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Reactions of enantiopure cyclic diols with sulfuryl chloride†

Derek R. Boyd, Narain D. Sharma, Magdalena Kaik, Peter B. A. M^cIntyre, John F. Malone and Paul J. Stevenson*

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Monocyclic allylic *cis*-1,2-diols reacted with sulfuryl chloride at 0 °C in a regio- and stereo-selective manner to give 2-chloro-1-sulfochloridates, which were hydrolysed to yield the corresponding *trans*-1,2-chlorohydrins. At −78 °C, with very slow addition of sulfuryl chloride, cyclic sulfates were formed in good yields, proved to be very reactive with nucleophiles and rapidly decomposed on attempted storage. Reaction of a cyclic sulfate with sodium azide yielded a *trans*-azidohydrin without evidence of allylic rearrangement occurring. An enantiopure bicyclic *cis*-1,2-diol reacted with sulfuryl chloride to give, exclusively, a *trans*-1,2-dichloride enantiomer with retention of configuration at the benzylic centre and inversion at the non-benzylic centre; a mechanism is presented to rationalise the observation.

Introduction

Enantiopure *cis*-dihydrodiol bacterial metabolites, derived from monosubstituted halobenzenes, are useful intermediates in organic synthesis.[1] Their unsubstituted alkene bonds can be chemoselectively functionalised and the halogen atom of the vinyl halide replaced with a wide range of additional functionality.[2] This versatile chemistry makes these substrates ideal for the synthesis of complex cyclohexane-based natural products.

Since the advent of the Sharpless asymmetric dihydroxylation reaction,[3] resulting in the ready availability of a wide range of chiral 1,2-diols, there has been increased activity in utilizing them as key chiral intermediates in organic synthesis. This has led to a resurgence of interest in cyclic sulfate derivatives of 1,2-diols,[4] as electrophiles for nucleophilic substitution reactions. Cyclic sulfates are generally more reactive towards nucleophilic attack than the corresponding epoxides. We were particularly interested in using the previously unreported cyclic sulfate esters of *cis*-tetrahydrodiol derivatives of aromatic compounds. The *cis*-1,2-dihydrodiol precursors are available in multi-gram quantities from our fermentation reactions.

Many reports on the preparation and use of sulfinate esters, derived from cyclic allylic diols, have appeared in the chemical literature.[5,6] These electrophiles are suitably activated to react, regioselectively, with nucleophiles at the allylic position and this methodology has been used in the synthesis of Tamiflu.[5,7] To date, only one example of a well characterised cyclic sulfate ester of a cyclic diol, having an allylic hydroxyl group, has been reported. However, this was prepared indirectly by the oxidation of a cyclic sulfinate ester followed by the subsequent introduction of unsaturation through dehydration.[8]

A number of methods are available for preparing cyclic sulfate esters and the subject has been reviewed.[9] The most direct route involves reaction of the *vic*-diol with sulfuryl chloride or 1,1′-sulfonylbis(1*H*-imidazole). This procedure works well with: (i) 1,2-diols containing electron withdrawing groups[10] (ii) cyclic diols[11] and (iii) some acyclic 1,2-diols. Recently, ionic liquids have been employed as solvents for such reactions, with the advantage that sulfuryl chloride is hydrolytically stable in this medium.[12] These direct methods are however not generally applicable and complex mixtures may result from simple alkyl substituted acyclic 1,2-diols. The problem has been attributed to: (a) the intrinsic ring strain of cyclic sulfates slowing down the final cyclisation, and (b) the innate chlorinating power of sulfuryl chloride. A more general approach involves assembling the comparatively less strained cyclic sulfinate esters (cyclic sulfites), derived from thionyl chloride, followed by their oxidation to yield cyclic sulfate esters. The Sharpless modification of this procedure, which demonstrated that the sulfinate esters could be oxidised to the sulfate esters, using sodium periodate and a catalytic quantity of ruthenium salts, led to a major advance in the routine use of cyclic sulfate esters in organic synthesis.[13]

School of Chemistry and Chemical Engineering, Queens University, Belfast, N Ireland BT9 5AG, UK. E-mail: p.stevenson@qub.ac.uk; Fax: +44 (0)289097 4687; Tel: +44 (0)2890974426

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Results and discussion

We have recently reported that the unsubstituted alkene bond in *cis*-1,2-dihydrodiols, derived from monosubstituted benzenes, can be chemoselectively reduced to give *cis*-tetrahydrodiols **1a–f**, Table 1.[14] Due to the enhanced stability of these derivatives, over the corresponding *cis*-dihydrodiols, they are ideal precursors for enantioselective synthesis. To explore the chemistry further by chemoselective activation of the allylic hydroxyl group, substitution reactions at the allylic position were carried out and synthesis of previously unreported reactive cyclic sulfate esters seemed to be the obvious choice.

Products obtained from selected reactions of *cis*-tetrahydrodiols **1a–f** and **6** with thionyl and sulfuryl chlorides, under various conditions (A–C), are presented in Scheme 1 and Table 1. Reaction of diol **1a** with thionyl chloride gave cyclic sulfite **2a** as a mixture (5 : 1) of diastereoisomers in 89% yield. Attempted oxidation of diastereoisomers **2a** to give cyclic sulfate ester **3a**, using the Sharpless procedure,[13] was unsuccessful. Only 20% of the starting material, containing none of the minor diastereoisomer, was recovered. It is known that alkenes are susceptible to oxidation under these conditions, and thus it is likely that the failure of this reaction was due to the formation of polar products, which were lost on aqueous workup. Problems in carrying out this type of oxidation, in the presence of alkene functionality, have been reported.[15,16] Our attention was next focussed on the direct formation of cyclic sulfate esters **3** using sulfuryl chloride.

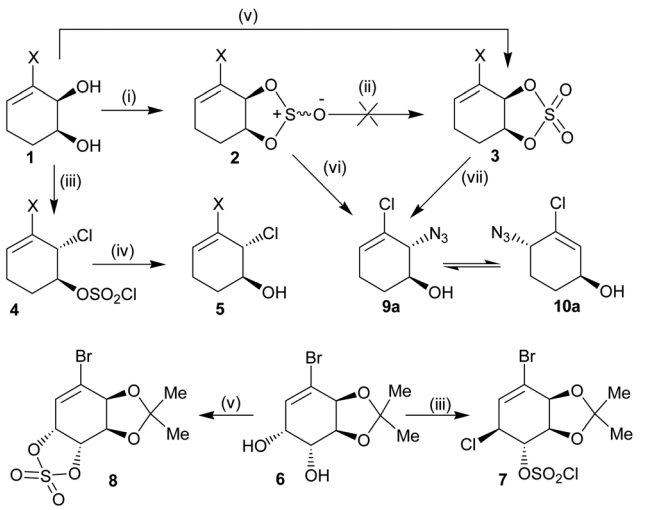
Reaction of *cis*-diols **1a–c** and **6** with excess sulfuryl chloride at 0 °C, in the presence of triethylamine, gave 2-chloro-1-sulfochloridates **4a–c**, and **7** (Table 1, conditions B). The triethylamine Lewis salt of sulfur trioxide, present in the crude mixture after aqueous workup, was removed by crystallisation from hexane. Surprisingly, significant proportions of 2-chloro-1-sulfochloridates **4a–c** and sulfochloridate **7** survived the aqueous work up, though hydrolysis might have been a contributing factor to the modest isolated yields (45–55%).

