Regio- and stereo-chemical outcomes in the nucleophilic ring cleavage reactions of mono-epoxides derived from *cis*-1,2-dihydrocatechols

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Reactions of the mono-epoxy derivatives, 4–7, of the *cis*-1,2-dihydrocatechols 1 and 2 with various oxygen-, nitrogen-, carbon- and halogen-centred nucleophiles have been studied. In both direct and acid-catalysed processes these epoxides react exclusively by the pathway involving nucleophilic attack at 5a-C of the substrate and such regioselectivity has been exploited in a synthesis of the fluoro-deoxy-conduritol 32. Palladium-catalysed nucleophilic additions to epoxide 4 proceed in the same regiochemical sense (attack at 5a-C) but with overall retention of configuration. A competing process associated with palladium-catalysed addition of phthalimide to epoxide 4 is isomerisation of the substrate to cyclohexenone 41. Product structures have been established by single-crystal X-ray analyses and chemical correlation studies.
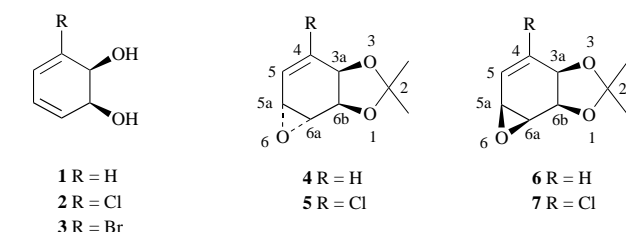
Introduction

Mutant strains of the micro-organism *Pseudomonas putida* have been employed in the microbial oxidation of various arenes and a number of the resulting *cis*-1,2-dihydrocatechols are produced commercially by this or related means. Notable members of this now readily available class of compound§ include those derived from benzene (*viz.* diol 1¶), chlorobenzene (diol 2¶) and bromobenzene (diol 3). Due to their unique combinations of functionality, all three of these *cis*-1,2-dihydrocatechols have found increasing use as starting

1 R = H
2 R = Cl
3 R = Br

4 R = H
5 R = Cl

6 R = H
7 R = Cl

materials in the preparation of various natural products (most notably cyclitols) and related molecules.[1] The early stages of such synthetic sequences often involve the preparation and nucleophilic ring-cleavage of mono-epoxy derivatives of compounds such as 1–3.[2] There has, however, been some apparent variation (see below) in the regiochemical outcomes of such ring-opening reactions. As part of a continuing series of studies on the applications of *cis*-1,2-dihydrocatechols to chemical syn-

thesis,[3] we had occasion to examine more closely the regio- and stereo-chemical outcomes of reactions involving nucleophilic ring-cleavage of the mono-epoxy derivatives, 4–7, of compounds 1 and 2.[4] We now detail the results of this study.
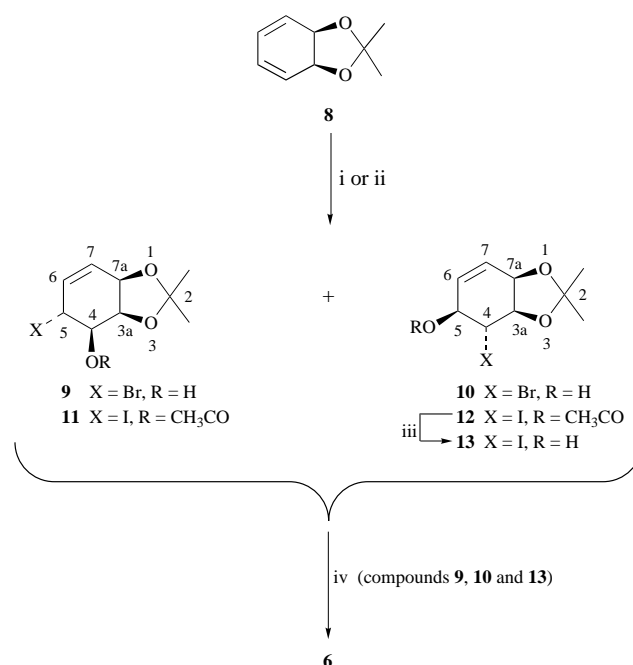
Results and discussion

Preparation of mono-epoxides 4–7

Whilst compounds 4 and 5 were readily prepared from the corresponding *cis*-1,2-dihydrocatechols using literature procedures,[5] syntheses of *cis-cisoid-cis* epoxides 6 and 7 were less straightforward. The key step in the ultimately successful route to substrate 6 (Scheme 1) involved reaction of compound 8,[5a]

8

i or ii

9 X = Br, R = H
11 X = I, R = CH₃CO

10 X = Br, R = H
12 X = I, R = CH₃CO
13 X = I, R = H

iv (compounds 9, 10 and 13)

6

Scheme 1 *Reagents and conditions:* i, NBS, DMSO, H₂O, 5 to 20 °C, 0.75 h, 64% combined yield; ii, I₂, CH₃CO₂Ag, CH₃CO₂H, H₂O, 20 °C, 46 h, 82%, 1 : 9 11 and 12; iii, K₂CO₃, CH₃OH, 20 °C, 2 h, 80%; iv, KH, THF, 2.5 h, 0 to 20 °C, 89%

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§ *Ca.* twenty diols derived from substituted aromatic compounds are available commercially from the following sources: Genencor International, Inc., Palo Alto, CA; ICI Fine Chemicals, Manchester, UK; Enzymatix, Cambridge, UK; Janssen Chimica, Geel, Belgium.
¶ All compounds except 1, 2, 3, 5, 7, 14, 16, 17, 24, 26–32 and 34–36 are racemic but only one enantiomer is depicted for clarity. Diol 1 is a *meso* compound. Diol 2 is obtained in > 99.9% ee[1c] so all compounds derived from it are assumed to be of comparable enantiomeric excess.

the acetonide derivative of **1**, with *N*-bromosuccinimide (NBS) in the presence of moist dimethyl sulfoxide (DMSO) according to the method of Dalton and Dutta.[6] In this way a *ca.* 1:2 mixture of bromohydrins **9**‖ and **10** was obtained (64% combined yield). These products could be separated from one another by column chromatography and each was fully characterised spectroscopically. In the ^{1}H NMR spectrum of the major diastereoisomer, **10**, the triplet at δ 3.93 was assigned (using H,C-COSY techniques) to 4-H and the magnitude of the observed coupling (J 8.5 Hz) suggests a *trans*-diaxial relationship between this proton and its immediate neighbours. In the analogous spectrum of the minor isomer, **9**, the magnitudes of the vicinal couplings ($J_{4,3a}$ 5.2 Hz and $J_{4,5}$ 9.0 Hz) associated with the signal due to 4-H (at δ 4.57) suggest a *trans*-diaxial arrangement between this proton and 5-H, together with a *cis*-relationship to 3a-H.
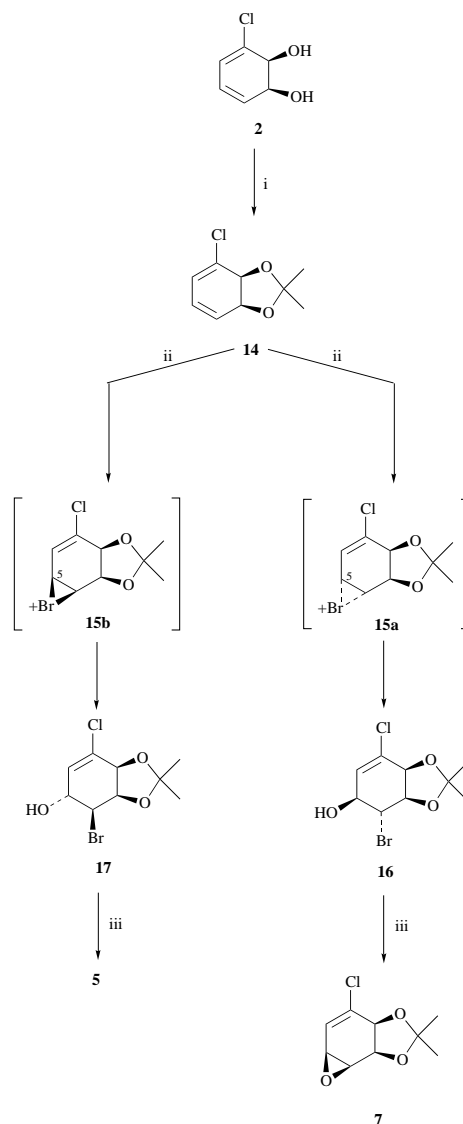
In related work, diene **8** was reacted with a 1:1 mixture of iodine and silver acetate in acetic acid containing water[7] to give an inseparable *ca.* 1:9 mixture (as judged by ^{1}H NMR analysis) of the regioisomeric iodoacetates **11** and **12**. Subjecting this mixture of acetates to hydrolysis with potassium carbonate in methanol then gave the corresponding mixture of iodohydrins from which the major component, tentatively assigned as compound **13**, could be isolated by fractional crystallisation.

Treatment of the mixture of bromohydrins **9** and **10** with potassium hydride in tetrahydrofuran (THF) at 20 °C resulted in smooth elimination of the elements of hydrogen bromide and formation of the desired epoxide **6**, which was isolated in 89% yield after column chromatography and recrystallisation. Reaction of iodohydrin **13** under the same conditions also afforded epoxide **6** (85%). The ^{1}H and {^{1}H}^{13}C NMR spectra obtained for this epoxide were in full accord with the proposed structure.

Interestingly, when compound **14**,[5b] the acetonide derivative of diol **2**, was treated with NBS in 1,2-dimethoxyethane (DME)–water a *ca.* 10:1 mixture of products **16** and **17** (34% combined yield) was obtained (Scheme 2). Bromohydrins **16** and **17**, unlike the products formed by treatment of acetonide **8** with NBS, were the result of hydrolytic opening of two different bromonium ion intermediates (**15a** and **15b**) at the allylic carbon (5-C). The structures of bromohydrins **16** and **17** were determined by ^{1}H NMR experiments and chemical correlation studies. Thus, whilst the magnitude of the observed coupling between 3a-H and 4-H ($J_{3a,4}$ 9.1 Hz) in the ^{1}H NMR spectrum of compound **16** was indicative of a *trans*-pseudoaxial orientation, the observed coupling between 4-H and 5-H ($J_{4,5}$ 4.4 Hz) was less convincing (of a *trans*-orientation). The minor bromohydrin **17** showed couplings ($J_{3a,4}$ 2.2 Hz and $J_{4,5}$ 9.0 Hz) indicative of a *cis*-orientation between 3a-H and 4-H and a *trans*-orientation between 4-H and 5-H. ^{1}H NMR decoupling experiments were used to determine the regiochemistry of bromohydrins **16** and **17**, whilst their base-promoted cyclisation to epoxides **7** and **5**, respectively, established their stereochemistry.

Reaction of substrates 4–7 with nucleophiles

(i) Acid-catalysed and base-promoted processes. Treatment of the *transoid*-epoxide **4** with a variety of nucleophiles in the presence of acid catalysts or base produced various differentially protected conduritol F derivatives (Scheme 3). The nucleophiles employed were benzoic acid, methanol, methoxide ion, azide ion[8] and diethyl malonate ion providing products **18** (78% at 64% conversion), **19** (56%), **20** (94% at 53% conversion), **21** (87%) and **22** (20%) respectively. Thus, in full accord with

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‖ The Chemical Abstracts numbering scheme (see structure **9**, Scheme 1) has been used throughout this paper for the 1,3-benzodioxolane ring system associated with compounds **9–14**, **16–18**, **20–24**, **27**, **29–31** and **33–41**. The α/β notation used refers to the stereochemistry around the central six-membered ring of the relevant molecule, with α being up and β being down with relation to the plane of the page.

Scheme 2 *Reagents and conditions:* i, $(H_3C)_2C(OCH_3)_2$, PTSA·H_2O, acetone, 20 °C, 0.33 h; ii, NBS, $H_3CO(CH_2)_2OCH_3$–H_2O, −5 to 0 °C, 10 h, 31% **16** and 3% **17**; iii, NaOH, Bu_4NHSO_4, CH_2Cl_2, reflux 2 h
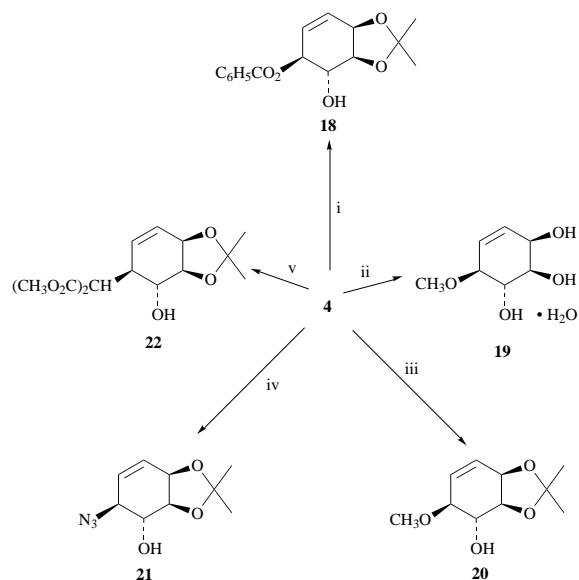
Scheme 3 *Reagents and conditions:* i, $C_6H_5CO_2H$, 20 mol% CSA, CH_2Cl_2, 20 °C, 14 h, 78% at 64% conversion; ii, CH_3OH, 14 mol% CSA, CH_2Cl_2, 20 °C, 22 h, 56%; iii, CH_3ONa, CH_3OH, 20 °C, 24 h, 94% at 53% conversion; iv, NaN_3, NH_4Cl, 8:1 H_2O–$CH_3O(CH_2)_2OH$, reflux, 5 h, 87%; v, $(CH_3O_2C)_2CHNa$, THF, 20 °C, 24 h, 20%

expectations, the reaction of compound **4** with all of the above nucleophiles involved diaxial epoxide ring-opening and exclusive formation (within the limits of detection) of the *trans*-1,2-addition products. The ^{1}H NMR spectra of all of these products were again assigned using H,C-COSY procedures and for compounds **18** and **20–22** the observed values of $J_{4,5}$ and $J_{4,3a}$ were of the order of 8.6 to 10.0 Hz—suggestive of *trans*-diaxially related protons on a cyclohexene ring. Preliminary assignments of the regiochemical outcomes associated with these ring-cleavage reactions were based largely on the assumption that nucleophilic attack should proceed preferentially at the allylic carbon (5a-C) of the epoxide ring, this preference being a reflection of the operation of favourable electronic factors (stabilisation of incipient carbocationic character) at the allylic position and (perhaps) less severe steric effects being exerted by the (*endo*)-2-C methyl group at the same position [by comparison with the homo-allylic (6a-C) position]. Definitive confirmation of several of these structural assignments was obtained by conducting single-crystal X-ray analyses on compounds **18**, **20** and **21**. The details of the structure determination for compound **21** are reported herein (see Fig. 1 and Experimental section) whilst the results of analogous studies on compounds **18** and **20** have been described elsewhere.[9]

A number of features associated with the reactions shown in Scheme 3 deserve further comment. Thus, in the case where epoxide **4** was treated with methanol in the presence of (+)-camphorsulfonic acid (CSA), ring-cleavage was accompanied by methanolysis of the acetonide moiety and the resulting triol was always isolated as its monohydrate **19**. The non-hydrated form of this material has been obtained previously.[5a] The rather disappointing yields associated with the sodium dimethyl malonate promoted ring-opening reaction of compound **4** appear to be due, at least in part, to the labile nature of the product **22**, which tends to decompose on standing or when subjected to chromatographic purification.

