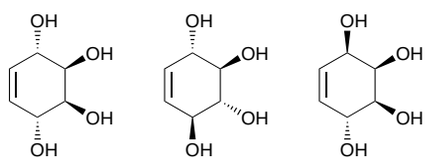
Hydroxyhalogenations of acyloxycyclohex-2-enes. Part 3.[1] Iterative 1,2-hydroxyiodination of acetoxycyclohex-2-ene: preparation of tetraacetyl conduritol D

Johannes Bange, Alan F. Haughan, J. R. Knight and Joseph Sweeney *,†

Department of Chemistry, University of Reading, Reading, UK RG6 6AD

Compound 22, the tetraacetyl derivative of conduritol D, has been synthesized by repeated hydroxyiodination reactions in nine steps from acetoxycyclohex-2-ene.

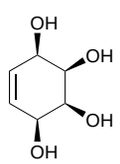
Oxidation of alkenes by means of addition of oxygen has been an area of research of great interest to organic chemists throughout the history of the subject. In particular, of late the study of asymmetric epoxidation[2] and dihydroxylation[3] reactions of alkenes has provided many of the most-used reactions of the modern synthetic chemist's armoury. Our group has had an interest in such oxygen addition reactions of alkenes for some time, and we have aimed during that time to develop new and useful synthetic methods of this type, with a view to enabling synthesis of cyclitols, such as the conduritol[4] family (conduritols A–F, **1**–**6**). We here disclose in full[5] the details of



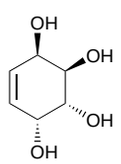
1

2

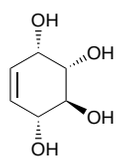
3



4



5



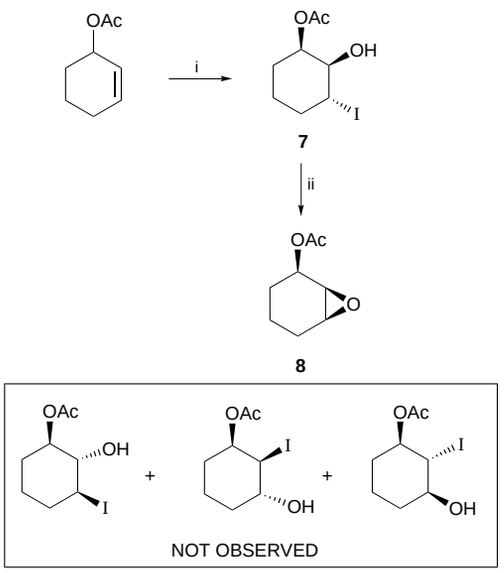
6

Conduritols A–F (**1**–**6**, respectively)

our recent endeavours in this area of research which have culminated in a synthesis of the peracetylated derivative of a *meso*-conduritol, conduritol D **4**.

Our work commenced with the investigation of the addition of 'I–OH' to acetoxycyclohex-2-ene, a reaction which could produce four compounds in two diastereomeric pairs (Scheme 1). In fact, a single product was obtained from this reaction, in 65% yield. Upon the basis of the values of ^{1}H NMR chemical shift and ^3J coupling constants, the structure was tentatively assigned as **7**, an assignment reinforced by conversion of the product of the reaction to *cis*-3-acetoxycyclohexene oxide **8**[6] upon reaction with DBU.

The pronounced selectivity of this hydroxyiodination reaction is rationalized by a mechanism involving the less stable[7] conformer **9** of the cycloalkene (Scheme 2). Thus, the preponderance of **7** may be explained if one accepts that iodonium ion **10**, produced by addition of iodenium ion to the face of the double bond distant from the ring substituent, is the predominant intermediate in the reaction. Compound **10** then reacts regiospecifically with water due to the constraint for *trans*-



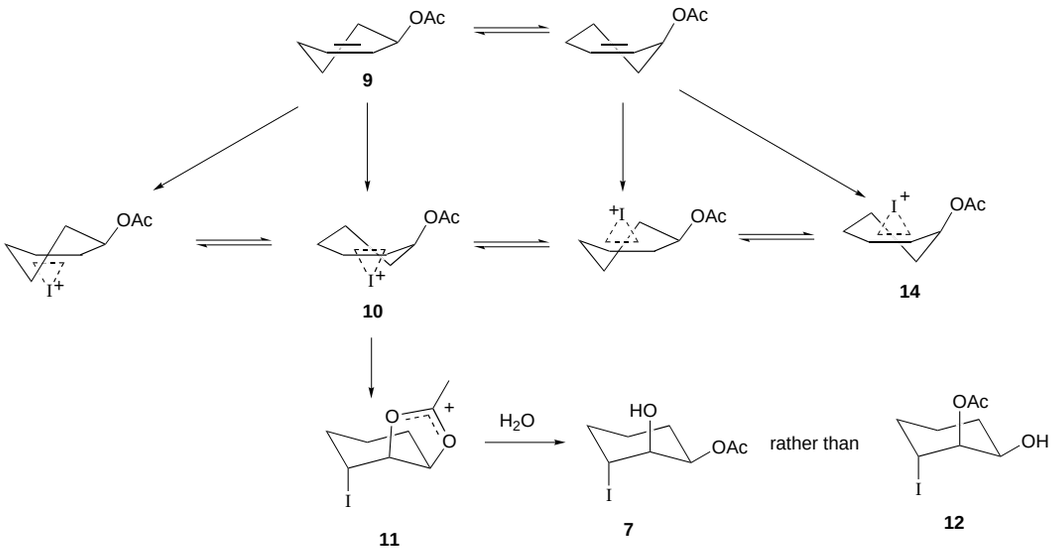
Scheme 1 *Reagents*: i, *N*-iodosuccinimide, water, CH_2Cl_2; ii, DBU, room temp.

diaxial ring-opening to give **7**. Because of the *trans*-diaxial requirement for ring-opening, iodonium ion **10** is the only intermediate which can furnish **7** as the product of the reaction. Since it is likely that the energetic barriers between the possible iodonium ions are small, it is perhaps the case that there is a neighbouring group effect in operation, whereby only iodonium ion **10** may react *via* intramolecular *trans*-diaxial ring-opening. Thus, even if ion **10** is not very much more stable than its counterparts, once it is formed, reaction to give dioxolonium ion **11** is rapid, thereby distorting the conformer population by Le Chatelier's principle. Dioxolonium ion **11** would then react with water to give **7**, in which the acetate remains in an equatorial position rather than migrating to an axial one. When the reaction to produce **7** was repeated on a large scale, however, a small amount of regioisomeric hydroxy iodide **12** was isolated, indicating that the acetate migration is occurring, albeit to a small extent (Scheme 3).

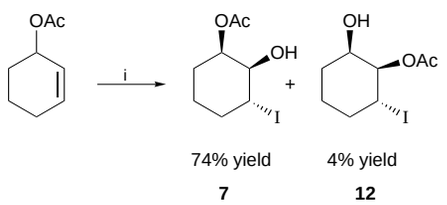
Given the appearance of this acetate-migrated isomer, we were keen to investigate further to see whether other factors could influence the product ratio of the reaction. When dichloromethane was replaced as solvent by acetonitrile, the product ratio **7**:**12** was improved to 34:1, although the reaction was low-yielding. When THF was employed as solvent, the major product was another isomeric hydroxy iodide **13**, produced *via* iodonium ion **14** as an intermediary (Scheme 4).

Having performed a brief examination of the solvent effect upon product distribution in the hydroxyiodination reaction, we next examined the role of the acyl substituent upon the

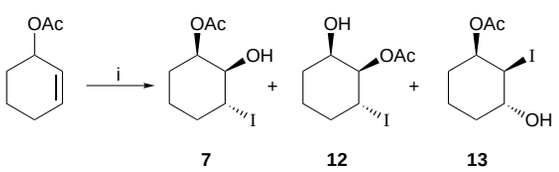
† E-Mail: j.b.sweeney@reading.ac.uk



Scheme 2



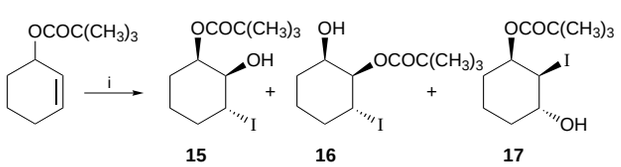
Scheme 3 *Reagents*: i, *N*-iodosuccinimide, water, CH_2Cl_2



Solvent	CH_2Cl_2	CH_3CN	THF
7:**12**:**13**	74:4:0	34:1:0	17:0:54

Scheme 4 *Reagents*: i, *N*-iodosuccinimide, water, solvent

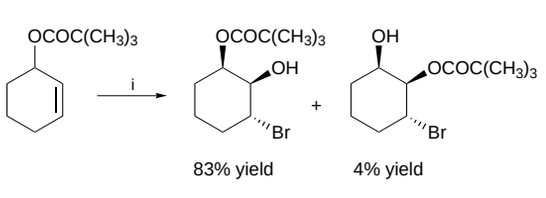
reaction. Thus, the acetyl sub-unit of the starting material was replaced by a pivaloyl group. When this compound was exposed to the reaction conditions previously referred to, the reaction trend was repeated (Scheme 5), although yields were lower.



