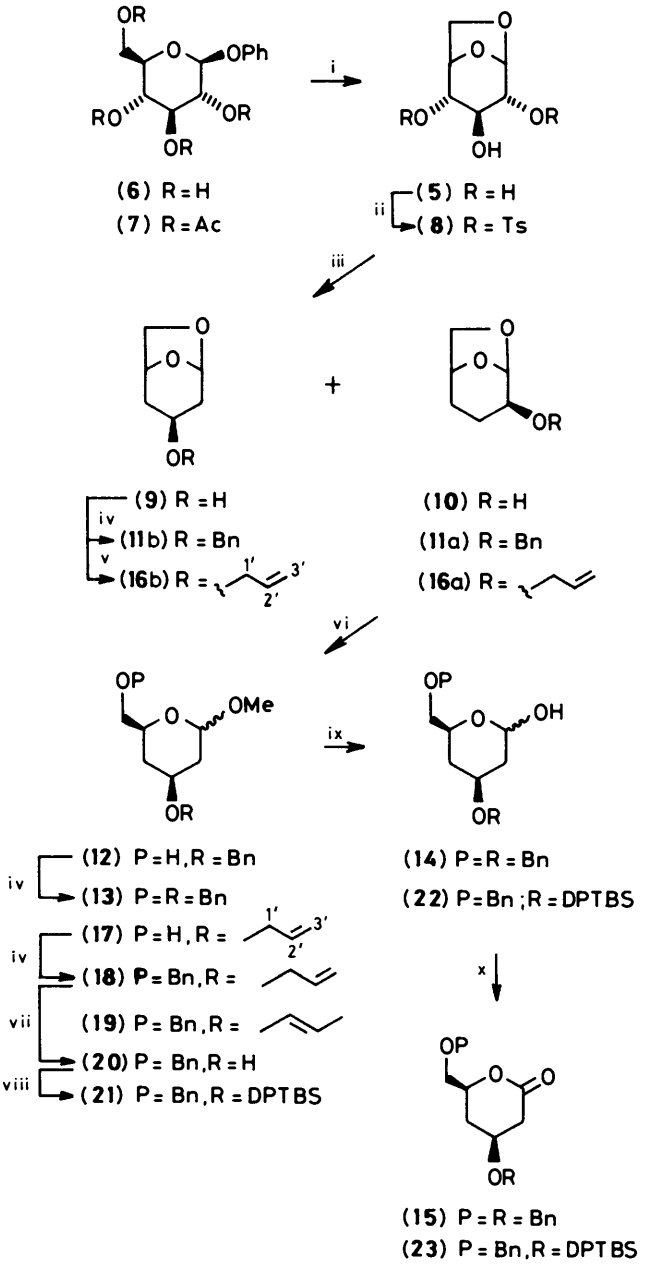
Within the spiroacetal moiety of the milbemycin/avermectin family there are two basic sources of variation, the alkyl group at C-25 and the different levels of oxidation at the C-22 and C-23 positions. The C-17 to C-21 ring segment is identical in all the milbemycins and avermectins.[1,2] A general entry into these families would require the flexibility for synthesis of all the analogues from a common advanced intermediate. With this objective in mind the chosen strategy was based on the coupling of a chiral acetylene (**4**) with the dioxygenated lactone (**3**). It was envisaged that the acetylene would contain the latent functionality to produce all the different oxidation levels required.

Preparation for Chiral Lactones (*Scheme 1*).—Laevoglucosan (**5**) contains several features required for the synthesis of the lactone (**3**). In particular, it provides the absolute stereochemistry at C-19 and C-17 and the oxygenation at C-21 and C-16. Laevoglucosan is available from the pyrolysis of starch.[28] However, although short, this route proved capricious. Alternative routes *via* basic hydrolysis of the phenyl glycosides (**6**) or (**7**) proved more convenient.[29,30] Treatment of laevoglucosan with 2 equiv. of toluene-*p*-sulphonyl chloride in a pyridine acetone mixture gave the ditosylate (**8**) in excellent yield.[31] Reduction of the ditosylate using lithium triethylborohydride [32] gave a mixture of two regioisomeric alcohols (**9**) and (**10**) in ratios varying from 3:1 to 13:1. These could be separated by column chromatography but subsequent results showed that this separation could be achieved more easily at a later stage (*vide infra*).

The alcohol was now protected as the benzyl ether (**11b**) and acid-catalysed methanolysis of the anhydro bridge afforded the methyl glycoside (**12**) in excellent overall yield. In addition it was noted that the acid-catalysed methanolysis of a mixture of the 2- and 3-benzyl ethers (**11a**) and (**11b**) caused exclusive cleavage of the 3-benzyl isomer (**11b**), the 2-benzyl ether being recovered unchanged from the reaction mixture. The selective cleavage of the anhydro bridge of the 3-substituted isomer is possibly due to the release of 1,3-diaxial interaction between the anhydro bridge and the axial C-3 benzyl ether. In the case of the isomeric ether (**11a**) this interaction is considerably reduced.

The primary alcohol was now protected as the benzyl ether (**13**) and the unveiling of the C-1 lactol moiety attempted. Treatment with aqueous acetic acid gave a very poor yield of the desired product. However, treatment of the methyl glycoside with a 10:1 mixture of tetrahydrofuran and 1M aqueous HCl at reflux for 6 h produced a 62% yield of the lactol (**14**) together with 31% of recovered methyl glycoside (**13**). Prolonged reaction times served only to reduce the yield of the desired product, presumably because of the slow hydrolysis of the benzyl ether. Oxidation of the lactol (**14**) to the required lactone (**15**) was achieved in 93% yield by the use of Fetizon's reagent.[33]

It was clear that it would be necessary at some point in the synthesis to differentiate between the two benzyl-protected hydroxy groups. Whilst selectivity of reaction between primary and secondary alcohols is well documented, an alternative solution would be to use differential protection. Accordingly a parallel study was undertaken to prepare a lactone with two different protecting groups. The alcohol (**9**) presents the first

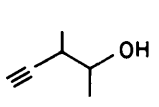


Scheme 1. *Reagents*: i, aq. KOH; ii, *p*-TsCl, py; iii, $LiEt_3BH$, THF; iv, NaH, $PhCH_2Br$; v, NaH, $CH_2{=}CHCH_2Br$; vi, MeOH, Amberlite IR 118; vii, $[Rh(PPh_3)_3]Cl$; MeOH, Amberlite IR 118; viii, DPTBSCl, KH; ix, THF–1M HCl, 10:1; x, Ag_2CO, Celite

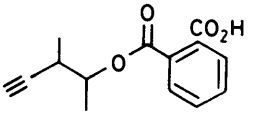
opportunity for selective protection of the secondary alcohol. Such a protecting group would have to withstand acid and basic reaction conditions and be sterically undemanding for introduction at such a hindered position. The allyl ether seemed best to serve these requirements. Reaction of the sodium alkoxide of alcohol (**9**) with allyl bromide gave the allyl ether (**16b**). Treatment with an acid catalyst in dry methanol afforded a mixture of the epimeric methyl glycosides (**17**). As in the case of the benzyl-protected ether (**11a**) the C-2 allyl ether (**16a**) remained inert under these conditions. The primary alcohol was now protected as the benzyl ether (**18**) in 93% yield. At this point it was decided to replace the allyl protecting group with the diphenyl-t-butylsilyl ether (DPTBS), which would be unaffected by the hydrogenation conditons employed at a later stage in the

synthesis. Introduction of this bulky protecting group in the presence of the anhydro bridge proved impossible. Removal of the allyl ether by treatment with Wilkinson's catalyst in methanol at reflux proceeded smoothly *via* the isomeric enol ether (**19**) to yield alcohol (**20**).[34] Subsequent reprotection as the DPTBS ether gave the required differentially protected product (**21**). Again, hydrolysis of the methylglycoside proved troublesome. However, treatment with a 20:1 mixture of tetrahydrofuran–1M HCl gave a 50% yield of the desired lactol (**22**) together with a substantial quantity of recovered starting material. Oxidation with Fetizon's reagent afforded the desired lactone (**23**) in excellent yield.

Preparation of the Chiral Acetylene.—We now turned our attention to the synthesis of the chiral acetylene (**3**) required for the spiroacetal moiety of milbemycin β_3. Our initial studies were centred on the resolution of the racemic compound. The racemic alcohol (**24**) was readily available from the reaction of lithium acetylide with *cis*-butene epoxide.[35] The alcohol (**24**)



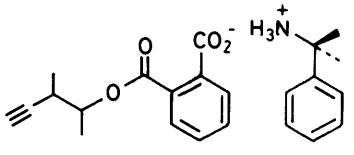
(**24**)



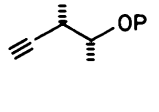
(**25**)

PhCH(Me)NH$_2$

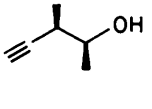
(**26**)



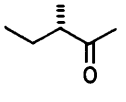
(**27**)



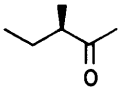
(**24b**) P = H
(**29**) P = THP



(**24a**)



(**28b**)