The observation that epoxide **4** reacts with sodium azide to give the azido alcohol **21** seemed to be at odds with an earlier report[5b] which suggested that reaction of chloro epoxide **5** with
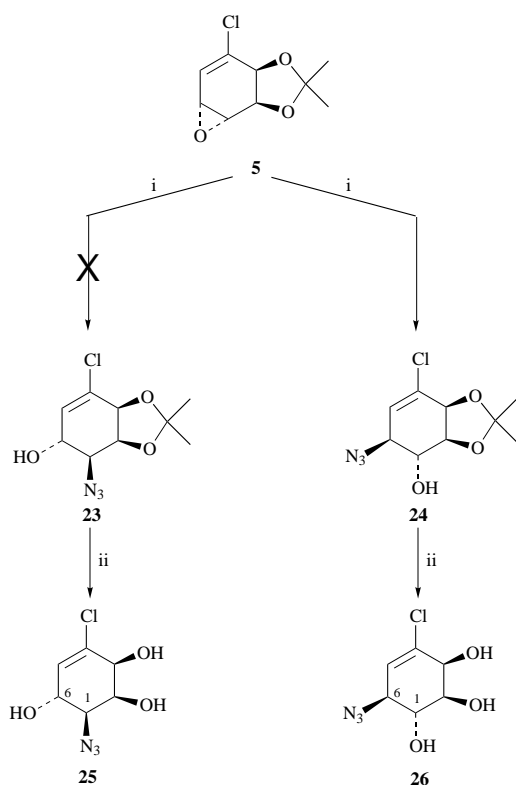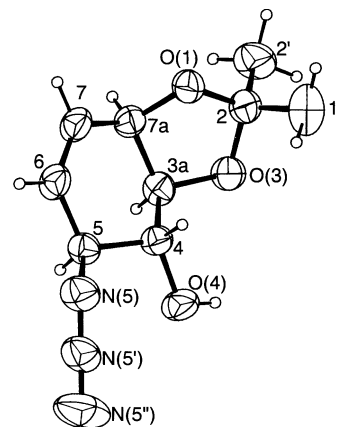

Fig. 1 ORTEP derived from the X-ray crystal structure of the (3a*S*,4*R*,5*S*,7a*R*)-enantiomer of azido alcohol **21**. (Thermal ellipsoids are drawn at the 50% probability level and hydrogen atoms are represented by spheres of arbitrary radius. The C symbol for the carbon atoms has been omitted.)
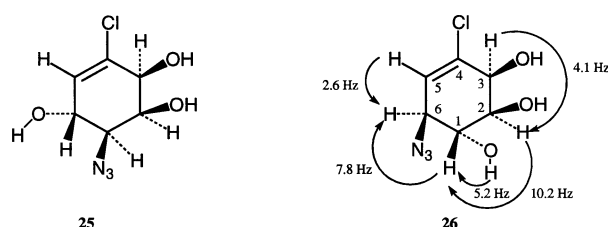

Fig. 2 Selected three- and four-bond couplings observed in the 270 MHz ^{1}H NMR spectrum of azido alcohol **26** which have allowed its differentiation from regioisomer **25**

the same nucleophile (and under essentially the same conditions) produces compound **23** (Scheme 4). To clarify matters, a sample of epoxide **5** was subjected to reaction with sodium azide and the single major product was found to have the same spectroscopic and physical properties as described in the earlier report.[5b] However, the strong spectroscopic resemblances between this compound and the azido alcohol **21** prompted consideration of the possibility that the compound derived from azide opening of epoxide **5** has structure **24** and not **23** as originally suggested.[5b] Further suspicions about the original structural assignment arose when the triol derived from deprotection of the azido alcohol was subjected to detailed spectroscopic analysis. Thus, in connection with a proposed synthesis of L-*threo*-sphingosine, the azido alcohol derived from epoxide **5** (and presumed, at this stage, to have structure **23**) was subjected to reaction with strongly acidic and wet Amberlyst 15 ion-exchange resin (in methanol). In this manner a single azido triol, presumed to have structure **25**, was obtained in 97% yield. However, careful scrutiny of the spectral data obtained for compound '**25**' revealed serious inconsistencies. The ^{1}H NMR spectrum of the presumed triol **25** was recorded in [^{2}H$_6$]DMSO and the addition of D$_2$O eliminated the exchangeable protons, thus largely simplifying the resonance patterns. The connectivity assignment began with the readily identifiable olefinic proton 5-H (δ 5.72, d, J 2.6 Hz, 1H; see Fig. 2). The only other proton resonance sharing the same coupling constant (J 2.6 Hz) was at δ 3.93 (J 7.8 and 2.6 Hz, 1H) and therefore must be 6-H, as supported by selective irradiation experiments. Surprisingly, the resonance pattern of this proton (6-H) appeared to be unchanged upon the addition of D$_2$O, indicating that no alcohol functionality was present at 6-C. Since the azide moiety was clearly present, as indicated by the IR spectrum, it seemed logical that the azide group resided at 6-C rather than 1-C. Further scrutiny of the spectra confirmed these observations and led to the conclusion that the azido triol obtained actually possessed structure **26** and not **25**. Consequently, azido alcohol

Scheme 4 *Reagents and conditions:* i, NaN$_3$, NH$_4$Cl, 3:3:2 EtOH–CH$_3$O(CH$_2$)$_2$OCH$_3$–H$_2$O, reflux, 4 h, 72%; ii, Amberlyst 15 (wet) ion-exchange resin (Aldrich), strongly acidic, CH$_3$OH, 20 °C, 192 h, 97%

23 is **NOT** formed under the reaction conditions previously reported,[5b] but rather regioisomer **24** is the single major product formed in 72% yield (Scheme 4). These conclusions were reported earlier in a corrigendum.[5c] The relative stereochemistry of triol **26** was determined by interpretation of the ^{1}H NMR coupling constants for 6-H and 1-H (Fig. 2), which suggest a *trans*-relationship between 6-H and 1-H ($J_{1,6}$ 7.8 Hz) and between 1-H and 2-H ($J_{1,2}$ 10.2 Hz).

In order to unequivocally prove the regio- and stereochemistry of azido alcohol **24**, a chemical correlation study was undertaken. Since benzylamino alcohol **27** (Scheme 5) is a
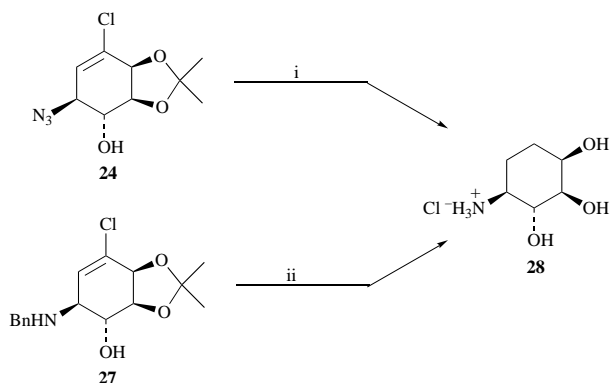
Scheme 5 *Reagents and conditions:* i, 80 psi H$_2$, PtO$_2$, CH$_3$OH, 20 °C, 6 h, 86%; ii, NH$_4^+$HCO$_2^-$, 10% Pd-C, CH$_3$OH, reflux, 0.16 h, 72%

known compound of proven structure,[5b] both this compound and azido alcohol **24** were degraded to the trihydroxyamine hydrochloride **28**. Thus, hydrogenolysis of azido alcohol **24** using Adams' catalyst afforded the ammonium salt **28** in 86% yield. Subjection of benzylamino alcohol **27** to the same reaction conditions afforded only a mixture of reduction products and the use of Pearlman's catalyst [10] [20% Pd(OH)$_2$] gave similar results. However, catalytic transfer hydrogenolysis [11] of compound **27** provided ammonium salt **28** in 72% yield. The two products obtained from the degradation of acetonides **24** and **27** were indistinguishable by ^{1}H and ^{13}C NMR spectroscopy as well as by $[a]_D$ comparison. This result served further to confirm the stereochemistry of azido alcohol **24**. Subsequent X-ray diffraction analysis [12] of azido alcohol **24**, in addition to the fact that azido alcohol **23** was later synthesised using an alternative route,[2c] further supported all of the above conclusions. Thus, there appears to be no exception, so far, to the rule that nucleophilic ring-opening of epoxides **4** and **5** involves predominant attack at the allylic (5a-C) carbon.

Further nucleophilic ring-cleavage reactions of epoxide **5** which have been exploited in a synthesis of fluoro-deoxyconduritol F **32** are summarised in Scheme 6. Thus, as previously reported,[5b] treatment of epoxide **5** with boron trifluoride–diethyl ether resulted in a *ca.* 1:1 mixture of the diastereoisomeric fluorohydrins **29** and **30** which could be separated from one another chromatographically. The lack of stereoselectivity in this reaction has been interpreted as meaning that an S$_N$1 process, involving an allylic cation, is in operation. Consequently, the use of a 'softer' fluoride ion source was examined in the expectation that this would favour the desired S$_N$2 process. In the event,[5b] reaction of epoxide **5** with tetrabutylphosphonium dihydrogen trifluoride afforded the fluorohydrin **30** (75%) in a completely regio- and stereo-selective manner. With useful quantities of this latter material in hand its conversion into compound **32** was achieved by tributyltin hydride promoted dechlorination (to give **31**) and subsequent acid-catalysed hydrolysis of the acetonide group. However, the reductive dechlorination step was low yielding (*ca.* 30%). A more efficient route to the target conduritol involved debromination of the bromo-analogue of compound **30**—a process which proceeded in 75% yield.
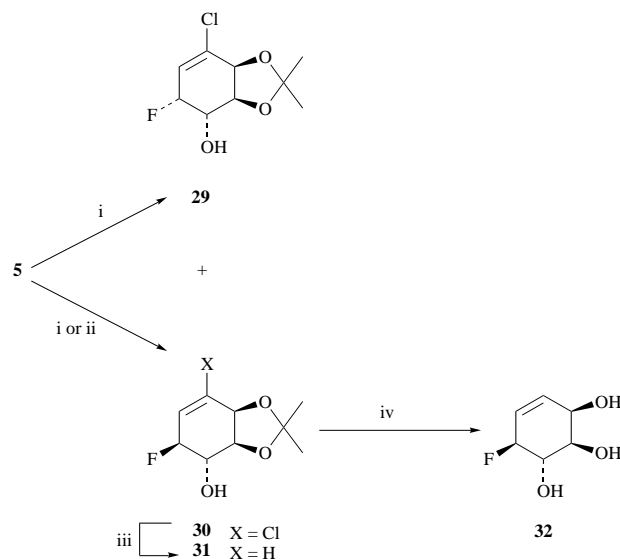
Scheme 6 *Reagents and conditions:* i, BF$_3$·OEt$_2$, Et$_2$O, benzene, 20 °C, 15 h, 21% **29** and 23% **30**; ii, H$_2$Bu$_4$PF$_3$, 105 °C, 24 h, 75%; iii, Bu$_3$SnH, AIBN, toluene, 111 °C, 7 h, 75%; iv, Amberlyst 15 (wet) ion-exchange resin (Aldrich), CH$_3$OH, 20 °C, 15 h, 94%

Epoxide **6** was subjected to reaction with the same range of nucleophiles as described above for isomer **4**, but the results were rather disappointing. Thus, only in the case where compound **6** was treated with methanol in the presence of CSA was any characterisable product obtained. The reaction appeared to be very clean and quite high yielding as judged by TLC analysis of the crude reaction mixture. Unfortunately, however, the reaction product proved to be very unstable and, after silica gel chromatography, only a 17% yield of the conduritol C derivative **33** was obtained. The illustrated 4α,5β-stereochemistry in compound **33** was assigned through analysis of the ^{1}H NMR
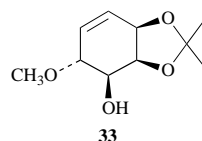

spectrum. The magnitude (1.0 Hz) of the coupling constant $J_{3a,4}$ was suggestive of a small dihedral angle between 3a-H and 4-H (molecular mechanics calculations suggest this angle should be *ca.* 60°), thus implying 4α-stereochemistry in **33**. The considerably greater coupling between 4-H and 5-H (J 8.1 Hz) is, once again, indicative of a *trans*-diaxial relationship between these protons [the dihedral angle H(4)–C(4)–C(5)–H(5) was determined to be *ca.* 170° by molecular mechanics calculations] and suggests 5β-stereochemistry. The placement of the methoxy group at 5-C in compound **33** derives from the assumption that, under the conditions of the reaction, nucleophilic attack on epoxide **6** will occur preferentially at the allylic (5a-C) position.

In contrast to the lack of useful reactivity shown by epoxide **6** towards nucleophiles, epoxide **7** was found to undergo ring-opening in the presence of LiBr or NaN$_3$, to afford compounds **34** and **35**, respectively, in high yield (Scheme 7). Subsequent treatment of bromohydrin **34** with azide ion generated compound **36**, an epimer of **35**. The regio- and stereo-chemical assignment of azido alcohols **36** and **35** was confirmed by their conversion into D-*erythro*- and D-*threo*-sphingosine, respectively, as reported previously.[13,14]

(ii) Palladium(0)-catalysed processes. Pioneering work by a number of groups [15] has established that reaction of 3,4-epoxycycloalkenes with nucleophiles in the presence of a palladium(0) catalyst often results in the highly selective formation of *syn*-1,4-addition products. The application of such processes

to epoxide **4** might be expected to produce conduritol A derivatives. In the event, treatment of a THF solution of compound **4** with benzoic acid (as nucleophile) and tetrakis(triphenylphosphine)palladium(0) (5 mol% with respect to **4**) resulted in

7

34

36

35

D-*erythro*-sphingosine

D-*threo*-sphingosine
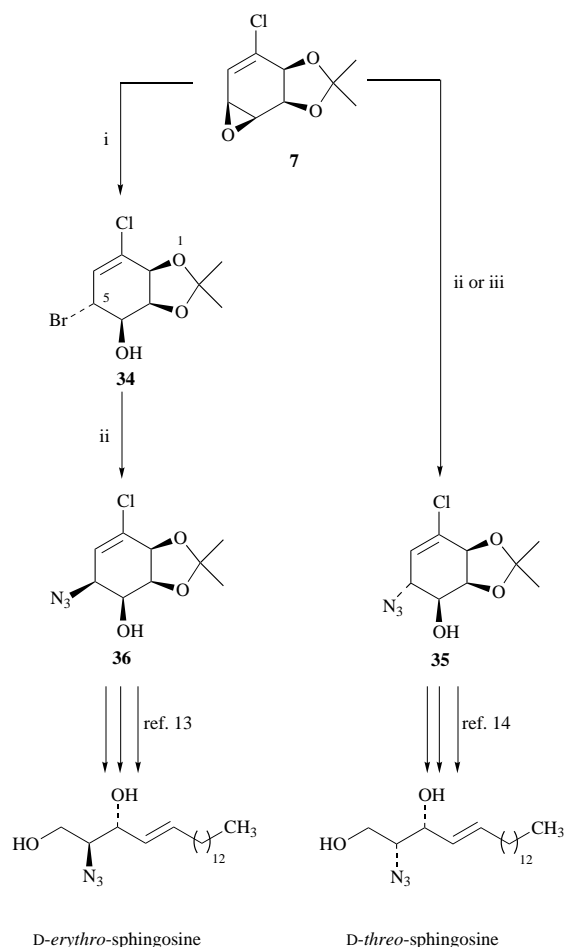
Scheme 7 *Reagents and conditions:* i, LiBr, ethyl acetoacetate, THF, 30 °C, 4 h, 94%; ii, NaN$_3$, DMSO paste, ultrasound, 45 °C, 4 h, 75% **36** and 22% **35**; iii, NaN$_3$, NH$_4$Cl, 13:10:8 H$_3$CO(CH$_2$)$_2$OCH$_3$–H$_3$CCH$_2$OH–H$_2$O, 55 °C, 1 h, 87%