Solvent	CH_2	THF
15:**16**:**17**	51:4:0	7:0:50

Scheme 5 *Reagents*: i, *N*-iodosuccinimide, water, solvent

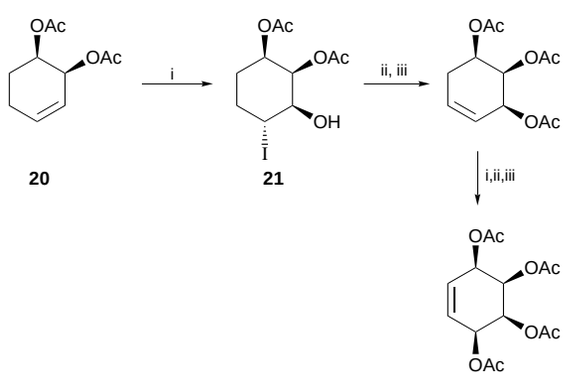
The same pivalate substrate was also reacted with NBS, again repeating the trend observed earlier (Scheme 6). In this



Scheme 6 *Reagents*: i, *N*-bromosuccinimide, water, CH_2Cl_2

reaction, the ratio of non-acyl migrated product **18** to acyl migrated product **19** was slightly better than in the reaction with NIS, and the yield was higher.

With this highly selective, previously unreported reaction in hand, we immediately realized that an iterative hydroxyiodination procedure would, if similar regio- and stereo-selectivity were exhibited, allow a conceptually unique synthesis of tetraacetyl conduritol D, as described diagrammatically in Scheme 7. Thus, we proposed to acetylate **7** and then eliminate

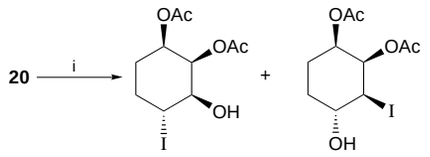


Scheme 7 *Reagents*: i, *N*-iodosuccinimide, water, CH_2Cl_2; ii, acetic anhydride, pyridine, DMAP; iii, DBU, toluene, reflux

HI to give 1,2-diacetoxycyclohex-3-ene **20** which, we hoped, would undergo a regio- and stereo-selective reaction with NIS and water in a fashion analogous to the reaction of monoacetoxycyclohexene, to give hydroxy iodide **21**. Double repetition of the acetylation–elimination–hydroxy iodination protocol would then eventually provide the desired cyclitol derivative **22**.

To commence the realization of this synthetic concept, compound **20** was prepared from **7** in 65% yield by reaction, firstly, with acetic anhydride in pyridine and, secondly, DBU in refluxing toluene. When **20** was reacted with NIS in dichloromethane at room temperature, only two products were obtained; our desired hydroxy iodide, 1,2-*trans*-2,3-*cis*-3,4-*cis*-3,4-diacetoxy-2-hydroxy-1-iodocyclohexane, **21**, and the undesired regioisomer **23** (Scheme 8). Although the reaction was reasonably stereoselective, in as much as only two diastereoisomers were produced, unfortunately, the undesired isomer **23** was the major product of the reaction.

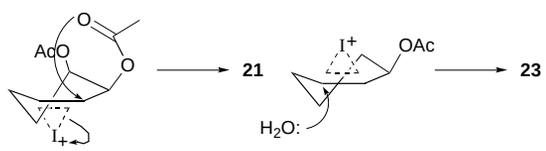
When a trace of acetic acid (1% v/v) was used in the reaction, the product ratio was shifted in favour of **21**, but the regioselectivity of the process was still relatively poor (*ca*. 5 : 3 in favour of **21**). As before, the use of acetonitrile as solvent proved bene-



Yield **21**	Yield **23**	Solvent
39%	52%	CH_2Cl_2
46%	27%	CH_2Cl_2–AcOH
60%	6%	CH_3CN

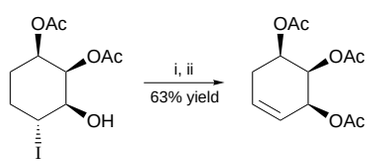
Scheme 8 *Reagents*: i, *N*-iodosuccinimide, water, solvent; ii, acetic anhydride, pyridine, DMAP; iii, DBU, toluene, reflux

ficial and the product ratio of the reaction improved drastically to lie heavily in favour of our desired regio- and diastereoisomer **21**. To yield **21** and **23**, iodonium ions **24a** and **24b**, respectively, are implicated in the mechanism (Scheme 9).

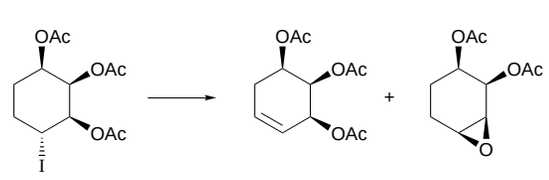


Scheme 9

Compound **21** was acylated in good yield and then dehydrohalogenated to give 1,2-*cis*-2,3-*cis*-1,2,3-triacetoxycyclohex-4-ene **25** in moderate overall yield (Scheme 10). The dehydrohalogenation reaction was slightly irksome, in that it proceeded slowly (although in good yield), taking 96 hours to reach completion for small-scale reactions (<30 mg substrate) and considerably longer for larger-scale reactions (120 h on 200 mg scale and 168 hours on > 800 mg scale). Furthermore, in the longest reaction, an additional product, epoxide **26** began to appear (Scheme 11).



Scheme 10 *Reagents*: i, acetic anhydride, pyridine, DMAP; ii, DBU, toluene, reflux



Reagents	DBU, toluene, reflux	P_4-Bu^t base, THF, –78 °C to rt
Time	168 hours	7 hours
Yield **25**	51%	16%
Yield **26**	4%	82%

Scheme 11

In an attempt to obviate these complications, we turned our attention to a stronger base for dehydrohalogenation and, accordingly, we next examined the use of Schwesinger's P_4-Bu^t phosphazene base **27**, a substance more basic than DBU by a factor of 10^{18}.[8] Using this base, dehydrohalogenation was much more rapid, with HI elimination being complete within a few hours when the reaction was performed from −78 °C to room temperature in THF solvent, but under these conditions the major product was epoxide **26**, obtained in 82% yield (Scheme 11).

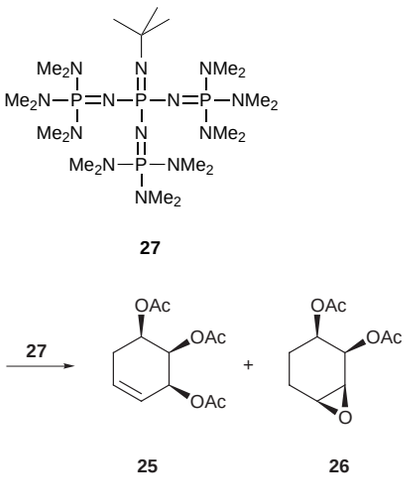


Table 1

Reaction time/h	Reaction temp.	Solvent	Yield (%) **25**	Yield (%) **26**
22	−130 °C to rt	Pentane	30	61
6	−100 °C to rt	THF	16	52
7	−78 °C to rt	THF	16	82
6	−78 °C	THF	0	21
18	−40 °C	THF	0	0*
6	0 °C	THF	0	0*

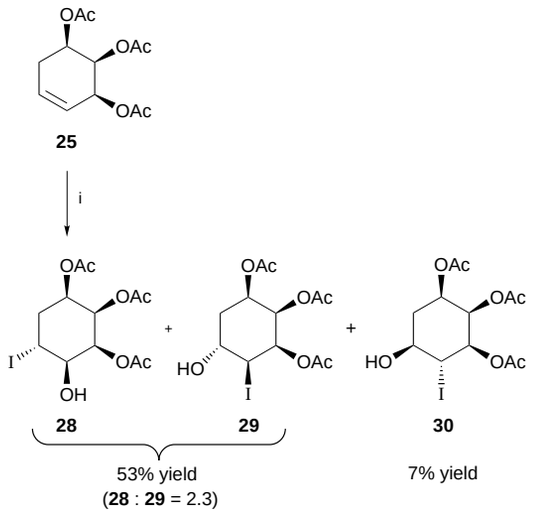
* Decomposition observed.