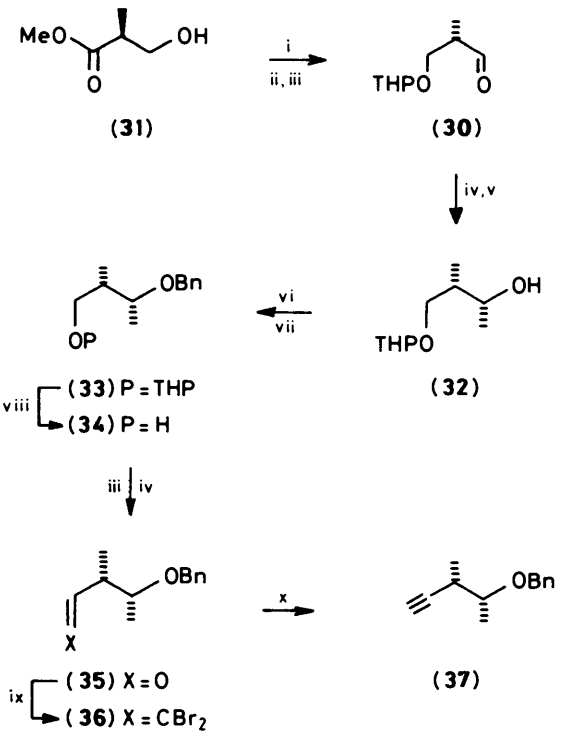


(**28a**)

was treated with phthalic anhydride to yield the half ester (**25**) in quantitative yield. Brucine, cinchonine, and cinchonidine all failed to yield crystalline salts, but treatment of the half ester with (−)-α-methylbenzylamine (**26**) did yield a crystalline salt (**27**). Repeated recrystallisation from a mixture of dichloromethane and acetone (1:1) yielded a salt with a constant optical rotation $[\alpha]_D$ − 1° (*c* 1, CH_2Cl_2). Degradation of the salt by treatment with 5M hydrochloric acid to release the half ester and saponification with aqueous sodium hydroxide gave the (−)-alcohol (**24a**) $[\alpha]_D$ − 20° in 81% yield from the salt. The enantiomeric excess was determined by formation of the MTPA ester[36] and analysis of the ^1H and ^{19}F n.m.r. spectra. The highest enantiomeric excess achieved was 88% e.e., and was routinely greater than 80% e.e. In a similar manner (+)-α-methylbenzylamine yielded the (+)-alcohol (**24b**).

All that remained was correlation of the absolute configuration with the optical rotation. Hydrogenation over palladium on charcoal followed by pyridinium chlorochromate (PCC) oxidation yielded the known chiral ketones (**28a**) and (**28b**).[37] Thus the required acetylene was (3*S*,4*R*)-(−)-3-methylpent-1-yn-4-ol (**24b**). Treatment of the alcohol (**24b**) with dihydropyran in the presence of an acid catalyst yielded the protected alcohol (**29**).

The difficulties encountered in performing the resolution led us to investigate an alternative approach (Scheme 2), taking

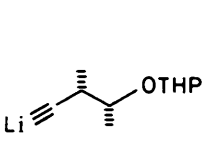


Scheme 2. *Reagents:* i, DHP, Et_2O, CSA; ii, $LiAlH_4$, Et_2O; iii, DMSO, $(COCl)_2$; iv, Et_3N; v, Me_2CuLi, Et_2O, −20 °C; vi, NaH, THF; vii, $PhCH_2Br$, viii, MeOH, CSA; ix, $Ph_3P{=}CBr_2$, THF, 0 °C; x, BuLi, THF, −80 °C

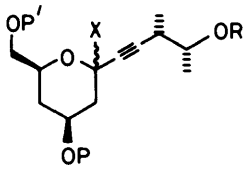
advantage of the work of Still *et al.* on chelation-controlled addition to β-oxy aldehydes.[38] The requisite aldehyde (**30**) was readily available from (*S*)-methyl-3-hydroxy-2-methylpropionate (**31**) by sequential protection, reduction, and oxidation. Treatment of the aldehyde (**30**) with lithium dimethylcuprate afforded the 'chelation controlled' product (**32**).[38] Protection of the alcohol as its benzyl ether (**33**) proceeded slowly, but the use of a catalytic amount of tetrabutylammonium iodide greatly accelerated the reaction. Deprotection of the primary alcohol (**34**) and preparation of the MTPA ester enabled the enantiomeric excess to be determined and shown to be greater than 95%. Swern oxidation[39] of the alcohol (**34**) yielded the aldehyde (**35**) and conversion into the dibromoolefin (**36**) followed by treatment with 2 equivalents of butyllithium afforded the required acetylene (**37**).[40]

Preparation of the Spiroacetals.—The scene was now set for the crucial union of the chiral lactone and acetylene and cyclisation to construct the spiro centre. Generation of the acetylide anion (**38**) at −60 °C followed by reaction of the lactone (**15**) for 1 h at −40 °C gave a poor yield of the desired hemiacetal together with substantial amounts of elimination products. Carrying out the reaction at −80 °C and quenching with an aqueous solution of sodium dihydrogen orthophosphate at −80 °C gave an excellent yield of the adduct (**39**). The hemiacetal exists in equilibrium with the open-chain hydroxy ketone (**40**). In order to aid purification, the equilibrium mixture was dissolved in methanol and treated with an acid catalyst. This served not only to trap the hemiacetal as the methoxyacetal but also removed the THP ether (**41**) to reveal the hydroxy function.

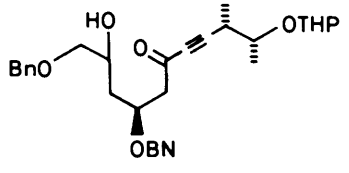
Hydrogenation and acid-catalysed cyclisation afforded the spiroacetal diol (**42**) as a white crystalline solid (m.p. 102 °C). A mono-protected spiroacetal could be prepared directly from the



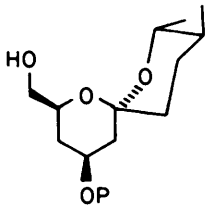
(38)



(39) P = P′ = Bn, R = THP, X = OH
(41) P = P′ = Bn, R = H, X = OMe
(43) P = DPTBS, P′ = Bn, R = THP, X = OH



(40)



(42) P = H
(44) P = DPTBS

differentially protected lactone (**21**). Reaction with the lithium acetylide (**38**) gave only a 30% yield of the desired hemiacetal (**43**). Despite considerable effort it proved impossible to improve the yield of this reaction. Following the protocol established previously, the hemiacetal was converted into the spiroacetal (**44**).[9] The acetylene (**37**) was also used in a similar manner, all the benzyl protecting groups being removed during the hydrogenation to yield the spiroacetal diol (**42**).

The cyclisation to form the spiro centre could, in theory, yield two diastereomeric products, each of which could exist in two different conformations. The single major product observed in each case can be explained by the preference for the desired spiroacetal to adopt the conformation in which all the substituents are equatorial and the ring oxygens are axially orientated to the adjacent ring thus gaining additional stabilisation from the anomeric effect.[41] Confirmation of the assigned structure of the spiroacetal was obtained by detailed examination of the highfield ^{1}H n.m.r. aided by 2D n.m.r. In particular the large coupling between 2-H and 3-H (J 10 Hz), indicating a *trans* diequatorial disposition of the methyl substituents, and the downfield shift of 10-H (δ 4.2) indicative of a 1,3-diaxial arrangement of 10-H and the anomeric oxygen of the adjacent ring.

With a chiral synthesis of the spiroacetal moiety of milbemycin β_3 in hand we turned our attention towards the total synthesis of (+)-milbemycin β_3 described in the following paper.[42] In addition, access to multigram amounts of the key chiral lactones (**15**) and (**23**), has provided common advanced intermediates for use in investigations into the development of a synthetic strategy towards the more highly functionalised spiroacetals of the milbemycin/avermectin families.[1,2]

Experimental

I.r. spectra were recorded on a Pye-Unicam SP3-100 spectrophotometer using polystyrene as standard. ^{1}H, ^{13}C, and ^{19}F n.m.r. spectra were recorded either on a Hitachi-Perkin-Elmer R-24B (60 MHz) spectrometer, a Varian Associates XL-100-12 (100 MHz) spectrometer, or a Bruker AM-360 (360 MHz) spectrometer; J values in Hz. Tetramethylsilane was used as standard, and deuteriochloroform used as solvent unless otherwise stated. Mass spectra were recorded using a Kratos MS-30 spectrometer equipped with a Nova-3 computer and a DS 50S data system, using electron impact (e.i.) or chemical ionization (c.i.). M.p.s were measured on a Reichert Koffler hot-stage melting point apparatus and are uncorrected. Optical rotations were measured on an Optical Activity Ltd. AA-100 polarimeter using a 5-cm cell. Flash chromatography was performed according to the procedure of Still *et al.*[43] using Macherey-Nagel Kieselgel 60 (230—400 mesh). High-pressure liquid chromatography (h.p.l.c.) was performed on a Waters 6000A chromatograph equipped with either a u.v. or refractive index detector. Normal phase separations were carried out using a Zorbax Sil column whilst reverse phase were carried out on a Zorbax ODS column. Gas liquid chromatography (g.l.c.) was performed on a Pye series 104 chromatograph equipped with a flame ionization detector. Elemental analyses were carried out by the microanalytical laboratory, University College, London. All solvents were purified before use; light petroleum refers to the fraction boiling in the range 40—60 °C, and ether refers to diethyl ether.