Determination of the molecular formulae of compounds **4a–c**, initially, proved difficult as these compounds did not provide meaningful mass spectroscopic data. However, the ^{13}C-NMR spectrum of compound **4a** clearly showed a signal at δ 55.6 ppm that was entirely consistent with the replacement of a hydroxyl group with a chlorine atom at the C-2 position. The huge increase in chemical shift of the homoallylic H-1 proton signal from δ 4.0 to δ 5.37 strongly suggested that the other hydroxyl group had been converted to an ester. A single crystal X-ray structure of compound **4c** (Fig. 1) established the gross structure as a 3-iodo-2-chloro-1-sulfochloridate and confirmed that the chlorine atom was introduced at the C-2 position with clean inversion of configuration. In the solid state, the molecule adopted a conformation in which the chlorine atom and chlorosulfonyl ester group were *trans*-diaxial. The same conformation was also prevalent in $CDCl_3$ solution,

Table 1 Reactions of *cis*-tetrahydrodiols **1** and **6** with $SOCl_2$ or SO_2Cl_2 to yield products **2–5**, **7** and **8**

		Conditions		
	Substituent	A	B	C
cis-Diol	X	Yield (%)	Yield (%)	Yield (%)
1a	Cl	**2a** (89)	**4a** (45)	**3a** (70)
1b	Br	na	**4b** (51)	**3b** (72)
1c	I	na	**4c** (55)	na
1d	CF_3	na	na	**3d** (61)
1e	CO_2Me	na	na	**3e** (34), **5e** (14)
1f	Ph	na	na	**5f** (29)[a]
6	Br, acetonide	na	**7** (46)	**8** (73)

Conditions A: $SOCl_2$, CH_2Cl_2, 0 °C; B: SO_2Cl_2, Et_3N, CH_2Cl_2, 0 °C; C: SO_2Cl_2, Et_3N, DMAP, CH_2Cl_2, −78 °C. [a] A sample of **5f**, as a 7 : 1 mixture of *trans* : *cis* diastereoisomers (29%) was isolated but the mixture was not characterised. na – not attempted.



Scheme 1 Reagents and conditions: (i) C_6H_5N, $SOCl_2$, CH_2Cl_2, 0 °C, 30 min; (ii) $RuCl_3$, $NaIO_4$, CH_3CN–H_2O, 0 °C, 1 h; (iii) SO_2Cl_2, Et_3N, CH_2Cl_2, 0 °C → RT, 12 h; (iv) NaI, MeOH–H_2O, 3.6 : 1, 25 °C, 5 min; (v) SO_2Cl_2, DMAP, CH_2Cl_2, −78 °C, 1.5 h; (vi) NaN_3, DMSO, 60 °C, 4 h, 93%; (vii) NaN_3, $(CH_3)_2CO$–H_2O (6 : 1), 0 °C → RT, 68%.

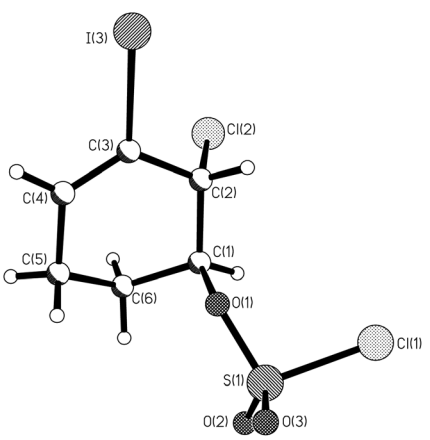


Fig. 1 X-ray crystal structure of (1*S*,2*R*)-3-iodo-2-chlorocyclohex-3-enyl sulfochloridate **4c**.

since proton H-2 appeared as a doublet, J 2.3 Hz, in the ^{1}H-NMR spectrum, indicating a predominant conformer with a diequatorial arrangement of the two adjacent hydrogen atoms. The allylic chloro substituent adopted a pseudoaxial position, presumably to minimise allylic 1,2-strain with the iodine atom and increase hyperconjugation of the polar bond with the alkene.

Racemic compounds, containing a chlorine atom and a sulfonyl chloride ester on adjacent carbons, have been prepared by the addition of chlorine chlorosulfate to alkenes at low temperature.[17] Chiral compounds of this nature, can also be prepared regioselectively, by the reaction of sulfuryl chloride with vinyl epoxides.[18] In carbohydrate chemistry, it is common to observe that, on reaction with sulfuryl chloride, chlorination occurs at the activated anomeric position, whilst other secondary alcohols are normally converted to chlorosulfonate esters.[19] In the case of diols **1a–c**, the more reactive pseudoequatorial homoallylic hydroxyl group on C-1 is likely to form a monochlorosulfonyl ester first. If the cyclisation to cyclic sulfate ester **3** is slow, then a second chlorosulfonyl ester may form through reaction with the allylic hydroxyl group at C-2. The pseudoaxial allylic chlorosulfonate ester is sufficiently activated to facilitate rapid nucleophilic attack of chloride ion and conversion into the allylic chloride, with inversion of configuration, giving rise to *trans* products, **4a–c** and **7**. When stored at room temperature for over a month, compounds **4a–c** and **7** were found to be stable, with no noticeable decomposition.

trans-2-Chloro-1-chlorosulfonate esters **4a** and **4b** were converted to *trans*-chlorohydrins **5a** and **5b** in 81% and 82% yields, respectively, using a standard procedure involving sodium iodide in aqueous methanol.[20] This two-step procedure provides a cheap alternative to the Mattock reagent,[21] for regio- and stereo-selectively converting cyclic allylic *cis*-diols **1a** and **1b** to *trans*-chlorohydrins **5a** and **5b** respectively (Scheme 1).

Reaction of *cis*-diols **1a,b,d,e** and **6**, at low temperature and high dilution, with very slow addition of sulfuryl chloride in the presence of DMAP (Table 1, conditions C, conditions used by Myers[15]), gave the desired cyclic sulfates **3a**, **3b**, **3d**, **3e** and **8** in moderate to good yields (34–73%). These conditions were essential to achieve the desired chemoselectivity and to favour intramolecular ring closure of the intermediate mono chlorosulfate ester and formation of the cyclic sulfate ester over other processes. Low temperature single crystal X-ray crystallography established the structure of cyclic sulfate **3a** (Fig. 2). In the case of *cis*-diol **1e** the modified conditions gave a 2.5 : 1 ratio of cyclic sulfate **3e** to chlorohydrin **5e** and similarly diol **1f** gave a modest yield (29%) of impure chlorohydrin **5f** but no cyclic sulfate **3f** indicating that these reactions were very substrate dependant. The cyclic allylic sulfate esters **3a**, **3b**, **3d**, **3e** and **8** were found to partially decompose at room temperature after 24 h.

We have recently reported[22] the synthesis of (1*S*,2*R*)-*trans*-1,2-azidohydrin **9a** as the predominant product from a ring opening reaction of the corresponding epoxide, and have demonstrated that this equilibrates with the isomeric

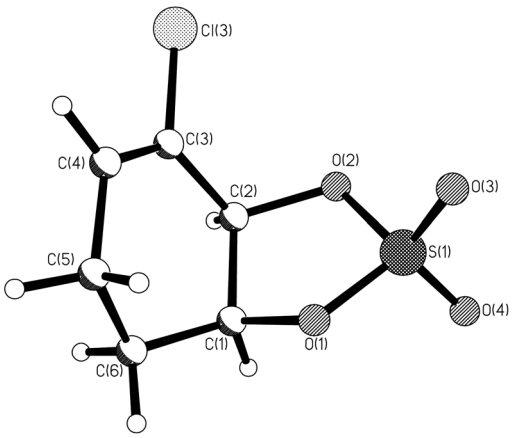
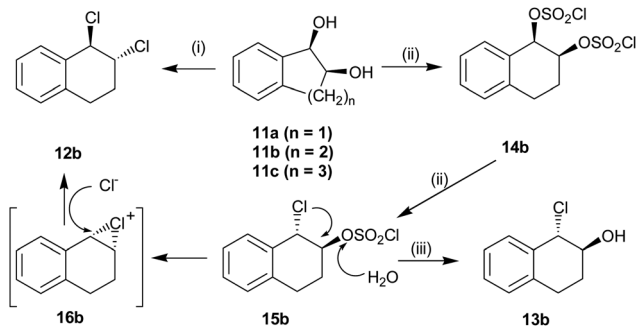


Fig. 2 X-ray crystal structure of (1*S*,2*S*)-3-chlorocyclohex-3-ene-1,2-cyclic sulfate **3a**.

azidohydrin **10a**, *via* an allyl azide [3,3] sigmatropic rearrangement on gentle heating, to give a 4 : 1 mixture of isomers **9a** : **10a**. Cyclic sulfate **3a** reacted with sodium azide, at room temperature, to give, exclusively, azidohydrin **9a** without evidence of azidohydrin isomer **10a**. The corresponding less reactive cyclic sulfite **2a** did not react with sodium azide under these conditions. However, on heating, with sodium azide in DMSO, cyclic sulfite **2a** formed azidohydrin **9a** together with the rearranged isomer **10a**. It is, therefore, advantageous, in some cases, to use the more reactive cyclic sulfate **3** rather than cyclic sulfite **2**.