Given this rather unexpected observation, we probed more deeply the effect of reaction temperature upon the dehydrohalogenation using the phosphazene base. The results of this investigation are collated in Table 1.

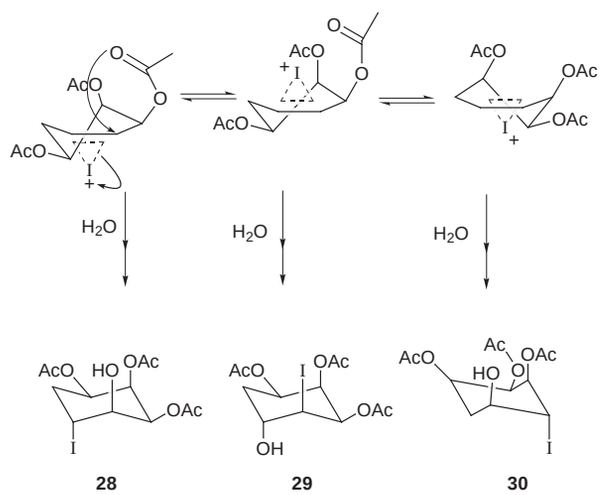
Thus, based on the results summarized in Table 1, it can be concluded that the formation of our desired cycloalkene **25** using the P_4-Bu^t base is only feasible at very low temperature, and that even at these temperatures, the predominant product is epoxide **26**. This epoxide presumably arises *via*, firstly, deacylation caused by hydroxide ion generated by reaction of **27** with trace amounts of water in the reaction mixture and, secondly, 3-*exo*-tet ring-closure. Whatever the origin of epoxide **26**, it is clear that DBU provides a much more reliable means of obtaining compound **25**.

Armed with sufficient quantities of **25** to bring a synthesis of tetraacetyl conduritol D in sight, we proceeded to the crucial final hydroxyiodination step. Thus, 1,2-*cis*-2,3-*cis*-1,2,3-triacetoxycyclohex-4-ene **25** was treated with NIS and water in dichloromethane at room temperature over a three-day period; three products were obtained from the reaction, in a combined yield of 60%, along with a small amount of unreacted starting material (8%) (Scheme 12). These three (previously unreported) compounds were identified as 1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-triacetoxy-5-iodocyclohexan-4-ol **28**, the regioisomeric 1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-triacetoxy-4-iodocyclohexan-5-ol **29** and 1,2-*cis*-2,3-*cis*-3,4-*trans*-4,5-*trans*-1,2,3-triacetoxy-4-iodocyclohexan-5-ol **30**. Compounds **28** and **29** were obtained in a yield of 53% and could not be separated by flash chromatography using a variety of solvents: these compounds were formed in a ratio of approximately 2:3 (as judged from ^{1}H NMR spectra), while **30** was purified by flash chromatography, after which it was obtained in 7% yield.

The conformational effects responsible for this product distribution are summarized diagrammatically in Scheme 13. Since the major product of the reaction is **29**, in which there has



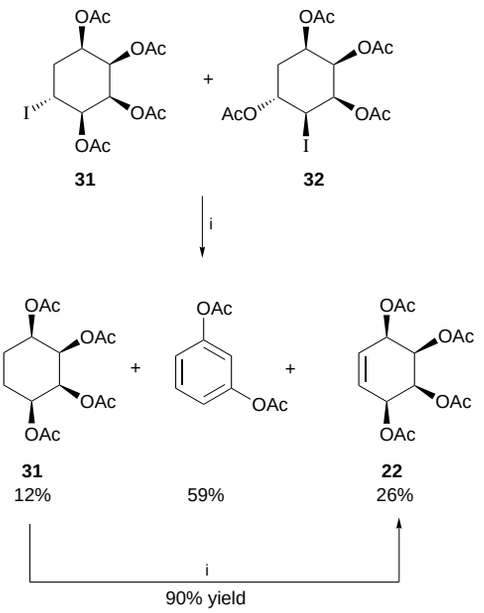
Scheme 12 *Reagents*: i, *N*-iodosuccinimide, water, CH_2Cl_2



Scheme 13

been no anchimeric assistance to ring-opening of an iodonium ion, we presume that the neighbouring group participation which we proposed to explain our initial observations is of relatively little importance when there is greater steric constraint present in the substrate, so that the primary concern is to minimize axiality (both proper and pseudo). Thus, **28** and **29** are favoured over **30** simply because they result from a reactive conformation in which there is a pseudoequatorial rather than a pseudoaxial allylic acetoxy substituent. Furthermore, the presence of **28** and **29** in roughly equal amounts implies a high-energy barrier for interconversion of the iodonium ions leading to **28** and **29**, since intramolecular ring-opening of iodonium might otherwise be expected to dominate the mechanism. There is no trace of a product in which acetate has migrated, presumably because such a process would incur a highly-disfavoured 1,3-diaxial interaction.

Although disappointed that **28** and **29** were not separable, we proceeded with the mixture of regioisomers in the hope that separation would be possible at a later stage. Thus, **28** and **29** were acylated in high yield, but even as the acetyl derivative the mixture remained inseparable. Treatment of the mixture of tetraacetates **31** and **32** with DBU in refluxing toluene induced a rapid reaction yielding three products, which were isolated by flash chromatography and proved to be unreacted tetraacetate **31**, 1,3-diacetoxybenzene and conduritol D tetraacetate **22**[9] in 12, 59 and 26% yields, respectively (Scheme 14). Although the yield of **22** from this reaction was disappointing, when now-pure tetraacetate **31** was re-exposed to the reaction conditions, a 90% yield of **22** was obtained. Clearly, if we were able to



Scheme 14 *Reagents*: i, DBU, toluene, reflux, 4 h

prepare **31** with greater selectivity as a pure compound, the final dehydrohalogenation reaction of the iteration sequence would be a very efficient reaction. The factors affecting the selectivity of the last hydroxyiodination reaction of the above sequence are the subject of close scrutiny in our laboratory at present.

Experimental

General

Where appropriate, solvents and reagents were purified using standard procedures. Light petroleum refers to the fraction with the boiling range 40–60 °C.

Melting points were recorded on either a Kofler hot-stage apparatus and were corrected, or an Electrothermal melting point apparatus and were uncorrected. Infra-red spectra were recorded on a Perkin-Elmer 881 spectrophotometer. Mass spectra were recorded on a Fisons Autospec spectrometer. NMR spectra were recorded on a JEOL GX-270 spectrometer, a JEOL GX-400 spectrometer or a JEOL Λ-300 spectrometer, using tetramethylsilane or chloroform as the internal standard. Chemical shifts in ^{1}H NMR spectra are expressed as ppm down field from tetramethylsilane, and in ^{13}C NMR relative to the internal solvent standard. Coupling constants (J) are quoted in Hz.

Reactions involving chemicals or intermediates sensitive to air and/or moisture were conducted under a nitrogen or argon atmosphere in flame- or oven-dried apparatus. Column chromatography was performed using Merck Kieselgel 60 or Fluka Kieselgel 60 silica gel. Preparative plate thin layer chromatography was carried out using Kieselgel 60 $PF_{254+366}$. Analytical thin layer chromatography was carried out using either precoated Merck Kieselgel 60 F_{254} glass backed plates, or precoated Merck Kieselgel 60 F_{254} aluminium backed plates and were visualized under UV at 346 nm and by staining with iodine and an acidic ammonium molybdate stain [20% w/v ammonium molybdate(VI) tetrahydrate in 10% v/v sulfuric acid].