1,6-*Anhydro*-β-D-gluco-*pyranose* (*Laevoglucosan*) (**5**).—A solution of β-phenylgucoside (100 g, 0.39 mol) in 1.3M aqueous potassium hydroxide (**11**) was heated at gentle reflux for 9 h. The dark solution was cooled to room temperature and neutralised with 10% aqueous sulphuric acid. The water was then evaporated under reduced pressure (10 mmHg) to yield a brown semisolid. This was extracted with absolute ethanol (3 × 500 ml). The extracts were then evaporated at reduced pressure to yield a buff-coloured oil which crystallised with time (59.8 g, 94%). This was sufficiently pure to use in the next step, but a small amount was further purified by recrystallisation from ethanol to yield the pure title compound (**5**) as a white crystalline solid, m.p. 172 °C (lit., 172 °C).[28]

1,6-*Anhydro*-2,4-*dideoxy*-β-D-threo-*hexopyranose* (**9**).—To a stirred solution of the 1,6-anhydro-2,4-bis(*p*-tolylsulphonyloxy)-β-D-*gluco*-hexapyranose (**8**)[31] (27 g, 57 mmol) in dry tetrahydrofuran (THF) (150 ml) under a nitrogen atmosphere at 0 °C was added lithium triethylborohydride (Super hydride) (1M in THF; 340 ml, 0.34 mol) over a period of 12 h. The reaction mixture was then stirred for 4 days at 20 °C. Water (40 ml) was then carefully added dropwise at 0 °C and this was followed by addition of 3M aqueous sodium hydroxide (130 ml) and 30% aqueous hydrogen peroxide (120 ml). The resulting solution was stirred for 4 h at room temperature; the mixture was then continuously extracted for 2 days with ether. The ethereal extracts were then dried ($MgSO_4$) and evaporated under reduced pressure. This afforded a pale yellow oil (13 g) which was purified by column chromatography on Florosil using ether as the eluant, to yield the title compound (**9**),[32] and 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hexopyranose (**10**)[32] (5.6 g, 75%) in a ratio of 13:1.

1,6-*Anhydro*-2,4-*dideoxy*-3-O-*benzyl*-β-D-threo-*hexopyranose* (**11b**).—To a slurry of pentane-washed sodium hydride (0.9 g, 38 mmol) in dry THF (20 ml) under an atmosphere of nitrogen at 0 °C was added a solution of the hexopyranose (**9**) (4.5 g, 35 mmol) in dry THF (50 ml). The mixture was then stirred for 1 h before the addition of benzyl bromide (6.5 g, 38 mmol). The reaction mixture was then stirred overnight at room temperature before the addition of water (40 ml). The organic phase was separated, the aqueous phase extracted with ether (2 × 20 ml), and the combined organic extracts were dried (K_2CO_3). The solvent was then removed under reduced pressure to yield a pale yellow oil. Purification by flash chromatography (ether–light petroleum) afforded the title compound (**11b**) (6.2 g, 80%); $\nu_{max.}$($CDCl_3$) 2 950, 2 920, 1 640, and 1 090 cm^{-1}; δ_H (60 MHz) 1.1—2.0 (4 H, m, 2 × CH_2), 3.5—3.8 (2 H, m, 3-H, *exo*-6-H), 4.3 (1 H, d, J 7, *endo*-6-H), 4.35 (1 H, m, 5-H), 4.6 (2 H, s, CH_2), and 7.3 (5 H, s, Ph); m/z 221 (M^+, 1%) 114 (5), 92 (15), and 91 (100).

Methyl 2,4-*Dideoxy*-3-O-*benzyl*-α- *and* β-D-threo-*hexopyranosides* (**12**).—The hexopyranose (**11b**) (4.3 g, 20 mmol) was dissolved in dry methanol (100 ml) and Amberlite IR118 (H^+) (110 mg) was added; the resulting suspension was stirred at room temperature until t.l.c. analysis indicated that the reaction was complete. The resin was then filtered off and the solvent removed at reduced pressure. Flash chromatography (ether) afforded the title compounds (**12**) (4.75 g, 95%), as a syrup (ratio 20:1); δ_H (60 MHz) 1.1—2.1 (4 H, m, 2 × CH_2), 2.3 (1 H, br s, OH), 3.1 and 3.3 (3 H combined, s, OMe), 3.5—3.9 (4 H, m, 2 × HCO + CH_2O), 4.5 (2 H, s, benzylic), 4.8 (1 H, br s, 1-H), and 7.3 (5 H, s, Ph). A small sample was repurified by flash chromatography (ether) to afford a pure sample of the major epimer methyl 2,4-dideoxy-3-*O*-benzyl-α-D-*threo*-hexopyranoside; $[\alpha]_D^{20}$ +111° (*c* 1.0, MeOH); $\nu_{max.}$(CH_2Cl_2) 3 430 (OH), 2 920, 2 890, 1 630, and 1 080 cm^{-1}; δ_H (360 MHz) 1.3 (1 H, ddd, *J* 12, 12, and 12, 4_{ax}-H), 1.49 (1 H, ddd, *J* 12, 11.4, 3.4, 2_{ax}-H), 1.91 (1 H, dddd, *J* 12, 5, 2.5, and 2, 4_{eq}-H), 2.04 (1 H, t, *J* 6, OH), 2.17 (1 H, dddd, *J* 12, 4, 2.4, and 2, 2_{eq}-H), 3.2 (3 H, s, OMe), 3.4—3.6 (2 H, m, CH_2O), 3.73 (1 H, dddd, *J* 12, 12, 2.5, and 2.5, 5-H), 3.83 (1 H, dddd, *J* 12, 11.4, 2.5, and 2.4, 3-H), 4.47 (2 H, s, benzylic), 4.82 (1 H, d, *J* 3.4, 1-H), and 7.25 (5 H, m, Ar); *m/z* 221 (1%, M^+ − OMe), 202 (1), 120 (8), 114 (11), 113 (10), 91 (100), and 70 (21).

Methyl 2,4-*Dideoxy*-3,6-*di*-O-*benzyl*-α- *and* β-D-threo-*hexopyranosides* (**13**).—A solution of the alcohol (**12**) in dry THF was added dropwise to a pentane-washed slurry of sodium hydride (0.8 g, 35 mmol) in dry THF at 0 °C under nitrogen. The resulting slurry was then stirred for 2 h at room temperature. Benzyl bromide (4.5 ml, 6.5 g, 38 mmol) was added dropwise and the reaction stirred at room temperature overnight. Water (50 ml) was then added and the resulting mixture extracted with ether (3 × 50 ml). The combined ether extracts were dried ($MgSO_4$) and the solvent removed at reduced pressure to yield an orange oil. Purification by flash chromatography (light petroleum–ether, 2:1) afforded the title compounds (**13**) as a syrup (5.05 g, 93%); δ_H (60 MHz) 1.0—2.1 (4 H, m, 2 × CH_2), 3.1—4.1 (7 H, m), 4.6 (4 H, s, 2 × CH_2Ph), 4.8 (1 H, br s, 1-H), and 7.3 (10 H, s, Ph); a small quantity of the mixture was subjected to flash chromatography (light petroleum) to afford a sample of pure methyl 2,4-dideoxy-3,6-*O*-benzyl-α-D-*threo*-hexopyranoside; $[\alpha]_D$ +80° (*c* 0.5, MeOH); $\nu_{max.}$($CHCl_3$) 2 920, 2 870, 1 650, and 1 120 cm^{-1}; δ_H (360 MHz) 1.44 (1 H, dm, *J* 12, 4_{ax}-H), 1.6 (1 H, ddd, *J* 12.5, 12, and 2.8, 2_{ax}-H), 2.07 (1 H, dddd, *J* 12, 4.5, 2.2, and 1.9, 4_{eq}-H), 2.2 (1 H, ddd, *J* 12.5, 4.7, 1.8, 2_{eq}-H), 3.34 (3 H, s, OMe), 3.53 (2 H, m, CHO), 3.9 (2 H, m, 5- and 3-H), 4.54 (2 H, s, benzylic), 4.58 (2 H, s, benzylic), 4.91 (1 H, d, *J* 2.8, 1-H), and 7.3 (10 H, m, Ar); *m/z* 219 (23%), 204 (4), 163 (2), 115 (3), 113 (6), 105 (4), and 91 (100).

2,4-*Dideoxy*-3,6-*di*-O-*benzyl*-α- *and* β-D-threo-*hexopyranoses* (**14**).—The methyl glycoside (**13**) (5 g, 146 mmol) was dissolved in THF (60 ml) and 1M hydrochloric acid (5 ml) added; further THF was added until the mixture appeared homogenous (*ca.* 20 ml). The resulting solution was heated under reflux under a nitrogen atmosphere for 7 h. The mixture was allowed to cool to room temperature and then diluted with ether (100 ml); the organic phase was separated and the aqueous phase extracted with ether (2 × 50 ml). The combined organic extracts were washed with brine (50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to afford an oil. Purification of this by flash chromatography yielded starting material (**13**) (1.55 g, 31%) and the title compounds (**14**) as an oil (2.97 g, 62%); $\nu_{max.}$($CDCl_3$) 3 500 (OH), 2 930, 2 800, 1 720 (CO), 1 650, and 1 120 cm^{-1}; δ_H (60 MHz) 1.2—2.2 (4 H, m, 2 × CH_2), 3.1—4.3 (4 H, m, 3- and 5-H, 2 × 6-H), 4.5 (4 H, s, CH_2Ph), 5.4 (1 H, br s, 1-H), and 7.3 (10 H, s, Ph); *m/z* 219 (10%), 115 (3), 113 (6), 105 (10), and 91 (100).