41

37 R = C$_6$H$_5$CO
38 R = H

4

40

39

+

+

41

22
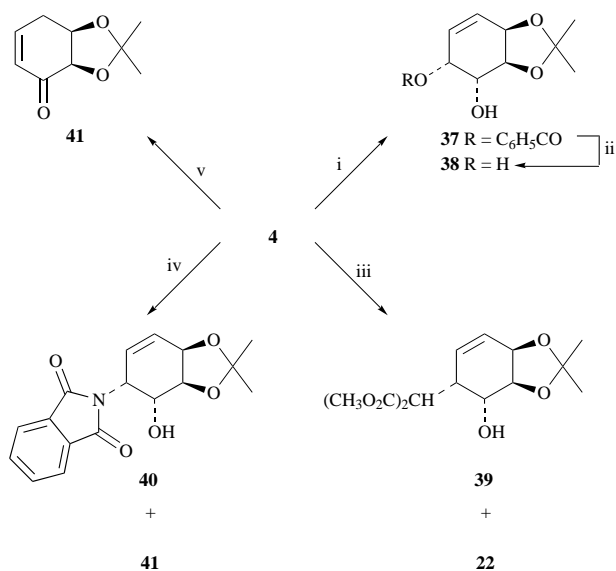
Scheme 8 *Reagents and conditions:* i, C$_6$H$_5$CO$_2$H, 5 mol% Pd[P(C$_6$H$_5$)$_3$]$_4$, THF, 20 °C, 72 h, 53%; ii, K$_2$CO$_3$, CH$_3$OH, 20 °C, 2 h, 98%; iii, (CH$_3$O$_2$C)$_2$CH$_2$, 5 mol% Pd[P(C$_6$H$_5$)$_3$]$_4$, THF, 20 °C, 36 h, 65%; iv, phthalimide, 10 mol% Pd[P(C$_6$H$_5$)$_3$]$_4$, THF, 20 °C, 72 h, 38% **40** and 45% **41**; v, Pd$_2$(DBA)$_3$·CHCl$_3$, DPPE, C$_6$H$_5$CO$_2$H, THF, 20 °C, 7 h, 70%

the formation of a nucleophilic addition product in 53% yield (Scheme 8). Hydrolytic removal of the benzoate moiety in the reaction product was accomplished with potassium carbonate in methanol and the {^{1}H}^{13}C NMR spectrum of the resulting diol exhibited nine signals. This observation immediately ruled out the possibility that the elements of benzoic acid had added to epoxide **4** in a *syn*-1,4-fashion, since hydrolysis of such a product would form a C_s symmetric diol for which only six ^{13}C NMR signals would be seen. Further study revealed that the product diol was identical with the compound derived from the osmium tetroxide mediated *cis*-dihydroxylation of diene **8**. Since electrophilic additions to diene **7** appear to involve exclusive attack at the β-face (due to steric shielding of the α-face by the *endo*-methyl of the dioxolane ring), the diol must have structure **38** and hence the original benzoate must have either structure **37** or be the regioisomer in which the positions (but not the stereochemistries) of the hydroxy and benzoyloxy groups have been interchanged. Final confirmation of the structure of hydroxybenzoate **37** was established by single-crystal X-ray analysis, details of which have been published elsewhere.[9]

As noted above, palladium(0)-catalysed additions of nucleophiles to 3,4-epoxycycloalkenes usually result in the formation of 1,4-addition products, although small amounts of 1,2-addition products have been observed.[16] Since it is known[15b] that carbon-centred nucleophiles sometimes show a greater propensity than heteroatom-centred nucleophiles to add to cycloalkadiene mono-epoxides in a 1,4-fashion, epoxide **4** was reacted with dimethyl malonate in the presence of Pd(PPh$_3$)$_4$. However, an inseparable 1:1 mixture of two diastereoisomeric addition products was obtained. {^{1}H}^{13}C NMR spectroscopic analysis of this mixture established that one of the components was identical with compound **22**, which had previously (see above) been obtained from the reaction of epoxide **4** with sodium diethyl malonate. On the basis that the ^{13}C NMR data for the second component were very similar to those of the first, and given that *syn*-1,2 addition is observed in the formation of **37** from **4**, this second component is tentatively assigned as malonate **39**. Interestingly, treatment of epoxide **4** with diethyl malonate in the presence of palladium bis(diphenylphosphino)ethane [Pd(DPPE)$_2$] [prepared *in situ* by reaction of Pd$_2$(DBA)$_3$·CHCl$_3$ (DBA = dibenzylideneacetone)[17] with two equivalents of diphenylphosphinoethane (DPPE)] gave the *anti*-1,2-addition compound **22** as the only characterisable product. However, given the low yield (21%) associated with this conversion, the concomitant formation of the *syn*-isomer cannot be discounted.

The reaction of epoxide **4** with phthalimide in the presence of Pd(PPh$_3$)$_4$ afforded two products which were readily separated by chromatography. The less mobile component was identified as the expected *syn*-1,2-addition product **40** (38%). Analysis of the ^{1}H NMR spectrum of compound **40** showed $J_{3a,4}$ 5.9 Hz which is suggestive of the illustrated 4β,5β-stereochemistry and this was subsequently confirmed by X-ray analysis (Fig. 3). Recently a chiral methoxymethyl (MOM)-derivative of compound **40** has been reported[18] by Johnson and co-workers, whilst Borchardt *et al.* have shown[5a] that treatment of epoxide **4** with adenine under [(Pr^{i}O)$_3$P]$_4$Pd catalysis leads to the exclusive formation of the *syn*-1,2-addition product. The second product isolated from the reaction of epoxide **4** with phthalimide in the presence of Pd(PPh$_3$)$_4$ was identified as cyclohexenone **41** (45%). In the {^{1}H}^{13}C NMR spectrum of enone **41** the signals at δ 196.2, 146.3 and 128.1 were assigned to the sp^2-carbons 4-C, 6-C and 5-C respectively. The infrared spectrum of this compound showed a strong absorption maximum at 1665 cm^{-1}, whilst the ^{1}H NMR spectrum was completely consistent with the assigned structure. Compound **41** has recently been prepared[19] (in monochiral form) during the course of a total synthesis of the natural product palitantin, however no spectral data were provided. The yields of compound **41** could be increased significantly (up to 70%) by using
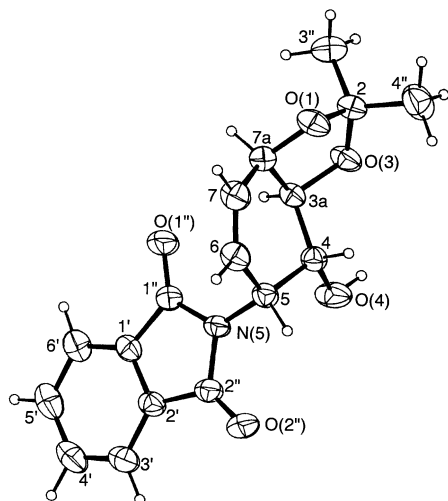
Fig. 3 ORTEP derived from the X-ray crystal structure of the (3aS,4R,5R,7aR)-enantiomer of compound 40. (Thermal ellipsoids are drawn at the 50% probability level and hydrogen atoms are represented by spheres of arbitrary radius. The C symbol for the carbon atoms has been omitted.)

[Pd(DPPE)₂], rather than Pd(PPh₃)₄, as catalyst. Curiously, whilst the conversion of epoxide **4** into enone **41** is formally an isomerisation process, the presence of either benzoic acid or phthalimide was required before rearrangement was observed.

A mechanistic rationalisation of the various outcomes described above is given in Scheme 9. It is proposed that in all
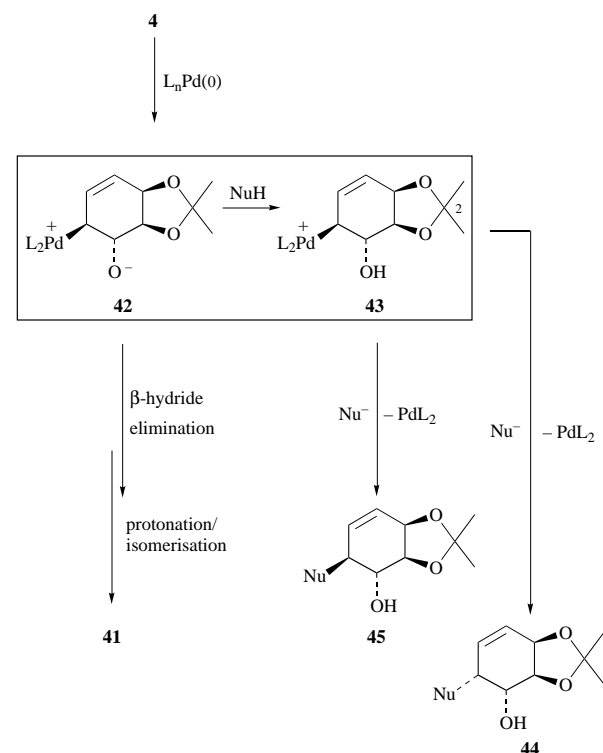
Scheme 9

of the palladium(0)-catalysed reactions the first step involves palladation of epoxide **4**. The stereoelectronic requirements of this process demand that the palladium-centred moiety be in a *syn*-relationship with the dioxolane ring. Due to the bulky nature of the latter moiety, it is assumed that the σ-allyl species **42** is formed in preference to its sterically more congested π-allyl isomer. An acid–base reaction between species **42** and the nucleophile would then give products **43** and Nu⁻, which could subsequently engage in an S_N2 process to form the observed *syn*-1,2-addition products **44**. Presumably an S_N2′ process

(which would deliver a 1,4-addition product) does not operate since the *endo*-methyl group (at 2-C) of the dioxolane ring prevents proper orbital alignment between the π-electrons of the double-bond and the adjacent C–Pd σ-bond. The formation of the *anti*-1,2-addition product **22** from the reaction of epoxide **4** with Pd⁰ could occur in one of two possible ways. Thus, the malonate anion, formed by reaction of the malonic ester with zwitterion **42**, could attack the palladium centre in **43** and subsequent reductive-elimination of Pd⁰ from the intermediate so-formed would afford the *anti*-1,2-addition product **45** (≡**22**). Alternately, direct attack by the malonate anion on epoxide **4** would also account for the formation of compound **22** as was demonstrated earlier (Scheme 3).

Isomerisation of 3,4-epoxycycloalkenes to the corresponding enone is often observed under Pd⁰-catalysis when the nucleophile does not react quickly enough with the initially produced palladium-complex.[20] This situation presumably prevails when cyclohexenone **41** is produced from **4** in the presence of Pd⁰ and the key step probably involves elimination of L₂PdH (β-hydride elimination) from complex **42**. Subsequent protonation and isomerisation steps would then produce the conjugated enone **41**.

Disappointingly, attempts to apply the palladium(0)-catalysed chemistry outlined above to epoxides **5** and **6** have not produced any useful results. Thus, reaction of compound **6** with various nucleophiles in the presence of several palladium catalysts led only to complex mixtures whilst the analogous treatment of epoxide **5** failed to produce any reaction whatsoever.

X-Ray structures of compounds 21 and 40

The molecular conformation of azide **21** is illustrated in Fig. 1. The cyclohexane ring is in a regular sofa conformation with C(4) lying 0.68(1) Å from the plane of the other ring atoms which are coplanar to within experimental limits. The *cis*-fused dioxolane ring adopts a O(1)β,C(7a)α half-chair conformation, with the pseudo-rotation parameters[21] $\Delta = -7.5°$ and $\varphi_m = 35.7°$. The N(5)–N(5′)–N(5″) bond angle of 172.6(2)° for the azido group indicates a significant distortion from linearity and the N(5)–N(5′) bond length, 1.226(4) Å, is significantly longer than that of the N(5′)–N(5″) bond, 1.127(4) Å. These features have also been observed in other azido moieties.

The molecular conformation of compound **40** is illustrated in Fig. 3. The atoms of the phthalimide moiety are coplanar [root mean square deviation 0.03 Å, $\delta_{max} = 0.06(1)$ Å for N(5)]. The cyclohexene ring is in the expected sofa form with C(4) lying 0.57(1) Å from the other ring atoms which are coplanar to within experimental limits. The *cis*-fused dioxolane ring adopts a conformation midway between an envelope and half-chair ($\Delta = 20.9$ and $\varphi_m = 35.6°$). The relative orientation of the phthalimide group to the benzodioxolanol moiety is given by the torsion angle, C(1″)–N(5)–C(5)–C(6) 57.5(3)°.

Experimental

Unless otherwise specified, ¹H and ¹³C NMR spectra were recorded in deuteriochloroform at 400 and 100 MHz, respectively. *J* Values are given in Hz. Positive-ion electron-impact mass spectra were recorded at 70 eV unless otherwise specified. Other general procedures have been reported elsewhere.[3c,5b]

(3aα,5aβ,6aβ,6bα)-2,2-Dimethyl-3a,5a,6a,6b-tetrahydro-oxireno[e]-1,3-benzodioxole 4

m-Chloroperbenzoic acid (4.14 g, 20.9 mmol, 85% peracid) was added in portions over 1 h to a chilled (ice–water) and magnetically stirred mixture of acetonide **8**[5a,22] (2.54 g, 16.7 mmol) and sodium hydrogen carbonate (2.48 g, 29.5 mmol) in CH₂Cl₂ (25 cm³). The reaction mixture was stirred for 5 h at 20 °C then poured into H₂O (100 cm³) and extracted with CH₂Cl₂ (3 × 50

cm³). The combined organic extracts were washed with sodium metabisulfite (2 × 50 cm³ of a 20% aqueous solution) and sodium hydrogen carbonate (2 × 100 cm³ of a saturated aqueous solution) before being dried, filtered and concentrated under reduced pressure to a light yellow oil. Kugelrohr distillation (80 °C/0.5 mmHg) of this material yielded the previously reported[5a] epoxide **4** (2.53 g, 90%) as a clear, colourless oil (Found: C, 64.3; H, 7.1. Calc. for $C_9H_{12}O_3$: C, 64.3; H, 7.2%); ν_{max}(NaCl)/cm⁻¹ 2986, 1379, 1370, 1243, 1167, 1068, 1052, 1000, 826 and 734; δ_H 6.06 (ddd, $J_{5,4}$ 10.0, $J_{5,5a}$ 3.7, $J_{5,3a}$ ca. 2.2, 1H, 5-H), 5.81 (dddd, $J_{4,5}$ 10.0, $J_{4,6b}$ ca. 2.7, $J_{4,3a}$ 2.2, $J_{4,5a}$ 1.0, 1H, 4-H), 4.78 (dm, $J_{6b,3a}$ 6.8, 1H, 6b-H), 4.46 (dt, $J_{3a,6b}$ 6.8, $J_{3a,5}$ 2.2, $J_{3a,4}$ 2.2, 1H, 3a-H), 3.55 (dd, $J_{6a,5a}$ 3.7, $J_{6a,6b}$ 2.0, 1H, 6a-H), 3.35 (tt, $J_{5a,5}$ 3.7, $J_{5a,6a}$ 3.7, $J_{5a,4}$ 1.0, $J_{5a,6b}$ 1.0, 1H, 5a-H) and 1.41 (s, 6H, 2 × CH₃); δ_C 131.9 (5-C), 123.5 (4-C), 110.3 (2-C), 70.7 (6b-C), 70.6 (3a-C), 49.0 (6a-C), 46.2 (5a-C), 27.6 (CH₃) and 25.8 (CH₃); m/z 153 [40%, (M − CH₃)⁺], 111 [25, [(M − CH₃ − CH₂CO)⁺], 81 (31) and 43 (100).

