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CARBOHYDRATE-LIKE CHIRAL SYNTHONS: SYNTHESIS OF THE *N*-TRIFLUOROACETYL DERIVATIVES OF 4-AMINO-2,4,6-TRIDEOXY-L-*lyxo*-, -L-*arabino*, AND -L-*ribo*-HEXOSE FROM THE (2*S*,3*R*)-2,3-DIOL FORMED FROM CINNAMALDEHYDE IN FERMENTING BAKER'S YEAST

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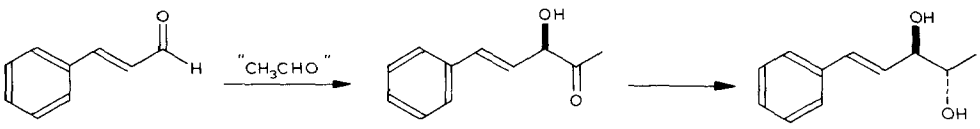
ABSTRACT

(2*S*,3*S*)-2,3-Isopropylidenedioxybutyraldehyde, produced by ozonolysis of the *O*-isopropylidenated (2*S*,3*R*)-2,3-diol formed from cinnamaldehyde in fermenting baker's yeast, affords, with diallyl-zinc, the C_7, carbohydrate-like, non-carbohydrate-derived adduct (2*S*,3*R*,4*R*)-2,3-isopropylidenedioxy-4-hydroxyhept-6-ene (**9**). This material is a stereochemically defined, functionalised, chiral synthon which is useful in the synthesis of enantiomerically pure products. The synthesis of the *N*-trifluoroacetyl derivatives of 4-amino-2,4,6-trideoxy-L-*lyxo* (**21**), -L-*arabino* (**22**), and -L-*ribo*-hexose (**23**) from **9** is reported. Key intermediates in the synthesis were the isomeric epoxy alcohols (2*S*,3*S*,4*S*)-3,4-epoxyhept-6-en-2-ol, (2*S*,3*R*,4*S*)-2,3-epoxyhept-6-en-4-ol, and (2*S*,3*R*,4*R*)-2,3-epoxyhept-6-en-4-ol. The nitrogen function is introduced by intramolecular epoxide-opening of the corresponding benzyl urethanes which gave, eventually, (2*S*,3*R*,4*S*)-3-*N*-trifluoroacetamidohept-6-en-2,4-diol, (2*S*,3*S*,4*S*)-3-*N*-trifluoroacetamidohept-6-en-2,4-diol, and (2*S*,3*S*,4*R*)-3-*N*-trifluoroacetamido-6-en-2,4-diol, from which the required C_6–N frameworks of **21–23** were obtained by ozonolysis.

INTRODUCTION

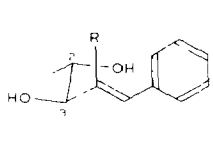
In a study of the steric course of the reduction of cinnamaldehyde to 3-phenylpropanol mediated by baker's yeast, we discovered a new synthetic capacity,



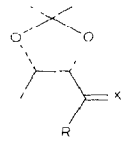
Scheme 1

0008-6215/85/$ 03.30

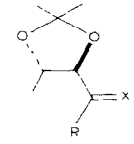
namely the conversion[1] of aromatic α,β-unsaturated aldehydes into C_6–C_5 methyl diols (Scheme 1). The reaction involves the formal addition of the equivalent of acetaldehyde, formed from the carbohydrates in the fermentation mixture, to the carbonyl carbon atom of the α,β-unsaturated aldehyde to form, in an asymmetric acyloin-type condensation, (*R*)-hydroxyketones. These products are then reduced stereospecifically to give the (2*S*,3*R*)-diols, isolated in yields of 25–30%. The (2*S*,3*R*)-diols **1** and **2**, obtained from cinnamaldehyde and α-methylcinnamal-



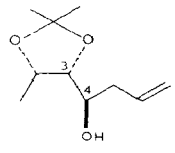
1 R = H
2 R = Me



3 R = H, X = O
4 R = Me, X = O
7 R = H, X = NSPh



5 R = H, X = O
6 R = Me, X = O
8 R = H, X = NSPh



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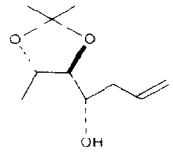