(4S,6S)-4-*Benzyloxy*-6-*benzyloxymethyltetrahydropyran*-2-*one* (**15**).—The lactol (**14**) (2.5 g, 7.6 mmol) was dissolved in dry toluene (70 ml) and freshly prepared Fetizons reagent (13 g, 23 mmol) (**19**) was added. The stirred suspension was heated at reflux until t.l.c. analysis (ether) indicated that the reaction was complete (*ca.* 3 h). The black precipitate was then removed by filtration through Celite and the filtrate evaporated under reduced pressure to afford an oil. Purification by flash chromatography (ether) afforded the title compound (**15**) as a colourless oil (2.3 g, 93%); $[\alpha]_D$ 15° (*c* 1, CH_2Cl_2); $\nu_{max.}$ 2 920, 2 870, 1 730 (CO), 1 640, and 1 130 cm^{-1}; δ_H (100 MHz) 1.5—2.2 (2 H, m, CH_2), 2.3—2.9 (2 H, m, CH_2CO), 3.6 (2 H, d, *J* 5, CH_2O), 3.8—4.4 (2 H, m, CHO), 4.5 (4 H, br s, CH_2Ar), and 7.2 (10 H, m, Ar); *m/z* (c.i., NH_3) 344 (3%, $M^+NH_4^+$), 327 (1, *M* + 1), 136 (3), 129 (4), 113 (3), 109 (2), 108 (28), 107 (32), 91 (100), and 79 (29).

1,6-*Anhydro*-2,4-*dideoxy*-3-O-*allyl*-β-D-threo-*hexopyranose* (**16b**).—To a slurry of pentane-washed sodium hydride (0.5 g, 21 mmol) in dry THF (20 ml) under nitrogen was added a solution of the hexopyranose (**9**) (2 g, 15 mmol) in dry THF (20 ml). The resulting suspension was stirred overnight at room temperature. Allyl bromide (5 ml, 7 g, 58 mmol) was added dropwise and the reaction mixture stirred at room temperature for a further 2 h; it was then cooled to 0 °C and water (30 ml) added cautiously. The mixture was then diluted with ether (50 ml) and the organic phase separated; the aqueous phase was extracted with ether (2 × 30 ml) and the combined organic phases were washed with brine (30 ml), dried (K_2CO_3), and evaporated under reduced pressure to yield a yellow oil which was purified by flash chromatography (ethyl acetate–light petroleum, 1:5) to yield the title compound (**16b**) as a colourless oil (1.75 g, 67%); $[\alpha]_D^{22}$ −70° (*c* 0.95, CH_2Cl_2); $\nu_{max.}$($CHCl_3$) 2 960, 2 900, 1 640, 1 330, 1 130, and 1 030 cm^{-1}; δ_H (60 MHz) 1.6—2.2 (4 H, m, 2 × CH_2), 3.5—3.8 (2 H, m), 3.9 (2 H, d, *J* 4, OCH_2), 4.3 (1 H, d, *J* 6, *endo*-6-H), 4.4—4.5 (1 H, m, 5-H), and 5.1 (1 H, br s, 1-H); *m/z* 129 (8%), 125 (14), 115 (60), 113 (25), 84 (21), 83 (39), 82 (14), 71 (27), 69 (100), 67 (57), 57 (32), 55 (41), and 41 (37).

Methyl 2,4-*Dideoxy*-3-O-*allyl*-α *and* β-D-threo-*hexopyranoside* (**17**).—Methanol-washed Amberlite IR 118 (H^+) (100 mg) was added to a stirred solution of the hexopyranose (**16b**) (1.5 g, 8.8 mmol) in dry methanol (20 ml) and the resulting suspension stirred overnight at room temperature. The resin was then filtered off and the filtrate evaporated under reduced pressure. The residue was purified by flash chromatography (ether) to yield the title compounds (**17**) (20:1) as a colourless oil (1.7 g, 95%); a small amount was repurified by flash chromatography to afford a pure sample of the major isomer methyl 2,4-dideoxy-3-*O*-allyl-α-D-*threo*-hexopyranoside as a colourless oil, $[\alpha]_D^{22}$ + 138° (*c* 1.0, CH_2Cl_2); $\nu_{max.}$($CHCl_3$) 3 440 (OH), 2 920, 1 630, 1 120, and 1 080 cm^{-1}; δ_H (100 MHz) 1.35 (1 H, m, 4_{ax}-H), 1.6 (1 H, m, 2_{ax}-H), 1.95 (1 H, m, 4_{eq}-H), 2.1 (1 H, m, 2_{eq}-H), 2.45 (1 H, br s, OH), 3.3 (3 H, s, OMe), 3.5—3.9 (4 H, m), 4.6 (2 H, d, *J* 6 Hz, OCH_2C=), 4.85 (1 H, br d, *J* 2 Hz, 1-H), 5.15 (1 H, br dd, *J* 12 and 2, < 1 Hz, *anti*-3′-H), 5.3 (1 H, dd, H 9 and < 1 Hz, *syn*-3′-H), and 5.9 (1 H, ddt, *J* 12, 9, and 6 Hz, 2′-H); *m/z* 171 (OMe, 19%), 115 (24), 113 (100), 85 (66), 84 (24), 71 (39), 67 (19), 58 (18), and 55 (20).

Methyl 2,4-*Dideoxy*-6-O-*benzyl*-3-O-*allyl*-α *and* β-D-threo-*hexopyranosides* (**18**).—A solution of the hexopyranosides (**17**) (1.6 g, 7.9 mmol) in THF (10 ml) was added to a slurry of pentane-washed sodium hydride (0.5 g, 10 mmol) in dry THF (20 ml). After the reaction had subsided, benzyl bromide (2 ml,

1.9 g, 16.8 mmol) in dry THF (20 ml) was then added and the resulting mixture stirred at room temperature for 2 h. Water (40 ml) was then added at 0 °C followed by ether (50 ml). The organic phase was separated, the aqueous phase extracted with ether (2 × 20 ml), and the combined organic extracts were washed with brine (30 ml) and dried (K_2CO_3). The solvent was removed at reduced pressure and the residue purified by flash chromatography (ethyl acetate–light petroleum, 1:5) to yield the title compounds (**18**) as a colourless oil (2.15 g, 93%); $\nu_{max.}$ 2 940, 2 900, 1 650, 1 110, and 1 060 cm^{-1}; δ_H (60 MHz) 1.0—2.3 (4 H, m, 2 × CH_2), 3.25 (3 H, s, OMe), 3.3—3.8 (4 H, m, 2 × OCH, CH_2O), 3.95 (2 H, d, *J* 6, allylic CH_2), 4.5 (2 H, s, CH_2Ph), 4.75 (1 H, br d, *J* × 1-H), 5.1 (1 H, dd, *J* 9, and 2, *syn*-3′-H), 5.2 (1 H, dd, *J* 15 and 2, *anti*-3′-H), 5.9 (1 H, ddt, *J* 15, 9, and 6, 2-H), and 7.3 (5 H, s, Ph); *m/z* 223 (2%), 131 (10), 113 (5), and 91 (100).

Methyl 2,4-*Dideoxy*-6-O-*benzyl*-α- *and* β-D-threo-*hexopyranosides* (**20**).—To a solution of the hexopyranosides (**18**) (2.15 g, 7.4 mmol) in dry methanol (20 ml) was added tris(triphenylphosphine)rhodium(I) chloride (100 mg). The resulting mixture was heated under reflux and the reaction monitored by t.l.c. (ethyl acetate–light petroleum, 1:5). After 2 h t.l.c. indicated the presence of a less-polar product and continued heating overnight afforded a single more-polar product. The solvent was removed under reduced pressure and the residue purified by flash chromatography (ethyl acetate) to yield the title compounds (**20**) (1.75 g, 95%) as a colourless oil; $\nu_{max.}$($CHCl_3$) 3 350 (OH), 2 950, 2 930, 1 640, and 1 340 cm^{-1}; δ_H (60 MHz) 1—2.1 (4 H, m, 2 × CH_2), 3.3 (3 H, s, OMe), 3.4—4.3 (5 H, m, OH, HCO, and CH_2O), 4.6 (2 H, s, CH_2Ph), 4.8 (1 H, br d, *J* 4, 1-H), and 7.4 (5 H, s, Ph); *m/z* 221 (M^+ − OMe, 2%) 202 (18), 131 (6), 113 (30), 107 (16), 91 (100), 87 (9), and 59 (13).

Methyl 2,4-*Dideoxy*-3-O-*diphenyl*-t-*butylsilyl*-6-O-*benzyl*-α- *and* β-D-threo-*hexopyranosides* (**21**).—A solution of the hexopyranosides (**20**) (1.9 g, 77.7 mmol) in dry dimethylformamide (DMF) (10 ml) were added to a solution of chloro(diphenyl)-t-butylsilane (2.1 g, 7.7 mmol) and imidazole (1.02 g, 15 mmol) in DMF (10 ml) and the resulting mixture was stirred at room temperature overnight. It was then diluted with a mixture (1:1) of ether–light petroleum (100 ml), washed with water (3 × 50 ml), and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue purified by flash chromatography (light petroleum–ether, 2:1) to afford the title compounds (**21**) (3.2 g, 86%); $\nu_{max.}$ 2 950, 2 900, 1 640, 1 620, 1 130, and 1 050 cm^{-1}; δ_H (60 MHz) 1.0 (9 H, s, Bu^t), 1.1—2.2 (4 H, m, 2 × CH_2), 3.1—3.8 (7 H, m, CHO, CH_2O, OMe), 4.5 (2 H, s, CH_2Ph), 4.7 (1 H, br s, 1-H), and 7.2—7.9 (15 H, m, Ar); *m/z* (c.i., NH_3) 508 ($M^+NH_4^+$, 11%), 265 (24), 234 (11), 233 (23), 217 (11), 216 (19), 207 (53), 203 (40), 199 (24), 157 (49), and 91 (100).