(3aα,4α,5β,7aα)-5-Bromo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 9 and (3aα,4β,5α,7aα)-4-bromo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-ol 10

Freshly recrystallised *N*-bromosuccinimide (1.16 g, 6.57 mmol) was added to a cooled (5 °C), magnetically stirred mixture of acetonide **8**[5a,22] (500 mg, 3.29 mmol), DMSO (5 cm³), potassium carbonate (454 mg, 3.27 mmol) and H_2O (89 cm³, 9.86 mmol) maintained under a N_2 atmosphere. The reaction mixture was warmed to 20 °C and stirred for 0.75 h before being diluted with H_2O (50 cm³) and extracted with Et_2O (4 × 30 cm³). The combined organic extracts were washed with sodium hydrogen carbonate (2 × 50 cm³ of a saturated aqueous solution) then dried, filtered and concentrated under reduced pressure to yield a pale-yellow oil. Column chromatography of this material (silica gel, 8 : 92 Et_2O–CH_2Cl_2 elution) yielded two fractions, A and B.

Concentration of fraction A (R_f 0.4) afforded a white solid which was recrystallised (CHCl₃ at −10 °C) to yield the *title compound* **9** (46 mg, 6%) as colourless needles, mp 119.5–121.0 °C [Found: (M − CH₃)⁺, 232.9813. $C_9H_{13}^{79}BrO_3$ requires (M − CH₃)⁺, 232.9813], ν_{max}(KBr)/cm⁻¹ 3431, 2987, 1376, 1224, 1161, 1081, 1066, 1032, 903 and 851; δ_H 5.88 (ddd, $J_{6,7}$ 10.3, $J_{6,5}$ 1.9, $J_{6,7a}$ 0.7, 1H, 6-H), 5.74 (dm, $J_{7,6}$ 10.3, 1H, 7-H), 4.66 (dm, $J_{3a,4}$ 5.2, 1H, 3a-H), 4.62 (m, 1H, 7a-H), 4.57 (ddd, $J_{4,5}$ 9.0, $J_{4,3a}$ 5.2, $J_{4,OH}$ 3.9, 1H, 4-H), 4.03 (dd, $J_{5,4}$ 9.0, $J_{5,6}$ 2.9, 1H, 5-H), 2.38 (d, $J_{OH,4}$ 3.9, 1H, OH), 1.41 (s, 3H, CH₃) and 1.40 (s, 3H, CH₃); δ_C 130.5 (6-C), 127.5 (7-C), 109.9 (2-C), 77.4 (3a-C), 73.5 (7a-C), 68.6 (4-C), 55.4 (5-C), 27.6 (CH₃) and 26.6 (CH₃); m/z (20 eV) 235 (100%), 233 [98, (M − CH₃)⁺], 175 (36), 173 [35, (M − CH₃ − CH₂CO − H₂O)⁺], 147 (28), 145 (27), 111 (34), 94 (31) and 43 (31).

Concentration of fraction B (R_f 0.5) afforded a white solid which was recrystallised (twice from Et_2O–hexane) to yield the *title compound* **10** (291 mg, 35%) as colourless plates, mp 46.0–46.5 °C (Found: C, 43.7; H, 5.05; Br, 32.2. $C_9H_{13}BrO_3$ requires C, 43.6; H, 4.9; Br, 32.2%); ν_{max}(KBr)/cm⁻¹ 3443, 1374, 1243, 1217, 1159, 1094, 1073, 1053, 893 and 856; δ_H 5.91 (ddd, $J_{6,7}$ 10.3, $J_{6,5}$ 2.2, $J_{6,7a}$ 1.0, 1H, 6-H), 5.83 (ddd, $J_{7,6}$ 10.3, $J_{7,7a}$ 3.4, $J_{7,5}$ 2.0, 1H, 7-H), 4.53 (m, 1H, 7a-H), 4.35 (dd, $J_{3a,4}$ 8.5, $J_{3a,7a}$ 5.9, 1H, 3a-H), 4.22 (m, 1H, 5-H), 3.93 (t, $J_{4,3a}$ 8.5, $J_{4,5}$ 8.5, 1H, 4-H), 3.12 (d, $J_{OH,5}$ 6.1, 1H, OH), 1.43 (s, 3H, CH₃) and 1.32 (s, 3H, CH₃); δ_C 132.6 (6-C), 124.5 (7-C), 110.8 (2-C), 77.5 (3a-C), 72.0 (7a-C), 70.1 (5-C), 56.5 (4-C), 28.0 (CH₃) and 25.9 (CH₃); m/z (15 eV) 235 (94%) 233 [100, (M − CH₃)⁺], 175 (27), 173 [29, (M − CH₃ − CH₂CO − H₂O)⁺], 147 (13), 145 (12) and 43 (20).

Fractions containing mixtures of the two isomers were combined [192 mg, 23% (64% total yield)] and again subjected to column chromatography to obtain further quantities of purified bromohydrins.

(3a′α,4′α,5′β,7a′α)-5′-Iodo-2′,2′-dimethyl-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-4′-yl ethanoate 11 and (3a′α,4′β,5′α,7a′α)-4-iodo-2′,2′-dimethyl-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl ethanoate 12

Finely ground iodine (834 mg, 3.28 mmol) was added in small portions over 0.5 h to a magnetically stirred mixture of acetonide **8**[5a,22] (500 mg, 3.28 mmol), silver acetate (1.10 g, 6.57 mmol) and acetic acid (30 cm³) maintained in the dark. Water (62 mm³, 3.45 mmol) was then added in one portion and the resulting mixture was stirred at 20 °C in the dark for 46 h. The mixture was then filtered through Celite (5 cm deep pad, CH_2Cl_2 elution, 50 cm³). The filtrate was washed with H_2O (2 × 50 cm³), sodium hydrogen carbonate (2 × 50 cm³ of a saturated aqueous solution), sodium metabisulfite (2 × 50 cm³ of a 20% aqueous solution) and H_2O (2 × 50 cm³) then dried, filtered and concentrated under reduced pressure to a yellow oil. This material was subjected to preparative TLC (silica gel, 9 : 1 hexane–EtOAc elution) and extraction (Et_2O) of the appropriate band (R_f 0.4) yielded a 1 : 9 mixture (as judged by ¹H NMR analysis) of *title compounds* **11** and **12** (911 mg, 82%) as a clear, viscous oil [Found: (M − CH₃)⁺, 322.9783. $C_{11}H_{15}IO_4$ requires (M − CH₃)⁺, 322.9782]; ν_{max}(NaCl)/cm⁻¹ 2985, 2934, 1743, 1371, 1218, 1183, 1152, 1080, 1042 and 861; δ_H(major isomer) 6.00 (ddd, $J_{7′,6′}$ 10.0, $J_{7′,5′}$ 3.6, $J_{7′,7a′}$ 2.1, 1H, 7′-H), 5.81 (dd, $J_{6′,7′}$ 10.0, $J_{6′,5′}$ 1.8, 1H, 6′-H), 5.50 (dm, $J_{5′,4′}$ 9.7, 1H, 5′-H), 4.53 (m, 1H, 7a′-H), 4.49 (dd, $J_{3a′,4′}$ 9.7, $J_{3a′,7a′}$ 5.8, 1H, 3a′-H), 4.01 (t, $J_{4′,3a′}$ 9.7, $J_{4′,5′}$ 9.7, 1H, 4′-H), 2.13 (s, 3H, CH₃CO), 1.49 (s, 3H, CH₃) and 1.39 (s, 3H, CH₃); δ_C(major isomer) 169.8 (C=O), 131.3 (6′-C), 125.4 (7′-C), 110.7 (2′-C), 78.7 (3a′-C), 72.6 (5′-C), 71.3 (7a′-C), 30.9 (4′-C), 28.1 (CH₃), 25.8 (CH₃) and 20.8 (CH₃CO); m/z 324 [29%, (M + H − CH₃)⁺], 222 (26), 95 (36) and 43 (100).

(3aα,4β,5α,7aα)-4-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-ol 13

Anhydrous potassium carbonate (401 mg, 2.90 mmol) was added to a magnetically stirred solution of compounds **11** and **12** (892 mg, 2.64 mmol) in anhydrous methanol (60 cm³) maintained under a N_2 atmosphere at 20 °C. After 2 h the reaction mixture was quenched with HCl (40 cm³ of a 1 M aqueous solution) and then extracted with CHCl₃ (4 × 20 cm³). The combined organic extracts were dried, filtered and concentrated under reduced pressure to yield a white solid. Recrystallisation (Et_2O) of this material yielded the *title compound* **13** (624 mg, 80%) as colourless cubes, mp 148.0 °C (subl.) (Found: C, 36.5; H, 4.25; I, 43.2. $C_9H_{13}IO_3$ requires C, 36.5; H, 4.4; I, 42.9%); ν_{max}(KBr)/cm⁻¹ 3381, 1370, 1229, 1129, 1068, 1053, 1028, 897, 749 and 723; δ_H 5.92–5.89 (dm, $J_{7,6}$ 10.0, 1H, 7-H), 5.78 (dm, $J_{6,7}$ 10.0, 1H, 6-H), 4.69 (m, 1H, 3a-H), 4.56–4.51 (complex m, 2H, 5-H, 7a-H), 4.12 (br dd, J 9.3 and 2.2, 1H, 4-H), 2.29 (d, $J_{OH,5}$ 4.4, 1H, OH), 1.49 (s, 3H, CH₃) and 1.40 (s, 3H, CH₃); δ_C 130.4, 127.5, 109.2, 78.7, 72.3, 69.4, 34.6, 27.6 and 26.5; m/z 281 [30%, (M − CH₃)⁺], 111 (64), 94 (43) and 43 (100).

(3aα,5aα,6aα,6bα)-2,2-Dimethyl-3a,5a,6a,6b-tetrahydro-oxireno[*e*]-1,3-benzodioxole 6

A pre-cooled solution of the bromohydrins **9** and **10** (540 mg, 2.17 mmol) in THF (20 cm³) was added to a solution of potassium hydride (114 mg, 2.82 mmol) in THF (15 cm³) maintained, with stirring, under a N_2 atmosphere at 0 °C (ice–H₂O bath). After stirring at 0 °C for 0.16 h the cooling bath was removed and stirring continued at 20 °C for 2.5 h. The reaction mixture was quenched by the slow addition of H_2O–Et_2O (20 cm³ of a 1 : 1 mixture) then poured into H_2O (50 cm³) and extracted with CH_2Cl_2 (3 × 30 cm³). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to yield a yellow oil. Subjection of this material to column chromatography (silica gel, 8 : 92 Et_2O–CH_2Cl_2 elution) and concentration of the appropriate fractions (R_f 0.7) afforded a white solid. Recrystallisation (Et_2O–hexane) of this material yielded the

title compound **6** (326 mg, 89%) as colourless cubes, mp 46.0–46.5 °C (Found: C, 64.6; H, 7.5. $C_9H_{12}O_3$ requires C, 64.3; H, 7.2%); ν_{max}(KBr)/cm^{-1} 2984, 1378, 1369, 1246, 1214, 1163, 1056, 974, 874 and 849; δ_H 6.37 (ddd, $J_{5,4}$ 10.0, $J_{5,5a}$ 4.4, $J_{5,3a}$ 0.5, 1H, 5-H), 6.14 (ddd, $J_{4,5}$ 10.0, $J_{4,3a}$ 5.4, $J_{4,5a}$ 1.7, 1H, 4-H), 4.61 (dddd, $J_{3a,6b}$ 6.6, $J_{3a,4}$ 5.4, $J_{3a,6a}$ 2.0, $J_{3a,5}$ 0.7, 1H, 3a-H), 4.40 (dd, $J_{6b,3a}$ 6.6, $J_{6b,6a}$ 2.7, 1H, 6b-H), 3.65 (ddd, $J_{6a,5a}$ 4.0, $J_{6a,6b}$ 2.7, $J_{6a,3a}$ 2.0, 1H, 6a-H), 3.46 (td, $J_{5a,5}$ 4.0, $J_{5a,6a}$ 4.0, $J_{5a,4}$ 1.7, 1H, 5a-H), 1.55 (s, 3H, CH$_3$) and 1.40 (s, 3H, CH$_3$); δ_C 129.6(3), 129.5(7) (4-C, 5-C), 107.8 (2-C), 72.8 (6b-C), 70.0 (3a-C), 56.1 (6a-C), 49.1 (5a-C), 27.4 (CH$_3$) and 25.2 (CH$_3$); *m/z* (20 eV) 153 [100%, (M − CH$_3$)$^+$], 111 (17) and 43 (27).

Reaction of the iodohydrin **13** under the same conditions as described above afforded the epoxide **6** in 85% yield.

(3a*R*,4*R*,5*S*,7a*S*)-4-Bromo-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-ol 16 and (3a*R*,4*S*,5*R*,7a*S*)-4-bromo-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-ol 17

A magnetically stirred solution of compound **2** (5.00 g, 34.1 mmol) in HPLC grade acetone (20 cm^3) was treated with 2,2-dimethoxypropane (30 cm^3) and toluene-*p*-sulfonic acid monohydrate (175 mg, 0.92 mmol). The reaction mixture was stirred at 20 °C for 0.33 h (at which time the starting material could not be detected by TLC) then poured into sodium hydrogen carbonate (100 cm^3 of a saturated aqueous solution) and extracted with CH$_2$Cl$_2$ (3 × 50 cm^3). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to give a yellow oil. The crude acetonide **14**[13] obtained in this manner was treated with 1,2-dimethoxyethane (140 cm^3) and distilled H$_2$O (35 cm^3). The solution so-formed was cooled to *ca.* −5 °C (ice–salt bath) and treated with NBS (9.72 g, 54.6 mmol, 1.6 mol equiv. with respect to **2**). The reaction mixture was maintained at 0 °C for 10 h then quenched with brine (100 cm^3) and extracted with EtOAc (3 × 50 cm^3). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to give a light yellow oil (4.20 g) which was dissolved in hot hexanes then decanted into another flask. Upon cooling the *title bromohydrin* **17** (270 mg, 2.8% from diol **2**) was obtained as white crystalline masses; δ_H(270 MHz) 6.00 (d, *J* 1.8, 1H), 4.70 (dd, *J* 9.0 and 2.2, 1H), 4.60 (br d, *J* 9.7, 1H), 4.57 (dd, *J* 5.1 and 2.1, 1H), 4.00 (dd, *J* 9.0 and 2.2, 1H), 2.42 (br s, 1H) and 1.42 (s, 6H); δ_C(67.5 MHz) 133.0, 128.3, 110.8, 77.8, 76.7, 53.3, 44.7, 27.3 and 26.4. R_f 0.30 (silica, 4:1 hexane–EtOAc elution).