A brief study of benzo-fused cyclic *cis*-diols **11a–c**, in which one of the hydroxyl groups was benzylic (Scheme 2), available as single enantiomer metabolites from earlier biotransformation studies, was undertaken. Reaction of 2,3-dihydro-1*H*-indene-1,2-diol **11a**, and 6,7-dihydro-5*H*-benzo[7]annulene **11c**, with sulfuryl chloride at 0 °C, gave complex mixtures of products whose separation was not attempted. In marked contrast, reaction of (1*R*,2*S*)-naphthalene *cis*-1,2,3,4-tetrahydrodiol **11b**,[23] under the same reaction conditions, proceeded smoothly and cleanly, to give dichloride **12b** in excellent yield. Analysis of the ^{1}H-NMR spectrum gave the coupling constant between H-1 and H-2, (J 2 Hz). This indicated that there was a



Scheme 2 Reagents and conditions: (i) SO_2Cl_2, Et_3N, CH_2Cl_2, 0 °C → RT 12 h; (ii) SO_2Cl_2, DMAP, Et_3N, CH_2Cl_2, −78 °C, 1.5 h; (iii) H_2O.

strong preference, in solution, for a conformer in which these two hydrogens were *trans*-diequatorial, confirming the structure of diastereoisomer **12b** as the *trans*-1,2-dichloride. Coupling constants of similar magnitude have been reported for the *trans*-1,2-diazides in the tetrahydronaphthalene series.[24] Surprisingly, one of the chlorine atoms was introduced with retention, whilst the other with inversion of configuration.

trans-Dichloride **12b** was found to be optically active but the magnitude of optical rotation ($[\alpha]_D$ +12.3), in comparison with the literature values,[25,26] suggested that the compound was of relatively low enantiopurity (*ca*. 20% ee). Chiral stationary phase HPLC analysis (Chiralcel OD), however, showed a baseline separation of the enantiomers of racemic *trans*-dichloride **12b** and an early eluting single peak for (+)-*trans*-dichloride **12b**, derived from (1*R*,2*S*)-diol **11b**, establishing that it was a single enantiomer. ^{1}H-NMR spectroscopy proved that one chiral centre had inverted whilst the other had retained its stereochemistry on chlorination, but could not link these stereochemical events to a discrete chiral centre. X-ray crystallographic analysis, on a single crystal of (+)-dichloride **12b**, determined both its relative and absolute configurations (Fig. 3). It confirmed: (i) the *trans* diaxial stereochemistry of (+)-dichloride **12b** in the solid state and (ii) that chlorination at the benzylic position proceeded with retention of configuration and at the non-benzylic position with inversion of configuration to give the (1*R*,2*R*) enantiomer.

Since many reactions which proceed with retention of configuration involve a double inversion,[27] the cyclic chloronium ion **16b** has been presented as a likely intermediate (Scheme 2). Cyclic chloronium ions have previously been postulated, to explain counterintuitive stereoselectivity in ring opening reactions of ω-chloroepoxides.[28] Chlorination with inversion of configuration at the more reactive benzylic position in the postulated intermediate **14b**, would give the anticipated product **15b** as a precursor of the cyclic chloronium ion **16b**. Ring opening of intermediate **16b** with chloride ion at the reactive benzylic position would complete the double inversion and account for the experimentally observed stereochemistry. Nicolaou has demonstrated catalytic asymmetric addition of chlorine to allylic alcohols, where regioselectivity of chloronium ion ring opening is a prerequisite for good ee values[29] and Denmark has recently demonstrated that chiral chloronium ions, containing alkyl groups, are configurationally stable.[30] The generality of this novel dichlorination reaction remains to be fully evaluated, but it is significant that it failed with two (**11a** and **11c**) out of three bicyclic substrates.

Reaction of *cis*-tetrahydrodiol **11b**, under Myers' conditions,[15] failed to give any of the corresponding cyclic sulfate and only the *trans*-chlorohydrin **13b** was isolated (71% yield). In this example, it was likely that the cyclic sulfate was slow to form and both the hydroxyl groups became chlorosulfonated to yield intermediate **14b** which eventually led to the formation of chlorohydrin **13b**, on warming the reaction mixture to room temperature followed by its aqueous workup.

The relative stereochemistry of chlorohydrin **13b**, a known literature compound,[24] was determined as *trans*, by comparison of the NMR spectroscopic data. It is noteworthy that the coupling constant in *trans*-chlorohydrin **13b** was much larger ($J_{1,2}$ 6.9 Hz) than the corresponding coupling constant in *trans*-dichloride **10** ($J_{1,2}$ 2.2 Hz). This is consistent with the conformational heterogeneity in chlorohydrin **13b**, with two dominant conformers contributing to the observed coupling constant. It may be the result of an intramolecular hydrogen bond, helping to stabilise the conformer in which the hydroxyl and chloro groups are diequatorial. The absolute configuration of compound (−)-**13b** was assumed to be (1*S*,2*S*) on the basis of its formation from intermediate **15b** and is in accord with the literature assignment.[24]

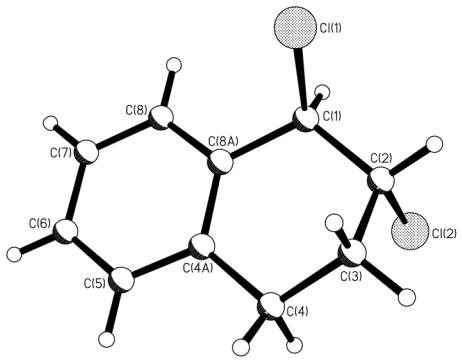


Fig. 3 X-ray crystal structure of (1*R*,2*R*)-1,2-dichloro-1,2,3,4-tetrahydronaphthalene **12b**.

Conclusion

It was demonstrated that the products, from reactions of chiral allyl- and benzyl-activated cyclic *cis*-diols with sulfuryl chloride, were dependent on both substrate structure and conditions. Up to four types of enantiopure products were identified from this reaction *i.e.* *trans*-chlorohydrin, *trans*-chloro-chlorosulfate ester, *cis*-cyclic sulfate ester and *trans*-dichloride. With monocyclic allylic diols, conditions were found that favoured either formation of the cyclic sulfate esters or chloro-chlorosulfate esters as precursors to *trans*-chlorohydrins. Cyclic sulfate esters and *trans*-chlorohydrins demonstrate stereo-complementarity, because the absolute configurations at the electrophilic allylic sites are opposite for each class of compound. It is noteworthy that reaction with sulfuryl chloride can yield either type of product, simply by modifying the reaction conditions. This is likely to enhance the importance of these species as intermediates in enantioselective synthesis.

Experimental

^{1}H and ^{13}C-NMR spectra were recorded on Bruker Avance 400, DPX-300 and DRX-500 instruments. Chemical shifts (δ) are reported in ppm relative to $SiMe_4$ and coupling constants (J)

are given in Hz. Mass spectra were run at 70 eV, on a VG Autospec mass spectrometer, using a heated inlet system. IR spectra were recorded on a Perkin-Elmer Model 983G instrument coupled to a Perkin-Elmer 3700 data station using potassium bromide (KBr) disks unless otherwise stated. Accurate molecular weights were determined by the peak matching method, with perfluorokerosene as the standard. Flash column chromatography and preparative layer chromatography (PLC) were performed on Merck Kieselgel type 60 (250–400 mesh) and $PF_{254/366}$ plates respectively. Merck Kieselgel type $60F_{254}$ analytical plates were employed for TLC. Diols **1a–f**,[14,31] **6**[32] and **11a–c**[23,33] were prepared by literature methods.