(±)-1,2-*cis*-2,3-*trans*-1-Acetoxy-3-iodocyclohexan-2-ol 7 and (±)-1,2-*cis*-2,3-*trans*-2-acetoxy-3-iodocyclohexan-1-ol 12

To a solution of 1-acetoxycyclohex-2-ene[10] (5.30 g, 37.81 mmol) in dichloromethane (100 ml) was added *N*-iodosuccinimide (11.06 g, 49.15 mmol) and distilled water (5 ml). The mixture was stirred at room temperature (24 h), washed with saturated aqueous sodium thiosulfate (50 ml) and the organic layer dried ($MgSO_4$) and concentrated *in vacuo*. Purifi-

cation by flash column chromatography (40% diethyl ether in light petroleum) yielded *hydroxy iodide* **7** as a colourless solid (8.00 g, 74%); R_f 0.37 (50% diethyl ether in light petroleum); mp 56–58 °C (Found: C, 34.07; H, 4.59; I, 44.88. $C_8H_{13}IO_3$ requires C, 33.82; H, 4.61; I, 44.67%); $\nu_{max}(CCl_4)/cm^{-1}$ 3446 (OH), 1741 (CO); δ_H(270 MHz, $CDCl_3$) 1.39–2.45 (6H, m, 3 × CH_2), 2.11 (3H, s, CH_3), 2.64 (1H, d, *J* 4.0, OH), 3.81 (1H, ddd, *J* 9.2, 4.0, 3.3, C*H*OH), 4.35 (1H, ddd, *J* 10.6, 9.5, 4.4, CHI), 5.26–5.30 (1H, m, CHOAc); δ_C(67.5 MHz, $CDCl_3$) 170.6 (CO), 75.4 (CH), 71.6 (CH), 36.5 (CH_2), 34.1 (CH), 28.3 (CH_2), 21.9 (CH_2), 21.2 (CH_3); *m*/*z* (CI) 285 (MH^+, 1.4%), 267 (12.0), 225 (74.0), 207 (24.0), 157 (10.0), 97 (100.0) [Found 284.9998. $C_8H_{14}IO_3$ (MH^+) requires 284.9988]; and *hydroxy iodide* **12** as a colourless oil (0.43 g, 4%); R_f 0.27 (50% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3614 (OH), 2948, 1753 (CO); δ_H(270 MHz, $CDCl_3$) 1.39–2.10 (6H, m, 3 × CH_2), 2.16 (3H, s, CH_3), 2.36–2.43 (1H, m, OH), 4.14 (1H, m, C*H*OH), 4.42 (1H, ddd, *J* 10.6, 9.8, 4.4, CHI), 5.01 (1H, dd, *J* 9.5, 2.6, CHOAc); δ_C(67.5 MHz, $CDCl_3$) 170.5 (CO), 78.4 (CH), 68.2 (CH), 34.8 (CH_2), 30.3 (CH_2), 27.1 (CH), 21.3 (CH_3), 21.2 (CH_2); *m*/*z* (CI) 225 (14.0%), 207 (11.0), 157 (M − I, 5.0) [Found 157.0867. $C_8H_{13}O_3$ (M − I)$^+$ requires 157.0865].

(±)-1,2-*cis*-2,3-*trans*-1-Acetoxy-3-iodocyclohexan-2-ol 7 and (±)-1,2-*cis*-2,3-*trans*-1-acetoxy-2-iodocyclohexan-3-ol 13

To a solution of 1-acetoxycyclohex-2-ene (110 mg, 0.785 mmol) in THF (2 ml) was added *N*-iodosuccinimide (265 mg, 1.178 mmol) and water (5 drops). The mixture was stirred at room temperature (20 h) and then concentrated *in vacuo*. The residue thus obtained was dissolved in dichloromethane (20 ml), washed with saturated aqueous sodium thiosulfate (10 ml), dried ($MgSO_4$) and evaporated *in vacuo*. Purification by flash column chromatography (50% diethyl ether in light petroleum) yielded *hydroxy iodide* **7** (37 mg, 17%), data as before, and *hydroxy iodide* **13** as a colourless oil (120 mg, 54%); R_f 0.29 (50% diethyl ether in light petroleum) (Found: C, 33.73; H, 4.75. $C_8H_{13}IO_3$ requires C, 33.82; H, 4.61; I, 4.75%); $\nu_{max}(CCl_4)/cm^{-1}$ 3568 (OH), 2947, 1747 (C=O); δ_H(270 MHz, $CDCl_3$) 1.40–2.20 (6H, m, 3 × CH_2), 2.13 (3H, s, CH_3), 2.25 (1H, d, *J* 3.1, OH), 4.01 (1H, ddt, *J* 9.4, 4.2, 2.9, C*H*OH), 4.23 (1H, dd, *J* 9.2, 2.9, CHI), 5.23–5.26 (1H, m, CHOAc); δ_C(75 MHz, $CDCl_3$) 170.0 (CO), 73.7 (CH), 71.7 (CH), 43.4 (CH), 32.5 (CH_2), 29.9 (CH_2), 21.2 (CH_3), 19.1 (CH_2); *m*/*z* (EI) 284 (M^+, 3.3%), 224 (7.6), 180 (4.7), 157 [(M − I)$^+$, 4.8].

(±)-*cis*-1-Acetoxy-2,3-epoxycyclohexane 8

To a solution of (±)-1,2-*cis*-2,3-*trans*-1-acetoxy-3-iodocyclohexan-2-ol **7** (60 mg, 0.211 mmol) in toluene (1 ml) was added DBU (0.04 ml, 0.267 mmol). The mixture was stirred at room temperature (0.5 h), concentrated *in vacuo* and the residue dissolved in dichloromethane (10 ml). The organic layer was washed with 5% hydrochloric acid (5 ml), saturated aqueous sodium hydrogen carbonate (5 ml), dried ($MgSO_4$) and concentrated *in vacuo* to yield *epoxide* **8**[11] as a colourless oil (30 mg, 91%); $\nu_{max}(CCl_4)/cm^{-1}$ 2946, 1741 (C=O), 1230; δ_H(270 MHz, $CDCl_3$) 1.24–1.88 (6H, m, 3 × CH_2), 2.11 (3H, s, CH_3), 3.28–3.30 [2H, m, CH(OAc)C*H*(O)C*H*], 5.10–5.16 [1H, m, CH(OAc)]; δ_C(67.5 MHz, $CDCl_3$) 170.9 (CO), 70.9 (CH), 54.2 (CH), 52.8 (CH), 24.4 (CH_2), 22.5 (CH_2), 21.2 (CH_3), 19.4 (CH_2); *m*/*z* (CI) 157 (MH^+, 2.8%), 153 (62.9), 97 (100.0) [Found 157.0861. $C_8H_{13}O_3$ (MH^+) requires 157.0865].

(±)-1,2-*cis*-2,3-*trans*-1-(2,2-Dimethylpropionyloxy)-3-iodocyclohexan-2-ol 15 and (±)-1,2-*cis*-2,3-*trans*-2-(2,2-dimethylpropionyloxy)-3-iodocyclohexan-1-ol 16