The mother liquors obtained from the crystallisation of bromohydrin **17** were subjected to column chromatography (silica gel, 1:50 acetone–CH$_2$Cl$_2$ elution) and concentration of the appropriate fractions (R_f 0.35, silica gel, 4:1 hexane–EtOAc elution) gave the *title bromohydrin* **16** (2.97 g, 31% from diol **2**) as white crystalline masses, mp 43–47 °C (Found: C, 38.0; H, 4.26. $C_9H_{12}BrClO_3$ requires: C, 38.1; H, 4.3%); $[a]_D^{23}$ +17.2 (*c* 1.16, CHCl$_3$); ν_{max}/cm^{-1} 3465, 3000, 2940, 1650, 1380, 1220 and 1060; δ_H 6.10 (d, *J* 4.4, 1H), 4.61 (dm, *J* 2.3, 2H), 4.35 (dddm, *J* 9.1, 4.4 and 4.2, 1H), 4.27 (m, 1H), 2.88 (dd, $J_{4,3a}$ 9.1, $J_{4,5}$ 4.4, 1H, 4-H), 1.51 (s, 3H) and 1.41 (s, 3H); δ_C 133.1 (C), 126.9 (CH), 112.2 (C), 78.1 (CH), 75.3 (CH), 70.2 (CH), 48.6 (CH), 27.9 (CH$_3$) and 26.4 (CH$_3$); *m/z* (CI, 70 eV) 285 (0.3%), 283 (0.4), 281 [0.3, (M − H)$^+$], 271 (10), 269 (40), 267 [38, (M − CH$_3$)$^+$], 211 (20), 209 (65), 207 {50, [M − (CH$_3$)$_2$-CO − OH]$^+$}, 181 (23), 145 (23), 128 (21) and 59 (100).

(3a*S*,5a*S*,6a*S*,6b*S*)-4-Chloro-2,2-dimethyl-3a,5a,6a,6b-tetrahydrooxireno[*e*]-1,3-benzodioxole 7

A solution of bromohydrin **16** (1.65 g, 5.83 mmol) in CH$_2$Cl$_2$ (25 cm^3) maintained under an argon atmosphere was treated with tetrabutylammonium hydrogen sulfate (195 mg, 0.56 mmol) and finely ground NaOH (300 mg, 5.75 mmol). The resulting mixture was heated at reflux for 1 h, stirred at 20 °C for another 12 h, then quenched with ammonium chloride (50

cm^3 of a saturated aqueous solution). The separated aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 30 cm^3) and the combined organic phases were dried, filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to column chromatography (silica gel, 9:1 to 7:3 hexane–EtAOc gradient elution) gave, after concentration of the appropriate fractions (R_f 0.45, silica, 2:1 hexane–EtOAc elution), a crystalline solid. Recrystallisation (hexane) of this material then gave the *title epoxide* **7** (806 mg, 68%) as a white solid, mp 89–90 °C (Found: C, 53.4; H, 5.6. $C_9H_{11}ClO_3$ requires: C, 53.3; H, 5.5%); $[a]_D^{23}$ −112 (*c* 1.05, CHCl$_3$); ν_{max}/cm^{-1} 3070, 2990, 2910, 2875, 1650, 1375, 1255, 1210, 1060 and 1040; δ_H 6.40 (d, *J* 4.3, 1H), 4.59 (dd, *J* 6.7 and 1.8, 1H), 4.52 (dd, *J* 6.8 and 2.6, 1H), 3.61 (ddd, *J* 4.2, 2.6 and 1.7, 1H), 3.48 (t, *J* 4.2, 1H), 1.52 (s, 3H) and 1.40 (s, 3H); δ_C 135.7 (C), 125.6 (CH), 109.1 (C), 75.5 (CH), 74.0 (CH), 54.5 (CH), 49.6 (CH), 27.1 (CH$_3$) and 25.3 (CH$_3$); *m/z* (CI, 70 eV) 203 [1.0%, (M + H)$^+$], 189 (25), 187 [80, (M − CH$_3$)$^+$], 147 (20), 145 {60, [M + H − (CH$_3$)$_2$CO)]$^+$}, 117 (70), 109 (75) and 59 (100).

(3a*S*,5a*R*,6a*R*,6b*S*)-4-Chloro-2,2-dimethyl-3a,5a,6a,6b-tetrahydrooxireno[*e*]-1,3-benzodioxole 5

The conversion of bromohydrin **17** into the title epoxide was effected in the same manner as described immediately above for the transformation of compound **16** into epoxide **7**. Compound **5** obtained in this manner was identical, in all respects, with an authentic sample[13] obtained by direct epoxidation of diene **14**.

(3a′*α*,4′*β*,5′*α*,7a′*α*)-4′-Hydroxy-2′,2′-dimethyl-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl benzoate 18

A mixture of benzoic acid (545 mg, 4.64 mmol), CSA (138 mg, 0.59 mmol, 20 mol%) and epoxide **4** (500 mg, 2.97 mmol) in CH$_2$Cl$_2$ (20 cm^3) was stirred under N$_2$ at 20 °C for 14 h. The reaction mixture was then diluted with H$_2$O (30 cm^3) and extracted with Et$_2$O (3 × 30 cm^3). The combined organic extracts were washed with sodium hydrogen carbonate (3 × 30 cm^3 of a saturated aqueous solution) then dried, filtered and concentrated under reduced pressure to yield a colourless oil. This material was subjected to preparative TLC (silica gel, 5:2 hexane–EtOAc elution) and afforded two major bands, A and B.

Extraction (Et$_2$O) of band A (R_f 0.7) yielded the epoxide **4** (178 mg, 36% recovery).

Extraction (Et$_2$O) of band B (R_f 0.4) yielded a clear, viscous oil that solidified upon standing. Recrystallisation (CH$_2$Cl$_2$–hexane) of this material yielded the *title compound* **18** (432 mg, 78% at 64% conversion) as cubic crystals, mp 135.0–137.0 °C (Found: C, 66.3; H, 6.0. $C_{16}H_{18}O_5$ requires C, 66.2; H, 6.25%); ν_{max}(KBr)/cm^{-1} 3493, 1711, 1281, 1258, 1209, 1117, 1087, 1056, 1036, 975 and 715; δ_H 8.09–8.06 (complex m, 2H), 7.61–7.56 (complex m, 1H), 7.47–7.43 (complex m, 2H), 5.99 (ddd, $J_{7',6'}$ 10.0, $J_{7',7a'}$ 3.7, $J_{7',5'}$ 2.2, 1H, 7′-H), 5.88 (dm, $J_{6',7'}$ 10.0, 1H, 6′-H), 5.57–5.30 (dm, $J_{5',4'}$ 9.0, 1H, 5′-H), 4.72 (m, 1H, 7a′-H), 4.24 (dd, $J_{3a',4'}$ 9.0, $J_{3a',7a'}$ 6.6, 1H, 3a′-H), 3.96 (t, $J_{4',3a'}$ 9.0, $J_{4',5'}$ 9.0, 1H, 4′-H), 2.62 (s, 1H, OH), 1.57 (s, 3H, CH$_3$) and 1.43 (s 3H, CH$_3$); δ_C 166.4 (C=O), 133.5, 130.8 (6′-C), 129.8, 129.6, 128.4, 124.9 (7′-C), 110.8 (2′-C), 77.7 (3a′-C), 73.3 (5′-C), 72.3 (7a′-C), 72.2 (4′-C), 28.1 (CH$_3$) and 25.8 (CH$_3$); *m/z* (15 eV) 275 [100%, (M − CH$_3$)$^+$], 122 (22) and 105 (82).

(1*β*,2*α*,3*α*,6*α*)-6-Methoxycyclohex-4-ene-1,2,3-triol monohydrate 19

CSA (51 mg, 0.22 mmol, 14 mol%) was added to a stirred mixture of epoxide **4** (260 mg, 1.55 mmol), CH$_2$Cl$_2$ (4 cm^3) and anhydrous methanol (7 cm^3) maintained at 20 °C under a N$_2$ atmosphere. The mixture was stirred for 22 h and then quenched with sodium hydrogen carbonate (10 cm^3 of a 1 M aqueous solution) and the resulting mixture subjected to continuous liquid–liquid extraction (Et$_2$O) for 24 h. Concentration of the dried organic phase afforded a clear oil that solidified on standing. Recrystallisation (CH$_2$Cl$_2$–hexane) of this material

yielded the *title compound* **19** (155 mg, 56%) as colourless needles, mp 65.5–67.0 °C (Found: C, 47.3; H, 7.5. Calc. for $C_7H_{14}O_5$: C, 47.2; H, 7.9%); ν_{max}(KBr)/cm^{-1} 3409 and 1074; δ_H 5.86 (ddd, J 10.0, 4.9 and 1.7, 1H), 5.81 (dd, J 10.0 and 1.7, 1H), 4.92 (br s, 2H, 2 × OH), 4.49 (br s, 1H, OH), 4.24 (s, 1H), 3.85 (t, $J_{3,4}$ 9.1, $J_{3,2}$ 9.1, 1H), 3.70 (d, J 7.8, 1H), 3.51 (m, 1H) and 3.46 (s, 3H, OCH$_3$) (resonance due to one proton not observed); δ_C 129.2, 127.4, 81.3, 71.1, 70.3, 66.3 and 56.8; m/z (15 eV) 100 [100%, (M − HOCH=CHOH)$^+$].

(3aα,4β,5α,7aα)-2,2-Dimethyl-5-methoxy-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 20

A solution of epoxide **4** (100 mg, 0.59 mmol) in anhydrous CH$_3$OH (3 cm^3) was added to a magnetically stirred solution of methanolic sodium methoxide [generated from elemental sodium (18 mg, 0.77 mmol) and CH$_3$OH (5 cm^3)] maintained under a N$_2$ atmosphere at 20 °C. After 24 h the reaction mixture was concentrated under reduced pressure and the residue partitioned between water (40 cm^3) and Et$_2$O (30 cm^3). The phases were separated and the aqueous phase was extracted with additional Et$_2$O (3 × 30 cm^3). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to yield a white solid which was subjected to column chromatography (silica gel, Et$_2$O elution).

Concentration of the less polar fractions (R_f 0.9) yielded the epoxide **4** (47 mg, 47% recovery).

Concentration of the more polar fractions (R_f 0.5) afforded a white solid recrystallisation (CHCl$_3$–hexane) of which yielded the *title compound* **20** (59 mg, 94% at 53% conversion) as colourless needles, mp 100.0–101.0 °C (Found: C, 60.0; H, 7.9. $C_{10}H_{16}O_4$ requires C, 59.9; H, 8.1%); ν_{max}(KBr)/cm^{-1} 3452, 2985, 2945, 2867, 1380, 1246, 1215, 1159, 1084 and 1057; δ_H 5.96 (dt, $J_{6,7}$ 10.0, $J_{6,5}$ 1.0, $J_{6,7a}$ 1.0, 1H, 6-H), 5.89 (ddd, $J_{7,6}$ 10.0, $J_{7,7a}$ 3.2, $J_{7,5}$ 2.0, 1H, 7-H), 4.65 (dm, $J_{7a,3a}$ 6.6, 1H, 7a-H), 4.12 (dd, $J_{3a,4}$ 8.8, $J_{3a,7a}$ 6.6, 1H, 3a-H), 3.68 (dm, $J_{5,4}$ 8.8, 1H, 5-H), 3.64 (td, $J_{4,5}$ 8.8, $J_{4,3a}$ 8.8, $J_{4,OH}$ 1.8, 1H, 4-H), 3.49 (s, 3H, OCH$_3$), 2.64 (d, $J_{4,OH}$ 1.8, 1H, OH), 1.52 (s, 3H, CH$_3$) and 1.39 (s, 3H, CH$_3$); δ_C 130.9, 123.9, 110.4, 79.7, 77.5, 73.1, 72.3, 57.1 (OCH$_3$), 28.0 and 25.6; m/z (20 eV) 185 [85%, (M − CH$_3$)$^+$], 125 (60), 113 (95), 101 (100), 100 (85), 93 (19), 55 (42) and 43 (24).

(3aα,4β,5α,7aα)-5-Azido-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 21

Ammonium chloride (200 mg, 3.75 mmol) and sodium azide (609 mg, 9.36 mmol) were added to a solution of epoxide **4** (315 mg, 1.87 mmol) in 2-methoxyethanol–H$_2$O (12 cm^3 of an 8:1 mixture). The resulting mixture was heated at reflux for 5 h then cooled to 20 °C and concentrated under reduced pressure. The residue was subjected to chromatographic filtration (1 cm deep pad of TLC grade silica gel, Et$_2$O elution, 80 cm^3) and the filtrate was concentrated under reduced pressure to yield a brown crystalline solid. Recrystallisation (CH$_2$Cl$_2$–hexane with charcoal) of this material afforded the *title compound* **21** (344 mg, 87%) as colourless prisms, mp 90.5–91.5 °C (Found: C, 51.2; H, 6.45; N, 19.8. $C_9H_{13}N_3O_3$ requires C, 51.2; H, 6.2; N, 19.9%); ν_{max}(KBr)/cm^{-1} 3478, 2983, 2113, 1288, 1262, 1245, 1221, 1086, 1070 and 871; δ_H 5.96 (ddd, $J_{7,6}$ 10.0, $J_{7,5}$ 3.7, $J_{7,7a}$ 2.7, 1H, 7-H), 5.76 (br d, $J_{6,7}$ 10.0, 1H, 6-H), 4.65 (m, 1H, 7a-H), 4.10 (dd, $J_{3a,4}$ 9.0, $J_{3a,7a}$ 6.5, 1H, 3a-H), 3.91 (dm, $J_{5,4}$ 9.0, 1H, 5-H), 3.65 (td, $J_{4,3a}$ 9.0, $J_{4,5}$ 9.0, $J_{4,OH}$ 2.7, 1H, 4-H), 2.84 (m, 1H, OH), 1.52 (s, 3H, CH$_3$) and 1.40 (d, J 0.5, 3H, CH$_3$); δ_C 130.0 (6-C), 125.4 (7-C), 110.7 (2-C), 77.8 (3a-C), 73.7 (4-C), 72.2 (7a-C), 61.6 (5-C), 28.1 (CH$_3$) and 25.7 (CH$_3$); m/z (15 eV) 196 [100%, (M − CH$_3$)$^+$], 168 [42, (M − CH$_3$ − N$_2$)$^+$] and 125 (62).

Dimethyl (3a′α,4′β,5′α,7a′α)-(2′,2′-dimethyl-4′-hydroxy-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl)malonate 22

Sodium metal (27 mg, 1.16 mmol) was added to a magnetically

stirred solution of dimethyl malonate (122 mm^3, 1.07 mmol) in THF (5 cm^3) maintained under N$_2$ at 20 °C. Once the sodium had completely reacted a solution of epoxide **4** (150 mg, 0.89 mmol) in THF (3 cm^3) was added. After 24 h the reaction mixture was poured into water (40 cm^3) and extracted with Et$_2$O (4 × 30 cm^3). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to yield a colourless oil. This material was subjected to column chromatography (silica gel, Et$_2$O elution) and concentration of the appropriate fractions (R_f 0.7) yielded the *title compound* **22** (50 mg, 20%) as a clear colourless oil (Found: M$^+$, 300.1209. $C_{14}H_{20}O_7$ requires M, 300.1209); ν_{max}(NaCl)/cm^{-1} 2985, 1735, 1435, 1380, 1371, 1241, 1218, 1160, 1058 and 867; δ_H 5.88–5.86 (complex m, 2H, 6′-H, 7′-H), 4.60 (m, 1H, 7a′-H), 4.01 (dd, $J_{3a',4'}$ 8.8, $J_{3a',7a'}$ 6.6, 1H, 3a′-H), 3.90 (d, $J_{2,5'}$ 5.1, 1H, 2-H), 3.72 (s, 3H, OCH$_3$), 3.71 (s, 3H, OCH$_3$), 3.56 (dm, $J_{4',5'}$ 10.0, 1H, 4′-H), 2.85 (m, 1H, 5′-H), 2.60 (d, $J_{OH,4'}$ 3.4, 1H, OH), 1.46 (s, 3H, CH$_3$) and 1.36 (s, 3H, CH$_3$); δ_C 169.2, 168.4, 130.8, 124.3, 109.6 (2′-C), 79.4, 72.4, 70.5, 52.6, 52.4, 50.7, 40.8, 28.1 (CH$_3$) and 25.6 (CH$_3$); m/z 300 (0.3%, M$^+$), 285 [54, (M − CH$_3$)$^+$], 241 (18), 225 (20) and 165 (100).