(3a*S*,7a*S*)-7-Chloro-3a,4,5,7a-tetrahydrobenzo[1.3.2]dioxathiol-2-oxide 2a

Thionyl chloride (3.24 g 27.2 mmol) was added dropwise to a stirred solution of diol **1a** (2.7 g, 18.2 mmol) and pyridine (2.6 g, 32.7 mmol) in DCM (100 mL) at −30 °C. The reaction mixture was allowed to warm to room temperature, water (100 mL) was added, the organic phase separated, washed with water (100 mL), dried ($MgSO_4$) and concentrated. The resulting crude yellow oil was purified by passing it through a pad of alumina and eluting with ethyl acetate–petroleum ether (1 : 1), to afford cyclic sulfite **2a** (3.15 g, 89%). Product **2a** was obtained as an oil consisting of an inseparable mixture (4 : 1) of two diastereoisomers, resulting from the newly generated chiral sulfur centre. HRMS (LC-TOFMS) (Found: $[M + 1]^+$ 194.9877. $C_6H_8ClO_3S$ requires 194.9877); *Major isomer*: ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H 6.18 (1 H, dd, *J* 4.9, 3.7, H-6), 5.21 (2 H, 2 × m, H-7a and H-3a), 2.32 (1 H, m, H-5), 2.18 (1 H, m, H-5′), 2.07–2.13 (2 H, 2 × m, H-4 and H-4′) and *Minor isomer*: 6.18 (1 H, m, H-6), 4.97 (1 H, bd, *J* 5.9 H-3a), 4.89 (1 H, td, *J* 5.9, 3.0, H-7a), 2.51 (1 H m, H-5), 2.03–2.40 (3 H, 3 × m, H-5′, H-3 and H-3′); *Major isomer*: ^{13}C-NMR ($CDCl_3$, 75 MHz) δ_C 131.45 (2C), 79.16, 77.96, 24.18, 21.84 and *Minor isomer*: 131.14, 127.25, 82.23, 80.05, 25.68, 21.80; ν_{max}/cm^{-1} (thin film) 1211.68 (S=O).

General procedure A for chloro sulfochloridate formation

Triethylamine (0.16 mL, 1.14 mmol) and sulfuryl chloride (0.09 mL, 1.14 mmol) were added to a solution of *cis*-diol **1** (0.57 mmol) in DCM (8 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The solution was diluted with DCM (5 mL), cooled to 0 °C and water (8 mL) was added. The DCM layer was separated and the remaining aqueous layer extracted with fresh DCM (2 × 5 mL). The combined organic extract was dried ($MgSO_4$) and the solvent removed to give a yellow oil. The oil was extracted with hexane (3 × 10 mL) and the extract evaporated at 40 °C, to give a concentrated solution, which was left for crystallisation to yield the title compound.

(1*S*,2*R*)-2,3-Dichlorocyclohex-3-enyl sulfochloridate 4a. General procedure A gave titled compound, yield: 45%; m. p. 49–50 °C (from hexane); R_f 0.9, (Et_2O–hexane, 1 : 1); $[\alpha]_D$ +153.3 (*c* 0.6, $CHCl_3$); (Found: C, 27.6; H, 2.7; S, 11.7. $C_6H_7Cl_3O_3S$ requires C, 27.1; H, 2.7; S, 12.1%); ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 2.50–2.22 (4 H, m, H-5, H-5, H-6, H-6), 4.58 (1 H, bm, H-2), 5.37 (1 H, dt, *J* 4.5, 2.4, H-1), 6.15 (1 H, dd, *J* 5.0, 2.9, H-4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 20.29, 21.27, 55.64, 85.91, 127.16, 129.76; ν_{max}/cm^{-1} (KBr) 3061.9, 2932.1, 1649.7, 1404.2, 1215.6, 1191.9, 934.9, 919.7.

(1*S*,2*R*)-3-Bromo-2-chlorocyclohex-3-enyl sulfochloridate 4b. General procedure A gave titled compound, yield: 51%; m. p. 68–70 °C (from hexane); R_f 0.82 (Et_2O–hexane, 1 : 1); $[\alpha]_D$ +119 (*c* 1.07, $CHCl_3$); (Found: C, 23.9; H, 2.3; S, 10.1. $C_6H_7BrCl_2O_3S$ requires C, 23.3; H, 2.3; S, 10.3%); ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 2.48–2.24 (4 H, m, H-5, H-5′ H-6, H-6′), 4.65 (1 H, bm, H-2), 5.37 (1 H, dt, *J* 4.4, 2.3, H-1), 6.37 (1 H, dd, *J* 5.2, 2.7, H-4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 20.31, 22.77, 57.47, 85.99, 116.72, 134.24; LRMS (EI) 310 (M^+, 1%), 194 (10), 159 (95), 157 (100), 113 (30); ν_{max}/cm^{-1} (KBr) 588.8, 737.3, 759.7, 918.8, 1190.6, 1214.4, 1402.3, 1639.4, 2361.9.

(1*S*,2*R*)-3-Iodo-2-chlorocyclohex-3-enyl sulfochloridate 4c. General procedure A gave titled compound yield 55%; m. p. 84–86 °C (from hexane); $[\alpha]_D$ +82.2 (*c* 1.07, $CHCl_3$); (Found: C, 20.8; H, 2.2; S, 8.5. $C_6H_7Cl_2IO_3S$ requires C, 20.2; H, 2.0; S, 9.0%); ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H 6.63 (1 H, dd, *J* 4.9, 2.8, H-4), 5.35 (1 H, dt, *J* 4.9, 2.8, H-1), 4.66 (1 H, bs, H-1), 2.52–2.28 (4 H, m, H-5, H-5′ H-6, H-6′); ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C 142.20, 90.11, 85.25, 60.48, 24.12, 19.83; ν_{max}/cm^{-1} (KBr) 2361.0, 1724.6, 1624.8, 1400.1, 1187.9, 1211.0, 915.8, 727.4, 591.0.

Crystal data for **4c**: $C_6H_7Cl_2IO_3S$, M = 357.0, orthorhombic, a = 5.936(1), b = 8.960(3), c = 20.683(6) Å, U = 1100.0(5) Å^3, T = 293(2) K, space group $P2_12_12_1$ (no. 19), Mo-Kα radiation, λ = 0.71073 Å, Z = 4, $F(000)$ = 680, D_x = 2.156 g cm^{-3}, μ = 3.560 mm^{-1}, Bruker P4 diffractometer, ω scans, 5.0° < 2θ < 55.0°, measured/independent reflections: 2047/1868, R_{int} = 0.094, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.072 for 1525 data with F_o > 4$\sigma(F_o)$, 119 parameters, ωR_2 = 0.198 (all data), GoF = 1.07, CCDC 971376. The absolute configuration is established as (1*S*,2*R*) from the anomalous scattering arising from the iodine atom; Flack parameter x = −0.04(9).

(3a*R*,4*S*,5*S*,7a*S*)-7-Bromo-5-chloro-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[*d*][1,3]dioxol-4-yl sulfochloridate 7. General procedure A gave titled compound, was obtained by as colourless plates, yield: 46%; m. p. 56–58 °C (Et_2O–hexane); $[\alpha]_D$ +20.0 (*c* 1.1, $CHCl_3$); HRMS (LC-TOFMS) (Found: $[M + H]^+$ 380.8957. $C_9H_{12}O_5Cl_2BrS$ requires 380.8960); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 1.45 (3 H, s, CH_3), 1.58 (3 H, s, CH_3), 4.44 (1 H, dd, *J* 7.3, 5.9, H-3a), 4.57 (1 H, ddd, *J* 6.8, 3.2, 1.1, H-5), 4.75 (1 H, d, *J* 5.9, H-7a), 5.17 (1 H, dd, *J* 7.2, 7.2, H-4), 6.28 (1H, d, *J* 3.2, H-6); ^{13}C NMR (300 MHz, $CDCl_3$) δ_C 26.3, 27.7, 53.1, 74.8, 76.6, 87.1, 112.7, 122.4, 130.1; ν_{max}/cm^{-1} (KBr) 2994, 2941, 1644, 1628, 1411, 1249, 1185, 981.