To a solution of 1-(2,2-dimethylpropionyloxy)cyclohex-2-ene (210 mg, 1.097 mmol) in dichloromethane (5 ml) was added *N*-iodosuccinimide (370 mg, 1.646 mmol) and water (8 drops). The mixture was stirred at room temperature (26 h) and then washed with saturated aqueous sodium thiosulfate (5 ml). The aqueous layer was saturated with sodium chloride and extracted with ethyl acetate (2 × 10 ml). The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (20% diethyl ether in light petroleum) yielded: *hydroxy iodide* **15** as a colourless oil (184 mg, 51%); R_f 0.38 (20% diethyl ether in light petroleum) (Found: C, 40.31; H, 5.99; I, 38.79. $C_{11}H_{19}IO_3$ requires C, 40.50; H, 5.87; I, 38.91%); $\nu_{max}(CCl_4)/cm^{-1}$ 3572 (OH), 2954, 1730 (C=O); δ_H(270 MHz, $CDCl_3$, 1.23 [9H, s, C(CH_3)$_3$], 1.46–1.68 [3H, m, C*H*(H)CH_2], 1.95–2.15 (2H, m, CH_2), 2.45–2.47 [1H, m, CH(*H*)], 2.46 (1H, d, *J* 4.4, OH), 3.81 (1H, ddd, *J* 9.7, 4.2, 3.1, C*H*OH), 4.29 (1H, ddd, *J* 11.3, 9.7, 4.3, CHI), 5.22–5.27 [1H, m, C*H*(OPiv)]; δ_C(67.5 MHz, $CDCl_3$) 178.0 (CO), 75.9 (CH), 71.3 (CH), 39.1 (C), 37.1 (CH_2), 34.4 (CH), 28.6 (CH_2), 27.2 (CH_3), 22.10 (CH_2); *m*/*z* (CI) 327 (MH^+, 57.3%), 309 (48.2), 225 (100.0), 199 (30.6), 131 (14.0) [Found 327.0463. $C_{11}H_{20}IO_3$ (MH^+) requires 327.0457]; and *hydroxy iodide* **16** as a colourless oil (14 mg, 4%); R_f 0.32 (20% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3617 (OH), 2953, 1737 (C=O); δ_H(270 MHz, $CDCl_3$) 1.28 [9H, s, C(CH_3)$_3$], 1.66–2.40 (6H, m, 3 × CH_2), 4.12–4.17 (1H, m, C*H*OH), 4.44 (1H, ddd, *J* 10.3, 9.5, 4.2, CHI), 4.99 [1H, dd, *J* 9.4, 2.6, C*H*(OPiv)]; δ_C(75 MHz, $CDCl_3$) 177.07 (CO), 77.9 (CH), 68.0 (CH), 39.1 (C), 30.2 (CH_2), 27.3 (CH_2), 26.8 (CH), 21.3 (CH_2), 19.1 (CH_2); *m*/*z* (CI) 372 (MH^+, 16.7%), 309 (44.5), 225 (57.3), 207 (62.2), 199 (31.9), 103 (41.0) [Found 327.0442. $C_{11}H_{20}IO_3$ (MH^+) requires 327.0457].

(±)-1,2-*cis*-2,3-*trans*-1-(2,2-Dimethylpropionyloxy)-3-iodocyclohexan-2-ol 15 and (±)-1,2-*cis*-2,3-*trans*-1-(2,2-dimethylpropionyloxy)-2-iodocyclohexan-3-ol 17

To a solution of 1-(2,2-dimethylpropionyloxy)cyclohex-2-ene (150 mg, 0.823 mmol) in THF (3 ml) was added *N*-iodosuccinimide (278 mg, 1.236 mmol) and water (8 drops). The mixture was stirred at room temperature (23 h), concentrated *in vacuo*, the residue dissolved in dichloromethane (10 ml) and washed with saturated aqueous sodium thiosulfate (7 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (40% diethyl ether in light petroleum) yielded *hydroxy iodide* **15** (20 mg, 7%), data as before, and *hydroxy iodide* **17** as a colourless oil (133 mg, 50%); R_f 0.28 (40% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3571 (OH), 2954, 1735 (C=O); δ_H(270 MHz, $CDCl_3$) 1.27 [9H, s, C(CH_3)$_3$], 1.35–1.88 [5H, m, CH_2CH_2C*H*(H)], 2.17–2.23 [1H, m, CH(*H*)], 2.45 (1H, d, *J* 3.0, OH), 3.96–4.05 (1H, m, C*H*OH), 4.23 (1H, dd, *J* 9.7, 2.9, CHI), 5.23–5.25 [1H, m, C*H*(OPiv)]; δ_C(75 MHz, $CDCl_3$) 177.14 (CO), 73.6 (CH), 71.8 (CH), 43.4 (CH), 39.2 (CH), 32.9 (CH_2), 29.9 (CH_2), 27.3 (CH_3), 19.1 (CH_2); *m*/*z* (CI) 327 (MH^+, 4.6%), 309 (39.4), 225 (25.2), 207 (33.9), 199 (6.0) [Found 327.0452. $C_{11}H_{20}IO_3$ (MH^+) requires 327.0457].

(±)-1,2-*cis*-2,3-*trans*-3-Bromo-1-(2,2-dimethylpropionyloxy)-cyclohexan-2-ol 18 and (±)-1,2-*cis*-2,3-*trans*-3-bromo-2-(2,2-dimethylpropionyloxy)cyclohexan-1-ol 19

To a solution of 1-(2,2-dimethylpropionyloxy)cyclohex-2-ene (150 mg, 0.823 mmol) in dichloromethane (3 ml) was added *N*-bromosuccinimide (220 mg, 1.236 mmol) and water (5 drops). The mixture was stirred at room temperature (25 h) and then washed with saturated aqueous sodium thiosulfate (5 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (50% diethyl ether in light petroleum) yielded *hydroxy bromide* **18** as a colourless oil (190 mg, 83%); R_f 0.37 (50% diethyl ether in light petroleum) (Found: C, 47.16; H, 6.79; Br, 28.31. $C_{11}H_{19}BrO_3$ requires C, 47.32; H, 6.86; Br, 28.62%); $\nu_{max}(CCl_4)/cm^{-1}$ 3587 (OH), 2973, 2955, 1735 (C=O); δ_H(270 MHz, $CDCl_3$) 1.23 [9H, s, C(CH_3)$_3$], 1.60–1.66 (4H, m, 2 × CH_2), 1.80–1.97 [1H, m, C*H*(H)], 2.30–2.39 [1H, m, CH(*H*)], 2.38 (1H, d, *J* 3.7, OH), 3.77 (1H, ddd, *J* 9.4, 3.3, 3.3, C*H*OH), 4.21 (1H, ddd, *J* 11.0, 9.3, 4.4, C*H*Br), 5.29–5.31 [1H,

m, C*H*(OPiv)]; δ_C(75 MHz, $CDCl_3$) 177.8 (CO), 75.3 (CH), 71.6 (CH), 55.3 (CH), 39.1 (C), 34.9 (CH_2), 28.4 (CH_2), 27.2 (CH_3), 20.9 (CH_2); *m*/*z* (CI) 199 [$(M - {}^{79}Br)^+$, 15.0%], 179 (12.0), 131 (33.0), 115 (29.0) [Found 199.1333. $C_{11}H_{19}O_3$ ($M - {}^{79}Br)^+$ requires 199.1334]; and *hydroxy bromide* **19** as a colourless oil (10 mg, 4%); R_f 0.30 (50% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3613 (OH), 2955, 1737 (C=O); δ_H(270 MHz, $CDCl_3$) 1.27 [9H, s, C(CH_3)$_3$], 1.62–1.99 [5H, m, CH_2CH_2-C*H*(H)], 2.27–2.37 [1H, m, CH(*H*)], 4.14–4.19 (1H, m, C*H*OH), 4.35 (1H, ddd, *J* 9.5, 9.5, 4.2, CHBr), 4.99 [1H, dd, *J* 9.2, 2.8, C*H*(OPiv)]; δ_C(75 MHz, $CDCl_3$) 177.7 (CO), 71.8 (CH), 68.5 (CH), 49.2 (CH), 39.1 (C), 34.7 (CH_2), 30.1 (CH_2), 27.2 (CH_3), 20.0 (CH_2); *m*/*z* (CI) 217 (0.15%), 207 (0.45), 199 [$(M - {}^{79}Br)^+$, 0.95], 149 (1.3), 137 (5.0), 131 (10.0), 123 (6.0).

(±)-*cis*-1,2-Diacetoxycyclohex-3-ene 20[12]

To a solution of (±)-1,2-*cis*-2,3-*trans*-1-acetoxy-3-iodocyclohexan-2-ol **7** (7.39 g, 26.01 mmol) in pyridine (90 ml) was added acetic anhydride (2.5 ml, 26.42 mmol) and DMAP (50 mg). The mixture was stirred at room temperature (18 h), diluted with ethyl acetate (100 ml), washed with saturated aqueous copper(II) sulfate (2 × 100 ml) and water (80 ml). The organic layer was separated, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (40% diethyl ether in light petroleum) yielded (±)-1,2-*cis*-2,3-*trans*-1,2-diacetoxy-3-iodocyclohexane as a colourless oil (7.18 g, 85%); R_f 0.70 (50% diethyl ether in light petroleum) (Found: C, 36.85; H, 4.67; I, 38.65. $C_{10}H_{15}IO_4$ requires C, 36.83; H, 4.64; I, 38.91%); $\nu_{max}(CCl_4)/cm^{-1}$ 1744 (C=O); δ_H(270 MHz, $CDCl_3$) 1.48–2.42 (6H, m, 3 × CH_2), 2.08 and 2.085 (6H, 2 × s, 2 × CH_3), 4.33 (1H, ddd, *J* 10.0, 4.4, CHI), 5.00 [1H, dd, *J* 9.9, 2.9, C*H*(OAc)-CHI], 5.32–5.36 [1H, m, CH_2CH(OAc)]; δ_C(67.5 MHz, $CDCl_3$) 169.7 (CO), 169.5 (CO), 75.6 (CH), 69.2 (CH), 36.6 (CH_2), 28.1 (CH_2), 26.1 (CH), 21.7 (CH_2), 20.9 (CH_3), 20.7 (CH_3); *m*/*z* (EI) 326 (M^+, 0.6%), 199 (57.0), 139 (31.9), 97 (100.0) [Found 199.0979. $C_{10}H_{15}O_4$ ($M - I)^+$ requires 199.0970].