(3aS,4R,5S,7aS)-5-Azido-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 24

Ammonium chloride (212 mg, 3.96 mmol) and sodium azide (643 mg, 9.89 mmol) were added to a solution of chloro epoxide **5** (401 mg, 1.98 mmol) in 1,2-dimethoxyethane–ethanol–H$_2$O (18 cm^3 of a 3:3:2 mixture). The resulting mixture was heated at reflux for 4 h then cooled to 20 °C and concentrated under reduced pressure. The residue was subjected to chromatographic filtration [1.5 cm deep pad of TLC grade silica gel, elution with CHCl$_3$ (80 cm^3) then EtOAc (80 cm^3)]. The filtrate was concentrated under reduced pressure, the residue was subjected to column chromatography (silica gel, 7:3 hexane–EtOAc elution) and the appropriate fractions (R_f 0.5) were concentrated under reduced pressure to yield a white solid. Recrystallisation (CH$_2$Cl$_2$–hexane) of this material afforded the title compound **24**[5b,c] (348 mg, 72%) as fine needles, mp 94–94.5 °C (lit.,[5b] mp 94–94.5 °C) [Found: (M − CH$_3$)$^+$, 230.0334. Calc. for $C_9H_{12}^{35}ClN_3O_3$: $(M − CH_3)^+$, 230.0332]; ν_{max}(KBr)/cm^{-1} 3452, 2113, 1383, 1333, 1248, 1210, 1158, 1073, 869 and 851; δ_H 5.88 (d, $J_{6,5}$ 2.2, 1H, H-6), 4.62 (dd, $J_{7a,3a}$ 6.6, $J_{7a,5}$ 1.5, 1H, H-7a), 4.17 (dd, $J_{3a,4}$ 8.8, $J_{3a,7a}$ 6.6, 1H, H-3a), 3.97 (ddd, $J_{5,4}$ 8.8, $J_{5,6}$ 2.2, $J_{5,7a}$ 1.5, 1H, H-5), 3.72 (t, $J_{4,3a}$ 8.8, $J_{4,5}$ 8.8, 1H, H-4), 2.81 (br s, 1H, OH), 1.55 (s, 3H, CH$_3$) and 1.43 (d, J 0.5, 3H, CH$_3$); δ_C 130.8 (C-7), 126.7 (C-6), 111.5 (C-2), 77.8, 75.6, 73.1, 61.2 (C-5), 28.1 (CH$_3$) and 25.9 (CH$_3$); m/z (70 eV) 232 (34%), 230 [100, (M − CH$_3$)$^+$], 101 (81), 58 (64) and 54 (41).

(1R,2S,3S,6S)-6-Azido-4-chlorocyclohex-4-ene-1,2,3-triol 26

A solution of acetonide **24** (513 mg, 2.09 mmol) in CH$_3$OH (25 cm^3) was treated with wet and strongly acidic Amberlyst 15 ion-exchange resin (1.60 g, Aldrich) and the resulting mixture stirred at 20 °C for 8 days. The reaction mixture was then filtered through a pad of Celite and the filtrate concentrated under reduced pressure to give a yellow oil (454 mg) which was subjected to column chromatography (silica gel, 1:4 hexane–EtOAc elution). Concentration of the appropriate fractions (R_f 0.5, EtOAc) afforded a white solid which was recrystallised (EtOAc) to give the *title compound* **26** (406 mg, 97%) as a white solid, mp 137–138 °C (Found: C, 35.2; H, 3.9. $C_6H_8ClN_3O_3$ requires C, 35.1; H, 3.9%); $[a]_D^{20}$ −11.0 (c 1.1, CH$_3$OH); ν_{max}(KBr)/cm^{-1} 3290, 3190, 2900, 2840, 2060, 1640, 1430 and 1240; δ_H[(CD$_3$)$_2$SO, 270 MHz] 5.72 (d, J 2.6, 1H), 5.51 (d, J 6.1, 1H), 5.38 (d, J 5.2, 1H), 4.98 (d, J 6.1, 1H), 3.98 (dd, J 6.1 and 4.1, 1H), 3.93 (dd, J 7.8 and 2.6, 1H), 3.62 (ddd, J 10.2, 7.8 and 5.2, 1H) and 3.45 (ddd, J 10.2, 6.1 and 4.1, 1H); δ_C[(CD$_3$)$_2$SO, 67.5 MHz] 135.4 (C), 125.0 (CH), 71.4 (CH), 71.0 (CH), 70.0 (CH) and 63.6 (CH); m/z (CI, 70 eV) 207 (5%), 205 (5, M$^+$),

182 (8), 180 (26), 178 (24), 160 (30), 145 (80), 116 (80) and 114 (100).

(1*R*,2*R*,3*R*,4*S*)-4-Aminocyclohexane-1,2,3-triol hydrochloride salt 28

Method A: A mixture of azido alcohol **24** (396 mg, 1.61 mmol), CH_3OH (14 cm³) and PtO_2 (45 mg, 0.20 mmol) was added to a Paar hydrogenator which was pressurised to 80 psi with hydrogen gas. After 6 h at 20 °C the residual hydrogen was removed from the reaction vessel and the reaction mixture was filtered through Celite. The filtrate was concentrated under reduced pressure to give a light brown oil. This material was treated with HCl (1 cm³ of a 2 M aqueous solution) and CH_3OH (4 cm³) and the resulting mixture stirred magnetically at room temperature for 0.1 h then evaporated to dryness. The residue was triturated with $CHCl_3$ (15 cm³) then the solvent was removed under reduced pressure. The trituration–evaporation process was repeated and the resulting material dissolved in CH_3OH (1–2 cm³) and the product was precipitated from solution by successive dropwise addition of hexane then Et_2O. The light-pink precipitate was removed by vacuum filtration then re-dissolved in CH_3OH and re-precipitated with hexane–Et_2O to give the *title salt* **28** (256 mg, 86%) as a white crystalline salt, mp >200 °C (Found: C, 39.2; H, 7.7. $C_6H_{14}ClNO_3$ requires: C, 39.2; H, 7.7%); $[a]_D^{24}$ −26 (*c* 1.0, H_2O); v_{max}(KBr)/cm⁻¹ 3410, 3320, 3050, 2940, 1660, 1595, 1515 and 1075; δ_H[(CD₃)₂SO, 270 MHz] 7.96 (br s, 3H), 5.36 (br s, 1H), 4.84 (br s, 1H), 4.60 (br s, 1H), 3.77 (s, 1H), 3.52 (t, *J* 9.8, 1H), 3.16 (d, *J* 8.4, 1H), 2.74 (br s, 1H), 1.67 (m, 3H) and 1.41 (m, 1H); δ_C[(CD₃)₂SO, 67.5 MHz], 74.5 (CH), 70.5 (CH), 68.0 (CH), 53.5 (CH), 27.4 (CH₂) and 22.4 (CH₂); *m/z* (CI, 70 eV) 148 (100%, M⁺), 112 [30, (M − 2H₂O)⁺], 85 (11) and 84 (9).

Method B: A solution of benzylamino alcohol **27**[5b] (249 mg, 0.80 mmol) in CH_3OH (4 cm³) was treated with 10% palladium on carbon (180 mg) and ammonium formate (250 mg, 3.97 mmol) and the resulting mixture heated under reflux for 0.16 h. The cooled reaction mixture was filtered through Celite and the filtrate concentrated under reduced pressure to give a brown oil. This material was treated in the same manner as described in method A immediately above. In this way the title salt **28** (106 mg, 72%) was obtained as a white crystalline solid which was identical, in all respects, with the material produced earlier.

(3a*S*,4*S*,5*S*,7a*R*)-2,2-Dimethyl-5-fluoro-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 31

A solution of chloro alkene **30**[5b] (627 mg, 2.35 mmol) in toluene (15 cm³) was purged with argon then treated with tributyltin hydride (2.73 g, 9.38 mmol) and azoisobutyronitrile (AIBN) (18 mg, 0.110 mmol). The resulting mixture was heated at reflux for 7 h then cooled and diluted with EtOAc (15 cm³). The solution obtained in this manner was washed with KF (3 × 10 cm³ of a one-quarter saturated aqueous solution) then brine (2 × 10 cm³) before being dried, filtered and concentrated under reduced pressure to give a light yellow oil (*ca.* 1.00 g). This material was subjected to flash chromatography[23] (silica gel, 4:1 hexane–EtOAc elution) and provided, after concentration of the appropriate fractions (R_f 0.4, 1:1 hexane–EtOAc elution), the *title compound* **31** (133 mg, 30%) as a white crystalline solid, mp 97.5–99.5 °C (Found: C, 57.5; H, 7.0. $C_9H_{13}FO_3$ requires: C, 57.4; H, 7.0%); $[a]_D^{23}$ −83 (*c* 1.2, $CHCl_3$); v_{max}(KBr)/cm⁻¹ 3415, 3060, 2995, 2942, 1620, 1385, 1260, 1220 and 1065; δ_H(270 MHz) 5.92 (m, 2H), 4.90 (ddm, *J* 50 and 8.4, 1H), 4.63 (dm, *J* 6.6, 1H), 4.11 (dd, *J* 8.9 and 6.6, 1H), 3.82 (dt, *J* 14.5 and 8.6, 1H), 2.78 (br s, 1H), 1.51 (s, 3H) and 1.38 (s, 3H); δ_C(75.4 MHz) 130.1 (CH, d, $J_{13C-19F}$ 25.2), 124.7 (CH, d, $J_{13C-19F}$ 9.6), 111.0 (C), 91.0 (CH, d, $J_{13C-19F}$ 170.2), 76.9 (CH, d, $J_{13C-19F}$ 12.1), 72.7 (CH, d, $J_{13C-19F}$ 17.1), 72.1 (CH), 27.9 (CH₃) and 25.5 (CH₃); δ_F(254 MHz) −193.9 (dm, J_{19F-1H} 50, 1F); *m/z* (CI, 70 eV) 189

[20%, (M + H)⁺], 173 [13, (M − CH₃)⁺], 131 (25), 111 {100, [M − (CH₃)₂CO − H₂O − H]⁺} and 83 (17).

(1*S*,2*R*,3*R*,6*S*)-6-Fluorocyclohex-4-ene-1,2,3-triol 32

A magnetically stirred solution of acetonide **31** (95 mg, 0.50 mmol) in CH_3OH (8 cm³) was treated with wet Amberlyst 15 ion-exchange resin (350 mg, Aldrich) and the resulting mixture stirred at 20 °C for 15 h. After this time the resin was removed by filtration and the filtrate concentrated under reduced pressure to give a white solid which was subjected to column chromatography (silica gel, 1:4 hexane–EtOAc elution). Concentration of the appropriate fractions (R_f 0.25) afforded the *title compound* **32** (70 mg, 94%) as a fluffy white solid, mp 105–107 °C (Found: C, 48.5; H, 6.1. $C_6H_9FO_3$ requires: C, 48.7; H, 6.1%); $[a]_D^{23}$ +123 (*c* 1.09, CH_3OH); v_{max}(KBr)/cm⁻¹ 3387, 3042, 2929, 2908, 1654, 1365, 1076 and 943; δ_H[(CD₃)₂SO, 270 MHz] 5.86 (ddt, *J* 10.1, 5.0 and 1.6, 1H), 5.70 (dt, *J* 10.1 and 2.1, 1H), 5.14 (d, *J* 4.8, 1H), 4.80 (d, *J* 5.2, 1H), 4.73 (ddm, *J* 49.7 and 7.1, 1H), 4.70 (d, *J* 5.9, 1H), 4.02 (dd, *J* 4.8, 1H), 3.70 (m, 1H) and 3.24 (ddm, *J* 10.3 and 4.1, 1H); δ_C[(CD₃)₂SO, 67.5 MHz], 130.7 (CH, d, $J_{13C-19F}$ 10.3), 126.7 (CH, d, $J_{13C-19F}$ 22.3), 93.0 (CH, d, $J_{13C-19F}$ 168.1), 70.0 (CH, d, *J* 8.7), 69.8 (CH) and 65.7 (CH); δ_F(D₂O, 254 MHz) −178.1 (dm, J_{19F-1H} 50, 1F).

(3a*α*,4*α*,5*β*,7a*α*)-2,2-Dimethyl-5-methoxy-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 33

CSA (174 mg, 0.75 mmol) was added to a magnetically stirred mixture of epoxide **6** (326 mg, 1.93 mmol) in $CHCl_3$ (4 cm³) and anhydrous CH_3OH (4 cm³) maintained under N_2 at 20 °C. After 8 h the reaction mixture was quenched by pouring into $CHCl_3$ (20 cm³) and washing the resulting solution with sodium hydrogen carbonate (40 cm³ of a saturated aqueous solution). The separated aqueous layer was washed with $CHCl_3$ (2 × 30 cm³) then the combined organic extracts were dried, filtered and concentrated under reduced pressure to yield a yellow oil. This material was subjected to preparative TLC (silica gel, 1:1 Et_2O–hexane elution) and extraction (Et_2O) of the appropriate band (R_f 0.1–0.3) yielded the *title compound* **33** (68 mg, 17%) as a yellow oil [Found: (M − CH₃)⁺, 185.0813. $C_{10}H_{16}O_4$ requires (M − CH₃)⁺, 185.0814]; v_{max}(NaCl)/cm⁻¹ 2984, 2931, 1379, 1369, 1234, 1161, 1135, 1105, 1032 and 880; δ_H 5.86 (ddd, $J_{6,7}$ 10.3, $J_{6,5}$ 2.0, $J_{6,7a}$ 1.0, 1H, 6-H), 5.70 (dm, $J_{7,6}$ 10.3, 1H, 7-H), 4.64 (m, 1H, 7a-H), 4.55 (ddd, $J_{3a,7a}$ 5.2, $J_{3a,7}$ 2.7, $J_{3a,4}$ 1.0, 1H, 3a-H), 3.99 (dm, $J_{5,4}$ 8.1, 1H, 5-H), 3.77 (br d, $J_{4,5}$ 8.1, 1H, 4-H), 3.51 (s, 3H, OCH₃), 2.90 (br s, 1H, OH), 1.40 (s, 3H, CH₃) and 1.39 (s, 3H, CH₃); δ_C 127.4 (6-C), 127.2 (7-C), 109.8 (2-C), 77.6 (5-C), 75.7 (3a-C), 73.4 (7a-C), 71.7 (4-C), 57.2 (OCH₃), 27.5 (CH₃) and 26.4 (CH₃); *m/z* 185 [38%, (M − CH₃)⁺], 113 (88), 100 (81), 55 (71) and 43 (100).