(1*S*,2*R*)-2,3-Dichlorocyclohex-3-enol 5a. A solution of sodium iodide (10%, 0.34 g, 2.26 mmol) in MeOH–H_2O (1 : 1,

3 mL) was added to chloro-chlorosulfate **4a** (0.65 mmol) in MeOH (4 mL). After stirring the mixture for 5 minutes, sodium thiosulfate (0.56 g, 2.26 mmol) was added to trap the evolved iodine. The reaction mixture was neutralised with sodium bicarbonate (0.19 g, 2.26 mmol), most of the methanol was removed under reduced pressure, and the remaining solution diluted with water (5 mL). The aqueous mixture was extracted with EtOAc (3 × 5 mL), the extract was dried ($MgSO_4$) and concentrated under reduced pressure. The crude yellow oil obtained was purified by PLC (Et_2O–hexane, 1 : 1), to give the title compound **5a** as a colourless oil. Yield: 82%; R_f 0.1 (EtOAc–hexane, 1 : 9); $[\alpha]_D$ + 87.0 (*c* 0.5, $CHCl_3$); HRMS (EI) (Found: $[M + H]^+$ 167.0021. $C_6H_8Cl_2O^+$ requires 167.0025); ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H 1.78 (1 H, m, H-6), 2.08 (1 H, m, H-6′), 2.20 (1 H, m, H-5), 2.26 (1 H, m, H-5′), 4.23 (1 H, dtd, *J* 6.6, 4.2, 2.5 H-1), 4.30 (1 H, d, *J* 4.2, H-2), 6.06 (1 H, t, *J* 4.2, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 22.2, 24.0, 62.4, 72.4, 128.9, 129.6; ν_{max}/cm^{-1} (thin film) 3377, 2935, 1646, 1062, 836, 769.

(1*S*,2*R*)-3-Bromo-2-chlorocyclohex-3-enol 5b. It was obtained following the procedure for the preparation of compound **5a**, substituting chloro-chlorosulfate **4b** (0.20 g, 0.65 mmol). Purification by PLC (Et_2O–hexane, 1 : 1) gave the title compound **5b** as a colourless oil. Yield: 0.11 g, 81%; R_f 0.45 (Et_2O–hexane, 1 : 1); HRMS (EI) (Found: $[M - OH]^+$ 194.9414. $C_6H_7BrCl^+$ requires 194.9402); ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H 1.78 (1 H, m, H-6), 2.07 (1 H, m, H-6′), 2.19 (1 H, m, H-5), 2.33 (1 H, m, H-5′), 4.21 (1 H, dt, *J* 6.0, 2.8, H-1), 4.38 (1 H, d, *J* 3.2, H-2), 6.29 (1 H, t, *J* 4.2, H-4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 20.7, 23.8, 64.2, 72.4, 119.5, 134.3.

General procedure B for cyclic sulfate formation

4-(Dimethylamino)pyridine (25 mg, 0.21 mmol) was added to a stirred solution of diol **1** (0.52 mmol) in DCM (10 mL) and the resulting solution cooled to −78 °C. Triethylamine (0.29 mL, 2.06 mmol) was added to the cooled solution and the stirring continued for 10 min. A solution of sulfuryl chloride (0.08 mL 0.98 mmol) in DCM (10 mL) was then slowly added to the cold reaction mixture *via* a glass syringe over a period of 1 h. After stirring at −78 °C for 30 min, the solution was diluted with DCM (10 mL) and a saturated solution (10 mL) of sodium bicarbonate was added to the reaction mixture. The organic layer was separated, washed, successively, with brine (10 mL) and water (10 mL), dried (Na_2SO_4) and concentrated. The crude product obtained was purified either by crystallisation or chromatography.

(1*S*,2*S*)-3-Chlorocyclohex-3-ene-1,2-cyclic sulfate 3a. Using general procedure B, diol **1a** gave a crude product, which was purified by PLC and then crystallised from Et_2O–hexane to give cyclic sulfate **3a** as colourless needles. Yield: 70%; m. p. 71–72 °C; R_f 0.4 (Et_2O–hexane, 1 : 1); $[\alpha]_D$ +106.0 (*c* 0.73, $CHCl_3$); (Found: C, 34.4; H, 2.8. $C_6H_7ClO_4S$ requires C, 34.2; H, 3.3%). HRMS (LC-TOFMS) (Found: $[M + NH_4]^+$ 228.0087. $C_6H_{11}ClNO_4S$ requires 228.0092); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.03 (1 H, m, H-6), 2.30 (2 H, m, H-5, H-6′), 2.50 (1 H, m, H-5′), 5.23 (1 H, d, *J* 5.8, H-2), 5.26 (1 H, td, *J* 5.8, 2.9, H-1), 6.39 (1 H, dd, *J* 5.3, 3.4, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 21.09, 24.04, 79.94, 80.48, 124.90, 133.49; ν_{max}/cm^{-1} (KBr) 3061.2, 2973.5, 2936.0, 1648.2, 1376.1, 1205.5, 961.9.

Crystal data for **3a**: $C_6H_7ClO_4S$, *M* = 210.6, orthorhombic, *a* = 6.6774(1), *b* = 10.9657(2), *c* = 11.0176(2) Å, *U* = 806.73(2) Å^3, *T* = 100(2) K, space group $P2_12_12_1$ (no. 19), Cu-Kα radiation, λ = 1.54180 Å, *Z* = 4, *F*(000) = 432, D_x = 1.734 g cm^{-3}, μ = 6.431 mm^{-1}, SuperNova Dual, Atlas CCD diffractometer, ω scans, 11.4° < 2θ < 153.4°, measured/independent reflections: 5964/1674, R_{int} = 0.025, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.023 for 1670 data with $F_o > 4\sigma(F_o)$, 109 parameters, ωR_2 = 0.060 (all data), GoF = 1.08, $\Delta\rho_{min,max}$ = −0.34/0.23 e Å^{-3}. CCDC 971378. The absolute configuration is established as (1*S*,2*S*) from the anomalous scattering arising from the chlorine and sulfur atoms; Flack parameter *x* = −0.006(14).

(1*S*,2*S*)-3-Bromocyclohex-3-ene-1,2-cyclic sulfate 3b. Following the general procedure B, diol **1b** gave a crude product, which crystallised from Et_2O to give cyclic sulfate **3b** as colourless solid. Yield: 95 mg, 72%; m. p. 73–74 °C; R_f 0.26 (Et_2O–hexane, 1 : 1); $[\alpha]_D$ +111.0 (*c* 0.88, $CHCl_3$); (Found: C, 28.4; H, 2.3; S, 12.4. $C_6H_7BrO_4S$ requires C, 28.3; H, 2.8; S, 12.6%); HRMS (LC-TOFMS): (Found: $[M + NH_4]^+$ 271.9585. $C_6H_{11}O_4SBrN$ requires 271.9587; ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.05 (1 H, m, H-6), 2.2 (1 H, m, H-5), 2.34 (1 H, m, H-6′), 2.45 (1 H, m, H-5′), 5.26 (1 H, td, *J* 5.7, 2.9, H-1) 5.29 (1 H, d, *J* 5.3, H-2), 6.62 (1 H, dd, *J* 5.31, 3.40, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 22.41, 24.05, 80.76, 81.15, 114.14, 137.95; ν_{max}/cm^{-1} (KBr) 3055.4, 2971.5, 2932.3, 2918.1, 1642.9 (C═C) 1374.7 (S═O), 1205.0 (S═O).

(1*S*,2*R*)-3-(Trifluoromethyl)cyclohex-3-ene-1,2-cyclic sulfate 3d. Following the general procedure B gave a crude product, which was purified by PLC to give the titled cyclic sulfate **3d** as a pale yellow oil. Yield: 61%; R_f 0.25 (Et_2O–hexane, 1 : 1); $[\alpha]_D$ +35.0 (*c* 1.2, $CHCl_3$); HRMS (LC-TOFMS) (Found: $[M + Na]^+$ 266.9913. $C_7H_7F_3NaO_4S^+$ requires 266.9909); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.07 (1 H, m, H-6), 2.34 (2 H, m, H-6′, H-5′), 2.58 (1 H, m, H-5), 5.25 (1 H, m, H-1), 5.46 (1 H, d, *J* 5.4, H-2) 6.98 (1 H, m, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 20.17, 23.75, 74.11, 79.42, 122.35 (q, *J* 273.5), 123.31 (q, *J* 32.3), 140.9 (q, *J* 5.0).

(5*S*,6*R*)-Methyl-5,6-cyclic-sulfate-cyclohex-1-enecarboxylate 3e. Using the general procedure B, diol **1e** (130 mg, 0.76 mmol) gave a crude product, which on purification by PLC (Et_2O–hexane, 3 : 1) gave cyclic sulfate **3e** as colourless oil. Yield: 60 mg, 34%; R_f 0.23 (Et_2O–hexane, 3 : 1); $[\alpha]_D$ +94.6 (*c* 0.75, $CHCl_3$); HRMS (LC-TOFMS) (Found $[M + H]^+$ 235.0275. $C_8H_{11}O_6S$ requires 235.0271); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.02 (1 H, m, H-4), 2.34 (2 H, m, H-3, H-4′), 2.61 (1 H, m, H-3′), 3.83 (3 H, s, CO_2Me), 5.24 (1 H, ddd, *J* 6.6, 5.5, 3.3, H-5), 5.72 (1 H, d, *J* 5.5, H-6), 7.49 (1 H, dd, *J* 4.8, 3.8, H-2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 21.08, 23.94, 52.43, 76.14, 79.69, 125.13,

147.53, 164.35; ν_{max}/cm^{-1} (thin film) 2959, 1721, 1654, 1383, 1268, 1205.