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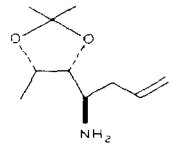

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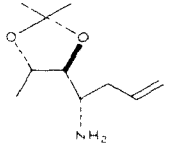
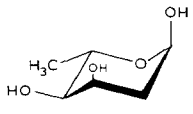


12

dehyde, respectively, have an absolute configuration matching that at positions 5 and 4 of 6-deoxy-L-sugars and they have been converted[2] into L-amicetose (2,3,6-trideoxy-L-*erythro*-hexose) and L-olivomycose (2,6-dideoxy-3-*C*-methyl-L-*arabino*-hexose). Thus, **1** and **2** can be considered as carbohydrate-like, non-carbohydrate-derived, chiral synthons, the value in synthesis of which is associated with the fact that is possible to obtain, from protected forms of **1** and **2**, the C_4 and C_5 chiral carbonyl compounds **3** and **4**, which can be converted by treatment with base into their α-epimers **5** and **6**.

The value of these compounds as chiral synthons is illustrated by the addition of carbon nucleophiles to the carbonyl carbon atom of **3–6** or the *N*-phenylsulfenimino derivatives **7** and **8** to afford, exclusively or preferentially, adducts arising by Cram or *anti*-Cram modes of addition[3], depending upon the nature of the nucleophile and/or the solvent. For instance, addition of diallylzinc in ether to **3, 5, 7,** and **8** gave the C_7 adducts **9–12** and also minute amounts of the C-4 epimers[4,5]. The carbohydrate-like intermediates **9–12** were converted into the 2,6-dideoxy- and 3-amino-2,3,6-trideoxy-L-sugars **13–16** by conventional chemical reactions. The synthetic value of such products as **9** and **10** is not limited to the preparation of sugar derivatives since they contain, in masked form, (*R*) and (*S*)-malaldehyde, the two carbonyl functions of which can be generated regioselectively by the appro-

priate choice of reagent. Moreover, in **9** and **10**, the three adjacent chiral centers can be manipulated easily by the appropriate use of protecting groups. Accordingly, **9** has been used, as an alternative to natural carbohydrates, as a chiral starting-material for the synthesis of (+)-*exo*brevicomin (**17**), (*R*)-γ-hexanolide (**18**), (5*R*,6*S*,7*S*)-6,7-isopropylidenedioxy-δ-octanolide[6] (**19**), and the (2*R*)-C_{10}-aldehyde **20**, a key intermediate in the synthesis of natural LTB_4. As further examples of the value of such chiral synthons as **9**, we report the synthesis therefrom of the *N*-trifluoroacetyl derivatives (**21–23**) of 4-amino-2,4,6-trideoxy-L-*lyxo*-, -L-*arabino*-, and -L-*ribo*-hexose.



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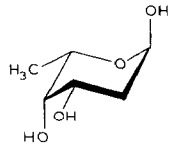

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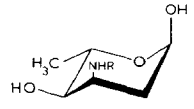
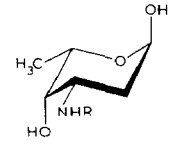
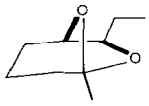


15 R = $COCF_3$



16 R = $COCF_3$



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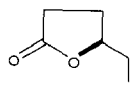

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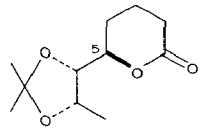

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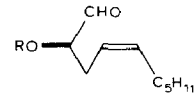
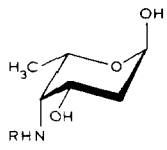
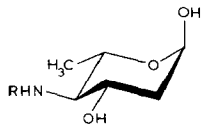


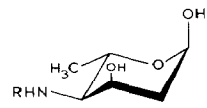
20 R = $SiPh_2Bu^t$



21 R = $COCF_3$



22 R = $COCF_3$



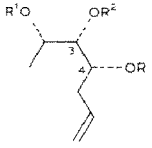
23 R = $COCF_3$

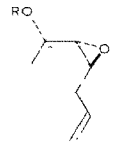
DISCUSSION

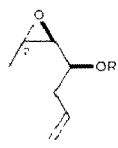
The route envisaged from **9** to **21–23** involved the epoxy alcohols **29–31**, which, following transformation into the benzylurethanes **32–34**, had to be cyclised according to Kishi's procedure[8] to give **35–37**. Application in sequence of *N*-debenzylation, basic hydrolysis, *N*-protection, and ozonolysis of the terminal vinyl group then leads to the aminodeoxy sugar derivatives **21–23**.