(3a*S*,4*R*,5*R*,7a*S*)-5-Bromo-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 34

A solution of epoxide **7** (5.00 g, 24.7 mmol) in freshly distilled THF (80 cm³) and maintained under an argon atmosphere was treated with lithium bromide (2.570 g, 29.60 mmol, 1.2 equiv.) then ethyl acetoacetate (6.24 cm³, 49.3 mmol). The resulting mixture was heated at 30 °C for 4 h then cooled and washed with NH_4Cl (3 × 100 cm³ of a saturated aqueous solution) before being dried, filtered and concentrated under high vacuum at 20 °C for 48 h (to remove ethyl acetoacetate). The residue was subjected to column chromatography (silica gel, 1:99 to 3:97 gradient elution with acetone–CH_2Cl_2) and concentration of the appropriate fractions (R_f 0.40 in 2:1 hexane–EtOAc) afforded a white solid which was recrystallised (hexane) to give the *title bromohydrin* **34** (6.54 g, 94%) as white crystalline masses, mp 66–67 °C (Found: C, 38.3; H, 4.2. $C_9H_{12}BrClO_3$ requires C, 38.1; H, 4.3%); $[a]_D^{23}$ −89.3 (*c* 1.00, $CHCl_3$). v_{max}(KBr)/cm⁻¹ 3420, 3070, 2995, 2935, 2905, 1630, 1370 and 1220; δ_H 6.06 (d, *J* 2.7, 1H), 4.75 (ddd, *J* 7.7, 2.6 and 1.7, 1H), 4.64 (dd, *J* 5.4 and 1.7, 1H), 4.60 (dd, *J* 5.4 and 2.4, 1H), 4.06

(dd, J 7.7 and 2.4, 1H), 1.43 (s, 3H) and 1.41 (s, 3H) (one resonance obscured or overlapping); δ_C 133.7 (C), 126.4 (CH), 111.2 (C), 76.1 (CH), 75.8 (CH), 72.7 (CH), 48.8 (CH), 27.2 (CH$_3$) and 26.1 (CH$_3$); m/z (CI, 70 eV) 287 (7.5%), 285 (22), 283 [19, (M + H)$^+$], 269 (14), 267 [11, (M − CH$_3$)$^+$], 209 (16), 203 (25), 147 (32), 145 {90, [M − (CH$_3$)$_2$CO − Br]$^+$} and 59 (100).

(3aS,4S,5R,7aS)-5-Azido-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 35

Epoxide 7 (250 mg, 1.23 mmol), 1,2-dimethoxyethane (13.0 cm^3), ethanol (10.0 cm^3), H$_2$O (8.0 cm^3), NaN$_3$ (320 mg, 4.92 mmol, 4 equiv.) and NH$_4$Cl (264 mg, 4.94 mmol) were added to a round-bottomed flask in the order listed. The round-bottomed flask was fitted with a reflux condenser and the apparatus placed in an oil bath maintained at 55 °C. After 1 h the reaction mixture was allowed to cool to 20 °C then treated with H$_2$O (40.0 cm^3). The resulting mixture was extracted with EtOAc (3 × 50 cm^3) then the combined organic extracts were dried, filtered and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, 3 : 1 to 2 : 1 gradient elution with hexane–EtOAc) and concentration of the appropriate fractions (R_f 0.5 in 2 : 1 hexane–EtOAc) afforded the *title azido alcohol* 35 (262 mg, 87%) as a clear colourless oil which darkened on standing at 20 °C for extended periods. This material was subjected to further column chromatography (silica gel, 1 : 99 to 2 : 98 gradient elution with acetone–CH$_2$Cl$_2$) affording an analytically pure sample of compound 35 (Found: C, 44.3; H, 5.0; N, 17.0. C$_9$H$_{12}$ClN$_3$O$_3$ requires C, 44.0; H, 4.9; N, 17.1%); $[a]_D^{22}$ −120 (c 1.00, CHCl$_3$); ν_{max}(NaCl)/cm^{-1} 3430, 2995, 2930, 2895, 2100, 1645, 1225 and 1040; δ_H 5.81 (d, J 2.0, 1H), 4.57 (m, 2H), 4.27 (dt, J 8.6 and 1.8, 1H), 3.81 (td, J 8.1 and 2.1, 1H), 2.54 (d, J 7.5, 1H, OH), 1.44 (s, 3H) and 1.43 (s, 3H); δ_C 134.2 (C), 123.9 (CH), 111.1 (C), 76.7 (CH), 76.3 (CH), 72.0 (CH), 60.9 (CH), 27.3 (CH$_3$) and 26.3 (CH$_3$); m/z (CI, 70 eV) 246 [3%, (M + H)$^+$], 160 (3), 145 (20), 133 (3), 117 (3), 114 (4), 101 (15), 96 (15) and 59 (100).

(3aS,4S,5S,7aS)-5-Azido-7-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 36

Bromohydrin 34 (6.04 g, 21.3 mmol) was treated with NaN$_3$ (22.0 g, 339 mmol) then DMSO (35.0 cm^3). The solid mass obtained in this manner was broken into much smaller pieces (**WARNING**: metal spatulas are known to initiate the explosion of solid NaN$_3$) and the ensuing material sonicated at 45 °C for 1.5 h. Additional DMSO (15.0 cm^3) was added and sonication continued for a further 2.5 h. The reaction mixture was diluted with sufficient H$_2$O to dissolve the residual NaN$_3$ and then extracted with EtOAc (5 × 40 cm^3). The combined organic phases were then dried, filtered and concentrated under reduced pressure to give a yellow oil. This material was subjected to column chromatography (silica gel, 85 : 15 to 70 : 30 gradient elution with hexane–EtOAc) and two fractions, A and B, were obtained.

Concentration of fraction A (R_f 0.35 in 2 : 1 hexane–EtOAc) afforded *azido alcohol* 36 (3.92 g, 75%) as a clear colourless oil (Found: C, 43.9; H, 4.9; N, 16.9. C$_9$H$_{12}$ClN$_3$O$_3$ requires C, 44.0; H, 4.9; N, 17.1%); $[a]_D^{23}$ +289 (c 1.06, CHCl$_3$); ν_{max}(NaCl)/cm^{-1} 3420, 3060, 2995, 2910, 2090 and 1635; δ_H 6.00 (d, J 5.0, 1H), 4.49 (m, 2H), 4.02 (m, 2H), 2.77 (br s, 1H), 1.51 (s, 3H) and 1.39 (s, 3H); δ_H 137.4 (C), 121.7 (CH), 111.6 (C), 75.9 (CH), 75.4 (CH), 67.0 (CH), 58.1 (CH), 27.4 (CH$_3$) and 25.7 (CH$_3$); m/z (CI, 70 eV) 246 [3%, (M + H)$^+$], 232 (19), 230 [53, (M − CH$_3$)$^+$], 220 (42), 218 (92), 205 (23), 203 [60, (M − N$_3$)$^+$], 182 (39) and 59 (100).

Concentration of fraction B (R_f 0.5 in 2 : 1 hexane–EtOAc) afforded azido alcohol 35 (1.14 g, 22%) as a light brown oil which was identical, in all respects, with the material obtained previously.

(3a′α,4′β,5′β,7a′α)-4′-Hydroxy-2′,2′-Dimethyl-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl benzoate 37

A pre-cooled (ice–H$_2$O) solution of epoxide 4 (369 mg, 2.19 mmol) in THF (5 cm^3) was added dropwise to a cooled (ice–H$_2$O) solution of benzoic acid (321 mg, 2.63 mmol) and tetrakis(triphenylphosphine)palladium(0) (127 mg, 0.11 mmol, 5 mol%) in THF (30 cm^3) maintained under a N$_2$ atmosphere in the dark. The mixture was allowed to warm to 20 °C then stirred at this temperature for 72 h. After this time the reaction mixture was concentrated under reduced pressure to give a bright yellow oil. Subjection of this material to preparative TLC (silica gel, 1 : 1 hexane–EtOAc elution) and extraction (Et$_2$O) of the appropriate band (R_f 0.6) yielded a white solid. Recrystallisation (CH$_2$Cl$_2$–hexane) of this material afforded the *title compound* 37 (336 mg, 53%) as colourless needles, mp 130.0–131.0 °C (Found: C, 66.2; H, 6.2. C$_{16}$H$_{18}$O$_5$ requires C, 66.2; H, 6.25%); ν_{max}(KBr)/cm^{-1} 3490, 1692, 1342, 1277, 1245, 1125, 1074, 1051, 865 and 713; δ_H 8.03 (dm, J 8.3, 2H), 7.58 (ddm, J 8.3 and 1.5, 1H), 7.44 (dt, J 8.3, 2H), 6.05 (m, 2H, 6′-H and 7′-H), 5.63 (m, 1H, 5′-H), 4.76 (m, 1H), 4.48 (dd, $J_{3a′,4′}$ 7.3, $J_{3a′,7a′}$ 5.9, 1H, 3a′-H), 4.21 (ddd, $J_{4′,3a′}$ 7.3, $J_{4′,OH}$ 4.4, $J_{4′,5′}$ 3.7, 1H, 4′-H), 2.32 (d, $J_{OH,4′}$ 4.4, 1H, OH), 1.50 (s, 3H, CH$_3$) and 1.42 (d, J 0.5, 3H, CH$_3$); δ_C(100 MHz) 165.9 (C=O), 133.5, 133.2, 129.7, 129.3 (6′-C or 7′-C), 128.4 (4-C), 126.6 (6′-C or 7′-C), 109.8 (2′-C), 75.8 (3a′-C), 71.9 (7a′-C), 70.0 (4′-C), 69.3 (5′-C), 27.9 (CH$_3$) and 25.8 (CH$_3$); m/z (15 eV) 275 [46%, (M − CH$_3$)$^+$] and 105 (100, C$_6$H$_5$CO$^+$).

(3aα,4β,5β,7aα)-2,2-Dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxole-4,5-diol 38

Method A: A mixture of acetonide 8 (500 mg, 3.29 mmol), *tert*-butyl alcohol (14 cm^3), water (4 cm^3), pyridine (0.58 cm^3) and trimethylamine *N*-oxide dihydrate (820 mg, 7.23 mmol) was treated in one portion with osmium tetroxide (0.27 cm^3 of a 2.5 wt% solution in *tert*-butyl alcohol). The resulting mixture was heated at reflux under N$_2$ for 14 h then cooled to 20 °C and treated with sodium metabisulfite (5 cm^3 of 20% aqueous solution). The resulting solution was stirred for 0.5 h and then concentrated to dryness. The residue was suspended in THF (20 cm^3) and the ensuing mixture was subjected to chromatographic filtration (4 cm deep pad of TLC grade silica gel, Et$_2$O elution, 200 cm^3). The filtrate was concentrated under reduced pressure to yield the title compound 38 as a white solid (392 mg, 64%). Recrystallisation (Et$_2$O–hexane) of this material yielded an analytically pure sample of compound 38 as colourless plates, mp 95.0–95.5 °C (Found: C, 58.1; H, 7.5; M$^+$, 186.0893. Calc. for C$_9$H$_{14}$O$_4$: C, 58.1; H, 7.6%; M, 186.0892); ν_{max}(KBr)/cm^{-1} 3292, 3240, 1377, 1370, 1222, 1124, 1109, 1082, 1039 and 1011; δ_H 5.92 (s, 2H, 6-H and 7-H), 4.65 (d, $J_{7a,3a}$ 6.1, 1H, 7a-H), 4.36 (dd, $J_{3a,4}$ 6.6, $J_{3a,7a}$ 6.1, 1H, 3a-H), 4.30 (br s, 1H, 5-H), 3.97 (dd, $J_{4,3a}$ 6.6, $J_{4,5}$ 3.7, 1H, 4-H), 2.82 (br s, 1H, OH), 2.66 (br s, 1H, OH), 1.44 (s, 3H, CH$_3$) and 1.38 (s, 3H, CH$_3$); δ_C 129.9, 127.5 (6-C, 7-C), 109.5 (2-C), 75.7 (3a-C), 71.8 (7a-C), 71.1 (4-C), 65.9 (5-C), 27.9 (CH$_3$) and 25.9 (CH$_3$); m/z (15 eV) 186 (0.4%, M$^+$), 171 [100, (M − CH$_3$)$^+$], 111 (28) and 101 (84).

Method B: Anhydrous potassium carbonate (87 mg, 0.63 mmol) was added to a magnetically stirred solution of benzoate 37 (182 mg, 0.63 mmol) in anhydrous CH$_3$OH (20 cm^3) maintained at 20 °C. The reaction mixture was stirred for 2 h, during which time it became homogenous but remained colourless. The solution was then neutralised with HCl (12 cm^3 of a 1 M aqueous solution) and extracted with CH$_2$Cl$_2$ (3 × 50 cm^3). The combined organic extracts were then dried, filtered and concentrated under reduced pressure to yield a clear oil that crystallised on standing. Recrystallisation (Et$_2$O–hexane) of this solid yielded the title compound 38 (115 mg, 98%) as colourless plates, mp 95.0–95.5 °C. This material was identical with that derived from *cis*-dihydroxylation of diene 8.

Dimethyl (3a′α,4′β,5′α,7a′α)-(2′,2′-dimethyl-4′-hydroxy-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl)malonate 22 and dimethyl (3a′α,4′β,5′β,7a′α)-(2′,2′-dimethyl-4′-hydroxy-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl)malonate 39

A pre-cooled (ice–H_2O) solution of epoxide **4** (100 mg, 0.59 mmol) in THF (5 cm^3) was added dropwise to a cooled (ice–H_2O) solution of dimethyl malonate (136 cm^3, 1.19 mmol) and tetrakis(triphenylphosphine)palladium(0) (69 mg, 0.06 mmol, 5 mol%) in THF (5 cm^3) maintained under N_2 in the dark. The resulting mixture was then allowed to warm to 20 °C and was stirred at this temerature for 36 h. The reaction mixture was then concentrated under reduced pressure to a bright yellow oil. Subjection of this material to preparative TLC (silica gel, 1:1 hexane–EtOAc) and extraction (Et$_2$O) of the appropriate band (R_f 0.4–0.6) yielded an inseparable and 1:1 mixture of the *title compounds* **22** and **39** (111 mg, 65%) as a colourless oil. δ_C (isomer **22**) 169.2, 168.4, 130.8, 124.3, 109.6 (2′-C), 79.4, 72.4, 70.5, 52.6, 52.4, 50.7, 40.8, 28.1 (CH$_3$) and 25.6 (CH$_3$); (isomer **39**) 168.8, 168.4, 131.5, 126.6, 109.2, 80.8, 74.3, 71.0, 52.7, 52.6, 40.8, 27.3, 24.9 and 14.2 (one signal obscured or overlapping).

Dimethyl (3a′α,4′β,5′α,7a′α)-(2′,2′-dimethyl-4′-hydroxy-3a′,4′,5′,7a′-tetrahydro-1′,3′-benzodioxol-5′-yl)malonate 22

Pd$_2$(DBA)$_3$·CHCl$_3$[17] (35 mg, 0.03 mmol) was added to a stirred solution of diphenylphosphinoethane (27 mg, 0.07 mmol) in THF (5 cm^3) which was protected from light and maintained under N_2. This mixture was stirred for 0.16 h and then dimethyl malonate was added (0.16 cm^3, 1.36 mmol) followed by a solution of epoxide **4** (115 mg, 0.68 mmol) in THF (3 cm^3). The resulting mixture was stirred at 20 °C for 40 h before being concentrated under reduced pressure to a bright yellow oil. Subjection of this material to preparative TLC (silica gel, 1:1 hexane–EtOAc elution) and extraction (Et$_2$O) of the appropriate band (R_f 0.4–0.6) yielded the title compound **22** which was contaminated with dimethyl malonate. Re-subjection of this material to preparative TLC (Et$_2$O elution) and extraction (Et$_2$O) of the appropriate band (R_f 0.6) yielded the title compound **22** as a colourless oil (44 mg, 21%). This material was identical with that obtained from the reaction of epoxide **4** with sodium dimethyl malonate.