2,4-*Dideoxy*-3-O-*diphenyl*-t-*butylsilyl*-6-O-*benzyl*-α- *and* β-D-threo-*hexopyranoses* (**22**).—The hexopyranosides (**21**) (2.3 g, 4.8 mmol) were dissolved in THF (30 ml) and 1M hydrochloric acid (2 ml) was added together with a small amount of THF (*ca.* 5 ml) to achieve an homogeneous solution. The resulting solution was heated at reflux for 5 h. After cooling, ether (50 ml) was added and the organic phase separated; the aqueous layer was extracted with ether (2 × 20 ml) and the combined ether phases were washed with water (30 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the resulting oil purified by flash chromatography (ethyl acetate–light petroleum, 1:4) to afford starting material (**21**) (0.85 g, 37%) and the title compounds (**22**) as a colourless oil (1.15 g, 52%); $\nu_{max.}$ 3 420 (OH), 2 930, 2 860, 1 740 (C=O), 1 140, and 700 cm^{-1}; δ_H (60 MHz) 1.0 (9 H, s, Bu^t), 1.2—2.2 (4 H, m, 2 × CH_2), 2.6 (1 H, br s, OH), 3.3—4.3 (4 H, m, 2 × HCO, CH_2O), 4.5 (2 H, s, CH_2Ph), 5.4 (1 H, br s, 1-H), and 7.3—7.9 (15 H, m, Ar); *m/z* (c.i., NH_3), 476 (M^+, 3%), 233 (23), 207 (30), 203 (23), 157 (47), and 91 (100).

(4S,6S)-3-*Diphenyl*-t-*butylsiloxy*-6-*benzyloxymethyltetrahydropyran*-2-*one* (**23**).—2,4-Dideoxy-3-*O*-diphenyl-t-butylsilyl-6-*O*-benzyl-α- and β-D-*threo*-hexopyranose (**22**) (1.1 g, 2.4 mmol) was dissolved in dry toluene (30 ml) and freshly prepared Fetizons reagent added (7 g, 12 mmol). The resulting suspension was heated under reflux until t.l.c. (ethyl acetate–light petroleum, 1:4) indicated that the reaction was complete. The precipitate was then filtered off and the filtrate evaporated under reduced pressure to yield a colourless oil. Purification by flash chromatography afforded the title compound (**23**); (0.79 g, 70%); $[\alpha]_D$ +10.4 (*c* 1.0, CH_2Cl_2); $\nu_{max.}$($CHCl_3$), 2 930, 2 860, 1 740 (C=O), 1 115, and 730 cm^{-1}; δ_H (360 MHz) 1.05 (9 H, s, Bu^t), 1.84 (1 H, ddd, $J_{4a,4eq}$ 13, $J_{4ax,3}$ 12, $J_{4ax,5}$ 9, 4_{ax}-H), 2.05 (1 H, dddd, $J_{4eq,4ax}$ 13, $J_{4eq,3}$ 5, $J_{4eq,3}$ 3.5, $J_{4eq,2eq}$ 1.5, 4_{eq}-H), 2.5 (1 H, dd, $J_{2ax,2eq}$ 17, $J_{2ax,3}$ 7.8, 2_{ax}-H), 2.68 (1 H, ddd, $J_{2eq,2ax}$ 17, $J_{2eq,3}$ 5.8, $J_{2eq,4eq}$ 1.5, 2_{eq}-H), 3.57 (2 H, m, CH_2O), 4.12 (1 H, m, 3-H), 4.18 (1 H, m, 5-H), 4.56 (2 H, s, benzylic H), and 7.2—7.7 (15 H, m, Ar); *m/z* (c.i., NH_3) 492 (33%, $M^+NH_4^+$), 274 (10), 249 (14), 236 (13), 199 (15), 105 (30), and 91 (100).

3-*Methylpent*-4-*yn*-2-*yl Hemiphthalate* (**25**).—(±)-3-Methylpent-4-yn-2-ol[35] (**24**) (6.9 g, 70 mmol) and phthalic anhydride (15.6 g, 105 mmol) were dissolved in a mixture of benzene (100 ml) and pyridine (50 ml). The resulting solution was heated at reflux for 12 h after which it was cooled and diluted with ether (150 ml); 1M hydrochloric acid was then added (500 ml). The two phases were vigorously mixed and the pH of the aqueous phase adjusted to pH 4 by the dropwise addition of concentrated hydrochloric acid. The aqueous phase was then separated and extracted with ether (2 × 25 ml). The combined ether extracts were extracted with 1M aqueous ammonia 2 × 250 ml). The combined aqueous extracts were acidified with concentrated hydrochloric acid, extracted with ether (2 × 250 ml), and the ether extracts dried ($MgSO_4$) and evaporated under reduced pressure to yield a colourless oil (17 g). This was purified by flash chromatography (ether–light petroleum, 2:1) to yield the title compound (**25**) as a white solid (16 g, 91%), m.p. 52—53 °C; $\nu_{max.}$ 3 320 (=CH), 2 500—3 000 (OH), 1 730 (CO ester), 1 700 (CO acid), 1 280, 1 120, and 1 080 cm^{-1}; δ_H (60 MHz), 1.2 (3 H, d, *J* 7, =CCHMe), 1.4 (3 H, d, *J* 6, OEt), 2.07 (1 H, d, *J* 3, CH), 2.8 (1 H, m, =CCH), 5.2 (1 H, m, CHO), and 7.7—7.9 (4 H, m, Ar); *m/z* 247 (M^+, 2%), 193 (1), 167 (10), 150 (10), 149 (100), 98 (9), 81 (15), and 65 (9).

Resolution of 3-*Methylpent*-4-*yn*-2-*yl Hemiphthalate* (**25**).—(−)-α-Methylbenzylamine (**26**) (20 g, 0.16 mol) was added to a warm (40 °C) stirred solution of the hemiphthalate (**25**) (44.7 g, 0.18 mol) in anhydrous acetone (500 ml). After the addition the solution was allowed to cool to room temperature overnight. The white precipitate produced was filtered off, washed with dry ether (100 ml), and recrystallised repeatedly (7×) from dichloromethane–acetone (1:1) to yield the *resolved salt* (**27**) (5.1 g, 17%), m.p. 154—156 °C; $[\alpha]_D$ −1° (*c* 1.0, CH_2Cl_2) (Found: C, 71.9; H, 6.9; N, 3.8. $C_{22}H_{25}NO_4$ requires C, 71.9; H, 6.7; N, 3.85%); $\nu_{max.}$ 3 300 (=CH), 2 560, 2 200, 1 720 CO, ester), 1 630 (CO, acid), 1 540, 1 270, and 1 080 cm^{-1}.

(3S,4R)-3-*Methylpent*-4-*yn*-2-*ol* (**24b**).—A suspension of the salt (**27**) (5.1 g, 13.9 mmol) in ether (150 ml) was vigorously stirred with 0.5M hydrochloric acid (100 ml) at room temperature for 2 h. The organic phase was separated, the aqueous phase extracted with ether (3 × 50 ml), and the

combined ether extracts were then washed with 1M hydrochloric acid (100 ml) and water (100 ml). The ether solution was then reduced to *ca.* 100 ml under reduced pressure and stirred with 1.5M aqueous sodium hydroxide (50 ml) at room temperature for 3 h. The organic phase was separated, the aqueous phase extracted with ether (2 × 50 ml), and the combined ether extracts were washed with water (100 ml), dried ($MgSO_4$), and the solvent removed under reduced pressure. The crude product was then purified by distillation under reduced pressure to yield the title compound (**24b**), b.p. 65 °C at 55 mmHg (lit.,[35] 65 °C at 55 mmHg), $[\alpha]_D^{20}$ −23° (*c* 2.4, CH_2Cl_2). In a similar manner, resolution yielded (3*R*,4*S*)-3-methylpent-4-yn-2-ol (**24a**), b.p. 65 °C at 55 mmHg; $[\alpha]_D^{20}$ +22.8° (*c* 2.3, CH_2Cl_2).

(S)-(+)-3-*Methylpentan*-2-*one* (**28b**).—To a solution of the pentynol (**24b**) (33 mg, 0.34 mmol) in pentane (10 ml) was added 10% palladium on charcoal (5 mg) and the suspension was stirred under an atmosphere of hydrogen. After complete reaction (g.l.c. FFAP at 85 °C) the catalyst was removed by filtration through Celite and the pentane distilled off at atmospheric pressure. The residue was dissolved in methylene dichloride (10 ml) and PCC (81 mg, 0.38 mmol) added. After being stirred under argon for 1 h, the reaction mixture was diluted with pentane (40 ml), filtered through a small pad of silica, and the filtrate evaporated at atmospheric pressure to yield the title compound (**28b**) (21 mg, 62%), b.p. 118 °C (lit.,[37] b.p. 118 °C); $[\alpha]_D^{22}$ +6.4° (*c* 1.5, CH_2Cl_2) (lit.,[37] $[\alpha]_D$ +8.4° neat). In a similar manner (3*R*,4*S*)-3-methylpent-4-yn-2-ol (**24a**) (38 mg, 0.39 mmol) afforded (*R*)-(−)-3-methylpentan-2-one (**28a**) (18 mg, 46%), b.p. 118 °C; $[\alpha]_D^{20}$ −5.9° (*c* 1.4, CH_2Cl_2).