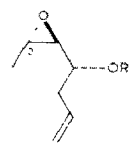
Thus, the tosylate of **9** was subjected to mild hydrolysis with acid to afford the diol **25**. Treatment of **25** with base gave the epoxy alcohol **29**, but, under the conditions required for the elimination of the tosyl group, partial isomerisation occurred yielding **30**, as shown by g.l.c. analysis and ^{1}H-n.m.r. data (see Experimental). Unfortunately, **29** and **30** could not be separated by conventional

chromatographic methods. Accordingly, the reaction sequence was continued with a ~4:1 mixture, which was converted into the corresponding benzylurethanes using the procedure of Bernet and Vasella[9]. Cyclisation of the resulting C_7–N derivatives **32** and **33** under basic conditions proceeded cleanly to afford a mixture of **35** and **36**, which was *N*-debenzylated with lithium in liquid ammonia; the products were hydrolysed with ethanolic lithium hydroxide. The resulting C_7–N 3-amino-2,4-diols were *N*-trifluoroacetylated to give **41** and **42**, ozonolysis of which in methanol at −40° and subsequent treatment with dimethyl sulphide afforded 2,4,6-trideoxy-4-*N*-trifluoroacetamido-L-*lyxo*-hexose (**21**) as an oil, $[\alpha]_D^{20}$ −49° (methanol), and 2,4,6-trideoxy-4-*N*-trifluoroacetamido-L-*arabino*-hexose (**22**), m.p. 200–202°, $[\alpha]_D^{20}$ −66° (methanol), in the ratio ~4:1; **21** and **22** were easily separated by column chromatography on silica gel.







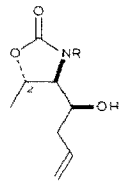


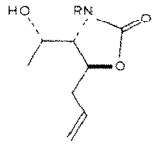
24 R = $SiPh_2Bu^t$, R^1,R^2 = $>CMe_2$
25 R = Ts, R^1 = R^2 = H
26 R = $SiPh_2Bu^t$, R^1 = R^2 = H
27 R = $SiPh_2Bu^t$, R^1 = Bz R^2 = H
28 R = $SiPh_2Bu^t$, R^1 = Bz, R^2 = Ms

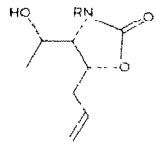
29 R = H
32 R = NHCOBzl

30 R = H
33 R = NHCOBzl

31 R = H
34 R = NHCOBzl



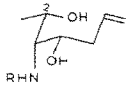


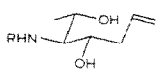


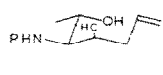
35 R = Bzl
38 R = H

36 R = Bzl
39 R = H

37 R = Bzl
40 R = H







41 R = $COCF_3$

42 R = $COCF_3$

43 R = $COCF_3$

In seeking to isomerise the epoxy alcohol **29** into **30**, **29** was treated with potassium carbonate in dry methanol at room temperature overnight. G.l.c. of the reaction mixture then indicated a ~2:3 mixture of **29** and **30**, but the subsequent

recovery of these compounds was very poor. Accordingly, a more efficient conversion of **9** into **22** *via* **30** was not sought.

The synthesis of the L-*ribo* compound **23** from **9**, using the above method for introduction of the nitrogen function, required an intermediate epoxy alcohol **31** with unchanged stereochemistry at positions 2 and 4. Thus, **9** was converted into the *O*-protected diol **26** which, on benzoylation, afforded, regioselectively, the 2-benzoate **27**. The 3-mesylate (**28**) of **27**, on treatment with base, yielded the *O*-protected epoxide which was then converted into the required epoxy alcohol **31**. The latter material, as described above, afforded the L-*ribo* compound **23**, m.p. 168°, $[\alpha]_D^{20}$ −131° (methanol).