(5*S*,6*S*)-Methyl-6-chloro-5-hydroxycyclohex-1-enecarboxylate 5e. Following the general procedure B, the titled compound was isolated as a byproduct in the above reactions as a pale yellow oil. Yield: 20 mg, 14%; R_f 0.52 (Et_2O–hexane, 3 : 1); $[\alpha]_D$ +89.0 (*c* 0.9, $CHCl_3$); HRMS (Found: M^+ 190.0401. $C_8H_{11}ClO_3$ requires 190.0391); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 1.86 (1 H, m, H-4), 1.90 (1 H, s, OH) 2.14 (1 H, m, H-4′), 2.35 (1 H, m, H-5), 2.48 (1 H, m, H-5′), 3.80 (3 H, s, CO_2Me), 4.30 (1 H, dt, *J* 5.01, 2.88, H-5), 4.73 (1 H, m, H-6), 7.18 (1 H, t, *J* 4.1 Hz, H-2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 21.35, 22.50, 52.16, 53.78, 69.84, 128.43, 143.38, 166.04; LRMS (EI): *m*/*z* 190 (M^+, 8%), 172 (4), 158 (52), 147 (93), 137 (42), 111 (100), 95 (50), 77 (62).

(1*S*,2*S*)-2-Chloro-3-phenylcyclohex-3-enol 5f and (1*S*,2*R*)-2-chloro-3-phenylcyclohex-3-enol as a 7 : 1 mixture. Following the general procedure B, diol **1e** (280 mg, 1.47 mmol) gave a crude product, which on purification by PLC (Et_2O–hexane, 3 : 1) gave a 7 : 1 mixture of *trans* and *cis*-chlorohydrins **5f** (90 mg 29%); R_f 0.48, (50% Et_2O–hexanes); $[\alpha]_D$ +39.9 (*c* 0.98, $CHCl_3$; ^{1}H-NMR major *trans* (400 MHz, $CDCl_3$) δ_H 1.84 (1 H, m, H-6), 2.21 (1 H, m, H-6′), 2.35 (1 H, m, H-5), 2.45 (1 H, m, H-5′), 4.27 (1 H, ddd, *J* 6.8, 4.4, 2.7, H-1), 4.82 (1 H, d, *J* 4.4, H-2), 6.19 (1 H, t, *J* 4.0, H-3), 7.23–7.46 (5 H, m, Ar); ^{13}C-NMR (100 MHz) δ_C 21.95, 24.49, 59.71, 71.79, 126.04 (2C), 127.47, 128.35 (2C), 129.32, 135.26, 139.50.

Selected peaks from minor *cis*-isomer: ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 5.13 (1 H, d, *J* 3.7, H-2), 4.05 (1 H, dt, *J* 11.9, 3.7, H-1); ^{13}C-NMR (100 MHz) δ_C 69.49, 63.39.

(3a*S*,4*R*,5*R*,7a*S*)-7-Bromo-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[*d*][1,3]dioxole-4,5-diol cyclic sulfate 8. General procedure B, using (200 mg, 0.75 mmol) of diol **6**, gave the crude product, which was purified by column chromatography (EtOAc–hexane, 1 : 19) to give cyclic sulfate **8** as a colourless oil. Yield: 73%; R_f 0.4 (EtOAc–hexane, 1 : 9); $[\alpha]_D$ +103.4 (*c* 1.03, $CHCl_3$); HRMS (LC-TOFMS) (Found $[M + H]^+$ 326.9540. $C_9H_{12}BrO_6S$ requires 326.9533); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 1.42 (3 H, s, Me), 1.43 (3 H, s, Me), 4.70–4.74 (2 H, m, H-3a, H-7a), 5.34 (1 H, ddd, *J* 5.6, 3.2, 1.3, H-5), 5.42 (1 H, ddd, *J* 5.6, 2.9, 1.2, H-4), 6.27 (1 H, dt, *J* 3.2, 1.2, H-6); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 26.32, 27.34, 72.01, 73.60, 76.56, 77.82, 111.65, 122.67, 130.18; ν_{max}/cm^{-1} (thin film) 2992, 1651, 1396, 1212, 936.

(1*S*,2*R*)-2-Azido-3-chlorocyclohex-3-enol 9a. Sodium azide (31 mg, 0.48 mmol) was added to a solution of cyclic sulfate **3a** (50 mg, 0.24 mmol) in a mixture of acetone–water (6 : 1, 5 mL) at 0 °C. The solution was stirred for 12 h and then allowed to warm to room temperature. The solvent was removed *in vacuo*, the white solid residue obtained was treated with a mixture of 20% H_2SO_4 and Et_2O (1 : 1, 6 mL) and the reaction mixture stirred for a further 8 h. It was diluted with Et_2O (20 mL), washed with aq. $NaHCO_3$ (2 × 15 mL), brine (15 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product, obtained as a yellow oil, was purified by PLC (EtOAc–hexane, 3 : 7) to furnish azide **9a** as a colourless oil. Yield: 28 mg, 68%; R_f 0.48 (EtOAc–hexane, 3 : 7); $[\alpha]_D$ +198.0 (*c* 0.7, $CHCl_3$); HRMS (LC-TOFMS) (Found: $[M + Na]^+$, 196.0245. $C_6H_8ClN_3NaO$ requires 196.0248); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 1.77 (1 H, m, H-6), 1.89 (1 H, m, H-6′), 1.96 (1 H, s, OH), 2.21–2.28 (2 H, m, H-5, H-5′), 3.87 (1 H, br d, *J* 5.6, H-2), 3.91 (1 H, ddd, *J* 8.5, 5.6, 3.1, H-1), 6.07 (1 H, t, *J* 4.1, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 22.8, 26.3, 67.6, 71.0, 128.3, 129.3; LRMS (EI): *m*/*z* 173 (M^+, 7%), 146 (26), 144 (78), 131 (81), 130 (75), 129 (72), 118 (73), 116 (82), 103 (64), 101 (100); ν_{max}/cm^{-1} (thin film) 3367, 2932, 2103, 1662, 1257.

(1*S*,2*R*)-2-Azido-3-chloro-3-cyclohexen-1-ol 9a and (1*S*,4*S*)-4-azido-3-chloro-3-cyclohexen-1-ol 10a. A solution of cyclic sulfite **2a** (2.01 g, 10.3 mmol) and sodium azide (1.14 g, 17.6 mmol) in DMSO (40 mL) was heated with stirring at 60 °C for 4 h. After cooling the mixture, it was diluted with water (40 mL) and extracted with ethyl acetate (60 mL). The organic phase was washed with brine (3 × 50 mL), dried (Na_2SO_4) and concentrated to give the crude product (1.67 g, 93%) as an inseparable mixture (3 : 1) of azides **9a** and **10a**. In addition to the NMR signals for the major isomer **9a**, additional signals for the compound **10a** were also present. ^{1}H-NMR (300 MHz, $CDCl_3$) δ_H 6.07 (1 H, d, *J* 4.6, H-2), 4.25(1 H, m, H-1), 3.93 (1 H, t, *J* 4.9, H-4) 2.30–2.20 (2 H, m, H-5), 1.93–1.80 (2 H, m, H-6); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 131.33, 128.51, 65.35, 61.19, 27.67, 26.29. The above data matched with that reported in the literature.[22]