(3S,4R)-4-*Tetrahydropyranyloxy*-3-*methylpent*-1-*yne* (**29**).—To a stirred solution of the pentynol (**24b**) (0.22 g, 2.2 mmol) in dry ether (50 ml) was added dihydropyran (0.7 g, 8.3 mmol) and camphorsulphonic acid (10 mg). The resulting mixture was stirred at room temperature for 3 h after which potassium carbonate (20 mg) was added and the stirring continued for 10 min. The solids were then filtered off and the filtrate evaporated under reduced pressure. The residue was purified by distillation at reduced pressure to afford the *title compound* (**29**) (0.36 g, 88%), b.p. 95 °C at 20 mmHg (Found: C, 72.8; H, 10.0. $C_{11}H_{18}O_2$ requires C, 72.8; H, 10.05%); $\nu_{max.}$ 3 300 (=CH), 2 100 (C=C), 1 140, 1 120, and 1 030 cm^{-1}; δ_H (60 MHz) 1.1—1.4 (6 H, m, 2 × CH_3), 1.6—1.9 (6 *H*, m, 3 × CH_2), 2.05 (1 H, d, *J* 3, CH), 2.7 (1 H, m, C=CCH), 4.1—3.6 (3 H, m, OCHCH, and OCH_2), and 4.7 (1 H, br s, OCHO).

(R)-(−)-2-*Methyl*-3-(*tetrahydropyran*-2-*yloxy*)*propan*-1-*ol*.—Camphorsulphonic acid (10 mg) was added to a solution of (*S*)-methyl 3-hydroxy-2-methylpropionate (**31**) (20 g, 0.17 mol) and dihydropyran (20 g, excess) in dry ether (150 ml), and the resulting mixture stirred overnight. Potassium carbonate (1 g) was then added and the suspension stirred for 10 min, filtered, and then added to a cooled (0 °C) suspension of lithium aluminium hydride (6 g, 0.16 mol) in dry ether (100 ml) under argon. The mixture was stirred overnight after which water (6 ml), 10% aqueous sodium hydroxide (6 ml), and water (20 ml) were added. The mixture was filtered and the filtrate dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by distillation to yield the title compound (28 g, 95%); b.p. 95—98 °C at 4 mmHg (lit.,[29] 96—99 °C at 4 mmHg).

(S)-2-*Methyl*-3-(*tetrahydropyran*-2-*yloxy*)*propan*-1-*al* (**30**).—A solution of dimethyl sulphoxide (DMSO) (14.04 g, 2.4 equiv.) in CH_2Cl_2 (30 ml) was added slowly to a solution of oxalyl chloride (10.4 g, 1.1 equiv.) in CH_2Cl_2 (30 ml) at −60 °C under argon. The mixture was stirred at −60 °C for 15 min after which a solution of the alcohol (**31**) (13 g, 74 mmol) in CH_2Cl_2 (30 ml) was added and the resulting cloudy solution stirred for 10 min; triethylamine (38 g) was then added and the reaction mixture allowed to warm to room temperature. The reaction mixture was then washed with water (50 ml), 10% hydrochloric acid (100 ml), 10% aqueous sodium hydrogen carbonate (100 ml), and brine (100 ml). The organic phase was dried (Na_2SO_4) and evaporated under reduced pressure to afford a colourless oil, distillation of which gave the title compound (**30**)[38] (12.5 g, 95%), short-path distillation, b.p. 55 °C at 0.1 mmHg.

(2R,3R)-2-*Methyl*-1-(*tetrahydropyran*-2-*yloxy*)*butan*-2-*ol* (**32**).—A solution of methyl-lithium in ether (1.1M solution; 123 ml, 135 mmol) was added dropwise to a vigorously stirred suspension of CuBr·SMe_2 (13.86 g, 67 mmol) in ether (80 ml) at −60 °C. The resulting buff-coloured solution was stirred for a further 10 min and then added *via* a cannula to a solution of the propanal (**30**) (11.6 g, 67 mmol) in ether (100 ml) at −80 °C. The resulting mixture was stirred for a further 1 h at −80 °C before addition of a saturated aqueous NH_4Cl (100 ml). The organic phase was separated and the aqueous phase extracted with ether (50 ml). The combined ether phases were dried (Na_2SO_4) and evaporated under reduced pressure to yield a colourless oil. Short-path distillation of this afforded the title compound (**32**)[38] (11.6 g, 92%), b.p. 50—60 °C at 0.1 mmHg.

(2R,3R)-2-*Methyl*-1-(*tetrahydropyran*-2-*yloxy*)*butan*-2-*ol Benzyl Ether* (**33**).—A solution of the butanol (**32**) (3.45 g, 18.35 mmol) was added to a slurry of pentane-washed sodium hydride (0.75 g, 31.25 mmol) in THF (20 ml) at room temperature. After 1 h, benzyl bromide (3.5 g, 20 mmol) and a catalytic amount of tetrabutylammonium iodide (20 mg) were added. The reaction mixture was heated under reflux for 24 h. Water (50 ml) was then added carefully, and the reaction mixture diluted with ether (50 ml). The aqueous phase was separated and extracted with ether (2 × 30 ml) and the combined extracts were washed with 10% hydrochloric acid (20 ml) followed by 10% aqueous sodium hydrogencarbonate (50 ml), and then dried (Na_2SO_4). The solvent was removed under reduced pressure to yield a colourless oil (4.1 g, 80%) which was normally used without further purification. A small sample was purified by flash chromatography to afford the *title compound* (**33**) as a colourless oil (Found: C, 73.4; H, 9.6. $C_{17}H_{26}O_3$ requires C, 73.3; H, 9.4%); $\nu_{max.}$ 1 610 and 1 500 cm^{-1}; δ_H (60 MHz) 0.95 (3 H, d, *J* 6, Me), 1.15 (3 H, d, *J* 6, Me), 1.2—2.3 (7 H, m, CH, 3 × CH_2), 3.1—4.0 (3 H, m, CHO, CH_2O), 4.5 (3 H, br s, OCHO, $PhCH_2$), and 7.25 (5 H, s, Ph); *m/z* 176 (8%), 135 (10), and 91 (100).

(2S,3R)-(−)-3-*Benzyloxy*-2-*methylbutan*-1-*ol* (**34**).—Crude compound (**33**) (4.1 g) was dissolved in methanol (100 ml) and a catalytic amount of camphorsulphonic acid (20 mg) added. The resulting solution was stirred for 16 h at room temperature after which time anhydrous potassium carbonate (1 g) was added and the methanol removed under reduced pressure. The oily residue was dissolved in ether (100 ml) and the solution washed with water (20 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (ether–light petroleum, 1:1) followed by vacuum distillation to afford the *title compound* (**34**) [2.47 g, 70% from (**32**)] as a colourless oil, b.p. 85 °C at 0.15 mmHg; $[\alpha]_D^{20}$ −41.7° (*c* 2.54, CH_2Cl_2) (Found: C, 74.2; H, 9.4. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%); $\nu_{max.}$ 3 500 (OH), 2 900, 1 450, 1 100, 740, and 700 cm^{-1}; δ_H (360 MHz) 0.9 (3 H, d, *J* 6, CHMe), 1.25 (3 H, d, *J* 6, MeCHO), 1.78 (1 H, m, CHMe), 3.5 (1 H, dq, *J* 6 and 6, CHO), 3.61 (2 H, m, CH_2O), 4.40 (1 H, d, *J* 12, benzylic H), 4.67 (1 H, d, *J* 12, benzylic H), and 7.35 (5 H, m, ArH); *m/z* 194.1347 (M^+, $C_{12}H_{18}O_2$ requires 194.1307, 1%), 176 ($M^+ - H_2O$, 4%), 135 (3), 107 (11), 139 (16), and 91 (100).

(2R,3S)-(−)-3-*Benzyloxy*-2-*methylbutanal* (**35**).—A solution of DMSO (2.19 g, 28 mmol) in CH_2Cl_2 (5 ml) was added dropwise to a solution of oxalyl chloride (1.71 g, 14 mmol) in CH_2Cl_2 (35 ml) at −60 °C under argon. After the addition was complete the reaction mixture was stirred for a further 10 min after which a solution of the butanol (**34**) (2.47 g, 12.7 mmol) in CH_2Cl_2 (10 ml) was added over 5 min. After a further 15 min at −60 °C, triethylamine (6.43 g, 63.7 mmol) was added and the reaction mixture allowed to warm to room temperature. Water (100 ml) was then added and the organic phase separated and the aqueous phase re-extracted with CH_2Cl_2 (2 × 30 ml). The combined organic extracts were washed with 10% hydrochloric acid (50 ml), 10% aqueous sodium hydrogen carbonate (50 ml), and brine (50 ml), and dried ($MgSO_4$). The solvent was then removed under reduced pressure to yield the title compound (**35**) (2.46 g, 100%) as a colourless oil which decomposed on attempted distillation; $[\alpha]_D^{20}$ −61.7° (*c* 2.5, CH_2Cl_2); $\nu_{max.}$ 2 960, 1 730 (CO), 1 450, 1 100, 740, and 700 cm^{-1}; δ_H (60 MHz) 1.05 (3 H, d, *J* 7, Me), 1.21 (3 H, *J* 7, Me), 2.50 (1 H, ddq, *J* 2, 7, and 7, MeCHCHO), 3.70 (1 H, dq, *J* 7 and 7, MeCHO), 4.30 (1 H, d, *J* 12, benzylic H), 4.57 (1 H, d, *J* 12, benzylic H), 7.3 (5 H, m, Ar), and 9.58 (1 H, d, *J* 2, CHO); *m/z* 192.1150 (M^+, $C_{12}H_{16}O_2$ requires 192.1150, 1%), 119 (2), 107 (18), 92 (55), 91 (100), and 79 (11).