The ^{1}H-n.m.r. data for the *N*-trifluoroacetylated-4-amino-2,4,6-trideoxy-L-hexoses **21–23** are reported in Table I. Their solutions in acetone-d_6 contained α,β-mixtures. Where possible, the data for the α and β forms have been reported. The values of the vicinal coupling constants indicated the configuration and showed that the $^1C_4$(L) conformations were adopted, as predicted[10] for pyranoses characterised by the presence of a conformation-stabilising substituent at C-5. A set of additivity constants has been reported[11] which are valid for predicting the vicinal coupling constants for conformationally pure pyranose rings. Since relatively few examples of 4-amino-2,4-dideoxypyranoses were used in compiling the data base, we have tested the validity of these additivity rules. Thus, the predicted values for $J_{3a,4e}$, $J_{3a,4a}$, $J_{3e,4a}$, $J_{4e,5a}$, and $J_{4a,5a}$ are 3.8, 10.1, 2.8, 1.5, and 10.1 Hz, respectively, which are in good agreement with the experimental values reported in Table I.

The ^{13}C chemical shifts for **21–23** are reported in Table II. The assignment of the signals was made by ^{1}H selective heteronuclear-decoupling experiments. Structural assignments are based on the variations of the chemical shifts of the signals of the ring carbon atoms according to the orientation of the substituents. Generally, an axial group is associated with larger shielding of the ring carbon atoms that are α, β, and γ to the substituent, than is an equatorial substituent. The upfield shifts due to such a configurational inversion usually are in the range 1–5 p.p.m. for hexopyranoses[12,13]. An important exception occurs when 1,3-*syn*-diaxial hydroxyl

TABLE I

^{1}H-N M.R DATA FOR THE 2,4,6-TRIDEOXY-4-TRIFLUOROACETAMIDO-L-HEXOSES[a]

Compound	*H-1*	*H-2*a	*H-2*e	*H-3*	*H-4*	*H-5*	*Me*	$J_{1,2e}$	$J_{1,2a}$	$J_{2e\,2a}$	$J_{3,2e}$	$J_{3,2a}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
21β	4.79	1.55	1.97	4.05	4.17	3.72	1.12	2.3	9.6	12.8	5.0	12.4	4.3	1.5	6.4
22α	5.28	1.64	2.09	4.10	3.52	4.05	1.10	1.4	3.5	12.6	4.8	11.3	9.9	10.3	6.3
22β	4.75	1.54	2.20	3.81	3.5	3.5	1.15	2.0	9.6	12.6	4.8	11.4	9.4	[b]	6.3
23α	5.23	1.95	2.05	4.04	3.72	4.29	1.15	1.4	3.3	14.4	3.3	3.3	2.9	10.5	6.2
23β	5.10	1.70	2.03	4.10	3.66	3.96	1.14	2.1	9.8	13.6	3.4	2.7	3.0	10.2	6.2

[a]Chemical shifts in p.p.m. from internal Me_4Si; coupling constants in Hz; solvent $(CD_3)_2CO$ + D_2O.
[b]Not detected.

TABLE II

^{13}C CHEMICAL SHIFTS[a] OF THE 2,4,6-TRIDEOXY-4-TRIFLUOROACETAMIDO-L-HEXOSES[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*Me*
21α	92.6	34.7	64.7	55.3	64.7	17.4
21β	95.3	37.7	68.0	54.2	69.6	17.3
22α	91.9	40.2	66.4[b]	60.5	65.7[b]	18.5
22β	94.5	42.5	69.0	59.9	71.0	18.5
23α	92.4	36.5	67.2	55.8	62.2	18.6
23β	92.6	41.2	66.9	55.8	68.8	18.9

[a]In p.p.m. from internal Me_4Si; solvent $(CD_3)_2CO$. [b]Assignments may be interchanged

groups are present. In this situation, the OH–OH interaction is associated[12] with a deshielding (0.4–1.1 p.p.m.) of carbons directly bonded to the hydroxyl groups. Thus, comparison between the α and β anomers allows the identification of the stereochemistry at C-3; in fact, C-3 is deshielded by 0.3 p.p.m. on going from **23**β to **23**α, and by 3 p.p.m. on going from **21**α and **22**α to **21**β and **22**β.