To a solution of (±)-1,2-*cis*-2,3-*trans*-1,2-diacetoxy-3-iodocyclohexane (5.53 g, 16.96 mmol) in toluene (40 ml) was added DBU (5.1 ml, 34.10 mmol). The mixture was heated to reflux until the reaction had gone to completion as evinced by ^1H NMR spectroscopy (*ca*. 3 days). Toluene was removed *in vacuo*, and the residue dissolved in dichloromethane (100 ml), washed with 5% hydrochloric acid (60 ml), saturated aqueous sodium hydrogen carbonate (60 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (30% diethyl ether in light petroleum) yielded *cyclohexene* **20** as a colourless oil (2.45 g, 73%); R_f 0.70 (50% diethyl ether in light petroleum) (Found: C, 60.32; H, 7.39. $C_{10}H_{14}O_4$ requires C, 60.59; H, 7.12%); $\nu_{max}(CCl_4)/cm^{-1}$ 1743 (C=O), 1665 (C=C); δ_H(270 MHz, $CDCl_3$) 1.75–2.35 (4H, m, 2 × CH_2), 2.05 and 2.08 (6H, 2 × s, 2 × CH_3), 5.10 [1H, ddd, *J* 10.4, 3.5, 3.5, C*H*(OAc)CH_2], 5.44–5.47 [1H, m, C*H*(OAc)CH=C*H*CH_2], 5.68 [1H, dddd, *J* 9.9, 4.4, 2.2, 2.2, CH(OAc)C*H*=CHCH_2], 5.99 [1H, ddd, *J* 9.7, 3.3, 3.1, CH(OAc)CH=C*H*CH_2]; δ_C(67.5 MHz, $CDCl_3$) 170.5 (CO), 170.4 (CO), 132.9 (CH), 123.3 (CH), 69.4 (CH), 66.5 (CH), 23.9 (CH_2), 23.1 (CH_2), 21.3 (CH_3), 21.1 (CH_3); *m*/*z* (CI) 199 (MH^+, 1.8%), 158 (5.8), 139 (34.9), 97 (43.4), 79 (100.0) [Found 139.0760. $C_8H_{10}O_2$ ($M - CH_3CO_2)^+$ requires 139.0759].

(±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2-Diacetoxy-4-iodocyclohexan-3-ol 21 and (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2-diacetoxy-3-iodocyclohexan-4-ol 23

Method A. To a solution of (±)-1,2-*cis*-1,2-diacetoxycyclohex-3-ene **20** (100 mg, 0.505 mmol) in acetonitrile (5 ml) was added *N*-iodosuccinimide (147 mg, 0.653 mmol). The mixture was stirred at room temperature (3 days), concentrated *in vacuo*, dissolved in ethyl acetate (20 ml), washed with saturated aqueous sodium thiosulfate (10 ml), dried ($MgSO_4$) and evaporated *in vacuo*. Purification by flash column chromatography (50% diethyl ether in light petroleum; foil covered column) yielded *hydroxy iodide* **21** as a colourless solid (103 mg, 60%); R_f 0.29 (50% diethyl ether in light petroleum); mp 108–109 °C (diethyl ether–light petroleum) (Found: C, 35.10; H, 4.46. $C_{10}H_{15}IO_5$ requires C, 35.11; H, 4.42; I, 37.09%); $\nu_{max}(CCl_4)/cm^{-1}$ 3577 (OH), 2956, 1753 (C=O); δ_H(270 MHz, $CDCl_3$) 1.62–1.68 [1H, m, 1H of CH(OAc)CH_2], 1.74–1.89 [1H, m, 1H of CH(OAc)CH_2], 2.01 and 2.14 (6H, 2 × s, 2 × CH_3), 2.04 (1H, m, 1H of CHICH_2), 2.43–2.53 (1H, m, 1H of CHICH_2), 2.63 (1H, d, *J* 4.6, OH), 3.82 (1H, ddd, *J* 10.1, 4.6, 3.1, C*H*OH), 4.20 (1H, ddd, *J* 11.7, 10.2, 4.4, CHI), 4.91 [1H, ddd, *J* 11.4, 4.9, 2.7, C*H*(OAc)CH_2], 5.51 [1H, ddd, *J* 2.7, 2.7, 1.5, CH(OAc)-C*H*(OAc)CHOH]; δ_C(67.5 MHz, $CDCl_3$) 170.4 (CO), 170.1 (CO), 74.7 (CH), 70.9 (CH), 70.2 (CH), 32.9 (CH_2), 31.2 (CH), 27.0 (CH_2), 20.9 (CH_3), 20.9 (CH_3); *m*/*z* (CI) 343 (MH^+, 2.0%), 342 (1.9), 325 (29.0), 283 (28.0), 223 (37.5), 143 (40.9), 97 (60.0) [Found 341.9978. $C_{10}H_{15}IO_5$ (M^+) requires 341.9964]; and *hydroxy iodide* **23** as a colourless oil (10 mg, 6%); R_f 0.19 (50% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3598 (OH), 2958, 1752 (C=O); δ_H(270 MHz, $CDCl_3$) 1.38–2.01 (4H, m, 2 × CH_2), 1.99 and 2.19 (6H, 2 × s, 2 × CH_3), 2.51 (1H, d, *J* 3.1, OH), 3.96 (1H, dddd, *J* 10.6, 10.6, 4.8, 3.1, C*H*OH), 4.16 (1H, dd, *J* 10.6, 2.6, CHI), 4.90 [1H, ddd, *J* 11.5, 5.5, 2.7, C*H*-(OAc)CH_2], 5.62 [1H, ddd, *J* 2.6, 2.6, 1.1, CHIC*H*(OAc)]; *m*/*z* (EI) 342 (M^+, 2.0%), 264 (2.6), 215 (31.2), 155 (46.1), 113 (46.6), 95 (56.9) [Found 341.9968. $C_{10}H_{15}IO_5$ (M^+) requires 341.9964].

Method B. To a solution of (±)-*cis*-1,2-diacetoxycyclohex-3-ene **20** (100 mg, 0.505 mmol) in dichloromethane (5 ml) was added *N*-iodosuccinimide (147 mg, 0.653 mmol) and acetic acid (0.06 ml, 1.04 mmol). The mixture was stirred at room temperature (48 h), then washed with saturated aqueous sodium thiosulfate (3 ml), water (3 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (50% diethyl ether in light petroleum) yielded *hydroxy iodide* **21** (80 mg, 46%), *hydroxy iodide* **23** (47 mg, 27%) and unreacted olefin (10 mg, 8%).

Method C. To a solution of (±)-*cis*-1,2-diacetoxycyclohex-3-ene **20** (100 mg, 0.505 mmol) in dichloromethane (5 ml) was added *N*-iodosuccinimide (147 mg, 0.653 mmol) and water (3 drops). The mixture was stirred at room temperature (10 days), then washed with saturated aqueous sodium thiosulfate (3 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (50% diethyl ether in light petroleum) yielded *hydroxy iodide* **21** (67 mg, 39%) and *hydroxy iodide* **23** (90 mg, 52%).