(3S,4R)-(+)-4-*Benzyloxy*-1,1-*dibromo*-2-*methylpent*-1-*ene* (**36**).—A solution of carbon tetrabromide (14.83 g, 4.5 mmol) in CH_2Cl_2 (50 ml) was added over 10 min to a solution of triphenylphosphine (23.65 g, 9.0 mmol) in CH_2Cl_2 (150 ml) at 0 °C under nitrogen. After being stirred for a further 10 min at 0 °C the reaction mixture was cooled to −20 °C and a solution of the butanal (**35**) (4.3 g, 2.2 mmol) in CH_2Cl_2 (100 ml) was added. The reaction mixture was stirred at −20 °C for 20 min, diluted with light petroleum (300 ml) with vigorous stirring, and allowed to warm to room temperature. The precipitate was removed by filtration through Florisil and the filtrate was evaporated under reduced pressure. The residual oil was purified by flash chromatography (light petroleum) to yield the title compound (**36**) as a colourless oil (8.0 g, 98%), b.p. 80 °C at 0.05 mmHg (Kugelrohr); $[\alpha]_D^{20}$ +16.4° (*c* 2, CH_2Cl_2); $\nu_{max.}$ 2 960, 1 450, 1 370, 1 060, and 700 cm^{-1}; δ_H (60 MHz) 1.04 (3 H, d, *J* 7, Me), 1.15 (3 H, d, *J* 7, Me), 2.55 (1 H, m, Me*CH*CH=), 3.4 (1 H, dq, *J* 6 and 7, C*H*OCH$_3$), 4.3 (1 H, d, *J* 12, benzylic H), 4.57 (1 H, d, *J* 12, benzylic H), 6.30 (1 H, d, *J* 10, HC=), and 7.3 (5 H, m, Ar); *m/z* 212 (2%), 135 (11), 107 (4), 91 (100), and 65 (5).

(3S,4R)-4-*Benzyloxy*-3-*methylpent*-1-*yne* (**37**).—Butyllithium (1.74M solution in hexane; 13.1 ml, 22.8 mmol) was added dropwise to a cooled (−80 °C) solution of the pentene (**36**) in THF (100 ml). The reaction mixture was stirred for 1 h at −80 °C and then allowed to warm to room temperature. Water (50 ml) was added, the organic phase separated, and the aqueous phase re-extracted with ether (50 ml). The combined organic extracts were dried ($MgSO_4$) and the solvent evaporated under reduced pressure to yield a pale yellow oil which was purified by vacuum distillation to afford the *title compound* (**37**) as a colourless oil (2.0 g, 94%), b.p. 55 °C at 12 mmHg; $[\alpha]_D^{20}$ −8.4 (*c* 0.68, CH_2Cl_2) (Found: C, 83.0; H, 8.6. $C_{13}H_{16}O$ requires C, 82.9; H, 8.56%); $\nu_{max.}$ 3 300 (≡CH), 3 000, 2 110 (C≡C), 1 460, 1 380, 1 110, 740, and 700 cm^{-1}; δ_H 1.15 (3 H, d, *J* 7, Me), 1.22 (3 H, d, *J* 6.3, Me), 2.04 (1 H, d, *J* 3, CH), 2.76 (1 H, ddq, *J* 3, 4.7, and 7, C*H*CMe), 3.55 (1 H, dq, *J* 4.7 and 6.3, CHO), 4.52 (1 H, d, *J* 12, benzylic H), 4.58 (1 H, d, *J* 12, benzylic H), and 9.23 (5 H, m, ArH); *m/z* 188.2188 (M^+, $C_{13}H_{16}O$ requires 188.2718, 1%), 187 (3), 147 (15), 143 (11), 105 (70), 91 (100), and 77 (28).

(4S,6S)-4-*Benzyloxy*-6-*benzyloxymethyl*-2-*hydroxy*-2-[(3S,4R)-3-*methyl*-4-*tetrahydropyranyloxypent*-1-*ynyl*]*tetrahydropyran* (**39**).—Butyl-lithium (1.45M solution in hexane; 2.6 ml) was added dropwise to a cooled (−80 °C) solution of the pentyne (**29**) (0.71 g, 3.9 mmol) in THF (30 ml) under argon. After the mixture had been stirred at −80 °C for 1 h a solution of the pyranone (**15**) (1.3 g, 3.98 mmol) in THF (30 ml) was added in one portion. The mixture was set aside for 1 h at −80 °C after which saturated aqueous sodium dihydrogen orthophosphate (100 ml) was added and the cooling bath removed. When the reaction mixture had warmed to room temperature, ether (100 ml) was added and the organic phase separated; the aqueous phase was then extracted with ether (3 × 50 ml). The combined organic extracts were washed with brine (100 ml), dried ($MgSO_4$) and evaporated under reduced pressure to afford the title compound (**39**) as a pale yellow oil (2.1 g, 100%) which was used without further purification; $\nu_{max.}$ 3 500 (OH), 2 200 (C–C), and 1 670 cm^{-1} (CO).

(4S,6S)-4-*Benzyloxy*-6-*benzyloxymethyl*-2-*methoxy*-2-[(3S,4R)-3-*methyl*-4-*hydroxypent*-1-*ynyl*]*tetrahydrofuran* (**41**).—The crude tetrahydropyran (**39**) was dissolved in anhydrous methanol (100 ml) and Amberlite IR118 (H+) resin (100 mg) was added; the resulting solution was then stirred overnight. The resin was filtered off and the filtrate concentrated under reduced pressure to afford an orange oil, purification of which by flash chromatography (light petroleum–ethyl acetate, 3:1) afforded the title compound (**41**) as a colourless oil (1.4 g, 80%); $\nu_{max.}$ 3 500 (OH), 2 900, 1 450, 1 360, 740, and 700 cm^{-1}; δ_H (60 MHz) 0.95 (3 H, d, *J* 7, Me), 1.15 (3 H, d, *J* 7, Me), 1.2—2.2 (5 H, m, 2 × CH_2, CHMe), 3.15 (3 H, s, OMe), 3.2—4.2 (5 H, m, CH_2O, 3 × HCO), 4.6 (4 H, s, benzylic H), and 7.3 (5 H, m, Ar); *m/z* 205 (1%), 107 (10), and 91 (100).

(2R,3S,6S,8S,10S)-(+)-10-*Hydroxy*-8-*hydroxymethyl*-2,3-*dimethyl*-1,7-*dioxaspiro*[5.5]*undecane* (**42**).—A solution of the tetrahydropyran (**41**) (1.4 g, 3.2 mmol) in methanol (10 ml) was added to a suspension of 10% palladium on charcoal (100 mg) in methanol (10 ml). The resulting suspension was stirred under an atmosphere of hydrogen until uptake had ceased. The catalyst was removed by filtration through Celite and the filtrate evaporated under reduced pressure to yield a colourless oil which solidified with time. Recrystallisation from ether afforded the title compound (**42**) (0.7 g, 98%), m.p. 102 °C (Found: C, 62.55; H, 9.7. $C_{12}H_{22}O_4$ requires C, 62.58; H, 9.63%); $[\alpha]_D^{22}$ +46.3° (*c* 1.07, CH_2Cl_2); $\nu_{max.}$ 3 400 (OH), 2 960, 1 470, and 1 390 cm^{-1}; δ_H (360 MHz) 0.75 (3 H, d, *J* 6.4, 3-Me), 1.02 (2 H, d, *J* 6.3, 2-Me), 1.12 (1 H, m, 3-H), 1.2 (1 H, m, 9_{ax}-H), 1.21 (1 H, dd, *J* 11.5 and 11, 11_{ax}-H), 1.35—1.5 (3 H, m, 4_{ax}-H, 4_{eq}-H, 5_{ax}-H), 1.6 (1 H, m, 5_{eq}-H), 1.80 (1 H, dddd, $J_{9eq,9ax}$ 12, $J_{9eq,8} = J_{9eq,10}$ 5, $J_{9eq,11eq}$ 1, 9_{eq}-H), 1.91 (1 H, ddd, $J_{11eq,11ax}$ 11.5, $J_{11eq,10}$ 5, $J_{11eq,9eq}$ 1, 11_{eq}-H), 3.1 (2 H, br s, OH), 3.2 (1 H, dq, *J* 10, and 6.3, 2-H), 3.34—3.6 (2 H, m, CH_2OH), 3.57 (1 H, m, 8-H), and 4.06 (1 H, dddd, $J_{10,9eq} = J_{10,11eq}$ = 5, $J_{10,11ax} = J_{10,9ax}$ 11, 10-H); *m/z* 199 (28%), 186 (31), 181 (13), 147 (16), 144 (56), 129 (25), 126 (89), 113 (44), 111 (48), 97 (12), 95 (75), 87 (19), 83 (54), 73 (24), 69 (79), 43 (100), and 41 (85).