Once the configuration at C-3 has been established, the stereochemistry at C-4 can be deduced on the basis of the above-mentioned effects. Thus, comparison of the data for **22**α and **22**β with those for **21**α and **21**β, respectively, reveals upfield shifts of the signals for C-4, C-5, C-3, and C-2 consistent with the predicted trend. In addition, the signal for the C-5 methyl group is shifted upfield by ~1 p.p.m. for compounds having an axial, in comparison with those having an equatorial, C-4 substituent. This behaviour has been found also for 3-benzoylamino-2,3,6-trideoxyhexoses[14] and 3-benzoylamino-2,3,6-trideoxy-3-*C*-methylhexoses[15], and should be a simple method for the determination of the configuration at C-4 for this kind of compound.

The synthesis of the 4-amino-2,4,6-trideoxy-L-hexose derivatives **21**–**23** from the carbohydrate-like, non-carbohydrate-derived product **1** emphasises the value of this approach[16] for the synthesis of enantiomerically pure forms of natural products and of their analogues. This method is based on the use of microbial transformations of non-conventional substrates as the source of chirality. The approach is a valid alternative to the use of natural carbohydrates as starting materials in the synthesis of the optically active forms of natural products containing relatively few chiral carbon atoms.

EXPERIMENTAL

(2S,3S,4R)-4-Tosyloxyhept-6-en-2,3-diol (**25**). — (2*S*,3*S*,4*R*)-2,3-Isopropylidenedioxyhept-6-en-4-ol (**9**; 9.3 g, 0.05 mol) in dry pyridine (90 mL) was treated conventionally for 48 h at 0° with tosyl chloride (28.6 g, 0.15 mol). The product was subjected to column chromatography on silica gel (200 g). Elution with hexane–ethyl acetate (9:1) gave an oily tosylate (14.5 g, 48 mmol, 96%) which decomposed

on storage. A solution of this product in ethanol (140 mL) and aqueous 20% acetic acid (140 mL) was kept at 25° for 48 h. The deketalisation, which was monitored by t.l.c., was then complete. The mixture was concentrated under vacuum at 40–45° to give **25** (10.5 g, 70%) as an oil which solidified on storage.

(2S,3S,4S)-3,4-Epoxyhept-6-en-2-ol (**29**) *and (2S,3R,4S)-2,3-epoxyhept-6-en-4-ol* (**30**). — A solution of **25** (10.5 g, 35 mmol) in methanol (100 mL) was stirred for 3 h at room temperature with potassium carbonate (2 g), filtered, concentrated to small volume, and diluted with ether (100 mL). The organic phase was washed with water (2 × 50 mL), dried, and concentrated. The residual oil (3.6 g, 80%) was shown by g.l.c. and ^{1}H-n.m.r. studies to be a ~4:1 mixture of **29** and **30**. ^{1}H-N.m.r. data ($CDCl_3$) for **29**: δ 1.25 (d, 3 H, $J_{1,2}$ 6.4 Hz, Me), 1.94 (d, 1 H, $J_{3,4}$ 2.4 Hz, HO-2), 2.2–2.4 (m, 2 H, CH_2-5), 2.81 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 2.4 Hz, H-3), 3.08 (m, 1 H, H-4), 3.97 (qdd, 1 H, $J_{1,2}$ 6.4, $J_{2,OH}$ 2.6, $J_{2,3}$ 3.4 Hz, H-2), 5.0–5.3 (m, 2 H, H-7), and 5.6–6.1 (m, 1 H, H-6); for **30**, δ 1.33 (d, 3 H, $J_{1,2}$ 5.3 Hz, Me), 1.98 (d, 1 H, $J_{4,OH}$ 2.5 Hz, HO-4), 2.2–2.4 (m, 2 H, CH_2-5), 2.75 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 3.6 Hz, H-3), 3.07 (qd, 1 H, $J_{1,2}$ 5.3, $J_{2,3}$ 2.3 Hz, H-2), 3.80 (m, 1 H, H-4), 5.0-5.3 (m, 2 H, H-7), and 5.6–6.1 (m, 1 H, H-6).