(±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2,3-Triacetoxy-4-iodocyclohexane

To a solution of (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2-diacetoxy-4-iodocyclohexan-3-ol **21** (181 mg, 0.529 mmol) in pyridine (4 ml) was added acetic anhydride (0.06 ml, 0.634 mmol) and DMAP (10 mg). The mixture was stirred at room temperature (18 h), then diluted with ethyl acetate (20 ml), washed with saturated aqueous copper(II) sulfate (2 × 15 ml), water (15 ml) and the organic layer dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (40–50% diethyl ether in light petroleum) yielded (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2,3-triacetoxy-4-iodocyclohexane as a colourless solid (158 mg, 78%); R_f 0.57 (50% diethyl ether in light petroleum); mp 77–78 °C (Found: C, 37.39; H, 4.83; I, 32.92. $C_{12}H_{17}IO_6$ requires C, 37.52; H, 4.46; I, 33.02%); $\nu_{max}(CCl_4)/cm^{-1}$ 2943, 1755 (C=O); δ_H(270 MHz, $CDCl_3$) 1.65–1.95 [2H, m, CH_2CH(OAc)], 2.05 (1H, m, 1H of CHICH_2), 2.00, 2.07 and 2.15 (9H, 3 × s, 3 × CH_3), 2.48–2.57 (1H, m, 1H of CHICH_2), 4.17 (1H, ddd, *J* 12.3, 11.2, 4.6, CHI), 4.94 [1H, ddd, *J* 11.4, 5.3, 2.7, CH_2CH(OAc)], 5.00 [1H, dd, *J* 11.2, 2.7, CHIC*H*(OAc)], 5.44–5.46 [1H, m, CH(OAc)C*H*(OAc)CH(OAc)]; δ_C(67.5 MHz, $CDCl_3$) 169.8 (CO), 169.7 (CO), 169.3 (CO), 75.0 (CH), 70.0 (CH), 69.5 (CH), 33.6 (CH_2), 30.4 (CH), 27.1 (CH_2), 23.0 (CH_3), 20.8 (CH_3), 20.7 (CH_3); *m*/*z* (EI) 257 [$(M - I)^+$, 100.0%], 155 (45.8), 113 (44.7).

(±)-1,2-*cis*-2,3-*cis*-1,2,3-Triacetoxycyclohex-4-ene 25

Method A. To a solution of (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2,3-triacetoxy-4-iodocyclohexane (270 mg, 0.703 mmol) in toluene (20 ml) was added DBU (0.26 ml, 1.739 mmol). The mixture was heated to reflux (5 days), after which time further DBU (0.21 ml, 1.404 mmol) was added and reflux continued (24 h). The toluene was removed *in vacuo*, and the residue dissolved in dichloromethane (20 ml), dried ($MgSO_4$) and evaporated *in vacuo*. Purification by flash column chromatography (30% diethyl ether in light petroleum) yielded (±)-1,2-*cis*-2,3-*cis*-1,2-diacetoxy-3,4-epoxycyclohexane **26** (5 mg, 3%) and *cyclohexene* **25** (91 mg, 51%) as a colourless oil; R_f 0.53 (50% diethyl ether in light petroleum) (Found: C, 56.32; H, 6.19. $C_{12}H_{16}O_6$ requires C, 56.24; H, 6.25%); $\nu_{max}(CCl_4)/cm^{-1}$ 2932, 1752 (C=O), 1666 (C=C); δ_H(270 MHz, $CDCl_3$) 2.04, 2.05 and 2.13 (9H, 3 × s, 3 × CH_3), 2.39–2.44 (2H, m, CH_2), 5.13 [1H, ddd, *J* 8.6, 7.0, 1.8, CH_2CH(OAc)], 5.51–5.60 [3H, m, CH(OAc)CH(OAc)-CH=CH], 5.83–5.90 (1H, m, CH=CHCH$_2$); δ_C(67.5 MHz, $CDCl_3$) 170.5 (CO), 170.2 (CO), 170.1 (CO), 127.5 (CH), 124.2 (CH), 68.2 (CH), 68.0 (CH), 67.9 (CH), 27.1 (CH_2), 21.0 (CH_3), 20.9 (2 × CH_3); *m*/*z* (CI) 257 (MH^+, 8.9%), 155 (41.0), 136 (14.6), 94 (100.0) (Found 257.1029. $C_{12}H_{17}O_6$ requires 257.1025).

Method B. To a solution of (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-1,2,3-triacetoxy-4-iodocyclohexane (55 mg, 0.143 mmol) in THF (2 ml) at −78 °C was added dropwise a solution of phosphazene base P_4-Bu^t **27** (0.14 ml of a 1 M solution in hexane, 0.143 mmol) in THF (1 ml). The mixture was stirred at −78 °C (1.5 h) then at room temperature (2 h). Solvent was then removed *in vacuo* and diethyl ether (5 ml) added. The resulting precipitate was filtered and washed with diethyl ether (5 × 5 ml). The combined filtrates were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (50–70% diethyl ether in light petroleum) yielded *cyclohexene* **25** (6 mg, 16%) and (±)-1,2-*cis*-2,3-*cis*-1,2-diacetoxy-3,4-epoxycyclohexane **26** (25 mg, 82%).

(±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-Triacetoxy-5-iodocyclohexan-4-ol 28, (±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-triacetoxy-4-iodocyclohexan-5-ol 29 and (±)-1,2-*cis*-2,3-*cis*-3,4-*trans*-4,5-*trans*-1,2,3-triacetoxy-4-iodocyclohexan-5-ol 30

To a solution of (±)-1,2-*cis*-2,3-*cis*-1,2,3-triacetoxycyclohex-4-ene **25** (360 mg, 1.405 mmol) in dichloromethane (10 ml) was added *N*-iodosuccinimide (632 mg, 2.810 mmol) and water (10 drops). The mixture was stirred at room temperature (2 days), washed with saturated aqueous sodium thiosulfate (5 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (50–70% diethyl ether in light petroleum; foil covered column) yielded *cyclohexene* **25** (30 mg, 8%) and *hydroxy iodides* **28** and **29** as an inseparable mixture and a colourless solid (296 mg, 53%); R_f 0.29 (75% diethyl ether in light petroleum); mp 141–143 °C; $\nu_{max}(CCl_4)/cm^{-1}$ 3582 (OH), 2981, 1755 (C=O); δ_H(270 MHz, $CDCl_3$) 1.71–1.81 (1H, m, H_{eq} of CH_2), 2.03, 2.09 and 2.16 (9H, 3 × s, 3 × CH_3), 2.36 (1H, d, *J* 2.9, OH), 2.39–2.48 (1H, m, H_{ax} of CH_2), 4.23–4.35 (2H, m, CHOH and CHI), 5.14 [1H, m, CH(OAc)CH(OAc)CH(OAc)], 5.41–5.45 [1H, m, CH_2CH(OAc)], 5.49–5.51 [1H, m, CH_2CH(OAc)CH(OAc)CH(OAc)]; *m*/*z* (EI) 400 (M^+, 1.2%), 340 (1.2), 273 (24.7), 213 (80.7), 110 (100.0) (Found 400.0048. $C_{12}H_{17}IO_7$ requires 400.0019). Also isolated was *hydroxy iodide* **30** as a colourless oil (37 mg, 7%); R_f 0.40 (75% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 3582 (OH), 2955, 1760 (C=O); δ_H(270 MHz, $CDCl_3$) 1.87–2.01 (1H, m, H_{eq} of CH_2), 2.02, 2.09 and 2.16 (9H, 3 × s, 3 × CH_3), 2.18–2.23 (1H, m, H_{ax} of CH_2), 2.70 (1H, d, *J* 2.4, OH), 3.86–3.97 (1H, m, CHOH), 4.18 (1H, dd, 11.5, 10.3, CHI), 4.98 [1H, ddd, *J* 12.6, 4.6, 2.7, CH_2CH(OAc)], 5.08 [1H, dd, *J* 11.7, 2.7, CH(OAc)CHI], 5.40 [1H, ddd, *J* 2.6, 2.6, 1.5, CH_2CH(OAc)CH(OAc)]; δ_C(67.5 MHz, $CDCl_3$) 169.8 (CO), 169.7 (CO), 169.3 (CO), 72.1 (CH), 70.8 (CH), 68.8 (CH), 66.8 (CH), 37.8 (CH), 32.3 (CH_2), 22.6 (CH_3), 20.8 (CH_3), 20.7 (CH_3); *m*/*z* (EI) 273 [$(M - I)^+$, 6.2%], 153 (1.6), 110 (7.1) [Found 273.0961. $C_{12}H_{17}O_7$ $(M - I)^+$ requires 273.0974].