(1*R*,2*R*)-1,2-Dichloro-1,2,3,4-tetrahydronaphthalene 12b. Triethylamine (0.47 mL, 3.04 mmol) and sulfuryl chloride (0.25 mL, 3.04 mmol) were added to a solution of *cis*-diol **8b** (250 mg, 1.52 mmol) in DCM (15 mL) at 0 °C. The reaction mixture was stirred for 15 min. at 0 °C, allowed to warm to room temperature and the stirring continued for another 45 min. It was diluted with a mixture of DCM (5 mL) and water (15 mL). The organic layer was separated, the remaining aqueous layer extracted with fresh DCM (2 × 10 mL), the organic extracts combined, dried ($MgSO_4$) and the solvent was removed to give the crude product as a pale yellow solid. Crystallisation of the crude product furnished colourless crystals of dichloride **12b**. Yield: 210 mg, 69%; m. p. 61–62 °C (from hexane); its spectral data matched with the literature values except for the optical rotation;[25] $[\alpha]_D$ +12.3 (*c* 0.81, $CHCl_3$, >98% ee); lit.[25] $[\alpha]_D$ +8.6 (*c* 0.4, $CHCl_3$, 14% ee); ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 2.13 (1 H, m, H-3) 2.67 (1 H, dddd, *J* 14.5, 11.3, 5.8, 2.4, H-3′), 2.87 (1 H, ddd, *J* 17.2, 5.8, 2.8, H-4), 3.15 (1 H, ddd, *J* 17.2, 11.3, 5.8, H-4′), 4.65 (1 H, dt, *J* 5.0, 2.8, H-2), 5.23 (1 H, d, *J* 2.5, H-1), 7.05–7.30 (4 H, m, Ar); ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 23.90, 25.04, 59.48, 59.77, 126.71, 128.81, 129.06, 131.05, 132.39, 135.88; ν_{max}/cm^{-1} (thin film) 2956, 2930, 1492, 1455, 1440, 1428, 738.

Crystal data for **12b**: $C_{10}H_{10}Cl_2$, *M* = 201.1, monoclinic, *a* = 7.4192(4), *b* = 7.6708(4), *c* = 8.1477(5) Å, *β* = 101.30(1)°, *U* = 454.70(4) Å^3, *T* = 150(2) K, space group $P2_1$ (no. 4), Mo-Kα radiation, *λ* = 0.71073 Å, *Z* = 2, *F*(000) = 208, D_x = 1.469 g cm^{-3}, *μ* = 0.650 mm^{-1}, Oxford Diffraction Gemini ultra diffractometer, *ω* scans, 5.6° < 2*θ* < 61.7°, measured/independent reflections: 2509/1797, R_{int} = 0.021, direct methods solution, full-matrix

least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.030 for 1578 data with $F_o > 4\sigma(F_o)$, 109 parameters, ωR_2 = 0.059 (all data), GoF = 1.04, $\Delta\rho_{min,max}$ = −0.26/0.29 e Å^{-3}. CCDC 971377. The absolute configuration is established as (1*R*,2*R*) from the anomalous scattering arising from the chlorine atom; Flack parameter x = 0.05(6).

(1*S*,2*S*)-1-Chloro-1,2,3,4-tetrahydronaphthalen-2-ol 13b. Triethylamine (0.34 mL, 2.42 mmol) was added to solution of (1*R*,2*S*)-*cis*-diol **11b** (100 mg, 0.61 mmol) and DMAP (0.03 g, 0.24 mmol) in DCM (10 mL). The mixture was cooled to −78 °C and stirred for 10 min. Sulfuryl chloride (0.09 mL, 1.15 mmol) was added dropwise over a period of 1 h and the mixture allowed to stir for a further 30 min at −78 °C. The reaction mixture was quenched with a saturated solution of sodium bicarbonate (3 mL), diluted with DCM (5 mL), and water (15 mL). The organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated on a rotary evaporator, to give a brown-coloured oil. The crude product was passed through a short silica gel column with Et_2O as eluent. This sample was further purified by PLC (Et_2O–hexane, 1 : 1), to give the chlorohydrin **13b** as a colourless oil. Yield: 81 mg, 73%. Its spectral properties were in general agreement‡ with the literature values;[24] R_f 0.42 (Et_2O–hexane, 1 : 1); $[\alpha]_D$ −123.7 (*c* 0.73, $CHCl_3$); lit[24] $[\alpha]_D$ −39 (*c* 0.7, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 1.89 (1 H, m, H-3), 2.33 (1 H, dtd, *J* 14.4, 5.8, 5.8, 3.3, H-3′), 2.43 (1 H, s, OH), 2.94 (2 H, appar t, *J* 6.2, H-4, H-4′), 4.15 (1 H, ddd, *J* 9.6, 6.9, 3.3, H-2), 5.02 (1 H, d, *J* 6.9, H-1), 7.11 (1 H, m, Ar), 7.23 (2 H, m, Ar), 7.53 (1 H, m, Ar); ^{13}C-NMR (100 MHz, $CDCl_3$) δ_C 26.33, 27.69, 64.56, 72.84, 126.53, 128.14, 128.54, 130.17, 133.92, 135.91.

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References

1 J. A. Griffen, S. J. Kenwright, S. Abou-Shehada, S. Wharry, T. S. Moody and S. E. Lewis, *Org. Chem. Front.*, 2014, DOI: 10.1039/c3qo00057e; D. R. Adams, J. van Kempen, J. R. Hudlicky and T. Hudlicky, *Heterocycles*, 2014, **88**, 1255; T. A. Reekie, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2013, **78**, 7100; X. Ma, M. G. Banwell and A. C. Willis, *J. Nat. Prod.*, 2013, **76**, 1514; H. S. Kim, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2013, **78**, 5103; B. D. Schwartz, E. Matousova, R. White, M. G. Banwell and A. C. Willis, *Org. Lett.*, 2013, **15**, 1934; V. Varghese and T. Hudlicky, *Synlett*, 2013, 369; D. Bon, M. G. Banwell, J. S. Ward and A. C. Willis, *Tetrahedron*, 2013, **69**, 1363; J. A. Griffen, J. C. White, G. Kociok-Kohn, M. D. Lloyd, A. Wells, T. C. Arnot and S. E. Lewis, *Tetrahedron*, 2013, **69**, 5989; M. K. Sharma, M. G. Banwell, A. C. Willis and A. D. Rae, *Chem.–Asian J.*, 2012, **7**, 676; V. Semak, T. A. Metcalf, M. A. A. Endoma-Arias, P. Mach and T. Hudlicky, *Org. Biomol. Chem.*, 2012, **10**, 4407; M. G. Banwell, N. Gao, X. H. Ma, L. Petit, L. V. White, B. D. Schwartz, A. C. Willis and I. A. Cade, *Pure Appl. Chem.*, 2012, **84**, 1329; D. R. Boyd, N. D. Sharma, M. Kaik, P. B. A. McIntyre, P. J. Stevenson and C. C. R. Allen, *Org. Biomol. Chem.*, 2012, **10**, 2774; D. R. Boyd, M. Bell, K. S. Dunne, B. Kelly, P. J. Stevenson, J. F. Malone and C. C. R. Allen, *Org. Biomol. Chem.*, 2012, **10**, 1388; S. Vshyvenko, J. Scattolon, T. Hudlicky, A. E. Romero, A. Kornienko, D. Ma, I. Tuffley and S. Pandey, *Can. J. Chem.*, 2012, **90**, 932; M. J. Palframan, G. Kociok-Kohn and S. E. Lewis, *Chem.–Eur. J.*, 2012, **18**, 4766; M. A. Khan, M. F. Mahon, J. P. Lowe, A. J. W. Stewart and S. E. Lewis, *Chem.–Eur. J.*, 2012, **18**, 13480; L. Werner, A. Machara, B. Sullivan, I. Carrera, M. Moser, D. R. Adams, T. Hudlicky and J. Andraos, *J. Org. Chem.*, 2011, **76**, 10050; M. A. A. Endoma-Arias and T. Hudlicky, *Tetrahedron Lett.*, 2011, **52**, 6632; L. Petit, M. G. Banwell and A. C. Willis, *Org. Lett.*, 2011, **13**, 5800; B. D. Schwartz, L. V. White, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2011, **76**, 8560; B. D. Schwartz, M. G. Banwell and I. A. Cade, *Tetrahedron Lett.*, 2011, **52**, 4526; D. Bon, M. G. Banwell and A. C. Willis, *Tetrahedron*, 2011, **67**, 5841; L. V. White, B. D. Schwartz, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2011, **76**, 6250; J. Duchek, D. R. Adams and T. Hudlicky, *Chem. Rev.*, 2011, **111**, 4223; J. Duchek, T. G. Piercy, J. Gilmet and T. Hudlicky, *Can. J. Chem.*, 2011, **89**, 709; D. R. Adams, C. Aichinger, J. Collins, U. Rinner and T. Hudlicky, *Synlett*, 2011, 1188; M. J. Palframan, G. Kociok-Kohn and S. E. Lewis, *Org. Lett.*, 2011, **13**, 3150; M. A. Khan, J. P. Lowe, A. L. Johnson, A. J. W. Stewart and S. E. Lewis, *Chem. Commun.*, 2011, **47**, 215; S. Pilgrim, G. Kociok-Kohn, M. D. Lloyd and S. E. Lewis, *Chem. Commun.*, 2011, **47**, 4799; D. R. Boyd, N. D. Sharma, C. A. Acaru, J. F. Malone, C. R. O'Dowd, C. C. R. Allen and P. J. Stevenson, *Org. Lett.*, 2010, **12**, 2206; D. R. Boyd, N. D. Sharma, N. I. Bowers, G. B. Coen, J. F. Malone, C. R. O'Dowd, P. J. Stevenson and C. C. R. Allen, *Org. Biomol. Chem.*, 2010, **8**, 1415; D. K. Winter, M. A. Endoma-Arias, T. Hudlicky, J. A. Beutler and J. A. Porco, *J. Org. Chem.*, 2013, **78**, 7617; J. F. Trant, J. Froese and T. Hudlicky, *Tetrahedron: Asymmetry*, 2013, **24**, 184.