To a stirred solution of the mixture of **29** and **30** (3 g, 23 mmol) in dry CH_2Cl_2 (30 mL) and dry pyridine (3 mL) at 0° was added portionwise 4-nitrophenyl chloroformate (5.7 g, 28 mmol). After 2 h, the temperature was raised to 25° and the mixture was treated with benzylamine (7.5 mL, 69 mmol). After 1 h, the mixture was poured into ice–water and extracted with CH_2Cl_2 (2 × 100 mL). The residue obtained on concentration of the dried organic phase was eluted from a column of silica gel (130 g) with hexane–ethyl acetate (7:3) to give an oily 4:1 mixture of the benzyl urethanes **32** and **33** (5.4 g, 90%), $[\alpha]_D^{20}$ −17° (*c* 1, chloroform).

A solution of the mixture of **32** and **33** (5 g, 19 mmol) in dry tetrahydrofuran (50 mL) was treated at −10° with Bu^{t}OK (2.13 g, 19 mmol) for 1 h. The mixture was then poured into ice–water and extracted with ethyl acetate (4 × 50 mL). The oily residue obtained upon concentration of the dried solution was eluted from a column of silica gel with hexane–ethyl acetate (1:1) to give an oily 4:1 mixture (3.5 g, 70%) of the cyclic urethanes **35** and **36**, $[\alpha]_D^{20}$ −27° (*c* 1, chloroform).

*(2S,3R,4S)-3-*N*-Trifluoroacetamidohept-6-en-2,4-diol* (**41**) *and (2S,3S,4S)-3-*N*-trifluoroacetamidohept-6-en-2,4-diol* (**42**). — To a solution of the foregoing mixture (3.5 g, 13 mmol) of **35** and **36** in dry tetrahydrofuran at −78° was added, dropwise, liquid ammonia (~20 mL) followed, portionwise, by Li (2.5 g) until the solution became deep blue. The solution was then stirred at −78° for 3 h, solid NH_4Cl and a few drops of methanol were added until the solution became colourless, the mixture was filtered, and the organic solution was concentrated to dryness. The residue was eluted from a short column of silica gel with ethyl acetate to give an oily ~4:1 mixture (2 g, 92%) of **38** and **39**, $[\alpha]_D^{20}$ −48° (*c* 1, chloroform).

A solution of this mixture in ethanol (15 mL) and water (15 mL) containing LiOH (0.9 g) was boiled under reflux for 2 h and then concentrated under reduced

pressure, and the aqueous phase was extracted with ethyl acetate (4 × 50 mL). The oily residue (1.7 g) obtained on concentration of the organic phase was dissolved in CH_2Cl_2 (5 mL) and stirred at 0° with trifluoroacetic anhydride (10 mL). After 3 h, the mixture was concentrated to dryness under reduced pressure. To a solution of the residue in methanol (50 mL) was added sodium methoxide (50 mg), and the mixture was boiled under reflux for 1 h, stored overnight at room temperature, neutralised with acetic acid, concentrated to small volume, and diluted with ethyl acetate (60 mL). The organic phase was washed with water (20 mL), dried, and concentrated to give an oily 4:1 mixture (2 g, 70%) of **41** and **42**, $[\alpha]_D^{20}$ +6° (*c* 1, chloroform).

2,4,6-Trideoxy-4-trifluoroacetamido-L-lyxo-*hexose* (**21**) *and 2,4,6-trideoxy-4-trifluoroacetamido*-L-arabino-*hexose* (**22**). — A solution of the mixture of **41** and **42** (2 g, 8.5 mmol) in dry methanol (50 mL) at −40° was ozonised until absorption was complete. Nitrogen was flushed through the mixture for 10 min and, at the same temperature, Me_2S (0.7 mL, 10 mmol) was added. The temperature of the mixture was slowly increased until refluxing occurred, which was maintained for 2 h. The residue obtained upon evaporation of the solvent crystallised from hot ethyl acetate–hexane (7:3) to give **22**, m.p. 200–202°, $[\alpha]_D^{20}$ −66° (*c* 1, methanol; 15 min) (Found: C, 39.8; H, 4.8; N, 5.7. $C_8H_{12}F_3NO_4$ calc.: C, 39.5; H, 5.0; N, 5.8%). The residue obtained upon evaporation of the mother liquors was purified by flash chromatography on silica gel (ethyl acetate) to give **21** (1.1 g) as an oil, $[\alpha]_D^{20}$ −49° (*c* 1, methanol; 15 min), and **22** (total yield, 0.36 g). The combined yield of **41** and **42** was ~73%.