(±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3,4-Tetraacetoxy-5-iodocyclohexane 31 and (±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3,5-tetraacetoxy-4-iodocyclohexane 32

To a solution of a 40:60 mixture of (±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-triacetoxy-5-iodocyclohexan-4-ol **28** and (±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3-triacetoxy-4-iodocyclohexan-5-ol **29** (263 mg, 0.657 mmol) in pyridine (5 ml) was added acetic anhydride (0.07 ml, 0.740 mmol) and DMAP (10 mg). The mixture was stirred at room temperature (18 h), diluted with ethyl acetate (20 ml), washed with saturated aqueous copper(II) sulfate (2 × 10 ml), water (10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (60% diethyl ether in light petroleum) yielded *tetraacetates* **31** and **32** as a mixture and a colourless solid (279 mg, 93%); R_f 0.24 (50% diethyl ether in light petroleum); mp 115–119 °C (Found: C, 38.31; H, 4.52; I, 29.01. $C_{14}H_{19}IO_8$ requires C, 38.02; H, 4.33; I, 28.70%); $\nu_{max}(CCl_4)/cm^{-1}$ 1760 (C=O); δ_H(270 MHz, $CDCl_3$) 1.78–1.89 (1H, m, H_{eq} of CH_2), 2.08, 2.09, 2.12 and 2.15 (12H, 4 × s, 4 × CH_3), 2.43–2.53 (1H, m, H_{ax} of CH_2), 4.32 (0.7H, dd, *J* 7.9, 4.0, CHI of **31**), 4.44 (0.3H, ddd, *J* 10.6, 10.1, 4.0, CHI of **32**), 5.20–5.49 [4H, m, 4 × CH(OAc)]; *m*/*z* (EI) 323 (0.8%), 315 [$(M - I)^+$, 43.3], 213 (28.1), 153 (63.8), 111 (82.3) [Found 315.1090. $C_{14}H_{19}O_8$ $(M - I)^+$ requires 315.1080].

(±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-1,2,3,4-Tetraacetoxycyclohex-5-ene 22 (conduritol D tetraacetate)[8]

To a solution of a 40:60 mixture of **31** and **32** (150 mg, 0.339 mmol) in toluene (10 ml) was added DBU (0.10 ml, 0.669 mmol). The mixture was heated to reflux (4 h), then cooled and dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (60% diethyl ether in petroleum ether) yielded the following, in order of elution.

1,3-Diacetoxybenzene. Colourless oil (39 mg, 59%); R_f 0.78 (50% diethyl ether in light petroleum); $\nu_{max}(CCl_4)/cm^{-1}$ 1780 (C=O), 1569, 1439, 1369; δ_H(270 MHz, $CDCl_3$) 2.28 (6H, 2 × s, 2 × CH_3), 7.15–7.26 (4H, m, aromatic H); *m*/*z* (CI) 195 (MH^+, 5.1%), 153 (100.0) [Found 195.0658. $C_{10}H_{11}O_4$. (MH^+) requires 195.0657].

(±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3,4-Tetraacetoxy-5-iodocyclohexane 31. Unreacted, as a colourless solid (18 mg, 12%); R_f 0.51 (50% diethyl ether in light petroleum); mp 133–134 °C (corrected); $\nu_{max}(CCl_4)/cm^{-1}$ 2931, 1754 (C=O), 1220; δ_H(270 MHz, $CDCl_3$) 2.02, 2.088, 2.094 and 2.12 (12H, 4 × s, 4 × CH_3), 2.25–2.31 (1H, m, 1H of CH_2), 2.60–2.66 (1H, m, 1H of CH_2), 4.44 (1H, ddd, *J* 10.6, 10.1, 4.0, CHI), 5.06–5.12 [2H, m, CHICH(OAc) and CH_2CH(OAc)CH(OAc)], 5.19–5.23 [1H, m, CH_2CH(OAc)], 5.51 [1H, ddd, *J* 3.3, 2.9, 0.9, CHICH-(OAc)CH(OAc)]; δ_C(75 MHz, $CDCl_3$) 169.8 (CO), 169.7 (CO), 169.6 (CO), 169.3 (CO), 73.6 (CH), 68.5 (2 × CH), 68.4 (CH), 36.1 (CH), 20.9 (CH_3), 20.7 (2 × CH_3), 20.6 (CH_3), 18.2 (CH_2); *m*/*z* (CI) 383 (M − OAc, 100.0%), 341 (20.0), 315 (M − I, 16.0), 281 (18.0), 221 (28.0) [Found 315.1069. $C_{14}H_{19}O_8$. $(M - I)^+$ requires 315.1080].

Conduritol D tetraacetate 22.[8] Colourless solid (18 mg, 26%); R_f 0.20 (50% diethyl ether in light petroleum); mp 103–104 °C (lit.,[8] 103–103.5 °C); $\nu_{max}(CCl_4)/cm^{-1}$ 1752 (C=O), 1368, 1264, 1227; δ_H(270 MHz, $CDCl_3$) 2.083 and 2.088 (12H, 2 × s, 4 × CH_3), 5.37 [2H, d, *J* 5.1, CH(OAc)CH(OAc)CH(OAc)-CH(OAc)], 5.58 [2H, dd, *J* 5.1, 1.5, CH(OAc)CH(OAc)-CH(OAc)CH(OAc)], 5.89 (2H, d, *J* 1.3, CH=CH); δ_C(75 MHz, $CDCl_3$) 170.0 (2 × CO), 127.5 (CH), 66.9 (CH), 65.7 (CH), 20.80 (CH_3), 20.7 (CH_3); *m*/*z* (CI) 315 (MH^+, 2.2%), 255 (76.1), 153 (89.9), 111 (100.0) [Found 255.0866. $C_{12}H_{15}O_6$. $(M - OAc)^+$ requires 255.0869].

(±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-1,2,3,4-Tetraacetoxycyclohex-5-ene 22 (conduritol D tetraacetate)[8]

To a solution of (±)-1,2-*cis*-2,3-*cis*-3,4-*cis*-4,5-*trans*-1,2,3,4-tetraacetoxy-5-iodocyclohexane **31** (15 mg, 0.034 mmol) in toluene (1 ml) was added DBU (0.01 ml, 0.067 mmol). The mixture was heated to reflux (4 h), then cooled and dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude product by flash column chromatography (60% diethyl ether in light petroleum) yielded conduritol D tetraacetate **22**[8] (9.7 mg, 90%). Spectral properties were as reported previously.

Acknowledgements

We acknowledge the financial support of the Nuffield Foundation, the EPSRC (quota awards to A. F. H. and J. R. K.) and Zeneca (award from the Strategic Research Fund to J. B. S.).

References

1 For Part 2, see ref. 5.
2 For pertinent reviews, see: L. A. Campbell and T. Kodadek, *J. Mol. Cat.*, *A*, 1996, **113**, 293; S. Pedragosamoreau, A. Archelas and R. Furstoss, *Bull. Soc. Chim. Fr.*, 1995, **132**, 769; T. Katsuki, *Coord. Chem. Rev.*, 1995, **140**, 189; D. J. Berrisford, C. Bolm, K. B. Sharpless, *Angew. Chem.*, *Int. Ed. Engl.*, 1995, **34**, 1059.
3 For pertinent reviews, see: K. B. Sharpless, *Tetrahedron*, 1994, **50**, 4235; H. C. Kolb, M. S. Vannieuwenhze, K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483; B. B. Lohray, *Tetrahedron*: *Asymmetry*, 1992, **3**, 1317.
4 M. Balci, Y. Sütbeyaz and H. Seçan, *Tetrahedron*, 1990, **46**, 3715.
5 Preliminary communication: J. R. Knight and J. B. Sweeney, *Tetrahedron Lett.*, 1996, **37**, 6579.
6 A. J. Pearson and S.-Y. Hsu, *J. Org. Chem.*, 1986, **51**, 2505.
7 A. Ouédraogo, M. T. P. Viet, J. K. Saunders, J. Lessard, *Can. J. Chem.*, 1987, **65**, 1761.
8 R. Schwesinger and H. Schlemper, *Angew. Chem.*, *Int. Ed. Engl.*, 1987, **26**, 1167.
9 R. Criegee and P. Becher, *Chem. Ber.*, 1957, **90**, 2516.
10 A. Kötz and K. Richter, *J. Prakt. Chem.*, 1925, **111**, 373.
11 P. Chamberlain, M. C. Roberts and G. H. Whitham, *J. Chem. Soc.* (*B*), 1970, 1374.
12 I. V. Machinskaya and V. A. Barkhash, *Zh. Obshch. Khim.*, 1956, **26**, 848.

Paper 7/09056K
Received 17*th December* 1997
Accepted 19*th December* 1997