(3aα,4β,5β,7aα)-5-Phthalimido-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-4-ol 40 and (3aα,7aα)-2,2-dimethyl-7,7a-dihydro-1,3-benzodioxol-4(3a*H*)-one 41

A pre-cooled (ice–H_2O) solution of epoxide **4** (227 mg, 1.35 mmol) in THF (10 cm^3) was added dropwise to a cooled (ice–H_2O) solution of phthalimide (118 mg, 1.35 mmol) and tetrakis(triphenylphosphine)palladium(0) (152 mg, 10 mol%) in THF (20 cm^3) maintained under N_2 in the dark. The mixture was allowed to warm to 20 °C and stirred at this temperature for 72 h then concentrated under reduced pressure to a bright yellow oil which was subjected to preparative TLC (silica gel, 8:92 Et$_2$O–CH$_2$Cl$_2$ elution). In this manner two bands, A and B, were obtained.

Extraction (Et$_2$O) of band A (R_f 0.1) afforded product contaminated by catalyst. This material was further purified by preparative TLC (silica gel, 3:2 Et$_2$O–hexane elution, 6 sweeps). Extraction (Et$_2$O) of the more mobile component yielded a white solid. Recrystallisation (Et$_2$O) of this material yielded the *title compound* **40** (160 mg, 38%) as colourless needles, mp 93.0–95.0 °C [Found: C, 64.5; H, 5.4; N, 4.6%; (M − CH$_3$)$^+$, 300.0872. C$_{17}$H$_{17}$NO$_5$ requires C, 64.8; H, 5.4; N, 4.4%; (M − CH$_3$)$^+$, 300.0872]; ν_{max}(KBr)/cm^{-1} 3423, 1776, 1705, 1696, 1393, 1375, 1333, 1082, 1040 and 721; δ_H(400 MHz) 7.86 (m, 2H), 7.75 (m, 2H), 6.09 (dt, $J_{7,6}$ 10.0, $J_{7,7a}$ 3.1, $J_{7,5}$ 3.1, 1H, 7-H), 5.70 (dm, $J_{6,7}$ 10.0, 1H, 6-H), 5.21 (m, 1H, 5-H), 4.82 (m, 1H, 7a-H), 4.43 (dt, $J_{3a,4}$ 5.9, $J_{3a,7a}$ 5.9, 1H, 3a-H), 4.26 (m, 1H, 4-H), 3.13 (d, $J_{OH,4}$ 5.4, 1H, OH), 1.48 (s, 3H, CH$_3$) and 1.42 (s, 3H, CH$_3$); δ_C(100 MHz) 169.0, 134.3, 131.6, 129.3 (7-C),

125.9 (6-C), 124.4, 109.3 (2-C), 76.1 (3a-C), 71.5 (4-C and 7a-C), 48.0 (5-C), 27.8 (CH$_3$) and 25.9 (CH$_3$); *m/z* 300 [6%, (M − CH$_3$)$^+$], 240 (23), 205 (33) and 94 (100).

Extraction (Et$_2$O) of band B (R_f 0.6) yielded a solid. Recrystallisation (Et$_2$O–hexane) of this material yielded the *enone* **41** (101 mg, 45%) as cubes, mp 87.0–88.0 °C (Found: M$^+$, 168.0786. Calc. for C$_9$H$_{12}$O$_3$: M$^+$, 168.0786); ν_{max}(KBr)/cm^{-1} 2950, 2907, 1665, 1395, 1372, 1365, 1244, 1073, 1047 and 850; δ_H(400 MHz) 6.83 (m, 1H, 6-H), 6.12 (ddd, $J_{5,6}$ 10.3, $J_{5,7′}$ 2.7, $J_{5,7}$ 1.5, 1H, 5-H), 4.63 (tt, $J_{7a,3a}$ 4.9, $J_{7a,7′}$ 4.9, $J_{7a,7}$ 1.7, $J_{7a,6}$ 1.7, 1H, 7a-H), 4.29 (d, $J_{3a,7a}$ 4.9, 1H, 3a-H), 2.88 (dm, $J_{7,7′}$ 20.3, 1H, 7-H), 2.79 (dm, $J_{7′,7}$ 20.3, 1H, 7′-H), 1.39 (d, J 0.7, 3H, CH$_3$) and 1.34 (3H, s, CH$_3$); δ_C(100 MHz) 196.2 (4-C), 146.3 (6-C), 128.1 (5-C), 109.1 (2-C), 75.4 (3a-C), 72.8 (7a-C), 27.6 (7-C), 27.3 and 25.9 (2 × CH$_3$); *m/z* 168 (6%, M$^+$), 153 [30, (M − CH$_3$)$^+$], 111 (30), 100 (63), 85 (34), 82 (100), 81 (81) and 51 (49).

(3aα,7aα)-2,2-Dimethyl-7,7a-dihydro-1,3-benzodioxol-4(3a*H*)-one 41

Pd$_2$(DBA)$_3$·CHCl$_3$ (31 mg, 0.03 mmol) was added to a stirred solution of DPPE (24 mg, 0.06 mmol) in THF (5 cm^3) maintained under N_2 and protected from light. This mixture was stirred at 20 °C for 0.16 h and then benzoic acid (87 mg, 0.71 mmol) was added followed by a solution of epoxide **4** (100 mg, 0.59 mmol) in THF (3 cm^3). The mixture was then stirred for 7 h and concentrated under reduced pressure to a bright yellow oil. The residue was subjected to chromatographic filtration (3 cm deep pad of TLC grade silica gel, 100 cm^3 CH$_2$Cl$_2$ elution) and the filtrate concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel, 1:1 hexane–EtOAc elution) and extraction (Et$_2$O) of the appropriate band (R_f 0.5) yielded the title compound **41** as a colourless solid (70 mg, 70%). Recrystallisation of this material yielded an analytically pure sample of the enone **41** which was identical with that obtained previously.

Single-crystal X-ray diffraction analysis of compounds 21 and 40

Crystal data. Compound **21**: C$_9$H$_{13}$N$_3$O$_3$, M = 211.2, monoclinic space group $P2_1/n$, a = 6.416(1), b = 10.579(1), c = 15.855(1) Å, β = 97.69(1)°, V = 1066.5(3) Å^3, λ = 1.5418 Å, Z = 4, D_m = 1.30(1), D_c = 1.315 g cm^{-3}. Colourless prisms. Crystal dimensions (distances of faces from centre): 0.256 (0 −1 1, 0 1 −1) × 0.385 (−1 0 1, 1 0 −1) × 0.462 (0 −1 −1, 0 1 1) mm, μ = 8.04 cm^{-1}.

Crystal data. Compound **40**: C$_{17}$H$_{17}$NO$_5$, M = 315.3, triclinic space group $P\bar{1}$ (confirmed on refinement), a = 10.940(1), b = 12.830(1), c = 5.785(1) Å, α = 93.23(2), β = 103.61(2), γ = 106.87(2)°, V = 748.4(4) Å^3, λ = 1.5418 Å, Z = 2, D_m = 1.392(5), D_c = 1.399 g cm^{-3}. Colourless platelets. Crystal dimensions (distances of faces from centre): 0.256 (0 −1 0, 0 1 0) × 0.256 (−1 0 0, 1 0 0) × 0.384 (−1 0 1, 1 0 −1) mm, μ = 8.21 cm^{-1}.

Data collection and processing. Accurate unit cell parameters were obtained by least-squares refinement on diffractometer angles from 25 automatically centred reflections. Rigaku-AFC diffractometer at 292(1) K, ω–2θ mode with scan range ($\Delta\omega$) 1.2° + 0.5° tan θ, 2θ scan rate 2° min^{-1}, graphite monochromated Cu-Kα radiation, data to $2\theta_{max}$ 130° recorded yielded for **21** 2032 unique reflections (h −7 to 7, k 0 to 12, l 0 to 18) and for compound **40** 2465 unique reflections (h −12 to 12, k −15 to 15, l 0 to 6). Analytical absorption corrections were made (max, min transmission factors for compound **21**, 0.836, 0.743 and for compound **40**, 0.844, 0.766 giving 1273 and 1804 respectively with $I \geq 2\sigma I$, which were used in the refinements). There was no crystal decay for compound **40** but a linear and approximately isotropic crystal decay of *ca.* 3.9% for compound **21** was corrected during processing.

Structure analysis and refinement. Direct methods with SHELX-86 were used,[24] with full-matrix least-squares refinement with all non-hydrogen atoms anisotropic. The hydrogen

atoms were given individual isotropic temperature factors which were refined together with their positional coordinates. For compound **21** the weighting scheme was $w = [\sigma^2(F_o) + 0.000\,75 F_o^2]^{-1}$, final R and R_w 0.049, 0.060, and $(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ were $+0.18$, -0.23 e Å^{-3}. For compound **40**, the weighting scheme was $w = [\sigma^2(F_o) + 0.000\,15 F_o^2]^{-1}$, final R and R_w 0.034, 0.043, and $(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ were $+0.18$, -0.20 e Å^{-3}. The intensities for both the structures were corrected for Lorentz and polarisation factors. The absorption and refinements [function minimised $\Sigma w(|F_o| - |F_c|)^2$] were made with SHELX-76[25] on a VAX8800 computer. Atomic scattering factors and anomalous dispersion factors applied to the non-H atoms were those supplied in SHELX-76.[25] Figs. 1 and 3 were prepared from the output of ORTEPII.[26] Bond lengths and valence angles for the non-hydrogen atoms, anisotropic thermal parameters and atomic parameters for the hydrogen atoms for both the structures, together with their estimated standard deviations, have been deposited at the Cambridge Crystallographic Data Centre (CCDC).** The molecular conformations of compounds **21** and **40** are illustrated in Figs. 2 and 3 respectively.

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** See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/105.

References

1 For reviews on the applications of *cis*-1,2-dihydrocatechols in synthesis see: (*a*) H. A. J. Carless, *Tetrahedron: Asymmetry*, 1992, **3**, 795; (*b*) D. A. Widdowson, D. W. Ribbons and S. D. Thomas, *Janssen Chim. Acta*, 1990, 3; (*c*) S. M. Brown and T. Hudlicky, *The Use of Arene* cis-*Diols in Synthesis*, in *Organic Synthesis: Theory and practice*, ed T. Hudlicky, JAI Press, Greenwich, CT, 1993, vol. 2, p. 113; (*d*) T. Hudlicky and J. W. Reed, *Advances in Asymmetric Synthesis*, ed. A. Hassner, JAI Press, Greenwich, CT 1995, vol. 1, p. 271; (*e*) T. Hudlicky and A. J. Thorpe, *Chem. Commun.*, 1996, 1993.

2 For some notable examples see (*a*) S. V. Ley and L. L. Yeung, *Synlett.*, 1992, 291; (*b*) T. Hudlicky, J. D. Price, F. Rulin and T. Tsunoda, *J. Am. Chem. Soc.*, 1990, **112**, 9439; (*c*) T. Hudlicky, J. Rouden, H. Luna and S. Allen, *J. Am. Chem. Soc.*, 1990, **116**, 5099.

3 For our earlier papers in this area see (*a*) M. Mandel and T. Hudlicky, *Synlett.*, 1993, 418; (*b*) J. Rouden and T. Hudlicky, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1095 and references therein; (*c*) M. G. Banwell and J. R. Dupuche, *Chem. Commun.*, 1996, 869 and references therein.

4 One of us has previously described the reaction of the title monoepoxides and the corresponding aziridines with certain carbon-centred nucleophiles: T. Hudlicky, X. Tian, K. Konisburger and J. Rouden, *J. Org. Chem.*, 1994, **59**, 4037; for a discussion of the possible mechanism plus further applications and details see T. Hudlicky, X. Tian, K. Königsberger, R. Maurya, J. Rouden and B. Fan, *J. Am. Chem. Soc.*, 1996, **118**, 10 752.

5 (*a*) Synthesis of (±)-**4**: see ref. 2(*b*) as well as K. Ramesh, M. S. Wolfe, Y. Lee, D. Vander Velde and R. T. Borchardt, *J. Org. Chem.*, 1992, **57**, 5861 and references therein; (*b*) Synthesis of **5**: T. Hudlicky, H. Luna, H. F. Olivo, C. Anderson, T. C. Nugent and J. D. Price, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2907; (*c*) Note the corrigendum regarding the structure of azido alcohol **23**: *J. Chem. Soc., Perkin Trans. 1*, 1993, 535.

6 D. R. Dalton, V. P. Datta and D. C. Jones, *J. Am. Chem. Soc.*, 1968, **90**, 5498.

7 A. A. Haines, *Methods for the Oxidation of Organic Compounds*, Academic Press, London, 1985, p. 86.

8 C. H. Behrens and K. B. Sharpless, *J. Org. Chem.*, 1985, **50**, 5696.

9 M. F. Mackay, M. G. Banwell, M. E. Reum and S. L. Richards, *Acta Crystallogr., Sect. C*, 1992, **48**, 70.

10 M. B. Smith, *Compendium of Organic Synthetic Methods*, Wiley, New York, 1992, vol. 7, p. 164.

11 (*a*) M. B. Smith, *Compendium of Organic Synthetic Methods*, Wiley, New York, 1992, vol. 7, p. 163; (*b*) S. Ram and L. D. Spicer, *Tetrahedron Lett.*, 1987, 515.

12 We thank Dr Joseph S. Merola, of Virginia Polytechnic Institute & State University, for providing us with the crystallographic data for azido alcohol **24**.

13 T. Hudlicky, T. Nugent and W. Griffith, *J. Org. Chem.*, 1994, **59**, 7944.

14 T. C. Nugent, PhD Dissertation, Virginia Polytechnic Institute & State University, August 1995.

15 (*a*) B. M. Trost and G. M. Molander, *J. Am. Chem. Soc.*, 1981, **103**, 5969; (*b*) B. M. Trost, G.-H. Kuo and T. Benneche, *J. Am. Chem. Soc.*, 1988, **110**, 621; (*c*) D. R. Tueting, A. E. Echavarren and J. K. Stille, *Tetrahedron*, 1989, **45**, 979.

16 T. Tsuda, Y. Horii, Y. Nakagawa, T. Ishida and T. Saegusa, *J. Org. Chem.*, 1989, **54**, 977.

17 T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet and T. A. Ibers, *J. Organomet. Chem.*, 1974, **65**, 253.

18 C. R. Johnson, P. A. Plé, L. Su, M. J. Heeg and J. P. Adams, *Synlett.*, 1992, 388.

19 X. Deruyttere, L. Dumortier, J. Van der Eycken and M. Vanderwalle, *Synlett.*, 1992, 51.

20 (*a*) T. Tsuda, Y. Horii, Y. Nakagawa, T. Ishida and T. Saegusa, *J. Org. Chem.*, 1989, **54**, 977; (*b*) M. Suzuki, Y. Oda and R. Noyori, *J. Am. Chem. Soc.*, 1979, **101**, 1623.

21 C. Altona, H. J. Geise and C. Romers, *Tetrahedron*, 1968, **24**, 13.

22 M. G. Banwell, *Org. Prep. Proced. Int.*, 1989, **21**, 255.

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

24 G. M. Sheldrick, SHELX-86. In *Crystallographic Computing 3*, ed. G. M. Sheldrick, C. Krüger and R. Goddard, Oxford University Press, 1985, pp. 175–189.

25 G. M. Sheldrick, SHELX-76, *Program for Crystal Structure Determination*, University of Cambridge, Cambridge, UK, 1976.

26 C. K. Johnson, ORTEPII, Report ORNL-5138, Oak Ridge National Laboratory, Tennessee, USA, 1976.