*(2S,3S,4R)-2,3-Isopropylidenedioxy-4-(*tert*-butyldiphenylsilyloxy)-hept-6-ene* (**24**). — A solution of **9** (18.6 g, 0.1 mol) in dry *N,N*-dimethylformamide (100 mL) was treated at room temperature for 16 h with imidazole (15 g, 22 mmol) and *tert*-butylchlorodiphenylsilane (30 g, 11 mmol). The mixture was then poured into ice–water (~500 mL) and extracted with hexane (3 × 150 mL). Concentration of the combined and dried extracts gave **24** (37 g, 90%) as an oil which was homogeneous in t.l.c. and had $[\alpha]_D^{20}$ −16.5° (*c* 1, chloroform).

*(2S,3S,4R)-4-(*tert*-Butyldiphenylsilyloxy)-hept-6-en-2,3-diol* (**26**). — A solution of **24** (37 g) in CH_3CN (900 mL) containing aqueous 50% acetic acid (300 mL) was kept on a steam bath for 6 h and then concentrated, and the oily residue was eluted from a column of silica gel (200 g) with hexane–ethyl acetate (7:3) to give **26** (29.5 g, 90%) as an oil, $[\alpha]_D^{20}$ −30° (*c* 1, chloroform).

(2S,3R,4R)-2,3-Epoxyhept-6-en-4-ol (**31**). — A solution of **26** (15 g, 40 mmol) in CH_2Cl_2 (150 mL) containing dry pyridine (3.2 mL) was treated dropwise at 0° with benzoyl chloride (5.6 g, 40 mmol). The mixture was kept at room temperature overnight, washed with 0.05M HCl (2 × 50 mL) and water (2 × 50 mL), dried, and concentrated under vacuum. Chromatography of the residue on silica gel with hexane–ethyl acetate (95:5) gave (2*S*,3*S*,4*R*) 2-benzoyloxy-4-(*tert*-butyldiphenylsilyloxy)-hept-6-en-3-ol (**27**) as an oil (15.2 g, 80%), $[\alpha]_D^{20}$ −9° (*c* 1, chloroform).

A solution of **27** (15 g) in dry CH_2Cl_2 (50 mL) and dry pyridine (10 mL) was treated at 0° with methanesulphonyl chloride (11.4 g, 0.1 mol). The mixture was kept at room temperature overnight and then poured into ice–water (500 mL). The organic phase was separated, the aqueous layer was extracted with CH_2Cl_2 (100 mL), and the combined organic solutions were washed with 0.05M HCl (2 × 50 mL) and aqueous 3% $NaHCO_3$ (2 × 50 mL), and concentrated. The residue was eluted from a column of silica gel with hexane–ethyl acetate (7:3) to give the 3-methanesulphonate **28** (16.7 g, 95%), $[\alpha]_D^{20}$ −16° (*c* 1, chloroform).

A solution of **28** (15 g, 27 mmol) in dry MeOH (150 mL) was stirred with K_2CO_3 (5 g) at 50° for ~2 h, filtered, concentrated to small volume, diluted with ether (150 mL), washed with water (3 × 50 mL), and concentrated. The oily residue was eluted from a column of silica gel (100 g) with hexane–ethyl acetate (4:1) to give the *tert*-butyldiphenylsilyl ether **31** as an oil (7.9 g, 80%), $[\alpha]_D^{20}$ −23° (*c* 1, chloroform). A solution of this product in tetrahydrofuran (80 mL) was treated with M tetrabutylammonium fluoride in tetrahydrofuran (44 mL) at room temperature for 1 h. The solution was then poured into acetone–water (1:1, 300 mL) and concentrated under reduced pressure at 40°. A solution of the residue in ether (150 mL) was washed with water (3 × 50 mL), dried, and concentrated. The residue was eluted from a column of silica gel with hexane–ethyl acetate (1:1) to give **31** (1.8 g, 65%) as an oil, $[\alpha]_D^{20}$ −20° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.30 (d, 3 H, $J_{1,2}$ 5.8 Hz, Me), 2.00 (b, 1 H, HO-4), 2.37 (t, 2 H, $J_{4,5} = J_{5,6}$ = 7.0 Hz, CH_2-5), 2.70 (dd, 1 H, $J_{2,3}$ 2.5, $J_{3,4}$ 5.0, H-3), 2.97 (qd, 1 H, $J_{2,3}$ 2.5, $J_{1,2}$ 5.8 Hz, H-2), 3.56 (m, 1 H, H-4), 4.95–5.15 (m, 2 H, H-7), and 5.5–6.0 (m, 1 H, H-6).