(4S,6S)-6-*Benzyloxymethyl*-4-*diphenyl*-*t*-*butylsiloxy*-2-*methoxy*-2-[(3S,4R)-3-*methyl*-4-*hydroxypent*-1-*ynyl*]*tetrahydropyran* (**43**).—Butyl-lithium (1.6M solution in hexane; 0.38 ml) was added dropwise to a cooled (−80 °C) solution of the pentyne (**29**) (0.107 g, 0.59 mmol) in THF (10 ml) under argon. The mixture was stirred at −80 °C for 1 h after which a solution of the pyranone (**23**) (280 mg, 0.59 mmol) in THF (10 ml) was added in one portion; after 1 h at −80 °C saturated aqueous sodium dihydrogen orthophosphate (100 ml) was also added and the cooling-bath removed. When the reaction mixture had

warmed to room temperature ether (50 ml) was added and the organic phase separated; the aqueous phase was then extracted with ether (3 × 20 ml). The combined organic extracts were washed with brine (100 ml), dried ($MgSO_4$), and evaporated under reduced pressure to afford a yellow oil (300 mg); $\nu_{max.}$ 3 400 (OH), 2 210 (C≡C), and 1 680 cm^{-1} (C=O). This was dissolved in methanol (20 ml) and Amberlite IRA (118) (H^+) (50 mg) added, the suspension was then stirred overnight. The resin was filtered off and the filtrate evaporated under reduced pressure to afford a red oil (200 mg), purification of which by flash chromatography (light petroleum–ethyl acetate, 3:1) afforded the title compound (**43**) (103 mg, 30%); $\nu_{max.}$ 3 500 (OH), 2 900, and 1 410 cm^{-1}; δ_H (60 MHz) 0.9 (3 H, d, *J* 7, Me), 1.1 (12 H, s, Bu^t, Me), 1.1—2.5 (5 H, m), 3.15 (3 H, s, OMe), 3.2—4.5 (5 H, m, CH_2O, 3 × CHO), 4.5 (2 H, s, benzylic H), and 7.2—7.6 (15 H, m, ArH).

(2R,3S,6S,8S,10S)-(+)-10-*Diphenyl-t-butylsiloxy*-18-*hydroxymethyl*-2,3-*dimethyl*-1,7-*dioxaspiro*[5.5]*undecane* (**44**).—A solution of the tetrahydropyran (**43**) (103 mg, 0.18 mmol) in methanol (10 ml) was added to a suspension of 10% palladium on charcoal (100 mg) in methanol (10 ml) and the resulting suspension was stirred under an atmosphere of hydrogen until uptake had ceased. The catalyst was removed by filtration through Celite and the filtrate evaporated under reduced pressure to yield a colourless oil which was purified by flash chromatography (light petroleum–ethyl acetate, 5:1) to afford the title compound (**44**) (65 mg, 80%); $[\alpha]_D$ +54° (*c* 1.0, CH_2Cl_2); $\nu_{max.}$ 3 500 (OH) and 2 900 cm^{-1}; δ_H (360 MHz) 0.76 (3 H, d, *J* 6, 3-Me), 0.96 (3 H, d, *J* 6, 2-Me), 1.03 (9 H, s, Bu^t), 1.2 (1 H, m, 3-H), 1.31 (1 H, ddd, $J_{9ax.9eq}$ 12, $J_{9ax.10}$ 11, $J_{9ax.8}$ 11, 9_{ax}-H), 1.41 (1 H, dd, $J_{11ax.10}$ 11, $J_{11ax.11eq}$ 12.5, 11_{ax}-H), 1.43—1.50 (3 H, m, 4_{ax}-H, 4_{eq}-H, 5_{eq}-H), 1.57 (1 H, m, $J_{9eq.9ax}$ 12, $J_{9eq.11eq}$ 2, 9_{eq}-H), 1.65 (1 H, m, 5_{ax}-H), 1.92 (1 H, ddd, $J_{11eq.11ax}$ 12.5, $J_{11eq.10}$ 5, $J_{11eq.10eq}$ 2, 11_{eq}-H), 2.05 (1 H, br s, OH), 3.15 (1 H, dq, *J* 6, $J_{2.3}$ 10, 2-H), 3.4—3.55 (3 H, m, H_2, CH_2O), 4.2 (1 H, dddd, $J_{10.9eq}$ 4.5, $J_{10.11ax}$ 11, $J_{10.11eq}$ 5, $J_{10.9ax}$ 11, 10-H), and 7.25—7.6 (10 H, m, ArH); *m/z* (c.i., with NH_3), 469 (71%), 411 (23), 33 (10), 241 (12), 213 (100), 207 (25), 199 (14), 181 (10), 127 (12), 83 (30), and 35 (45).

Acknowledgements

Thanks are due to S.E.R.C. for financial support.

References

1 Y. Takiguchi, H. Mishima, M. Okuda, M. Terao, A. Aoki, and R. Fukunda, *J. Antibiot.*, 1980, **33**, 1120.
2 G. Albers-Schonberg, B. H. Arison, J. C. Chabala, A. W. Douglas, P. Eskola, M. H. Fischer, A. Lusi, H. Mrozik, J. L. Smith, and R. L. Tolman, *J. Am. Chem. Soc.*, 1981, **103**, 4216.
3 I. S. Kass, C. C. Wang, J. P. Walrond, and A. O. W. Stretton, *Proc. Natl. Acad. Sci., USA*, 1982, **104**, 4015.
4 W. C. Campbell, *Vet. Res. Commun.*, 1982, **5**, 251.
5 R. Baker, R. H. Herbert, P. E. Howse, O. T. Jones, W. Franke, and W. Reich, *J. Chem. Soc., Chem. Commun.*, 1980, 52.
6 W. Wieranga, 'Total Synthesis of Ionophores,' in 'Total Synthesis of Natural Products,' ed. J. Apsimon, Wiley, New York, 1981, vol. 4, 263.
7 D. G. Lynn, N. J. Phillips, W. C. Hutton, J. Shabonowitz, D. I. Fennell, and R. J. Cole, *J. Am. Chem. Soc.*, 1982, **104**, 7319.
8 A. B. Smith III, S. R. Schow, J. D. Bloom, A. S. Tompson, and K. N. Winzenberg, *J. Am. Chem. Soc.*, 1982, **104**, 4015.
9 D. R. Williams, B. A. Barner, K. Nishitani, and J. G. Phillips, *J. Am. Chem. Soc.*, 1982, **104**, 4708.
10 P. Kocienski and S. D. A. Street, *J. Chem. Soc., Chem. Commun.*, 1984, 571.
11 R. Baker, R. H. O. Boyes, D. M. P. Broom, J. A. Devlin, and C. J. Swain, *J. Chem. Soc., Chem. Commun.*, 1983, 830.
12 S. V. Attwood, A. G. M. Barrett, and J.-C. Florent, *J. Chem. Soc., Chem. Commun.*, 1981, 556.
13 S. Hanessian, A. Ugolini, and M. Therien, *J. Org. Chem.*, 1983, **48**, 4427.
14 R. Baker, J. C. Head, and C. J. Swain, *J. Chem. Soc., Chem. Commun.*, 1985, 309.
15 R. Baker, R. H. Herbert, and A. H. Parton, *J. Chem. Soc., Chem. Commun.*, 1982, 601.
16 S. L. Schreiber and T. J. Sommer, *Tetrahedron Lett.*, 1983, **24**, 4781.
17 A. P. Kozikowski and J. G. Scripko, *J. Am. Chem. Soc.*, 1984, **106**, 353.
18 D. A. Evans, C. E. Sacks, R. A. Whitney, and N. G. Mandel, *Tetrahedron Lett.*, 1978, 727.
19 S. V. Ley and B. Lygo, *Tetrahedron Lett.*, 1984, **25**, 113.
20 S. V. Ley, B. Lygo, and A. Wonnacott, *Tetrahedron Lett.*, 1985, **26**, 535.
21 P. Kocienski and C. Yeates, *J. Chem. Soc., Chem. Commun.*, 1984, 151.
22 A. M. Doherty, S. V. Ley, B. Lygo, and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1317.
23 B. A. Barner and D. R. Williams, *Tetrahedron Lett.*, 1983, **24**, 427.
24 M. Yamamoto, M. Yoshitake, and K. Yamada, *J. Chem. Soc., Chem. Commun.*, 1983, 991.
25 S. J. Danishefsky and W. H. Pearson, *J. Org. Chem.*, 1983, **48**, 3866.
26 I. T. Kay and E. G. Williams, *Tetrahedron Lett.*, 1983, **24**, 5915.
27 R. Baker and M. A. Brimble, *J. Chem. Soc., Chem. Commun.*, 1985, 78.
28 R. B. Ward, *Methods Carbohydr. Chem.*, 1963, **2**, 394.
29 G. H. Coleman, *Methods Carbohydr. Chem.*, 1963, **2**, 367.
30 M. P. Edwards, S. V. Ley, S. G. Lister, B. D. Palmer, and D. J. Williams, *J. Org. Chem.*, 1984, **49**, 3503.
31 M. Cerny, L. Kolvada, and J. Pacak, *Collect. Czech. Chem. Commun.*, 1968, **33**, 1143.
32 A. G. Kelly and J. S. Roberts, *Carbohydr. Res.*, 1978, **77**, 231.
33 M. Fetizon and M. Golfier, *C.R. Acad. Sci. Ser. C*, 1968, **267**, 900.
34 F. Kong and C. Schuerch, *Carbohydr. Res.*, 1983, **112**, 141.
35 M. A. Adams, A. J. Duggan, J. Smolanoff, and J. Meinwald, *J. Am. Chem. Soc.*, 1979, **101**, 5364.
36 J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543.
37 P. D. Bartlett and C. H. Stauffer, *J. Am. Chem. Soc.*, 1935, **57**, 2580.
38 J. A. Scheider and W. C. Still, *Tetrahedron Lett.*, 1980, **21**, 1035.
39 A. J. Mancuso and D. Swern, *Synthesis*, 1981, 165.
40 E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 1972, 3769.
41 P. Deslongchamps, D. D. Rowan, N. Pothier, T. Sauve, and J. K. Saunders, *Can. J. Chem.*, 1981, **59**, 1105.
42 R. Baker, M. J. O'Mahony, and C. J. Swain, *J. Chem. Soc., Perkin Trans. 1*, following paper.
43 W. C. Still, M. Khan, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2932.

Received 4*th September* 1986; *Paper* 6/1781