‡Signals are within 0.2 ppm except for signal at 72.84 does not match the literature value of 69.1 ppm.

2 D. R. Boyd, N. D. Sharma, M. Kaik, M. Bell, M. V. Berberian, P. B. A. McIntyre, B. Kelly, C. Hardacre, P. J. Stevenson and C. C. R. Allen, *Adv. Synth. Catal.*, 2011, **353**, 2455.
3 H. C. Kolb, M. S. Vannieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483; E. N. Jacobsen, I. Marko, W. S. Mungall, G. Schroder and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 1968.
4 T. L. Lowary, E. Eichler and D. R. Bundle, *Can. J. Chem.*, 2002, **80**, 1112; T. J. Tewson, *J. Org. Chem.*, 1983, **48**, 3507.
5 H. Sun, Y. J. Lin, Y. L. Wu and Y. K. Wu, *Synlett*, 2009, 2473.
6 T. L. Shih, W. S. Kuo and Y. L. Lin, *Tetrahedron Lett.*, 2004, **45**, 5751; A. Bianco, M. Brufani, F. Manna and C. Melchioni, *Carbohydr. Res.*, 2001, **332**, 23; C. U. Kim, W. Lew, M. A. Williams, H. T. Liu, L. J. Zhang, S. Swaminathan, N. Bischofberger, M. S. Chen, D. B. Mendel, C. Y. Tai, W. G. Laver and R. C. Stevens, *J. Am. Chem. Soc.*, 1997, **119**, 681; M. Cakmak, P. Mayer and D. Trauner, *Nat. Chem.*, 2011, **3**, 543.
7 L. D. Nie, W. Ding, X. X. Shi, N. Quan and X. Lu, *Tetrahedron: Asymmetry*, 2012, **23**, 742; L. D. Nie, X. X. Shi, N. Quan, F. F. Wang and X. Lu, *Tetrahedron: Asymmetry*, 2011, **22**, 1692.
8 J. K. Sutherland, R. C. Whitehead and G. M. Davies, *J. Chem. Soc., Chem. Commun.*, 1993, 464.
9 H. S. Byun, L. L. He and R. Bittman, *Tetrahedron*, 2000, **56**, 7051.
10 M. Alonso and A. Riera, *Tetrahedron: Asymmetry*, 2005, **16**, 3908.
11 M. S. Berridge, M. P. Franceschini, E. Rosenfeld and T. J. Tewson, *J. Org. Chem.*, 1990, **55**, 1211.
12 C. Hardacre, M. E. Migaud and K. A. Ness, *New J. Chem.*, 2012, **36**, 2316; C. Hardacre, I. Messina, M. E. Migaud, K. A. Ness and S. E. Norman, *Tetrahedron*, 2009, **65**, 6341.
13 Y. Gao and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 7538.
14 D. R. Boyd, N. D. Sharma, M. V. Berberian, K. S. Dunne, C. Hardacre, M. Kaik, B. Kelly, J. F. Malone, S. T. McGregor and P. J. Stevenson, *Adv. Synth. Catal.*, 2010, **352**, 855.
15 A. G. Myers and S. D. Goldberg, *Angew. Chem., Int. Ed.*, 2000, **39**, 2732.
16 F. E. McDonald and P. Vadapally, *Tetrahedron Lett.*, 1999, **40**, 2235.
17 N. S. Zefirov, A. S. Kozmin and V. D. Sorokin, *J. Org. Chem.*, 1984, **49**, 4086.
18 S. Barluenga, E. Moulin, P. Lopez and N. Winssinger, *Chem.–Eur. J.*, 2005, **11**, 4935.
19 H. J. Jennings and J. K. N. Jones, *Can. J. Chem.*, 1962, **40**, 1408.
20 H. J. Jennings and J. K. N. Jones, *Can. J. Chem.*, 1963, **41**, 1151.
21 A. R. Mattocks, *J. Chem. Soc.*, 1964, 1918.
22 D. R. Boyd, N. D. Sharma, T. Belhocine, J. F. Malone, S. T. McGregor, J. Atchison, P. A. B. McIntyre and P. J. Stevenson, *J. Phys. Org. Chem.*, 2013, **26**, 997.
23 D. R. Boyd, N. D. Sharma, N. A. Kerley, G. McConville, C. C. R. Allen and A. J. Blacker, *ARKIVOC*, 2003, 32.
24 F. Orsini, G. Sello and G. Bestetti, *Tetrahedron: Asymmetry*, 2001, **12**, 2961.
25 S. A. Snyder, D. S. Treitler and A. P. Brucks, *J. Am. Chem. Soc.*, 2010, **132**, 14303.
26 A. P. Brucks, D. S. Treitler, S. A. Liu and S. A. Snyder, *Synthesis*, 2013, 1886.
27 A. El Moncef, E. M. El Hadrami, M. A. Gonzalez, E. Zaballos and R. J. Zaragoza, *Tetrahedron*, 2010, **66**, 5173; S. J. Coote, S. G. Davies, A. M. Fletcher, P. M. Roberts and J. E. Thomson, *Chem.–Asian J.*, 2010, **5**, 589; S. Besli, S. J. Coles, D. B. Davies, R. J. Eaton, M. B. Hursthouse, A. Kilic and R. A. Shaw, *Eur. J. Inorg. Chem.*, 2005, 959; X. Q. Yu, A. Hirai and M. Miyashita, *Chem. Lett.*, 2004, **33**, 764; A. Hirai, X. Q. Yu, T. Tonooka and M. Miyashita, *Chem. Commun.*, 2003, 2482; M. Sasaki, K. Tanino and M. Miyashita, *J. Org. Chem.*, 2001, **66**, 5388.
28 D. K. Bedke, G. M. Shibuya, A. Pereira, W. H. Gerwick, T. H. Haines and C. D. Vanderwal, *J. Am. Chem. Soc.*, 2009, **131**, 7570; C. Nilewski, R. W. Geisser and E. M. Carreira, *Nature*, 2009, **457**, 573.
29 K. C. Nicolaou, N. L. Simmons, Y. C. Ying, P. M. Heretsch and J. S. Chen, *J. Am. Chem. Soc.*, 2011, **133**, 8134.
30 S. E. Denmark, M. T. Burk and A. J. Hoover, *J. Am. Chem. Soc.*, 2010, **132**, 1232.
31 D. R. Boyd, N. D. Sharma, N. M. Llamas, G. P. Coen, P. K. M. McGeehin and C. C. R. Allen, *Org. Biomol. Chem.*, 2007, **5**, 514.
32 T. Hudlicky, J. D. Price, F. Rulin and T. Tsunoda, *J. Am. Chem. Soc.*, 1990, **112**, 9439.
33 C. C. R. Allen, D. R. Boyd, H. Dalton, N. D. Sharma, I. Brannigan, N. A. Kerley, G. N. Sheldrake and S. C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1995, 117.