2,4,6-Trideoxy-4-trifluoroacetamido-L-ribo-*hexose* (**23**). — The conversion of **31** into **23** followed a sequence analogous to that described for the conversion of **30** into **22**. The intermediate benzyl urethane **34** had $[\alpha]_D^{20}$ −31° (*c* 1, chloroform), and was obtained as an oil (85%). The cyclic urethane **37** was also an oil (73%) and had $[\alpha]_D^{20}$ +9° (*c* 1, chloroform). The (2*S*,3*S*,4*R*)-4-trifluoroacetamido-hept-6-en-2,4-diol (**43**) was obtained (45%) as an oil, $[\alpha]_D^{20}$ −13° (*c* 1, chloroform). The product **23** had m.p. 168° (from ethyl acetate–hexane), $[\alpha]_D^{20}$ −131° (*c* 1, methanol; 15 min) (Found: C, 39.4; H, 4.9; N, 5.6. $C_8H_{12}F_3NO_4$ calc.: C, 39.5; H, 5.0; N, 5.8%).

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REFERENCES

1 C. FUGANTI AND P. GRASSELLI, *Chem. Ind. (London)*, (1977) 983.
2 C. FUGANTI AND P. GRASSELLI, *J. Chem. Soc., Chem. Commun.*, (1978) 299–300.
3 M. N. PADDON-ROW, N. RONDAN, AND K. N. HOUK, *J. Am. Chem. Soc.*, 104 (1982) 7162–7166.
4 G. FRONZA, C. FUGANTI, P. GRASSELLI, G. PEDROCCHI-FANTONI, AND C. ZIROTTI, *Tetrahedron Lett.*, (1982) 4143–4146.

5 C. FUGANTI, P. GRASSELLI, AND G. PEDROCCHI-FANTONI, *J Org. Chem.*, 48 (1983) 909–910.
6 C. FUGANTI, P. GRASSELLI, G PEDROCCHI-FANTONI, S. SERVI, AND C. ZIROTTI, *Tetrahedron Lett.*, (1983) 4143–4146.
7 C. FUGANTI, S. SERVI, AND C. ZIROTTI, *Tetrahedron Lett.*, (1983) 5285–5288.
8 N MINAMI, S. S. KO, AND Y. KISHI, *J. Am. Chem. Soc*, 104 (1982) 1109–1111
9 B. BERNET AND A. VASELLA, *Tetrahedron Lett.*, (1983) 5491–5494.
10 S. J. ANGYAL, *Angew. Chem., Int. Ed. Engl.*, 8 (1969) 157–166.
11 C ALTONA AND C. A. G. HAASNOOT, *Org. Magn. Reson.*, 13 (1980) 417–429.
12 A. S. PERLIN, B. CASU, AND H. J. KOCH, *Can. J. Chem.*, 48 (1970) 2596–2606.
13 D. E. DORMAN AND J. D. ROBERTS, *J. Am. Chem. Soc.*, 92 (1970) 1355–1366.
14 G. FRONZA, C. FUGANTI, AND P. GRASSELLI, *J Chem. Soc., Perkin Trans. 1*, (1982) 885–891.
15 G FRONZA, C FUGANTI, P GRASSELLI, AND G PEDROCCHI-FANTONI, *J Carbohydr. Chem.*, 2 (1983) 225–248.
16 G FRONZA, C. FUGANTI, P. GRASSELLI, L. MAJORI, G. PEDROCCHI-FANTONI, AND F. SPREAFICO, *J. Org. Chem*, 47 (1982) 3289–3296.